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Global Stability Analysis of CHIKV Dynamics Model with Adaptive Immunity and Distributed Time Delays

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Abstract

The application of mathematical biology and dynamical systems has proven to be an effective approach for studying viral infection models. To contribute to this research, our paper proposes a new CHIKV model that takes into account an adaptive immune response and distributed time delays, which accurately reflects the time lag between initial viral contacts and the production of new active CHIKV particles. By analyzing the model's qualitative behavior, we establish a biological threshold number that can predict whether CHIKV will be cleared from or persist in the body. We demonstrate the global stability of both CHIKV-present and CHIKV-free steady states using the Lyapunov functional method and LaSalle's invariance principle. In addition, we conduct numerical simulations to examine how time delays can affect the stability of the steady states. Through these simulations, we gain insights into how varying time delays can influence the persistence or clearance of CHIKV within the host.

Keywords: Chikungunya virus; Adaptive immune response; Distributed time delays; Global stability; Lyapunov functionals

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1. Introduction

Chikungunya virus (CHIKV) disease is a persistent and evolving mosquito-borne viral infection that continues to pose a significant public health concern in many regions across the globe (Cotella et al. (2022)). The virus was first identified in Tanzania in the 1950s, and the name "chikungunya" comes from the Makonde language of southern Tanzania and northern Mozambique, where the virus was first identified. The name means "that which bends up," referring to the posture of infected individuals due to the severe joint pain caused by the virus. CHIKV is found in many countries in Africa, Asia, Europe, and the Americas. Outbreaks of chikungunya have occurred in several parts of the world in recent years, including the Caribbean, Central and South America, and the Indian Ocean (Galán-Huerta et al. (2015), Da Silva-Júnior et al. (2017)). The virus is most commonly found in tropical and subtropical regions and is transmitted by mosquitoes, which are more abundant in these areas. The impact of CHIKV is manifested through its severity, prevalence, and geographical spread, which collectively contribute to the escalating public health challenge posed by the virus in affected regions (Cotella et al. (2022)).

The main mode of transmission for CHIKV to humans is through female mosquito bites, specifically the Aedes aegypti and Aedes albopictus (El Hajji et al. (2022)). Once a mosquito is infected with the virus, it can spread the virus to other humans through bites. The virus can also be transmitted from an infected mother to her fetus during pregnancy or childbirth, and in rare cases, the virus can be transmitted through blood transfusions or organ transplants (Besbassi et al. (2020)). Due to its mode of transmission via mosquitoes, the virus is categorized as an arbovirus or arthropod borne virus (Raghavendhar et al. (2019)). CHIKV falls under the *Alphavirus* genus, which is a part of the *Togariridae* family's classification (Galán-Huerta et al. (2015)) and is the underlying viral agent responsible for the onset of chikungunya fever (Elaiw et al. (2018a)).

The symptoms of chikungunya virus typically develop 3-7 days after the bite of an infected mosquito. The symptoms of the illness can last for several days to several weeks, and in some cases, the joint pain associated with the illness can persist for months or even years (Bettis et al. (2022)).

CHIKV can have a significant impact on populations, particularly in areas where mosquitoes are abundant and access to healthcare is limited. The virus can cause severe joint pain, leading to long-term disability and reduced quality of life. In addition, the virus can place a significant burden on healthcare systems and economies, particularly in developing countries (Galán-Huerta et al. (2015)).

There is currently no specific treatment for chikungunya virus infection. The symptoms can be managed with rest, hydration, and over-the-counter pain medications. In severe cases, hospitalization may be necessary (Raghavendhar et al. (2019)).

Over the past few decades, numerous mathematicians have developed mathematical models that describe the interactions between viruses and host organisms, shedding light on the dynamics of virus spread and replication. (Examples of viruses include human immunodeficiency virus (HIV),

hepatitis B virus (HBV), hepatitis C virus (HCV), Zika virus (ZIKV), dengue virus (DENV), chikungunya virus (CHIKV), and Rift Valley fever virus (RVFV)) (see, e.g., Nowak and May (2000); Liu and Stechlinski (2015); Sadki et al. (2022); Alade et al. (2021a); Alade (2021); Alade et al. (2021b); Mann Manyombe et al. (2020); Olaniyi (2018); Olaniyi et al. (2023); Falowo et al. (2023); Okyere et al. (2020); Alade et al. (2021c); Elaiw et al. (2019b); Abidemi et al. (2019); Abidemi and Aziz (2020); El Hajji (2021)). The utilization of mathematical modeling in studying human viruses serves as an essential tool for both the advancement of antiviral medications and the acquisition of valuable understandings regarding interactions between viruses and their hosts. It is an effective means of predicting the progression of diseases caused by these viruses. The exploration of stability analysis in these models is vital for a comprehensive understanding of how viruses replicate and the underlying mechanisms involved. The adaptive immune response is also a crucial factor in combating viruses and preventing their growth. The recognition of a foreign substance or antigen initiates the activation of the adaptive immune response, which in turn mobilizes immune cells to launch an attack against the antigen, aiming to eliminate it from the body. The immune response against CHIKV infection involves the coordinated action of two key components: cytotoxic T-lymphocytes (CTL) cells and the antibody immune response. Cytotoxic T-lymphocytes, also known as killer T-cells, play a crucial role in directly combating CHIKV-infected cells. These specialized cells recognize specific viral antigens presented on the surface of infected cells and initiate a targeted attack to eliminate them. By releasing cytotoxic molecules, such as perforin and granzymes, CTL cells induce apoptosis (cell death) in the infected cells, preventing the virus from replicating further (Tanabe et al. (2018), Hoarau et al. (2010)).

On the other hand, the antibody immune response works to neutralize CHIKV infections. B cells, a type of white blood cell, produce antibodies that are specifically designed to recognize and bind to CHIKV antigens. These antibodies can directly neutralize the virus by inhibiting its ability to enter host cells, blocking viral replication, and marking it for destruction by other immune cells (Tanabe et al. (2018)). Additionally, antibodies can activate complement proteins, leading to the formation of membrane attack complexes that can directly lyse CHIKV particles (Silva et al. (2017)).

Together, the cytotoxic T-lymphocytes and the antibody immune response act in a coordinated manner to effectively combat CHIKV infections. Their combined efforts help limit the spread of the virus, clear infected cells, and ultimately contribute to the resolution of CHIKV-associated symptoms.

In light of the recent CHIKV outbreaks, the scientific literature has extensively focused on the transmission dynamics of the disease between mosquito populations and human populations, as evidenced by numerous mathematical models (Dumont and Chiroleu (2010); Dumont and Tchuenche (2012); Moulay et al. (2011); Moulay et al. (2012); Manore et al. (2014); Yakob and Clements (2013)). Although there have been some mathematical models developed for studying the dynamics of CHIKV, only a few have focused on within-host dynamics. Moreover, there is a significant gap in the current research as no studies have been conducted on the adaptive immune response of CHIKV dynamics models with time delay. Most recently, authors in Alade et al. (2023) considered the need to incorporate cytotoxic T-lymphocytes (CTL) cells representing adaptive immune response into a within-host CHIKV model proposed by Wang and Liu (2017).

However, to the best of our knowledge, a mathematical model for a within-host CHIKV dynamics incorporating essential features such as saturated incidence, adaptive immune response, latency and distributed time delays has not been studied in the literature. Therefore, the objective of this paper is to expand upon the previously examined model studied in Alade et al. (2023) by taking into account all the aforementioned essential features. Incorporating distributed time delays into mathematical models of CHIKV dynamics is essential in accurately predicting the spread and behavior of virus. This time delays account for the time it takes for a CHIKV to replicate and spread throughout a host organism or between hosts, and how this process may vary across different individuals or populations. It can also help to identify critical time points in the disease progression, which can aid in the development of effective intervention strategies.

The study is organized as follows. Section 2 presents an in-depth exploration of the within-host CHIKV transmission dynamics model, specifically focusing on the formulation and analysis of the model considering the adaptive immune response and distributed time delays. This is followed up by the establishment of the global stability analysis of the model in Section 3. Numerical simulations of the proposed model are carried out in Section 4, while the concluding remarks are provided in Section 5.

2. Model Formulation

We consider a model that characterizes the dynamics of within-host CHIKV, incorporating an adaptive immune response and accounting for distributed time delays as:

$$\dot{W}(t) = \mu - \xi W(t) - \frac{bG(t)W(t)}{1+\pi G(t)}, \tag{1}$$

$$\dot{X}(t) = (1-\nu)b\int_0^{\kappa_1} \varpi_1(\tau)e^{-\varkappa_1\tau}\frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}d\tau - (\theta+\Omega)X(t), \tag{2}$$

$$\dot{U}(t) = \nu b\int_0^{\kappa_2} \varpi_2(\tau)e^{-\varkappa_2\tau}\frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}d\tau + \Omega X(t) - (d+\epsilon Z(t))U(t), \tag{3}$$

$$\dot{G}(t) = mU(t) - rG(t) - qG(t)A(t), \tag{4}$$

$$\dot{A}(t) = \eta + cA(t)G(t) - \delta A(t), \tag{5}$$

$$\dot{Z}(t) = \gamma + wU(t)Z(t) - \alpha Z(t). \tag{6}$$

In this context, we have the concentrations of different entities represented by W, X, U, G, A, and Z, which correspond to uninfected cells, latently infected cells, actively infected cells, CHIKV particles, antibodies, and CTL cells respectively. The death rate of uninfected cells is given by the parameter ξ, while the birth rate of uninfected cells is represented by μ. The infection of uninfected cells occurs at a rate determined by the product of b, the rate constant of CHIKV-target incidence, W, and G. The saturation parameter is denoted as π. When cells become actively infected, they generate an average of m CHIKV particles, which are targeted by antibodies at a rate of qGA and die at a rate of rG. Upon encountering an antigen, the antibodies undergo continuous growth at a steady rate denoted by η, proliferate at a rate of cAG, and die at a rate of δA.

In this model, it is assumed that a fraction of $(1-\nu)$ of infected cells are in a latent state, while the remaining fraction ν becomes actively infected cells, where $0 < \nu < 1$. The latently infected cells can transmit their infection to actively infected cells at a rate of ΩX, but they also die at a rate of θX. The actively infected cells, on the other hand, die at a rate of dU and are also targeted and killed by the CTL (Cytotoxic T Lymphocyte) response at a rate of ϵUZ. The CTL response expands at a constant rate of γ, proliferates at a rate of wUZ, and dies at a rate of αZ. The term $\varpi_1(\tau)e^{-\varkappa_1\tau}$ represents the probability that uninfected cells, contacted by CHIKV at time $t-\tau$, survive for a duration of τ units of time within the range $[0,\kappa_1]$, and subsequently become latently infected cells at time t. Here, κ_1 denotes the upper limit of this delay. Similarly, $\varpi_2(\tau)e^{-\varkappa_2\tau}$ represents the probability that uninfected cells, contacted by CHIKV at time $t-\tau$, survive for a duration of τ units of time within the range $[0,\kappa_2]$, and later become actively infected cells at time t. In this case, κ_2 represents the upper limit of this delay. The functions $\varpi_1(\tau)$ and $\varpi_2(\tau)$ represent probability distributions that adhere to the conditions $\varpi_1(\tau) > 0$ and $\varpi_2(\tau) > 0$, and

$$\int_0^{\kappa_1} \varpi_1(\tau)d\tau = \int_0^{\kappa_2} \varpi_2(\tau)d\tau = 1,$$
$$\int_0^{\kappa_1} \varpi_1(u)e^{nu}du < \infty, \quad \int_0^{\kappa_2} \varpi_2(u)e^{nu}du < \infty, \tag{7}$$

where n is a positive number. Let

$$E = \int_0^{\kappa_1} \varpi_1(\tau)e^{-\varkappa_1\tau}d\tau \text{ and } \quad K = \int_0^{\kappa_2} \varpi_2(\tau)e^{-\varkappa_2\tau}d\tau.$$

The values of E and K in this model are constrained to fall within the range of 0 to 1, inclusive, denoted as $0 < E \leq 1$ and $0 < K \leq 1$. The initial conditions for the model (1)-(6) are given by the following form:

$$\begin{aligned} &W(\varsigma) = \psi_1(\varsigma), && X(\varsigma) = \psi_2(\varsigma), && U(\varsigma) = \psi_3(\varsigma), \\ &G(\varsigma) = \psi_4(\varsigma), && A(\varsigma) = \psi_5(\varsigma), && Z(\varsigma) = \psi_6(\varsigma), \\ &\psi_j(\varsigma) \geq 0, && \varsigma \in [-\ell, 0], \text{ and} && \psi_j \in C([-\ell,0],\mathbb{R}_{\geq 0}),\ j = 1,...,5, \end{aligned} \tag{8}$$

where $\ell = \max\{\kappa_1, \kappa_2\}$, and C is the Banach space of continuous functions from $[-\ell, 0]$ into $\mathbb{R}_{\geq 0}$ with norm $\|\psi_j\| = \sup_{-\ell\leq\varsigma\leq 0} |\psi_j(\varsigma)|$. This constraint ensures that the system has a unique solution (Hale and Verduyn Lunel (1993)).

2.1. Basic analytical results

In this study, we examine the properties of nonnegativity and boundedness of the solution for the proposed CHIKV dynamics model.

Lemma 2.1.

The solutions of the system described by Equations (1)-(6), given the initial states (8), exhibit nonnegativity and eventually reach a bounded state.

Proof:

By utilizing Equations (1), (5), and (6), we can deduce that, for $W = 0$, it follows that $\dot{W}\Big|_{W=0} = \mu > 0$, and similarly, $\dot{A}\Big|_{A=0} = \eta > 0$ and $\dot{Z}\Big|_{Z=0} = \gamma > 0$. As a result, we can conclude that $W(t) > 0$, $A(t) > 0$, and $Z(t) > 0$ for all $t \geq 0$. Furthermore, within the interval $t \in [0, \tau]$, we have that

$$
\begin{aligned}
X(t) &= e^{-(\theta+\Omega)t}\psi_2(0) \\
&\quad + (1-\nu)b\int_0^t e^{-(\theta+\Omega)(t-u)}\int_0^{\kappa_1} e^{-\varkappa_1\tau}\varpi_1(\tau)\frac{W(u-\tau)G(u-\tau)}{1+\pi G(u-\tau)}d\tau du \geq 0, \\
U(t) &= e^{-\int_0^t (d+\epsilon Z(u))du}\psi_3(0) \\
&\quad + \nu b\int_0^t e^{-\int_\omega^t (d+\epsilon Z(u))du}\left(\int_0^{\kappa_2} e^{-\varkappa_2\tau}\varpi_2(\tau)\frac{W(\omega-\tau)G(\omega-\tau)}{1+\pi G(\omega-\tau)}d\tau + \ \Omega X(\omega)\right)d\omega \geq 0, \\
G(t) &= e^{-\int_0^t (r+qA(u))du}\psi_4(0) \\
&\quad + \int_0^t mU(\omega)e^{-\int_\omega^t (r+qA(u))du}d\omega \geq 0.
\end{aligned}
$$

Using Equation (1), we can deduce that $\limsup_{t\to\infty} W(t) \leq \frac{\mu}{\xi}$.

Let us define $T_1(t) = (1-\nu)\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}W(t-\tau)d\tau + X(t)$. Then,

$$
\begin{aligned}
\dot{T}_1(t) &= (1-\nu)\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\left(\mu - \xi W(t-\tau) - \frac{bG(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}\right)d\tau \\
&\quad + (1-\nu)b\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}d\tau - (\theta+\Omega)X(t) \\
&\leq \mu(1-\nu)E - \bar{\sigma}_3\left((1-\nu)\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}W(t-\tau)d\tau + X(t)\right) \\
&\leq \mu(1-\nu) - \bar{\sigma}_3 T_1(t),
\end{aligned}
$$

where $\bar{\sigma}_3 = \min\{\xi, \theta+\Omega\}$. It follows that $\limsup_{t\to\infty} T_1(t) \leq \bar{N}_1$. Since $\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}W(t-\tau)d\tau > 0$, then $\limsup_{t\to\infty} X(t) \leq \bar{N}_1$, where $\bar{N}_1 = \frac{\mu(1-\nu)}{\bar{\sigma}_3}$. Let

$$
T_2(t) = \nu\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}W(t-\tau)d\tau + U(t) + \frac{d}{2m}G(t) + \frac{dq}{2mc}A(t) + \frac{\epsilon}{w}Z(t),
$$

then we have

$$\begin{aligned}
\dot{T}_2(t) &= \nu \int_0^{\kappa_2} \varpi_2(\tau) e^{-\varkappa_2 \tau} \left(\mu - \xi W(t-\tau) - \frac{bG(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)} \right) d\tau \\
&\quad + \nu b \int_0^{\kappa_2} \varpi_2(\tau) e^{-\varkappa_2 \tau} \frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)} d\tau + \Omega X(t) - (d+\epsilon Z(t))U(t) \\
&\quad + \frac{d}{2m}\left(mU(t) - rG(t) - qG(t)A(t)\right) + \frac{dq}{2mc}\left(\eta + cA(t)G(t) - \delta A(t)\right) \\
&\quad + \frac{\epsilon}{w}(\gamma + wU(t)Z(t) - \alpha Z(t)) \\
&\leq \mu\nu K + \Omega \bar{N}_1 + \frac{dq\eta}{2mc} + \frac{\epsilon\gamma}{w} \\
&\quad - \bar{\sigma}_4 \left(\nu \int_0^{\kappa_2} \varpi_2(\tau) e^{-\varkappa_2 \tau} W(t-\tau) d\tau + U(t) + \frac{d}{2m} G(t) + \frac{dq}{2mc} A(t) + \frac{\epsilon}{w} Z(t) \right) \\
&\leq \mu\nu + \Omega \bar{N}_1 + \frac{dq\eta}{2mc} + \frac{\epsilon\gamma}{w} - \bar{\sigma}_4 T_2(t),
\end{aligned}$$

where $\bar{\sigma}_4 = \min\{\xi, \frac{d}{2}, r, \delta, \alpha\}$. Then $\limsup_{t\to\infty} T_2(t) \leq \bar{N}_2$. It follows that $\limsup_{t\to\infty} U(t) \leq \bar{N}_2$, $\limsup_{t\to\infty} G(t) \leq \bar{N}_3$, $\limsup_{t\to\infty} A(t) \leq \bar{N}_4$, and $\limsup_{t\to\infty} Z(t) \leq \bar{N}_5$. As a result, $W(t)$, $X(t)$, $U(t)$, $G(t)$, $A(t)$, and $Z(t)$ are ultimately bounded. ■

2.2. Steady states and threshold parameter

In this subsection, we demonstrate the presence of steady states in model (1)-(6). To achieve this, we utilize the approach introduced by Diekmann et al. (1990) and Van den Driessche and Watmough (2002). These methods enable us to express the basic reproduction number of system (1)-(6) as

$$\mathcal{R}_0^D = \frac{\Psi m b \mu \delta \alpha}{\xi(\alpha d + \epsilon\gamma)(r\delta + q\eta)(\theta + \Omega)},$$

where $\Psi = \Omega(1-\nu)e^{-\varkappa_1 \tau} + \nu e^{-\varkappa_2 \tau}(\theta + \Omega)$.

Considering the right-hand side (RHS) of system (1)-(6) as zero, we have the following expressions:

$$0 = \mu - \xi W - \frac{bGW}{1+\pi G}, \tag{9}$$

$$0 = E(1-p)\frac{bGW}{1+\pi G} - (\theta + \Omega)X, \tag{10}$$

$$0 = \frac{KpbWG}{1+\pi G} + \Omega X - (d+\epsilon Z)U, \tag{11}$$

$$0 = mU - rG - qGA, \tag{12}$$

$$0 = \eta + cAG - \delta A, \tag{13}$$

$$0 = \gamma + wUZ - \alpha Z. \tag{14}$$

System (1)-(6) admits a virus-free steady state $Q_0(W_0, 0, 0, 0, A_0, Z_0)$, where $W_0 = \frac{\mu}{\xi}$, $A_0 = \frac{\eta}{\delta}$, and $Z_0 = \frac{\gamma}{\alpha}$.

It is worth mentioning that each equation of the coupled Equations (9)-(14) is nonlinear. Therefore, we omit solving analytical expression for the nontrivial steady state $Q_1(W_1, X_1, U_1, G_1, A_1, Z_1)$ due to the complexity of the system.

However, the existence of the endemic state of the system is confirmed through numerical simulations.

3. Global stability analysis

This section presents the establishment of global stability for the two steady states of system (1)-(6) through the construction of suitable Lyapunov functionals, following the approach presented in Ghaleb et al. (2022)-Elaiw et al. (2018b).

Theorem 3.1.

Suppose that $\mathcal{R}_0^D \leq 1$. Then, Q_0 exhibits global asymptotic stability.

Proof:

Let us define $Y_0^D(W, X, U, G, A, Z)$ as:

$$Y_0^D = \frac{\Psi}{\theta+\Omega} W_0 H\left(\frac{W}{W_0}\right) + \frac{\Omega}{\theta+\Omega} X + U \tag{15}$$

$$+ \frac{(d+\epsilon Z_0)}{m} G + \frac{(d+\epsilon Z_0)q}{mc} A_0 H\left(\frac{A}{A_0}\right)$$

$$+ \frac{\epsilon}{w} Z_0 H\left(\frac{Z}{Z_0}\right) \tag{16}$$

$$+ \frac{\Omega(1-\nu)b}{\theta+\Omega} \int_0^{\kappa_1} \varpi_1(\tau) e^{-\varkappa_1 \tau} \int_0^{\tau} \frac{G(t-\varrho)W(t-\varrho)}{1+\pi G(t-\varrho)} d\varrho d\tau$$

$$+ \nu b \int_0^{\kappa_2} \varpi_2(\tau) e^{-\varkappa_2 \tau} \int_0^{\tau} \frac{G(t-\varrho)W(t-\varrho)}{1+\pi G(t-\varrho)} d\varrho d\tau. \tag{17}$$

Note that $Y_0^D(W, X, U, G, A, Z) > 0$ for all $W, X, U, G, A, Z > 0$ and $Y_0^D(W_0, 0, 0, 0, A_0, Z_0) = 0$. By differentiating Y_0^D with respect to time along the trajectories of (1)-(6), we obtain the ex-

pression as

$$\begin{aligned}
\frac{dY_0^D}{dt} &= \frac{\Psi}{\theta+\Omega}\left(1-\frac{W_0}{W}\right)\left(\mu-\xi W-\frac{bGW}{1+\pi G}\right)\\
&\quad+\frac{\Omega}{\theta+\Omega}\left((1-\nu)b\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}d\tau-(\theta+\Omega)X\right)\\
&\quad+\nu b\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}d\tau+\Omega X-(d+\epsilon Z)U\\
&\quad+\frac{(d+\epsilon Z_0)}{m}\left(mU-rG-qGA\right)\\
&\quad+\frac{(d+\epsilon Z_0)q}{mc}\left(1-\frac{A_0}{A}\right)(\eta+cAG-\delta A)+\frac{\epsilon}{w}\left(1-\frac{Z_0}{Z}\right)(\gamma+wUZ-\alpha Z)\\
&\quad+\frac{\Omega(1-\nu)}{\theta+\Omega}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\left(\frac{bGW}{1+\pi G}-\frac{bG(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}\right)d\tau\\
&\quad+\nu b\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\left(\frac{bGW}{1+\pi G}-\frac{bG(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}\right)d\tau\\
&=\frac{\Psi}{\theta+\Omega}\left(1-\frac{W_0}{W}\right)(\xi W_0-\xi W)+\left(\frac{\Psi}{\theta+\Omega}\right)\frac{bW_0G}{1+\pi G}\\
&\quad-\frac{(d+\epsilon Z_0)rG}{m}-\frac{(d+\epsilon Z_0)qA_0G}{m}\\
&\quad+\frac{(d+\epsilon Z_0)q}{mc}\left(1-\frac{A_0}{A}\right)(\delta A_0-\delta A)+\frac{\epsilon}{w}\left(1-\frac{Z_0}{Z}\right)(\alpha Z_0-\alpha Z)\\
&=-\frac{\xi\Psi}{\theta+\Omega}\frac{(W-W_0)^2}{W}-\frac{(d+\epsilon Z_0)q\delta}{mc}\frac{(A-A_0)^2}{A}-\frac{\epsilon\alpha}{w}\frac{(Z-Z_0)^2}{Z}\\
&\quad+\frac{(d+\epsilon Z_0)(r\delta+q\eta)}{m}\left(\frac{\Psi bm\mu\delta\alpha}{\xi(\theta+\Omega)(1+\pi G)(\alpha d+\epsilon\gamma)(r\delta+q\eta)}-1\right)G\\
&=-\frac{\xi\Psi}{\theta+\Omega}\frac{(W-W_0)^2}{W}-\frac{(d+\epsilon Z_0)q\delta}{mc}\frac{(A-A_0)^2}{A}-\frac{\epsilon\alpha}{w}\frac{(Z-Z_0)^2}{Z}\\
&\quad+\frac{(\alpha d+\epsilon\gamma)(r\delta+q\eta)}{m\alpha\delta}(\mathcal{R}_0^D-1)G-\frac{(\alpha d+\epsilon\gamma)(r\delta+q\eta)\mathcal{R}_0^D\pi G^2}{m\alpha\delta(1+\pi G)}. \qquad (18)
\end{aligned}$$

Therefore, $\frac{dY_0^D}{dt}\leq 0$ holds if $\mathcal{R}_0^D\leq 1$. Furthermore, $\frac{dY_0^D}{dt}=0$ if and only if $W=W_0$, $A=A_0$, $Z=Z_0$, and $G=0$. The solutions of system (1)-(6) converge to Γ, the largest invariant set of $\{(W,X,U,G,A,Z):\frac{dY_0^D}{dt}=0\}$. For any element in Γ satisfies $G(t)=\dot{G}(t)=0$. Then, from Equation (4) we have $U(t)=0$. According to the LaSalle's invariance principle (Hale and Verduyn Lunel (1993)), Q_0 is proven to exhibit global asymptotic stability. ∎

Theorem 3.2.

Suppose that Q_1 exists. Then, it is globally asymptotically stable.

Proof:

Define the function

$$
\begin{aligned}
Y_1^D(W,X,U,G,A,Z) = {} & \frac{\Psi}{\theta+\Omega}W_1H\left(\frac{W}{W_1}\right)+\frac{\Omega}{\theta+\Omega}X_1H\left(\frac{X}{X_1}\right)+U_1H\left(\frac{U}{U_1}\right)\\
& +\frac{(d+\epsilon Z_1)}{m}G_1H\left(\frac{G}{G_1}\right)+\frac{(d+\epsilon Z_0)q}{mc}A_1H\left(\frac{A}{A_1}\right)+\frac{\epsilon}{w}Z_1H\left(\frac{Z}{Z_1}\right)\\
& +\frac{\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\\
& \times\int_0^{\tau}H\left(\frac{G(t-\varrho)W(t-\varrho)(1+\pi G_1)}{W_1G_1\left(1+\pi G(t-\varrho)\right)}\right)d\varrho d\tau\\
& +\frac{\nu bW_1G_1}{1+\pi G_1}\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\int_0^{\tau}H\left(\frac{G(t-\varrho)W(t-\varrho)(1+\pi G_1)}{W_1G_1\left(1+\pi G(t-\varrho)\right)}\right)d\varrho d\tau.
\end{aligned}
$$

We have $Y_1^D(W,X,U,G,A,Z) > 0$ for all $W,X,U,G,A,Z > 0$ and $Y_1^D(W_1,X_1,U_1,G_1,A_1,Z_1)=0$.

Calculating $\frac{dY_1^D}{dt}$ along the system (1)-(6), we get

$$
\begin{aligned}
\frac{dY_1^D}{dt} = {} & \frac{\Psi}{\theta+\Omega}\left(1-\frac{W_1}{W}\right)\left(\mu-\xi W-\frac{bGW}{1+\pi G}\right)\\
& +\frac{\Omega}{\theta+\Omega}\left(1-\frac{X_1}{X}\right)\left((1-\nu)b\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}d\tau-(\theta+\Omega)X\right)\\
& +\left(1-\frac{U_1}{U}\right)\left(\nu b\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\frac{G(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}d\tau+\Omega X-(d+\epsilon Z)U\right)\\
& +\frac{(d+\epsilon Z_1)}{m}\left(1-\frac{G_1}{G}\right)(mU-rG-qGA)+\frac{(d+\epsilon Z_1)q}{mc}\left(1-\frac{A_1}{A}\right)(\eta+cAG-\delta A)\\
& +\frac{\epsilon}{w}\left(1-\frac{Z_1}{Z}\right)(\gamma+wUZ-\alpha Z)\\
& +\frac{\Omega(1-\nu)}{(\theta+\Omega)}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\left(\frac{bGW}{1+\pi G}-\frac{bG(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}\right)d\tau\\
& +\frac{\Omega(1-\nu)}{(\theta+\Omega)}\frac{bW_1G_1}{1+\pi G_1}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\left(1+\pi G(t-\tau)\right)}\right)d\tau\\
& +\nu\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\left(\frac{bGW}{1+\pi G}-\frac{bG(t-\tau)W(t-\tau)}{1+\pi G(t-\tau)}\right)d\tau\\
& +\frac{\nu bW_1G_1}{1+\pi G_1}\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\left(1+\pi G(t-\tau)\right)}\right)d\tau. \qquad (19)
\end{aligned}
$$

Applying

$$\mu=\xi W_1+\frac{bW_1G_1}{1+\pi G_1},\ \eta=\delta A_1-cA_1G_1,\ \gamma=\alpha Z_1-wU_1Z_1,$$

we obtain

$$\begin{aligned}
\frac{dY_1^D}{dt} &= \frac{\Psi}{\theta+\Omega}\left(1-\frac{W_1}{W}\right)(\xi W_1-\xi W)\\
&+\left(\frac{\Psi}{\theta+\Omega}\right)\frac{bW_1G_1}{1+\pi G_1}\left(1-\frac{W_1}{W}\right)\\
&+\frac{\Psi}{\theta+\Omega}\frac{bW_1G}{1+\pi G}\\
&-\frac{\Omega(1-\nu)b}{\theta+\Omega}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\frac{G(t-\tau)W(t-\tau)X_1}{(1+\pi G(t-\tau))\,X}d\tau\\
&+\Omega X_1-\nu b\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\frac{G(t-\tau)W(t-\tau)U_1}{(1+\pi G(t-\tau))\,U}d\tau\\
&-\frac{\Omega XU_1}{U}+(d+\epsilon Z)U_1\\
&-\frac{(d+\epsilon Z_1)UG_1}{G}-\frac{(d+\epsilon Z_1)rG}{m}\\
&+\frac{(d+\epsilon Z_1)rG_1}{m}+\frac{(d+\epsilon Z_1)qAG_1}{m}+\frac{(d+\epsilon Z_1)q}{mc}\left(1-\frac{A_1}{A}\right)(\delta A_1-\delta A)\\
&-\frac{(d+\epsilon Z_1)qA_1G}{m}-\frac{(d+\epsilon Z_1)qA_1G_1}{m}\\
&+\frac{(d+\epsilon Z_1)qA_1G_1}{m}\left(\frac{A_1}{A}\right)\\
&-\epsilon U_1Z_1+\epsilon U_1Z_1\left(\frac{Z_1}{Z}\right)+\frac{\epsilon}{w}\left(1-\frac{Z_1}{Z}\right)(\alpha Z_1-\alpha Z)\\
&+\frac{\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\,(1+\pi G(t-\tau))}\right)d\tau\\
&+\frac{\nu bW_1G_1}{1+\pi G_1}\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\,(1+\pi G(t-\tau))}\right)d\tau.
\end{aligned}$$

The components forming the steady state Q_1 satisfy the conditions

$$\begin{aligned}
E(1-\nu)\frac{bW_1G_1}{1+\pi G_1} &= (\theta+\Omega)X_1,\\
K\nu\frac{bW_1G_1}{1+\pi G_1}+\Omega X_1 &= (d+\epsilon Z_1)U_1,\\
mU_1 &= rG_1+qA_1G_1,
\end{aligned}$$

then

$$\begin{aligned}
(d+\epsilon Z_1)U_1 &= \frac{\Psi}{\theta+\Omega}\frac{bW_1G_1}{(1+\pi G_1)},\\
\frac{(d+\epsilon Z_1)rG_1}{m} &= \frac{\Psi}{\theta+\Omega}\frac{bW_1G_1}{(1+\pi G_1)}-\frac{(d+\epsilon Z_1)qA_1G_1}{m},
\end{aligned}$$

and

$$\begin{aligned}
\frac{dY_1^D}{dt} &= -\frac{\xi\Psi}{\theta+\Omega}\frac{(W-W_1)^2}{W} + \frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\left(1-\frac{W_1}{W}\right)\\
&+ K\nu\frac{bW_1G_1}{(1+\pi G_1)}\left(1-\frac{W_1}{W}\right) + \left(\frac{\Psi}{\theta+\Omega}\right)\frac{bW_1G_1}{1+\pi G_1}\left(\frac{(1+\pi G_1)G}{(1+\pi G)G_1}-\frac{G}{G_1}\right)\\
&- \frac{\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)X_1}{(1+\pi G(t-\tau))W_1G_1X}d\tau\\
&+ \frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{(1+\pi G_1)}\\
&- \frac{\nu bW_1G_1}{1+\pi G_1}\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)U_1}{(1+\pi G(t-\tau))W_1G_1U}d\tau\\
&- \frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\frac{U_1X}{X_1U}\\
&+ \frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{(1+\pi G_1)} + K\nu\frac{bW_1G_1}{(1+\pi G_1)}\\
&- \frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\frac{UG_1}{U_1G}\\
&- K\nu\frac{bW_1G_1}{1+\pi G_1}\frac{UG_1}{U_1G} + \frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{(1+\pi G_1)} + K\nu\frac{bW_1G_1}{(1+\pi G_1)}\\
&- \frac{2(d+\epsilon Z_1)qA_1G_1}{m} + \frac{(d+\epsilon Z_1)qAG_1}{m} + \frac{(d+\epsilon Z_1)qA_1G_1}{m}\left(\frac{A_1}{A}\right)\\
&- \frac{(d+\epsilon Z_1)q\delta}{mc}\frac{(A-A_1)^2}{A} - 2\epsilon U_1Z_1 + \epsilon U_1Z + \epsilon U_1Z_1\left(\frac{Z_1}{Z}\right) - \frac{\epsilon\alpha}{w}\frac{(Z-Z_1)^2}{Z}\\
&+ \frac{\Omega(1-\nu)}{(\theta+\Omega)}\frac{bW_1G_1}{1+\pi G_1}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\,(1+\pi G(t-\tau))}\right)d\tau\\
&+ \frac{\nu bW_1G_1}{1+\pi G_1}\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\,(1+\pi G(t-\tau))}\right)d\tau.
\end{aligned}$$

By using the subsequent equalities,

$$\begin{aligned}
\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\,(1+\pi G(t-\tau))}\right) &= \ln\left(\frac{W_1}{W}\right) + \ln\left(\frac{UG_1}{U_1G}\right) + \ln\left(\frac{1+\pi G}{1+\pi G_1}\right) + \ln\left(\frac{XU_1}{X_1U}\right)\\
&\quad + \ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)X_1}{(1+\pi G(t-\tau))W_1G_1X}\right),\\
\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G)}{GW\,(1+\pi G(t-\tau))}\right) &= \ln\left(\frac{W_1}{W}\right) + \ln\left(\frac{UG_1}{U_1G}\right) + \ln\left(\frac{1+\pi G}{1+\pi G_1}\right)\\
&\quad + \ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)U_1}{(1+\pi G(t-\tau))W_1G_1U}\right),
\end{aligned}$$

we have

$$\begin{aligned}
\frac{dY_1^D}{dt} &= -\frac{\xi\Psi}{\theta+\Omega}\frac{(W-W_1)^2}{W} + \frac{\Psi}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\left(-1+\frac{(1+\pi G_1)G}{(1+\pi G)G_1}-\frac{G}{G_1}+\frac{1+\pi G}{1+\pi G_1}\right)\\
&+\frac{E\Omega(1-\nu)}{(\theta+\Omega)}\frac{bW_1G_1}{(1+\pi G_1)}\left[1-\frac{W_1}{W}+\ln\left(\frac{W_1}{W}\right)\right]\\
&+\frac{E\Omega(1-\nu)}{(\theta+\Omega)}\frac{bW_1G_1}{(1+\pi G_1)}\left[1-\frac{UG_1}{U_1G}+\ln\left(\frac{UG_1}{U_1G}\right)\right]\\
&+\frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\frac{1}{E}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}\left[1-\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)X_1}{(1+\pi G(t-\tau))W_1G_1X}\right.\\
&\left.+\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)X_1}{(1+\pi G(t-\tau))W_1G_1X}\right)\right]d\tau\\
&+\frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\left[1-\frac{1+\pi G}{1+\pi G_1}+\ln\left(\frac{1+\pi G}{1+\pi G_1}\right)\right]\\
&+\frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{(1+\pi G_1)}\left[1-\frac{XU_1}{X_1U}+\ln\left(\frac{XU_1}{X_1U}\right)\right]\\
&+K\nu\frac{bW_1G_1}{(1+\pi G_1)}\left[1-\frac{W_1}{W}+\ln\left(\frac{W_1}{W}\right)\right]+K\nu\frac{bW_1G_1}{1+\pi G_1}\left[1-\frac{UG_1}{U_1G}+\ln\left(\frac{UG_1}{U_1G}\right)\right]\\
&+K\nu\frac{bW_1G_1}{1+\pi G_1}\frac{1}{K}\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}\left[1-\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)U_1}{(1+\pi G(t-\tau))W_1G_1U}\right.\\
&\left.+\ln\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)U_1}{(1+\pi G(t-\tau))W_1G_1U}\right)\right]d\tau\\
&+K\nu\frac{bW_1G_1}{(1+\pi G_1)}\left[1-\frac{1+\pi G}{1+\pi G_1}+\ln\left(\frac{1+\pi G}{1+\pi G_1}\right)\right]\\
&-\frac{(d+\epsilon Z_1)q\delta}{mc}\frac{(A-A_1)^2}{A}-\frac{(d+\epsilon Z_1)qA_1G_1}{m}\left[2-\frac{A}{A_1}-\frac{A_1}{A}\right]-\frac{\epsilon\alpha}{w}\frac{(Z-Z_1)^2}{Z}\\
&-\epsilon U_1Z_1\left[2-\frac{Z}{Z_1}-\frac{Z_1}{Z}\right] \qquad (20)
\end{aligned}$$

$$\begin{aligned}
&= -\xi\left(\frac{\Psi}{\theta+\Omega}\right)\frac{(W-W_1)^2}{W}-\left(\frac{\Psi}{\theta+\Omega}\right)\frac{\pi bW_1(G-G_1)^2}{(1+\pi G)(1+\pi G_1)^2}-\frac{(d+\epsilon Z_1)q\eta}{mcA_1}\frac{(A-A_1)^2}{A}\\
&-\frac{\epsilon\gamma}{wZ_1}\frac{(Z-Z_1)^2}{Z}-\frac{E\Omega(1-\nu)}{\theta+\Omega}\frac{bW_1G_1}{1+\pi G_1}\left[H\left(\frac{W_1}{W}\right)+H\left(\frac{UG_1}{U_1G}\right)+H\left(\frac{1+\pi G}{1+\pi G_1}\right)\right.\\
&\left.+H\left(\frac{XU_1}{X_1U}\right)+\frac{1}{E}\int_0^{\kappa_1}\varpi_1(\tau)e^{-\varkappa_1\tau}H\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)X_1}{(1+\pi G(t-\tau))W_1G_1X}\right)d\tau\right]\\
&-K\nu\frac{bW_1G_1}{(1+\pi G_1)}\left[H\left(\frac{W_1}{W}\right)+H\left(\frac{UG_1}{U_1G}\right)+H\left(\frac{1+\pi G}{1+\pi G_1}\right)\right.\\
&\left.+\frac{1}{K}\int_0^{\kappa_2}\varpi_2(\tau)e^{-\varkappa_2\tau}H\left(\frac{G(t-\tau)W(t-\tau)(1+\pi G_1)U_1}{(1+\pi G(t-\tau))W_1G_1U}\right)d\tau\right].
\end{aligned}$$

It can be seen that if Q_1 exists, then $W_1, X_1, U_1, G_1, A_1, Z_1 > 0$ and $\frac{dY_1^D}{dt} \leq 0$ for all

$W, X, U, G, A, Z > 0$. We have $\frac{dY_1^D}{dt} = 0$ if and only if $W = W_1$, $X = X_1$, $U = U_1$, $G = G_1$, $A = A_1$, $Z = Z_1$, and $H = 0$. Then, from LaSalle's invariance principle, Q_1 is globally asymptotically stable. ■

4. Numerical simulations

We perform numerical simulations for the system (1)-(6) with particular distribution functions $\varpi_1(\tau)$ and $\varpi_2(\tau)$ as:

$$\varpi_i(\tau) = \delta(\tau - \varkappa_i),\ i = 1, 2, \tag{21}$$

where $\delta(.)$ is the Dirac delta function, $\varkappa_1$ and $\varkappa_2$ are positive constants. Then, we can see that,

$$\begin{aligned} \int_0^{\kappa_1} \varpi_1(\tau)d\tau = \int_0^{\kappa_2} \varpi_2(\tau)d\tau = 1, \\ E = \int_0^{\kappa_1} \delta(\tau - \varkappa_1)e^{-\varkappa_1\tau}d\tau = e^{-\varkappa_1\tau_1}, \\ K = \int_0^{\kappa_2} \delta(\tau - \varkappa_2)e^{-\varkappa_2\tau}d\tau = e^{-\varkappa_2\tau_2}. \end{aligned} \tag{22}$$

$$\int_0^{\kappa_i} \delta(\tau - \delta_i)e^{-\delta\tau}\zeta(t-\tau)d\tau = e^{-\delta_i\tau_i}\zeta(t-\tau_i),\ i = 1, 2, \tag{23}$$

for any function ζ. From Equations (21), (22) and (23), system (1)-(6) leads to:

$$\dot{W}(t) = \mu - \xi W(t) - \frac{bG(t)W(t)}{1 + \pi G(t)}, \tag{24}$$

$$\dot{X}(t) = \frac{(1-\nu)e^{-\varkappa_1\tau_1}bG(t-\tau_1)W(t-\tau_1)}{1 + \pi G(t-\tau_1)} - (\theta + \Omega)X(t), \tag{25}$$

$$\dot{U}(t) = \frac{\nu e^{-\varkappa_2\tau_2}bG(t-\tau_2)W(t-\tau_2)}{1 + \pi G(t-\tau_2)} + \Omega X(t) - (d + \epsilon Z(t))U(t), \tag{26}$$

$$\dot{G}(t) = mU(t) - rG(t) - qA(t)G(t), \tag{27}$$

$$\dot{A}(t) = \eta + cA(t)G(t) - \delta A(t), \tag{28}$$

$$\dot{Z}(t) = \gamma + wU(t)Z(t) - \alpha Z(t). \tag{29}$$

The basic reproduction number for system (24)-(29) is defined as:

$$\mathcal{R}_0 = \frac{\beta m b \mu \delta \alpha}{\xi(\alpha d + \epsilon\gamma)(r\delta + q\eta)(\theta + \Omega)},$$

where $\beta = \Omega(1-\nu)e^{-\varkappa_1\tau_1} + \nu e^{-\varkappa_2\tau_2}(\theta + \Omega)$.

Now, we conduct numerical simulations for system (24)-(29) with parameter values: $\mu = 1.826$, $\theta = 0.5$, $m = 2.02$, $q = 0.5964$, $\tau_1, \tau_2 =$ varied, $\Omega = 0.1$, $\varkappa_1 = 0.5$, $r = 0.4418$, $\epsilon = 0.4441$,

$\pi = 0.1$, $c = 0.5$, $\gamma = 0.5$, $\eta = 1.402$, $\alpha = 1.2$, $\delta = 1.251$, $\xi = 0.7979$, $\varkappa_2 = 0.5$, $\nu = 0.5$, $b =$ varied, $w = 0.5$, $d = 0.5$. We discuss the effect of the incidence rate constant b on the qualitative behavior of the system by considering two sets and assume $\tau_e = \tau_1 = \tau_2 = 0.5$. We perform the following:

Set (I): We take $b = 0.05$, and compute $\mathcal{R}_0 = 0.1381 < 1$. The results depicted in Figure 1 indicate that the concentrations of uninfected cells, antibodies, and CTL cells tend to stabilize at their normal levels of $W_0 = 2.2885$, $A_0 = 1.1207$ and $Z_0 = 0.4167$, respectively. Meanwhile, the concentrations of latently and actively infected cells as well as CHIKV particles are seen to decay and eventually reach zero. Therefore, the system's solutions ultimately lead to the CHIKV-free steady state Q_0, which is proven to be globally asymptotically stable in Theorem 3.1. These results provide evidence that the CHIKV can be eradicated through this model.

Set (II): By selecting $b = 1.5$ and calculating $\mathcal{R}_0 = 4.1421 > 1$, we determine that the system possesses two positive steady states, denoted as Q_0 and Q_1. Notably, the state Q_1 is globally asymptotically stable (GAS). Figure 1 illustrates the changes in concentration of various cell types and CHIKV particles over time. Specifically, the concentration of uninfected cells is observed to decrease while the concentrations of latently and actively infected cells as well as CHIKV particles are seen to increase. The increase in CHIKV particles and actively infected cells results in an upsurge in the proliferation rates of both antibodies and CTL cells, leading to an increase in their respective concentrations. Ultimately, the system reaches a steady state $Q_1 = (0.8931, 0.7226, 0.6686, 0.9065, 1.7575, 0.5776)$, which is consistent with the findings presented in Theorem 3.2.

Subsequently, we proceed to examine the impact of time delays on the stability of the steady states. While keeping $b = 1.5$ fixed, we explore the parameter τ_e over a range of values. We then examine the system's behavior using the following initial conditions:

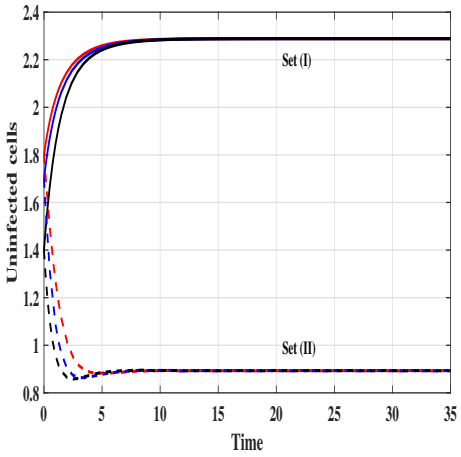
$$\varsigma_1(\varrho) = 1.4, \varsigma_2(\varrho) = 0.3, \varsigma_3(\varrho) = 0.4, \varsigma_4(\varrho) = 0.4, \varsigma_5(\varrho) = 1.7,\ \varsigma_6(\varrho) = 0.5,\ \varrho \in [-\tau_e, 0]$$

Figure 2 illustrates the temporal evolution of the states of system W, X, U, G, A, and Z. Observing the system's dynamics, we find that for smaller values of τ_e, specifically $\tau_e = 0.0, 0.5, 1.5$, and 3.0, the calculated $\mathcal{R}_0$ values all exceed 1. This implies that the system's trajectory tends towards the steady state Q_1, in accordance with the findings of Theorem 3.2. However, as τ_e increases to larger values, for instance $\tau_e = 3.5$ and 5.0, the value of $\mathcal{R}_0$ becomes less than 1, indicating the existence of a positive steady state Q_0, in accordance with the findings of Theorem 3.1. In this scenario, the body's immune responses effectively eliminate CHIKV particles, leading to their successful clearance from the host.

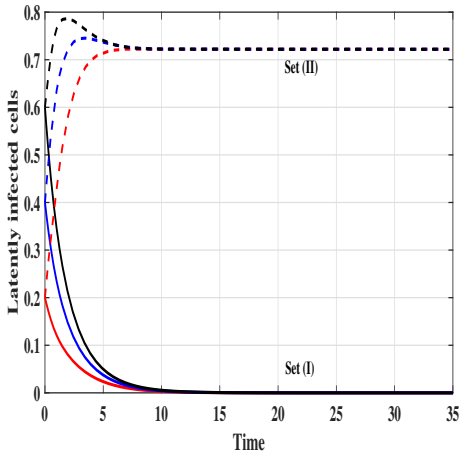
Let denote τ^{cr} as the critical threshold of the parameter τ_e, such that

$$\mathcal{R}_0 = \frac{mb\mu\delta\alpha\left(\Omega(1-\nu)e^{-\varkappa_1\tau^{cr}} + \nu e^{-\varkappa_2\tau^{cr}}(\theta+\Omega)\right)}{\xi(\alpha d + \epsilon\gamma)(r\delta + q\eta)\left(\theta + \Omega\right)} = 1.$$

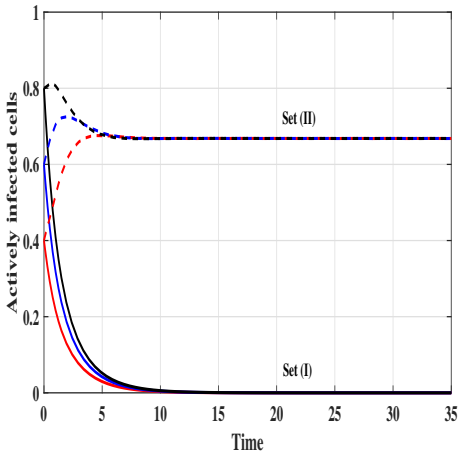
Based on the data presented in Table 1, the critical value of τ is determined to be $\tau^{cr} = 3.34243$. Subsequently, Table 2 provides the values of $\mathcal{R}_0$ for various values of τ_e. It can be observed that as τ_e increases, the value of $\mathcal{R}_0$ decreases. Furthermore, the following scenarios can be identified:



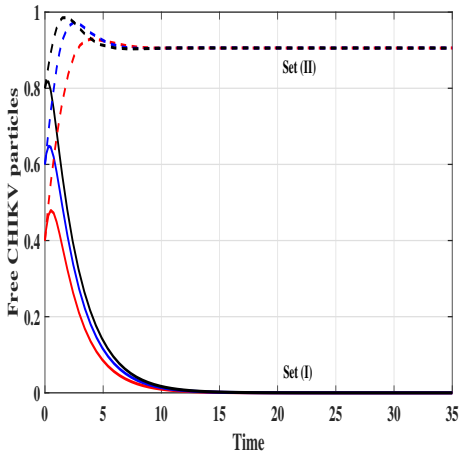
(a) The uninfected cells.



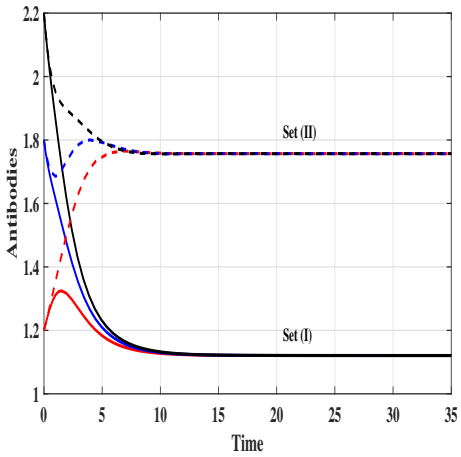
(b) The latently infected cells.



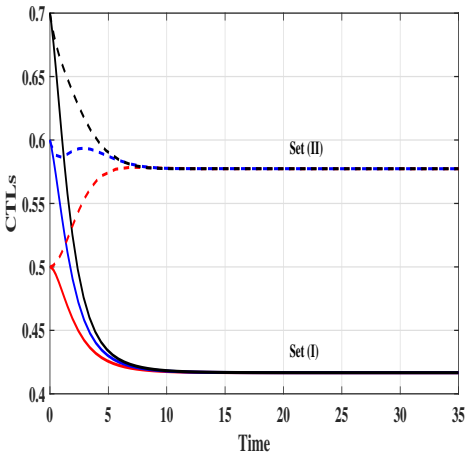
(c) The actively infected cells.



(d) The CHIKV particles.



(e) The antibodies.



(f) The CTLs.

Figure 1. Impact of the incidence rate parameter b on the stability of the steady states

(i) if $0 \leq \tau_e < 3.34243$, then Q_1 exists and it is globally asymptotically stable,

(ii) if $\tau_e \geq 3.34243$, then Q_0 is globally asymptotically stable. Obviously, as the time delay increases, the system exhibits a stabilization effect, converging towards the steady state Q_0. From a biological perspective, time delays in the CHIKV dynamics model can have a comparable effect to that of antiviral treatment, which is used to eliminate the virus. Specifically, our findings suggest that delays of sufficient magnitude can decrease CHIKV replication and aid in the eradication of the virus.

Table 1. Steady state values and $\mathcal{R}_0$ for model (24)-(29) with different τ_e

τ_e	Steady states	R_0
0.0	$Q_1 = (0.8052, 0.9863, 0.8730, 1.0864, 1.9809, 0.6549)$	5.3186
0.5	$Q_1 = (0.8931, 0.7226, 0.6686, 0.9065, 1.7575, 0.5776)$	4.1421
1.0	$Q_1 = (1.0114, 0.5151, 0.4920, 0.7200, 1.5736, 0.5241)$	3.2259
1.5	$Q_1 = (1.1684, 0.3518, 0.3439, 0.5373, 1.4272, 0.4864)$	2.5123
2.0	$Q_1 = (1.3747, 0.2235, 0.2223, 0.3666, 1.3131, 0.4592)$	1.9566
2.5	$Q_1 = (1.6436, 0.1229, 0.1237, 0.2132, 1.2251, 0.4393)$	1.5238
3.0	$Q_1 = (1.9924, 0.0439, 0.0447, 0.0797, 1.1576, 0.4246)$	1.1867
3.34243	$Q_0 = (2.2885, 0, 0, 0, 1.1207, 0.4167)$	1.0000
3.5	$Q_0 = (2.2885, 0, 0, 0, 1.1207, 0.4167)$	0.9242
4.0	$Q_0 = (2.2885, 0, 0, 0, 1.1207, 0.4167)$	0.7198
4.5	$Q_0 = (2.2885, 0, 0, 0, 1.1207, 0.4167)$	0.5606
5.0	$Q_0 = (2.2885, 0, 0, 0, 1.1207, 0.4167)$	0.4366

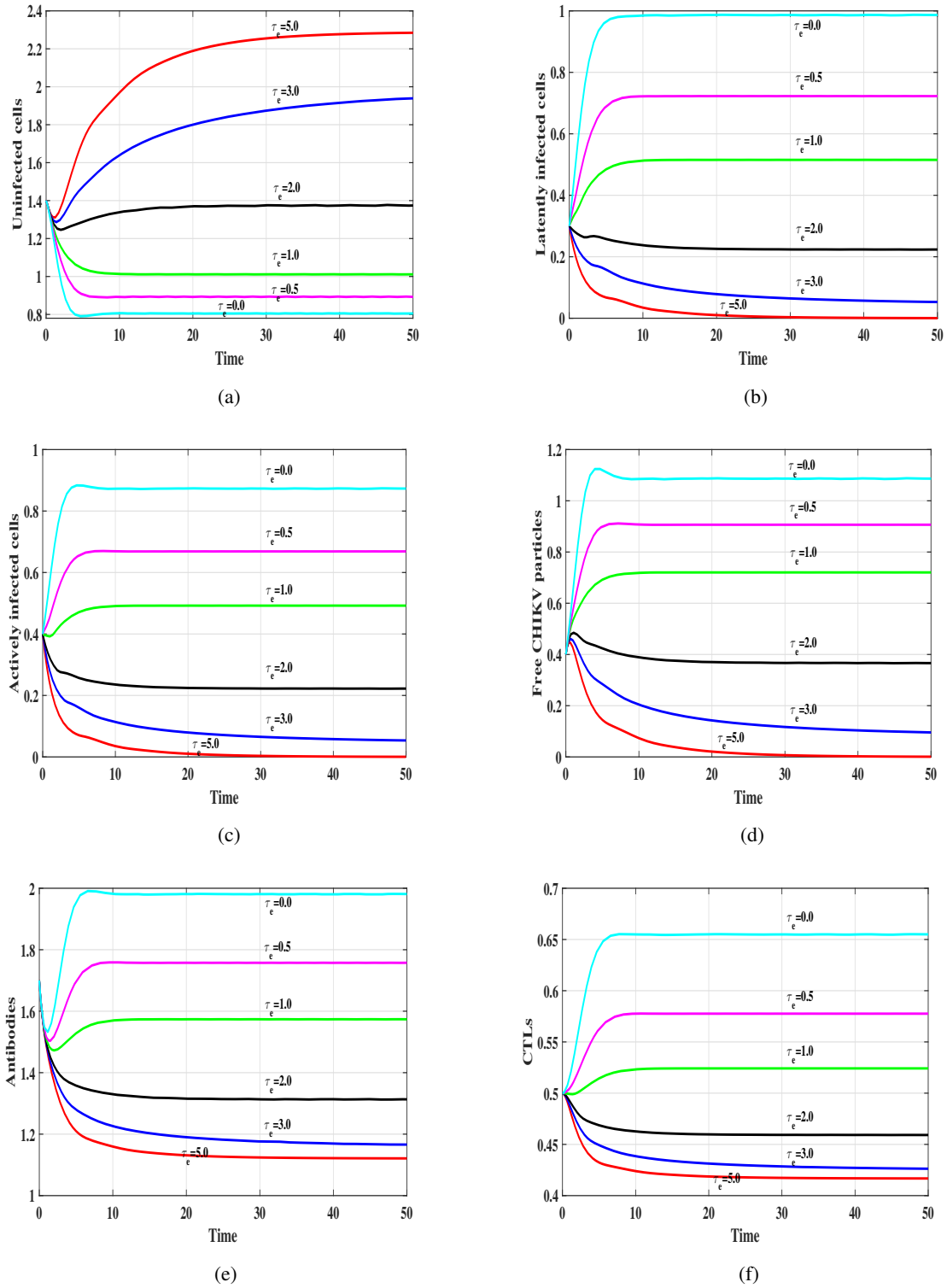


Figure 2. Impact of delay parameter τ_e on the stability of the steady states (a) uninfected cells, (b) latently infected cells, (c) actively infected cells, (d) CHIKV particles, (e) antibodies and (f) CTLs

5. Conclusion

A new mathematical model for the within-host transmission of Chikungunya virus (CHIKV) has been formulated and analyzed. Different from the existing CHIKV mathematical models in the

literature, the within-host CHIKV model formulated in this study was designed to capture some features such as saturated incidence rate, adaptive immune response and distributed time delays. We proved the nonnegativity and boundedness of the solution of the new within-host CHIKV model describing the interaction of six mutually exclusive concentrations of healthy cells, latently infected cells, actively infected cells, CHIKV particles, antibodies and cytotoxic T-lymphocytes cells. More importantly, we constructed suitable Lyapunov functionals to investigate the global dynamics of the CHIKV model about the virus-free and virus-present (endemic) steady states. We showed that the model has a globally-asymptotically stable virus-free steady state when the basic reproduction number is less than one, and a globally asymptotically stable endemic state was proved when the basic reproduction number is greater than one.

Furthermore, visualization of the qualitative analysis of the model was done by conducting numerical simulations to investigate the effect of time delays on the stability of the steady states. The simulations established the asymptotic convergence of solutions to both virus-free and endemic steady states at different initial concentrations of healthy cells, latently infected cells, actively infected cells, CHIKV particles, antibodies and cytotoxic T-lymphocytes cells. Particularly, we obtained the critical value of time delay, and it was revealed that the system stabilized around the endemic state when the time delay is below the critical value. Conversely, it was shown that the system stabilized around the virus-free steady state when the time delay is above the critical value. In essence, simulations demonstrated that an increase in time delay corresponds to a decrease in the basic reproduction number of the within-host CHIKV model. Thus, time delays have the capacity to hinder the replication of within-host chikungunya virus.

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