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Stability Properties and Hopf Bifurcation of a Delayed HIV Dynamics Model with Saturation Functional Response, Absorption Effect and Cure Rate

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Abstract. In this paper, stability properties of an HIV infection model with saturation functional response, logistic proliferation term of susceptible CD4$^+$T cells, cure rate of infected CD4$^+$T cell, virus absorption effect, intracellular delay, and maturation delay are investigated. According to our mathematical analysis, the basic reproduction number R_0 of the model completely determines its stability features. Using the characteristic equation of the model, we establish that the infection-free equilibrium point and the infected equilibrium point are locally asymptotically stable when $R_0 \leq 1$ and $R_0 > 1$, respectively. By means of appropriate Lyapunov functionals and LaSalle's invariance principle for delay models, if $R_0 \leq 1$, we study the global asymmetric stability of the infection-free equilibrium point of the model. When $R_0 > 1$, we establish the occurrence of Hopf bifurcations and determine conditions for the permanence of the model. Finally, numerical simulations are also presented to confirm the analytical results.

1. Introduction

The human immunodeficiency virus, also known as HIV, targets and weakens the immune system of the body and making it more challenging to fight off infections and diseases. HIV causes acquired immunodeficiency syndrome (AIDS) when it substantially compromises the human immune system [42]. Mathematical modeling is a promising approach to study the population dynamics between target cells and virus particles. Moreover, viral models are helpful in improving our knowledge of diseases and different medication therapy approaches for treating them. The mathematical proofs of stability of the basic virus dynamics model proposed by Bangham and Nowak in [23] has been established by Korobenikov in [18]. The HIV virus v, infected cells y,

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and healthy $CD4^+T$ cells x are all included in this model, which describes the immune system and its interaction with HIV. Based on the basic idea of HIV pathogenesis, some improvements or expansions have been taken into consideration in the recent literature ([25], [29], [40]).

The HIV dynamic models in ([6], [23]) and some references therein) took into account the bilinear infection incidence rate between free virus and uninfected $CD4^+T$ cells. However the true incidence rate is frequently nonlinear over the whole range of v and x, a nonlinear infection rate (sigmoidal function) was proposed by Roland [30] and Yumei [49]. Perelson et al. included intracellular latency in their presentation of the biology of the HIV life cycle in [26]. The term “intracellular delay" refers to the time interval between a virus’s entry into a target cell and the start of HIV virions production by the infected cells. Numerous modeling investigations were sparked by this study ([20], [24], [25]). Researchers in ([21], [46], [47]) and some references therein) have included a saturation infection rate in the HIV infection model with the intracellular delay and studied the stability properties of the models. In addition, some authors used the Beddington-DeAngelis functional response ([12], [20], [25], [29], [48]) which was proposed by Beddington [4] and DeAngelis [7] in place of the bilinear incidence rate and investigated the stability of the models. Li-Ming et al. investigated the HIV-1 infection model in [20] adding Beddington-DeAngelis functional response and intracellular time delay. The authors demonstrated the permanency and the global asymptotic stability of the equilibrium of this model. Biologically, when HIV enters the human body, it binds to $CD4^+T$ receptors on the surface of $CD4^+T$ cells and infects the cells. The virus then uses the cells’ machinery to replicate itself and spread to other $CD4^+T$ cells. This process may eventually result in a decrease in $CD4^+T$ cell counts, which can impair immunity and give rise to a variety of opportunistic infections and diseases. This process in known as absorption effect of HIV. Therefore, some authors have considered the HIV infection models together with absorption effect, intracellular delay and different nonlinear functional responses ([25], [29], [31]).

The virus has no metabolic processes of its own and cannot reproduce without a host cell. Generally, viruses go through different stages in their life cycle, which include various processes such as attachment to host cells, entry into cells, replication, assembly and release from cells. But, viruses that are just released cannot attack $CD4^+T$ cells and require some maturation time. Hence, maturity of a virus is a consideration of its ability to effectively infect and replicate in host cells. Therefore, we can increase the biological sense of the mathematical model by including maturation delay into the model. Hence, researches have applied the absorption effect and intracellular delay along with the maturation delay to their mathematical models and studied the stability of the models ([27], [31]). Rathnayaka et al. in [31] investigated the HIV-1 dynamics model by incorporating the Beddington-DeAngelis incidence rate, intracellular and maturation time delay into the model. The authors demonstrated the global asymptotic stability of the equilibrium points and permanency of this model.

In order to investigate the development of medication resistance, Rong et al. [34] developed a model that included anti-retroviral effects. Three groups of $CD4^+$T cells were taken into consideration by them: productively infected cells, uninfected cells, and infected cells in the eclipse phase. The idea is based on the finding that a virus may not fully reverse transcribe its RNA into DNA when it infects a $CD4^+$T cell that is at rest [50]. The reverse transcription can be completed if the cell is activated soon after infection. However, the un-integrated virus that is present in the resting cell may become progressively decay over time, and incomplete DNA transcripts are labile and degrade rapidly [51]. As a result, some infected cells that are at rest turn back into uninfected ones [8]. By using the above viral behavior concept, Prashant and Chandra [35], proposed a mathematical dynamics model of $CD4^+$T cells and HIV during the primary infection and analyzed the stability of infected state. Zhou et al. introduced an HIV infection model with a cure rate in [52], and they investigated the global asymptotic stability of all equilibrium points of the model. In [43], Kaifa et al. presented and enhanced the HBV mathematical model, which included a standard incidence function and cure rate. They also examined the stability of the model's equilibrium point. Sun and Min [36] modified the HIV-1 dynamic model with the cure rate proposed by Rong [34] by including a saturated infection rate, and analyzed the local and global asymmetric stability of the equilibrium of the model. Moreover, the authors performed numerical simulations to verify their theoretical calculations using clinical data from the Stanford University HIV Drug Resistance Database.

Some authors studied virus dynamics models that included more general nonlinear infection rates with delays ([13], [22], [33]). Recently, Alexander [33] studied a viral infection model with intracellular state-dependent delay and general incidence rate of the form $f(x, v)$. The author used the Lyapunov functionals technique to analyze the stability of the proposed model and it was further verified by using the Beddington–DeAngelis functional response and Crowley–Martin incidence rate. The authors in ([14], [53]) studied the global stabilities of virus dynamics models by incorporating the more general form incidence functions $f(y, v)x, f(x, y, v)v$ along with the cure rate of infected cells.

The authors of ([15], [37]), show that the generation rate of $CD4^+$T cells in the body slows down as the number of $CD4^+$T cell increases. Therefore, a further refinement of the basic viral model is considered by including the logistic growth term that characterizes the growth rate of the uninfected $CD4^+$T cell. Perelson et al. [28] improved the basic virus dynamics model by incorporating the logistic proliferation of the susceptible $CD4^+$T cells into the model in form $\gamma x(t)\left(1-\frac{x(t)}{X_{max}}\right)$, where γ represent the growth rate of healthy $CD4^+$T cells population and X_{max} represents the $x(t)$ population density at which the expansion of cells stops. Some researchers developed the basic model by incorporating the full logistic proliferation term for healthy $CD4^+$T cells ([2], [3], [5], [9]). In [1], Eric et al. studied a model of HCV with the saturation incident rate with intracellular delay and full Logistic proliferation term. The authors of the paper confirmed the global and local stability of the system and the occurrence of a Hopf bifurcation in the model. Eric

et al. [2], further developed the above mathematical model by adding the cure rate into the model and established the local and global stability of the system and the occurrence of a Hopf bifurcation in the model. Wang et al. [44], presented a delay HIV dynamics model with immune response by incorporating the logistic growth of target cells and they study local and global stability of the model and the occurrence of a Hopf bifurcation.

Inspired by the aforementioned research endeavors, we propose a following novel delayed HIV dynamics model with saturation functional response, absorption effect, cure rate and two time delays.

$$\begin{aligned}
\dot{x}(t) &= \lambda + \gamma x(t)\left(1 - \frac{x(t)}{X_{max}}\right) - \frac{\beta x(t)v(t)}{1+bv(t)} - dx(t) + \delta y(t),\\
\dot{y}(t) &= e^{-p\tau}\frac{\beta x(t-\tau)v(t-\tau)}{1+bv(t-\tau)} - (p+\delta)y(t),\\
\dot{v}(t) &= ke^{-u\sigma}y(t-\sigma) - uv(t) - \frac{\beta x(t)v(t)}{1+bv(t)}.
\end{aligned} \tag{1.1}$$

The concentration of susceptible host cells, infected host cells (which can form new viruses), and free virus are denoted by $x(t), y(t)$ and $v(t)$, and their decline rates are d, p and u respectively (naturally, $p \geq d$ ([18], [35]). Generate rate of the susceptible host cell is indicated by the parameter λ. During virus replication, free-virus and uninfected cells generate infected cells at a rate β. Non-cytolytic mechanisms may cure infected cells at a steady rate δ. New viral particles are produced by infected cells at a rate k ($k > \beta$ [18]). The incidence rate of infection is considered by the saturation infection rate $\frac{\beta x(t)v(t)}{1+bv(t)}$ for positive constant b. The intracellular time delay denoted by $\tau \geq 0$ and the surviving probability from $t-\tau$ to t is denoted by $e^{-p\tau}$. The maturity delay is denoted by $\sigma \geq 0$, and the surviving probability from $t-\sigma$ to t is denoted by a term $e^{-u\sigma}$. All parameters are taken as non-negative constants for biological relevance.

Consider $\xi = max\{\tau, \sigma\}$ and $C([-\xi, 0], \mathbb{R}^3_+])$ be the Banach space of continuous functions that map the interval $[-\xi, 0]$ to $\mathbb{R}^3_+$ with sup norm, where

$$\mathbb{R}^3_+ = \{(x(t), y(t), v(t)) \in \mathbb{R}^3 : x(t) \geq 0, y(t) \geq 0 \,\text{and}\, v(t) \geq 0\}, \tag{1.2}$$

Consider the following biologically plausible history of the host for model (1.1):

$$\begin{aligned}
x(\theta) = \psi_1(\theta), y(\theta) = \psi_2(\theta), v(\theta) = \psi_3(\theta), \text{ and}\\
\psi_i(\theta) \geq 0 \quad \text{for} \quad i = 1, 2, 3.
\end{aligned} \tag{1.3}$$

where $\theta \in [-\xi, 0]$ and $\psi = (\psi_1(\theta), \psi_2(\theta), \psi_3(\theta))^T \in C$.

The remaining sections of manuscript are arranged as follows. In Section 2, we discuss the limitations of the solution of model (1.1) and the positivity of the solution. The threshold parameter R_0 (i.e $R_0(\tau, \sigma)$) of model (1.1) was derived, and the presence of the equilibrium point in relation to the $R_0(\tau, \sigma)$ was examined in Section 3. We examined the local asymptotic stability and global asymptotic stability of the infection-free and infected equilibriums in Section 4. Additionally, we determined the circumstances under which the model's Hopf bifurcation would occur. In Section 5,

we examine the permanence of the model. To corroborate our analytical results, we have included some numerical simulations in Section 6. The work is concluded with a brief remarks in Section 7.

2. Boundedness and Positivity of Solutions

We know that the initial values of the variables in the model are non-negative. Consequently, in this section we show that every solution of model (1.1) is ultimately non-negative and bounded.

Theorem 2.1. *Let $(x(t), y(t), v(t))$ be the solution of model (1.1) with initial condition (1.3), then $x(t)$, $y(t)$, and $v(t)$ are positive for all $t \geq 0$, where $x(0) > 0$, $y(0) \geq 0$, and $v(0) \geq 0$.*

Proof. From the second equation of model (1.1), we have

$$y(t) = y(0)e^{-(p+\delta)t} + \beta e^{-p\tau} \int_0^t \frac{e^{-(p+\delta)(t-\eta)} x(\eta-\tau) v(\eta-\tau)}{1 + bv(\eta-\tau)} d\eta. \tag{2.1}$$

Let $t \in [0, \xi]$, then we have $\eta - \xi \in [-\xi, 0]$ for all $\eta \in [0, \xi]$. Then by (1.3) and (2.1), we have $y(t) \geq 0$ for $t \in [0, \xi]$. Next we need to prove that $x(t)$ is positive for $t \in [0, \xi]$. If it is not true, let $t_1 \leq \xi$ be the initial value of t satisfying $x(t) > 0$ such that $t \in [0, t_1)$ and $x(t_1) = 0$. Then, from the first and third equations of model (1.1), we get

$$\begin{aligned} \dot{x}(t) &= \lambda + \delta y(t) > 0, \text{ and} \\ \dot{v}(t) &= ke^{-u\sigma} y(t-\sigma) - uv(t). \end{aligned} \tag{2.2}$$

Then, the first equation of (2.2), giving us contradiction, as it implies there exist some $\epsilon_1 \in [0, t_1)$ such that $x(t) < 0$ for $t \in (t_1 - \epsilon_1, t_1)$. This is contradiction with $x(t) > 0$ for $t \in [0, \xi]$, hence $x(t) > 0$ for any $t \in [0, \xi]$. From the second equation of (2.2), we obtain

$$v(t) = e^{-ut} v(0) + ke^{-u\sigma} \int_0^t e^{-u(t-\eta)} y(\eta - \sigma) d\eta. \tag{2.3}$$

Let $t \in [0, \xi]$. Then, we have $\eta - \xi \in [-\xi, 0]$ for all $\eta \in [0, \xi]$. Then from the initial condition (1.3) and (2.3), we have $v(t) \geq 0$ for $t \in [0, \xi]$. We may now reiterate this argument to demonstrate the positivity of $x(t), y(t)$, and $v(t)$ on the interval $[\xi, 2\xi]$ and then on the consecutive interval $[n\xi, (n+1)\xi]$ for $n \geq 2$. As a result, every solution in model (1.1) is positive. □

Theorem 2.2. *Any positive solution $(x(t), y(t), v(t))$ of model (1.1) with the initial condition (1.3), is bounded by a positive constant M for all $t \geq 0$. Further*

$$\Gamma = \{(x(t), y(t), v(t)) \in \mathbb{R}^3_+ : x(t), y(t), v(t) \leq M, \text{for } t \geq 0\}, \tag{2.4}$$

is the positive invariant set of (1.1).

Proof. For each non-negative solution $(x(t), y(t), v(t))$ of (1.1) with condition (1.3), define a functional as

$$h_1(t) = x(t) + y(t) + \beta \int_{t-\tau}^t \frac{e^{-p(t-\eta)} x(\eta) v(\eta)}{1 + bv(\eta)} d\eta. \tag{2.5}$$

Taking the derivative of $h_1(t)$ along (1.1) and simplifying, we have

$$\frac{dh_1(t)}{dt} \leq \lambda + \frac{\gamma X_{max}}{4} - dx(t) - py(t) - \beta p \int_{t-\tau}^{t} \frac{e^{-p(t-\eta)}x(\eta)v(\eta)}{1+bv(\eta)}d\eta.$$

Then, from equation (2.5), we have

$$\frac{dh_1(t)}{dt} \leq \lambda + \frac{\gamma X_{max}}{4} - qh_1(t), \text{ where } q_1 = min\{d, p\}. \tag{2.6}$$

Hence, $\limsup_{t\to+\infty} h(t) \leq \frac{4\lambda+\gamma X_{max}}{4q_1} = M_0$. Now, we define

$$h_2(t) = y(t) + v(t) + \beta \int_{t-\tau}^{t} \frac{e^{-p(t-\eta)}x(\eta)v(\eta)}{1+bv(\eta)}d\eta + k\int_{t-\sigma}^{t} e^{-u(t-\eta)}y(\eta)d\eta. \tag{2.7}$$

Taking the derivative of $h_2(t)$ along (1.1) and simplifying, we get

$$h_2(t) \leq ky(t) - py(t) - uv(t) - p\beta \int_{t-\tau}^{t} \frac{e^{-p(t-\eta)}x(\eta)v(\eta)}{1+bv(\eta)}d\eta - ku\int_{t-\sigma}^{t} e^{-u(t-\eta)}y(\eta)d\eta.$$

Then, from equation (2.7), we have

$$\frac{dh_2(t)}{dt} \leq ky(t) - q_2h_2(t), \text{ where } q_2 = min\{u, p\}. \tag{2.8}$$

Then, we can obtain $\limsup_{t\to+\infty} h_2(t) \leq \frac{kM_0}{q_2}$. Let $M = max\{M_0, \frac{kM_0}{q_2}\}$. Hence, the solutions $(x(t), y(t), v(t))$ of (1.1) are uniformly bounded. Therefore, Γ is a positive invariant set and solutions of the model are attracted to a subset of Γ. □

3. Equilibrium Points and Reproduction Number

Biology requires that the body cannot contain a negative number of uninfected cells in the absence of virus, this just easy to show that the infection-free equilibrium of model (1.1) is $E_{IF}(x_0, y_0, v_0) \equiv (x_0, 0, 0)$, where

$$x_0 = \frac{\gamma - d + \sqrt{(\gamma-d)^2 + 4\lambda\gamma X_{max}^{-1}}}{2\gamma X_{max}^{-1}}. \tag{3.1}$$

It is obvious that population needs to be reduced if it ever reaches X_{max}. Hence, we can enforce the constraint $dX_{max} > \lambda$. Then, from equation (3.1), we get that $x_0 \leq X_{max}$.

By applying the next generation matrix method [41], we can determine the basic reproduction number R_0 of model (1.1), which is denoted by

$$R_0(\tau, \sigma) = \frac{k\beta x_0 e^{-p\tau - u\sigma}}{(p+\delta)(u+\beta x_0)}, \tag{3.2}$$

which is useful us to determine whether or not viruses are cleared over time. If $R_0(\tau,\sigma) > 1$, we can show that the infected equilibrium of model (1.1) is $E_{IE} = (x_1, y_1, v_1)$, where

$$x_1 = \frac{X_{max}}{2\gamma}\left[A_1 + \sqrt{A_1^2 + B_1}\right],\ y_1 = \frac{\beta x_0 u v_1 e^{-p\tau}}{u(p+\delta)R_0(\tau,\sigma) + (R_0(\tau,\sigma)-1)(p+\delta)\beta x_0},$$
$$v_1 = \frac{g(x_1)[u(p+\delta)R_0(\tau,\sigma) + \beta x_0(R_0(\tau,\sigma)-1)(p+\delta)]}{u\beta x_0[p+\delta(1-e^{-p\tau})]},$$

where

$$g(x) = \lambda + \gamma x\left(1 - \frac{x}{X_{max}}\right) - dx, \qquad A_1 = (\gamma - d) - \frac{[p + (1-e^{-p\tau})\delta]\beta}{b(p+\delta)}, \quad \text{and}$$
$$B_1 = \frac{4\gamma}{X_{max}}\left[\frac{u\beta x_0[p+(1-e^{-p\tau})\delta]}{b[u(p+\delta)R_0(\tau,\sigma) + \beta x_0(R_0(\tau,\sigma)-1)(p+\delta)]} + \lambda\right].$$

4. Stability Analysis

In this section, we analyze the local and global stability of E_{IF} and E_{IE} using the Routh Hurwitz criterion, the appropriate Lyapunov functionals, and LaSalle's invariance principle.

4.1. **Local stability of the infection-free equilibrium.**

Theorem 4.1. *If $R_0(\tau,\sigma) < 1$, the infection-free equilibrium E_{IF} is locally asymptotically stable. If $R_0(\tau,\sigma) > 1$, E_{IF} is unstable, and if $R_0(\tau,\sigma) = 1$, E_{IF} is linearly stable.*

Proof. At the infection-free equilibrium state, the characteristic equation of model (1.1) can be obtained as follows.

$$\left(s + d - \gamma + \frac{2\gamma x_0}{X_{max}}\right)\Big(s^2 + (u + \beta x_0 + p + \delta)s + (p+\delta)(u+\beta x_0)$$
$$-\beta k x_0 e^{-u\sigma - s\sigma - p\tau - s\tau}\Big) = 0. \tag{4.1}$$

Then, from the first factor of equation (4.1), we have $s = \gamma - d - \frac{2\gamma x_0}{X_{max}} = -\left(\frac{\gamma x_0}{X_{max}} + \frac{\lambda}{x_0}\right)$, is a negative root and the other roots of (4.1) can be obtained by the following lateral polynomial equation.

$$s^2 + (u + \beta x_0 + p + \delta)s + (p+\delta)(u+\beta x_0) - \beta k x_0 e^{-u\sigma - s\sigma - p\tau - s\tau} = 0. \tag{4.2}$$

Then, equation (4.2) can be simplified as

$$s^2 + (u + \beta x_0 + p + \delta)s + (p+\delta)(u+\beta x_0)(1 - R_0(\tau,\sigma)e^{-s\sigma - s\tau}) = 0. \tag{4.3}$$

Hence, it is clear that, if $R_0(\tau,\sigma) \neq 1$, $s = 0$ is not a solution of (4.2) for any $\tau, \sigma \geq 0$.

When $\tau = 0$ and $\sigma = 0$, the equation (4.3) becomes

$$s^2 + (u + \beta x_0 + p + \delta)s + (p+\delta)(u+\beta x_0)(1 - R_0(0,0)) = 0. \tag{4.4}$$

It is obvious that, if $R_0(0,0) < 1$, $(u + \beta x_0 + p + \delta) > 0$ and $(p+\delta)(u+\beta x_0)(1 - R_0(0,0)) > 0$. Hence, by Routh-Hurwitz criterion, all roots of (4.4) have negative real parts. This implies that, if $R_0(0,0) < 1$, E_{IF} is locally asymptotically stable when $\tau = 0$ and $\sigma = 0$.

Now suppose $\tau, \sigma > 0$ and $s = i\omega_1$ $(\omega_1 > 0)$ be a solution of equation (4.2). Then, by substituting $s = i\omega_1$ into (4.2) and separating the imaginary and real components, we have

$$\begin{aligned} -\omega_1^2 + (p+\delta)(u+\beta x_0) &= kx_0\beta e^{-u\sigma - p\tau}\cos\omega_1(\tau+\sigma), \quad (4.5)\\ \omega_1(u+p+\delta+\beta x_0) &= -kx_0\beta e^{-u\sigma-p\tau}\sin\omega_1(\tau+\sigma). \quad (4.6)\end{aligned}$$

By squaring and adding (4.5) and (4.6), we obtain

$$\omega_1^4 + \left[(p+\delta)^2 + (u+\beta x_0)^2\right]\omega_1^2 + (p+\delta)^2(u+\beta x_0)^2 - (kx_0\beta e^{-u\sigma-p\tau})^2 = 0. \quad (4.7)$$

Equation (4.7) can be further simplified as

$$\omega_1^4 + \left[(p+\delta)^2 + (u+\beta x_0)^2\right]\omega_1^2 + (p+\delta)^2(u+\beta x_0)^2(1-R_0^2(\tau,\sigma)) = 0. \quad (4.8)$$

Let $z = \omega_1^2$, $A_2 = (p+\delta)^2 + (u+\beta x_0)^2$ and $B_2 = (p+\delta)^2(u+\beta x_0)^2(1-R_0^2(\tau,\sigma))$. Then equation (4.8) becomes

$$z^2 + A_2 z + B_2 = 0. \quad (4.9)$$

It is clear that $A_2 > 0$ and $B_2 > 0$ if $R_0(\tau,\sigma) < 1$. Hence, the roots of equation (4.9) are negative. This implies that equation (4.2) cannot have roots such that $s = i\omega_1(\omega_1 > 0)$ for all $\tau, \sigma \geq 0$. Therefore, if $R_0(\tau,\sigma) < 1$, all the roots of (4.1) have negative real parts. Thus, using the Theorem 3.4.1 in [19], E_{IF} is locally asymptotically stable.

Further, if $R_0(\tau,\sigma) > 1$, we assume that the left-hands side of (4.3) is

$$f_1(s,\sigma,\tau) = s^2 + (u+\beta x_0+p+\delta)s + (p+\delta)(u+\beta x_0)(1-R_0(\tau,\sigma)e^{-s\sigma-s\tau}). \quad (4.10)$$

Then, for $R_0(\tau,\sigma) > 1$, we obtain

$$\begin{aligned} f_1(0,\sigma,\tau) &= (p+\delta)(u+\beta x_0)(1-R_0(\tau,\sigma)) < 0 \quad \text{and}\\ \lim_{s\to+\infty} f_1(s,\sigma,\tau) &\to +\infty.\end{aligned}$$

Hence, it is clear that, if $R_0(\tau,\sigma) > 1$, $f_1(s,\sigma,\tau) = 0$ has at least one positive root. Therefore, when $R_0(\tau,\sigma) > 1$, E_{IF} is unstable.

When $R_0(\tau,\sigma) = 1$, equation (4.3) becomes

$$s^2 + (u+\beta x_0+p+\delta)s + (p+\delta)(u+\beta x_0)(1-e^{-s\sigma-s\tau}) = 0. \quad (4.11)$$

It is clear, $s = 0$ is a simple root of (4.11) and we can show that any other root of (4.11) is negative. Supposed that $s = q_1 + iq_2$ satisfy (4.11) for any $q_1, q_2 > 0$ and $\tau, \sigma > 0$. Then, substituting this root into (4.11) and separating its real and imaginary parts, we obtain

$$\begin{aligned} q_1^2 - q_2^2 + q_1(u+p+\delta+\beta x_0) + (p+\delta)(u+\beta x_0)&\\ = (p+\delta)(u+\beta x_0)e^{-q_1(\sigma+\tau)}\cos q_2(\sigma+\tau),&\\ 2q_1q_2 + q_2(u+p+\delta+\beta x_0)&\\ = -(p+\delta)(u+\beta x_0)e^{-q_1(\sigma+\tau)}\sin q_2(\sigma+\tau).& \end{aligned} \quad (4.12)$$

By squaring the first and second equation of (4.12), we can obtain the following inequality

$$\begin{aligned}[q_1^2 - q_2^2 + q_1(u+p+\delta+\beta x_0) + (p+\delta)(u+\beta x_0)]^2 \\ +[2q_1q_2 + q_2(u+p+\delta+\beta x_0)]^2 \leq [(p+\delta)(u+\beta x_0)]^2.\end{aligned} \tag{4.13}$$

It is clear that inequality (4.13) is never satisfied and leads to a contradiction. This implies that the any root of (4.11) has negative real part except s = 0: □

4.2. **Global stability of the infection-free equilibrium.** Here, we employ the analytical technique outlined in ([10], [11]) to demonstrate the global stability of the E_{IF} of model (1.1) using the relevant Lyapunov functional and LaSalle's invariant principle.

Define

$$G = \left\{\psi = (\psi_1, \psi_2, \psi_3)^T \in C([-\xi, 0], \mathbb{R}^3_+) \,:\, x_0 \geq \psi_1 \geq 0\right\} \subset C^+ := C([-\xi, 0], \mathbb{R}^3_+).$$

Theorem 4.2. *If $R_0(\tau, \sigma) \leq 1$, the infection-free equilibrium E_{IF} is globally asymptotically stable in C^+ for any $\tau, \sigma \geq 0$.*

Proof. If $R_0(\tau, \sigma) \leq 1$, from Theorem 4.1, we know that E_{IF} is locally asymptotically stable. Therefore, we only need to prove that E_{IF} of C^+ is globally attractive when $R_0(\tau, \sigma) \leq 1$. We prove Theorem 4.2 under the following two cases.

Case I: Let $ke^{-p\tau-u\sigma} > p + \delta$. To investigate the global stability of E_{IF} in G, we define the following Liapunov functional,

$$L(\psi) = \psi_1(0) - x_0 - x_0 \ln \frac{\psi_1(0)}{x_0} + k_1\psi_2(0) + k_2\psi_3(0) + k_2ke^{-u\sigma}I_1 + k_1\beta e^{-p\tau}J_1, \tag{4.14}$$

where

$$\begin{aligned} I_1 &= \int_{-\sigma}^{0} \psi_2(\theta)d\theta, \quad J_1 = \int_{-\tau}^{0} \frac{\psi_1(\theta)\psi_3(\theta)}{1 + b\psi_3(\theta)}d\theta, \\ k_1 &= \frac{ke^{-u\sigma}}{ke^{-u\sigma-p\tau} - (p+\delta)}, \quad \text{and} \quad k_2 = \frac{p+\delta}{ke^{-u\sigma-p\tau} - (p+\delta)}. \end{aligned}$$

Let $z_t = z_t(\psi) = (x_t, y_t, v_t)^T$ be the solution of model (1.1) with any $\psi \in C^+$, which is defined as $z_t(\theta) = z(t+\theta), \theta \in [-\xi, 0]$. From Theorem 2.2, it is easy to see that ψ is bounded and it follows $\omega(\psi) \subset G$ which is compact, where $\omega(\phi)$ is the ω-limit set of ϕ for model (1.1). Therefore, for any $\phi \in \omega(\psi)$, we have

$$\begin{aligned} w(\phi) &= \left(\frac{\lambda}{x_0\phi_1(0)} + \frac{\gamma}{X_{max}}, \frac{\delta}{\phi_1(0)}(x_0 - \phi_1(0)), \frac{(p+\delta)(u+\beta x_0)(1-R_0(\tau,\sigma))}{ke^{-u\sigma-p\tau} - (p+\delta)}\right) \\ &\geq \left(\frac{\lambda}{x_0^2} + \frac{\gamma}{X_{max}}, \frac{\alpha\delta}{x_0}, \frac{(p+\delta)(u+\beta x_0)(1-R_0(\tau,\sigma))}{ke^{-u\sigma-p\tau} - (p+\delta)}\right) \equiv w_0. \end{aligned}$$

Hence, if $R_0(\tau, \sigma) \leq 1$ and $\alpha \in G$, then $w_0 \geq 0$.
Let $h(\phi) = \left((x_0 - \phi_1(0))^2, \phi_2(0), \phi_3(0)\right)^T$. Then $w_0h(\phi) = 0$, implies that $\phi(0) = E_{IF}$.

Taking the derivative of L along the solution z_t of model (1.1) for $t \geq \tau$ and $t \geq \sigma$, we have

$$\dot{L}(z_t) = \left(1 - \frac{x_0}{x(t)}\right)[g(x(t)) - g(x_0)] + (x(t) - x_0)\frac{\delta y(t)}{x(t)} + \left(\frac{\beta x_0}{1 + bv(t)} - k_2 u\right)v(t), \tag{4.15}$$

where $g(x_0) = 0$. Then equation (4.15), can be simplify as

$$\begin{aligned}
\dot{L}(z_t) &= -\left(\frac{\gamma x_0}{X_{max}} + d - \gamma\right)\frac{(x(t) - x_0)^2}{x(t)} - \frac{\gamma(x(t) - x_0)^2}{X_{max}} - \left(\frac{\delta x_0}{x(t)} - \delta\right)y(t) \\
&\qquad + \left(\frac{\beta x_0}{1 + bv(t)} - k_2 u\right)v(t), \\
&= -\left(\frac{\lambda}{x_0 x(t)} + \frac{a}{X_{max}}\right)(x(t) - x_0)^2 - \left(\frac{\delta x_0}{x(t)} - \delta\right)y(t) \\
&\qquad + \left(\frac{\beta x_0}{1 + bv(t)} - k_2 u\right)v(t),
\end{aligned}$$

$$\begin{aligned}
\dot{L}(z_t) &\leq -\left(\frac{\lambda}{x_0 x(t)} + \frac{a}{X_{max}}\right)(x(t) - x_0)^2 - \left(\frac{\delta x_0}{x(t)} - \delta\right)y(t) \\
&\qquad - \frac{(p + \delta)(u + \beta x_0)(1 - R_0(\tau, \sigma))}{ke^{-u\sigma - p\tau} - (p + \delta)}v(t), \\
&= -w(z_t)h(z_t).
\end{aligned}$$

Therefore, according to Theorem 3.1 in [10], E_{IF} is globally attractive in C^+.

Case II: When $ke^{-p\tau - u\sigma} \leq p + \delta$, we define a Lyapunov functional as

$$L_2(t) = e^{p\tau}y(t) + v(t) + ke^{-u\sigma}\int_{-\sigma}^{0} y(t + \theta)d\theta + \beta\int_{-\tau}^{0}\frac{x(t + \theta)v(t + \theta)}{1 + \alpha v(t + \theta)}d\theta. \tag{4.16}$$

Then, for $t \geq 0$, taking the derivative of $L_2(t)$ through the solutions of model (1.1), equation (4.16) can be derived as

$$\dot{L}_2(t) = e^{p\tau}\left(ke^{-u\sigma - p\tau} - (p + \delta)\right) - uv(t).$$

It is clear that, if $ke^{-p\tau - u\sigma} \leq p + \delta$, for all $t \geq 0$, $\dot{L}_2(t) \leq 0$. This implies that E_{IF} is stable. The equality is valid if and only if $y = v = 0$, for all $t \geq 0$. Next we show that E_{IF} is globally attractive. We define the subset

$$E = \left\{(\psi_1, \psi_2, \psi_3)^T \in C^+ \mid \dot{L}_2(\psi_1, \psi_2, \psi_3) = 0\right\}.$$

Assume that M is the largest invariant subset of E. Then for any $(\psi_1, \psi_2, \psi_3)^T \in M$, consider $(x_t, y_t, v_t)^T$ be the solution of (1.1) with condition (1.3), where

$$x_t = x(t + \theta),\ y_t = y(t + \theta),\ v_t = v(t + \theta), \text{ for } -\xi \leq \theta \leq 0, \text{ and } t \geq 0,\ \xi = max\{\tau, \sigma\}.$$

By the invariance of the subset M, for all $t \in \mathbb{R}$, $(x_t, y_t, v_t)^T \in M \subset E$. Hence, for any $t \geq 0$, $y(t) = 0$ and $v(t) = 0$. By the invariance of the subset M, it further implies that $y_t = \psi_2 = 0$ and $v_t = \psi_3 = 0$ for any $t \in \mathbb{R}$. Therefore, from the first equation of (1.1) and the invariance of the subset M, we obtain, for any $t \geq 0$, $x(t) = x_0$. This shows that $M = \{E_0\}$. Hence, from Lasalle's invariance

principle, E_{IF} is globally asymptotically stable when $R_0(\tau,\sigma) \leq 1$. The proof is completed. Next we study the stability of E_{IE} of model (1.1). □

4.3. **Stability of the infected equilibrium and bifurcation analysis.** In this section, we examine the effect of time delay for the stability of E_{IE} and bifurcation of model (1.1). At E_{IE}, the characteristic equation of model (1.1) can be represented as

$$\begin{aligned}\left(s+d-\gamma+\frac{2\gamma x_1}{X_{max}}+\frac{\beta v_1}{1+bv_1}\right)&\left((s+p+\delta)\left(s+u+\frac{\beta x_1}{(1+bv_1)^2}\right)\right.\\ &\left.-\frac{k\beta x_1 e^{-u\sigma-s\sigma-p\tau-s\tau}}{(1+bv_1)^2}\right)\\ &+\delta\left(\frac{-\beta v_1 e^{-p\tau-s\tau}}{1+bv_1}\left(s+u+\frac{\beta x_1}{(1+bv_1)^2}\right)+\frac{\beta^2 x_1 v_1 e^{-p\tau-s\tau}}{(1+bv_1)^3}\right)\\ &+\frac{\beta x_1}{(1+bv_1)^2}\left(\frac{k\beta v_1 e^{-p\tau-s\tau-u\sigma-s\sigma}}{1+bv_1}-\frac{\beta v_1}{1+bv_1}(s+p+\delta)\right)=0. \end{aligned} \tag{4.17}$$

Let $h = d-\gamma+\dfrac{\gamma x_1}{X_{max}}$. Then, equation (4.17) can be simplified as the following form.

$$f_2(s,\tau,\sigma) = s^3+a_2s^2+a_1s+a_0+(b_1s+b_0)e^{-s\tau-s\sigma}+(c_1s+c_0)e^{-s\tau}=0, \tag{4.18}$$

where,

$$\begin{aligned}
a_2 &= p+\delta+u+\frac{\beta x_1}{(1+bv_1)^2}+h+\frac{\gamma x_1}{X_{max}}+\frac{\beta v_1}{1+bv_1},\\
a_1 &= (p+\delta)\left(u+\frac{\beta x_1}{(1+bv_1)^2}\right)+\left(h+\frac{\gamma x_1}{X_{max}}+\frac{\beta v_1}{1+bv_1}\right)(p+\delta+u)\\
&\quad+\frac{\beta x_1}{(1+bv_1)^2}\left(h+\frac{\gamma x_1}{X_{max}}\right),\\
a_0 &= u(p+\delta)\left(h+\frac{\gamma x_1}{X_{max}}+\frac{\beta v_1}{1+bv_1}\right)+(p+\delta)\left(h+\frac{\gamma x_1}{X_{max}}\right)\frac{\beta x_1}{(1+bv_1)^2},\\
b_1 &= -(p+\delta)\left(\frac{u}{1+bv_1}+\frac{\beta x_1}{(1+bv_1)^2}\right),\\
b_0 &= -\left(h+\frac{\gamma x_1}{X_{max}}\right)(p+\delta)\left(\frac{u}{1+bv_1}+\frac{\beta x_1}{(1+bv_1)^2}\right),\\
c_1 &= \frac{-\delta\beta v_1 e^{-p\tau}}{1+bv_1} \quad \text{and} \quad c_0 = \frac{-\delta\beta v_1 u e^{-p\tau}}{1+bv_1}.
\end{aligned}$$

Case I: When $\tau=\sigma=0$, equation (4.18) is reduced as

$$f_2(s,0,0) = s^3+a_2s^2+A_3s+B_3=0, \tag{4.19}$$

and if $h \geq 0$ (equivalently $d-\gamma(1-\frac{x_1}{X_{max}}) \geq 0$), we get $a_2>0$, and

$$\begin{aligned}A_3 = \left(h+\frac{\gamma x_1}{X_{max}}\right)&\left(p+\delta+u+\frac{\beta x_1}{(1+bv_1)^2}\right)+(p+u)\frac{\beta v_1}{1+bv_1}\\ &+(\delta+p)\frac{ubv_1}{1+bv_1}>0,\end{aligned}$$

$$B_3 = \frac{p\beta uv_1}{1+bv_1} + u(p+\delta)\left(h + \frac{\gamma x_1}{X_{max}}\right)\frac{bv_1}{1+bv_1} > 0,$$

$$C_3 = \left(p+\delta+h+\frac{\beta x_1}{(1+bv_1)^2} + \frac{\beta v_1}{1+bv_1} + \frac{\gamma x_1}{X_{max}}\right)\times \left[\frac{(p+u)\beta v_1}{1+bv_1} + \left(h+\frac{\gamma x_1}{X_{max}}\right)\left(p+\delta+u+\frac{\beta x_1}{(1+bv_1)^2}\right)\right] + \left(p+\delta+u+\frac{\beta x_1}{(1+bv_1)^2}\right)\left[\frac{(p+\delta)ubv_1}{1+bv_1} + u\left(h+\frac{\gamma x_1}{X_{max}}\right)\right] + \frac{\beta uv_1}{1+bv_1}\left(u+\frac{(p+\delta)bv_1}{1+bv_1}\right)$$

where, $A_3 = a_1 + b_1 + c_1$, $B_3 = a_0 + b_0 + c_0$, and $C_3 = a_2A_3 - B_3 > 0$. According to the Routh-Hurwitz criterion, it follows that any root of (4.19) has negative real parts. Hence, E_{IE} of model (1.1) is locally asymptotically stable. Accordingly, the above result can be stated as following theorem.

Theorem 4.3. *If $R_0(0,0) > 1$ and $d - \gamma(1 - \frac{x_1}{X_{max}}) \geq 0$, the infected equilibrium E_{IE} of model (1.1) is locally asymptotically stable for $\tau = \sigma = 0$.*

Case II: When $\tau > 0$ and $\sigma = 0$, $R_0(\tau, 0) > 1$ implies that $\tau < \hat{\tau}_1$, where

$$\hat{\tau}_1 = \frac{1}{p}\ln\frac{\beta k x_0}{(p+\delta)(u+\beta x_0)}. \tag{4.20}$$

In overword, the values of τ need to be in $[0, \hat{\tau}_1)$ to satisfy $R_0(\tau, 0) > 1$.
Further, if $\tau > 0$ and $\sigma = 0$, equation (4.18) can be written as

$$f_3(s,\tau,0) = s^3 + a_2s^2 + a_1s + a_0 + [(b_1+c_1)s + (b_0+c_0)]\,e^{-s\tau} = 0. \tag{4.21}$$

We will now investigate the possibility of equation (4.21) having purely imaginary roots $s = i\omega_2(\omega_2 > 0)$. By substituting $s = i\omega_2$ into (4.21) and separating the real and imaginary parts, we have

$$-\omega_2^3 + a_1\omega_2 = -\omega_2(b_1+c_1)\cos\omega_2\tau + (b_0+c_0)\sin\omega_2\tau, \tag{4.22}$$

$$-a_2\omega_2^2 + a_0 = -\omega_2(b_1+c_1)\sin\omega_2\tau - (b_0+c_0)\cos\omega_2\tau. \tag{4.23}$$

By squaring equations (4.22) and (4.23) and adding the resulting equations together, we obtain

$$\omega_2^6 + (a_2^2 - 2a_1)\omega_2^4 + (a_1^2 - 2a_0a_2 - (b_1+c_1)^2)\omega_2^2 + a_0^2 - (b_0+c_0)^2 = 0. \tag{4.24}$$

Then, from equation (4.24), we have

$$z_2^3 + (a_2^2 - 2a_1)z_2^2 + (a_1^2 - 2a_0a_2 - (b_1+c_1)^2)z_2 + a_0^2 - (b_0+c_0)^2 = 0, \tag{4.25}$$

where, $z_2 = \omega_2^2$. Hence, if $d - \gamma(1 - \frac{x_1}{X_{max}}) \geq 0$, by direct calculation, we have $a_2^2 - 2a_1 > 0$, $a_1^2 - 2a_0a_2 - (b_1+c_1)^2 > 0$, $a_0^2 - (b_0+c_0)^2 > 0$. Hence, equation (4.25) does not have positive roots for ω_2^2. This suggests that all roots of equation (4.24) have negative real parts. Thus, the infected equilibrium of model (1.1) is locally asymptotically stable from the theorem 3.4.1 in [19]. Thus, from the above theoretical calculation, we can state the following theorem.

Theorem 4.4. *Supposed* $R_0(\tau,0) > 1\,(i.e\,\tau < \hat{\tau}_1)$, *if* $d-\gamma(1-\frac{x_1}{X_{max}}) \geq 0$, *the infected equilibrium* $E_{IE}(x_1,y_1,v_1)$ *of model (1.1) is locally asymptotically stable for* $\tau > 0$ *and* $\sigma = 0$.

4.3.1. *Hopf Bifurcation from the infected equilibrium when maturation delay zero.* Theorem 4.4 stated that if some conditions are satisfied, E_{IE} of model (1.1) are locally asymptotically stable independently of delay term τ. If the conditions in Theorem 4.4 are not satisfied, the stability of E_{IE} depends on the delay term τ and the infectious equilibrium may become unstable as the delay changes, leading to oscillations. Consequently, τ can be treated as a bivariate parameter and the solutions of equation (4.25) as a function of intracellular delay.

Let $s(\tau) = \eta_2(\tau) + i\omega_2(\tau)$ be the solution of (4.25) and for some initial value of bifurcation parameter $\hat{\tau}_{2,0}$, we have $\eta_2(\hat{\tau}_{2,0}) = 0$ and $\omega_2(\hat{\tau}_{2,0}) = \hat{\omega}_0$ (To avoid loss of normality, assume $\hat{\omega}_0 > 0$).

Then from equations (4.22) and (4.23) we have

$$\hat{\tau}_{2,n} = \frac{1}{\hat{\omega}_0}\arccos\left(\frac{(b_1+c_1)\hat{\omega}_0^4 + (a_2(b_0+c_0) - a_1(b_1+c_1))\hat{\omega}_0^2 - a_0(b_0+c_0)}{(b_0+c_0)^2 + (b_1+c_1)^2\hat{\omega}_0^2}\right) + \frac{2n\pi}{\hat{\omega}_0},\ n = 0,1,\ldots \tag{4.26}$$

Then, to establish the Hopf bifurcation of system (1.1) at $\tau = \hat{\tau}_{2,0}$, we have to show that $\left.\frac{Re\,s(\tau)}{d\tau}\right|_{s=i\hat{\omega}_0} > 0$. Differentiating equation (4.21) with respect to τ, we obtain

$$\frac{ds(\tau)}{d\tau} = \frac{s[(b_1+c_1)s + (b_0+c_0)]e^{-s\tau}}{3s^3 + 2a_2s + a_1 + (b_1+c_1)e^{-s\tau} - \tau e^{-s\tau}[(b_1+c_1)s + (b_0+c_0)]}. \tag{4.27}$$

Equation (4.27) can be written as

$$\left(\frac{ds(\tau)}{d\tau}\right)^{-1} = \frac{3s^3 + 2a_2s^2 + a_1s + (b_1+c_1)se^{-s\tau}}{s^2e^{-s\tau}[(b_1+c_1)s + (b_0+c_0)]} - \frac{\tau}{s}. \tag{4.28}$$

Using equation (4.21), we can rewrite equation (4.28) as

$$\left(\frac{ds(\tau)}{d\tau}\right)^{-1} = \frac{2s^3 + a_2s^2 - a_0}{-s^2(s^3 + a_2s^2 + a_1s + a_0)} - \frac{b_0+c_0}{s^2[(b_1+c_1)s + (b_0+c_0)]} - \frac{\tau}{s}. \tag{4.29}$$

Thus, $sign\left\{\frac{dRe\,s(\tau)}{d\tau}\right\}_{s=i\hat{\omega}_0} = sign\left\{Re\left(\frac{ds(\tau)}{d\tau}\right)^{-1}\right\}_{s=i\hat{\omega}_0}$

$$= sign\left\{Re\left[\frac{2s^3 + a_2s^2 - a_0}{-s^2(s^3 + a_2s^2 + a_1s + a_0)}\right]_{s=i\hat{\omega}_0} - Re\left[\frac{b_0+c_0}{s^2[(b_1+c_1)s + (b_0+c_0)]}\right]_{s=i\hat{\omega}_0} - Re\left[\frac{\tau}{s}\right]_{s=i\hat{\omega}_0}\right\}.$$

$$= sign\left\{\frac{-2\hat{\omega}_0^3(a_1\hat{\omega}_0 - \hat{\omega}_0^3) - (a_0 + a_2\hat{\omega}_0^2)(a_0 - a_2\hat{\omega}_0^2)}{\hat{\omega}_0^2\left[(a_1\hat{\omega}_0 - \hat{\omega}_0^3)^2 + (a_0 - a_2\hat{\omega}_0^2)^2\right]} + \frac{(b_0 + c_0)^2}{\hat{\omega}_0^2\left[(b_1 + c_1)^2\hat{\omega}_0^2 + (b_0 + c_0)^2\right]}\right\}.$$

Using Equations (4.22) and (4.23), the above equation can be further simplified as

$$sign\left\{\frac{dRe\,s(\tau)}{d\tau}\right\}_{s=i\hat{\omega}_0} = sign\left\{\frac{2\hat{\omega}_0^6 + (a_2^2 - 2a_1)\hat{\omega}_0^4 - a_0^2 + (b_0 + c_0)^2}{\hat{\omega}_0^2\left[(a_1\hat{\omega}_0 - \hat{\omega}_0^3)^2 + (a_0 - a_2\hat{\omega}_0^2)^2\right]}\right\}. \tag{4.30}$$

Using equation (4.24), equation (4.30) can be further simplified as

$$sign\left\{\frac{dRe\,s(\tau)}{d\tau}\right\}_{s=i\hat{\omega}_0} = sign\left\{\frac{3\hat{\omega}_0^4 + 2(a_2^2 - 2a_1)\hat{\omega}_0^2 + (a_1^2 - 2a_0a_2 - (b_1 + c_1)^2)}{(a_1\hat{\omega}_0 - \hat{\omega}_0^3)^2 + (a_0 - a_2\hat{\omega}_0^2)^2}\right\}. \tag{4.31}$$

Assume that the left-hands side of equation (4.25) is

$$g(z) = z^3 + (a_2^2 - 2a_1)z^2 + (a_1^2 - 2a_0a_2 - (b_1 + c_1)^2)z + a_0^2 - (b_0 + c_0)^2. \tag{4.32}$$

Thus, we have

$$\frac{dg(z)}{dz} = 3z^2 + 2(a_2 - 2a_1)z + (a_1^2 - 2a_0a_2 - (b_1 + c_1)^2). \tag{4.33}$$

As $\hat{\omega}_0$ is the largest positive simple root of equation (4.24), according to the lemma 3.3.2 in [45], we have

$$\left.\frac{dg(z)}{dz}\right|_{z=\hat{\omega}_0^2} = 3\hat{\omega}_0^4 + 2(a_2^2 - 2a_1)\hat{\omega}_0^2 + a_1^2 - 2a_0a_2 - (b_1 + c_1)^2 > 0.$$

Therefore,

$$\left.\frac{Re\,s(\tau)}{d\tau}\right|_{s=i\hat{\omega}_0} = \frac{\frac{dg(\hat{\omega}_0^2)}{dz}}{(a_1\hat{\omega}_0 - \hat{\omega}_0^3)^2 + (a_0 - a_2\hat{\omega}_0^2)^2} > 0. \tag{4.34}$$

Thus, by the above theoretical calculation, we can state the following theorem.

Theorem 4.5. *Let $R_0(\tau, 0) > 1$. If $d - \tau(1 - \frac{x_1}{X_{max}}) < 0$ is satisfied, and the largest simple root of equation (4.24) is $\hat{\omega}_0$, then infected equilibrium $E_{IE}(x_1, y_1, v_1)$ of model (1.1) is asymptotically stable when $\tau < \hat{\tau}_{2,0}$ and unstable when $\tau > \hat{\tau}_{2,0}$, with a Hopf bifurcation occurring when $\tau = \hat{\tau}_{2,0}$.*

Case III: When $\sigma > 0$ and $\tau = 0$, $R_0(0, \sigma) > 1$, implies that $\sigma < \hat{\sigma}_1$, where

$$\hat{\sigma}_1 = \frac{1}{u}\ln\frac{\beta k x_0}{(p + \delta)(u + \beta x_0)}. \tag{4.35}$$

In other words, $\sigma \in [0, \hat{\sigma}_1)$ is satisfy that $R_0(0, \sigma) > 1$.

Further, if $\sigma > 0$ and $\tau = 0$, equation (4.18) can be written as

$$f_4(s, 0, \sigma) = s^3 + a_2s^2 + (a_1 + c_1)s + (a_0 + c_0) + (b_1s + b_0)e^{-s\sigma} = 0. \tag{4.36}$$

We will now investigate the possibility of equation (4.36) having purely imaginary roots $s = i\omega_3$. Substituting $s = i\omega_3$ into (4.36) and separate the imaginary and real parts, we get.

$$-\omega_3^3 + (a_1 + c_1)\omega_3 = -b_1\omega_3 \cos\omega_3\sigma + b_0 \sin\omega_3\sigma, \tag{4.37}$$

$$-a_2\omega_3^2 + (a_0 + c_0) = -b_1\omega_3 \sin\omega_3\sigma - b_0 \cos\omega_3\sigma. \tag{4.38}$$

By squaring equation (4.37) and (4.38) and adding the resulting equations together, we get

$$\omega_3^6 + (a_2^2 - 2(a_1 + c_1))\omega_3^4 + ((a_1 + c_1)^2 - 2a_2(a_0 + c_0) - b_1^2)\omega_3^2 + (a_0 + c_0)^2 - b_0^2 = 0 \tag{4.39}$$

Let $z_3 = \omega_3^2$, $A_4 = a_2^2 - 2(a_1 + c_1)$, $C_4 = C_{41}C_{42}$, where $C_{41} = a_0 + c_0 - b_0$ and $C_{42} = a_0 + c_0 + b_0$ and $H_2 : B_4 = (a_1 + c_1)^2 - 2a_2(a_0 + c_0) - b_1^2$. Then equation (4.39) can be written as

$$z_3^3 + A_4 z_3^2 + B_4 z_3 + C_4 = 0 \tag{4.40}$$

By the direct calculation, if $h \geq 0$, it is easy to show that $A_4 > 0$, $C_{41} > 0$, $C_{42} > 0$. Hence, equation (4.40) does not have positive real roots for ω_3^2. This suggests that all roots of equation (4.39) have negative real components, i.e., the infected equilibrium E_{IE} of model (1.1) is locally asymptotically stable. Therefore, the aforementioned result can be expressed using the following theorem.

Theorem 4.6. *Suppose $R_0(0, \sigma) > 1$ (i.e $\sigma < \hat{\sigma}_1$), if H_2 is true and $d - \gamma\left(1 - \frac{x_1}{X_{max}}\right) \geq 0$ hold, then the infected equilibrium $E_{IE}(x_1, y_1, v_1)$ of model (1.1) is locally asymptotically stable for $\sigma > 0$ and $\tau = 0$.*

4.3.2. *Hopf Bifurcation from the infected equilibrium when intracellular delay zero.* According to Theorem 4.6, if some conditions are satisfied, infected equilibrium E_{IE} of model (1.1) is locally asymptotically stable. However, if the criteria of Theorem 4.6 are not met and $C_4 < 0$ is preserved, the stability of E_{IE} depends on the delay σ and when delay changes, the infectious equilibrium may become unstable and leading to oscillation. Thus, σ can be treated as a bifurcation parameter and the solutions of (4.40) as a function of σ.

Let $s(\sigma) = \eta_3(\sigma) + i\omega_3(\sigma)$ be the solution of (4.40) and for some initial value of bifurcation parameter $\hat{\sigma}_{2,0}$, we have $\eta_3(\hat{\sigma}_{2,0}) = 0$ and $\omega_3(\hat{\sigma}_{2,0}) = \hat{\omega}_1$ (In order not to lose generality, we can assume $\hat{\omega}_1 > 0$).

Then, from equations (4.37) and (4.38), we get

$$\hat{\sigma}_{2,n} = \frac{1}{\hat{\omega}_1} \arccos\left(\frac{b_1\hat{\omega}_1^4 + (b_0a_2 - b_1(a_1 + c_1))\hat{\omega}_1^2 - b_0(a_0 + c_0)}{b_0^2 + b_1^2\hat{\omega}_1^2}\right) + \frac{2n\pi}{\hat{\omega}_1}, n = 1, 2, ... \tag{4.41}$$

Then, to establish the Hopf bifurcation of model (1.1) at $\sigma = \hat{\sigma}_{2,0}$, we have to show that $\left.\frac{Re\, s(\sigma)}{d\sigma}\right|_{s=i\hat{\omega}_1} > 0$. Differentiating equation (4.36) with respect to σ, we obtain

$$\left(\frac{ds(\sigma)}{d\sigma}\right)^{-1} = \frac{3s^2 + 2a_2s + (a_1 + c_1) + b_1e^{-s\sigma}}{s(b_1s + b_0)e^{-s\sigma}} - \frac{\sigma}{s}. \tag{4.42}$$

Using equation (4.36), equation (4.42) can be written as

$$\left(\frac{ds(\sigma)}{d\sigma}\right)^{-1} = \frac{2s^3 + a_2s^2 - (a_0 + c_0)}{-s^2[s^3 + a_2s^2 + (a_1 + c_1)s + (a_0 + c_0)]} - \frac{b_0}{s^2(b_1s + b_0)} - \frac{\sigma}{s}. \tag{4.43}$$

$$\begin{aligned}
\text{Thus, } sign\left\{\frac{dRe\,s(\sigma)}{d\sigma}\right\}_{s=i\hat{\omega}_1} &= sign\left\{Re\left(\frac{ds(\sigma)}{d\sigma}\right)^{-1}\right\}_{s=i\hat{\omega}_1} \\
&= sign\left\{Re\left[\frac{2s^3 + a_2s^2 - (a_0 + c_0)}{-s^2[s^3 + a_2s^2 + (a_1 + c_1)s + (a_0 + c_0)]}\right]_{s=i\hat{\omega}_1}\right. \\
&\qquad \left. -Re\left[\frac{b_0}{s^2(b_1s + b_0)}\right]_{s=i\hat{\omega}_1} - Re\left[\frac{\sigma}{s}\right]_{s=i\hat{\omega}_1}\right\}, \\
&= sign\left\{\frac{-2\hat{\omega}_1^3((a_1 + c_1)\hat{\omega}_1 - \hat{\omega}_1^3) - ((a_0 + c_0) - a_2\hat{\omega}_1^2)((a_0 + c_0) + a_2\hat{\omega}_1^2)}{\hat{\omega}_1^2\left[((a_1 + c_1)\hat{\omega}_1 - \hat{\omega}_1^3)^2 + ((a_0 + c_0) - a_2\hat{\omega}_1^2)^2\right]}\right. \\
&\qquad \left. + \frac{b_0^2}{\hat{\omega}_1^2(b_1^2\hat{\omega}_1^2 + b_0^2)}\right\}.
\end{aligned}$$

Using Equations (4.37) and (4.38), the last equation can be further simplified as

$$sign\left\{\frac{dRe\,s(\sigma)}{d\sigma}\right\}_{s=i\hat{\omega}_1} = sign\left\{\frac{2\hat{\omega}_1^6 + (a_2^2 - 2(a_1 + c_1))\hat{\omega}_1^4 - (a_0 + c_0)^2 + b_0^2}{\hat{\omega}_1^2\left[((a_1 + c_1)\hat{\omega}_1 - \hat{\omega}_1^3)^2 + ((a_0 + c_0) - a_2\hat{\omega}_1^2)^2\right]}\right\}. \tag{4.44}$$

Using equation (4.39), equation (4.44) can be simplified as

$$\begin{aligned}
&sign\left\{\frac{dRe\,s(\sigma)}{d\sigma}\right\}_{s=i\hat{\omega}_1} \\
&\quad = sign\left\{\frac{3\hat{\omega}_1^4 + 2(a_2^2 - 2(a_1 + c_1))\hat{\omega}_1^2 + ((a_1 + c_1)^2 - 2a_2(a_0 + c_0) - b_1^2)}{((a_1 + c_1)\hat{\omega}_1 - \hat{\omega}_1^3)^2 + ((a_0 + c_0) - a_2\hat{\omega}_1^2)^2}\right\}, \\
&\quad = sign\left\{\frac{3\hat{\omega}_1^4 + 2A_4\hat{\omega}_1^2 + B_4}{((a_1 + c_1)\hat{\omega}_1 - \hat{\omega}_1^3)^2 + ((a_0 + c_0) - a_2\hat{\omega}_1^2)^2}\right\}.
\end{aligned}$$

Therefore, we have

$$sign\left\{\frac{dRe\,s(\sigma)}{d\sigma}\right\}_{s=i\hat{\omega}_1} = sign\{3\hat{\omega}_1^4 + 2A_4\hat{\omega}_1^2 + B_4\}.$$

It is clear that $A_4 > 0$, $B_4 > 0$. Hence, we have, $\left.\frac{Re\,s(\sigma)}{d\sigma}\right|_{s=i\hat{\omega}_1} > 0$. Thus, the transverse condition for Hopf bifurcation is verified and from the above analytical result, we can confirm the following theorem.

Theorem 4.7. *Let $R_0(0,\sigma) > 1$, if H_2 hold, $d - \gamma\left(1 - \frac{x_1}{X_{max}}\right) < 0$ satisfied and $\hat{\omega}_1$ is the positive root of equation (4.39), then the infected equilibrium $E_{IE}(x_1, y_1, v_1)$ of model (1.1) is locally asymptotically stable when $\sigma < \hat{\sigma}_2$ and unstable $\sigma > \hat{\sigma}_2$, with a Hopf bifurcation occurring when $\sigma = \hat{\sigma}_2$.*

Case IV: When $\tau > 0$ and $\sigma > 0$, stability and bifurcation analysis of the infected equilibrium E_{IE}. Here, we consider τ as the bifurcation parameter.
By substituting $s = i\omega_4\ (\omega_4 > 0)$ in equation (4.18) and separating the imaginary and real parts, we get

$$a_1\omega_4 - \omega_4^3 = b_0 \sin\omega_4(\tau+\sigma) - b_1\omega_4 \cos\omega_4(\tau+\sigma) + c_0 \sin\omega_4\tau - c_1\omega_4 \cos\omega_4\tau. \tag{4.45}$$

$$a_0 - a_2\omega_4^2 = -b_0 \cos\omega_4(\tau+\sigma) - b_1\omega_4 \sin\omega_4(\tau+\sigma) - c_0 \cos\omega_4\tau - c_1\omega_4 \sin\omega_4\tau. \tag{4.46}$$

By squaring equation (4.45) and (4.46) and adding the resulting equations, we get

$$A_1(\omega_4) + A_2(\omega_4)\cos(\omega_4\sigma) + A_3(\omega_4)\sin(\omega_4\sigma) = 0. \tag{4.47}$$

where,

$$\begin{aligned}
A_1(\omega_4) &= \omega_4^6 + (a_2^2 - 2a_1)\omega_4^4 + (a_1^2 - 2a_0a_2 - b_1^2 - c_1^2)\omega_4^2 + (a_0^2 - b_0^2 - c_0^2),\\
A_2(\omega_4) &= -2(b_0c_0 + b_1c_1\omega_4^2),\\
A_3(\omega_4) &= 2(b_0c_1 - b_1c_0)\omega_4.
\end{aligned}$$

(H_3):there are finite positive roots ω_{4k}, $k = 1, 2, \ldots, l$ for equation (4.47).
For some critical value of bifurcation parameter τ, from equations (4.45) and (4.46), we have

$$\tau_{2k}^n = \frac{1}{\omega_{4k}} \arccos\left(\frac{A_4(\omega_{4k}^3 - a_1\omega_{4k}) + A_5(a_2\omega_{4k}^2 - a_0)}{A_4^2 + A_5^2}\right) + \frac{2n\pi}{\omega_{4k}},\ n = 0, 1, 2, \ldots \tag{4.48}$$

where,

$$\begin{aligned}
A_4 &= c_1\omega_{4k} + b_1\omega_{4k}\cos(\omega_{4k}\sigma) - b_0\sin(\omega_{4k}\sigma),\\
A_5 &= c_0 + b_1\omega_{4k}\sin(\omega_{4k}\sigma) + b_0\cos(\omega_{4k}\sigma).
\end{aligned}$$

Let $\hat{\tau}_3 = min\left\{\tau_{2k}^0\right\}$ and $\omega_{4k}(\hat{\tau}_3) = \hat{\omega}_2$. Then, to establish the Hopf bifurcation of model (1.1) at $\hat{\tau}_3$, we need to show that $\left.\frac{Re\, s(\tau)}{d\tau}\right|_{s=i\hat{\omega}_2} \neq 0$.
Differentiating equation (4.18) with respect to τ, we get

$$\frac{ds}{d\tau} = \frac{s(c_1s + c_0)e^{-s\tau} + s(b_1s + b_0)e^{-s\tau-s\sigma}}{3s^2 + 2a_2s + a_1 + b_1e^{-s\tau-s\sigma} - (b_1s + b_0)(\tau+\sigma)e^{-s\tau-s\sigma} + A_6}, \tag{4.49}$$

where $A_6 = (c_1 - \tau(c_1s + c_0))e^{-s\tau}$. Using (4.18), equation (4.49) can be written as

$$\left(\frac{ds}{d\tau}\right)^{-1} = \frac{2s^3 + a_2s^2 - a_0}{-s^2(s^3 + a_2s^2 + a_1s + a_0)} + \frac{(b_0 + \sigma s(b_1s + b_0))e^{-s\tau-s\sigma}}{s^2(s^3 + a_2s^2 + a_1s + a_0)} + \frac{c_0e^{-s\tau}}{s^2(s^3 + a_2s^2 + a_1s + a_0)} - \frac{\tau}{s}. \tag{4.50}$$

$$\text{Thus, } sign\left\{\frac{dRe\,s(\tau)}{d\tau}\right\}_{s=i\hat{\omega}_2} = sign\left\{Re\left(\frac{ds(\tau)}{d\tau}\right)^{-1}\right\}_{s=i\hat{\omega}_2}$$
$$= sign\left\{Re\left[\frac{2s^3+a_2s^2-a_0}{-s^2(s^3+a_2s^2+a_1s+a_0)}\right]_{s=i\hat{\omega}_2}\right.$$
$$\left.+Re\left[\frac{(b_0+\sigma s(b_1s+b_0))e^{-s\tau-s\sigma}}{s^2(s^3+a_2s^2+a_1s+a_0)}\right]_{s=i\hat{\omega}_2}+Re\left[\frac{c_0e^{-s\tau}}{s^2(s^3+a_2s^2+a_1s+a_0)}\right]_{s=i\hat{\omega}_2}\right\},$$
$$= sign\left\{\frac{d_{13}+d_{23}+d_{33}}{\omega_4^2\left[(a_1\omega_4-\omega_4^3)^2+(a_0-a_2\omega_4^2)^2\right]}\right\}.$$

Therefore, we have

$$sign\left\{\frac{dRe\,s(\tau)}{d\tau}\right\}_{s=i\hat{\omega}_2} = sign\left\{d_{13}+d_{23}+d_{33}\right\},$$

where

$$d_{13} = 2\omega_4^6+(a_2^2-2a_1)\omega_4^3-a_0^2,$$
$$d_{23} = (a_1\omega_4-\omega_4^3)\left[(b_0-\sigma b_1\omega_4^2)\sin\omega_4(\tau+\sigma)+\sigma b_0\omega_4\cos\omega_4(\tau+\sigma)\right]$$
$$-(a_0-a_2\omega_4^2)\left[(b_0-\sigma b_1\omega_4^2)\cos\omega_4(\tau+\sigma)+\sigma b_0\omega_4\sin\omega_4(\tau+\sigma)\right],$$
$$d_{33} = c_0\left[(a_1\omega_4-\omega_4^3)\sin\omega_4\tau-(a_0-a_2\omega_4^2)\cos\omega_4\tau\right].$$

Hence, considering the Hypothesis (H_4)

$$sign\left\{\frac{dRe\,s(\tau)}{d\tau}\right\}_{s=i\hat{\omega}_2} = sign\left\{Re\left(\frac{ds(\tau)}{d\tau}\right)^{-1}\right\}_{s=i\hat{\omega}_2}$$
$$= sign\left\{d_{13}+d_{23}+d_{33}\right\}\neq 0.$$

Thus, the above theoretical calculation can be stated as the following theorem.

Theorem 4.8. *Let $R_0(\tau,\sigma) > 1$ and $\tau > 0$, $\sigma > 0$, if (H_3, H_4) hold and $\hat{\omega}_2$ is the first positive root of equation (4.47), then infected equilibrium E_{IE} of model (1.1) is locally asymptotically stable when $\tau < \hat{\tau}_3$ and unstable $\tau > \hat{\tau}_3$, Hopf bifurcation occurs when $\tau = \hat{\tau}_3$.*

5. Permanence

Permanence or uniform persistence, as used in biology, is referring to the ability of certain biological traits or characteristics to remain consistent or persistent over time within a population or species. It implies that specific features or properties are maintained relatively unchanged across generations or within individuals throughout their lifespan. Hence, permanence of HIV highlights the complex nature of the virus and its ability to establish a chronic infection within the human body when $R_0(\tau,\sigma) > 1$ and its further recalled that infection-free state is unstable.

The solution of model (1.1) is known to exist and is bounded in Γ, which means that model (1.1) is dissipative. We concur with the approaches and strategies used in [1] and [20] to demonstrate

the uniform persistence of model (1.1), and we state the conditions of Theorem 5.1.1 of [38] as follows.

Theorem 5.1. *Let $R_0(\tau,\sigma) > 1$, then, for any $\tau,\sigma \geq 0$, model (1.1) is uniformly persistent in Γ if there exist $\vartheta > 0$ (independent of initial value) such that any solution $(x(t), y(t), v(t))$ of the model with condition (1.3) satisfy*

$$\liminf_{t\to+\infty} x(t) \geq \vartheta,\ \liminf_{t\to+\infty} y(t) \geq \vartheta \text{ and } \liminf_{t\to+\infty} v(t) \geq \vartheta.$$

Proof. We begin by introducing the theory for infinite dimensional systems from Hale [16]. Supposed that X be complete matric space with matric d. Let $Q(t)$ be defined the family of solutions operators corresponding to model (1.1) for $t \geq 0$. Then $Q(t) : X \to X$ be a C_0- semigroup on X. i.e $Q(0) = I$ (the identity operator on X), $Q(t+s) = Q(t)Q(s)$ for $t,s \geq 0$. Q is continuous.

Define, $X^0 = \{(u_1,u_2,u_3) \in X : u_2(\theta) > 0,\ u_3(\theta) > 0,\ \theta \in [-\xi,0],\ \xi = max\{\tau,\sigma\}\}$ and $X_0 = X \setminus X^0 = \{(u_1,u_2,u_3) \in X : u_2(\theta) = 0 \text{ or } u_3(\theta) = 0, \theta \in [-\xi,0]\},\ \xi = max\{\tau,\sigma\}\}$. Then, according to the Theorem 2.1 and 2.2, the matric space X is the closure of the open set X^0 such that $X = X^0 \cup X_0$. Here X_0 is the boundary of X^0 and $X_0 \subset X$, $X^0 \subset X, X_0 \cap X^0 = \emptyset$ and from the Theorem 2.2, X^0 is positively invariant. Further, $Q(t)$ is a C_0- semigroup on X satisfies

$$Q(t) : X^0 \to X^0, \quad Q(t) : X_0 \to X_0. \tag{5.1}$$

Let $Q_\rho(t) = Q(t)|_{X_0}$ and define G_ρ as global attractor for $Q_\rho(t)$. Further, $\omega-$ limit set is defined as $\omega(\varrho) = \{\varrho_1 \in X | \text{there exists a sequence } t_n \to \infty \text{ as } n \to \infty \text{ with } Q(t_n)\varrho \to \varrho_1 \text{ as } n \to \infty\}$.

Lemma 5.1. *Let $Q(t)$ satisfies (5.1) and we have following*

(i) there is a $t_0 \geq 0$ such that $Q(t)$ is compact for all $t > t_0$.

(ii) $Q(t)$ is point dissipative in X.

(iii) $\bar{G}_\rho = \cup_{x\in G_\rho}\omega(x)$ is isolated and there exist an acyclic covering $\bar{N}$. Then $\bar{N} = \cup_{i=1}^{k} N_i$, where each N_i pairwise disjoint, compact, isolated invariant set for Q_ρ and also an isolated invariant set for Q.

(iv) $\omega^s(N_i) \cap X^0 = \emptyset$, for $i = 1,2,3,\ldots,n$, where ω^s is the attracting set or stable set of a compact invariant set which is defined as $\omega^s(N_i) = \{x_1 | x_1 \in X, \omega(x_1) \neq \emptyset, \omega(x_1) \subset N_i\}$.

Then X_0 is a uniform repeller with respect to X^0. It implies that, there exists an $\epsilon > 0$ such that

$$\liminf_{t\to+\infty} d(Q(t)x, X_0) \geq \epsilon.$$

for any $x \in X^0$, where d is the distance of $Q(t)x$ from X_0.

It is clear that bounded of solution of system (1.1) does not depend on (1.3). Therefore, any bounded set D in X, the positive orbit $\Gamma^+(D) = \cup_{t>0} Q(t)D$ through $D \in X$ is bounded in X. Therefore, $Q(t)$ is asymptotically smooth and for any nonempty bounded and closed set $D \in X$ for which $Q(t)D \subset B$, there is a compact set $D_0 \subset B$ such that D_0 attracts D [16,17]. Let us define a subset of X as

$$M_{\delta_1} = \{\varrho \in X : Q(t)\varrho \text{ satisfy system } (1.1) \text{ and } Q(t)\varrho \in X_0, \forall t \geq 0\},$$

and we claim that $M_{\delta_1} = \{x_0, 0, 0\}$. Assume any $Q(t) \in M_{\delta_1}$ for $t \geq 0$. Then, first we show that $y(t) = v(t) = 0$ for all $t \geq 0$. By using contradiction, we continue to prove this claim. Assume that, there exist $t_0 > 0$ such that either (i). $y(t_0) > 0,\ v(t_0) = 0$. or (ii). $y(t_0) = 0,\ v(t_0) > 0$. For case (i), from the third equation of system (1.1), we have

$$\left.\frac{dv(t)}{dt}\right|_{t=t_0} > 0.$$

This suggests that $v(t)$ is increasing at $t = t_0$. Then, there exists a sufficient small constant $\epsilon_0 > 0$ such that $v(t) > 0$ for all $t \in (t_0, t_0 + \epsilon_0)$. Since, $y(t_0) > 0$, we can find arbitrary small constant $\epsilon_1 (0 < \epsilon_1 < \epsilon_0)$ such that $y(t) > 0$ for all $t \in (t_0, t_0 + \epsilon_1)$. This implies that both $y(t) > 0$ and $v(t) > 0$ for all $t \in (t_0, t_0 + \epsilon_1)$. This is contradiction. Similarly, we can use the second equation of system (1.1) for case (ii) as $x(t) > 0$ for all $t \in X_0$.

Let $\bar{G}_\rho = \cup_{x \in G_\rho} \omega(x)$, where G_ρ be the global attractor of $Q(t)$ restricted to X_0. That is $Q_\rho(t) = Q(t)|_{X_0}$. Now we need to show that $\bar{G}_\rho = \{E_{IF}\}$. In fact $\bar{G}_\rho \subseteq M_{\delta_1}$ and in the set X_0, from the first equation of system (1.1), we have

$$\dot{x}(t) = \frac{-\gamma}{X_{max}}(x - x_0)(x - \hat{x}), \tag{5.2}$$

where, $\hat{x} = \dfrac{X_{max}}{2\gamma}\left[(\gamma - d) - \sqrt{(\gamma - d)^2 + 4\lambda\gamma X_{max}^{-1}}\right]$. By integrating equation (5.2), we have

$$x(t) = \frac{x_0 - \hat{x}e^{-\frac{(x_0 - \hat{x})\gamma t}{X_{max}} + c}}{1 - e^{-\frac{(x_0 - \hat{x})\gamma t}{X_{max}} + c}}, \tag{5.3}$$

where beginning conditions can be used to determine the constant c, and $\lim_{t\to\infty} x(t) = x_0$. Thus, it is clear that $\{E_{IF}\}$ is isolated invariant and a compact set in X. Therefore, the covering is simply $\{E_{IF}\}$, which is an acyclic, it suggests that there is not an orbit in X that joins E_{IF} to itself. Moreover, from Theorem 2.2, $Q(t)$ is point dissipative in X. Therefore, the conditions from $(i) - (iii)$ of lemma 5.1 be satisfied.

Next, we need to prove that $\omega^s(E_{IF}) \cap X^0 = \emptyset$, where $\omega^s(E_{IF})$ is the attracting (stable) set of a compact invariant set E_{IF}. To prove this result by contrary, we assume any positive solution $(x(t), y(t), v(t)) \in X^0$ such that

$$\lim_{t\to\infty} x(t) \to x_0,\ \lim_{t\to\infty} y(t) \to 0,\ \text{and}\ \lim_{t\to\infty} v(t) \to 0.$$

Then, there exists a positive constant $t_1 = t_1(\epsilon_2)$ such that

$$x_0 - \epsilon_2 < x(t) < x_0 + \epsilon_2,\ 0 < y(t) < \epsilon_2,\ \text{and}\ 0 < v(t) < \epsilon_2,\ \text{for all}\ t > t_1,$$

and the sufficiently small $\epsilon_2 > 0$. Then, for the chosen constant ϵ_2, from the last two equations of system (1.1), for $t > t_1 + \tau$ and $t_1 > t_1 + \sigma$, we have

$$\begin{aligned} \dot{y}(t) &\geq \frac{e^{-p\tau}\beta(x_0 - \epsilon_2)v(t - \tau)}{1 + b\epsilon_2} - (p + \delta)y(t), \\ \dot{v}(t) &\geq ke^{-u\sigma}y(t - \sigma) - uv(t) - \frac{\beta(x_0 + \epsilon_2)v(t)}{1 + b\epsilon_2}. \end{aligned} \tag{5.4}$$

It is clear that, the right-hand side of first and second equations increase with respect to the delay variable $v(t-\tau)$ and $y(t-\sigma)$, respectively. These properties provide the system (5.4) with a quasi-monotone structure [20,29].

Now, we take the following differential system into consideration and apply the comparison principle:

$$\begin{aligned} \dot{w_1}(t) &= \frac{e^{-p\tau}\beta(x_0-\epsilon_2)w_2(t-\tau)}{1+b\epsilon_2} - (p+\delta)w_1(t), \\ \dot{w_2}(t) &= ke^{-u\sigma}w_1(t-\sigma) - uw_2(t) - \frac{\beta(x_0+\epsilon_2)w_2(t)}{1+b\epsilon_2}, \ t \geq t_1-\xi, \end{aligned} \tag{5.5}$$

with initial condition $w_1(t) = y(t)$ and $w_2(t) = v(t)$, for all $t \in [t_1, t_1+\xi]$, where $\xi = max\{\tau, \sigma\}$. It is obvious that, all solution $(w_1(t), w_2(t))$ of system (5.5) are non-negative.

Then, we use the notations of Theorem 5.1.1 of [38] and define $(f_1(t,\phi_2), f_2(t,\phi_3)) = (y(t,\phi_2), v(t,\phi_3))$ and $(g_1(t,\phi_2), g_2(t,\phi_3)) = (w_1(t,\phi_2), w_2(t,\phi_3))$ in order to validate the criteria of Theorem 5.1.1 of [38].

From Theorem 2.2, we know that $(y(t), v(t))$ is bounded ; As a result, it is clear that for systems (5.4) and (5.5), $(f_1(t,\phi_2), f_2(t,\phi_3))$ and $(g_1(t,\phi_2), g_2(t,\phi_3))$ are continuous, and Lipschitz on each compact subset of X and $(f_1(t,\phi_2), f_2(t,\phi_3))$ satisfies the criterion (Q):whenever $\psi \leq \phi$ and $\psi_i(0) \leq \phi_i(0)$ for some i, then $f_i(\psi) \leq f_i(\psi)$. Therefore, system (5.4) satisfy the all necessary conditions of Theorem 5.1.1 of [38]. Thus, by the comparison principle in [38], since we have presumed that $(y(t), v(t)) \to (0,0)$ as $t \to \infty$, the solutions $(w_1(t), w_2(t))$ of system (5.5) is also converge to $(0,0)$ with the aforementioned initial conditions.

Define

$$\begin{aligned} L_3(t) = w_1(t) + \frac{e^{-p\tau}\beta(x_0-\epsilon_2)}{u(1+b\epsilon_2)+\beta(x_0+\beta_2)}w_2(t) + \frac{e^{-p\tau}\beta(x_0-\epsilon_2)}{1+b\epsilon_2}\int_{t-\tau}^{t} w_2(\eta)d\eta \\ + \frac{k\beta e^{-u\sigma-p\tau}(x_0-\epsilon_2)}{u(1+b\epsilon_2)+\beta(x_0+\epsilon_2)}\int_{t-\sigma}^{t} w_1(\eta)d\eta. \end{aligned} \tag{5.6}$$

From the solutions $(w_1(t), w_2(t)) \to (0,0)$ as $t \to \infty$, then we have

$$\lim_{t\to\infty} L_3(t) \to 0. \tag{5.7}$$

By taking the derivative of $L_3(t)$ along the solution of (5.5), we obtain

$$\dot{L}_3(t) = \left[\frac{ke^{-u\sigma-p\tau}\beta(x_0-\epsilon_2)}{u(1+b\epsilon_2)+\beta(x_0+\epsilon_2)} - (p+\delta)\right]w_1(t). \tag{5.8}$$

Since $R_0(\tau,\sigma) > 1$, it is possible to select a sufficiently small constant ϵ_2, such that

$$\frac{ke^{-u\sigma-p\tau}\beta(x_0-\epsilon_2)}{u(1+b\epsilon_2)+\beta(x_0+\epsilon_2)} - (p+\delta) = (R_0(\tau,\sigma)-1)(p+\delta)w_1(t) > 0, \text{ for all } t > 0.$$

Hence, it is clear that $L_3(t)$ goes to a positive number or infinity when $t \to \infty$. This is a contradiction with equation (5.7). Thus, we have $\omega^s(E_{IF}) \cap X^0 = \emptyset$. Therefore, by applying Lemma 5.1, for some

constant $\zeta_1 > 0$, we obtain

$$\liminf_{t\to+\infty} y(t) > \zeta_1, \text{ and } \liminf_{t\to+\infty} v(t) > \zeta_1.$$

Further, from equation (2.8), for any $\epsilon_3 > 0$, there exist $t_3 > 0$, such that $v(t) \leq \frac{kM_0}{q_3} + \epsilon_3$ for all $t \geq t_3$. Hence, from the first equation of the system (1.1), we have

$$\frac{dx(t)}{dt} \geq \lambda + \gamma x(t)\left(1 - \frac{x(t)}{X_{max}}\right) - dx(t) - \beta x(t)\left(\frac{kM_0}{q_3} + \epsilon_3\right). \tag{5.9}$$

Since, ϵ_3 is sufficiently small constant, from equation (5.9), we obtain

$$\liminf_{t\to\infty} x(t) \geq \frac{X_{max}}{2\gamma}\left[\gamma - d - \frac{\beta k M_0}{q_3} + \sqrt{\left(\gamma - d - \frac{\beta k M_0}{q_3}\right)^2 + \frac{4\lambda\gamma}{X_{max}}}\right] = \zeta_2. \tag{5.10}$$

Hence, the proof of Theorem 5.1 is completed, and incorporating this result with Theorem 2.2, it is clear that system (1.1) is permanent. □

6. Numerical Simulations

In this section, we provide some numerical simulations of cases that support our theoretical results that were obtained in Sections 3 and 4 using the sets of parameter values described in the literature that were similar to those in ([2,31,40,44,52] and references therein).

When we consider the set of parameter values:

$$\begin{aligned} &\lambda = 5, \gamma = 0.8, d = 0.01, \beta = 0.00024, \delta = 0.01, b = 0.001, p = 0.5, k = 600, \\ &u = 3, X_{max} = 1200, \tau = 2.0 \text{ and } \sigma = 1.5, \end{aligned} \tag{6.1}$$

we obtain $R_0(2, 1.5) = 0.4183 < 1$, infection free equilibrium $E_{IF} = (1191.2957, 0, 0)$ and the values of $ke^{-u\sigma - p\tau} - (p + \delta) = 1.9421 > 0$. Hence, by Theorem 4.2 the infection-free equilibrium E_{IF} is globally asymptotically stable. Figure 1 shows the time series of solutions of model (1.1) with three different initial conditions $\psi(100, 50, 80)$, $\psi(200, 80, 90)$ and $\psi(400, 100, 120)$.

When the set of parameter values:

$$\begin{aligned} &\lambda = 5, \gamma = 0.03, d = 0.04, \beta = 0.000024, \delta = 0.01, b = 0.0001, p = 0.5, k = 600, \\ &u = 3, X_{max} = 1500, \tau = 0.1 \text{ and } \sigma = 0, \end{aligned} \tag{6.2}$$

we obtain $R_0(0.1, 0) = 2.7597 > 1$, $d - \gamma(1 - \frac{x_1}{X_{max}}) = 0.01253 \geq 0$ and $\hat{\tau}_1 = \frac{1}{p} \ln \frac{\beta k x_0}{(p+\delta)(u+\beta x_0)} = 2.13036 > \tau$. Then the conditions of Theorem 4.4 are satisfied and solution trajectory converges to the infected equilibrium $E_{IE}(126.30907, 6.49594, 1298.02786)$. The graphs (a), (b) and (c) in Figure 2 show the stability of the solution trajectories for the three τ values and the graph (d) of Figure 2 shows the solution trajectory in phase diagram of model (1.1) which illustrate the stability of E_{IE} with four initial conditions $\psi(20, 50, 50)$, $\psi(50, 50, 50)$, $\psi(70, 50, 50)$ and $\psi(90, 50, 50)$.

When we consider the set of parameter values:

$$\lambda = 10, d = 0.02, \gamma = 0.8, \beta = 0.00024, \delta = 0.01, b = 0.0001, p = 0.5, k = 600,$$
$$u = 3, X_{max} = 1500, \tau = 1.2 \text{ and } \sigma = 0, \tag{6.3}$$

we have $R_0(1.2, 0) = 68.1553 > 1$, $E_{IE}(34.7462, 39.6594, 7919.5973)$, $d - \gamma(1 - \frac{x_1}{X_{max}}) = -0.7615 < 0$ and the constant coefficient of equation (4.24), $a_0^2 - (b_0 + c_0)^2 = -0.14635$ and the largest positive simple root $\hat{\omega}_0 = 0.2209$. Then $\hat{\tau}_2 = 7.9253$. Hence, infected equilibrium E_{IE} of model (1.1) asymptotically stable when $\tau < \hat{\tau}_2 = 7.9253$. Therefore the conditions of Theorem 4.5 are satisfied. The graphs (a), (b) and (c) in Figure 3 show the stability of the solution trajectories for the two τ values $\tau = 1.2, 1.6$ and the graph (d) of Figure 3 shows the solution trajectory in phase diagram of model (1.1) which illustrate the stability of E_{IE} with two initial conditions $\psi(10, 20, 40)$, $\psi(50, 10, 30)$.

When we consider the parameter values:

$$\lambda = 10, d = 0.02, \gamma = 0.8, \beta = 0.00024, \delta = 0.01, b = 0.00001, p = 0.5, k = 600,$$
$$u = 3, X_{max} = 1500, \tau = 2 \text{ and } \sigma = 0, \tag{6.4}$$

we have $R_0 = 45.6859$, $E_{IE}(30.3410, 24.1041, 4809.6719)$, $d - \gamma(1 - \frac{x_1}{X_{max}}) = -0.7638 < 0$ and the constant coefficient of equation (4.24) , $a_2^2 - (b_0 + c_0)^2 = -0.880064$ and the largest positive simple root $\hat{\omega}_0 = 0.4896$. Then we have $\hat{\tau}_2 = 1.3891$. Therefore, the conditions of Theorem 4.5 are satisfied and the infected equilibrium point E_{IE} of model (1.1) unstable when $\tau > \hat{\tau}_2 = 1.3891$. Hence, The Hopf bifurcation occurs when $\tau = \hat{\tau}_2 = 1.3891$, and it is numerically confirmed by the Figure 4. The graph (d) of Figure 4 shows the phase trajectory of model (1.1) after Hopf bifurcation occurs by considering two initial conditions $\psi(80, 45, 7000)$ and $\psi(30, 24, 3500)$. Then, it is clear that the solution trajectory starting from E_{IE} converges to a limit cycle. This implies that the E_{IE} becomes unstable and we have a stable limit cycle under the condition of Theorem 4.5.

When we consider the parameter values:

$$\lambda = 5, d = 0.04, \gamma = 0.03, \beta = 0.00024, \delta = 0.01, b = 0.0001, p = 2, k = 600, u = 3,$$
$$X_{max} = 1500, \tau = 0 \text{ and } \sigma = 0.1, \tag{6.5}$$

we have $R_0(0, 0.1) = 5.3349$, $d - \gamma(1 - \frac{x_1}{X_{max}}) = 0.01117 > 0$. Therefore, the condition of Theorem 4.6 is satisfied. Then, the solution trajectory of model (1.1) converges to the infected equilibrium E_{IE}(58.6017, 2.1726, 320.45205) as shown in Figure 5. The graphs (a), (b) and (c) in Figure 5 show the stability of the solution trajectories of model (1.1) for the three σ values $\sigma = 0.1, 0.2, 0.5$ and the graph (d) of Figure 5 shows the solution trajectory in phase diagram of model (1.1) which illustrate the stability of E_{IE} with two initial conditions $\psi(20, 50, 1000)$, $\psi(80, 10, 20)$.

When we consider the parameter values:

$$\lambda = 5, d = 0.04, \gamma = 0.8, \beta = 0.00024, \delta = 0.01, b = 0.0001, p = 0.5, k = 600, u = 3,$$
$$X_{max} = 1500, \tau = 0 \text{ and } \sigma = 0.2, \tag{6.6}$$

then, $R_0(0, 0.2) = 66.3455$, $E_{IE}(31.4488, 56.7473, 6219.0653)$, the condition $H_2 = 1.96358, d - \gamma(1 - \frac{x_1}{X_{max}}) = -0.743227 < 0$ and the largest simple root $\hat{\omega}_1 = 0.3555$. Then $\hat{\sigma}_2 = 2.3911$. Therefore, the conditions of Theorem 4.7 are satisfied. Hence, the infected equilibrium E_{IE} of model (1.1) is asymptotically stable when $\sigma < \hat{\sigma}_2 = 2.3911$. The graphs (a), (b) and (c) in Figure 6 show the stability of the solution trajectories for the three σ values $\sigma = 0.05, 0.2, 0.3$ and the graph (d) of Figure 6 shows the solution trajectory in phase diagram of system (1.1) which illustrate the stability of E_{IE} with two initial conditions $\psi(20, 20, 10)$, $\psi(80, 10, 20)$.

When we consider the parameter values:

$$\begin{aligned} &\lambda = 5, d = 0.01, \gamma = 0.8, \beta = 0.00024, \delta = 0.01, b = 0.00001, p = 0.5, k = 600, \\ &u = 3, X_{max} = 1500, \tau = 0 \text{ and } \sigma = 0.9, \end{aligned} \tag{6.7}$$

we have $R_0(0, \sigma) = 8.4084$, $E_{IE} = (165.2645, 241.9847, 3211.4044)$, $d - \gamma(1 - \frac{x_1}{X_{max}}) = -0.7019 < 0$. The largest positive simple root $\hat{\omega}_1 = 0.51689$, and $\hat{\sigma}_2 = 0.24984$. Therefore, the conditions of Theorem 4.7 are satisfied. Hence, the infected equilibrium E_{IE} of model (1.1) is unstable when $\sigma > \hat{\sigma}_2 = 0.24984$ and Hopf bifurcation occurs when $\sigma = \hat{\sigma}_2 = 0.24984$. This result numerically confirmed by Figure 7. The graph (d) of Figure 7 shows the phase trajectory of model(1.1) after Hopf bifurcation occurs by considering two initial conditions $\psi(30, 50, 800)$ and $\psi(160, 240, 3000)$. It is clear that the solution trajectory starting from E_{IE} converges to a limit cycle since the condition of Theorem 4.7 are satisfied. This implies that the E_{IE} is unstable and we have a stable limit cycle.

When we consider the parameter values:

$$\begin{aligned} &\lambda = 5, d = 0.01, \gamma = 0.8, \beta = 0.00024, \delta = 0.01, b = 0.0001, p = 0.5, k = 600, u = 3, \\ &X_{max} = 1200, \tau = 1.39 \text{ and } \sigma = 0.9, \end{aligned} \tag{6.8}$$

we have $R_0(1.39, 0.9) = 3.4334$, $E_{IE} = (333.1895, 191.9272, 2514.3369), H_4 = 0.5240 > 0$, $\hat{\omega}_2 = 0.3048 (H_3)$, and $\hat{\tau}_3 = 1.8553$. Hence, the conditions of Theorem 4.8 are satisfied. Therefore, the infected equilibrium E_{IE} of model (1.1) is asymptotically stable for $\tau < \hat{\tau}_3 = 1.8553$. The graphs (a), (b) and (c) in Figure 8 show the stability of solution trajectories of model (1.1) for the three τ values keeping $\sigma = 0.9$ constant. Graph (d) in Figure 8 shows the trajectory in the phase diagram of model (1.1), which illustrate the stability of infected equilibrium E_{IE} with the initial condition $\psi(300, 80, 100)$.

When we consider the parameter values:

$$\begin{aligned} &\lambda = 5, d = 0.01, \gamma = 0.8, \beta = 0.00024, \delta = 0.01, b = 0.00001, p = 0.5, k = 600, \\ &u = 3, X_{max} = 1200, \tau = 1.2 \text{ and } \sigma = 0.9, \end{aligned} \tag{6.9}$$

we have $R_0(1.2, 0.9) = 3.7756, E_{IE} = (302.5752, 199.0686, 2614.0378), H_4 = 0.9543 > 0$, $\hat{\omega}_2 = 0.3561$ (H_3), and $\tau > \hat{\tau}_3 = 0.8491$. Thus, the conditions of Theorem 4.8 are satisfied. Therefore, the infected equilibrium E_{IE} of model (1.1) is unstable when $\tau > \hat{\tau}_3 = 0.8491$ and $\sigma = 0.9$, and Hopf bifurcation occurs when $\tau = \hat{\tau}_3$. This results numerically confirmed by the Figure 9. Graph (d) of Figure 9 shows the phase trajectory of model (1.1) after Hopf bifurcation occurs by considering two

initial conditions $\psi(302, 199, 2614)$ and $\psi(300, 80, 100)$ when $\tau = 1.2$ and $\sigma = 0.9$. It is clear that the solution trajectory starting from E_{IE} converges to a limit cycle since the condition of Theorem 4.8 are satisfied. This implies that the E_{IE} is unstable and we have a stable limit cycle.

Model (1.1) has a process from stability to oscillation and then returns to stability when τ changes from 0 to 7 ($\sigma = 0.25$) as shown in Figure 11. The infected steady state is asymptotically stable at the left end of the τ range, up to $\tau = 0.25001$, although virulence decreases. Recurrent oscillations are produced when the infected steady state becomes unstable due to the time delay, which rises as τ. The infected steady state once more becomes asymptotically stable and the virulence level falls as τ increases from $\tau = 5.95001$. These findings suggest that the dynamics of the model are impacted by the time delays.

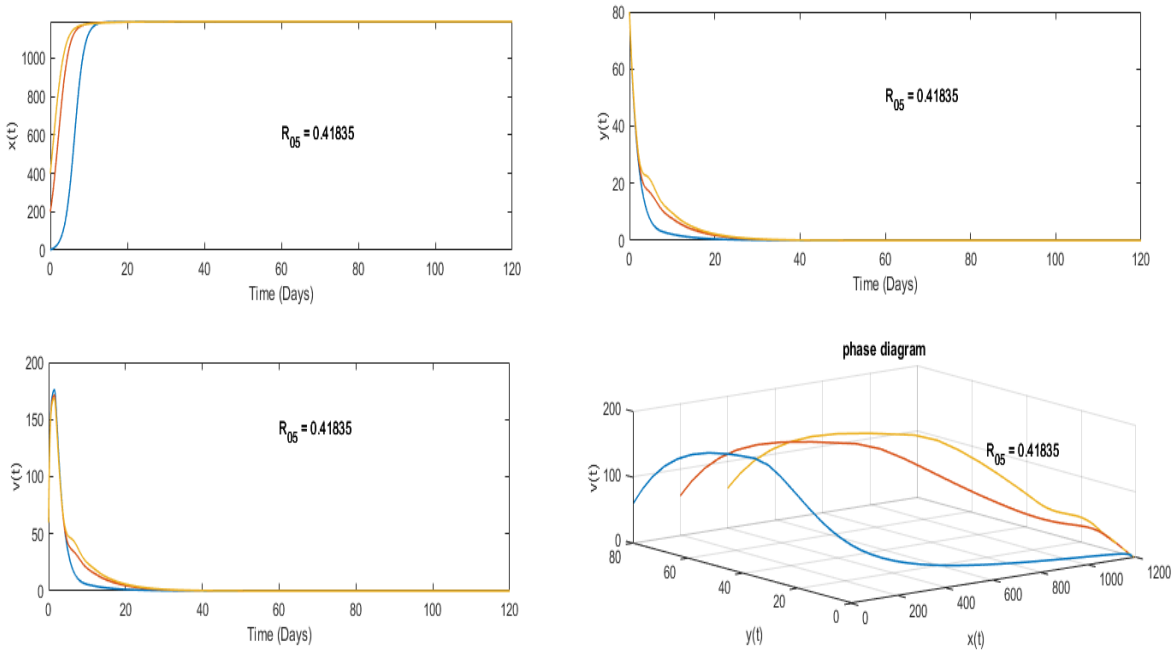


FIGURE 1. Dynamics of model (1.1) for the set of parameters in (6.1). Then, $R_0 = 0.41835$ and solution trajectory converges to the equilibrium point $E_{IF}(1191.2957, 0, 0)$.

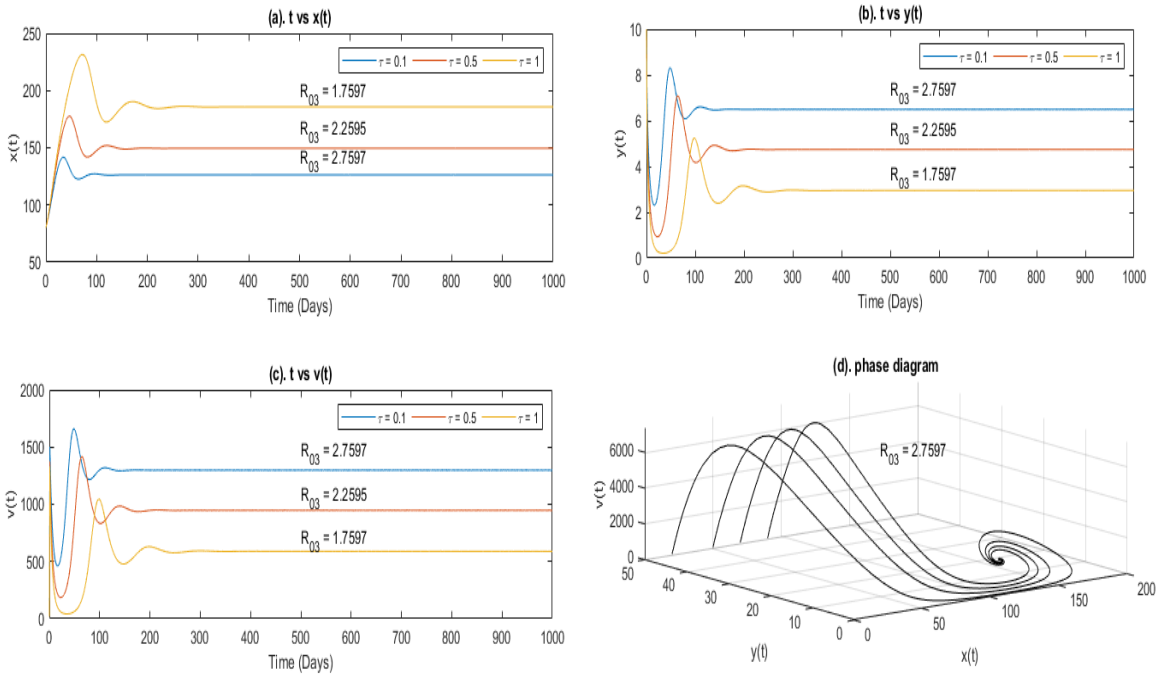


FIGURE 2. Dynamics of model (1.1) for the set of parameters in (6.2). The infected equilibrium E_{IE} of model (1.1) is asymptotically stable when $\tau > 0$ and $\sigma = 0$.

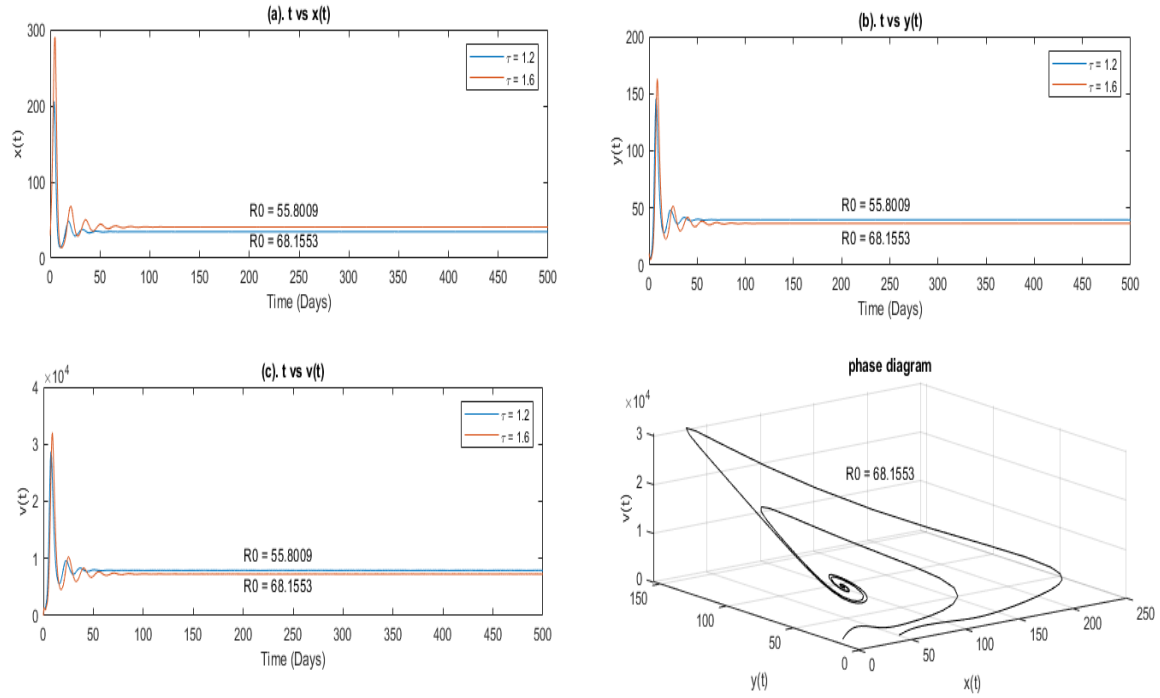


FIGURE 3. For the parameters in (6.3), the infected equilibrium of model (1.1) is asymptotically stable when $0 < \tau < \hat{\tau}_2 = 7.9253$. and $\sigma = 0$.

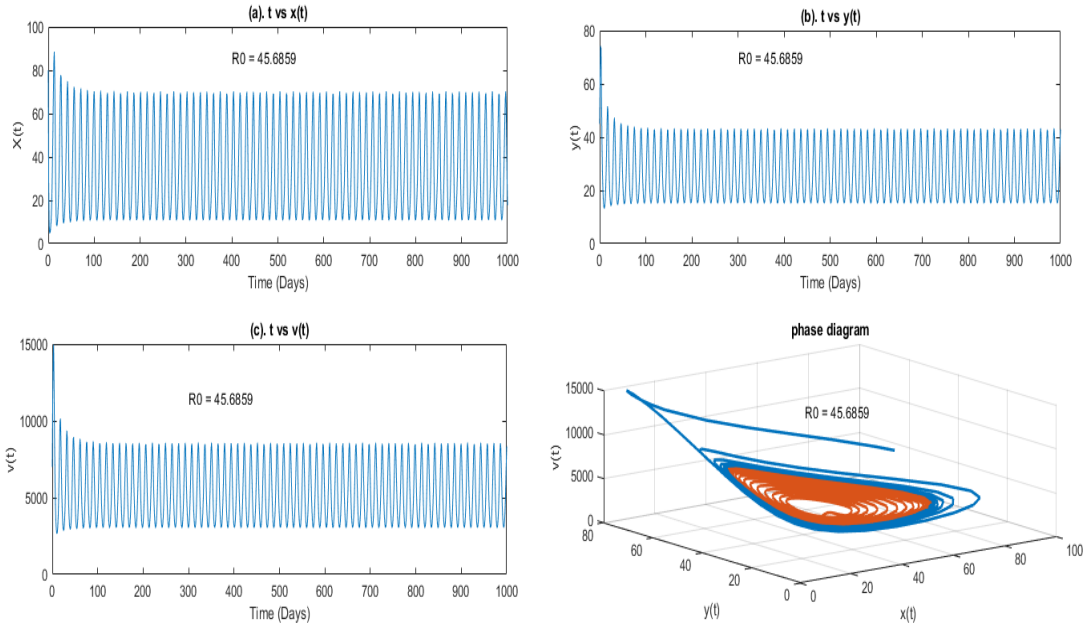


FIGURE 4. Dynamics of model (1.1) after Hopf bifurcation occurs for parameter values (6.4) with $\sigma = 0$ and $\tau = \hat{\tau}_2 = 1.3891$. Here E_{IE} is unstable and have a stable limit cycle.

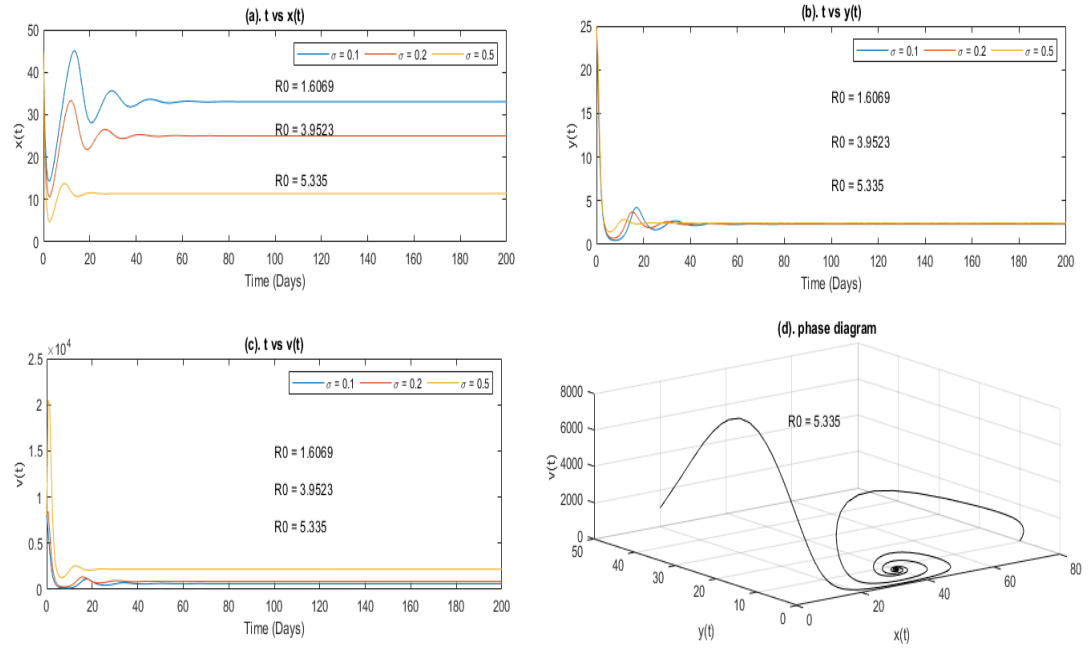


FIGURE 5. For the parameter values (6.5), the solution trajectory of model (1.1) is converge to the infected equilibrium E_{IE} when $\tau = 0$ and $\sigma > 0$.

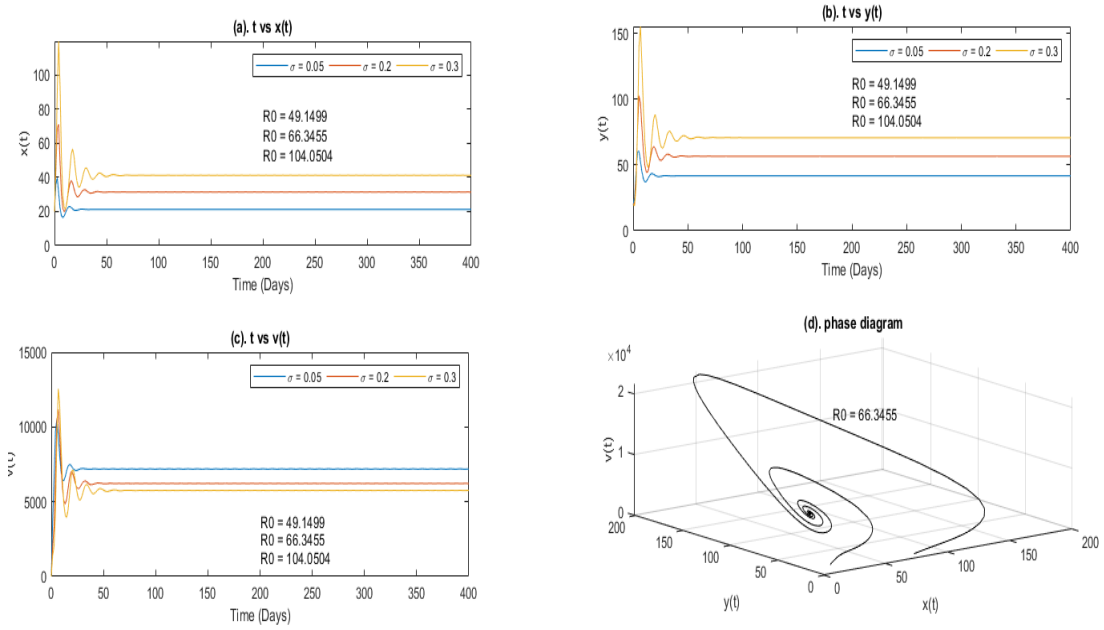


FIGURE 6. Dynamics of the system for the parameters values (6.6) with $\sigma = 0.05, 0.2, 0.3$. Here positive infected equilibrium E_{IE} is asymptotically stable when $\sigma < \hat{\sigma}_2 = 2.39116$ and $\tau = 0$.

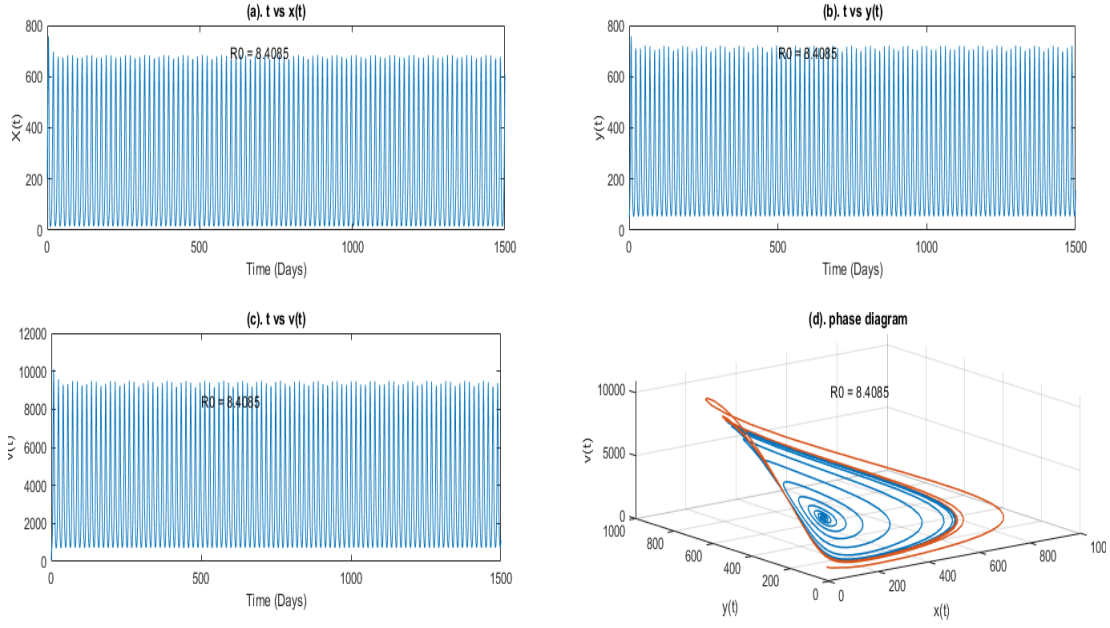


FIGURE 7. Dynamics of model (1.1) after Hopf bifurcation occurs for the parameter values (6.7) with $\sigma = \hat{\sigma}_2 = 0.2498$ and $\tau = 0$. E_{IE} is unstable and have a stable limit cycle.

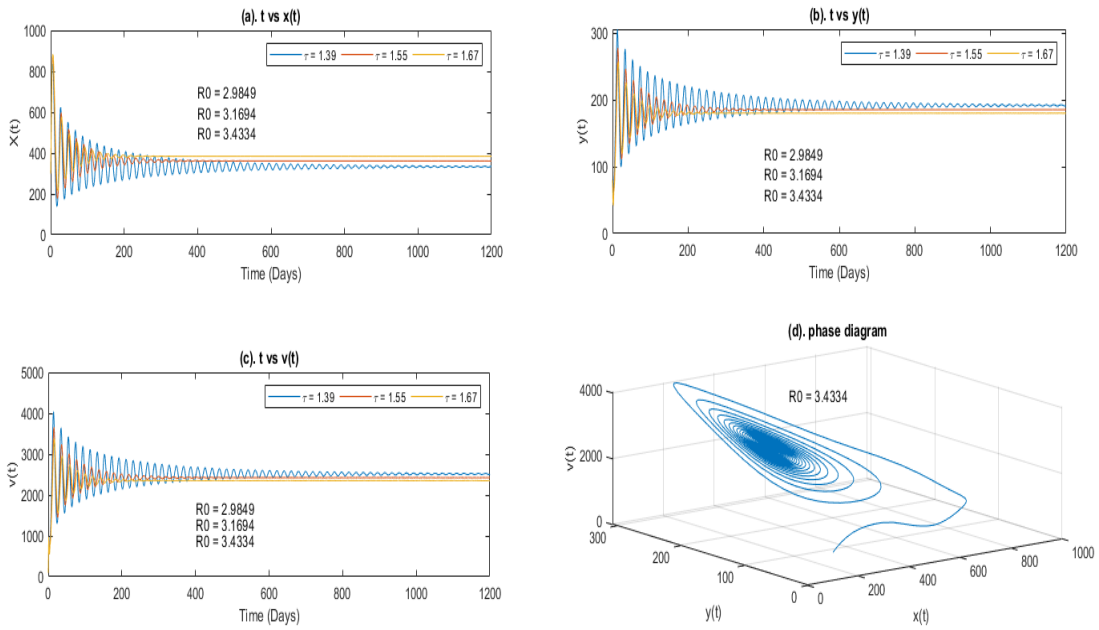


FIGURE 8. Dynamics of model (1.1) for the parameters in (6.8). Here, positive infected equilibrium E_{IE} is asymptotically stable when $0 < \tau < \hat{\tau}_3$ and $\sigma > 0$.

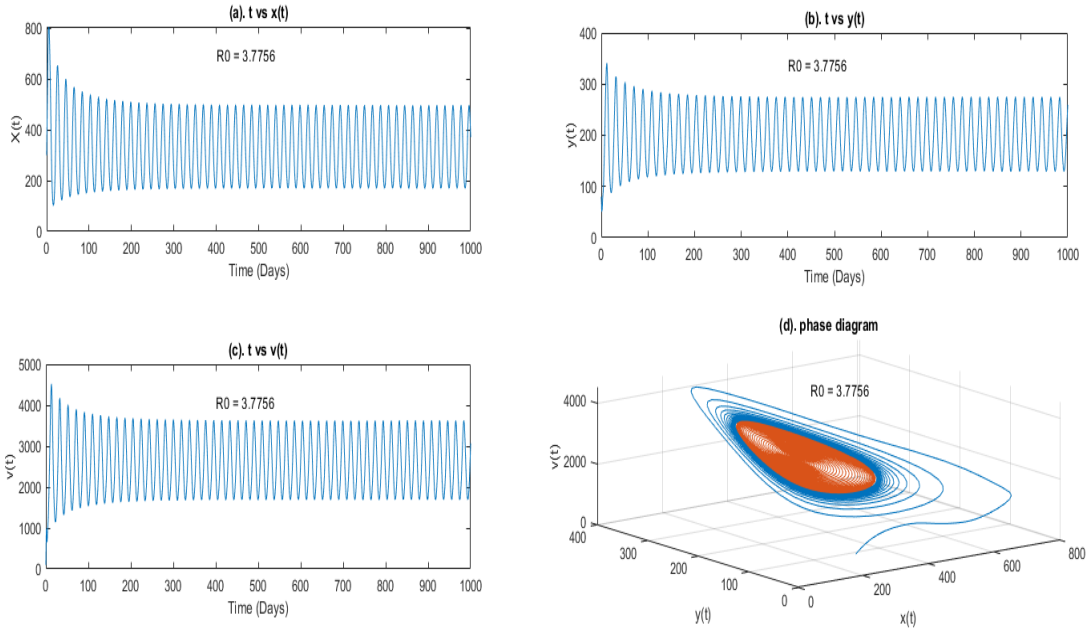


FIGURE 9. Dynamics of model (1.1) after Hopf bifurcation occurs for the parameter values in (6.9) with $\tau = \hat{\tau}_3 = 0.8491$ and $\sigma > 0$.

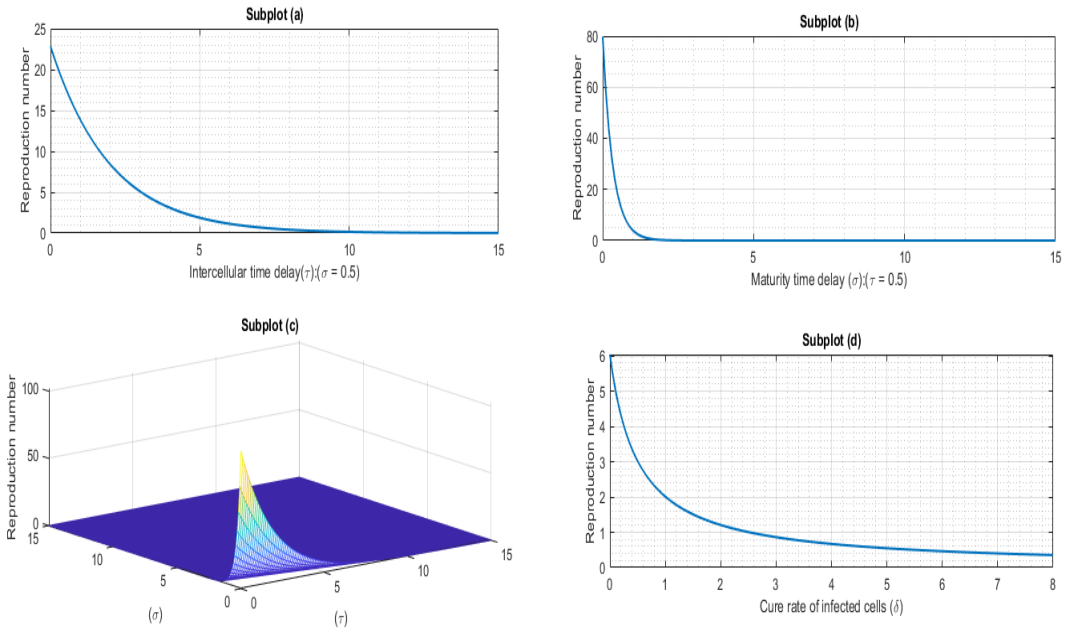
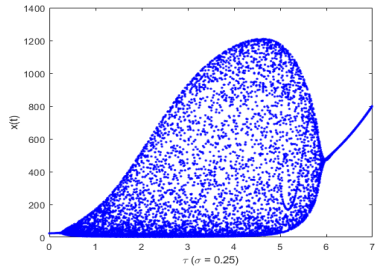
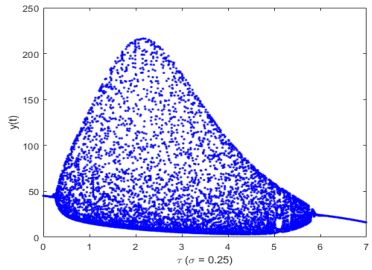


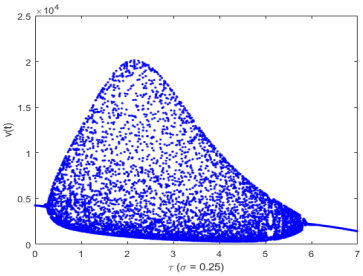
FIGURE 10. Dynamics of $R_0(\tau,\sigma)$ vs. $\tau(\sigma = 0.5)$, $\sigma(\tau = 0.5)$ and δ for the parameter values (6.1).



(A) τ vs. x(t) when $\sigma = 0.25$.



(B) τ vs. y(t) when $\sigma = 0.25$.



(C) τ vs. v(t) when $\sigma = 0.25$.

FIGURE 11. Bifurcation diagram of model (1.1) for the parameter values in (6.1), time delay τ varying from 0 to 7, and $\sigma = 0.25$.

7. Conclusion

In this paper, we have proposed and analysed a delayed HIV dynamics model with saturation functional response, virus absorption effect, cure rate of the infected cell, intracellular time delay and maturation time delay. We showed that there are two equilibrium points in this model, the infection-free equilibrium point and the infected equilibrium point. Further, we showed that the stability properties are completely determined by the basic reproduction number $R_0(\tau, \sigma)$ of the model. If $R_0(\tau, \sigma) \leq 1$, by examining the characteristic equation at the infection-free equilibrium point and considering the appropriate Lyapunov functional and LaSalle's invariance principle, we investigated that infection-free equilibrium E_{IF} of the model is locally and globally asymptotically stable for any $\tau, \sigma \geq 0$. The results are shown in Theorem 4.1 and Theorem 4.2 respectively. In this instance, it is biologically implied that the virus can be eliminated from the body by activating the body's immune system or by providing external medical treatment. That is, the host will not be infected and will recover within a certain period of time.

On the other hand, if $R_0(\tau, \sigma) > 1$, the infection-free equilibrium is unstable and infected equilibrium becomes a steady chronic infection or a periodic orbit. In Theorems 4.3, 4.4, 4.6 and 4.8, we established the necessary conditions to guarantee the locally asymptotically stability of infected equilibrium of model (1.1) under the four cases of delay τ and σ. In these conditions, the immune system or medications are unable to manage the host getting infected, resulting in a chronic and persistent infection. It has been further demonstrated in Theorem 5.1 that, uniform persistence takes place when the basic reproduction number exceeds unit. Moreover, we showed that the commencement of damped oscillation takes place via a Hopf bifurcation. In theorems 4.5, 4.7 and 4.8 respectively, we showed that when the models present with intracellular time delay, maturation delay, and both delays, the model exhibits the Hopf bifurcation based on the delay terms under certain conditions.

As a viral infection control measure, it is crucial to examine the rate at which infected cells revert to their uninfected form. We plot δ versus $R_0(\tau, \sigma)$ for certain maturation and intracellular delays, varying the values of δ from 0 to 8 as shown in graph (d) in Figure 10. We observed that if $\delta = 0$, then $R_0(0.3, 0.9) = 6.0397$, and if the value of the infected cells' cure rate rises, then $R_0(\tau, \sigma)$ falls below one. Therefore, the relevant conclusion of model (1.1) is that viral infection can be eliminated if δ becomes larger. Furthermore, we can observe that intracellular time delay and maturation time delay play an important role in reducing the basic reproductive number in model (1.1). The graphs (a), (b) and (c) in Figure 10 show that, assuming all the other parameter remains constant, we can choose sufficiently large enough τ and σ values to satisfy the condition $R_0(\tau, \sigma) \leq 1$. It shows that increasing τ and σ values can control the virus load in the model. Therefore, our research findings may contribute to the development of new therapeutic approaches to control viral infections and improve the understanding of viral pathogenesis.

Conflicts of Interest: The authors declare that there are no conflicts of interest regarding the publication of this paper.

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