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Research Article

Global Analysis of a Virus Dynamics Model with General Incidence Function and Cure Rate

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A virus dynamics model with logistic function, general incidence function, and cure rate is considered. By carrying out mathematical analysis, we show that the infection-free equilibrium is globally asymptotically stable if the basic reproduction number $\mathscr{R}_0 \leq 1$. If $\mathscr{R}_0 > 1$, then the infection equilibrium is globally asymptotically stable under some assumptions. Furthermore, we also obtain the conditions for which the model exists an orbitally asymptotically stable periodic solution. Examples are provided to support our analytical conclusions.

1. Introduction

Mathematical models have proven valuable in understanding the virus dynamics. The basic viral infection model was proposed by Nowak et al. [1, 2] in the following form:

$$\begin{aligned} \dot{x} &= \lambda - dx - \beta xv, \\ \dot{y} &= \beta xv - ay, \\ \dot{v} &= ky - uv, \end{aligned} \tag{1}$$

where x, y, and v denote uninfected cells, infected cells, and free virus particles, respectively. The uninfected cells are produced at a constant λ and die at rate dx. The infected cells are produced from uninfected cells and free virus at rate βxv and die at rate ay. Free virus is produced from infected cells at rate ky and declines at rate uv.

The incidence function in model (1) is based on the law of mass action. However, many researchers suggested that the bilinear incidence function is not sufficient to describe the infection process in detail, and some nonlinear incidence functions were proposed. For example, Li and Ma [3] considered a HIV-1 model with Holling type II function. Min et al. [4] considered a HBV model with standard incidence function. Elaiw [5] considered a virus dynamics model with a more general nonlinear incidence function, which satisfies some conditions.

When HBV infects a cell, infected cells may also revert to the uninfected state by loss of all covalently closed circular DNA (cccDNA) from their nucleus [6]. Then HBV infection has been modelled using the model including cytokine-mediated "cure" of infected cells [7–9]. Wang et al. [10] considered an improved HBV model with standard incidence function and cure rate. According to the virological basis found in [11], when a HIV enters a resting $CD4^+$ T-cell, the viral RNA may not be completely reverse transcribed into DNA. If the cell is activated shortly following infection, reverse transcription can proceed to completion. However, the unintegrated virus harbored in resting cells may decay with time and partial DNA transcripts are labile and degrade quickly [12]. Hence a proportion of resting infected cells can revert to the uninfected state [13]. Recently, Zhou et al. [14] considered a model of HIV infection of $CD4^+$ T-cells with bilinear incidence function and cure rate. Hattaf et al. [15] considered a virus dynamics model with general incidence function and cure rate. However, Tian and Liu [16] have pointed out that the proof for the main results in [15] is not corrected. They introduced a more general nonlinear incidence function including the form in [15].

The population dynamics of target cells is not well understood. Many models with logistic uninfected cell proliferation terms have been introduced. For example, Culshaw and Ruan [17] considered a delay-differential equation model of HIV infection of $CD4^+$ T-cells with logistic function term. Ji et al. [18] considered a viral infection model of HBV infection with logistic function. Li and Shu [19] considered an in-host model

with a logistic mitosis term for the uninfected target cells and a finite intracellular delay in the incidence term.

In this paper, we aim to study the following model with logistic function, general incidence function, and cure rate:

$$\begin{aligned}\dot{x} &= \lambda - dx + rx\left(1 - \frac{x}{x_{\max}}\right) - f(x, y, v)\, v + \rho y,\\ \dot{y} &= f(x, y, v)\, v - (a + \rho)\, y,\\ \dot{v} &= ky - uv,\end{aligned} \tag{2}$$

with initial condition $(x(0), y(0), v(0)) \in \mathbb{R}^3_+$. Here λ,d,a,k, and u defined as earlier. r is the maximum proliferation rate of uninfected cells and $x_{\max}$ is the maximum capacity of host's organ cells. $f(x, y, v)v$ is the incidence of new infections. $\rho \geq 0$ is the rate of cure, that is, noncytolytic loss of infected cells. The function $f(x, y, v)$ satisfies the following conditions:

(i) $f(0, y, v) = 0$ for all $y \geq 0$ and $v \geq 0$;

(ii) $\partial f(x, y, v)/\partial x > 0$, for all $x > 0$, $y \geq 0$, and $v \geq 0$;

(iii) $\partial f(x, y, v)/\partial y \leq 0$ and $\partial f(x, y, v)/\partial v \leq 0$, for all $x \geq 0$, $y \geq 0$, and $v \geq 0$;

(iv) $(\partial f(x, y, v)/\partial v)v + f(x, y, v) > 0$, for all $x > 0$, $y \geq 0$, and $v \geq 0$.

Several models for viral dynamics fit model (2). For example, Song and Neumann [20] considered a viral model with $f(x, y, v) = \beta x/(1 + \alpha x)$ and $\rho = 0$, where β is the infection rate constant and α is a positive constant. Ji et al. [18] considered a viral infection model of HBV infection with $f(x, y, v) = \beta x$ and $\rho = 0$. Zhou et al. [14] considered a model of HIV infection of $CD4^+$ T-cells with $f(x, y, v) = \beta x$.

The paper is organized as follows. In Section 2, we carry out mathematical analysis of the model. In Section 3, the local stability of equilibria is proved. In Section 4, the global stability of the infection-free equilibrium or the infection equilibrium is established, respectively. The conditions for the existence of an orbitally asymptotically stable periodic solution are obtained. In Section 5, two examples are provided to illustrate our theorems. The conclusion is given in Section 6.

2. Mathematical Analysis

First, we show that solution of system (2) is bounded.

Theorem 1. *The solution of system* (2) *is positive and bounded.*

Proof. Let

$$L_1(t) = x(t) + y(t). \tag{3}$$

Computing the derivation of L_1 along the solution of system (2), we have

$$\begin{aligned}\dot{L}_1 &= \lambda - dx + rx\left(1 - \frac{x}{x_{\max}}\right) - ay,\\ &= \lambda - dx - \frac{r}{x_{\max}}\left(x - \frac{x_{\max}}{2}\right)^2 + \frac{rx_{\max}}{4} - ay\\ &\leq \lambda + \frac{rx_{\max}}{4} - \min\{a, d\}\, L_1,\end{aligned} \tag{4}$$

which implies that

$$L_1(t) \leq \frac{\delta_1}{\delta_2} + \left(L(0) - \delta_1\right) e^{-\delta_2 t}, \tag{5}$$

where $\delta_1 = \lambda + rx_{\max}/4$ and $\delta_2 = \min\{a, d\}$. Obviously, $x(t)$ and $y(t)$ are bounded. From the third equation of system (2) and the boundedness of $y(t)$, it is easy to see that $v(t)$ is also bounded. This completes the proof. □

It can then be verified that the bounded set

$$\Omega = \left\{(x, y, v) \in \mathbb{R}^3_+ : 0 < x + y \leq \frac{\delta_1}{\delta_2},\ 0 < v \leq \frac{k\delta_1}{u\delta_2}\right\} \tag{6}$$

is positively invariant with respect to system (2) and is convex.

Following the computation of the basic reproduction number in [21], we have the basic reproduction number

$$\mathscr{R}_0 = \frac{kf(x_0, 0, 0)}{u(a + \rho)}. \tag{7}$$

For mathematical convenience, let

$$n(x) = \lambda - dx + rx\left(1 - \frac{x}{x_{\max}}\right), \tag{8}$$

and x_0 is the positive root of $n(x) = 0$. It is clear that $n'(x_0) < 0$ and system (2) has an infection-free equilibrium $E_0(x_0, 0, 0)$ when $\mathscr{R}_0 \leq 1$.

Theorem 2. *If* $\mathscr{R}_0 > 1$ *and* $d - r + 2rx/x_{\max} > 0$ *for arbitrary* $x \geq 0$, *then there exists a unique infection equilibrium* $E_*(x_*, y_*, v_*)$.

Proof. In order to find the infection equilibrium, set

$$\begin{aligned}n(x) - f(x, y, v)\, v + \rho y &= 0,\\ f(x, y, v)\, v - (a + \rho)\, y &= 0,\\ ky - uv &= 0,\end{aligned} \tag{9}$$

which yields

$$n(x) = ay = \frac{au}{k} v. \tag{10}$$

Substituting the expression of y and v by x, we have

$$G(x) = f\left(x, \frac{n(x)}{a}, \frac{kn(x)}{au}\right) - \frac{u(a + \rho)}{k}. \tag{11}$$

It is obvious that $G(0) = -u(a + \rho)/k < 0$ and

$$\begin{aligned}G(x_0) &= f(x_0, 0, 0) - \frac{u(a + \rho)}{k}\\ &= \frac{u(a + \rho)}{k}(\mathscr{R}_0 - 1) > 0.\end{aligned} \tag{12}$$

This implies that there exists $x_* \in (0, x_0)$ such that $G(x_*) = 0$. Suppose, to the contrary, there exists another infection equilibrium $E^*(x^*, y^*, v^*)$. Without loss of generality, we assume that $x_* < x^*$. Since $d - r + 2rx/x_{\max} > 0$, we have $n(x_*) > n(x^*)$. This yields $y_* > y^*$ and $v_* > v^*$. Hence, we get $f(x_*, y_*, v_*) < f(x^*, y^*, v^*)$. On the other hand, we have that $f(x_*, y_*, v_*) = f(x^*, y^*, v^*) = u(a + \rho)/k$. This is a contradiction. Therefore, E_* is the unique infection equilibrium. □

3. Local Stability of Equilibria

In this section, we discuss the local stability of the infection-free equilibrium E_0 and the infection equilibrium E_* of system (2), respectively.

Theorem 3. *If $\mathscr{R}_0 \leq 1$, then the infection-free equilibrium E_0 is locally asymptotically stable and becomes unstable when $\mathscr{R}_0 > 1$.*

Proof. The Jacobian matrix of system (2) at E_0 is

$$J(E_0) = \begin{pmatrix} n'(x_0) & \rho & -f(x_0,0,0) \\ 0 & -(a+\rho) & f(x_0,0,0) \\ 0 & k & -u \end{pmatrix}. \quad (13)$$

One eigenvalue of $J(E_0)$ is $\lambda_1 = n'(x_0) < 0$. The remaining two eigenvalues are solutions of the quadratic equation

$$\lambda^2 + (a+u+\rho)\lambda + u(a+\rho)(1-\mathscr{R}_0) = 0. \quad (14)$$

By the Routh-Hurwitz theorem, E_0 is locally asymptotically stable when $\mathscr{R}_0 \leq 1$. When $\mathscr{R}_0 > 1$, $J(E_0)$ has a positive eigenvalue and E_0 is unstable. □

Theorem 4. *If $\mathscr{R}_0 > 1$ and $d - r + 2rx/x_{\max} > 0$ for arbitrary $x \geq 0$, then the unique endemic equilibrium E_* is locally asymptotically stable.*

Proof. The Jacobian matrix of system (2) at E_* is

$$J(E_*) = \begin{pmatrix} n'(x_*) - \dfrac{\partial f(x_*,y_*,v_*)}{\partial x}v_* & -\dfrac{\partial f(x_*,y_*,v_*)}{\partial y}v_* + \rho & -\dfrac{\partial f(x_*,y_*,v_*)}{\partial v}v_* - f(x_*,y_*,v_*) \\ \dfrac{\partial f(x_*,y_*,v_*)}{\partial x}v_* & \dfrac{\partial f(x_*,y_*,v_*)}{\partial y}v_* - (a+\rho) & \dfrac{\partial f(x_*,y_*,v_*)}{\partial v}v_* + f(x_*,y_*,v_*) \\ 0 & k & -u \end{pmatrix}. \quad (15)$$

The characteristic equation of $J(E_*)$ can be written as

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0, \quad (16)$$

with

$$\begin{aligned} a_1 &= a + \rho + u - n'(x_*) \\ &\quad + \frac{\partial f(x_*,y_*,v_*)}{\partial x}v_* - \frac{\partial f(x_*,y_*,v_*)}{\partial y}v_*, \\ a_2 &= (a+u)\frac{\partial f(x_*,y_*,v_*)}{\partial x}v_* \\ &\quad - n'(x_*)\left(a + \rho + u - \frac{\partial f(x_*,y_*,v_*)}{\partial y}v_*\right) \\ &\quad - k\frac{\partial f(x_*,y_*,v_*)}{\partial v}v_* - u\frac{\partial f(x_*,y_*,v_*)}{\partial y}v_*, \\ a_3 &= au\frac{\partial f(x_*,y_*,v_*)}{\partial x}v_* + un'(x_*)\frac{\partial f(x_*,y_*,v_*)}{\partial y}v_* \\ &\quad + kn'(x_*)\frac{\partial f(x_*,y_*,v_*)}{\partial v}v_*. \end{aligned} \quad (17)$$

Since $d - r + 2rx/x_{\max} > 0$, we have $n'(x_*) < 0$. Therefore,

$$a_1 > 0, \qquad a_2 > 0, \qquad a_3 > 0. \quad (18)$$

By direct calculation, we have $a_1a_2 - a_3 > 0$. Then the Routh-Hurwitz theorem implies that the infection equilibrium E_* is locally asymptotically stable. □

4. Global Stability of Equilibria

In this section, we study the global stability of the infection-free equilibrium E_0 and the infection equilibrium E_* of system (2), respectively.

Theorem 5. *If $\mathscr{R}_0 \leq 1$, then the infection-free equilibrium E_0 is globally asymptotically stable.*

Proof. Consider a Lyapunov function

$$L_2(y,v) = y + \frac{a+\rho}{k}v. \quad (19)$$

Calculating the time derivative of $L_2(y,v)$ along solutions of system (2), we obtain

$$\begin{aligned} \dot{L}_2(y,v) &= \left(f(x,y,v) - \frac{u(a+\rho)}{k}\right)v \\ &\leq \left(f(x_0,0,0) - \frac{u(a+\rho)}{k}\right)v \\ &= \frac{u(a+\rho)}{k}(\mathscr{R}_0 - 1)v. \end{aligned} \quad (20)$$

If $\mathscr{R}_0 < 1$, from Corollary 5.2 of Kuang [22], E_0 is globally asymptotically stable. Also, for $\mathscr{R}_0 = 1$, $\dot{L}_2(y,v) = 0$ implies that $x(t) = x_0$. It is easy to show that the largest invariant set where $\dot{L}_2(y,v) = 0$ is the singleton $\{E_0\}$. By the LaSalle invariance principle, E_0 is globally asymptotically stable. □

Next, we prove that the infection equilibrium E_* is globally asymptotically stable. We need the following theorem.

Theorem 6. *If $\mathscr{R}_0 > 1$, then system (2) is uniformly persistent.*

Proof. The result follows from an application of Theorem 4.6 in [23], with $X_1 = \operatorname{int}(\mathbb{R}^3_+)$ and $X_2 = \partial\mathbb{R}^3_+$. We only need to prove that E_0 is a weak repeller for X_1.

Suppose that there exists a solution $(x(t), y(t), v(t))$ such that $(x(t), y(t), v(t)) \to E_0$. When t is sufficiently large, we have

$$x_0 - \varepsilon < x < x_0 + \varepsilon, \tag{21}$$

where ε is an arbitrarily small positive constant satisfying $0 < \varepsilon < x_0$. Then,

$$\dot{y} \geq f(x_0 - \varepsilon, y, v)\, v - (a + \rho)\, y. \tag{22}$$

Consider the following auxiliary system:

$$\begin{aligned} \dot{u}_1 &= f(x_0 - \varepsilon, u_1, u_2)\, u_2 - (a + \rho)\, u_1 \\ \dot{u}_2 &= k u_1 - u u_2. \end{aligned} \tag{23}$$

System (23) always has a trivial equilibrium $(0, 0)$. Since $\mathscr{R}_0 > 1$ and continuously differentiable of the function $f(x, y, v)$, we have

$$\mathscr{R}_0^{\varepsilon} := \frac{k f(x_0 - \varepsilon, 0, 0)}{u(a + \rho)} > 1, \tag{24}$$

for some $\varepsilon > 0$ sufficiently small. By calculation, system (23) has a unique positive equilibrium (u_1^*, u_2^*), where u_1^* satisfies the root equation

$$f\left(x_0 - \varepsilon, u_1, \frac{k u_1}{u}\right) - \frac{u(a + \rho)}{k} = 0. \tag{25}$$

The Jacobian matrix of system (23) at (u_1^*, u_2^*) is

$$J_{(u_1^*, u_2^*)} = \begin{pmatrix} \dfrac{\partial f(x_0 - \varepsilon, u_1^*, u_2^*)}{\partial u_1} u_2^* - (a + \rho) & \dfrac{\partial f(x_0 - \varepsilon, u_1^*, u_2^*)}{\partial u_2} u_2^* + f(x_0 - \varepsilon, u_1^*, u_2^*) \\ k & -u \end{pmatrix}. \tag{26}$$

The eigenvalues λ_1 and λ_2 of $J_{(u_1^*, u_2^*)}$ satisfy

$$\begin{aligned} \lambda_1 + \lambda_2 &= \frac{\partial f(x_0 - \varepsilon, u_1^*, u_2^*)}{\partial u_1} u_2^* - (a + \rho + u), \\ \lambda_1 \lambda_2 &= -u \frac{\partial f(x_0 - \varepsilon, u_1^*, u_2^*)}{\partial u_1} u_2^* \\ &\quad - k \frac{\partial f(x_0 - \varepsilon, u_1^*, u_2^*)}{\partial u_2} u_2^*. \end{aligned} \tag{27}$$

We get $\lambda_1 + \lambda_2 < 0$ and $\lambda_1 \lambda_2 > 0$. Hence, (u_1^*, u_2^*) is locally asymptotically stable when $\mathscr{R}_0 > 1$.

Denote the right-hand sides of system (23) by B_1 and B_2, respectively. We have

$$\begin{aligned} \frac{\partial B_1}{\partial u_1} + \frac{\partial B_2}{\partial u_2} &= \frac{\partial f(x_0 - \varepsilon, u_1^*, u_2^*)}{\partial u_1} u_2^* \\ &\quad - (a + \rho + u) < 0. \end{aligned} \tag{28}$$

Therefore, (u_1^*, u_2^*) is globally asymptotically stable by the Bendixson criterion for two-dimensional ordinary differential equations. By the comparison theorem, we have that $y(t) \geq u_1^*$ as $t \to \infty$ for system (23). This is a contradiction to $y(t) \to 0$. Hence, E_0 is a weak repeller for X_1. □

By looking at the Jacobian matrix of system (2) and choosing the matrix H as

$$\begin{pmatrix} 1 & 0 & 0 \\ 0 & -1 & 0 \\ 0 & 0 & 1 \end{pmatrix}, \tag{29}$$

system (2) is competitive in Ω, with respect to the partial order defined by the orthant $K = \{(x, y, v) \in \mathbb{R}^3 : x \geq 0,\ y \leq 0,\ v \geq 0\}$.

Theorem 7. *Suppose $\mathscr{R}_0 > 1$ and $d - r + 2rx/x_{\max} > 0$ for arbitrary $x \geq 0$; then the infection equilibrium E_* of system (2) is globally asymptotically stable.*

Proof. Let $P(t) = (x(t), y(t), v(t))$ be a periodic solution whose orbit is contained in $\mathrm{int}(\mathbb{R}^3_+)$. The second compound equation is the following periodic linear system:

$$Z'(t) = \frac{\partial f^{[2]}}{\partial x}(P(t))\, Z(t), \tag{30}$$

where $Z = (Z_1, Z_2, Z_3)^T$ and $\partial f^{[2]}/\partial x$ is the second additive compound matrix of the Jacobian matrix of system (2).

The Jacobian matrix of system (2) is

$$J = \begin{pmatrix} n'(x) - m_1 & -m_2 + \rho & -m_3 \\ m_1 & m_2 - (a + \rho) & m_3 \\ 0 & k & -u \end{pmatrix}, \tag{31}$$

and its second additive compound matrix is

$$J^{[2]} = \begin{pmatrix} n'(x) - m_1 + m_2 - (a + \rho) & m_3 & m_3 \\ k & n'(x) - m_1 - u & -m_2 + \rho \\ 0 & m_1 & m_2 - (a + \rho + u) \end{pmatrix}, \tag{32}$$

where

$$m_1 = \frac{\partial f(x,y,v)}{\partial x} v, \qquad m_2 = \frac{\partial f(x,y,v)}{\partial y} v, \qquad m_3 = \frac{\partial f(x,y,v)}{\partial v} v + f(x,y,v). \tag{33}$$

For the solution $P(t)$, system (30) becomes

$$\begin{aligned} \dot{Z}_1 &= \left(n'(x) - m_1 + m_2 - (a+\rho)\right) \times Z_1 + m_3 (Z_2 + Z_3), \\ \dot{Z}_2 &= kZ_1 + \left(n'(x) - m_1 - u\right) Z_2 + (\rho - m_2) Z_3, \\ \dot{Z}_3 &= m_1 Z_2 + (m_2 - (a+\rho+u)) Z_3. \end{aligned} \tag{34}$$

Now, define the function

$$\begin{aligned} V(t) &= V(Z_1, Z_2, Z_3; x, y, v) \\ &= \sup\left\{|Z_1|, \frac{y}{v}(|Z_2| + |Z_3|)\right\}, \end{aligned} \tag{35}$$

which is a Lyapunov function for system (30). Then, we have

$$\begin{aligned} \left|\dot{Z}_1\right| &\le \left(n'(x) - m_1 + m_2 - (a+\rho)\right)|Z_1| + m_3 (|Z_2| + |Z_3|), \\ \left|\dot{Z}_2\right| &\le k|Z_1| + \left(n'(x) - m_1 - u\right)|Z_2| + (\rho - m_2)|Z_3|, \\ \left|\dot{Z}_3\right| &\le m_1 |Z_2| + (m_2 - (a+\rho+u))|Z_3|. \end{aligned} \tag{36}$$

From system (36), we have

$$\begin{aligned} &D_+ \frac{y}{v}(|Z_2| + |Z_3|) \\ &= \frac{y}{v}\left(\frac{\dot{y}}{y} - \frac{\dot{v}}{v}\right)(|Z_2| + |Z_3|) + \frac{y}{v} D_+ (|Z_2| + |Z_3|) \\ &\le \frac{y}{v}\left(\frac{\dot{y}}{y} - \frac{\dot{v}}{v}\right)(|Z_2| + |Z_3|) + \frac{ky}{v}|Z_1| \\ &\quad - \frac{y}{v}\left(\left(u - n'(x)\right)|Z_2| + (a+u)|Z_3|\right) \\ &\le \frac{ky}{v}|Z_1| + \frac{y}{v}\left(\frac{\dot{y}}{y} - \frac{\dot{v}}{v} - \eta - u\right)(|Z_2| + |Z_3|), \end{aligned} \tag{37}$$

where $0 < \alpha^* = -\max_{x\in[0,x_0]} n'(x)$ and $\eta = \min\{\alpha^*, a\}$. Therefore,

$$D_+ V(t) \le \sup\{g_1(t), g_2(t)\} V(t), \tag{38}$$

where

$$\begin{aligned} g_1(t) &= n'(x) - m_1 + m_2 - (a+\rho) + m_3 \frac{v}{y}, \\ g_2(t) &= \frac{ky}{v} + \left(\frac{\dot{y}}{y} - \frac{\dot{v}}{v} - \eta - u\right). \end{aligned} \tag{39}$$

From the second and third equations of system (2), we have

$$\begin{aligned} \frac{\dot{y}}{y} &= \frac{f(x,y,v)\, v}{y} - (a+\rho), \\ \frac{\dot{v}}{v} &= \frac{ky}{v} - u. \end{aligned} \tag{40}$$

Hence,

$$\begin{aligned} g_1(t) &= n'(x) - m_1 + m_2 - (a+\rho) + m_3 \frac{v}{y} \\ &= \frac{\dot{y}}{y} + n'(x) - m_1 + m_2 + \frac{v}{y}\frac{\partial f(x,y,v)}{\partial v} v \\ &\le \frac{\dot{y}}{y} - \left(-n'(x)\right) \\ &\le \frac{\dot{y}}{y} - \alpha^*, \end{aligned} \tag{41}$$

$$g_2(t) = \frac{ky}{v} + \left(\frac{\dot{y}}{y} - \frac{\dot{v}}{v} - \eta - u\right) = \frac{\dot{y}}{y} - \eta.$$

Therefore,

$$\sup\{g_1(t), g_2(t)\} \le \frac{\dot{y}}{y} - \eta. \tag{42}$$

We have

$$\begin{aligned} \int_0^\omega \sup\{g_1(t), g_2(t)\}\, dt &\le \log y(t)\Big|_0^\omega - \eta\omega \\ &= -\eta\omega < 0, \end{aligned} \tag{43}$$

which implies that $V(t) \to 0$ as $t \to \infty$. This means that $(Z_1(t), Z_2(t), Z_3(t)) \to (0,0,0)$ as $t \to \infty$, so the linear system (34) is asymptotically stable and the periodic solution is asymptotically orbitally stable.

According to Theorem 4.1 in [24], system (2) satisfies the Poincare-Bendixson property. Using Theorem 1, Theorems 4 and 6, we have that all conditions of Theorem 2.2 in [25] are satisfied for system (2). This completes the proof. □

If the condition $d - r + 2rx/x_{\max} > 0$ in Theorem 4 could not be satisfied, there would exist an orbitally asymptotically stable periodic solution. We have the following theorem.

Theorem 8. *Suppose $\mathcal{R}_0 > 1$ and $a_1 a_2 < a_3$; then system (2) has an orbitally asymptotically stable periodic solution.*

Proof. The nonlinearities in system (2) are analytic in Ω. We obtain that the conclusion follows from Theorem 1.2 in [26]. Take the domain for system (2) to be the interior of the positive orthant, in which the only steady state is E_*. If $\mathcal{R}_0 > 1$ and $a_1 a_2 < a_3$, then E_* is unstable. The dissipativity hypothesis of Theorem 1.2 in [26] follows from Theorems 1 and 6. System (2) is competitive in Ω and $|J_{E_*}| = -a_3 < 0$. Hence, all conditions of Theorem 1.2 in [26] are satisfied. This completes the proof. □

5. Examples

In this section, we give two examples to show the application of our theorems.

Example 1. Consider the following system:

$$\begin{aligned}\dot{x} &= \lambda - dx + rx\left(1 - \frac{x}{x_{\max}}\right) - \frac{\beta x v}{x + y},\\ \dot{y} &= \frac{\beta x v}{x + y} - ay,\\ \dot{v} &= ky - uv,\end{aligned} \tag{44}$$

which is a special case of system (2) by letting $f(x, y, v) = \beta x/(x + y)$ and $\rho = 0$. This model has been investigated by Ji et al. [18]. Applying Theorem 5, Theorems 7 and 8, we have the following result.

Theorem 9.

(i) *If $\mathcal{R}_0 \le 1$, then the infection-free equilibrium $E_0(x_0, 0, 0)$ of system (44) is globally asymptotically stable.*

(ii) *If $\mathcal{R}_0 > 1$ and $r \le d$, then the unique infection equilibrium $E_*(x_*, y_*, v_*)$ of system (44) is globally asymptotically stable.*

(iii) *If $\mathcal{R}_0 > 1$ and $a_1 a_2 < a_3$, then system (44) exists an orbitally asymptotically stable periodic solution.*

Example 2. Consider the following system:

$$\begin{aligned}\dot{x} &= \lambda - dx + rx\left(1 - \frac{x}{x_{\max}}\right) - \beta x v + \rho y,\\ \dot{y} &= \beta x v - (a + \rho)\, y,\\ \dot{v} &= ky - uv,\end{aligned} \tag{45}$$

which is a special case of system (2) by letting $f(x, y, v) = \beta x$. This model has been studied by Zhou et al. [14]. By Theorem 5, Theorem 7, and Theorem 8, we get the following result.

Theorem 10.

(i) *If $\mathcal{R}_0 \le 1$, then the infection-free equilibrium $E_0(x_0, 0, 0)$ of system (45) is globally asymptotically stable.*

(ii) *If $\mathcal{R}_0 > 1$ and $d - r + 2rx/x_{\max} > 0$ for arbitrary $x \ge 0$, then the unique infection equilibrium $E_*(x_*, y_*, v_*)$ of system (45) is globally asymptotically stable.*

(iii) *If $\mathcal{R}_0 > 1$ and $a_1 a_2 < a_3$, then system (45) exists an orbitally asymptotically stable periodic solution.*

6. Conclusion

In this paper, we have considered a virus dynamics model with logistic function, general incidence function, and cure rate. The basic reproduction number is obtained and it determines the global dynamics of this model. If $\mathcal{R}_0 \le 1$, then the infection-free equilibrium is globally asymptotically stable. If $\mathcal{R}_0 > 1$, then the virus persists in the host, and solutions approach either an infection equilibrium or a periodic orbit. Our model is a generalization of several models that appeared in the literature as its special cases.

Conflict of Interests

The author declares that there is no conflict of interests regarding the publication of this paper.

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References

[1] M. A. Nowak and C. R. M. Bangham, "Population dynamics of immune responses to persistent viruses," *Science*, vol. 272, no. 5258, pp. 74–79, 1996.

[2] M. A. Nowak, S. Bonhoeffer, A. M. Hill, R. Boehme, H. C. Thomas, and H. Mcdade, "Viral dynamics in hepatitis B virus infection," *Proceedings of the National Academy of Sciences of the United States of America*, vol. 93, no. 9, pp. 4398–4402, 1996.

[3] D. Li and W. Ma, "Asymptotic properties of a HIV-1 infection model with time delay," *Journal of Mathematical Analysis and Applications*, vol. 335, no. 1, pp. 683–691, 2007.

[4] L. Min, Y. Su, and Y. Kuang, "Mathematical analysis of a basic virus infection model with application to HBV infection," *Rocky Mountain Journal of Mathematics*, vol. 38, no. 5, pp. 1573–1585, 2008.

[5] A. M. Elaiw, "Global properties of a class of virus infection models with multitarget cells," *Nonlinear Dynamics*, vol. 69, pp. 423–435, 2012.

[6] L. G. Guidotti, R. Rochford, J. Chung, M. Shapiro, R. Purcell, and F. V. Chisari, "Viral clearance without destruction of infected cells during acute HBV infection," *Science*, vol. 284, no. 5415, pp. 825–829, 1999.

[7] S. M. Ciupe, R. M. Ribeiro, P. W. Nelson, and A. S. Perelson, "Modeling the mechanisms of acute hepatitis B virus infection," *Journal of Theoretical Biology*, vol. 247, no. 1, pp. 23–35, 2007.

[8] H. Dahari, E. Shudo, R. M. Ribeiro, and A. S. Perelson, "Modeling complex decay profiles of hepatitis B virus during antiviral therapy," *Hepatology*, vol. 49, no. 1, pp. 32–38, 2009.

[9] A. S. Perelson, "Modelling viral and immune system dynamics," *Nature Reviews Immunology*, vol. 2, no. 1, pp. 28–36, 2002.

[10] K. Wang, A. Fan, and A. Torres, "Global properties of an improved hepatitis B virus model," *Nonlinear Analysis: Real World Applications*, vol. 11, no. 4, pp. 3131–3138, 2010.

[11] J. A. Zack, S. J. Arrigo, S. R. Weitsman, A. S. Go, A. Haislip, and I. S. Y. Chen, "HIV-1 entry into quiescent primary lymphocytes: molecular analysis reveals a labile, latent viral structure," *Cell*, vol. 61, no. 2, pp. 213–222, 1990.

[12] J. A. Zack, A. M. Haislip, P. Krogstad, and I. S. Y. Chen, "Incompletely reverse-transcribed human immunodeficiency virus type 1 genomes in quiescent cells can function as intermediates in the retroviral life cycle," *Journal of Virology*, vol. 66, no. 3, pp. 1717–1725, 1992.

[13] P. Essunger and A. S. Perelson, "Modeling HIV infection of $CD4^+$ t-cell subpopulations," *Journal of Theoretical Biology*, vol. 170, no. 4, pp. 367–391, 1994.

[14] X. Zhou, X. Song, and X. Shi, "A differential equation model of HIV infection of $CD4^+$ T-cells with cure rate," *Journal of Mathematical Analysis and Applications*, vol. 342, no. 2, pp. 1342–1355, 2008.

[15] K. Hattaf, N. Yousfi, and A. Tridane, "Mathematical analysis of a virus dynamics model with general incidence rate and cure rate," *Nonlinear Analysis: Real World Applications*, vol. 13, no. 4, pp. 1866–1872, 2012.

[16] Y. Tian and X. Liu, "Global dynamics of a virus dynamical model with general incidence rate and cure rate," *Nonlinear Analysis: Real World Applications*, vol. 16, pp. 17–26, 2014.

[17] R. V. Culshaw and S. Ruan, "A delay-differential equation model of HIV infection of $CD4^+$ T-cells," *Mathematical Biosciences*, vol. 165, no. 1, pp. 27–39, 2000.

[18] Y. Ji, L. Min, and Y. Ye, "Global analysis of a viral infection model with application to HBV infection," *Journal of Biological Systems*, vol. 18, no. 2, pp. 325–337, 2010.

[19] M. Y. Li and H. Shu, "Joint effects of mitosis and intracellular delay on viral dynamics: two-parameter bifurcation analysis," *Journal of Mathematical Biology*, vol. 64, no. 6, pp. 1005–1020, 2012.

[20] X. Song and A. U. Neumann, "Global stability and periodic solution of the viral dynamics," *Journal of Mathematical Analysis and Applications*, vol. 329, no. 1, pp. 281–297, 2007.

[21] P. van den Driessche and J. Watmough, "Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission," *Mathematical Biosciences*, vol. 180, pp. 29–48, 2002.

[22] Y. Kuang, *Delay Differential Equations with Applications in Population Dynamics*, Academic Press, Boston, Mass, USA, 1993.

[23] H. R. Thieme, "Persistence under relaxed point-dissipativity (with application to an endemic model)," *SIAM Journal on Mathematical Analysis*, vol. 24, pp. 407–435, 1993.

[24] H. L. Smith, *Monotone Dynamical Systems, An Introduction To the Theory of Competitive and Cooperative Systems*, American Mathematical Society, Providence, RI, USA, 1995.

[25] M. Y. Li and L. Wang, "Global stability in some SEIR epidemic models," in *Mathematical Approaches For Emerging and Reemerging Infectious Diseases: Models, Methods, and Theory*, vol. 126 of *The IMA Volumes in Mathematics and its Applications*, pp. 295–311, 2002.

[26] H. R. Zhu and H. L. Smith, "Stable periodic orbits for a class of three dimensional competitive systems," *Journal of Differential Equations*, vol. 110, no. 1, pp. 143–156, 1994.