Available online at www.isr-publications.com/jmcs
J. Math. Computer Sci., 19 (2019), 65–73
Research Article

Online: ISSN 2008-949X

Journal of Mathematics and Computer Science

Journal Homepage: www.isr-publications.com/jmcs

Global dynamics of humoral immunity Chikungunya virus with two routes of infection and Holling type-II

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Abstract

In this work, we analyze the global dynamics of within-host Chikungunya virus (CHIKV) infection model with humoral immune response. We incorporate two modes of infections, attaching a CHIKV to a host monocyte, and contacting an infected monocyte with an uninfected monocyte. The infection incident rate is given by Holling type-II. The basic reproduction number $\mathcal{R}_0$ is used to prove that the CHIKV-free equilibrium E_0 is globally asymptotically stable when $\mathcal{R}_0 \leqslant 1$ and the infected equilibrium E_1 is globally asymptotically stable when $\mathcal{R}_0 > 1$. Numerical simulations have been performed to confirm the theoretical results.

Keywords: Chikungunya virus, holling type-II, global stability, Lyapunov function, viral and cellular infections.

2010 MSC: 34D23, 93D20, 93D05, 93C55.

1. Introduction

Mosquito is one of the dangerous insect throughout the world. It can carry and spread viruses to humans and animals causes many of deaths every year. A great efforts has been paid to develop and analyze mathematical models that describe the population dynamics of mosquito-borne diseases such as Zika [2, 4, 7], dengue [1, 27, 43, 48], malaria [3, 5, 6, 36], yellow fever [40] and chikungunya [8–10, 34, 37–39, 46]. Chikungunya virus (CHIKV) is transmitted to humans by infected Aedes albopictus and Aedes agypti mosquito. CHIKV causes severe joint and muscle pain, fever, rash, headache, nausea and fatigue. Wang and Liu [45] have proposed and studied a within-host CHIKV dynamics model which contains four compartments, uninfected-monocytes (s), infected monocytes (y), free CHIKV particles (p) and antibodies (x). The model has been extended in [13, 14] by considering general CHIKV-monocyte incidence rate. In [13, 14, 45] it has been assumed that the uninfected monocyte becomes infected by contacting with CHIKV (CHIKV-to-monocyte transmission). Long and Heise [35] have reported that the CHIKV can also spread by infected-to-monocyte transmission. Mathematical models of different viruses with both cellular and

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doi: 10.22436/jmcs.019.02.01

Received: 2016-04-13 *Revised:* 2019-03-31 *Accepted:* 2019-04-04

viral infections have been studied in several works [24, 25, 31–33, 41, 44, 47]. In a very recent work, Elaiw et al. [15] have studied the dynamics of CHIKV model with two routes of infection, however, they did not consider the holling-II. The aim of the present paper is to propose and analyze a CHIKV dynamics model where the infection rate is given by Holling type-II incidence. The proposed model is given as:

$$\dot{s}(t) = \beta - \delta s(t) - \frac{\eta_1 s(t)p(t)}{1+\omega s(t)} - \frac{\eta_2 s(t)y(t)}{1+\omega s(t)}, \tag{1.1}$$

$$\dot{y}(t) = \frac{\eta_1 s(t)p(t)}{1+\omega s(t)} + \frac{\eta_2 s(t)y(t)}{1+\omega s(t)} - \epsilon y(t), \tag{1.2}$$

$$\dot{p}(t) = \pi y(t) - cp(t) - rx(t)p(t), \tag{1.3}$$

$$\dot{x}(t) = \lambda + \rho x(t)p(t) - mx(t). \tag{1.4}$$

The uninfected monocytes are generated monocytes by rate β, die with rate $\delta s(t)$ and be infected by CHIKV and infected monocytes with rate $\frac{\eta_1 s(t)p(t)}{1+\omega s(t)} + \frac{\eta_2 s(t)y(t)}{1+\omega s(t)}$, where ω is the uninfected monocyte Holling type-II constant, and η_1, and η_2 are the incidence rate constants. Constants ϵ, c, and m represent, respectively, the death rate constants of the infected monocytes, CHIKV, and antibodies. Constant π is the production rate constant of the CHIKV from infected monocytes. Antibodies attack the CHIKV at rate $rx(t)p(t)$. Once antigen is encountered, the antibodies expand at a constant rate λ and proliferate at rate $\rho x(t)p(t)$. All the parameters of the model are positive.

1.1. Basic properties

The following lemma establishes the nonnegativity and boundedness of the solutions of system (1.1)-(1.4).

Lemma 1.1. *There exist* $M_1, M_2, M_3 > 0$*, such that the following compact set is positively invariant for system* (1.1)-(1.4)*;*

$$\Gamma = \{(s, y, p, x) \in \mathbb{R}^4_{\geqslant 0} : 0 \leqslant s, y \leqslant M_1, 0 \leqslant p \leqslant M_2, 0 \leqslant x \leqslant M_3\}.$$

Proof. We have

$$\begin{aligned}
\dot{s}\mid_{s=0} &= \beta > 0,\\
\dot{y}\mid_{y=0} &= \frac{\eta_1 sp}{1+\omega s} \geqslant 0 \;\text{ for all } s, p \geqslant 0,\\
\dot{p}\mid_{p=0} &= \pi y \geqslant 0 \;\text{ for all } y \geqslant 0,\\
\dot{x}\mid_{x=0} &= \lambda > 0.
\end{aligned}$$

This shows that $(s(t), y(t), p(t), x(t)) \in \mathbb{R}^4_{\geqslant 0}$ with $(s(0), y(0), p(0), x(0)) \in \mathbb{R}^4_{\geqslant 0}$. Let us define

$$H_1(t) = s(t) + y(t), \qquad H_2(t) = p(t) + \frac{r}{\rho}x(t).$$

Then from Eqs. (1.1)-(1.4) we get

$$\dot{H}_1(t) = \beta - \delta s(t) - \epsilon y(t) \leqslant \beta - \sigma_1(s(t) + y(t)) = \beta - \sigma_1 H_1(t),$$

where, $\sigma_1 = \min\{\delta, \epsilon\}$. Hence $H_1(t) \leqslant M_1$, if $H_1(0) \leqslant M_1$, where $M_1 = \frac{\beta}{\sigma_1}$. It follows that $0 \leqslant s(t), y(t) \leqslant M_1$ if $0 \leqslant s(0) + y(0) \leqslant M_1$. Moreover, we have

$$\dot{H}_2(t) = \pi y(t) - cp(t) + \frac{r}{\rho}\lambda - \frac{mr}{\rho}x(t) \leqslant \pi M_1 + \frac{r}{\rho}\lambda - \sigma_2\left(p(t) + \frac{r}{\rho}x(t)\right) = \pi M_1 + \frac{r}{\rho}\lambda - \sigma_2 H_2(t),$$

where, $\sigma_2 = \min\{c, m\}$. Hence $H_2(t) \leqslant M_2$, if $H_2(0) \leqslant M_2$, where $M_2 = \frac{\pi M_1 + \frac{r}{\rho}\lambda}{\sigma_2}$. Since $p(t)$ and $x(t)$ are all non-negative, then $0 \leqslant p(t) \leqslant M_2$ and $0 < x(t) \leqslant M_3$ if $0 < p(0) + \frac{r}{\rho}x(0) \leqslant M_2$, where $M_3 = \frac{\rho M_2}{r}$. □

1.2. Equilibria

We define the basic reproduction number as:

$$\mathcal{R}_0 = \frac{(\eta_1 \pi m + \eta_2 c m + \eta_2 r \lambda)\beta}{\epsilon(cm + r\lambda)(\delta + \beta\omega)}.$$

Lemma 1.2. *Consider system (1.1)-(1.4), then*

- *if $\mathcal{R}_0 \leqslant 1$, then there exists only one equilibrium $E_0 \in \Gamma$, and*
- *if $\mathcal{R}_0 > 1$, then there exist two equilibria $E_0 \in \Gamma$ and $E_1 \in \mathring{\Gamma}$, where $\mathring{\Gamma}$ is the interior of Γ.*

Proof. Let $E(s, y, p, x)$ be any equilibrium satisfying

$$0 = \beta - \delta s - \frac{\eta_1 s p}{1 + \omega s} - \frac{\eta_2 s y}{1 + \omega s}, \tag{1.5}$$

$$0 = \frac{\eta_1 s p}{1 + \omega s} + \frac{\eta_2 s y}{1 + \omega s} - \epsilon y, \tag{1.6}$$

$$0 = \pi y - c p - r x p, \tag{1.7}$$

$$0 = \lambda + \rho x p - m x. \tag{1.8}$$

By solving Eqs. (1.5)-(1.8) we get two equilibria a CHIKV-free equilibrium $E_0 = (s_0, 0, 0, x_0)$, where $s_0 = \frac{\beta}{\delta}$ and $x_0 = \frac{\lambda}{m}$. Moreover, we have

$$\frac{C_1 p^3 + C_2 p^2 + C_3 p + C_4}{\bar{C_1} p + \bar{C_2}} = 0,$$

where

$$\begin{aligned}
C_1 &= c\epsilon\rho^2(-\pi\eta_1 - c\eta_2 + c\epsilon\omega),\\
C_2 &= C_{21} + C_{22} + C_{23} + C_{24} + C_{25},\\
C_3 &= C_{31} + C_{32} + C_{33} + C_{34} + C_{35} + C_{36},\\
C_4 &= m\pi(m\pi\beta\eta_1 - cm(\delta\epsilon - \beta\eta_2 + \beta\ \epsilon\omega) - r\lambda(\delta\epsilon - \beta\eta_2 + \beta\ \epsilon\omega)),\\
\bar{C_1} &= \bar{C_{11}} + \bar{C_{12}},\\
\bar{C_2} &= \bar{C_{21}} + \bar{C_{22}},
\end{aligned}$$

and

$$\begin{aligned}
&C_{21} = \rho\pi\eta_1(r\epsilon\lambda + \pi\beta\rho), && C_{22} = 2\rho c^2 m\epsilon(\eta_2 - \epsilon\omega), && C_{23} = 2\rho c m\pi\epsilon\eta_1,\\
&C_{24} = 2\rho c r\epsilon\lambda(\eta_2 - \epsilon\omega), && C_{25} = -\pi\rho^2 c(\delta\epsilon - \beta\eta_2 + \beta\epsilon\omega), && C_{31} = -m\pi\eta_1(r\epsilon\lambda + 2\pi\beta\rho),\\
&C_{32} = c^2 m^2\epsilon(-\eta_2 + \epsilon\omega), && C_{33} = r^2\lambda^2\epsilon(-\eta_2 + \epsilon\omega), && C_{34} = r\lambda\pi\rho(\delta\epsilon - \beta\eta_2 + \beta\epsilon\omega),\\
&C_{35} = cm(-m\pi\epsilon\eta_1 + 2r\epsilon\lambda(-\eta_2 + \epsilon\omega)), && C_{36} = 2cm\pi\rho(\delta\epsilon - \beta\eta_2 + \beta\epsilon\omega), && \bar{C_{11}} = \pi\rho r\lambda(\eta_2 - \epsilon\omega),\\
&\bar{C_{12}} = 2\pi\rho m(\pi\eta_1 + c(\eta_2 - \epsilon\omega)), && \bar{C_{21}} = -m\pi(m\pi\eta_1 + cm(\eta_2 - \epsilon\omega)), && \bar{C_{22}} = -m\pi r\lambda(\eta_2 - \epsilon\omega).
\end{aligned}$$

Let define a function $X(p)$ as:

$$X(p) = \frac{C_1 p^3 + C_2 p^2 + C_3 p + C_4}{\bar{C_1} p + \bar{C_2}} = 0,$$

we obtain

$$X(0) = \frac{\beta(cm\epsilon + r\epsilon\lambda)(\delta + \beta\omega)(\mathcal{R}_0 - 1)}{\epsilon(cm + r\lambda)(\delta + \beta\omega)(\mathcal{R}_0 - 1) + \epsilon\delta(cm + r\lambda)}, \qquad \lim_{p \to \left(\frac{m}{\rho}\right)^-} X(p) = -\frac{mr\epsilon\lambda}{\rho^2} < 0.$$

Therefore, if $\mathcal{R}_0 > 1$ then $X(0) > 0$ and there exists $p_1 \in (0, \frac{m}{\rho})$ such that $X(p_1) = 0$. It follows from Eqs. (1.6)-(1.8) that

$$x_1 = \frac{\lambda}{m - \rho p_1} > 0, \quad y_1 = \frac{p_1(c + r x_1)}{\pi} > 0,$$
$$s_1 = \frac{-\delta - p_1\eta_1 - y_1\eta_2 + \beta\omega + \sqrt{4\beta\delta\omega + (-\delta - p_1\eta_1 - y_1\eta_2 + \beta\omega)^2}}{2\delta\omega} > 0.$$

Therefore, if $\mathcal{R}_0 > 1$, then the system has an infected equilibrium $E_1 = (s_1, y_1, p_1, x_1)$. Now we show that $E_0 \in \Gamma$ and $E_1 \in \overset{\circ}{\Gamma}$. Clearly, $E_0 \in \Gamma$. From the equilibria conditions of E_1 we have

$$\beta = \delta s_1 + \frac{\eta_1 s_1 p_1}{1 + \omega s_1} + \frac{\eta_2 s_1 y_1}{1 + \omega s_1} \Rightarrow \delta s_1 + \epsilon y_1 = \beta \Rightarrow 0 < s_1 < \frac{\beta}{\delta} \leqslant M_1, 0 < y_1 < \frac{\beta}{\epsilon} \leqslant M_1.$$

Moreover, from Eqs. (1.7) and (1.8) we have

$$c p_1 = \pi y_1 + \frac{r}{\rho}\lambda - \frac{mr}{\rho} x_1 \Rightarrow c p_1 + \frac{mr}{\rho} x_1 = \pi y_1 + \frac{r}{\rho}\lambda < \pi M_1 + \frac{r}{\rho}\lambda,$$
$$p_1 < \frac{\pi M_1 + \frac{r}{\rho}\lambda}{c} \leqslant M_2, \quad x_1 < \frac{\rho}{r}\frac{\pi M_1 + \frac{r}{\rho}\lambda}{m} \leqslant \frac{\rho M_2}{r} = M_3.$$

It follows that, $E_1 \in \overset{\circ}{\Gamma}$. □

2. Global properties

To investigate the global stability of the equilibria we construct Lyapunov functions using the method presented [30] and followed by [11, 12, 15–24, 26, 28, 29, 42]. Define $F(v) = v - 1 - \ln v$.

Theorem 2.1. *For system (1.1)-(1.4), if $\mathcal{R}_0 \leqslant 1$, then E_0 is globally asymptotically stable in Γ.*

Proof. Let $\mathcal{R}_0 \leqslant 1$ and construct a Lyapunov function $U_0(s, y, p, x)$ as:

$$U_0(s, y, p, x) = s - s_0 - \int_{s_0}^{s} \frac{s_0(1 + \omega\theta)}{\theta(1 + \omega s_0)} d\theta + y + \frac{\eta_1 s_0}{(c + r x_0)(1 + \omega s_0)} p + \frac{r\eta_1 s_0}{\rho(c + r x_0)(1 + \omega s_0)} x_0 F\left(\frac{x}{x_0}\right).$$

Clearly, $U_0(s, y, p, x) > 0$ for all $s, y, p, x > 0$ and $U_0(s_0, 0, 0, x_0) = 0$. Calculating $\frac{dU_0}{dt}$ along system (1.1)-(1.4) we obtain

$$\begin{aligned} \frac{dU_0}{dt} &= \left(1 - \frac{s_0(1 + \omega s)}{s(1 + \omega s_0)}\right)\left(\beta - \delta s - \frac{\eta_1 s p}{1 + \omega s} - \frac{\eta_2 s y}{1 + \omega s}\right) + \frac{\eta_1 s p}{1 + \omega s} + \frac{\eta_2 s y}{1 + \omega s} - \epsilon y \\ &\quad + \frac{\eta_1 s_0}{(c + r x_0)(1 + \omega s_0)}\left(\pi y - c p - r x p\right) + \frac{r\eta_1 s_0}{\rho(c + r x_0)(1 + \omega s_0)}\left(1 - \frac{x_0}{x}\right)\left(\lambda + \rho x p - m x\right) \\ &= \left(1 - \frac{s_0(1 + \omega s)}{s(1 + \omega s_0)}\right)\left(\beta - \delta s\right) + \frac{\eta_2 s_0 y}{1 + \omega s_0} - \epsilon y + \frac{\eta_1 s_0}{(c + r x_0)(1 + \omega s_0)}\pi y \\ &\quad + \frac{r\eta_1 s_0}{\rho(c + r x_0)(1 + \omega s_0)}\left(1 - \frac{x_0}{x}\right)\left(\lambda - m x\right). \end{aligned}$$

Substituting $\beta = \delta s_0$ and $\lambda = m x_0$ we get

$$\begin{aligned} \frac{dU_0}{dt} &= -\delta\frac{(s - s_0)^2}{s(1 + \omega s_0)} + \epsilon\left(\frac{\eta_2 s_0}{\epsilon(1 + \omega s_0)} + \frac{\eta_1 s_0 \pi}{\epsilon(c + r x_0)(1 + \omega s_0)} - 1\right) y - \frac{r\eta_1 s_0 m}{\rho(c + r x_0)(1 + \omega s_0)}\frac{(x - x_0)^2}{x} \\ &= -\delta\frac{(s - s_0)^2}{s(1 + \omega s_0)} - \frac{r\eta_1 s_0 m}{\rho(c + r x_0)(1 + \omega s_0)}\frac{(x - x_0)^2}{x} + \epsilon(\mathcal{R}_0 - 1) y. \end{aligned}$$

If $\mathcal{R}_0 \leqslant 1$, then $\frac{dU_0}{dt} \leqslant 0$ for all $s, y, p, x > 0$ and $\frac{dU_0}{dt} = 0$ when $s = s_0, x = x_0$ and $y = 0$. It can be easily shown that $\frac{dU_0}{dt} = 0$ at E_0 . Applying LaSalle's invariance principle, we get E_0 is globally asymptotically stable when $\mathcal{R}_0 \leqslant 1$. □

Theorem 2.2. *For system* (1.1)-(1.4)*, if* $\mathcal{R}_0 > 1$*, then* E_1 *is globally asymptotically stable in* $\overset{\circ}{\Gamma}$.

Proof. Let a function $U_1(s, y, p, x)$ be defined as:

$$U_1(s,y,p,x) = s - s_1 - \int_{s_1}^{s} \frac{s_1(1+\omega\theta)}{\theta(1+\omega s_1)} d\theta + y_1 F\left(\frac{y}{y_1}\right) + \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} p_1 F\left(\frac{p}{p_1}\right) + \frac{r\eta_1 s_1 p_1}{\rho\pi y_1(1+\omega s_1)} x_1 F\left(\frac{x}{x_1}\right).$$

Clearly, $U_1(s, y, p, x) > 0$ for all $s, y, p, x > 0$ and $U_1(s_1, y_1, p_1, x_1) = 0$. Calculating $\frac{dU_1}{dt}$ along the trajectories of (1.1)-(1.4) we obtain

$$\begin{aligned}
\frac{dU_1}{dt} &= \left(1 - \frac{s_1(1+\omega s)}{s(1+\omega s_1)}\right)\left(\beta - \delta s - \frac{\eta_1 sp}{1+\omega s} - \frac{\eta_2 sy}{1+\omega s}\right) + \left(1 - \frac{y_1}{y}\right)\left(\frac{\eta_1 sp}{1+\omega s} + \frac{\eta_2 sy}{1+\omega s} - \epsilon y\right) \\
&\quad + \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)}\left(1 - \frac{p_1}{p}\right)\left(\pi y - cp - rxp\right) + \frac{r\eta_1 s_1 p_1}{\rho\pi y_1(1+\omega s_1)}\left(1 - \frac{x_1}{x}\right)\left(\lambda + \rho xp - mx\right) \\
&= \left(1 - \frac{s_1(1+\omega s)}{s(1+\omega s_1)}\right)\left(\beta - \delta s\right) + \frac{\eta_1 s_1 p}{1+\omega s_1} + \frac{\eta_2 s_1 y}{1+\omega s_1} - \frac{\eta_1 sp}{1+\omega s}\frac{y_1}{y} - \frac{\eta_2 sy}{1+\omega s}\frac{y_1}{y} - \epsilon y + \epsilon y_1 \\
&\quad + \frac{\eta_1 s_1 p_1}{1+\omega s_1}\frac{y}{y_1} - \frac{\eta_1 s_1 p_1}{1+\omega s_1}\frac{p_1 y}{p y_1} - \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} cp + \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} cp_1 + \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} rxp_1 \\
&\quad - \frac{r\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} x_1 p + \frac{r\eta_1 s_1 p_1}{\rho\pi y_1(1+\omega s_1)}\left(1 - \frac{x_1}{x}\right)\left(\lambda - mx\right).
\end{aligned}$$

Applying the equilibrium conditions for E_1

$$\beta = \delta s_1 + \frac{\eta_1 s_1 p_1}{1+\omega s_1} + \frac{\eta_2 s_1 y_1}{1+\omega s_1}, \quad \epsilon y_1 = \frac{\eta_1 s_1 p_1}{1+\omega s_1} + \frac{\eta_2 s_1 y_1}{1+\omega s_1}, \quad cp_1 = \pi y_1 - rx_1 p_1, \quad \lambda = mx_1 - \rho x_1 p_1.$$

we get

$$\begin{aligned}
\frac{dU_1}{dt} &= -\delta\frac{(s-s_1)^2}{s(1+\omega s_1)} + \left(1 - \frac{s_1(1+\omega s)}{s(1+\omega s_1)}\right)\left(\frac{\eta_1 s_1 p_1}{1+\omega s_1} + \frac{\eta_2 s_1 y_1}{1+\omega s_1}\right) \\
&\quad - \frac{\eta_1 s_1 p_1}{1+\omega s_1}\frac{spy_1(1+\omega s_1)}{s_1 p_1 y(1+\omega s)} - \frac{\eta_2 s_1 y_1}{1+\omega s_1}\frac{s(1+\omega s_1)}{s_1(1+\omega s)} + \frac{\eta_1 s_1 p_1}{1+\omega s_1} + \frac{\eta_2 s_1 y_1}{1+\omega s_1} \\
&\quad - \frac{\eta_1 s_1 p_1}{1+\omega s_1}\frac{p_1 y}{p y_1} + \frac{\eta_1 s_1 p_1}{1+\omega s_1} - 2\frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} rx_1 p_1 + \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} rxp_1 \\
&\quad + \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} rx_1 p_1 \frac{x_1}{x} - \frac{r\eta_1 s_1 p_1 m}{\rho\pi y_1(1+\omega s_1)}\frac{(x-x_1)^2}{x}.
\end{aligned} \tag{2.1}$$

Eq. (2.1) can be simplified as:

$$\begin{aligned}
\frac{dU_1}{dt} &= -\delta\frac{(s-s_1)^2}{s(1+\omega s_1)} + \frac{\eta_1 s_1 p_1}{1+\omega s_1}\left[3 - \frac{s_1(1+\omega s)}{s(1+\omega s_1)} - \frac{spy_1(1+\omega s_1)}{s_1 p_1 y(1+\omega s)} - \frac{p_1 y}{p y_1}\right] \\
&\quad + \frac{\eta_2 s_1 y_1}{1+\omega s_1}\left[2 - \frac{s_1(1+\omega s)}{s(1+\omega s_1)} - \frac{s(1+\omega s_1)}{s_1(1+\omega s)}\right] - \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)} rx_1 p_1\left[2 - \frac{x}{x_1} - \frac{x_1}{x}\right] \\
&\quad - \frac{r\eta_1 s_1 p_1 m}{\rho\pi y_1(1+\omega s_1)}\frac{(x-x_1)^2}{x} \\
&= -\delta\frac{(s-s_1)^2}{s(1+\omega s_1)} - \frac{\eta_1 s_1 p_1}{\pi y_1(1+\omega s_1)}\frac{r\lambda}{\rho x_1}\frac{(x-x_1)^2}{x} + \frac{\eta_1 s_1 p_1}{1+\omega s_1}\left[3 - \frac{s_1(1+\omega s)}{s(1+\omega s_1)} - \frac{spy_1(1+\omega s_1)}{s_1 p_1 y(1+\omega s)} - \frac{p_1 y}{p y_1}\right] \\
&\quad + \frac{\eta_2 s_1 y_1}{1+\omega s_1}\left[2 - \frac{s_1(1+\omega s)}{s(1+\omega s_1)} - \frac{s(1+\omega s_1)}{s_1(1+\omega s)}\right].
\end{aligned}$$

Using the rule

$$\frac{1}{n}\sum_{i=1}^{n} a_i \geqslant \sqrt[n]{\prod_{i=1}^{n} a_i}, \quad \text{where,} \quad a_i \geqslant 0, i = 1, 2, \ldots, n,$$

we get

$$\frac{1}{3}\left(\frac{s_1(1+\omega s)}{s(1+\omega s_1)} + \frac{spy_1(1+\omega s_1)}{s_1 p_1 y(1+\omega s)} + \frac{p_1 y}{p y_1}\right) \geqslant 1, \quad \frac{1}{2}\left(\frac{s_1(1+\omega s)}{s(1+\omega s_1)} + \frac{s(1+\omega s_1)}{s_1(1+\omega s)}\right) \geqslant 1.$$

Therefore, $\frac{dU_1}{dt} \leqslant 0$ for all $s, y, p, x > 0$ and $\frac{dU_1}{dt} = 0$ if and only if $s = s_1, y = y_1, p = p_1$ and $x = x_1$. It follows that the global stability of E_1 is induced from LaSalle's invariance principle. □

3. Numerical simulations

Using the values in Table 1, we consider two cases as follows:

Case 1: We simulate system (1.1)-(1.4) with the following initial conditions:

IC1: $s(0) = 14.0, y(0) = 1.0, p(0) = 1.5$, and $x(0) = 1.5$;
IC2: $s(0) = 8.0, y(0) = 2.0, p(0) = 3.0$, and $x(0) = 4.0$;
IC3: $s(0) = 4.0, y(0) = 3.5, p(0) = 6.0$, and $x(0) = 7.0$.

We fix $\omega = 0.09$ and consider the values of η_1 and η_2 as following sets:

Set (I): We let $\eta_1 = \eta_2 = 0.001$. Computing $\mathcal{R}_0 = 0.0857 < 1$, Figures (1)-(4) show that, $E_0 = (s_0, 0, 0, x_0)$ is globally asymptotically stable, where $s_0 = \frac{\beta}{\delta} = 20$ and $x_0 = \frac{\lambda}{m} = 1.4$, which agrees with the result of (2.1).

Set (II): We choose $\eta_1 = \eta_2 = 0.05$. Calculating $\mathcal{R}_0 = 4.2857 > 1$, we compute the equilibria as $E_0(20.0, 0, 0, 1.4)$ and $E_1 = (6.66, 2.66, 3.73, 5.51)$. We have observed that in Figures (1)-(4), when $\mathcal{R}_0 > 1$, the solution of the system tend to E_1 for IC1-IC3 and (2.2) is confirmed.

Case 2. We fixed the value $\eta_1 = \eta_2 = 0.06$, by using the following initial conditions $s(0) = 7, y(0) = 2.0, p(0) = 3.0$, and $x(0) = 4.0$, we can see from Figures (5)-(8) that the evolution of the system's states with different values of ω. We have observed that $\mathcal{R}_0 > 1$, and the trajectory of the system converges to the equilibrium E_1 for smaller values of ω e.g. $\omega = 0.0, 0.2, 0.4$. Whereas, $\mathcal{R}_0 \leqslant 1$, and the system has one equilibrium E_0 when ω become larger e.g. $\omega = 2, 5$. Let ω^{ct} be the critical value of the parameter ω, such that

$$\mathcal{R}_0 = \frac{(\eta_1 \pi m + \eta_2 c m + \eta_2 r \lambda)\beta}{\epsilon(cm + r\lambda)(\delta + \beta\omega^{ct})} = 1.$$

Using the data given in Table 1, we obtain $\omega^{ct} = 0.67$. The variation of $\mathcal{R}_0$ w.r.t. ω are listed in Table 2. We can observed that as ω is increased then $\mathcal{R}_0$ is decreased. Moreover, we have the following cases:

(i) if $0 \leqslant \omega < 0.67$, then E_1 exists and it is globally asymptotically stable,
(ii) if $\omega \geqslant 0.67$, then E_0 is globally asymptotically stable.

Table 1: The value of the parameters of model (1.1)-(1.4).

Parameter	Value	Parameter	Value
β	2	δ	0.1
η_1	varied	η_2	varied
π	4	c	0.1
r	0.5	λ	1.4
m	1	ρ	0.2
ω	varied	ϵ	0.5

Table 2: The value of $\mathcal{R}_0$ for different values of ω.

ω	Equilibria	$\mathcal{R}_0$
0.0	(3.77, 3.24, 3.91, 6.43)	14.3997
0.2	(8.93, 2.21, 3.54, 4.80)	2.8800
0.4	(15.93, 0.08, 2.25, 2.60)	1.6000
0.67	(20.00, 0.00, 0.00, 1.40)	1.00
1	(20.00, 0.00, 0.00, 1.40)	0.6857
5	(20.00, 0.00, 0.00, 1.40)	0.1426

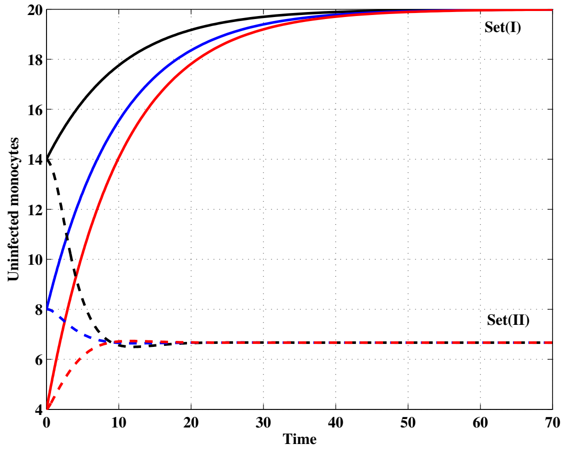

Figure 1: Uninfected monocytes.

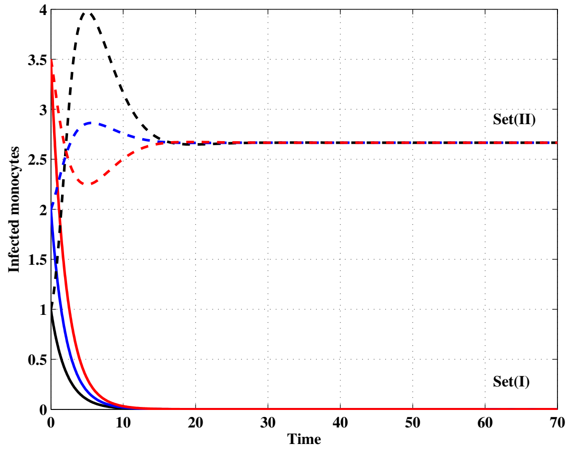

Figure 2: Infected monocytes.

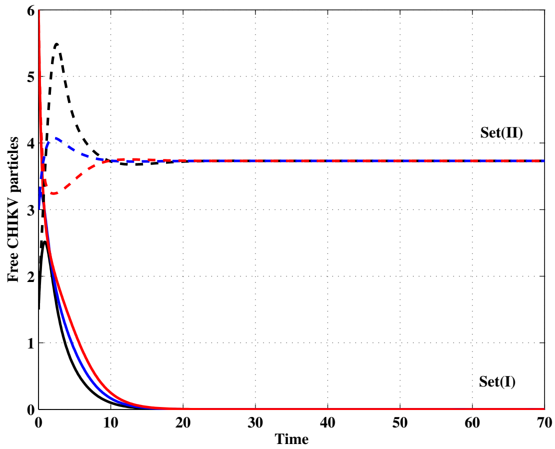

Figure 3: Free CHIKV particles.

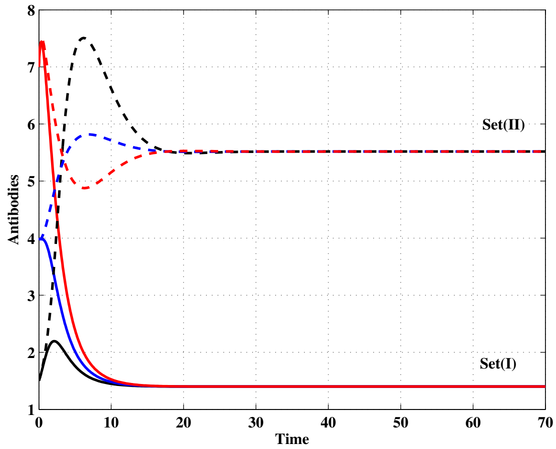

Figure 4: Antibodies.

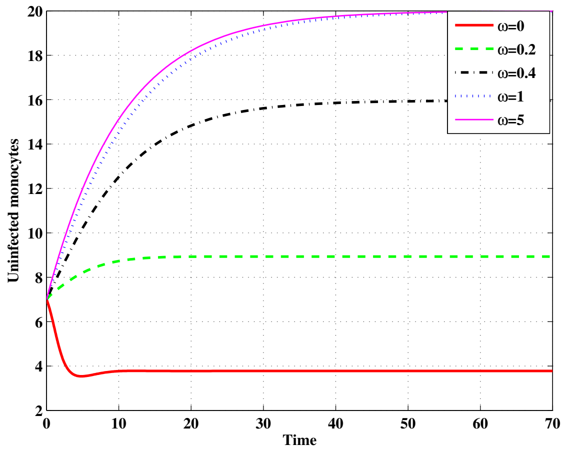

Figure 5: Uninfected monocytes.

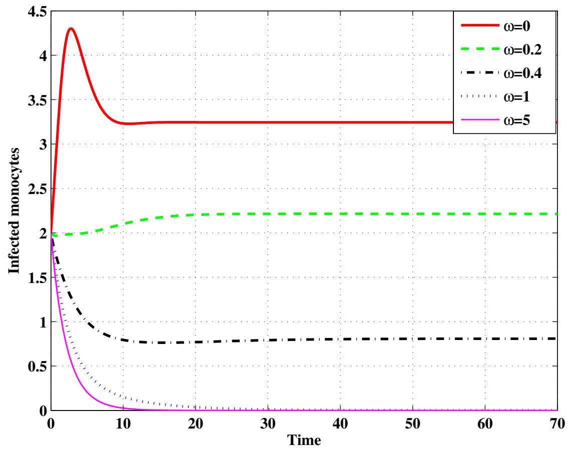

Figure 6: Infected monocytes.

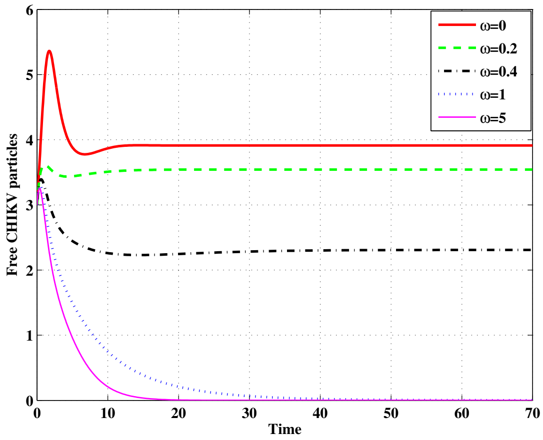

Figure 7: Free CHIKV particles.

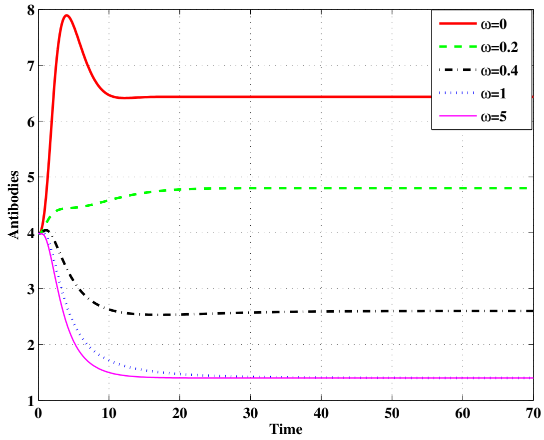

Figure 8: Antibodies.

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