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ANALYSIS OF AN HIV INFECTION MODEL WITH DELAYS

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Abstract. In this article, we present an HIV infection model with CTL immune response, immune impairment, and intracellular delay. Firstly, we study the well-posedness of the HIV infection model, then we give the basic reproduction number $\mathcal{R}_0$ and the existence of the equilibria. Secondly, we show that the basic reproduction number determines the stability of the equilibria. That is, by analyzing the distribution of the roots of the characteristic equation and constructing two appropriate Lyapunov functionals, we give the stability of the equilibria. Finally, two numerical simulations illustrate the theoretical analysis.

1. Introduction

Acquired immune deficiency syndrome (AIDS) is a devastating infectious disease caused by infection with a virus that attacks the body's immune system. It takes the most important $CD4^+T$ lymphocytes in the human immune system as the main target and destroys a large number of cells, so that the human body losses its immune function. Therefore, human infection leads to immune deficiency and being prone to various diseases, and the occurrence of malignant tumors. A classical viral infection model was proposed in [1],

$$\begin{aligned} \dot{x}(t) &= \lambda - dx(t) - \beta x(t)v(t), \\ \dot{y}(t) &= \beta x(t)v(t) - ay(t), \\ \dot{v}(t) &= ky(t) - \mu v(t), \end{aligned} \tag{1.1}$$

where $x(t)$, $y(t)$, and $v(t)$ represent the concentrations of susceptible cells, infected cells, and free HIV virions, respectively. The constants λ and d denote the production and mortality rates of susceptible cells; β is the effective contact rate between susceptible cells and HIV virions; a denotes the mortality rate of infected target cells; k represents the average rate at which each infected target cell produces free virions; μ is the virus clearance rate. By constructing Lyapunov functions, Korobeinikov [9] established the global dynamics of model (1.1).

To study the pathogenesis and transmission mechanism of AIDS, many researchers have studied the dynamic model of HIV infection in the host (see [11, 14, 15, 19, 22] and the references cited therein). We note that [14] focus on eliminating or controlling the spread of the virus, taking into account the immune response that the virus has during infection. The rapid and nonspecific immune response initially induced in the host during viral infection is mainly achieved by natural killer cells. Natural killer cells are part of the immune system, and they play an important role in the early stages of viral infection. It is able to quickly identify and attack cells infected by the virus, thus preventing its replication and spread. But in most viral infections, cytotoxic T lymphocyte (CTL) cells that attack infected cells and antibody cells that attack the virus play a key role in antiviral defense. To investigate the role of the population dynamics of viral infection with CTL response, Nowak and Bangham [15] introduced a mathematical model describing the basic dynamics of the interaction between activated $CD4^+$ T cells $x(t)$, infected $CD4^+$ T cells

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$y(t)$, viruses $v(t)$ and immune cells $z(t)$. The model is

$$\begin{aligned}\dot{x}(t) &= \lambda - dx(t) - \beta x(t)v(t),\\ \dot{y}(t) &= \beta x(t)v(t) - ay(t) - py(t)z(t),\\ \dot{v}(t) &= ky(t) - \mu v(t),\\ \dot{z}(t) &= cy(t) - bz(t).\end{aligned} \tag{1.2}$$

On the basis of this model, Song and Neumann [21] proposed the assumption that the clearance rate of each cell to the infected target cell for the cellular immune process is constant, that is, the principle of mass action is followed, but it only considers the antigen to stimulate immunity but ignores the immune damage caused by it. In [21], bilinear rate $\beta x(t)v(t)$ was replaced by infection rate $\frac{\beta x(t)v(t)}{1+\alpha v(t)}$ with saturation effect. Combined with the actual situation, $py(t)z(t)$ was proposed in [6, 17, 18] to represent immune damage and included in the study of HIV dynamics.

A large number of studies have shown that host immunity can be inhibited or even destroyed by certain pathogens, especially under the condition of excessive pathogen load, so antigens can impair immunity (see, [18, 23]). Combined with the situation of saturation incidence and intracellular delay, Xu [25] emphasized that the nonlinear function can better reproduce the saturation reaction in the process of cellular immunity. Therefore, motivated by the ideas [6, 12, 22, 23], Deng and Xu [3] used the nonlinear function $\frac{py(t)z(t)}{1+\omega z(t)}$ instead of the bilinear function $py(t)z(t)$, and considered the model

$$\begin{aligned}\dot{x}(t) &= \lambda - dx(t) - \frac{\beta x(t)v(t)}{1+\alpha v(t)},\\ \dot{y}(t) &= \frac{\beta e^{-m\tau}x(t-\tau)v(t-\tau)}{1+\alpha v(t-\tau)} - ay(t) - \frac{py(t)z(t)}{1+\omega z(t)},\\ \dot{v}(t) &= ky(t) - \mu v(t),\\ \dot{z}(t) &= cy(t) - bz(t) - ny(t)z(t).\end{aligned} \tag{1.3}$$

Here, α, p, c, b, n are positive constants. α represents the constant rate of inhibition effect produced by the crowding effect of free virions; τ is the time it takes from the entry of the virus into the susceptible cell to the production of new virions, and $e^{-m\tau}$ denotes the survival probability of the infected cell from time $t-\tau$ to time t, n is the rate of immune damage, p represents the clearance rate of T cells to infected cells, c and b represent the T cell production rate and death rate, respectively. ω represents the inhibition rate of CTL immune response, and the meanings of other variables and parameters are the same as those in models (1.1) and (1.2).

In [3], the authors assumed that the production rate of susceptible cells in model (1.3) is a constant, that is, they did not take into account that susceptible cells would also grow in the body. However, the results of the biological experiment indicate that the proliferation rate of $CD4^+$T cell is negatively correlates with its absolute concentration (see, e.g.,[2]). Thus, many scholars (see, e.g., [7, 10, 16, 24, 26]) recently proposed and studied that the $CD4^+$T proliferation is subject to logistic growth rate $rx(t)\big(1-\frac{x(t)}{x_{\max}}\big)$, where r is the rate of growth and $x_{\max}$ is the maximum capacity of $CD4^+$ T in the human body.

From the biological perspective, we know that a viral infection or immune response is not transient in vivo, there may be time-lapse, and a time delay is essential to explain a range of processes. It takes some time for infected cells to become active and produce virus particles; new virions also mature to become infectious; and a time interval for antigen stimulation of immune cells. Therefore, it is necessary and important to consider time delays when modeling viral spread and immune response.

Based on the above analysis, in this paper, we consider the delayed HIV infection model.

$$\begin{aligned}
\dot{x}(t) &= \lambda - dx(t) + rx(t)\Big(1 - \frac{x(t)}{x_{\max}}\Big) - \frac{\beta x(t)v(t)}{1+\alpha v(t)},\\
\dot{y}(t) &= \frac{\beta e^{-m\tau_1}x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)} - ay(t) - \frac{py(t)z(t)}{1+\omega z(t)},\\
\dot{v}(t) &= ke^{-m\tau_2}y(t-\tau_2) - \mu v(t),\\
\dot{z}(t) &= ce^{-m\tau_3}y(t-\tau_3) - bz(t) - ny(t)z(t).
\end{aligned} \tag{1.4}$$

Here, uninfected target cells are assumed to be produced at a constant rate λ and die at a per capita rate d. The proliferation of uninfected target cells is described by the logistic term $rx(t)\big(1-\frac{x(t)}{x_{\max}}\big)$, where r is the intrinsic mitosis rate and $x_{\max}$ is the carrying capacity. The delays during the processes of viral production, and CTLs recruitment are τ_2 and τ_3, respectively. The term $e^{-m\tau_2}$ describes the survival probability that start budding from activated infected cells at time t and become free mature viruses at τ_2 time later. The term $e^{-m\tau_3}$ represents the survival rate of virus-specific CTLs during the delay between cell encounters and subsequent recruitment. All parameters are positive constants. The other variables and parameters have the same meaning as model (1.3).

The paper is structured as follows. In section 2, we study the well-posedness of model (1.4). Then we give the basic reproduction number $\mathcal{R}_0$ and the existence of the equilibria of model (1.4). In section 3, we show the basic reproduction number $\mathcal{R}_0$ determine stability of the equilibria of model (1.4). Then the locally and global asymptotic stability of the infection-free and the infection equilibrium are derived. In section 4, we illustrate the theoretical results with numerical simulations. Finally, in section 5, we provide a brief summary.

2. Preliminaries

In this section, we present some preliminary results including the well-posedness, and the formula of the basic reproduction number and existence of equilibria.

2.1. **Well-posedness of model** (1.4)**.** Let $C = C([-\tau, 0]; \mathbb{R}^4_+)$ (where $\tau = \max\{\tau_1, \tau_2, \tau_3\}$) be the Banach space of continuous functions from $[-\tau, 0]$ to $\mathbb{R}$ with the norm $||\phi|| = \max_{\theta\in[-\tau,0]} |\phi(\theta)|$ for any $\phi \in C$. For any given continuous function $u = (x, y, v, z) : [-\tau, \sigma)$ with $\sigma > 0$, we define

$$u_t := (x(t+\cdot), y(t+\cdot), v(t+\cdot), z(t)) \in C \times C \times C \times \mathbb{R}_+ \quad \text{for } t \in [-\tau, \sigma).$$

Let

$$\mathbb{X}^+ = C([-\tau, 0], \mathbb{R}_+) \times C([-\tau, 0], \mathbb{R}_+) \times C([-\tau, 0], \mathbb{R}_+) \times \mathbb{R}_+.$$

We first investigate the well-posedness of model (1.4).

Theorem 2.1. *For any $\phi \in \mathbb{X}^+$, model (1.4) has a unique nonnegative solution $u(t, \phi)$ on $[0, \infty)$ with $u_0 = \phi$, and $u_t(\phi) \in \mathbb{X}^+$ for all $t > 0$. Further, the solution semiflow $u_t : \mathbb{X}^+ \to \mathbb{X}^+$, $t > 0$, has a compact global attractor.*

Proof. For any $\phi = (\phi_1, \phi_2, \phi_3, \phi_4) \in \mathbb{X}^+$, we define

$$f(\phi) := (f_1, f_2, f_3, f_4)(\phi),$$

with

$$\begin{aligned}
f_1(\phi) &= \lambda - d\phi_1(0) + r\phi_1(0)\Big(1 - \frac{\phi_1(0)}{x_{\max}}\Big) - \frac{\beta\phi_1(0)\phi_3(0)}{1+\alpha\phi_3(0)},\\
f_2(\phi) &= \frac{\beta e^{-m\tau_1}\phi_1(-\tau_1)\phi_3(-\tau_1)}{1+\alpha\phi_3(-\tau_1)} - a\phi_2(0) - \frac{p\phi_2(0)\phi_4(0)}{1+\omega\phi_4(0)},\\
f_3(\phi) &= ke^{-m\tau_2}\phi_2(-\tau_2) - \mu\phi_3(0),\\
f_4(\phi) &= ce^{-m\tau_3}\phi_2(-\tau_3) - b\phi_4(0) - n\phi_2(0)\phi_4(0).
\end{aligned}$$

Noting that $f(\phi)$ is continuous in $\phi \in \mathbb{X}^+$ and $f(\phi)$ is Lipschitz in ϕ on each compact subset of $\mathbb{X}^+$, then it implies that model (1.4) admits a unique solution $u(t, \phi)$ through $(0, \phi)$ on its maximal

interval $[0,\sigma_\phi)$ (see [5, Theorem 2.2.1 and Theorem 2.2.3]). Further, let $\phi := (\phi_1,\phi_2,\phi_3,\phi_4) \in \mathbb{X}^+$ be given, we can show that if $\phi_i(0) = 0$ for $1 \le i \le 4$, then $f_i(\phi) \ge 0$. By [20, Theorem 5.2.1 Remark 5.2.1], it follows that for any $(t,\phi) \in \mathbb{R}_+ \times \mathbb{X}^+$, the unique solution $u(t,\phi)$ of model (1.4) with $u_0 = \phi$ satisfies $u_t(\phi) \in \mathbb{X}^+$ for all $t \in [0,\sigma_\phi)$.

Next, we study the boundedness of solutions of model (1.4). Let

$$L(t) = x(t) + e^{m\tau_1} y(t+\tau_1).$$

Then, in view of the first and second equations of (1.4), we obtain

$$\begin{aligned} L'(t) &= \lambda - dx(t) + rx(t)\Big(1 - \frac{x(t)}{x_{\max}}\Big) - \frac{\beta x(t)v(t)}{1+\alpha v(t)} \\ &\quad + \frac{\beta x(t)v(t)}{1+\alpha v(t)} - ae^{m\tau_1} y(t+\tau_1) - \frac{pe^{m\tau_1} y(t+\tau_1)z(t+\tau_1)}{1+\omega z(t+\tau_1)} \\ &\leqslant \lambda - dx(t) + rx(t)\Big(1 - \frac{x(t)}{x_{\max}}\Big) - ae^{m\tau_1} y(t+\tau_1) \\ &\leqslant \lambda + \frac{1}{4} r x_{\max} - dx(t) - ae^{m\tau_1} y(t+\tau_1) \\ &\leqslant \lambda + \frac{1}{4} r x_{\max} - \delta L(t), \end{aligned} \tag{2.1}$$

where $\delta = \min\{d,a\}$. By the comparison theorem, we see $L(t)$ is bounded on $[0,\sigma_\phi)$, it implies $x(t)$ and $y(t)$ are all bounded on $[0,\sigma_\phi)$. As a result, we assume that there is $M > 0$ such that $|y(t)| \le M$ for all $t \in [0,\sigma_\phi)$. It then follows from the third and the last equation of (1.4) that we have

$$\frac{dv(t)}{dt} \leqslant kMe^{-m\tau_2} - \mu v(t), \tag{2.2}$$

$$\frac{dz(t)}{dt} \leqslant cMe^{-m\tau_3} - bz(t). \tag{2.3}$$

Hence, both $v(t)$ and $z(t)$ are bounded on $[0,\sigma_\phi)$, and then [5, Theorem 2.3.1] follows that $\sigma = \infty$. By the differential inequalities (2.1)-(2.3) and the comparison theorem, it then follows that solutions of model (1.4) are uniformly bounded and ultimately bounded in $\mathbb{X}^+$. Consequently, [5, Corollary 3.6.2 and Theorem 4.5.2] imply the existence of a compact global attractor for the solution semiflow of model (1.4) on $\mathbb{X}^+$. □

2.2. **Basic reproductive number and equilibria.** In this subsection, we give the basic reproduction number for model (1.4), and then establish the existence of equilibria of model (1.4). Obviously, model (1.4) always has an infection-free equilibrium $E_0 = (x_0, 0, 0, 0)$, where

$$x_0 = \frac{x_{\max}}{2r}\Big(r - d + \sqrt{(r-d)^2 + \frac{4r\lambda}{x_{\max}}}\Big). \tag{2.4}$$

Linearizing (1.4) at E_0, we obtain the following three infection related equations for variables y, v and z satisfied

$$\begin{aligned} \dot{y}(t) &= \beta e^{-m\tau_1} x_0 v(t-\tau_1) - ay(t), \\ \dot{v}(t) &= ke^{-m\tau_2} y(t-\tau_2) - \mu v(t), \\ \dot{z}(t) &= ce^{-m\tau_3} y(t-\tau_3) - bz(t). \end{aligned}$$

Let u_1, u_2 and u_3 be the number of infected cells, HIV and CTL cell at $t = 0$, respectively. Then the remaining numbers of infected cells HIV and CTL cell at time t are given by

$$u_1(t) = u_1 e^{-at}, \quad u_2(t) = u_2 e^{-\mu t}, \quad u_3(t) = u_3 e^{-bt}.$$

The total numbers of newly infected cells, produced HIV and CTL cell are

$$\bar{u}_1 = \int_{\tau_1}^{\infty} \beta e^{-m\tau_1} x_0 u_2(t-\tau_1)dt = \frac{\beta}{\mu} e^{-m\tau_1} x_0 u_2,$$

$$\bar{u}_2 = \int_{\tau_2}^{\infty} ke^{-m\tau_2}u_1(t-\tau_2)dt = \frac{k}{a}e^{-m\tau_2}u_1,$$
$$\bar{u}_3 = \int_{\tau_3}^{\infty} ce^{-m\tau_3}u_1(t-\tau_3)dt = \frac{c}{b}e^{-m\tau_3}u_1,$$

which can be rewritten as

$$\begin{pmatrix}\bar{u}_1\\ \bar{u}_2\\ \bar{u}_3\end{pmatrix} = \mathcal{M}_0\begin{pmatrix}u_1\\ u_2\\ u_3\end{pmatrix}, \quad \text{where } \mathcal{M}_0 = \begin{pmatrix}0 & \frac{\beta}{\mu}e^{-m\tau_1}x_0 & 0\\ \frac{k}{a}e^{-m\tau_2} & 0 & 0\\ \frac{c}{b}e^{-m\tau_3} & 0 & 0\end{pmatrix}.$$

Then, we can see the matrix $\mathcal{M}_0$ is the next infection operator [4]. As usual, the spectral radius of $\mathcal{M}_0$ is called the basic reproduction number $\mathcal{R}_0$, which is

$$\mathcal{R}_0 = \sqrt{\frac{k\beta x_0}{a\mu}e^{-m(\tau_1+\tau_2)}}.$$

Next, we shall establish the existence of the infection equilibrium of model (1.4). The infection equilibrium denoted by $E^* = (x^*, y^*, v^*, z^*)$ satisfies the system

$$\begin{aligned} h(x) - \frac{\beta xv}{1+\alpha v} &= 0,\\ \frac{\beta e^{-m\tau_1}xv}{1+\alpha v} - ay - \frac{pyz}{1+\omega z} &= 0,\\ ke^{-m\tau_2}y - \mu v &= 0,\\ ce^{-m\tau_3}y - bz - nyz &= 0, \end{aligned} \tag{2.5}$$

where $h(x) = \lambda - dx(t) + rx(t)(1 - \frac{x(t)}{x_{\max}})$. It follows from the first equation of (2.5) that

$$\frac{r}{x_{\max}}x^2 + \Big(d - r + \frac{\beta v}{1+\alpha v}\Big)x - \lambda = 0.$$

Clearly, the positive root x^* of the above equation is

$$x^* = \frac{x_{\max}}{2r}\Big(r - d - \frac{\beta v}{1+\alpha v} + \sqrt{\Big(r - d - \frac{\beta v}{1+\alpha v}\Big)^2 + \frac{4r\lambda}{x_{\max}}}\ \Big) < x_0.$$

Obviously, $\beta x^* - \alpha h(x^*) \neq 0$. From the first equation of (2.5) again, we obtain

$$v = \frac{h(x)}{\beta x - \alpha h(x)}.$$

By the third and fourth equations of (2.5), respectively, we obtain

$$y = \frac{\mu}{k}e^{m\tau_2}v, \quad z = ce^{-m\tau_3}\frac{y}{b+ny}.$$

Substituting $y = \frac{\mu}{k}e^{m\tau_2}v$ into $z = ce^{-m\tau_3}\frac{y}{b+ny}$, we have

$$z = \frac{Bv}{1+Cv}, \quad \text{where} \quad B = \frac{c\mu}{kb}e^{-m\tau_3+m\tau_2}, \ C = \frac{n\mu}{kb}e^{m\tau_2}.$$

Putting $z = \frac{Bv}{1+Cv}$ into the second equation of (2.5), we obtain

$$h(x) = \Big(a + \frac{pBv}{1+Cv+\omega Bv}\Big)Av, \quad \text{where} \quad A = \frac{\mu}{k}e^{m(\tau_1+\tau_2)},$$

that is,

$$h(x)(1+Cv+\omega Bv) = A(a + (aC + a\omega B + pB)v)v.$$

Substituting $v = \frac{h(x)}{\beta x - \alpha h(x)}$ into the above equation and noting that $h(x) \neq 0$, we obtain

$$\Big[\beta x - \alpha h(x) + (C+\omega B)h(x)\Big](\beta x - \alpha h(x)) = A\Big[a(\beta x - \alpha h(x)) + (aC + a\omega B + pB)h(x)\Big].$$

We define

$$\begin{aligned} H(x) &= \Big[\beta x - \alpha h(x) + (C+\omega B)h(x)\Big](\beta x - \alpha h(x)) \\ &\quad - A\Big[a(\beta x - \alpha h(x)) + (aC + a\omega B + pB)h(x)\Big] \quad \text{for } 0 < x < x_0. \end{aligned} \tag{2.6}$$

Now, we claim that there is a positive root x^* in the following equation

$$H(x) = 0, \quad 0 < x < x_0.$$

In fact, it is easy to see the equation $\alpha h(x) - \beta x = 0$ has the positive root

$$\tilde{x} = \frac{x_{\max}}{2r}\Big(r - d - \frac{\beta}{\alpha} + \sqrt{\Big(r - d - \frac{\beta}{\alpha}\Big)^2 + \frac{4r\lambda}{x_{\max}}}\Big),$$

and $0 < \tilde{x} < x_0$.

Since $h(\tilde{x}_0) - \beta\tilde{x}_0 = 0$, we have

$$H(\tilde{x}_0) = -A\beta(aC + a\omega B + pB)\tilde{x}_0 < 0.$$

And also, if $\mathcal{R}_0 > 1$, noting that $h(x_0) = 0$, we then obatin

$$H(x_0) = (\beta x_0)^2 - Aa\beta x_0 = \frac{a\mu}{k}\beta x_0 e^{m(\tau_1+\tau_2)}(\mathcal{R}_0^2 - 1) > 0.$$

Therefore, there is a $x^* \in (\tilde{x}_0, x_0)$ such that $H(x^*) = 0$.

Summarizing the above discussion, we establish the existence of equilibria of model (1.4).

Theorem 2.2. *(1) Model* (1.4) *always has the infection-free equilibrium* $E_0(x_0, 0, 0, 0)$ *with* x_0 *defined by* (2.1).

(2) Model (1.4) *has the infection equilibrium* $E^* = (x^*, y^*, v^*, z^*)$ *if* $\mathcal{R}_0 > 1$, *where* x^* *is the positive root of* $H(x) = 0$, *and*

$$v^* = \frac{h(x^*)}{\beta x^* - \alpha h(x^*)}, \quad y^* = \frac{u}{k}e^{m\tau_2}v^*, \quad z^* = \frac{u}{k}e^{m\tau_2}v^*,$$

where $H(x)$ *is defined by* (2.6).

3. Stability analysis

Here we establish the local and global stabilities of the equilibria of model (1.4).

3.1. **Local stability of equilibria of model** (1.4)**.** By analyzing the distribution of the roots of the corresponding characteristic equation, we study the local stability of the infection-free and infection equilibrium of model (1.4). First, we have the following result.

Theorem 3.1. *Let* $\tau_i \geqslant 0,\ i = 1, 2, 3$. *The infection-free equilibrium* E_0 *is locally asymptotically stable for* $\mathcal{R}_0 < 1$ *and it is unstable for* $\mathcal{R}_0 > 1$.

Proof. Linearizing (1.4) at E_0, we can see the Jacobian matrix at E_0 as follows

$$J_{E_0} = \begin{pmatrix} -d + r - \frac{2r}{x_{\max}}x_0 & 0 & -\beta x_0 & 0 \\ 0 & -a & \beta x_0 e^{-(\xi+m)\tau_1} & 0 \\ 0 & ke^{-(\xi+m)\tau_2} & -\mu & 0 \\ 0 & ce^{-(\xi+m)\tau_3} & 0 & -b \end{pmatrix}.$$

Then the characteristic equation of J_{E_0} is

$$(\xi + b)\Big(\xi + d - r + \frac{2r}{x_{\max}}x_0\Big)\Big((\xi + a)(\xi + \mu) - k\beta x_0 e^{-(\xi+m)(\tau_1+\tau_2)}\Big) = 0. \tag{3.1}$$

It is clear that equation (3.1) has two negative roots

$$\xi_1 = -b \quad \text{and} \quad \xi_2 = -\Big(d - r + \frac{2r}{x_{\max}}x_0\Big),$$

since

$$d - r + \frac{2r}{x_{\max}}x_0 = \sqrt{(r-d)^2 + \frac{4r\lambda}{x_{\max}}} > 0.$$

Hence, the remaining roots of equation (3.1) are determined by the equation

$$\kappa(\xi) =: (\xi + a)(\xi + \mu) - k\beta x_0 e^{-(\xi+m)(\tau_1+\tau_2)} = 0.$$

Obviously, the equation $\kappa(\xi) = 0$ is equivalent to the equation

$$1 = \frac{k\beta x_0}{(\xi + a)(\xi + \mu)} e^{-(\xi+m)(\tau_1+\tau_2)}. \tag{3.2}$$

Let $\xi = x+iy$ with $x > 0$ is a solution of equation (3.2), and the modulus on both sides of equation (3.2), we have

$$1 = \Big|\frac{k\beta x_0}{(\xi + a)(\xi + \mu)} e^{-(\xi+m)(\tau_1+\tau_2)}\Big| \leqslant \Big|\frac{k\beta x_0}{a\mu}\Big| |e^{-m(\tau_1+\tau_2)}| = \mathcal{R}_0^2 < 1,$$

which implies $1 \leq \mathcal{R}_0 < 1$, a contradiction. Hence all roots of equation (3.2) have negative real parts if $\mathcal{R}_0 < 1$, it follows that E_0 is locally asymptotically stable for $\mathcal{R}_0 < 1$.

Noting that

$$\kappa(0) = a\mu(1 - \mathcal{R}_0^2) < 0, \quad \lim_{\xi\to+\infty} \kappa(\xi) = +\infty.$$

Hence, the equation $\kappa(\xi) = 0$ has a positive root if $\mathcal{R}_0 > 1$. It follows that E_0 is unstable if $\mathcal{R}_0 > 1$. □

Theorem 3.2. *Let $\tau_i \geqslant 0$, $i = 1, 2$, and $\tau_3 = 0$. The infection equilibrium E^* is locally asymptotically stable for $\mathcal{R}_0 > 1$.*

Proof. Linearizing the system (1.4) at E^*, we can get the Jacobian matrix at E^* given by

$$J_{E^*} = \begin{pmatrix} -d + r - \frac{2r}{x_{\max}} x^* - \frac{\beta v^*}{1+\alpha v^*} & 0 & -\frac{\beta x^*}{(1+\alpha v^*)^2} & 0 \\ \frac{\beta v^*}{1+\alpha v^*} e^{-(\xi+m)\tau_1} & -a - \frac{pz^*}{1+\omega z^*} & \frac{\beta x^*}{(1+\alpha v^*)^2} e^{-(\xi+m)\tau_1} & -\frac{pz^*}{(1+\omega z^*)^2} \\ 0 & ke^{-(\xi+m)\tau_2} & -\mu & 0 \\ 0 & c - nz^* & 0 & -b - ny^* \end{pmatrix}.$$

Thus, we obtain the following characteristic equation of (1.4) at E^* as follows

$$\begin{aligned} &\Big(\xi + d - r + \frac{2r}{x_{\max}} x^* + \frac{\beta v^*}{1 + \alpha v^*}\Big)(\xi + \mu) \\ &\times \Big(\Big(\xi + a + \frac{pz^*}{1 + \omega z^*}\Big)(\xi + b + ny^*) + \frac{py^*}{(1 + \omega z^*)^2}(c - nz^*)\Big) \\ &= \frac{k\beta x^*}{(1 + \alpha v^*)^2}\Big(\xi + d - r + \frac{2r}{x_{\max}} x^*\Big)(\xi + b + ny^*) e^{-(\xi+m)(\tau_1+\tau_2)}. \end{aligned} \tag{3.3}$$

Next, we claim all roots of equation (3.3) have negative real parts when $\mathcal{R}_0 > 1$. Otherwise, equation (3.3) has a root $\xi = x + iy$ with $x > 0$, and note that

$$c - nz^* = \frac{bz^*}{y^*}, \quad y^* = \frac{u}{k} e^{m\tau_2} v^*, \quad \frac{\beta x^* v^*}{(1 + \alpha v^*)y^*} = a + \frac{pz^*}{1 + \omega z^*}.$$

Thus,

$$\Big|\xi + d - r + \frac{2r}{x_{\max}} x^* + \frac{\beta v^*}{1 + \alpha v^*}\Big| > \Big|\Big(\xi + d - r + \frac{2r}{x_{\max}} x^*\Big) e^{-\xi(\tau_1+\tau_2)}\Big|, \tag{3.4}$$

and

$$\begin{aligned}
&\Big|(\xi+\mu)\Big(\Big(\xi+a+\frac{pz^*}{1+\omega z^*}\Big)(\xi+b+ny^*)+\frac{py^*}{(1+\omega z^*)^2}(c-nz^*)\Big)\Big|\\
&=\Big|(\xi+\mu)\Big(\Big(\xi+a+\frac{pz^*}{1+\omega z^*}\Big)(\xi+b+ny^*)+\frac{bpz^*}{(1+\omega z^*)^2}\Big)\Big|\\
&\geqslant\Big|\mu(\xi+b+ny^*)\Big(a+\frac{pz^*}{1+\omega z^*}\Big)\Big| \qquad (3.5)\\
&\geqslant\Big|(\xi+b+ny^*)\frac{k\beta x^*}{1+\alpha v^*}e^{-m(\tau_1+\tau_2)}\Big|\\
&>\Big|(\xi+b+ny^*)\frac{k\beta x^*}{(1+\alpha v^*)^2}e^{-m(\tau_1+\tau_2)}\Big|.
\end{aligned}$$

In view of inequalities (3.4) and (3.5), we obtain that $\xi=x+iy$ with $x>0$ is not the root of (3.3), which leads that equation (3.3) can not have any root with positive real part. Hence, the infection equilibrium $E^*=(x^*,y^*,v^*,z^*)$ of model (1.4) is locally asymptotically stable for $\mathcal{R}_0>1$. □

3.2. **Global stability of equilibria of model** (1.4)**.** Constructing Lyapunov functionals, we study the global asymptotic stability of the equilibria of model (1.4). To this end, we introduce the fundamental function

$$g(x)=x-1-\ln x \quad \text{for } x>0.$$

Clearly, the function $g(x)\geqslant 0$ for all $x>0$, and $g(x)=0$ if and only if $x=1$.

We start with the globally asymptotic stability of the infection-free equilibrium E_0.

Theorem 3.3. *Let $\tau_i\geqslant 0,\ i=1,2,3$. If $\mathcal{R}_0\leq 1$, then the infection-free equilibrium E_0 of model* (1.4) *is globally asymptotically stable.*

Proof. We define the Lyapunov functional

$$M(t)=M_1(t)+M_2(t),$$

where

$$\begin{aligned}
M_1(t)&=x_0g\Big(\frac{x(t)}{x_0}\Big)+e^{m\tau_1}y(t)+\frac{\beta x_0}{\mu}e^{m(\tau_1+\tau_2)}v(t)+e^{m(\tau_1+\tau_3)}(1-\mathcal{R}_0^2)z(t),\\
M_2(t)&=\int_{t-\tau_1}^{t}\frac{\beta x(s)v(s)}{1+\alpha v(s)}ds+\mathcal{R}_0^2ae^{-m\tau_2}\int_{t-\tau_2}^{t}y(s)ds+ae^{m\tau_1}(1-\mathcal{R}_0^2)\int_{t-\tau_3}^{t}y(s)ds.
\end{aligned}$$

It can be easily verified that $M(t)\geq 0$ with $M(t)=0$ if and only if $x=x_0$, $y=0$, $v=0$ and $z=0$. Differentiating $M(t)$ along any positive solution of model (1.4), we have

$$\begin{aligned}
M_1'(t)=&-\frac{(x_0-x(t))^2}{x(t)}\Big(d-r+\frac{rx_0}{x_{\max}}+\frac{rx(t)}{x_{\max}}\Big)-\frac{\beta x(t)v(t)}{1+\alpha v(t)}+\frac{\beta x(t)v(t)}{1+\alpha v(t)}\frac{x_0}{x(t)}\\
&+\frac{\beta x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}-ae^{m\tau_1}y(t)-\frac{pe^{m\tau_1}y(t)z(t)}{1+\omega z(t)}\\
&+\frac{k\beta x_0}{\mu}e^{m\tau_1}y(t-\tau_2)-\beta x_0e^{m(\tau_1+\tau_2)}v(t)\\
&+ae^{m\tau_1}(1-\mathcal{R}_0^2)y(t-\tau_3)-\frac{a}{c}e^{m(\tau_1+\tau_3)}(1-\mathcal{R}_0^2)(bz(t)+ny(t)z(t)),
\end{aligned}$$

and

$$\begin{aligned}
M_2'(t)=&\frac{\beta x(t)v(t)}{1+\alpha v(t)}-\frac{\beta x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}+\mathcal{R}_0^2ae^{-m\tau_2}y(t)-\mathcal{R}_0^2ae^{-m\tau_2}y(t-\tau_2)\\
&+ae^{m\tau_1}(1-\mathcal{R}_0^2)y(t)-ae^{m\tau_1}(1-\mathcal{R}_0^2)y(t-\tau_3).
\end{aligned}$$

Thus, we obtain

$$\begin{aligned}
M'(t)=&-\frac{(x_0-x(t))^2}{x(t)}\Big(d-r+\frac{rx_0}{x_{\max}}+\frac{rx(t)}{x_{\max}}\Big)+\frac{\beta x(t)v(t)}{1+\alpha v(t)}\frac{x_0}{x(t)}-\frac{pe^{m\tau_1}y(t)z(t)}{1+\omega z(t)}\\
&-\frac{a}{c}e^{m(\tau_1+\tau_3)}(1-\mathcal{R}_0^2)(bz(t)+ny(t)z(t))+\mathcal{R}_0^2ae^{-m\tau_2}y(t)-\mathcal{R}_0^2ae^{-m\tau_1}y(t)
\end{aligned}$$

$$
\begin{aligned}
&= -\frac{(x_0 - x(t))^2}{x(t)}\Big(d - r + \frac{rx_0}{x_{\max}} + \frac{rx(t)}{x_{\max}}\Big) - \beta x_0 v(t)\Big(e^{m(\tau_1+\tau_2)} - \frac{1}{1+\alpha v(t)}\Big)\\
&\quad - \mathcal{R}_0^2 a e^{-m\tau_1} y(t)(1 - e^{-m(\tau_1+\tau_2)}) - \frac{p e^{m\tau_1} y(t) z(t)}{1+\omega z(t)}\\
&\quad - \frac{a}{c} e^{m(\tau_1+\tau_3)}(1-\mathcal{R}_0^2)(bz(t) + ny(t)z(t)).
\end{aligned}
$$

Note that $d - r + \frac{rx_0}{x_{\max}} > 0$. If $\mathcal{R}_0 < 1$, then $M'(t) \leqslant 0$ and the equality holds if and only if $x(t) = x_0$, $y(t) = 0$, $v(t) = 0$ and $z(t) = 0$. Hence, the largest invariant set in the set $\{(x, y, v, z) \colon M'(t) = 0\}$ is the singleton set E_0. Therefore, by the LaSalle's invariance principle [5], the infection-free equilibrium E_0 is globally asymptotically stable when $\mathcal{R}_0 < 1$.

Now, if $\mathcal{R}_0 = 1$, we obtain

$$
\begin{aligned}
M'(t) &= -\frac{(x_0 - x(t))^2}{x(t)}\Big(d - r + \frac{rx_0}{x_{\max}} + \frac{rx(t)}{x_{\max}}\Big) - \beta x_0 v(t)\Big(e^{m(\tau_1+\tau_2)} - \frac{1}{1+\alpha v(t)}\Big)\\
&\quad - a e^{-m\tau_1} y(t)(1 - e^{-m(\tau_1+\tau_2)}) - \frac{p e^{m\tau_1} y(t) z(t)}{1+\omega z(t)},
\end{aligned}
$$

which follows $M'(t) \leqslant 0$ and the equality holds if and only if $x(t) = x_0$, $y(t) = 0$, $v(t) = 0$. Then one can easily show that the largest invariant set of $\{(x, y, v, z) : M'(t) = 0\}$ is the singleton $\{E_0\}$. Hence, using LaSalle's invariance principle [5], we also get E_0 is globally asymptotically stable when $\mathcal{R}_0 = 1$. □

Theorem 3.4. *Let $\tau_i \geqslant 0$, $i = 1, 2$, and $\tau_3 = 0$. If $\mathcal{R}_0 > 1$ and that $x_{\max}(r - d) < rx^*$, then the infection equilibrium E^* of model (1.4) is globally asymptotically stable.*

Proof. We define the Lyapunov function

$$
N(t) = N_1(t) + N_2(t),
$$

where

$$
\begin{aligned}
N_1(t) &= x^* g\Big(\frac{x(t)}{x^*}\Big) + e^{m\tau_1} g\Big(\frac{y(t)}{y^*}\Big) + \frac{\beta x^* v^*}{(1+\alpha v^*) k y^*} e^{m\tau_2} v^* g\Big(\frac{v(t)}{v^*}\Big) + \frac{p y^* z^*}{b(1+\omega z^*)^2} e^{m\tau_1} g\Big(\frac{z(t)}{z^*}\Big),\\
N_2(t) &= \frac{\beta x^* v^*}{1+\alpha v^*} \int_{t-\tau_1}^{t} g\Big(\frac{x(s)v(s)(1+\alpha v^*)}{x^* v^* (1+\alpha v(s))}\Big) ds + \frac{\beta x^* v^*}{1+\alpha v^*} \int_{t-\tau_2}^{t} g\Big(\frac{y(s)}{y^*}\Big) ds.
\end{aligned}
$$

Then, differentiating $N(t)$ along any positive solution of model (1.4) for $t \geq 0$, we obtain

$$
\begin{aligned}
N_1'(t) &= \Big(1 - \frac{x^*}{x(t)}\Big)\Big(\lambda - dx(t) - \frac{\beta x(t) v(t)}{1+\alpha v(t)}\Big)\\
&\quad + e^{m\tau_1}\Big(1 - \frac{y^*}{y(t)}\Big)\Big(\frac{\beta e^{-m\tau} x(t-\tau) v(t-\tau)}{1+\alpha v(t-\tau)} - a y(t) - \frac{p y(t) z(t)}{1+\omega z(t)}\Big)\\
&\quad + \frac{\beta x^* v^*}{1+\alpha v^*} \frac{1}{k y^*} e^{m\tau_2}\Big(1 - \frac{v^*}{v(t)}\Big)(k e^{-m\tau_2} y(t-\tau_2) - \mu v(t))\\
&\quad + \frac{p y^*}{b(1+\omega z^*)^2} e^{m\tau_1}\Big(1 - \frac{x^*}{x(t)}\Big)(cy(t) - bz(t) - ny(t)z(t))\\
&= \Big(1 - \frac{x^*}{x(t)}\Big)\Big(\lambda - dx(t) - \frac{\beta x(t) v(t)}{1+\alpha v(t)}\Big) + \frac{\beta x(t-\tau_1) v(t-\tau_1)}{1+\alpha v(t-\tau_1)} - a e^{m\tau_1} y(t)\\
&\quad - \frac{p e^{m\tau_1} y(t) z(t)}{1+\omega z(t)} - \frac{\beta x(t-\tau_1) v(t-\tau_1)}{1+\alpha v(t-\tau_1)} \frac{y^*}{y(t)} + a e^{m\tau_1} y^* + \frac{p e^{m\tau_1} y^* z(t)}{1+\omega z(t)}\\
&\quad + \frac{\beta x^* v^*}{1+\alpha v^*} \frac{y(t-\tau_2)}{y^*} - \frac{\beta x^* v^*}{1+\alpha v^*} \frac{\mu}{k y^*} e^{m\tau_2} v(t) - \frac{\beta x^* v^*}{1+\alpha v^*} \frac{y(t-\tau_2)}{y^*} \frac{v^*}{v(t)}\\
&\quad + \frac{\beta x^* v^*}{1+\alpha v^*} \frac{\mu v^*}{k y^*} e^{m\tau_2} + \frac{p y^*}{b(1+\omega z^*)^2} e^{m\tau_1} \frac{z(t) - z^*}{z(t)} (cy(t) - bz(t) - ny(t)z(t)),
\end{aligned}
$$

and

$$N_2'(t) = \frac{\beta x(t)v(t)}{1+\alpha v(t)} - \frac{\beta x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)} + \frac{\beta x^* v^*}{1+\alpha v^*} \ln \frac{x(t-\tau_1)v(t-\tau_1)(1+\alpha v(t))}{x(t)v(t)(1+\alpha v(t-\tau_1))} + \frac{\beta x^* v^*}{1+\alpha v^*} \frac{y(t)}{y^*} - \frac{\beta x^* v^*}{1+\alpha v^*} \frac{y(t-\tau_2)}{y^*} + \frac{\beta x^* v^*}{1+\alpha v^*} \ln \frac{y(t-\tau_2)}{y(t)}.$$

Noting that the infection equilibrium $E^*(x^*, y^*, v^*, z^*)$ satisfies the equations

$$\lambda = dx^* - rx^*\Big(1 - \frac{x^*}{x_{\max}}\Big) + \frac{\beta x^* v^*}{1+\alpha v^*},$$

$$\frac{\beta e^{-m\tau_1} x^* v^*}{1+\alpha v^*} = ay^* + \frac{py^* z^*}{1+\omega z^*}, \quad ke^{-m\tau_2} y^* = \mu v^*, \quad cy^* = bz^* + ny^* z^*,$$

we then have

$$\begin{aligned}
N'(t) &= -\frac{(x^*-x(t))^2}{x(t)}\Big(d - r + \frac{rx^*}{x_{\max}} + \frac{rx(t)}{x_{\max}}\Big) + \frac{\beta x^* v^*}{1+\alpha v^*} - \frac{\beta x(t)v(t)}{1+\alpha v(t)} - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{x^*}{x(t)} \\
&\quad + \frac{\beta x(t)v(t)}{1+\alpha v(t)}\frac{x^*}{x(t)} + \frac{\beta x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)} - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{y(t)}{y^*} + \frac{py^* z^*}{1+\omega z^*}e^{m\tau_1}\frac{y(t)}{y^*} \\
&\quad - \frac{pe^{m\tau_1} y(t)z(t)}{1+\omega z(t)} - \frac{\beta x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}\frac{y^*}{y(t)} + \frac{\beta x^* v^*}{1+\alpha v^*} - \frac{py^* z^*}{1+\omega z^*}e^{m\tau_1} \\
&\quad + \frac{pe^{m\tau_1} y^* z(t)}{1+\omega z(t)} + \frac{\beta x^* v^*}{1+\alpha v^*}\frac{y(t-\tau_2)}{y^*} - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{\mu}{ky^*}e^{m\tau_2} v(t) - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{y(t-\tau_2)}{y^*}\frac{v^*}{v(t)} \\
&\quad + \frac{\beta x^* v^*}{1+\alpha v^*} + \frac{pe^{m\tau_1} y^*(z(t)-z^*)}{bz(t)(1+\omega z^*)^2}\Big(ny(t)(z^*-z(t)) + \frac{by(t)z^* - by^* z(t)}{y^*}\Big) \\
&\quad + \frac{\beta x(t)v(t)}{1+\alpha v(t)} - \frac{\beta x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)} + \frac{\beta x^* v^*}{1+\alpha v^*}\ln\frac{x(t-\tau_1)v(t-\tau_1)(1+\alpha v(t))}{x(t)v(t)(1+\alpha v(t-\tau_1))} \\
&\quad + \frac{\beta x^* v^*}{1+\alpha v^*}\frac{y(t)}{y^*} - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{y(t-\tau_2)}{y^*} + \frac{\beta x^* v^*}{1+\alpha v^*}\ln\frac{y(t-\tau_2)}{y(t)} \\
&= -\frac{(x^*-x(t))^2}{x(t)}\Big(d - r + \frac{rx^*}{x_{\max}} + \frac{rx(t)}{x_{\max}}\Big) + \frac{\beta x^* v^*}{1+\alpha v^*} - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{x^*}{x(t)} + \frac{\beta x(t)v(t)}{1+\alpha v(t)}\frac{x^*}{x(t)} \\
&\quad - \frac{\beta x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}\frac{y^*}{y(t)} + \frac{\beta x^* v^*}{1+\alpha v^*} - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{v(t)}{v^*} - \frac{\beta x^* v^*}{1+\alpha v^*}\frac{y(t-\tau_2)}{y^*}\frac{v^*}{v(t)} \\
&\quad + \frac{\beta x^* v^*}{1+\alpha v^*} + \frac{py^* z^*}{1+\omega z^*}e^{m\tau_1}\frac{y(t)}{y^*} - \frac{pe^{m\tau_1} y(t)z(t)}{1+\omega z(t)} - \frac{py^* z^*}{1+\omega z^*}e^{m\tau_1} + \frac{pe^{m\tau_1} y^* z(t)}{1+\omega z(t)} \\
&\quad + \frac{pe^{m\tau_1}(z(t)-z^*)(y(t)z^* - y^* z(t))}{z(t)(1+\omega z^*)^2} - \frac{npy^* y(t)e^{m\tau_1}(z(t)-z^*)^2}{bz(t)(1+\omega z^*)^2} \\
&\quad + \frac{\beta x^* v^*}{1+\alpha v^*}\ln\frac{x(t-\tau_1)v(t-\tau_1)(1+\alpha v(t))}{x(t)v(t)(1+\alpha v(t-\tau_1))} + \frac{\beta x^* v^*}{1+\alpha v^*} ln\frac{y(t-\tau_2)}{y(t)} \\
&= -\frac{(x^*-x(t))^2}{x(t)}\Big(d - r + \frac{rx^*}{x_{\max}} + \frac{rx(t)}{x_{\max}}\Big) + \frac{\beta x^* v^*}{1+\alpha v^*}\Big(1 - \frac{x^*}{x(t)} + \frac{1+\alpha v^*}{1+\alpha v(t)}\frac{v(t)}{v^*} \\
&\quad - \frac{x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}\frac{y^*}{y(t)}\frac{1+\alpha v^*}{x^* v^*} + 1 - \frac{v(t)}{v^*} - \frac{y(t-\tau_2)}{y^*}\frac{v^*}{v(t)} + 1 \\
&\quad + \ln\frac{x(t-\tau_1)v(t-\tau_1)(1+\alpha v(t))}{x(t)v(t)(1+\alpha v(t-\tau_1))} + \ln\frac{y(t-\tau_2)}{y(t)}\Big) - \frac{pe^{m\tau_1}(z(t)-z^*)(y(t)-y^*)}{(1+\omega z(t))(1+\omega z^*)} \\
&\quad + \frac{pe^{m\tau_1}(z(t)-z^*)(y(t)z^* - y^* z(t))}{z(t)(1+\omega z^*)^2} - \frac{npy^* y(t)e^{m\tau_1}(z(t)-z^*)^2}{bz(t)(1+\omega z^*)^2} \\
&= -\frac{(x^*-x(t))^2}{x(t)}\Big(d - r + \frac{rx^*}{x_{\max}} + \frac{rx(t)}{x_{\max}}\Big) + \frac{\beta x^* v^*}{1+\alpha v^*}\Big(1 - \frac{x^*}{x(t)} + \ln\frac{x^*}{x(t)} \\
&\quad + 1 - \frac{x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}\frac{y^*}{y(t)}\frac{1+\alpha v^*}{x^* v^*} + \ln\frac{x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}\frac{y^*}{y(t)}\frac{1+\alpha v^*}{x^* v^*}
\end{aligned}$$

$$
\begin{aligned}
&+1-\frac{y(t-\tau_2)}{y^*}\frac{v^*}{v(t)}+\ln\frac{y(t-\tau_2)}{y^*}\frac{v^*}{v(t)}+\ln\frac{1+\alpha v(t)}{1+\alpha v^*}-\frac{1+\alpha v(t)}{1+\alpha v^*}+1\\
&+\frac{1+\alpha v^*}{1+\alpha v(t)}\frac{v(t)}{v^*}-\frac{v(t)}{v^*}+\frac{1+\alpha v(t)}{1+\alpha v^*}-1\Big)\\
&-\frac{pe^{m\tau_1}(z(t)-z^*)^2(y(t)+\omega y^* yz(t))}{z(t)(1+\omega z(t))(1+\omega z^*)}-\frac{npy^*y(t)e^{m\tau_1}(z(t)-z^*)^2}{bz(t)(1+\omega z^*)^2}\\
=&-\frac{(x^*-x(t))^2}{x(t)}\Big(d-r+\frac{rx^*}{x_{\max}}+\frac{rx(t)}{x_{\max}}\Big)-\frac{\beta x^*v^*}{1+\alpha v^*}\Big(g\Big(\frac{x^*}{x(t)}\Big)\\
&+g\Big(\frac{x(t-\tau_1)v(t-\tau_1)}{1+\alpha v(t-\tau_1)}\frac{y^*}{y(t)}\frac{1+\alpha v^*}{x^*v^*}\Big)+g\Big(\frac{y(t-\tau_2)}{y^*}\frac{v^*}{v(t)}\Big)+g\Big(\frac{1+\alpha v(t)}{1+\alpha v^*}\Big)\\
&+\frac{\alpha(v(t)-v^*)^2}{v^*(1+\alpha v(t))(1+\alpha v^*)}\Big)-\frac{pe^{m\tau_1}(z(t)-z^*)^2(y(t)+\omega y^* yz(t))}{z(t)(1+\omega z(t))(1+\omega z^*)}\\
&-\frac{npy^*y(t)e^{m\tau_1}(z(t)-z^*)^2}{bz(t)(1+\omega z^*)^2}.
\end{aligned}
$$

Using the fact $x_{\max}(r-d)<rx^*$, we have $\big(d-r+\frac{rx^*}{x_{\max}}+\frac{rx(t)}{x_{\max}}\big)>0$. Thus, it follows that $N'(t)\le 0$ and $N'(t)=0$ holds if and only if $x(t)=x^*$, $y(t)=y^*$, $v(t)=v^*$, $z(t)=z^*$. Furthermore, it can be shown that the largest invariant set of $\{(x,y,v,z)\colon N'(t)=0\}$ is the singleton E^*. Therefore, By LaSalle's invariance principle [5], we see the infection equilibrium E^* is globally asymptotically stable. □

4. Numerical simulations

We illustrate the theoretical results of model (1.4) by numerical simulations. The model parameters listed in Table 1 are based on biological data from [3, 8, 13].

When $\tau_1=0.5$, $\tau_2=0.43$, $\tau_3=0.42$, in view of the simple calculations, we obtain the disease-free equilibrium $E_0=(549.5098,0,0,0)$ and $\mathcal{R}_0^2=0.2658<1$. Figure 1 shows that the infection-free equilibrium E_0 of model (1.4) is globally asymptotically stable, consistent with Theorem 3.3. This result stems from the relatively low viral infection coefficient $\beta=7.8\times10^{-4}\mu l^{-1}d^{-1}$, which limits the efficiency of the virus in infecting new cells. Eventually, the virus will be eliminated by the immune system, and the system will converge to the infection-free equilibrium without developing a chronic infection.

On the other hand, when $\tau_1=0.5$, $\tau_2=0.43$, $\tau_3=0$, we also compute the infection equilibrium $E^*=(386.4550,10.3804,19.0720,4.1226)$ and the basic reproduction number $\mathcal{R}_0^2=2.3607>1$. This result stems from the relatively viral infection coefficient $\beta=2.6\times10^{-3}\mu l^{-1}d^{-1}$. That is, the infection equilibrium E^* of model (1.4) is globally asymptotically stable, which completely conforms with Theorem 3.2.

5. Summary

Motivated by Deng and Xu's recent work [3], we introduce the logistic term $rx(t)\big(1-\frac{x(t)}{x_{\max}}\big)$ and delays τ_2,τ_3 into model (1.3) and then present an HIV infection model (1.4) with CTL immune response, immune impairment and intracellular delay. Subsequently, we give the basic reproduction $\mathcal{R}_0$ for model (1.4). Based on the value of the basic reproduction $\mathcal{R}_0$, we establish the existence and stability of the equilibria of model (1.4).

(i) If $\mathcal{R}_0<1$, then there exists the infection-free equilibrium of (1.4), and it is globally asymptotically stable.

(ii) If $\mathcal{R}_0>1$, then there exists the infection equilibrium of (1.4), and it is globally asymptotically stable.

When there is no logistic growth $rx(t)\big(1-\frac{x(t)}{x_{\max}}\big)$, theorems 3.1–3.4 reduce to Theorems 4.1–4.4 for model (1.3) in [3]. Thus, our analytic results generalize those in [3] for model (1.3).

Our global stability results (Theorems 3.3 and 3.4) show that the basic reproduction ratio $\mathcal{R}_0$ may be used to design the control strategies of the infection transmission and to estimate the

TABLE 1. Biologically parameter ranges (values)

Parameter	Value	Range	Ref.
λ	$50\mu l^{-1}d^{-1}$	$[10, 200]$	[3]
d	$0.11d^{-1}$	$[0.01, 0.2]$	[8]
r	$0.03d^{-1}$	$[0, 0.1]$	[13]
$x_{\max}$	$1500\mu l^{-1}$	1500	[13]
α	0.01		Assumed
k	$1.1349d^{-1}$	$[0, 2]$	[3]
μ	$0.5d^{-1}$	$[0, 1]$	[3]
m	$1.39d^{-1}$	$[0, 2]$	[3]
a	$1.005d^{-1}$	$[0.01, 2]$	[8]
p	$0.1\mu l^{-1}d^{-1}$	$[0, 1]$	[8]
w	0.01		Assumed
c	$0.2d^{-1}$	$[0, 1]$	[8]
b	$0.4d^{-1}$	$[0, 1]$	[8]
n	$0.01\mu l^{-1}d^{-1}$	$[0, 1]$	[8]

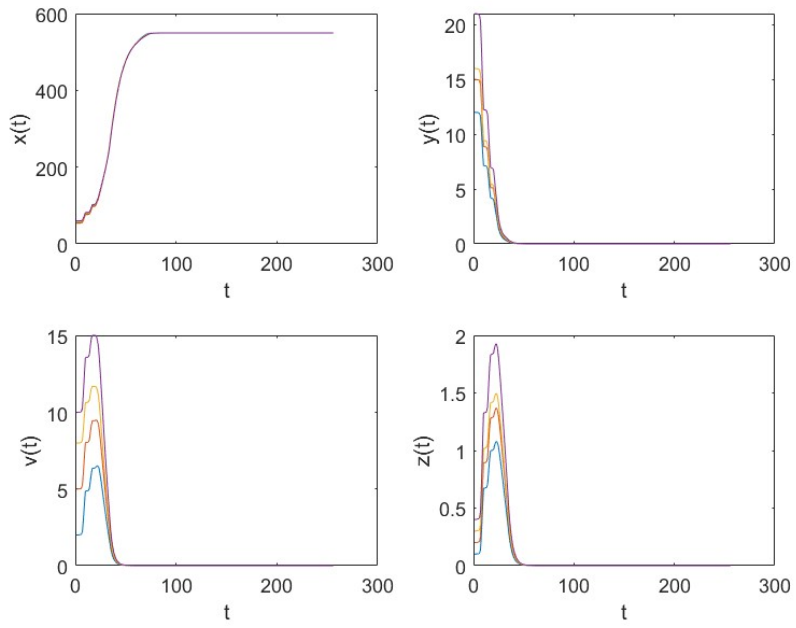

FIGURE 1. Solutions $x(t)$, $y(t)$, $v(t)$, and $z(t)$ of (1.4). Here the infection-free equilibrium E_0 of (1.4) is globally asymptotically stable.

infection level. In the case where $\mathcal{R}_0 > 1$, we may obtain an approximate value of the infection level from the globally stable infection equilibrium, and then change some parameters to drive $\mathcal{R}_0 < 1$ so that the infection can be eradicated ultimately.

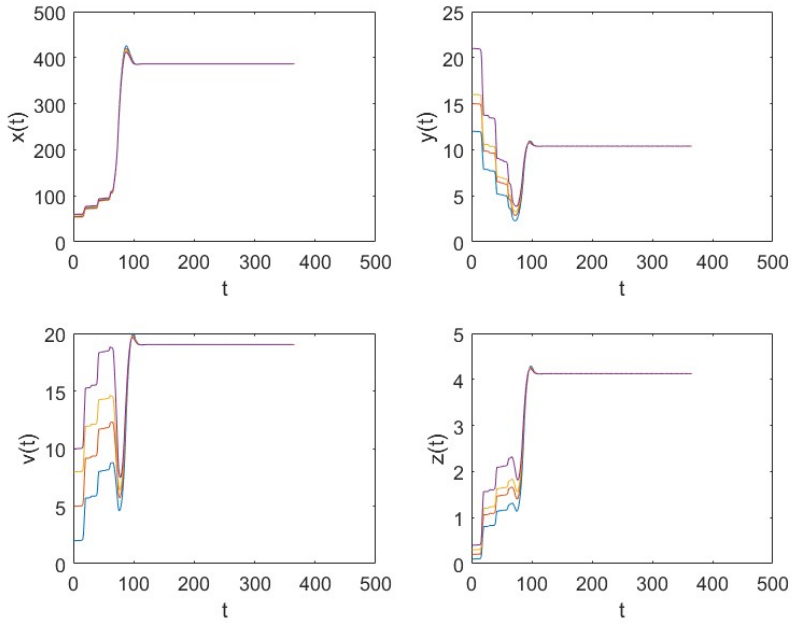

FIGURE 2. Solutions $x(t)$, $y(t)$, $v(t)$ and $z(t)$ of (1.4). Here the infection equilibrium E^* of (1.4) is globally asymptotically stable.

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REFERENCES

[1] S. Bonhoeffer, R. M. May, G. M. Shaw, M. A. Nowak; *Virus dynamics and drug therapy*, Proc. Natl. Acad. Sci. USA, 94 (1997) 6971-6976.

[2] F. A. T. Boshier, D. B. Reeves, E. R. Duke, et al.; *Substantial uneven proliferation of $CD4^+$ T cells during recovery from acute HIV infection is sufficient to explain the observed expanded clones in the HIV reservoir*. J. Virus. Erad. 8(4) (2022), 100091.

[3] Y. Deng, R. Xu; *Stability analysis of a dynamic model of HIV infection with CTL immune response and immune impairment*, Acta Math. Sci. 42(A) (2022) 1592-1600.

[4] P. van den Driessche, J. Watmough; *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Math. Biosci. 180 (2002) 29-48.

[5] J. K. Hale, S. M. Verduyn Lumel; *Introduction to Functional Differential Equations*, Springer, New York, 1993.

[6] Z. X. Hu, J. J. Zhang, H. Wang, F. Liao; *Dynamics analysis of a delayed viral infection model with logistic growth and immune impairment*, Appl. Math. Model. 38 (2014) 524-534.

[7] M. Li, K. Guo, W. Ma; *Uniform persistence and global attractivity in a delayed virus dynamic model with apoptosis and both virus-to-cell and cell-to-cell infections*. Mathematics, 10 (2022) 975.

[8] X. Jia, R. Xu; *Global dynamics of a delayed HTLV-I infection model with Beddington-DeAngelis incidence and immune impairment*, Chaos Solitons Fractals. 155 (2022) 111733.

[9] A. Korobeinikov; *Global properties of basic virus dynamics models*. Bull. Math. Biol. 66(4) (2004) 879-883.

[10] M. Y. Li, H. Shu; *Joint effects of mitosis and intracellular delay on viral dynamics: two-parameter bifurcation analysis*, J. Math. Biol. 64 (2012) 1005-1020.

[11] M. Y. Li, L. Wang; *Backward bifurcation in a mathematical model for HIV infection in vivo with anti-retroviral treatment*, Nonlinear Anal: Real World Appl. 17 (2014) 147-160.

[12] J. Z. Lin, R. Xu, X. H. Tian; *Threshold dynamics of an HIV-1 model with both viral and cellular, cell-mediated and humoral immune responses*, Math. Biosci. Eng. 16 (2019) 292-319.

[13] S. Marino, Ian B. Hogue, C. J. Ray, D. E. Kirschner; *A methodology for performing global uncertainty and sensitivity analysis in systems biology*, J. Theoret. Biol. 254 (2008) 178-196.

[14] M. A. Nowak, R. M. Anderson, M. C. Boerlijst, S. Bonhoeffer, R. M. May; *HIV-1 evolution and disease progression*, Science. 274 (1996) 1008-1011.

[15] M. A. Nowak, C. R. M. Bangham; *Population dynamics of immune response to persistent viruses*, Science. 272 (1996) 74-79.
[16] X. Pan, Y. Chen, H. Shu; *Rich dynamics in a delayed HTLV-I infection model: Stability switch, multiple stable cycles, and torus*, J. Math. Anal. Appl. 479 (2) (2019) 2214-2235.
[17] K. Qi, D. Q. Jiang, T. Hayat, A. Alsaedi; *The stationary distribution and extinction of a double thresholds HTLV-I infection model with nonlinear CTL immune response disturbed by white noise*, Int. J. Biomath. 12 (2019) 1950058.
[18] R. R. Regoes, D. Wodarz, M. A. Nowak; *Virus dynamics: the effect of target cell limitation and immune responses on virus evolution*, J. Theoret. Biol. 191 (1998) 451-462.
[19] G. P. Samanta; *Permanence and extinction of a nonautonomous HIV/AIDS epidemic model with distributed time delay*, Nonlinear Anal: Real World Appl. 12 (2011) 1163-1177.
[20] H. L. Smith; *Monotone dynamical systems: An introduction to the theory of competitive and cooperative systems*. Mathematical Surveys and Monographs, American Mathematical Society. Providence, RI, 1995.
[21] X. Song, A. U. Neumann; *Global stability and periodic solution of the viral dynamics*, J. Math. Anal. Appl. 329 (2007) 281-297.
[22] L. W. Wang, Z. J. Liu, Y. Li, D. Xu; *Complete dynamical analysis for a nonlinear HTLV-I infection model with distributed delay, CTL response and immune impairment*, Discrete Contin. Dyn. Syst. Ser. B. 25 (2020) 917-933.
[23] S. L. Wang, X. Y. Song, Z. H. Ge; *Dynamics analysis of a delayed viral infection model with immune impairment*, Appl. Math. Model. 35 (2011) 4877-4885.
[24] Y. Wang, M. Lu, J. Liu; *Global stability of a delayed virus model with latent infection and Beddington-DeAngelis infection function*, Appl. math. letters, 107 (2020) 106463.
[25] R. Xu; *Global stability of an HIV-1 infection model with saturation infection and intracellular delay*. J. Math. Anal. Appl. 375 (2011) 75-81.
[26] X. Zhou, L. Zhang, T. Zheng, H. L. Li, Z. Teng; *Global stability for a delayed HIV reactivation model with latent infection and Beddington-DeAngelis incidence*, Appl. Math. Letters, 117 (2021) 107047.

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