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A GENERALIZED MODEL OF CHIKUNGUNYA VIRUS WITH BOTH MODES OF TRANSMISSION AND HUMORAL IMMUNITY

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Abstract. In this paper, we develop a mathematical model to describe the interactions between Chikungunya virus (CHIKV), host cells and antibodies. The proposed model considers two types of infected cells and incorporates two modes of transmission, the classical virus-to-cell infection and the direct cell-to-cell transmission. These both modes are modeled by two general incidence functions that include many special cases existing in the literature. We first prove the well-posedness of the model, including the positivity and boundedness of solutions. The stability and instability of equilibria are established by means of direct and indirect Lyapunov methods. Furthermore, numerical simulations are presented in order to support our analytical results.

Keywords: chikungunya virus infection; humoral immunity; mathematical modeling; stability.

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1. INTRODUCTION

Chikungunya virus (CHIKV) is a mosquito-borne virus responsible for periodic and explosive outbreaks of a febrile disease that is characterized by severe and sometimes prolonged

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polyarthritis [1]. CHIKV was first identified in Tanzania in the early 1952 and has caused periodic outbreaks in Asia and Africa since the 1960s [2]. On 9 December 2013, the Pan American Health Organization (PAHO) has issued an alert about the transmission of CHIKV in the Americas [3]. Since then, the transmission of CHIKV was confirmed in 44 countries and territories in the region, with more than 2 millions reported cases and 403 deaths.

In the literature, many mathematical models have been proposed to understand the dynamics of CHIKV infection. Most of them describe the disease transmission in mosquito and human populations [4, 5, 6, 7, 8, 9, 10]. However, there are only few within-host CHIKV infection models. For this, Wang and Liu proposed and analysed a within-host CHIKV model [11]. An extension of this model was given by Elaiw et al. [12]. These within-host models are based on the assumption that the cell infection is caused only by contact with free virus.

To better describe the dynamics of CHIKV in within human body by taking into account virus-to-cell infection and cell-to-cell transmission via direct contact [13, 14, 15], we propose the following model:

$$
\left\{
\begin{array}{ll}
\dot{T} & = \lambda - dT - f(T,I,V)V - g(T,I)I, \\
\dot{L} & = (1-p)\Big(f(T,I,V)V + g(T,I)I\Big) - (\delta+\gamma)L, \\
\dot{I} & = p\Big(f(T,I,V)V + g(T,I)I\Big) + \gamma L - aI, \\
\dot{V} & = kI - \mu V - qBV, \\
\dot{B} & = \eta + cBV - hB,
\end{array}
\right. \tag{1}
$$

where $T(t)$, $L(t)$, $I(t)$, $V(t)$ and $B(t)$ are the concentrations of susceptible monocytes, latently infected monocytes, actively infected monocytes, CHIKV particles and antibodies at time t, respectively. The susceptible monocytes are produced at a constant λ, die at rate d and become infected either by free virus at rate $f(T,I,V)V$ or by direct contact with actively infected monocyte at rate $g(T,I)I$. So, the term $f(T,I,V)V + g(T,I)I$ denotes the total infection rate of susceptible monocytes. A fraction $(1-p)$ of infected monocytes is assumed to be latently infected monocytes and the remaining p becomes actively infected monocytes, where $0 < p < 1$. The parameters δ, a, μ and h are the death rates of latently infected monocytes, actively infected monocytes, CHIKV particles and antibodies, respectively. The latently infected monocytes are

transmitted to actively infected monocytes at rate γL. The CHIKV particles are produced at rate kI and neutralized by antibodies at rate qVB. The antibodies are created at rate η and proliferated at rate cBV.

As in [16, 17], the incidence functions $f(T,I,V)$ and $g(T,I)$ for both modes are continuously differentiable and satisfy the following hypotheses:

- (H_0) $g(0,I) = 0$, for all $I \geq 0$; $\frac{\partial g}{\partial T}(T,I) \geq 0$ $\big($or $g(T,I)$ is a strictly monotone increasing function with respect to T when $f \equiv 0\big)$ and $\frac{\partial g}{\partial I}(T,I) \leq 0$, for all $T \geq 0$ and $I \geq 0$.
- (H_1) $f(0,I,V) = 0$, for all $I \geq 0$ and $V \geq 0$,
- (H_2) $f(T,I,V)$ is a strictly monotone increasing function with respect to T $\big($or $\frac{\partial f}{\partial T}(T,I,V) \geq 0$ when $g(T,I)$ is a strictly monotone increasing function with respect to $T\big)$, for any fixed $I \geq 0$ and $V \geq 0$,
- (H_3) $f(T,I,V)$ is a monotone decreasing function with respect to I and V.

It is very important to note that the model presented by system (1) extends and generalizes some special cases existing in the literature. For example, we get the within-host CHIKV infection model with latency [18] when $f(T,I,V) = \frac{\beta_1 T}{1+\alpha_1 V}$ and $g(T,I) = 0$, where β_1 is the virus-to-cell infection rate and α_1 is a non-negative constant that measures the saturation effect. When $f(T,I,V) = \frac{\beta_1 T}{1+\alpha_1 V}$ and $g(T,I) = \frac{\beta_2 T}{1+\alpha_2 I}$ with β_2 is the cell-to-cell transmission rate and α_2 is the saturation constant, we obtain the CHIKV infection model with CHIKV-monocyte and infected-monocyte saturated incidences [19].

The rest of the paper is organized as follows. The next section focused on well-posedness of the model and the existence of equilibria. The section 3 is devoted to stability analysis of equilibria. An application and some numerical simulations are presented in section 4. The paper ends with mathematical and biological conclusions in section 5.

2. WELL-POSEDNESS AND EQUILIBRIA

In this section, we first prove that our model (1) is well-posed by showing the nonnegativity and boundedness of solutions. After, we derive the threshold parameters for the existence of equilibria.

Theorem 2.1. *All solutions of model (1) starting from non-negative initial conditions remain non-negative and bounded for all $t > 0$.*

Proof. We have

$$\begin{aligned}
\dot{T}|_{T=0} &= \lambda > 0, \quad \dot{L}|_{L=0} = (1-p)(f(T,I,V)V + g(T,I)I) \geq 0 \text{ for all } T,I,V \geq 0,\\
\dot{I}|_{I=0} &= p(f(T,0,V)V + \gamma L \geq 0 \text{ for all } T,L,V \geq 0,\\
\dot{V}|_{V=0} &= kI \geq 0 \text{ for all } I \geq 0, \quad \dot{B}|_{B=0} = \eta > 0.
\end{aligned}$$

Then $\mathbf{R}^5_+$ is positively invariant with respect (1). It remains to prove the boundedness of solutions. Denote

$$G(t) = T(t) + L(t) + I(t) + \frac{a}{2k}V(t) + \frac{aq}{2kc}B(t).$$

Then

$$\begin{aligned}
\frac{dG}{dt} &= \dot{T}(t) + \dot{L}(t) + \dot{I}(t) + \frac{a}{2k}\dot{V}(t) + \frac{aq}{2kc}\dot{B}(t)\\
&= \lambda - dT(t) - \delta L(t) - \frac{a}{2}I(t) - \frac{a\mu}{2k}V(t) + \frac{aq\eta}{2kc} - \frac{aqh}{2kc}B(t)\\
&\leq \lambda + \frac{aq\eta}{2kc} - \rho G(t),
\end{aligned}$$

where $\rho = \min\{\frac{a}{2}, d, \delta, \mu, h\}$. Thus,

$$\limsup_{t\to\infty} G(t) \leq \frac{\lambda}{\rho} + \frac{aq\eta}{2kc\rho}.$$

Consequently, $T(t)$, $L(t)$, $I(t)$, $V(t)$ and $B(t)$ are bounded.

It is clear that model (1) has always one infection-free equilibrium $E_0(T_0,0,0,0,B_0)$, where $T_0 = \dfrac{\lambda}{d}$ and $B_0 = \dfrac{\eta}{h}$. Therefore, we define the basic reproduction number of (1) as follows

$$R_0 = \frac{(\delta p + \gamma)\left[kf(T_0,0,0) + (\mu + qB_0)g(T_0,0)\right]}{a(\delta+\gamma)(\mu+qB_0)}. \tag{2}$$

The other equilibrium of model (1) satisfies the following equations:

$$\lambda - dT - f(T,I,V)V - g(T,I)I = 0, \tag{3}$$

$$(1-p)\Big(f(T,I,V)V + g(T,I)I\Big) - (\delta+\gamma)L = 0, \tag{4}$$

$$p\Big(f(T,I,V)V + g(T,I)I\Big) + \gamma L - aI = 0, \tag{5}$$

$$kI - \mu V - qBV = 0, \tag{6}$$

$$\eta + cBV - hB = 0. \tag{7}$$

By (3)-(7), we have $B = \dfrac{\eta}{h-cV}$, $I = \dfrac{\mu(h-cV)+q\eta}{k(h-cV)}V = \varphi_1(V)$, $L = \dfrac{(1-p)a}{\delta p+\gamma}I = \dfrac{(1-p)a}{\delta p+\gamma}\varphi_1(V)$, $T = \dfrac{\lambda(\delta p+\gamma)-(\delta+\gamma)a\varphi_1(V)}{d(\delta p+\gamma)} = \varphi_2(V)$ and

$$k(\delta p+\gamma)(h-cV)f\big(T,I,V\big) + (\delta p+\gamma)\big[\mu(h-cV)+q\eta\big]g\big(T,I\big) = a(\delta+\gamma)\big[\mu(h-cV)+q\eta\big].$$

Since $B = \dfrac{\eta}{h-cV} \geq 0$, we have $V < \dfrac{h}{c}$. Then there is no biological equilibrium when $V \geq \dfrac{h}{c}$. So, we consider the function ψ defined on $[0, \frac{h}{c})$ by

$$\begin{aligned}\psi(V) &= k(\delta p+\gamma)(h-cV)f\big(\varphi_2(V),\varphi_1(V),V\big) + (\delta p+\gamma)\big[\mu(h-cV)+q\eta\big]g\big(\varphi_2(V),\varphi_1(V)\big)\\ &\quad -a(\delta+\gamma)\big[\mu(h-cV)+q\eta\big].\end{aligned}$$

We have $\varphi_2(0) = \frac{\lambda}{d} > 0$, $\lim\limits_{V\to(\frac{h}{c})^-}\varphi_2(V) = -\infty$ and

$\varphi_2'(V) = -\dfrac{(\delta+\gamma)a}{d(\delta p+\gamma)}\varphi_1'(V) < 0$ with $\varphi_1'(V) = \dfrac{\mu(h-cV)^2+q\eta h}{k(h-cV)^2} > 0$.

Then the equation $\varphi_2(V) = 0$ admits a unique solution $\widetilde{V} \in (0, \frac{h}{c})$. Thus, $\widetilde{B} = \frac{\eta}{h-c\widetilde{V}} > 0$ and $\psi(\widetilde{V}) = -a(\delta+\gamma)[\mu(h-c\widetilde{V})+q\eta] < 0$. Since $\psi(0) = a(\delta+\gamma)(\mu h+q\eta)(R_0-1) > 0$, we deduce that there exists a $V_1 \in (0,\widetilde{V})$ such that $\psi(V_1) = 0$. Hence,

$$B_1 = \frac{\eta}{h-cV_1} > 0,\ I_1 = \frac{\mu+qB_1}{k}V_1 > 0,\ L_1 = \frac{(1-p)}{(\delta p+\gamma)}aI_1 > 0.$$

Substituting $V = V_1$ and $I = I_1$ in (3) and define a function φ_3 as

$$\varphi_3(T) = \lambda - dT - f(T,I_1,V_1)V_1 - g(T,I_1)I_1.$$

Since $\varphi_3(0) = \lambda > 0$, $\varphi_3(\frac{\lambda}{d}) = -f(\frac{\lambda}{d}, I_1, V_1)V_1 - g(\frac{\lambda}{d}, I_1)I_1 < 0$ and φ_3 is a strictly decreasing function of T, then there exists a unique $T_1 \in (0, \frac{\lambda}{d})$ such that $\varphi_3(T_1) = 0$. Thus, model (1) has a unique chronic infection equilibrium $E_1(T_1, L_1, I_1, V_1, B_1)$ when $R_0 > 1$.

The pervious discussions are summarized in the following theorem.

Theorem 2.2.

(i) If $R_0 \leq 1$, then model (1) has a unique infection-free equilibrium $E_0(T_0, 0, 0, 0, B_0)$, where $T_0 = \dfrac{\lambda}{d}$ and $B_0 = \dfrac{\eta}{h}$.

(ii) If $R_0 > 1$, then model (1) has a unique chronic infection equilibrium $E_1(T_1, L_1, I_1, V_1, B_1)$ besides E_0, where $T_1 \in (0, \frac{\lambda}{d})$, $L_1 > 0$, $I_1 > 0$, $V_1 > 0$ and $B_1 > 0$.

3. Stability Analysis

This section investigates the stability of the two equilibria E_0 and E_1. Firstly, the following theorem characterizes the global stability of the free-infection equilibrium E_0.

Theorem 3.1. *The infection-free equilibrium E_0 is globally asymptotically stable when $R_0 \leq 1$ and becomes unstable when $R_0 > 1$.*

Proof. Define

$$\Gamma = \left\{ (T, L, I, V, B) \in \mathbf{R}^5_+ : T \leq \frac{\lambda}{d} \text{ and } B \geq \frac{\eta}{h} \right\}.$$

We see that any solution $(T(t), L(t), I(t), V(t), B(t))$ starting in Γ remains there forever. Indeed, it follows from Theorem 2.1 that $(T(t), L(t), I(t), V(t), B(t)) \in \mathbf{R}^5_+$. It remains to prove that $T(t) \leq \frac{\lambda}{d}$ with $T(0) \leq \frac{\lambda}{d}$ and $B(t) \geq \frac{\lambda}{d}$ with $B(0) \geq \frac{\lambda}{d}$. From the first and fifth equations of (1), we get

$$\begin{aligned} T(t) &\leq \frac{\lambda}{d} + \left(T(0) - \frac{\lambda}{d} \right) e^{-dt}, \\ B(t) &\geq \frac{\eta}{h} + \left(B(0) - \frac{\eta}{h} \right) e^{-ht}. \end{aligned}$$

This implies that $T(t) \leq \frac{\lambda}{d}$ and $B(t) \geq \dfrac{\eta}{h}$. So, $(T(t), L(t), I(t), V(t), B(t)) \in \Gamma$.

Construct a Lyapunov functional as follows

$$U(t) = \frac{\gamma + \delta}{\delta p + \gamma} I(t) + \frac{\gamma}{\delta p + \gamma} L(t) + \frac{f(\frac{\lambda}{d}, 0, 0)}{\mu + q\frac{\eta}{h}} V(t).$$

Calculating the time derivative of U along the solutions of (1), we obtain

$$\begin{aligned}\frac{dU}{dt} &= \left(f(T,I,V)-\frac{\mu+qB}{\mu+q\frac{\eta}{h}}f(\frac{\lambda}{d},0,0)\right)V+a\left(\frac{kf(\frac{\lambda}{d},0,0)+(\mu+q\frac{\eta}{h})g(T,I)}{a(\mu+q\frac{\eta}{h})}-\frac{\gamma+\delta}{\delta p+\gamma}\right)I\\ &\leq \left(f(T,0,0)-f(\frac{\lambda}{d},0,0)\right)V+a\frac{\gamma+\delta}{\delta p+\gamma}(R_0-1)I\\ &\leq a\frac{\gamma+\delta}{\delta p+\gamma}(R_0-1)I.\end{aligned}$$

Since $R_0\leq 1$, we have $\frac{dU}{dt}(t)\leq 0$. Further, it is not hard to prove that the largest invariant set in $\left\{(T,L,I,V,B)|\frac{dU}{dt}=0\right\}$ is the singleton $\{E_0\}$. It follows from LaSalle's invariance principle [20] that E_0 is globally asymptotically stable when $R_0\leq 1$.

On the other hand, the characteristic equation at E_0 is given by

$$(\xi+d)(\xi+h)P(\xi)=0,$$

where

$$\begin{aligned}P(\xi) &= \xi^3+\left(\gamma+\delta+a+\mu+q\frac{\eta}{h}-pg(\frac{\lambda}{d},0)\right)\xi^2+\Big((\mu+q\frac{\eta}{h})(\gamma+\delta+a-pg(\frac{\lambda}{d},0))\\ &\quad -kpf(\frac{\lambda}{d},0,0)+a(\gamma+\delta)-(\delta p+\gamma)g(\frac{\lambda}{d},0)\Big)\xi\\ &\quad -a(\mu+q\frac{\eta}{h})(\gamma+\delta)(R_0-1).\end{aligned}$$

When $R_0>1$, we have $P(0)=-a(\mu+q\frac{\eta}{h})(\gamma+\delta)(R_0-1)<0$. Since $\lim\limits_{\xi\to+\infty}P(\xi)=+\infty$, we deduce that there exists a $\xi_0\in(0,+\infty)$ such that $P(\xi_0)=0$. Then E_0 is unstable. This completes the proof.

Finally, we investigate the global stability of the chronic infection equilibrium E_1. So, we assume that $R_0>1$ and the functions f and g satisfy, for all $T,I,V>0$, the following hypothesis:

$$(H_4)\qquad \begin{aligned}&\left(1-\frac{f(T,I,V)}{f(T,I_1,V_1)}\right)\left(\frac{f(T,I_1,V_1)}{f(T,I,V)}-\frac{V}{V_1}\right)\leq 0,\\ &\left(1-\frac{f(T_1,I_1,V_1)g(T,I)}{f(T,I_1,V_1)g(T_1,I_1)}\right)\left(\frac{f(T,I_1,V_1)g(T_1,I_1)}{f(T_1,I_1,V_1)g(T,I)}-\frac{I}{I_1}\right)\leq 0.\end{aligned}$$

Theorem 3.2. *Assume that (H_4) holds. If $R_0>1$, then the chronic infection equilibrium E_1 is globally asymptotically stable.*

Proof. Consider the following Lyapunov functional

$$\begin{aligned} W(t) &= T(t)-T_1-\int_{T_1}^{T}\frac{f(T_1,I_1,V_1)}{f(X,I_1,V_1)}dX+\frac{\gamma}{\delta p+\gamma}L_1\Phi\left(\frac{L(t)}{L_1}\right)+\frac{\gamma+\delta}{\delta p+\gamma}I_1\Phi\left(\frac{I(t)}{I_1}\right)\\ &\quad+\frac{f(T_1,I_1,V_1)V_1}{kI_1}V_1\Phi\left(\frac{V(t)}{V_1}\right)+\frac{qf(T_1,I_1,V_1)V_1}{ckI_1}B_1\Phi\left(\frac{B(t)}{B_1}\right), \end{aligned}$$

where $\Phi(x)=x-1-\ln x$, $x>0$.

Calculating the time derivative of W along the positive solutions of (1) and using:
$\lambda = dT_1+f(T_1,I_1,V_1)V_1+g(T_1,I_1)I_1$, $kI_1=\mu V_1+qB_1V_1$, $\eta = hB_1-cB_1V_1$,
$(\delta+\gamma)L_1=(1-p)(f(T_1,I_1,V_1)V_1+g(T_1,I_1)I_1)$ and $\dfrac{(\delta+\gamma)}{\delta p+\gamma}aI_1=f(T_1,I_1,V_1)V_1+g(T_1,I_1)I_1$,
we obtain

$$\begin{aligned} \frac{dW}{dt} &= dT_1\left(1-\frac{T}{T_1}\right)\left(1-\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}\right)-\frac{q\eta f(T_1,I_1,V_1)V_1}{ckI_1B_1B}\left(B-B_1\right)^2\\ &\quad+f(T_1,I_1,V_1)V_1\left(3-\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}+\frac{f(T,I,V)V}{f(T,I_1,V_1)V_1}-\frac{V}{V_1}-\frac{IV_1}{I_1V}\right)\\ &\quad+\frac{\gamma(1-p)}{\delta p+\gamma}f(T_1,I_1,V_1)V_1\left(1-\frac{f(T,I,V)VL_1}{f(T_1,I_1,V_1)V_1L}-\frac{I_1L}{IL_1}-\frac{p(\gamma+\delta)f(T,I,V)VI_1}{\gamma(1-p)f(T_1,I_1,V_1)V_1I}\right)\\ &\quad+g(T_1,I_1)I_1\left(2-\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}+\frac{f(T_1,I_1,V_1)g(T,I)I}{f(T,I_1,V_1)g(T_1,I_1)I_1}-\frac{I}{I_1}\right)\\ &\quad+\frac{\gamma(1-p)}{\delta p+\gamma}g(T_1,I_1)I_1\left(1-\frac{I_1L}{IL_1}-\frac{g(T,I)IL_1}{g(T_1,I_1)I_1L}-\frac{p(\gamma+\delta)g(T,I)}{\gamma(1-p)g(T_1,I_1)}\right). \end{aligned}$$

Hence,

$$\begin{aligned} \frac{dW}{dt} &= dT_1\left(1-\frac{T}{T_1}\right)\left(1-\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}\right)-\frac{q\eta f(T_1,I_1,V_1)V_1}{ckI_1B_1B}\left(B-B_1\right)^2\\ &\quad+f(T_1,I_1,V_1)V_1\left(-1-\frac{V}{V_1}+\frac{f(T,I,V)V}{f(T,I_1,V_1)V_1}+\frac{f(T,I_1,V_1)}{f(T,I,V)}\right)\\ &\quad+g(T_1,I_1)I_1\left(-1-\frac{I}{I_1}+\frac{f(T_1,I_1,V_1)g(T,I)I}{f(T,I_1,V_1)g(T_1,I_1)I_1}+\frac{f(T,I_1,V_1)g(T_1,I_1)}{f(T_1,I_1,V_1)g(T,I)}\right)\\ &\quad-\frac{\gamma(1-p)}{\delta p+\gamma}f(T_1,I_1,V_1)V_1\left[\Phi\left(\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}\right)+\Phi\left(\frac{f(T,I_1,V_1)}{f(T,I,V)}\right)\right.\\ &\quad\left.+\Phi\left(\frac{f(T,I,V)VL_1}{f(T_1,I_1,V_1)V_1L}\right)+\Phi\left(\frac{I_1L}{IL_1}\right)+\Phi\left(\frac{IV_1}{I_1V}\right)\right]\\ &\quad-\frac{(\gamma+\delta)p}{\delta p+\gamma}f(T_1,I_1,V_1)V_1\left[\Phi\left(\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}\right)+\Phi\left(\frac{f(T,I_1,V_1)}{f(T,I,V)}\right)\right. \end{aligned}$$

$$+\Phi\left(\frac{f(T,I,V)VI_1}{f(T_1,I_1,V_1)V_1I}\right)+\Phi\left(\frac{IV_1}{I_1V}\right)\Bigg]$$
$$-\frac{\gamma(1-p)}{\delta p+\gamma}g(T_1,I_1)I_1\left[\Phi\left(\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}\right)+\Phi\left(\frac{f(T,I_1,V_1)g(T_1,I_1)}{f(T_1,I_1,V_1)g(T,I)}\right)\right.$$
$$\left.+\Phi\left(\frac{g(T,I)IL_1}{g(T_1,I_1)I_1L}\right)+\Phi\left(\frac{I_1L}{IL_1}\right)\right]$$
$$-\frac{(\gamma+\delta)p}{\delta p+\gamma}g(T_1,I_1)I_1\left[\Phi\left(\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}\right)+\Phi\left(\frac{f(T,I_1,V_1)g(T_1,I_1)}{f(T_1,I_1,V_1)g(T,I)}\right)+\Phi\left(\frac{g(T,I)}{g(T_1,I_1)}\right)\right].$$

By (H_2), we deduce that

$$\left(1-\frac{T}{T_1}\right)\left(1-\frac{f(T_1,I_1,V_1)}{f(T,I_1,V_1)}\right)\leq 0.$$

By (H_4), we obtain

$$-1-\frac{V}{V_1}+\frac{f(T,I,V)V}{f(T,I_1,V_1)V_1}+\frac{f(T,I_1,V_1)}{f(T,I,V)}=\left(1-\frac{f(T,I,V)}{f(T,I_1,V_1)}\right)\left(\frac{f(T,I_1,V_1)}{f(T,I,V)}-\frac{V}{V_1}\right)\leq 0$$

and

$$-1-\frac{I}{I_1}-\frac{f(T_1,I_1,V_1)g(T,I)I}{f(T,I_1,V_1)g(T_1,I_1)I_1}+\frac{f(T,I_1,V_1)g(T_1,I_1)}{f(T_1,I_1,V_1)g(T,I)}$$
$$=\left(1-\frac{f(T_1,I_1,V_1)g(T,I)}{f(T,I_1,V_1)g(T_1,I_1)}\right)\left(\frac{f(T,I_1,V_1)g(T_1,I_1)}{f(T_1,I_1,V_1)g(T,I)}-\frac{I}{I_1}\right)\leq 0.$$

Since $\Phi(x)\geq 0$, we have $\dfrac{dW}{dt}\leq 0$ with equality if and only if $T=T_1$, $L=L_1$, $I=I_1$, $V=V_1$ and $B=B_1$. From LaSalle's invariance principle, we conclude that the chronic infection equilibrium E_1 is globally asymptotically stable when $R_0>1$.

4. Application and Numerical Simulations

In this section, we first apply our main results to the following model

$$\begin{cases}\dot{T} &= \lambda-dT-\dfrac{\beta_1TV}{1+\alpha_1V}-\dfrac{\beta_2TI}{1+\alpha_2I},\\ \dot{L} &= (1-p)\left(\dfrac{\beta_1TV}{1+\alpha_1V}+\dfrac{\beta_2TI}{1+\alpha_2I}\right)-(\delta+\gamma)L,\\ \dot{I} &= p\left(\dfrac{\beta_1TV}{1+\alpha_1V}+\dfrac{\beta_2TI}{1+\alpha_2I}\right)+\gamma L-aI,\\ \dot{V} &= kI-\mu V-qBV,\\ \dot{B} &= \eta+cBV-hB,\end{cases} \tag{8}$$

Parameter	Value	Parameter	Value
λ	1.826	a	0.4441
d	0.7979	k	2.02
p	0.5	μ	0.4418
α_1	0.01	q	0.5946
α_2	0.01	η	1.402
δ	0.5	c	1.2129
γ	0.1	h	1.251
β_1	Varied	β_2	Varied

TABLE 1. Parameter values of model (8).

which is a special case of model (1) by letting $f(T,I,V) = \frac{\beta_1 T}{1+\alpha_1 V}$ and $g(T,I) = \frac{\beta_2 T}{1+\alpha_2 I}$. Clearly, the assumptions (H_0)-(H_3) hold. In addition, we have

$$\left(1 - \frac{f(T,I,V)}{f(T,I_1,V_1)}\right)\left(\frac{f(T,I_1,V_1)}{f(T,I,V)} - \frac{V}{V_1}\right) = \frac{-\alpha_1(V-V_1)^2}{V_1(1+\alpha_1 V)(1+\alpha_1 V_1)} \leq 0$$

and

$$\left(1 - \frac{f(T_1,I_1,V_1)g(T,I)}{f(T,I_1,V_1)g(T_1,I_1)}\right)\left(\frac{f(T,I_1,V_1)g(T_1,I_1)}{f(T_1,I_1,V_1)g(T,I)} - \frac{I}{I_1}\right) = \frac{-\alpha_2(I-I_1)^2}{I_1(1+\alpha_2 I)(1+\alpha_2 I_1)} \leq 0.$$

Then the assumption (H_4) is satisfied. By applying Theorems 3.1 and 3.2, we have the following result.

Corollary 4.1.

(i) If $R_0 \leq 1$, then the infection-free equilibrium E_0 of model (8) is globally asymptotically stable.

(ii) If $R_0 > 1$, then the infection-free equilibrium E_0 becomes unstable and the chronic infection equilibrium E_1 of model (8) is globally asymptotically stable.

For the numerical simulations, we consider β_1 and β_2 as free parameters and the other parameter values are given in Table 1.

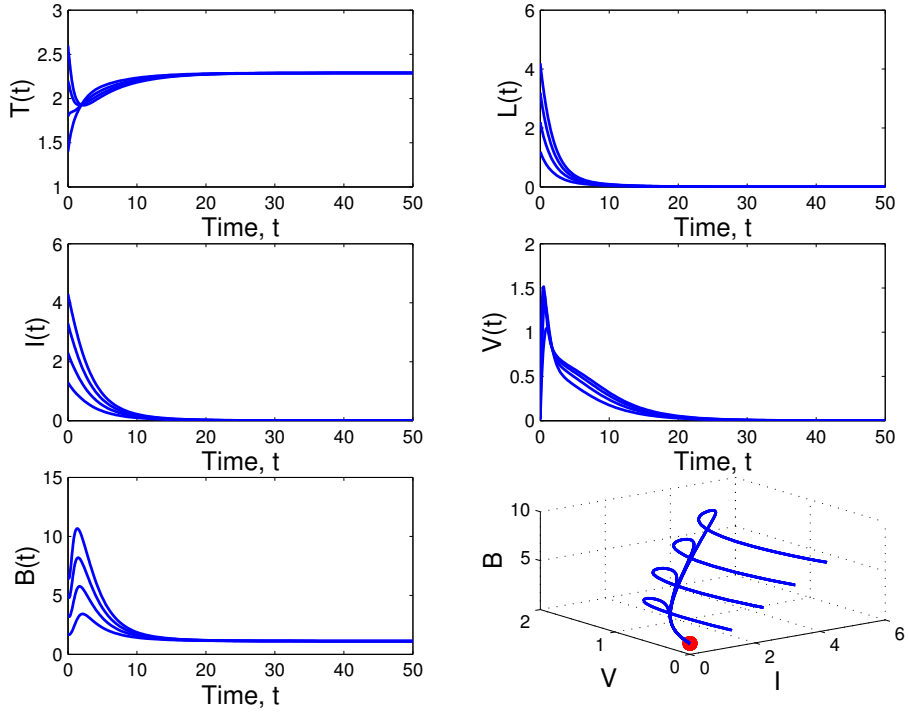

FIGURE 1. Dynamics of the model (8) when $R_0 = 0.7582 \leq 1$.

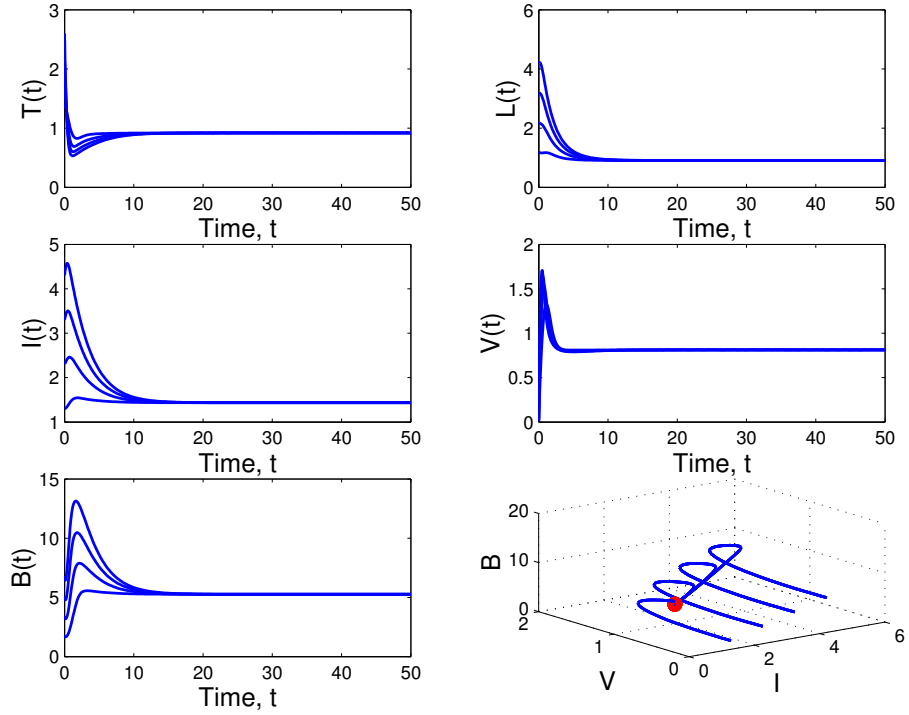

FIGURE 2. Dynamics of the model (8) when $R_0 = 7.5819 > 1$.

Firstly, we choose $\beta_1 = 0.05$ and $\beta_2 = 0.04$. By a simple calculation, we have $R_0 = 0.7582 \leq 1$. Hence, model (8) has an infection-free equilibrium $E_0(2.2885, 0, 0, 0, 1.1207)$. From Corollary 4.1 (i), we know that E_0 is globally asymptotically stable. Figure 1 demonstrates this result.

Secondly, we choose $\beta_1 = 0.5$ and $\beta_2 = 0.3$. In this case, we have $R_0 = 7.5819 > 1$. It follows from Corollary 4.1 (ii) that the chronic infection equilibrium $E_1(0.9116, 0.9102, 1.4419, 0.8313, 5.1502)$ is globally asymptotically stable (see Figure 2).

5. Conclusions

In this work, we have presented a within-host CHIKV infection model with humoral immunity, two modes of transmission and two classes of infected monocytes that are actively infected monocytes and latently infected monocytes. We have investigated the well-posedness of the model by studying the existence, positivity and boundedness of solutions. By constructing suitable Lyapunov functionals, we found sufficient conditions for the global stability of equilibria. Our study showed that the global dynamics of the model is completely determined by the basic reproduction number R_0. More particularly, if $R_0 \leq 1$ the infection-free equilibrium is globally asymptotically stable, which leads to the removal of virus in the host. When $R_0 > 1$, the infection-free equilibrium loses its stability and a unique chronic infection equilibrium appears and it is globally asymptotically stable, which means that the CHIKV persists in the host. Furthermore, the more recent works presented in [12, 18, 19] are extended and generalized.

Conflict of Interests

The author(s) declare that there is no conflict of interests.

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