# Effect of antibodies and latently infected cells on HIV dynamics with differential drug efficacy in cocirculating target cells

A. M. Shehata[a,b], A. M. Elaiw[c] and E. Kh. Elnahary[d]

[a]Department of Electrical, Electronic and Computer Engineering, University of Pretoria, South Africa

[b]Department of Mathematics, Faculty of Science, Al-Azhar University, Assiut, Egypt.

[c]Department of Mathematics, Faculty of Science, King Abdulaziz University, P.O. Box 80203, Jeddah 21589, Saudi Arabia.

[d]Department of Mathematics, Faculty of Science, Sohag University, Sohag, Egypt.

Emails: ah moukh81@yahoo.com (A. M. Shehata), a m elaiw@yahoo.com (A.M.Elaiw), e elnahary@yahoo.com (E. Kh. Elnahary).

**Abstract**

In this paper, we investigate the qualitative behaviors of three viral infection models with two types of cocirculating target cells. The models take into account both antibodies and latently infected cells. The incidence rate is represented by bilinear, saturation and general function. For the first two models, we have derived two threshold parameters, $R_0$ and $R_1$ which completely determined the global properties of the models. Lyapunov functions are constructed and LaSalle's invariance principle is applied to prove the global asymptotic stability of all equilibria of the models. For the third model, we have established a set of conditions on the general incidence rate function which are sufficient for the global stability of the equilibria of the model. Theoretical results have been checked by numerical simulations.

**Keywords:** Virus infection; Global stability; Latently infected cells; cocirculating target cells; Lyapunov function.

## 1 Introduction

Mathematical modeling and model analysis of virus infection in vivo have attracted the interests of mathematicians during the recent years. Such virus infection models can be very useful in the control of epidemic diseases and provide insights into the dynamics of viral load in vivo. Therefore, mathematical analysis of the virus infection models can play a significant role in the development of a better understanding of diseases and various drug therapy strategies.Many authors have formulated mathematical models to describe the population dynamics of several viruses such as, human immunodeficiency virus (HIV) (see e.g. [1]-[10]), hepatitis B virus (HBV) [11]-[13], hepatitis C virus (HCV) [14]-[15], human T cell leukemia HTLV [16] and dengue virus [17], etc. During viral infections, the host immune system reacts with antigen-specific immune response. The immune system has two main responses to viral infections. The first is based on the Cytotoxic T Lymphocyte (CTL) cells which are responsible to attack and kill the infected cells. The second immune response is based on the antibodies that are produced by the B cells. The function of the antibodies is to attack the viruses [1]. In some infections such as in malaria, the CTL immune response is less effective than the antibody immune response [18]. Several mathematical models have been proposed to consider the antibody immune response into the viral infection models ([19]-[24]). The basic model of viral infection with antibody immune response has been introduced by Murase et. al. [19] and Wang and Zou [21] as:

$$\dot{x} = \lambda - dx - \bar{\beta}xv, \tag{1}$$
$$\dot{y} = \bar{\beta}xv - ay, \tag{2}$$
$$\dot{v} = ky - cv - rzv, \tag{3}$$
$$\dot{z} = gzv - \mu z, \tag{4}$$

where $x, y, v$ and $z$ represent, respectively, the concentrations of uninfected cells, infected cells, free viruses and the antibody immune cells. Parameters $\lambda$, $k$ and $g$ represent respectively, the rate of new uninfected cells that are generated from sources within the body, the rate of free virus production and the proliferation rate constant of the antibody immune cells. Parameters $d, a, c$ and $\mu$ are the natural death rate constant of uninfected cells, infected cells, free virus particles and the antibody immune cells respectively. Parameter $\bar{\beta}$ is the infection rate constant at which a target cell becomes infected via contacting with virus and $r$ is the removal rate constant of the virus due to the antibodies. Model (1)-(4) is based on the assumption that the infection could occur and that the viruses are produced from infected cells instantaneously, once the uninfected cells are contacted by the virus particles. Other accurate models incorporate the latently infected cells which are due to the delay between the time of infection and the time when the infected cell becomes active to produce infectious viruses. In [26], model (1)-(4) was extended to take into consideration both latently and actively infected cells as:

$$\dot{x} = \lambda - dx - \bar{\beta}xv, \tag{5}$$
$$\dot{w} = (1-\alpha)\bar{\beta}xv - (e+b)w, \tag{6}$$
$$\dot{y} = \alpha\bar{\beta}xv + bw - ay, \tag{7}$$
$$\dot{v} = ky - cv - rvz, \tag{8}$$
$$\dot{z} = gvz - \mu z, \tag{9}$$

where $w$ and $y$ are the concentrations of latently infected and actively infected cells, respectively. Eq. (6) describes the population dynamics of the latently infected cells and show that they are converted to actively infected cells with rate constant $b$. The parameters $e$ and $a$ are the death rate constants of the latently and actively infected cells, respectively. The fractions $(1-\alpha)$ where, $0 < \alpha < 1$ are the probabilities that upon infection, an uninfected cell will become either latently infected or actively infected. Model (5)-(9) it have been assumed that, the HIV has one class of target cells, $CD4^{+}$T cells. However, Perelson et al. in [25] have shown that, HIV infects the macrophages in addition to the $CD4^{+}$T cells. Recently, many efforts have been devoted to study various mathematical models of HIV dynamics with two classes of target cells (see e.g. [3]).

Our primary goal of the present paper is to propose the global stability analysis of three viral infection models with two types of target cells, $CD4^{+}$T cells and macrophages taking into consideration the latently, actively infected cells and antibody immune response. The infection rate is represented by bilinear incidence and saturated incidence in the first and the second models, respectively, while it is given by a general function in the third one. The global stability of the three models is established using Lyapunov functionals.

## 2 HIV model with bilinear incidence rate

In this section, we introduce an HIV dynamics model which describes two cocirculation populations of target cells, $CD4^{+}$ T cells and macrophages and takes into account the antibody immune response. We consider two types of infected cells, the latently infected and actively infected cells.

$$\dot{x}_i = \lambda_i - d_i x_i - \beta_i x_i v, \qquad i = 1, 2, \tag{10}$$
$$\dot{w}_i = (1-\alpha_i)\beta_i x_i v - (e_i + b_i)w_i, \qquad i = 1, 2, \tag{11}$$
$$\dot{y}_i = \alpha_i \beta_i x_i v + b_i w_i - a_i y_i, \qquad i = 1, 2, \tag{12}$$
$$\dot{v} = \sum_{i=1}^{2} k_i y_i - cv - rvz, \tag{13}$$
$$\dot{z} = gvz - \mu z. \tag{14}$$

Here $i = 1, 2$ correspond to the CD4$^+$ T cells and macrophages and $\beta_1 = (1-\varepsilon)\bar{\beta}_1,\ \beta_2 = (1-\varepsilon f)\bar{\beta}_2$. The model incorporates RTI drug therapy where in the CD4$^+$T cells, the drug efficacy is $\varepsilon$ and $0 \leqslant \varepsilon < 1$, while in the macrophages the drug efficacy $\varepsilon f$ is reduced by a factor $f$ and $0 < f < 1$. All the parameters and variables of the model have the same meanings as given in (5)-(9).

## 2.1 Properties of solutions

One can easily show that the non-negative orthant $\mathbb{R}^8 \geq 0$ by model (10)-(14).

**Proposition 1.** There exist positive numbers $L_j,\ j = 1, 2, 3, 4$ such that the compact set $\Omega = \left\{(x_i, w_i, y_i, v, z) \in \mathbb{R}^8 \geq 0 : 0 \leq x_i, w_i, y_i \leq L_i,\ 0 \leq v \leq L_3,\ 0 \leq z \leq L_4,\ i = 1, 2\right\}$ is positively invariant.

**Proof**. To show the boundedness of the solutions of system (10)-(14) we let $T_i(t) = x_i(t) + w_i(t) + y_i(t)$, then

$$\dot{T}_i(t) = \lambda_i - d_i x_i(t) - e_i w_i(t) - a_i y_i(t) \leq \lambda_i - \rho_i T_i(t),$$

where $\rho_i = \min\{d_i, a_i, e_i\}, i = 1, 2$. Hence $T_i(t) \leq L_i$, if $T_i(0) \leq L_i$, where $L_i = \dfrac{\lambda_i}{\rho_i}$. Since $x_i(t)$, $w_i(t)$ and $y(t)$ are all non-negative, then $0 \leq x_i(t),\ w_i(t),\ y_i(t) \leq L_i$, for all $t \geq 0$, if $0 \leq x_i(0) + w_i(0) + y_i(0) \leq L_i$, $i = 1, 2$. On the other hand, let $G(t) = v(t) + \dfrac{r}{g} z(t)$, then

$$\dot{G}(t) = \sum_{i=1}^{2} k_i y_i - cv - \frac{r\mu}{g} z \leq \sum_{i=1}^{2} k_i L_i - \delta\left(v + \frac{r}{g} z\right) = \sum_{i=1}^{2} k_i L_i - \delta G(t),$$

where $\delta = \min\{c, \mu\}$. Hence $G(t) \leq L_3$, if $G(0) \leq L_3$, where $L_3 = \dfrac{1}{\delta}\sum\limits_{i=1}^{2} k_i L_i$. Since $v(t) \geq 0$ and $z(t) \geq 0$, then $0 \leq v(t) \leq L_3$ and $0 \leq z(t) \leq L_4$ if $0 \leq v(0) + \dfrac{r}{g} z(0) \leq L_3$, where $L_4 = \dfrac{g L_3}{r}$.

## 2.2 Equilibria and biological thresholds

Let $\overset{\circ}{\Omega}$ be the interior of $\Omega$.

**Lemma 1**. For system (10)-(14) we have (i) There exist only one uninfected equilibrium $E_0 = (x_1^0, x_2^0, 0, 0, 0, 0, 0, 0) \in \Omega$, when $R_0 \leq 1$.

(ii) There exist $E_0$ and a chronic-infection equilibrium without antibody immune response $E_1 = (\tilde{x}_1, \tilde{x}_2, \tilde{w}_1, \tilde{w}_2, \tilde{y}_1, \tilde{y}_2, \tilde{v}, 0, ) \in \Omega$, when $R_1 \leq 1 < R_0$.

(iii) There exist $E_0$, $E_1$ and a chronic-infection equilibrium with antibody immune response $E_2 = (\bar{x}_1, \bar{x}_2, \bar{w}_1, \bar{w}_2, \bar{y}_1, \bar{y}_2, \bar{v}, \bar{z}) \in \overset{\circ}{\Omega}$, when $R_1 > 1$.

**Proof**. The equilibria of (10)-(14) satisfy the following equations:

$$\lambda_i - d_i x_i - \beta_i x_i v = 0, \tag{15}$$

$$(1-\alpha_i)\beta_i x_i v - (e_i + b_i) w_i = 0, \tag{16}$$

$$\alpha_i \beta_i x_i v + b_i w_i - a_i y_i = 0, \tag{17}$$

$$\sum_{i=1}^{2} k_i y_i - cv - rvz = 0, \tag{18}$$

$$gvz - \mu z = 0. \tag{19}$$

Eq. (19) has two possible solutions $z = 0$ or $v = \dfrac{\mu}{g}$. If $z = 0$, then from Eqs.(15)-(17) we get

$$x_i = \frac{x_i^0}{(1 + \eta_i v)}, \qquad w_i = \frac{(1-\alpha_i)\beta_i x_i^0}{(e_i + b_i)(1 + \eta_i v)} v, \qquad y_i = \frac{(e_i \alpha_i + b_i)\beta_i x_i^0}{a_i (e_i + b_i)(1 + \eta_i v)} v, \tag{20}$$

where $x_i^0 = \dfrac{\lambda_i}{d_i}$, $\eta_i = \dfrac{\beta_i}{d_i}$, $i = 1, 2$. From Eq. (18) we obtain

$$\left(\sum_{i=1}^{2} \frac{(e_i \alpha_i + b_i) k_i \beta_i x_i^0}{a_i c (e_i + b_i)(1 + \eta_i v)} - 1\right) cv = 0. \tag{21}$$

We note that $v = 0$ is a solution for Eq. (21) which leads to the disease-free equilibrium $E_0 = (x_1^0, x_2^0, 0, 0, 0, 0, 0, 0)$. If $v \neq 0$, we have

$$\sum_{i=1}^{2} \frac{\Phi_i}{1+\eta_i v} = 1. \tag{22}$$

where $\Phi_i = \dfrac{(e_i\alpha_i + b_i)k_i\beta_i x_i^0}{a_i c(e_i+b_i)}$. Equation (22) can be written as:

$$Av^2 + Bv - C = 0, \tag{23}$$

where

$$A = \eta_1\eta_2, \quad B = \eta_1\Phi_1 + \eta_2\Phi_2 + (1 - \Phi_1 - \Phi_2)(\eta_1 + \eta_2), \quad C = \Phi_1 + \Phi_2 - 1$$

The solutions of Eq. (23) is given by

$$v^{\pm} = \frac{-B \pm \sqrt{B^2 + 4AC}}{2A}.$$

We have $A > 0$, therefore if $C > 0$, then $v^+ > 0$ and $v^- < 0$. Let $\tilde{v} = v^+$, then from Eq. (20) we get

$$\tilde{x}_i = \frac{x_i^0}{1+\eta_i\tilde{v}}, \quad \tilde{w}_i = \frac{(1-\alpha_i)\beta_i x_i^0}{(e_i+b_i)(1+\eta_i\tilde{v})}\tilde{v}, \quad \tilde{y}_i = \frac{(e_i\alpha_i + b_i)\beta_i x_i^0}{a_i(e_i+b_i)(1+\eta_i\tilde{v})}\tilde{v}, \quad i = 1, 2. \tag{24}$$

Therefore, a chronic-infection equilibrium without antibody immune response $E_1 = (\tilde{x}_1, \tilde{x}_2, \tilde{w}_1, \tilde{w}_2, \tilde{y}_1, \tilde{y}_2, \tilde{v}, 0)$ exists when $C > 0$ or $(\Phi_1 + \Phi_2 > 1)$. Now we are ready to define the basic infection reproduction number $R_0$ as

$$R_0 = \Phi_1 + \Phi_2 = \sum_{i=1}^{2} R_{0i} = \sum_{i=1}^{2} \frac{k_i\beta_i x_i^0(e_i\alpha_i + b_i)}{a_i c(e_i+b_i)}.$$

If $v = \dfrac{\mu}{g}$, then we obtain the chronic-infection equilibrium with antibody immune response $E_2 = (\bar{x}_1, \bar{x}_2, \bar{w}_1, \bar{w}_2, \bar{y}_1, \bar{y}_2, \bar{v}, \bar{z})$, where

$$\bar{x}_i = \frac{g\lambda_i}{gd_i + \mu\beta_i}, \quad \bar{w}_i = \frac{(1-\alpha_i)\lambda_i\beta_i\mu}{(e_i+b_i)(gd_i+\mu\beta_i)}, \quad \bar{y}_i = \frac{(e_i\alpha_i + b_i)\lambda_i\beta_i\mu}{a_i(e_i+b_i)(gd_i+\mu\beta_i)}, \quad i = 1, 2,$$
$$\bar{v} = \frac{\mu}{g}, \qquad \bar{z} = \frac{c}{r}\left(\sum_{i=1}^{2} \frac{gk_i\beta_i\lambda_i(e_i\alpha_i + b_i)}{a_i c(e_i+b_i)(gd_i+\mu\beta_i)} - 1\right).$$

We note that $E_2$ exists when $\sum_{i=1}^{2} \dfrac{gk_i\beta_i\lambda_i(e_i\alpha_i + b_i)}{a_i c(e_i+b_i)(gd_i+\mu\beta_i)} > 1$. Let us define the antibody immune response activation number as

$$R_1 = \sum_{i=1}^{2} \frac{gk_i\beta_i\lambda_i(e_i\alpha_i + b_i)}{a_i c(e_i+b_i)(gd_i+\mu\beta_i)} = \sum_{i=1}^{2} \frac{R_{0i}}{1 + \frac{\mu\beta_i}{gd_i}},$$

which determines whether or not a persistent antibody immune response can be established. Then we can write $\bar{z} = \dfrac{c}{r}(R_1 - 1)$. Clearly $R_1 < R_0$.

Now, we show that $E_0,\ E_1 \in \Omega$ and $E_2 \in \mathring{\Omega}$. Clearly, $E_0 \in \Omega$. Let $R_0 > 1$, then from Eq. (20) we have $\tilde{x}_i < x_i^0$, then

$$0 < \tilde{x}_i < \frac{\lambda_i}{d_i} \leq \frac{\lambda_i}{\rho_i} = L_i.$$

From Eqs. (10)-(12), we get

$$\lambda_i = d_i\tilde{x}_i + e_i\tilde{w}_i + a_i\tilde{y}_i.$$

Thus,

$$0 < \tilde{w}_i < \frac{\lambda_i}{e_i} \leq \frac{\lambda_i}{\rho_i} = L_i, \qquad 0 < \tilde{y}_i < \frac{\lambda_i}{a_i} \leq \frac{\lambda_i}{\rho_i} = L_i.$$

Also, $\tilde{v} = \frac{1}{c}\sum_{i=1}^{2} k_i\tilde{y}_i < \frac{1}{c}\sum_{i=1}^{2} k_iL_i \leq \frac{1}{\delta}\sum_{i=1}^{2} k_iL_i = L_3$. Moreover, $\tilde{z} = 0$, and then, $E_1 \in \Omega$. Let $R_1 > 1$, then one can show that $0 < \bar{x}_i < L_i$, $0 < \bar{w}_i < L_i$ and $0 < \bar{y}_i < L_i$. Now we show that $0 < \bar{v} < L_3$ and $0 < \bar{z} < L_4$. From Eq. (13), we have $c\bar{v} + r\bar{v}\bar{z} = \sum_{i=1}^{2} k_i\bar{y}_i$. Then

$$c\bar{v} < \sum_{i=1}^{2} k_i\bar{y}_i \Rightarrow 0 < \bar{v} < \frac{1}{c}\sum_{i=1}^{2} k_iL_i \leqslant \frac{1}{\delta}\sum_{i=1}^{2} k_iL_i = L_3,$$

$$r\bar{v}\bar{z} < \sum_{i=1}^{2} k_i\bar{y}_i \Rightarrow 0 < \bar{z} < \frac{g}{r\mu}\sum_{i=1}^{2} k_i\bar{y}_i < \frac{g}{r\delta}\sum_{i=1}^{2} k_iL_i = \frac{gL_3}{r} = L_4.$$

It follows that, $E_2 \in \mathring{\Omega}$.

## 2.3 Global stability

Let us define the function $F(s) = s - 1 - \ln s$.

**Theorem 1.** The infection-free equilibrium $E_0$ of system (10)-(14) is GAS when $R_0 \leq 1$.

**Proof.** Define a Lyapunov function $W_0$ as follows:

$$W_0 = \sum_{i=1}^{2} \gamma_i \left[ x_i^0 F\left(\frac{x_i}{x_i^0}\right) + \frac{b_i}{e_i\alpha_i + b_i} w_i + \frac{e_i + b_i}{e_i\alpha_i + b_i} y_i \right] + v + \frac{r}{g} z, \tag{25}$$

where $\gamma_i = \dfrac{k_i(e_i\alpha_i + b_i)}{a_i(e_i + b_i)}$, $\quad i = 1, 2$. The time derivative of $W_0$ along the trajectories of (10)-(14) satisfies

$$\begin{aligned}\frac{dW_0}{dt} &= \sum_{i=1}^{2} \gamma_i \left[ \left(1 - \frac{x_i^0}{x_i}\right)(\lambda_i - d_ix_i - \beta_ix_iv) + \frac{b_i}{e_i\alpha_i + b_i}((1-\alpha_i)\beta_ix_iv - (e_i + b_i)w_i) \right. \\ &\left. + \frac{e_i + b_i}{e_i\alpha_i + b_i}(\alpha_i\beta_ix_iv + b_iw_i - a_iy_i) \right] + \sum_{i=1}^{2} k_iy_i - cv - rvz + \frac{r}{g}(gvz - \mu z). \end{aligned} \tag{26}$$

Collecting terms of Eq. (26) we get

$$\begin{aligned}\frac{dW_0}{dt} &= \sum_{i=1}^{2} \gamma_i \left[ d_i\left(1 - \frac{x_i^0}{x_i}\right)(x_i^0 - x_i) + \beta_ix_i^0v \right] - cv - \frac{r\mu}{g}z \\ &= -\sum_{i=1}^{2} \gamma_id_i\frac{(x_i - x_i^0)^2}{x_i} + \sum_{i=1}^{2} \frac{k_i(e_i\alpha_i + b_i)}{a_i(e_i + b_i)}\beta_ix_i^0v - cv - \frac{r\mu}{g}z \\ &= -\sum_{i=1}^{2} \gamma_id_i\frac{(x_i - x_i^0)^2}{x_i} + \left(\sum_{i=1}^{2} \frac{k_i\beta_ix_i^0(e_i\alpha_i + b_i)}{a_ic(e_i + b_i)} - 1\right)cv - \frac{r\mu}{g}z \\ &= -\sum_{i=1}^{2} \gamma_id_i\frac{(x_i - x_i^0)^2}{x_i} + (R_0 - 1)cv - \frac{r\mu}{g}z. \end{aligned} \tag{27}$$

If $R_0 \leq 1$ then $\frac{dW_0}{dt} \leq 0$ for all $x_i, v, z > 0$. Thus, the solutions of system (10)-(14) converge to $\Omega$, the largest invariant subset of $\left\{\frac{dW_0}{dt} = 0\right\}$ [27]. Clearly, it follows from Eq. (26) that $\frac{dW_0}{dt} = 0$ if and only if $x_i = x_i^0$, $v = 0$ and $z = 0$. The set $\Omega$ is invariant and for any element belongs to $\Omega$ satisfies $v = 0$ and $z = 0$, then $\dot{v} = 0$. We can see from Eq. (13) that $0 = \dot{v} = \sum_{i=1}^{2} k_iy_i$, and thus $y_i = 0$. Moreover, from Eq. (12) we get $w_i = 0$. Hence $\frac{dW_0}{dt} = 0$ occurs at $E_0$. From LaSalle's invariance principle, $E_0$ is GAS.

**Theorem 2.** The chronic-infection equilibrium without antibody immune response $E_1$ of system (10)-(14) is GAS when $R_1 \leq 1 < R_0$.

**Proof.** We construct the following Lyapunov function

$$W_1 = \sum_{i=1}^{2} \gamma_i \left[ \tilde{x}_i F(\frac{x_i}{\tilde{x}_i}) + \frac{b_i}{e_i\alpha_i + b_i} \tilde{w}_i F\left(\frac{w_i}{\tilde{w}_i}\right) + \frac{e_i + b_i}{e_i\alpha_i + b_i} \tilde{y}_i F\left(\frac{y_i}{\tilde{y}_i}\right) \right] + \tilde{v} F\left(\frac{v}{\tilde{v}}\right) + \frac{r}{g} z.$$

Calculating $\frac{dW_1}{dt}$ along the trajectories of (10)-(14) we get

$$\frac{dW_1}{dt} = \sum_{i=1}^{2} \gamma_i \left[ \left(1 - \frac{\tilde{x}_i}{x_i}\right)(\lambda_i - d_i x_i - \beta_i x_i v) + \frac{b_i}{e_i\alpha_i + b_i}\left(1 - \frac{\tilde{w}_i}{w_i}\right)((1-\alpha_i)\beta_i x_i v - (e_i + b_i) w_i) \right.$$
$$\left. + \frac{e_i + b_i}{e_i\alpha_i + b_i}\left(1 - \frac{\tilde{y}_i}{y_i}\right)(\alpha_i\beta_i x_i v + b_i w_i - a_i y_i) \right] + \left(1 - \frac{\tilde{v}}{v}\right)\left(\sum_{i=1}^{2} k_i y_i - cv - rvz\right) + \frac{r}{g}(gvz - \mu z). \quad (28)$$

Collecting terms of Eq. (28) we get

$$\frac{dW_1}{dt} = \sum_{i=1}^{2} \gamma_i \left[ \left(1 - \frac{\tilde{x}_i}{x_i}\right)(\lambda_i - d_i x_i) + \beta_i \tilde{x}_i v - \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\frac{\beta_i x_i v \tilde{w}_i}{w_i} + \frac{e_i + b_i}{e_i\alpha_i + b_i} b_i \tilde{w}_i - \frac{\alpha_i (e_i + b_i)}{e_i\alpha_i + b_i}\frac{\beta_i x_i v \tilde{y}_i}{y_i} \right.$$
$$\left. - \frac{b_i (e_i + b_i)}{e_i\alpha_i + b_i}\frac{w_i \tilde{y}_i}{y_i} + \frac{e_i + b_i}{e_i\alpha_i + b_i} a_i \tilde{y}_i \right] - cv - \frac{\tilde{v}}{v}\sum_{i=1}^{2} k_i y_i + c\tilde{v} + r\tilde{v}z - \frac{r\mu}{g} z. \quad (29)$$

Using the value of $\tilde{x}_i$ given in Eq. (24) we get $\left(\sum_{i=1}^{2} \gamma_i \beta_i \tilde{x}_i - c\right) v = 0$. Applying $\lambda_i = d_i\tilde{x}_i + \beta_i \tilde{x}_i \tilde{v}$, we obtain

$$\frac{dW_1}{dt} = \sum_{i=1}^{2} \gamma_i \left[ \left(1 - \frac{\tilde{x}_i}{x_i}\right)(d_i\tilde{x}_i - d_i x_i) + \beta_i \tilde{x}_i \tilde{v}\left(1 - \frac{\tilde{x}_i}{x_i}\right) - \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\frac{\beta_i x_i v \tilde{w}_i}{w_i} + \frac{e_i + b_i}{e_i\alpha_i + b_i} b_i \tilde{w}_i \right.$$
$$\left. - \frac{\alpha_i (e_i + b_i)}{e_i\alpha_i + b_i}\frac{\beta_i x_i v \tilde{y}_i}{y_i} - \frac{b_i (e_i + b_i)}{e_i\alpha_i + b_i}\frac{w_i \tilde{y}_i}{y_i} + \frac{e_i + b_i}{e_i\alpha_i + b_i} a_i \tilde{y}_i \right] - \frac{\tilde{v}}{v}\sum_{i=1}^{2} k_i y_i + c\tilde{v} + r\tilde{v}z - \frac{r\mu}{g} z. \quad (30)$$

Using the equilibrium condition for $E_1$

$$(1-\alpha_i)\beta_i \tilde{x}_i \tilde{v} = (e_i + b_i)\tilde{w}_i, \quad \alpha_i\beta_i \tilde{x}_i \tilde{v} + b_i \tilde{w}_i = a_i \tilde{y}_i, \quad c\tilde{v} = \sum_{i=1}^{2} k_i \tilde{y}_i = \sum_{i=1}^{2} \gamma_i \beta_i \tilde{x}_i \tilde{v},$$

$$\frac{e_i + b_i}{e_i\alpha_i + b_i} a_i \tilde{y}_i = \beta_i \tilde{x}_i \tilde{v} = \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v} + \frac{(e_i + b_i)\alpha_i}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v}.$$

we have

$$\frac{dW_1}{dt} = \sum_{i=1}^{2} \gamma_i \left[ -d_i \frac{(x_i - \tilde{x}_i)^2}{x_i} + \beta_i \tilde{x}_i \tilde{v}\left(1 - \frac{\tilde{x}_i}{x_i}\right)\left(\frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i} + \frac{(e_i + b_i)\alpha_i}{e_i\alpha_i + b_i}\right) - \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v}\frac{x_i \tilde{w}_i v}{\tilde{x}_i w_i \tilde{v}} \right.$$
$$+ \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v} - \frac{(e_i + b_i)\alpha_i}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v}\frac{x_i \tilde{y}_i v}{\tilde{x}_i y_i \tilde{v}} - \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v}\frac{w_i \tilde{y}_i}{\tilde{w}_i y_i} + \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v} + \frac{(e_i + b_i)\alpha_i}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v}$$
$$\left. - \left(\frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i} + \frac{(e_i + b_i)\alpha_i}{e_i\alpha_i + b_i}\right)\beta_i \tilde{x}_i \tilde{v}\frac{y_i \tilde{v}}{\tilde{y}_i v} + \left(\frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i} + \frac{(e_i + b_i)\alpha_i}{e_i\alpha_i + b_i}\right)\beta_i \tilde{x}_i \tilde{v} \right] + (\tilde{v} - \bar{v})\, rz.$$
$$= \sum_{i=1}^{2} \gamma_i \left[ -d_i \frac{(x_i - \tilde{x}_i)^2}{x_i} + \frac{b_i(1-\alpha_i)}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v}\left(4 - \frac{\tilde{x}_i}{x_i} - \frac{x_i \tilde{w}_i v}{\tilde{x}_i w_i \tilde{v}} - \frac{y_i \tilde{v}}{\tilde{y}_i v} - \frac{w_i \tilde{y}_i}{\tilde{w}_i y_i}\right) \right.$$
$$\left. + \frac{(e_i + b_i)\alpha_i}{e_i\alpha_i + b_i}\beta_i \tilde{x}_i \tilde{v}\left(3 - \frac{\tilde{x}_i}{x_i} - \frac{y_i \tilde{v}}{\tilde{y}_i v} - \frac{x_i \tilde{y}_i v}{\tilde{x}_i y_i \tilde{v}}\right) \right] + (\tilde{v} - \bar{v})\, rz. \quad (31)$$

We have $x_i, w_i, y_i, v > 0$ when $R_0 > 1$. Since the geometrical mean is less than or equal to the arithmetical mean, the second and the third terms are less than or equal to zero. Now we show that if $R_1 \leq 1$ then $\tilde{v} \leq \frac{\mu}{g} = \bar{v}$.

Using the steady state conditions for $E_1$ we have $\sum_{i=1}^{2}\frac{k_i\beta_i\lambda_i(e_i\alpha_i+b_i)}{a_icd_i(e_i+b_i)(1+\eta_i\tilde{v})}=1$, then

$$\begin{aligned}R_1-1&=\sum_{i=1}^{2}\frac{gk_i\beta_i\lambda_i(e_i\alpha_i+b_i)}{a_ic(e_i+b_i)(gd_i+\mu\beta_i)}-\sum_{i=1}^{2}\frac{k_i\beta_i\lambda_i(e_i\alpha_i+b_i)}{a_id_ic(e_i+b_i)(1+\eta_i\tilde{v})}\\&=\sum_{i=1}^{2}\frac{k_i\beta_i\lambda_i(e_i\alpha_i+b_i)}{a_id_ic(e_i+b_i)(1+\eta_i\bar{v})}-\sum_{i=1}^{2}\frac{k_i\beta_i\lambda_i(e_i\alpha_i+b_i)}{a_id_ic(e_i+b_i)(1+\eta_i\tilde{v})}=(\tilde{v}-\bar{v})\chi,\end{aligned}\tag{32}$$

where $\chi=\sum_{i=1}^{2}\frac{k_i\beta_i\lambda_i\eta_i(e_i\alpha_i+b_i)}{a_id_ic(e_i+b_i)(1+\eta_i\bar{v})(1+\eta_i\tilde{v})}$. It follows that, if $R_1\leq 1$ then $\frac{dW_1}{dt}\leq 0$ for all $x_i,w_i,y_i,v,z>0$. Thus, the solutions of system (10)-(14) limit to $\Omega$, the largest invariant subset of $\left\{\frac{dW_1}{dt}=0\right\}$ [27]. It can be seen that, $\frac{dW_1}{dt}=0$ occurs at $E_1$. Applying LaSalle's invariance principle we obtain that $E_1$ is GAS.

**Theorem 3.** The chronic-infection equilibrium with antibody immune response $E_2$ of system (10)-(14) is GAS when $R_1>1$.

**Proof.** Consider the following Lyapunov function

$$W_2=\sum_{i=1}^{2}\gamma_i\left[\bar{x}_iF(\frac{x_i}{\bar{x}_i})+\frac{b_i}{e_i\alpha_i+b_i}\bar{w}_iF\left(\frac{w_i}{\bar{w}_i}\right)+\frac{e_i+b_i}{e_i\alpha_i+b_i}\bar{y}_iF\left(\frac{y_i}{\bar{y}_i}\right)\right]+\bar{v}F\left(\frac{v}{\bar{v}}\right)+\frac{r}{g}\bar{z}F\left(\frac{z}{\bar{z}}\right).$$

Calculating the derivative of $W_2$ along the trajectories of (10)-(14) we get

$$\begin{aligned}\frac{dW_2}{dt}=&\sum_{i=1}^{2}\gamma_i\left[\left(1-\frac{\bar{x}_i}{x_i}\right)(\lambda_i-d_ix_i-\beta_ix_iv)+\frac{b_i}{e_i\alpha_i+b_i}\left(1-\frac{\bar{w}_{\bar{\imath}}}{w_i}\right)((1-\alpha_i)\beta_ix_iv-(e_i+b_i)w_i)\right.\\&\left.+\frac{e_i+b_i}{e_i\alpha_i+b_i}\left(1-\frac{\bar{y}_i}{y_i}\right)(\alpha_i\beta_ix_iv+bw_i-a_iy_i)\right]+\left(1-\frac{\bar{v}}{v}\right)(\sum_{i=1}^{2}k_iy_i-cv-rvz)+\frac{r}{g}\left(1-\frac{\bar{z}}{z}\right)(gvz-\mu z).\end{aligned}\tag{33}$$

Collecting terms of Eq. (33) we get

$$\begin{aligned}\frac{dW_2}{dt}=&\sum_{i=1}^{2}\gamma_i\left[\left(1-\frac{\bar{x}_i}{x_i}\right)(\lambda_i-d_ix_i)+\beta_i\bar{x}_iv-\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\frac{\beta_ix_iv\bar{w}_{\bar{\imath}}}{w_i}+\frac{e_i+b_i}{e_i\alpha_i+b_i}b_i\bar{w}_{\bar{\imath}}\right.\\&\left.-\frac{\alpha_i\left(e_i+b_i\right)}{e_i\alpha_i+b_i}\frac{\beta_ix_iv\bar{y}_i}{y_i}-\frac{b_i\left(e_i+b_i\right)}{e_i\alpha_i+b_i}\frac{w_i\bar{y}_i}{y_i}+\frac{e_i+b_i}{e_i\alpha_i+b_i}a_i\bar{y}_i\right]-cv-\frac{\bar{v}}{v}\sum_{i=1}^{2}k_iy_i+c\bar{v}-rv\bar{z}+\frac{r\mu}{g}\bar{z}.\end{aligned}\tag{34}$$

Applying $\lambda_i=\ d_i\bar{x}_i+\beta\bar{x}_i\bar{v}$ , we get

$$\begin{aligned}\frac{dW_2}{dt}=&\sum_{i=1}^{2}\gamma_i\left[\left(1-\frac{\bar{x}_i}{x_i}\right)(d_i\bar{x}_i-d_ix_i)+\beta_i\bar{x}_i\bar{v}\left(1-\frac{\bar{x}_i}{x_i}\right)+\beta_i\bar{x}_iv-\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\frac{\beta_ix_iv\bar{w}_{\bar{\imath}}}{w_i}+\frac{e_i+b_i}{e_i\alpha_i+b_i}b_i\bar{w}_{\bar{\imath}}\right.\\&\left.-\frac{\alpha_i\left(e_i+b_i\right)}{e_i\alpha_i+b_i}\frac{\beta_ix_iv\bar{y}_i}{y_i}-\frac{b_i\left(e_i+b_i\right)}{e_i\alpha_i+b_i}\frac{w_i\bar{y}_i}{y_i}+\frac{e_i+b_i}{e_i\alpha_i+b_i}a_i\bar{y}_i\right]-cv-\frac{\bar{v}}{v}\sum_{i=1}^{2}k_iy_i+c\bar{v}-rv\bar{z}+\frac{r\mu}{g}\bar{z}.\end{aligned}\tag{35}$$

Using the equilibrium conditions for $E_2$

$$(1-\alpha_i)\beta_i\bar{x}_i\bar{v}=(e_i+b_i)\bar{w}_i,\quad \alpha_i\beta_i\bar{x}_i\bar{v}+b_i\bar{w}_i=a_i\bar{y}_i,\quad c\bar{v}+r\bar{v}\bar{z}=\sum_{i=1}^{2}k_i\bar{y}_i=\sum_{i=1}^{2}\gamma_i\beta_i\bar{x}_i\bar{v},$$

$$\frac{e_i+b_i}{e_i\alpha_i+b_i}a_i\bar{y}_i=\beta_i\bar{x}_i\bar{v}=\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v}+\frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}\beta_i\bar{x}_i\bar{v},\quad \sum_{i=1}^{2}\gamma_i\beta_i\bar{x}_i\bar{v}-c\bar{v}-r\bar{v}\bar{z}=0,$$

we have

$$\frac{dW_2}{dt} = \sum_{i=1}^{2}\gamma_i\Bigg[-d_i\frac{(x_i-\bar{x}_i)^2}{x_i} + \beta_i\bar{x}_i\bar{v}\left(1-\frac{\bar{x}_i}{x_i}\right)\left(\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}+\frac{(e_i+b_i)\alpha_i}{e_i\alpha_i+b_i}\right) - \frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v}\frac{x_i\bar{w}_iv}{\bar{x}_iw_i\bar{v}}$$
$$+\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v} - \frac{(e_i+b_i)\alpha_i}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v}\frac{x_i\bar{y}_iv}{\bar{x}_iy_i\bar{v}} - \frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v}\frac{w_i\bar{y}_i}{\bar{w}_iy_i} + \frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v} + \frac{(e_i+b_i)\alpha_i}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v}$$
$$-\left(\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}+\frac{(e_i+b_i)\alpha_i}{e_i\alpha_i+b_i}\right)\beta_i\bar{x}_i\bar{v}\frac{y_i\bar{v}}{\bar{y}_iv} + \left(\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}+\frac{(e_i+b_i)\alpha_i}{e_i\alpha_i+b_i}\right)\beta_i\bar{x}_i\bar{v}\Bigg]$$
$$= \sum_{i=1}^{2}\gamma_i\Bigg[-d_i\frac{(x_i-\bar{x}_i)^2}{x_i} + \frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}\beta_i\bar{x}_i\bar{v}\left[4-\frac{\bar{x}_i}{x_i}-\frac{x_i\bar{w}_iv}{\bar{x}_iw_i\bar{v}}-\frac{y_i\bar{v}}{\bar{y}_iv}-\frac{w_i\bar{y}_i}{\bar{w}_iy_i}\right]$$
$$+\frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}\beta_i\bar{x}_i\bar{v}\left[3-\frac{\bar{x}_i}{x_i}-\frac{y_i\bar{v}}{\bar{y}_iv}-\frac{x_i\bar{y}_iv}{\bar{x}_iy_i\bar{v}}\right]\Bigg].$$

Thus, if $R_1 > 1$, then $\bar{x}_i, \bar{w}_i, \bar{y}_i, \bar{v}, \bar{z} > 0$. Using the relation between arithmetical and geometrical means, we get $\frac{dW_2}{dt} \le 0$. Clearly, $\frac{dW_2}{dt} = 0$ if and only if $x_i = \bar{x}_i$, $w_i = \bar{w}_i$, $y_i = \bar{y}_i$ and $v = \bar{v}$. If $v = \bar{v}$, then $\dot{v} = 0$ and from Eq. (13) we have $0 = \sum_{i=1}^{2} k_i\bar{y}_i - c\bar{v} - r\bar{v}\bar{z}$, which give $z = \bar{z}$. Therefore, $\frac{dW_2}{dt}$ equal to zero at $E_2$. The global stability of $E_2$ follows from LaSalle's invariance principle.

# 3 Model with saturation functional response

In this section, we modify model (10)-(14) by taking into account the saturation functional response as:

$$\dot{x}_i = \lambda_i - d_ix_i - \frac{\beta_ix_iv}{1+\sigma_iv}, \qquad i = 1,2, \tag{36}$$
$$\dot{w}_i = \frac{(1-\alpha_i)\beta_ix_iv}{1+\sigma_iv} - (e_i+b_i)w_i, \qquad i = 1,2, \tag{37}$$
$$\dot{y}_i = \frac{\alpha_i\beta_ix_iv}{1+\sigma_iv} + b_iw_i - a_iy_i, \qquad i = 1,2, \tag{38}$$
$$\dot{v} = \sum_{i=1}^{2} k_iy_i - cv - rvz, \tag{39}$$
$$\dot{z} = gvz - \mu z, \tag{40}$$

where $\sigma_i > 0, i = 1,2$, is the saturation constant, and all the variables and parameters of the model have the same definition as given in (10)-(14). We mention that the compact set $\Omega$ given in Section 2 is also positively invariant with respect to system (36)-(40).

## 3.1 Equilibria

**Lemma 2**. For system (36)-(40) we have (i) There exist only one uninfected equilibrium $E_0 = (x_1^0, x_2^0, 0, 0, 0, 0, 0, 0) \in \Omega$, when $R_0 \le 1$.

(ii) There exist $E_0$ and a chronic-infection equilibrium without antibody immune response $E_1 = (\tilde{x}_1, \tilde{x}_2, \tilde{w}_1, \tilde{w}_2, \tilde{y}_1, \tilde{y}_2, \tilde{v}, 0, ) \in \Omega$, when $R_1 \le 1 < R_0$.

(iii) There exist $E_0$, $E_1$ and a chronic-infection equilibrium with antibody immune response $E_2 = (\bar{x}_1, \bar{x}_2, \bar{w}_1, \bar{w}_2, \bar{y}_1, \bar{y}_2, \bar{v}, \bar{z}) \in \mathring{\Omega}$, when $R_1 > 1$.

**Proof**. We let the right-hand side of Eqs.(36)-(40) equal zero, then we obtain the following: Eq. (40) has two possible solutions $z = 0$ or $v = \frac{\mu}{g}$.

If $z = 0$, then from Eqs.(36)-(38) we have

$$x_i = \frac{x_i^0(1+\sigma_iv)}{(1+\xi_iv)}, \qquad w_i = \frac{(1-\alpha_i)\beta_ix_i^0}{(e_i+b_i)(1+\xi_iv)}v, \qquad y_i = \frac{(e_i\alpha_i+b_i)\beta_ix_i^0}{a_i(e_i+b_i)(1+\xi_iv)}v, \tag{41}$$

where $x_i^0 = \dfrac{\lambda_i}{d_i},\ \xi_i = \sigma_i + \dfrac{\beta_i}{d_i},\ i = 1, 2$. From Eq. (39) we find

$$\left(\sum_{i=1}^{2} \frac{(e_i\alpha_i + b_i)k_i\beta_i x_i^0}{a_i c(e_i + b_i)(1 + \xi_i v)} - 1\right) cv = 0. \tag{42}$$

Eq. (42) has also two possible solutions $v = 0$ or $\sum_{i=1}^{2} \dfrac{(e_i\alpha_i + b_i)k_i\beta_i x_i^0}{a_i c(e_i + b_i)(1 + \xi_i v)} - 1 = 0$.

If $v = 0$, then substituting it in Eq. (41) we get the disease-free equilibrium $E_0 = (x_1^0, x_2^0, 0, 0, 0, 0, 0, 0)$.

If $v \neq 0$, we have

$$\sum_{i=1}^{2} \frac{\Psi_i}{(1 + \xi_i v)} = 1. \tag{43}$$

where $\Psi_i = \dfrac{(e_i\alpha_i + b_i)k_i\beta_i x_i^0}{a_i c(e_i + b_i)}$. Eq. (43) can be written as:

$$A_1 v^2 + B_1 v - C_1 = 0 \tag{44}$$

where

$$A_1 = \xi_1\xi_2, \quad B_1 = \xi_1\Psi_1 + \xi_2\Psi_2 + (1 - \Psi_1 - \Psi_2)(\xi_1 + \xi_2), \quad C_1 = \Psi_1 + \Psi_2 - 1$$

The solutions of Eq. (23) is given by:

$$v^{\pm} = \frac{-B_1 \pm \sqrt{B_1^2 + 4A_1C_1}}{2A}.$$

We have $A_1 > 0$, therefore $v^+ > 0$ and $v^- < 0$ when $C_1 > 0$. Let $\tilde{v} = v^+$, then from Eq. (41) we get

$$\tilde{x}_i = \frac{x_i^0(1 + \sigma_i\tilde{v})}{(1 + \xi_i\tilde{v})} > 0, \qquad \tilde{w}_i = \frac{(1 - \alpha_i)\beta_i x_i^0}{(e_i + b_i)(1 + \xi_i\tilde{v})}\tilde{v} > 0, \qquad \tilde{y}_i = \frac{(e_i\alpha_i + b_i)\beta_i x_i^0}{a_i(e_i + b_i)(1 + \xi_i\tilde{v})}\tilde{v} > 0, \quad i = 1, 2.$$

Therefore, an endemic equilibrium $E_1 = (\tilde{x}_1, \tilde{x}_2, \tilde{w}_1, \tilde{w}_2, \tilde{y}_1, \tilde{y}_2, \tilde{v}, 0, )$ exists when $C_1 > 0$ or $(\Psi_1 + \Psi_2 > 1)$.

Now we are ready to define the basic reproduction number $R_0$ as

$$R_0 = \sum_{i=1}^{2} R_{0i} = \sum_{i=1}^{2} \Psi_i = \sum_{i=1}^{2} \frac{(e_i\alpha_i + b_i)k_i\beta_i x_i^0}{a_i c(e_i + b_i)}.$$

If $v = \dfrac{\mu}{g}$, then we obtain the chronic-infection equilibrium with antibody immune response $E_2 = (\bar{x}_1, \bar{x}_2, \bar{w}_1, \bar{w}_2, \bar{y}_1, \bar{y}_2, \bar{v}, \bar{z})$, where

$$\bar{x}_i = \frac{(g + \mu\sigma_i)x_i^0}{g + \mu\xi_i}, \quad \bar{w}_i = \frac{(1 - \alpha_i)\beta_i\mu x_i^0}{(e_i + b_i)(g + \mu\xi_i)}, \quad \bar{y}_i = \frac{(e_i\alpha_i + b_i)\beta_i\mu x_i^0}{a_i(e_i + b_i)(g + \mu\xi_i)}, \quad i = 1, 2,$$
$$\bar{v} = \frac{\mu}{g}, \qquad \bar{z} = \frac{c}{r}\left(\sum_{i=1}^{2} \frac{(e_i\alpha_i + b_i)k_i\beta_i g x_i^0}{a_i c(e_i + b_i)(g + \mu\xi_i)} - 1\right).$$

We note that $E_2$ exists when $\sum_{i=1}^{2} \dfrac{(e_i\alpha_i + b_i)k_i\beta_i g x_i^0}{a_i c(e_i + b_i)(g + \mu\xi_i)} > 1$. This equilibrium represents the state that both the viruses and antibodies are present. Let us define the antibody immune response activation number as

$$R_1 = \sum_{i=1}^{2} \frac{(e_i\alpha_i + b_i)k_i\beta_i g x_i^0}{a_i c(e_i + b_i)(g + \mu\xi_i)} = \sum_{i=1}^{2} \frac{R_{0i}}{\left(1 + \dfrac{\mu}{g}\xi_i\right)},$$

which determines whether a persistent antibody immune response can be established. Then we can write $\bar{z} = \dfrac{c}{r}(R_1 - 1)$. Clearly $R_1 < R_0$. Similar to Section 2.2, one can show that, $E_0,\ E_1 \in \Omega$ and $E_2 \in \mathring{\Omega}$

### 3.2 Global stability

**Theorem 4.** The disease-free equilibrium $E_0$ of system (36)-(40) is GAS when $R_0 \le 1$.

**Proof.** We define a Lyapunov function $W_0$ as:

$$W_0 = \sum_{i=1}^{2} \gamma_i \left[ x_i^0 F\left(\frac{x_i}{x_i^0}\right) + \frac{b_i}{e_i\alpha_i + b_i} w_i + \frac{e_i + b_i}{e_i\alpha_i + b_i} y_i \right] + v + \frac{r}{g} z. \tag{45}$$

We calculate $\frac{dW_0}{dt}$ along the trajectories of (36)-(40)

$$\begin{aligned}\frac{dW_0}{dt} = \sum_{i=1}^{2} \gamma_i \Bigg[ &\left(1 - \frac{x_i^0}{x_i}\right)\left(\lambda_i - d_i x_i - \frac{\beta_i x_i v}{1+\sigma_i v}\right) + \frac{b_i}{e_i\alpha_i + b_i}\left(\frac{(1-\alpha_i)\beta_i x_i v}{1+\sigma_i v} - (e_i + b_i) w_i\right) \\ &+ \frac{e_i + b_i}{e_i\alpha_i + b_i}\left(\frac{\alpha_i \beta_i x_i v}{1+\sigma_i v} + b_i w_i - a_i y_i\right)\Bigg] + \sum_{i=1}^{2} k_i y_i - cv - rvz + \frac{r}{g}(gvz - \mu z).\end{aligned} \tag{46}$$

Collecting terms of Eq. (46) we get

$$\begin{aligned}\frac{dW_0}{dt} &= \sum_{i=1}^{2} \gamma_i \left[ d_i \left(1 - \frac{x_i^0}{x_i}\right)(x_i^0 - x_i) + \frac{\beta_i x_i^0 v}{1+\sigma_i v}\right] - cv - \frac{r\mu}{g} z \\ &= -\sum_{i=1}^{2} \gamma_i d_i \frac{(x_i - x_i^0)^2}{x_i} + \sum_{i=1}^{2} \frac{(e_i\alpha_i + b_i) k_i \beta_i x_i^0}{a_i (e_i + b_i)(1+\sigma_i v)} v - cv - \frac{r\mu}{g} z \\ &= -\sum_{i=1}^{2} \gamma_i d_i \frac{(x_i - x_i^0)^2}{x_i} + \left(\sum_{i=1}^{2} \frac{R_{0i}}{(1+\sigma_i v)} - 1\right) cv - \frac{r\mu}{g} z \\ &= -\sum_{i=1}^{2} \gamma_i d_i \frac{(x_i - x_i^0)^2}{x_i} + (R_0 - 1)cv - \sum_{i=1}^{2} \frac{c\sigma_i R_{0i} v^2}{(1+\sigma_i v)} - \frac{r\mu}{g} z.\end{aligned} \tag{47}$$

If $R_0 \le 1$ then $\frac{dW_0}{dt} \le 0$ for all $x_i, v, z > 0$. Similar to the proof of Theorem 1, one can easily show that $\frac{dW_0}{dt} = 0$ at $E_0$. Then using LaSalle's invariance principle, we can show the global stability of $E_0$.

Next, we show that the endemic equilibrium $E_1$ is GAS.

**Theorem 5.** The chronic-infection equilibrium without antibody immune response $E_1$ of system (36)-(40) is GAS when $R_1 \le 1 < R_0$.

**Proof.** We consider the following Lyapunov function

$$W_1 = \sum_{i=1}^{2} \gamma_i \left[ \tilde{x}_i F\left(\frac{x_i}{\tilde{x}_i}\right) + \frac{b_i}{e_i\alpha_i + b_i} \tilde{w}_i F\left(\frac{w_i}{\tilde{w}_i}\right) + \frac{e_i + b_i}{e_i\alpha_i + b_i} \tilde{y}_i F\left(\frac{y_i}{\tilde{y}_i}\right)\right] + \tilde{v} F\left(\frac{v}{\tilde{v}}\right) + \frac{r}{g} z.$$

Calculating $\frac{dW_1}{dt}$ along the solutions of (36)-(40) we get

$$\begin{aligned}\frac{dW_1}{dt} = \sum_{i=1}^{2} \gamma_i \Bigg[ &\left(1 - \frac{\tilde{x}_i}{x_i}\right)\left(\lambda_i - d_i x_i - \frac{\beta_i x_i v}{1+\sigma_i v}\right) + \frac{b_i}{e_i\alpha_i + b_i}\left(1 - \frac{\tilde{w}_i}{w_i}\right)\left(\frac{(1-\alpha_i)\beta_i x_i v}{1+\sigma_i v} - (e_i + b_i) w_i\right) \\ &+ \frac{e_i + b_i}{e_i\alpha_i + b_i}\left(1 - \frac{\tilde{y}_i}{y_i}\right)\left(\frac{\alpha_i \beta_i x_i v}{1+\sigma_i v} + b_i w_i - a_i y_i\right)\Bigg] + \left(1 - \frac{\tilde{v}}{v}\right)\left(\sum_{i=1}^{2} k_i y_i - cv - rvz\right) + \frac{r}{g}(gvz - \mu z).\end{aligned} \tag{48}$$

Collecting terms of Eq. (48) we have:

$$\begin{aligned}\frac{dW_1}{dt} = \sum_{i=1}^{2} \gamma_i \Bigg[ &\left(1 - \frac{\tilde{x}_i}{x_i}\right)(\lambda_i - d_i x_i) + \frac{\beta_i \tilde{x}_i v}{1+\sigma_i v} + \frac{b_i}{e_i\alpha_i + b_i}\left(-\frac{(1-\alpha_i)\beta_i x_i v \tilde{w}_i}{(1+\sigma_i v) w_i} + (e_i + b_i)\tilde{w}_i\right) \\ &+ \frac{e_i + b_i}{e_i\alpha_i + b_i}\left(-\frac{\alpha_i \beta_i x_i v \tilde{y}_i}{(1+\sigma_i v) y_i} + \frac{b_i w_i \tilde{y}_i}{y_i} + a_i \tilde{y}_i\right)\Bigg] - cv - \frac{\tilde{v}}{v}\sum_{i=1}^{2} k_i y_i + c\tilde{v} + r\tilde{v}z - \frac{\mu r}{g} z.\end{aligned}$$

Using the equilibrium condition for $E_1$:

$$\lambda_i = d_i\tilde{x}_i + \frac{\beta\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}}, \quad \frac{(1-\alpha_i)\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}} = (e_i+b_i)\tilde{w}_i, \quad a_i\tilde{y}_i = \frac{\alpha_i\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}} + b_i\tilde{w}_i = \frac{e_i\alpha_i+b_i}{e_i+b_i}\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}},$$

$$c\tilde{v} = \sum_{i=1}^{2} k_i\tilde{y}_i = \sum_{i=1}^{2}\gamma_i\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}}, \quad \frac{\tilde{v}}{v}\sum_{i=1}^{2}k_iy_i = \sum_{i=1}^{2}\gamma_i\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}}\frac{y_i\tilde{v}}{\tilde{y}_iv}, \quad cv = \frac{v}{\tilde{v}}\sum_{i=1}^{2}\gamma_i\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}},$$

$$\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}} = \frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}\frac{\beta_i\tilde{x}_i\tilde{v}}{(1+\sigma_i\tilde{v})} + \frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}\frac{\beta_i\tilde{x}_i\tilde{v}}{(1+\sigma_i\tilde{v})},$$

we obtain

$$\begin{aligned}
\frac{dW_1}{dt} &= \sum_{i=1}^{2}\gamma_i\Bigg[\left(1-\frac{\tilde{x}_i}{x_i}\right)\left(d_i\tilde{x}_i + \frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}} - d_ix_i\right) + \frac{\beta_i\tilde{x}_iv}{1+\sigma_iv} + \frac{b_i}{e_i\alpha_i+b_i}\left(-\frac{(1-\alpha_i)\beta_ix_iv\tilde{w}_i}{(1+\sigma_iv)w_i} + \frac{(1-\alpha_i)\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}}\right) \\
&\quad + \frac{e_i+b_i}{e_i\alpha_i+b_i}\left(-\frac{\alpha_i\beta_ix_iv\tilde{y}_i}{(1+\sigma_iv)y_i} + \frac{b_iw_i\tilde{y}_i\tilde{w}_i}{y_i\tilde{w}_i} + \frac{e_i\alpha_i+b_i}{e_i+b_i}\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}}\right) - \frac{y_iv}{\tilde{y}_i\tilde{v}}\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}} - \frac{v}{\tilde{v}}\frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}} + \frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}}\Bigg] + r\tilde{v}z - \frac{\mu r}{g}z. \\
&= \sum_{i=1}^{2}\gamma_i\Bigg[-d_i\frac{(x_i-\tilde{x}_i)^2}{x_i} + \frac{\beta_i\tilde{x}_i\tilde{v}}{1+\sigma_i\tilde{v}}\left(-1+\frac{v(1+\sigma_i\tilde{v})}{\tilde{v}(1+\sigma_iv)} - \frac{v}{\tilde{v}} + \frac{1+\sigma_iv}{1+\sigma_i\tilde{v}}\right) \\
&\quad + \frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}\frac{\beta_i\tilde{x}_i\tilde{v}}{(1+\sigma_i\tilde{v})}\left(5-\frac{\tilde{x}_i}{x_i} - \frac{x_i\tilde{w}_iv(1+\sigma_i\tilde{v})}{\tilde{x}_iw_i\tilde{v}(1+\sigma_iv)} - \frac{y_i\tilde{v}}{\tilde{y}_iv} - \frac{w_i\tilde{y}_i}{\tilde{w}_iy_i} - \frac{1+\sigma_iv}{1+\sigma_i\tilde{v}}\right) \\
&\quad + \frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}\frac{\beta_i\tilde{x}_i\tilde{v}}{(1+\sigma_i\tilde{v})}\left(4-\frac{\tilde{x}_i}{x_i} - \frac{x_i\tilde{y}_iv(1+\sigma_i\tilde{v})}{\tilde{x}_iy_i\tilde{v}(1+\sigma_iv)} - \frac{y_i\tilde{v}}{\tilde{y}_iv} - \frac{1+\sigma_iv}{1+\sigma_i\tilde{v}}\right)\Bigg] + \left(\tilde{v}-\frac{\mu}{g}\right)rz \\
&= \sum_{i=1}^{2}\gamma_i\Bigg[-d_i\frac{(x_i-\tilde{x}_i)^2}{x_i} - \frac{\beta_i\tilde{x}_i\tilde{v}}{(1+\sigma_i\tilde{v})}\frac{\sigma_i(v-\tilde{v})^2}{(1+\sigma_iv)(1+\sigma_i\tilde{v})\tilde{v}} \\
&\quad + \frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}\frac{\beta_i\tilde{x}_i\tilde{v}}{(1+\sigma_i\tilde{v})}\left(5-\frac{\tilde{x}_i}{x_i} - \frac{x_i\tilde{w}_iv(1+\sigma_i\tilde{v})}{\tilde{x}_iw_i\tilde{v}(1+\sigma_iv)} - \frac{y_i\tilde{v}}{\tilde{y}_iv} - \frac{w_i\tilde{y}_i}{\tilde{w}_iy_i} - \frac{1+\sigma_iv}{1+\sigma_i\tilde{v}}\right) \\
&\quad + \frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}\frac{\beta_i\tilde{x}_i\tilde{v}}{(1+\sigma_i\tilde{v})}\left(4-\frac{\tilde{x}_i}{x_i} - \frac{x_i\tilde{y}_iv(1+\sigma_i\tilde{v})}{\tilde{x}_iy_i\tilde{v}(1+\sigma_iv)} - \frac{y_i\tilde{v}}{\tilde{y}_iv} - \frac{1+\sigma_iv}{1+\sigma_i\tilde{v}}\right)\Bigg] + \left(\tilde{v}-\frac{\mu}{g}\right)rz. \qquad (49)
\end{aligned}$$

As the same proof of Eq. (32) we can show that $(\tilde{v}-\bar{v}) = \frac{1}{\omega}(R_1-1)$, where $\omega = \sum_{i=1}^{2}\frac{k_i\beta_i\lambda_i\xi_i(e_i\alpha_i+b_i)}{a_id_ic(e_i+b_i)(1+\xi_i\bar{v})(1+\xi_i\tilde{v})}$. So, if $R_1 \le 1$ then $\tilde{v} \le \frac{\mu}{g} = \bar{v}$. We have $x_i, w_i, y_i, v > 0$ when $R_0 > 1$. Since the geometrical mean is less than or equal to the arithmetical mean, then the third and fourth terms of Eq. (49) are less than or equal zero, then if $R_1 \le 1$ then $\frac{dW_1}{dt} \le 0$ for all $x_i, w_i, y_i, v, z > 0$. Clearly, $\frac{dW_1}{dt} = 0$ occurs at $E_1$. LaSalle's invariance principle implies global stability of $E_1$.

**Theorem 6.** The chronic-infection equilibrium with antibody immune response $E_2$ of system (36)-(40) is GAS when $R_1 > 1$.

**Proof.** Define Lyapunov function $W_2$ as:

$$W_2 = \sum_{i=1}^{2}\gamma_i\left[\bar{x}_iF\left(\frac{x_i}{\bar{x}_i}\right) + \frac{b_i}{e_i\alpha_i+b_i}\bar{w}_iF\left(\frac{w_i}{\bar{w}_i}\right) + \frac{e_i+b_i}{e_i\alpha_i+b_i}\bar{y}_iF\left(\frac{y_i}{\bar{y}_i}\right)\right] + \bar{v}F\left(\frac{v}{\bar{v}}\right) + \frac{r}{g}\bar{z}F\left(\frac{z}{\bar{z}}\right).$$

The time derivative of $W_2$ along the trajectories of (36)-(40) is given by

$$\begin{aligned}
\frac{dW_2}{dt} &= \sum_{i=1}^{2}\gamma_i\Bigg[\left(1-\frac{\bar{x}_i}{x_i}\right)\left(\lambda_i - d_ix_i - \frac{\beta_ix_iv}{1+\sigma_iv}\right) + \frac{b_i}{e_i\alpha_i+b_i}\left(1-\frac{\bar{w_\imath}}{w_i}\right)\left(\frac{(1-\alpha_i)\beta_ix_iv}{1+\sigma_iv} - (e_i+b_i)w_i\right) \\
&\quad + \frac{e_i+b_i}{e_i\alpha_i+b_i}\left(1-\frac{\bar{y}_i}{y_i}\right)\left(\frac{\alpha_i\beta_ix_iv}{1+\sigma_iv} + bw_i - a_iy_i\right)\Bigg] + \left(1-\frac{\bar{v}}{v}\right)\left(\sum_{i=1}^{2}k_iy_i - cv - rvz\right) + \frac{r}{g}\left(1-\frac{\bar{z}}{z}\right)(gvz-\mu z). \qquad (50)
\end{aligned}$$

Collecting terms of Eq. (50) and using the equilibrium condition for $E_2$

$$\lambda_i = d_i\bar{x}_i + \frac{\beta\bar{x}_i\bar{v}}{1+\sigma_i\bar{v}}, \ \frac{(1-\alpha_i)\beta_i\bar{x}_i\bar{v}}{1+\sigma_i\bar{v}} = (e_i+b_i)\bar{w}_i, \ \frac{\alpha_i\beta_i\bar{x}_i\bar{v}}{1+\sigma_i\bar{v}} + b_i\bar{w}_i = a_i\bar{y}_i, \ c\bar{v} + r\bar{v}\bar{z} = \sum_{i=1}^{2}k_i\bar{y}_i,$$

$$\frac{e_i+b_i}{e_i\alpha_i+b_i}a_i\bar{y}_i = \frac{\beta_i\bar{x}_i\bar{v}}{1+\sigma_i\bar{v}} = \frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}\frac{\beta_i\bar{x}_i\bar{v}}{(1+\sigma_i\bar{v})} + \frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}\frac{\beta_i\bar{x}_i\bar{v}}{(1+\sigma_i\bar{v})}$$

Eq. (50) becomes

$$\begin{aligned}\frac{dW_2}{dt} &= \sum_{i=1}^{2}\gamma_i\Bigg[-d_i\frac{(x_i-\bar{x}_i)^2}{x_i} - \frac{\beta_i\bar{x}_i\bar{v}}{(1+\sigma_i\bar{v})}\frac{\sigma_i(v-\bar{v})^2}{\bar{v}(1+\sigma_i v)(1+\sigma_i\bar{v})} \\ &+ \frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}\frac{\beta_i\bar{x}_i\bar{v}}{(1+\sigma_i\bar{v})}\left(5-\frac{\bar{x}_i}{x_i}-\frac{x_i\bar{w}_i v(1+\sigma_i\bar{v})}{\bar{x}_i w_i\bar{v}(1+\sigma_i v)}-\frac{y_i\bar{v}}{\bar{y}_i v}-\frac{w_i\bar{y}_i}{\bar{w}_i y_i}-\frac{1+\sigma_i v}{1+\sigma_i\bar{v}}\right) \\ &+ \frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}\frac{\beta_i\bar{x}_i\bar{v}}{(1+\sigma_i\bar{v})}\left(4-\frac{\bar{x}_i}{x_i}-\frac{x_i\bar{y}_i v(1+\sigma_i\bar{v})}{\bar{x}_i y_i\bar{v}(1+\sigma_i v)}-\frac{y_i\bar{v}}{\bar{y}_i v}-\frac{1+\sigma_i v}{1+\sigma_i\bar{v}}\right)\Bigg]\end{aligned}$$

Thus, if $R_1 > 1$ then $x_i, w_i, y_i, v$ and $z > 0$. Similar to the proof of Theorem 3, one can show that $E_2$ is GAS.

# 4 Model with general incidence rate

In this section, we propose a viral infection model with latently infected cells and antibody immune response. The incidence rate of infection is represented by a general function of the populations of the uninfected target cells and free viruses.

$$\dot{x}_i = \lambda_i - d_i x_i - f_i(x_i, v), \qquad i = 1, 2, \tag{51}$$

$$\dot{w}_i = (1-\alpha_i)f_i(x_i, v) - (e_i + b_i)w_i, \qquad i = 1, 2, \tag{52}$$

$$\dot{y}_i = \alpha_i f_i(x_i, v) + b_i w_i - a_i y_i, \qquad i = 1, 2, \tag{53}$$

$$\dot{v} = \sum_{i=1}^{2} k_i y_i - cv - rvz, \tag{54}$$

$$\dot{z} = gvz - \mu z, \tag{55}$$

where the function $f_i(x_i, v)$ represents the rate of the uninfected target cells to be infected by the viruses.

**Assumption A1** For $i = 1, 2$, function $f_i$ satisfies:
(i) $f_i(x_i, v)$ is positive, continuous, and differentiable,
(ii) $\dfrac{\partial f_i(x_i, v)}{\partial v} > 0$ and $\dfrac{\partial f_i(x_i, v)}{\partial x_i} > 0$ for any $x_i$,$v > 0$. Furthermore, $\dfrac{\partial f_i(x_i, 0)}{\partial v} > 0$ for any $x_i > 0$,
(iii) $f_i(x_i, 0) = f_i(0, v) = 0$, for all $x_i > 0$ and $v > 0$.

**Assumption A2** For $i = 1, 2$, function $f_i$ satisfies:
(i) $f_i(x_i, v) \le v\dfrac{\partial f_i(x_i, 0)}{\partial v}$, for all $v > 0$.
(ii) $\frac{d}{dx_i}\left(\dfrac{\partial f_i(x_i, 0)}{\partial v}\right) > 0$

## 4.1 Equilibria and biological thresholds

We define the basic infection reproduction number of system (51)-(55) as:

$$R_0 = \sum_{i=1}^{2}\frac{k_i(e_i\alpha_i + b_i)}{a_i c(e_i + b_i)}\frac{\partial f_i(x_i^0, 0)}{\partial v}.$$

The equilibria of (51)-(55) satisfy the following equations:

$$\lambda_i - d_i x_i - f_i(x_i, v) = 0, \tag{56}$$

$$(1-\alpha_i)f_i(x_i, v) - (e_i + b_i)w_i = 0, \tag{57}$$

$$\alpha_i f_i(x_i, v) + b_i w_i - a_i y_i = 0, \tag{58}$$

$$\sum_{i=1}^{2} k_i y_i - cv - rvz = 0, \tag{59}$$

$$(gv - \mu)z = 0. \tag{60}$$

Equation (60) has two possible solutions, $z = 0$ or $v = \mu/g$. When $z = 0$, we obtain two equilibria, the infection-free equilibrium $E_0 = (x_1^0, x_2^0, 0, 0, 0, 0, 0, 0)$, where $x_i^0 = \dfrac{\lambda_i}{d_i}$, $i = 1, 2$ and the infected steady state without antibody immune response $E_1 = (\tilde{x}_1, \tilde{x}_2, \tilde{w}_1, \tilde{w}_2, \tilde{y}_1, \tilde{y}_2, \tilde{v}, 0, )$, where the coordinates satisfy the equalities:

$$\lambda_i = d_i\tilde{x}_i + f_i(\tilde{x}_i, \tilde{v}), \quad (1-\alpha_i)f_i(\tilde{x}_i, \tilde{v}) = (e_i + b_i)\tilde{w}_i, \; \alpha_i f_i(\tilde{x}_i, \tilde{v}) + b_i\tilde{w}_i = a_i\tilde{y}_i, \; \sum_{i=1}^{2} k_i\tilde{y}_i = c\tilde{v}. \tag{61}$$

The other possibility of Eq. (60) $z \neq 0$ leads to $\bar{v} = \dfrac{\mu}{g}$. Substitute the value of $\bar{v}$ in Eq. (56) and let

$$\Pi(x_i) = \lambda_i - d_i x_i - f_i(x_i, \bar{v}) = 0.$$

According to Assumptions A1, $\Pi$ is a strictly decreasing function of $x_i$. Besides, $\Pi(0) = \lambda_i > 0$ and $\Pi(x_i^0) = -f_i(x_i^0, \bar{v}) < 0$. Thus, there exists a unique $\bar{x}_i \in (0, x_i^0)$ such that $\Pi(\bar{x}_i) = 0$. From Eqs. (57)-(59) we have

$$\bar{w}_i = \frac{(1-\alpha_i)f_i(\bar{x}_i, \bar{v})}{(e_i + b_i)}, \quad \bar{y}_i = \frac{(e_i\alpha_i + b_i)f_i(\bar{x}_i, \bar{v})}{a_i(e_i + b_i)}, \quad \bar{z} = \frac{c}{r}\left[\sum_{i=1}^{2} \frac{k_i(e_i\alpha_i + b_i)f_i(\bar{x}_i, \bar{v})}{a_i c(e_i + b_i)\bar{v}} - 1\right].$$

Thus $\bar{w}_i > 0$ and $\bar{y}_i > 0$, moreover, $\bar{z} > 0$ when $\sum_{i=1}^{2} \dfrac{k_i(e_i\alpha_i + b_i)f_i(\bar{x}_i, \bar{v})}{a_i c(e_i + b_i)\bar{v}} > 1$. Now we define the antibody immune response activation number as:

$$R_1 = \sum_{i=1}^{2} \frac{k_i(e_i\alpha_i + b_i)f_i(\bar{x}_i, \bar{v})}{a_i c(e_i + b_i)\bar{v}}.$$

Hence, $\bar{z}$ can be rewritten as $\bar{z} = \frac{c}{r}(R_1 - 1)$. It follows that, there exists a chronic-infection equilibrium with antibody immune response $E_2 = (\bar{x}_1, \bar{w}_1, \bar{y}_1, \bar{x}_2, \bar{w}_2, \bar{y}_2, \bar{v}, \bar{z})$ when $R_1 > 1$. Clearly from **Assumptions A1** and **A2**, we have

$$R_1 = \sum_{i=1}^{2} \frac{k_i(e_i\alpha_i + b_i)f_i(\bar{x}_i, \bar{v})}{a_i c(e_i + b_i)\bar{v}} < \sum_{i=1}^{2} \frac{k_i(e_i\alpha_i + b_i)}{a_i c(e_i + b_i)\bar{v}} \frac{\partial f_i(\bar{x}_i, 0)}{\partial \bar{v}}\bar{v} < \sum_{i=1}^{2} \frac{k_i(e_i\alpha_i + b_i)}{a_i c(e_i + b_i)} \frac{\partial f_i(x_i^0, 0)}{\partial v} = R_0.$$

## 5 Global stability analysis

**Theorem 7.** Let Assumptions A1-A2 be hold true and $R_0 \leq 1$, then the infection-free equilibrium $E_0$ for system (51)-(55) is GAS.

**Proof.** Define a Lyapunov functional $W_0$ as follows:

$$W_0 = \sum_{i=1}^{2} \gamma_i \left[x_i - x_i^0 - \int_{x_i^0}^{x_i} \lim_{v \to 0^+} \frac{f_i(x_i^0, v)}{f_i(s_i, v)} ds_i + \frac{b_i}{e_i\alpha_i + b_i} w_i + \frac{e_i + b_i}{e_i\alpha_i + b_i} y_i\right] + v + \frac{r}{g}z.$$

Calculating $\dfrac{dW_0}{dt}$ along the trajectories of (51)-(55) as:

$$\begin{aligned}
\frac{dW_0}{dt} &= \sum_{i=1}^{2} \gamma_i \Bigg[ \left(1 - \lim_{v \to 0^+} \frac{f_i(x_i^0, v)}{f_i(x_i, v)}\right)(\lambda_i - d_i x_i - f_i(x_i, v)) + \frac{b_i}{e_i\alpha_i + b_i}((1-\alpha_i)f_i(x_i, v) - (e_i + b_i)w_i) \\
&\quad + \frac{e_i + b_i}{e_i\alpha_i + b_i}(\alpha_i f_i(x_i, v) + b_i w_i - a_i y_i)\Bigg] + \sum_{i=1}^{2} k_i y_i - cv - rvz + \frac{r}{g}(gvz - \mu z) \\
&= \sum_{i=1}^{2} \gamma_i\lambda_i \left(1 - \frac{\partial f_i(x_i^0, 0)/\partial v}{\partial f_i(x_i, 0)/\partial v}\right)\left(1 - \frac{x_i}{x_i^0}\right) + (R_0 - 1)cv - \frac{r\mu}{g}z.
\end{aligned} \tag{62}$$

Based on Assumption A2, the first term of Eq. (62) is less than or equal zero. Therefore if $R_0 \leq 1$, then $\frac{dW_0}{dt} \leq 0$ for all $x_i, v, z > 0$. Similar to the previous sections, one can show that $E_0$ is GAS.

Now we need to the following Assumption to proof that, $E_1$ and $E_2$ for the system (51)-(55) are GAS.
**Assumption A3** Function $f_i(x_i, v)$ satisfies the following:

$$\left(\frac{f_i(x_i,v)}{f_i(x_i,\tilde{v})}-\frac{v}{\tilde{v}}\right)\left(1-\frac{f_i(x_i,\tilde{v})}{f_i(x_i,v)}\right)\leq 0, \quad \left(\frac{f_i(x_i,v)}{f_i(x_i,\bar{v})}-\frac{v}{\bar{v}}\right)\left(1-\frac{f_i(x_i,\bar{v})}{f_i(x_i,v)}\right)\leq 0, \quad x_i, v>0,$$

**Theorem 8.** Suppose that Assumptions A1-A3 are satisfied, $E_1$ exists and $R_1 \leq 1$, then $E_1$ for system (51)-(55) is GAS.

**Proof.** We construct the following Lyapunov functional

$$W_1=\sum_{i=1}^{2}\gamma_i\left[x_i-\tilde{x}_i-\int_{\tilde{x}_i}^{x_i}\frac{f_i(\tilde{x}_i,\tilde{v})}{f_i(s_i,\tilde{v})}ds_i+\frac{b_i}{e_i\alpha_i+b_i}\tilde{w}_iF\left(\frac{w_i}{\tilde{w}_i}\right)+\frac{e_i+b_i}{e_i\alpha_i+b_i}\tilde{y}_iF\left(\frac{y_i}{\tilde{y}_i}\right)\right]+\tilde{v}F\left(\frac{v}{\tilde{v}}\right)+\frac{r}{g}z.$$

The time derivative of $W_1$ along the trajectories of (51)-(55) is given by

$$\begin{aligned}\frac{dW_1}{dt}&=\sum_{i=1}^{2}\gamma_i\left[\left(1-\frac{f_i(\tilde{x}_i,\tilde{v})}{f_i(x_i,\tilde{v})}\right)(\lambda_i-d_ix_i-f_i(x_i,v))+\frac{b_i}{e_i\alpha_i+b_i}\left(1-\frac{\tilde{w}_i}{w_i}\right)((1-\alpha_i)f_i(x_i,v)-(e_i+b_i)w_i)\right.\\&\left.+\frac{e_i+b_i}{e_i\alpha_i+b_i}\left(1-\frac{\tilde{y}_i}{y_i}\right)(\alpha_if_i(x_i,v)+b_iw_i-a_iy_i)\right]+\left(1-\frac{\tilde{v}}{v}\right)(\left(\sum_{i=1}^{2}k_iy_i-cv-rvz\right)+\frac{r}{g}(gvz-\mu z).\end{aligned} \tag{63}$$

Collecting terms of Eq. (63) we get

$$\begin{aligned}\frac{dW_1}{dt}&=\sum_{i=1}^{2}\gamma_i\left[\left(1-\frac{f_i(\tilde{x}_i,\tilde{v})}{f_i(x_i,\tilde{v})}\right)(\lambda_i-d_ix_i)+f_i(x_i,v)\frac{f_i(\tilde{x}_i,\tilde{v})}{f_i(x_i,\tilde{v})}-\frac{b_i(1-\alpha_i)}{e_i\alpha_i+b_i}f_i(x_i,v)\frac{\tilde{w}_i}{w_i}\right.\\&\left.+\frac{(e_i+b_i)}{e_i\alpha_i+b_i}b_i\tilde{w}_i-\frac{(e_i+b_i)\alpha_i}{e_i\alpha_i+b_i}f_i(x_i,v)\frac{\tilde{y}_i}{y_i}-\frac{(e_i+b_i)b_iw_i}{e_i\alpha_i+b_i}\frac{\tilde{y}_i}{y_i}-\frac{e_i+b_i}{e_i\alpha_i+b_i}a_i\tilde{y}_i\right]\\&-cv-\sum_{i=1}^{2}k_iy_i\frac{\tilde{v}}{v}+c\tilde{v}+r\tilde{v}z-\frac{r\mu}{g}z.\end{aligned}$$

Using the equilibrium condition for $E_1$:

$$\lambda_i=d_i\tilde{x}_i+f_i(\tilde{x}_i,\tilde{v}),\quad (1-\alpha_i)f_i(\tilde{x}_i,\tilde{v})=(e_i+b_i)\tilde{w}_i,\quad a_i\tilde{y}_i=\alpha_if_i(\tilde{x}_i,\tilde{v})+b_i\tilde{w}_i,\quad cv=\frac{v}{\tilde{v}}\sum_{i=1}^{2}\gamma_if_i(\tilde{x}_i,\tilde{v}),$$

$$c\tilde{v}=\sum_{i=1}^{2}k_i\tilde{y}_i=\sum_{i=1}^{2}\gamma_if_i(\tilde{x}_i,\tilde{v}),\quad \frac{e_i+b_i}{e_i\alpha_i+b_i}a_i\tilde{y}_i=f_i(\tilde{x}_i,\tilde{v})=\frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}f_i(\tilde{x}_i,\tilde{v})+\frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}f_i(\tilde{x}_i,\tilde{v}),$$

we obtain

$$\begin{aligned}\frac{dW_1}{dt}&=\sum_{i=1}^{2}\gamma_i\left[d_i\tilde{x}_i\left(1-\frac{f_i(\tilde{x}_i,\tilde{v})}{f_i(x_i,\tilde{v})}\right)\left(1-\frac{x_i}{\tilde{x}_i}\right)+\left(1-\frac{f_i(x_i,\tilde{v})}{f_i(x_i,v)}\right)\left(\frac{f_i(x_i,v)}{f_i(x_i,\tilde{v})}-\frac{v}{\tilde{v}}\right)\right.\\&+\frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}f_i(\tilde{x}_i,\tilde{v})\left(5-\frac{f_i(\tilde{x}_i,\tilde{v})}{f_i(x_i,\tilde{v})}-\frac{\tilde{w}_if_i(x_i,v)}{w_if_i(\tilde{x}_i,\tilde{v})}-\frac{w_i\tilde{y}_i}{\tilde{w}_iy_i}-\frac{y_i\tilde{v}}{\tilde{y}_iv}-\frac{vf_i(x_i,\tilde{v})}{\tilde{v}f_i(x_i,v)}\right)\\&\left.+\frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}f_i(\tilde{x}_i,\tilde{v})\left(4-\frac{f_i(\tilde{x}_i,\tilde{v})}{f_i(x_i,\tilde{v})}-\frac{\tilde{y}_if_i(x_i,v)}{y_if_i(\tilde{x}_i,\tilde{v})}-\frac{y_i\tilde{v}}{\tilde{y}_iv}-\frac{vf_i(x_i,\tilde{v})}{\tilde{v}f_i(x_i,v)}\right)\right]+r\left(\tilde{v}-\frac{\mu}{g}\right)z.\end{aligned} \tag{64}$$

From **Assumptions A1 and A3**, we get that the first and second terms of Eq. (64) are less than or equal zero. Because the geometrical mean is less than or equal to the arithmetical mean, then the third and fourth terms of Eq. (64) are less than or equal zero. Now we show that if $R_1 \leq 1$ then $\tilde{v} \leq \frac{\mu}{r} = \bar{v}$. This can be achieved if we show that

$$sgn(\bar{x}_i-\tilde{x}_i)=sgn(\tilde{v}-\bar{v})=sgn(R_1-1).$$

Applying **Assumptions A1-A2**, we have

$$(f_i(\bar{x}_i,\tilde{v})-f_i(\tilde{x}_i,\tilde{v}))\,(\bar{x}_i-\tilde{x}_i)>0, \tag{65}$$

$$(f_i(\tilde{x}_i,\bar{v})-f_i(\tilde{x}_i,\tilde{v}))\,(\bar{v}-\tilde{v})>0, \quad (f_i(\bar{x}_i,\bar{v})-f_i(\bar{x}_i,\tilde{v}))\,(\bar{v}-\tilde{v})>0. \tag{66}$$

Using **Assumption A3** with $x_i=\tilde{x}_i$ and $v=\bar{v}$, we get

$$(f_i(\tilde{x}_i,\bar{v})\tilde{v}-f_i(\tilde{x}_i,\tilde{v})\bar{v})\,(f_i(\tilde{x}_i,\bar{v})-f_i(\tilde{x}_i,\tilde{v}))\le 0$$

It follows from inequality (66) that

$$((f_i(\tilde{x}_i,\bar{v})\tilde{v}-f_i(\tilde{x}_i,\tilde{v})\bar{v}))\,(\tilde{v}-\bar{v})>0. \tag{67}$$

Suppose that, $sgn\,(\bar{x}_i-\tilde{x}_i)=sgn\,(\bar{v}-\tilde{v})$. Using the conditions of the equilibria $E_1$ and $E_2$ we have

$$(\lambda_i-d_i\bar{x}_i)-(\lambda_i-d_i\tilde{x}_i)=f_i(\bar{x}_i,\bar{v})-f_i(\tilde{x}_i,\tilde{v})=f_i(\bar{x}_i,\bar{v})-f_i(\bar{x}_i,\tilde{v})+f_i(\bar{x}_i,\tilde{v})-f_i(\tilde{x}_i,\tilde{v}),$$

and from inequalities (65) and (66) we get $sgn\,(\tilde{x}_i-\bar{x}_i)=sgn\,(\bar{x}_i-\tilde{x}_i)$, which leads to contradiction. Thus, $sgn\,(\bar{x}_i-\tilde{x}_i)=sgn\,(\tilde{v}-\bar{v})$. Using the equilibrium conditions for $E_1$ we have $\sum\limits_{i=1}^{2}\frac{k_i(e_i\alpha_i+b_i)f_i(\tilde{x}_i,\tilde{v})}{a_ic(e_i+b_i)\tilde{v}}=1$, then

$$\begin{aligned}R_1-1&=\sum_{i=1}^{2}\frac{k_i(e_i\alpha_i+b_i)}{a_ic(e_i+b_i)}\left(\frac{f_i(\bar{x}_i,\bar{v})}{\bar{v}}-\frac{f_i(\tilde{x}_i,\tilde{v})}{\tilde{v}}\right)\\&=\sum_{i=1}^{2}\frac{k_i(e_i\alpha_i+b_i)}{a_ic(e_i+b_i)}\left(\frac{1}{\bar{v}}\,(f_i(\bar{x}_i,\bar{v})-f_i(\tilde{x}_i,\bar{v}))+\frac{1}{\tilde{v}\bar{v}}\,(f_i(\tilde{x}_i,\bar{v})\tilde{v}-f_i(\tilde{x}_i,\tilde{v})\bar{v})\right).\end{aligned}$$

From inequalities (65) and (67) we get $sgn\,(R_1-1)=sgn\,(\tilde{v}-\bar{v})$. It follows that, if $R_1\le 1$ then $\tilde{v}\le\frac{\mu}{r}=\bar{v}$. Therefore, if $R_1\le 1$ then $\frac{dW_1}{dt}\le 0$ for all $x_i,w_i,y_i,v,z>0$, where the equality occurs at the equilibrium $E_1$. LaSalle's invariance principle implies the global stability of $E_1$.

**Theorem 9.** Let **Assumptions A1-A3** be hold true and $R_1>1$, then chronic-infection equilibrium with antibody immune response $E_2$ for system (51)-(55) is GAS.

**Proof.** We construct the following Lyapunov functional

$$W_2=\sum_{i=1}^{2}\gamma_i\left[x_i-\bar{x}_i-\int_{\bar{x}_i}^{x_i}\frac{f_i(\bar{x}_i,\bar{v})}{f_i(s_i,\bar{v})}ds_i+\frac{b_i}{e_i\alpha_i+b_i}\bar{w}_iF\left(\frac{w_i}{\bar{w}_i}\right)+\frac{e_i+b_i}{e_i\alpha_i+b_i}\bar{y}_iF\left(\frac{y_i}{\bar{y}_i}\right)\right]+\bar{v}F\left(\frac{v}{\bar{v}}\right)+\frac{r}{g}\bar{z}F\left(\frac{z}{\bar{z}}\right).$$

We calculate the time derivative of $W_2$ along the trajectories of (51)-(55) as:

$$\begin{aligned}\frac{dW_2}{dt}&=\sum_{i=1}^{2}\gamma_i\left[\left(1-\frac{f_i(\bar{x}_i,\bar{v})}{f_i(x_i,\bar{v})}\right)(\lambda_i-d_ix_i-f_i(x_i,v))+\frac{b_i}{e_i\alpha_i+b_i}\left(1-\frac{\bar{w}_i}{w}\right)((1-\alpha_i)f_i(x_i,v)-(e_i+b_i)w_i)\right.\\&\left.+\frac{e_i+b_i}{e_i\alpha_i+b_i}\left(1-\frac{\bar{y}_i}{y}\right)(\alpha_if_i(x_i,v)+b_iw_i-a_iy_i)\right]+\left(1-\frac{\bar{v}}{v}\right)(\sum_{i=1}^{2}k_iy_i-cv-rvz)+\frac{r}{g}\left(1-\frac{\bar{z}}{z}\right)(gvz-\mu z).\end{aligned} \tag{68}$$

Collecting terms of Eq. (68) and using the equilibrium conditions for $E_2$

$$\lambda_i=d_i\bar{x}_i+f_i(\bar{x}_i,\bar{v}),\quad (1-\alpha_i)f_i(\bar{x}_i,\bar{v})=(e_i+b_i)\bar{w}_i,\quad a_i\bar{y}_i=\alpha_if_i(\bar{x}_i,\bar{v})+b_i\bar{w}_i,\quad c\bar{v}=\sum_{i=1}^{2}\gamma_if_i(\bar{x}_i,\bar{v})-r\bar{v}\bar{z},$$

$$cv=\frac{v}{\bar{v}}\sum_{i=1}^{2}\gamma_if_i(\bar{x}_i,\bar{v})-rv\bar{z},\quad \frac{e_i+b_i}{e_i\alpha_i+b_i}a_i\bar{y}_i=f_i(\bar{x}_i,\bar{v})=\frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}f_i(\bar{x}_i,\bar{v})+\frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}f_i(\bar{x}_i,\bar{v}),$$

we get

$$\frac{dW_2}{dt} = \sum_{i=1}^{2}\gamma_i\Bigg[d_i\bar{x}_i\left(1-\frac{f_i(\bar{x}_i,\bar{v})}{f_i(x_i,\bar{v})}\right)(1-\frac{x_i}{\bar{x}_i}) + f_i(\bar{x}_i,\bar{v})\left(1-\frac{f_i(x_i,\bar{v})}{f_i(x_i,v)}\right)\left(\frac{f_i(x_i,v)}{f_i(x_i,\bar{v})}-\frac{v}{\bar{v}}\right)$$
$$+\frac{b_i(1-\alpha_i)}{(e_i\alpha_i+b_i)}f_i(\bar{x}_i,\bar{v})\left(5-\frac{f_i(\bar{x}_i,\bar{v})}{f_i(x_i,\bar{v})}-\frac{\bar{w}_i f_i(x_i,v)}{w_i f_i(\bar{x}_i,\bar{v})}-\frac{\bar{y}_i w_i}{y_i\bar{w}_i}-\frac{y_i\bar{v}}{\bar{y}_i v}-\frac{v f_i(x_i,\bar{v})}{\bar{v} f_i(x_i,v)}\right)$$
$$+\frac{(e_i+b_i)\alpha_i}{(e_i\alpha_i+b_i)}f_i(\bar{x}_i,\bar{v})\left(4-\frac{f_i(\bar{x}_i,\bar{v})}{f_i(x_i,\bar{v})}-\frac{\bar{y}_i f_i(x_i,v)}{y_i f_i(\bar{x}_i,\bar{v})}-\frac{y_i\bar{v}}{\bar{y}_i v}-\frac{v f_i(x_i,\bar{v})}{\bar{v} f_i(x_i,v)}\right)\Bigg] \quad (69)$$

Thus, if $R_1 > 1$ then $\bar{x}_i, \bar{w}_i, \bar{y}_i, \bar{v}$ and $\bar{z} > 0$. From Assumptions A1 and A3, we get that the first and second terms of Eq. (69) are less than or equal zero. Since the arithmetical mean is greater than or equal to the geometrical mean, then $\frac{dW_2}{dt} \le 0$. It can be seen that, $\frac{dW_2}{dt} = 0$ if and only if $x_i = \bar{x}_i$, $w_i = \bar{w}_i$ and $v = \bar{v}$. From Eq. (54), if $v = \bar{v}$ and $y_i = \bar{y}_i$ then $\dot{v} = 0$ and $0 = \sum_{i=1}^{2} k\bar{y}_i - c\bar{v} - r\bar{v}\bar{z} = 0$, which yields $z = \bar{z}$ and hence $\frac{dW_2}{dt}$ equal to zero at $E_2$. LaSalle's invariance principle implies global stability of $E_2$.

## 5.1 Special forms of the incidence rate

By using the Lyapunov direct method, we have established a set of conditions on $f_i(x_i, v)$, $i = 1, 2$ ensuring the global asymptotic stability of the equilibria of model (51)-(55). Now we introduce some forms of the incidence rate and verify A1-A3.

(1) Bilinear incidence rate: $f_i(x_i, v) = \beta_i x_i v$,
(2) Saturation functional response: $f_i(x_i, v) = \frac{\beta_i x_i v}{1+\eta_i v}$,
(3) Beddington-DeAngelis functional response: $f_i(x_i, v) = \frac{\beta_i x_i v}{1+\gamma_i x_i+\eta_i v}$,
(4) Crowley-Martin functional response: $f_i(x_i, v) = \frac{\beta_i x_i v}{(1+\gamma_i x_i)(1+\eta_i v)}$,
(5) Hill type incidence rate: $f_i(x_i, v) = \frac{\beta_i x_i^n v}{\gamma_i^n + x_i^n}$, where $\beta_i, \gamma_i, n > 0$.

One can easily show that A1-A3 for the functions $f_i$, $i = 1, 2$ given above.

Now we verify Assumptions A1-A3 for the function $f_i(x_i, v) = \frac{\beta_i x_i^n v}{\gamma_i^n + x_i^n}$, $i = 1, 2$. We have $f_i(x_i, v) > 0$ for all $x_i > 0$, $v > 0$, $f_i(0, v) = f_i(x_i, 0) = 0$ and

$$\frac{\partial f_i(x_i,v)}{\partial x_i} = \frac{n\beta_i\gamma_i^n x_i^{n-1} v}{(\gamma_i^n + x_i^n)^2}, \qquad \frac{\partial f_i(x_i,v)}{\partial v} = \frac{\beta_i x_i^n}{\gamma_i^n + x_i^n} = \frac{\partial f_i(x_i,0)}{\partial v}.$$

Then, for all $x_i > 0, v > 0$, we have $\frac{\partial f_i(x_i,v)}{\partial x_i} > 0$, $\frac{\partial f_i(x_i,v)}{\partial v} > 0$ and $\frac{\partial f_i(x_i,0)}{\partial v} > 0$ if $n > 0$. Therefore Assumptions A1 is satisfied. We have also

$$f_i(x_i,v) = \frac{\beta_i x_i^n v}{\gamma_i^n + x_i^n} = v\frac{\beta_i x_i^n}{\gamma_i^n + x_i^n} = v\frac{\partial f_i(x_i,0)}{\partial v},$$
$$\frac{d}{dx_i}\left(\frac{\partial f_i(x_i^0,0)/\partial v}{\partial f_i(x_i,0)/\partial v}\right) = -\frac{n\gamma_i^n (x_i^0)^n}{(\gamma_i^n + (x_i^0)^n)x_i^{n+1}} < 0,$$

then, Assumptions A2 is satisfied. Moreover,

$$\left(\frac{f_i(x_i,v)}{f_i(x_i,\tilde{v})}-\frac{v}{\tilde{v}}\right)\left(1-\frac{f_i(x_i,\tilde{v})}{f_i(x_i,v)}\right) = \left(\frac{v}{\tilde{v}}-\frac{v}{\tilde{v}}\right)\left(1-\frac{\tilde{v}}{v}\right) = 0.$$

Thus, Assumptions A3 is satisfied. In this case, $R_0$ and $R_1$ are given by

$$R_0 = \sum_{i=1}^{2}\frac{k_i(e_i\alpha_i+b_i)}{a_i c(e_i+b_i)}\frac{\partial f_i(x_i^0,0)}{\partial v} = \sum_{i=1}^{2}\frac{k_i(e_i\alpha_i+b_i)}{a_i c(e_i+b_i)}\frac{\beta_i (x_i^0)^n}{\gamma_i^n + (x_i^0)^n},$$
$$R_1 = \sum_{i=1}^{2}\frac{k_i(e_i\alpha_i+b_i)f_i(\bar{x}_i,\bar{v})}{a_i c(e_i+b_i)\bar{v}} = \sum_{i=1}^{2}\frac{k_i(e_i\alpha_i+b_i)}{a_i c(e_i+b_i)}\frac{\beta_i \bar{x}_i^n}{\gamma_i^n + \bar{x}_i^n}.$$

# 6 Numerical simulations

In this section, we will perform some numerical simulations to confirm our theoretical results. Let us consider model (51)-(55) with the incidence rate $f_i(x_i, v) = \frac{\beta_i x_i^n v}{\gamma_i^n + x_i^n}$, $i = 1, 2$. In Table 1, we provide the values of some parameters of model (51)-(55) with the incidence rate given by the function $f_i$. The effect of the parameter $\varepsilon$ on the dynamical behavior of the system will be discussed below in details.In order to investigate the theoretical results involved in Theorems 7-9, we shall study the following cases:

Table 1: The values of the parameters of model (51)-(55).

| *Parameter* | $\lambda_1$ | $\lambda_2$ | $\bar{\beta}_1$ | $\bar{\beta}_2$ | $d_1$ | $d_2$ | $\alpha_1$ | $\alpha_2$ | $e_1$ | $e_2$ | $b_1$ | $b_2$ | $\gamma_1$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Value* | 6.03198 | 0.03198 | 0.05 | 0.08 | 0.01 | 0.01 | 0.5 | 0.5 | 0.02 | 0.02 | 0.2 | 0.2 | 0.1 |
| *Parameter* | $\gamma_2$ | $k_1$ | $k_2$ | $a_1$ | $a_2$ | $f$ | $r$ | $c$ | $\mu$ | $g$ | $n$ | $\varepsilon$ | |
| *Value* | 0.5 | 10 | 5 | 0.3 | 0.1 | 0.3 | 0.5 | 3 | 0.07 | 0.1 | 1 | Varied | |

Case (I): $R_0 \leq 1$. Choosing $\varepsilon = 0.85$ and using the data in Table 1, we have $R_0 = 0.899$ and $R_1 = 0.641$. Since $R_0 < 1$, then according to Theorem 7, the infection-free equilibrium $E_0$ is GAS. Evidently, Figures 1-8 show that, the numerical results are consistent with the theoretical results of Theorem 7. We can see that, the concentration of uninfected target cells tends to its normal value $\frac{\lambda_1}{d_1} = 603.198$, $\frac{\lambda_2}{d_2} = 3.198$, respectively, while the concentrations of latently infected cells, actively infected cells, free virus particles and antibody immune cells are decreasing and tend to zero. In this case, the treatment succeeded to eliminate the HIV viruses from the blood.

Case (II): $R_1 \leq 1$. By taking $\varepsilon = 0.40$, we have $R_1 = 0.915 < 1$ and $E_1$ exists where $E_1 = (601.504, 0.780, 0.038, 0.055, 0.054, 0.231, 0.565, 0.000)$. Based on Theorem 8, $E_1$ is GAS. Figures 1-8 show that the numerical simulations confirm our theoretical result presented in Theorem 8. We observe that, the trajectory of the system will converge to the chronic-infection equilibrium without antibody immune response $E_1$. In such situation, the infection becomes chronic but without antibody immune response.

Case (III): $R_1 > 1$.We choose, $\varepsilon = 0.0$. Then, we calculate $R_0 = 1.631$ and $R_1 = 1.149 > 1$, this means that, $E_2$ exists and it is GAS. From Figures 1-8, we can see that, our simulation results are consistent with the theoretical results of Theorem 9. We observe that, the trajectory of the system tend to the chronic-infection equilibrium with antibody immune response $E_2 = (599.699, 0.474, 0.079, 0.062, 0.111, 0.260, 0.700, 0.896)$. In this case, the infection becomes chronic but with persistent antibody immune response. Figures 1 and 7 demonstrate that, when $R_1 > 1$, the antibody immune response is activated and it reduces the concentration of free virus particles and increases the concentration of uninfected cells. In case (i) we calculate the critical drug efficacy (i.e, the efficacy needed in order stabilize the system around the disease-free equilibrium). For system (51)-(55), $E_0$ is GAS when $R_0 \leq 1$ i.e.

$$\varepsilon_1^{crit} \leq \varepsilon < 1, \qquad \varepsilon_1^{crit} = \max\left\{0, \frac{\bar{R}_0 - 1}{\bar{R}_{01} + f\bar{R}_{02}}\right\},$$

where, $\bar{R}_0 = R_0\,|_{\varepsilon=0}$ and $\bar{R}_{0i} = R_{0i}\,|_{\varepsilon=0}$ , $i = 1, 2$. Using the data in Table 1, we have $\varepsilon_1^{crit} = 0.7332$. Also, in case (ii) we can calculate the critical drug efficacy $\varepsilon_2^{crit} = 0.2566$.

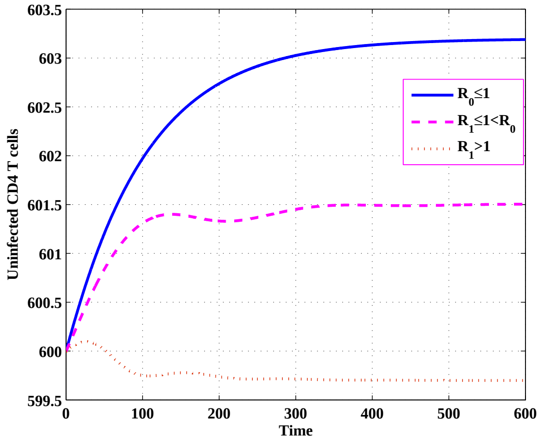


Figure 1: The evolution of uninfected CD4+T cells for model (51)-(55).

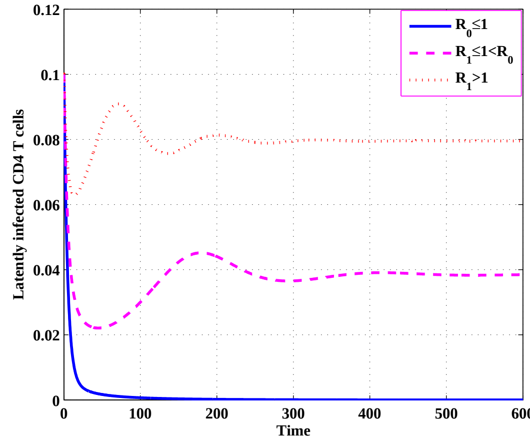


Figure 2: The evolution of uninfected macrophage cells for model (51)-(55).

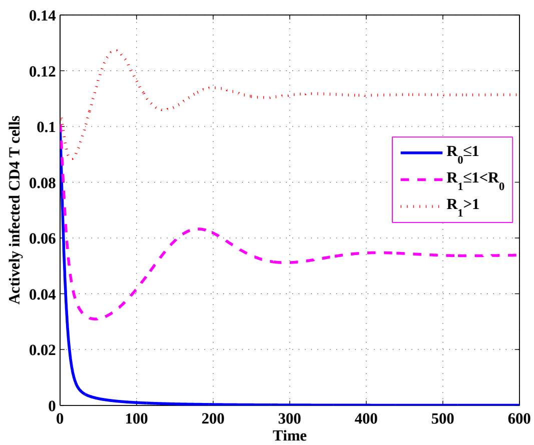


Figure 3: The evolution of actively infected CD4+T cells for model (51)-(55).

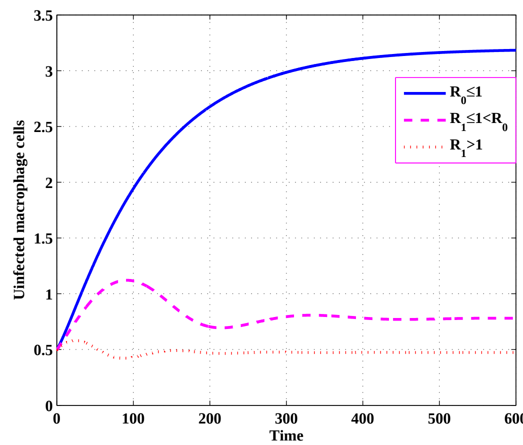


Figure 4: The evolution of uninfected macrophage cells for model (51)-(55).

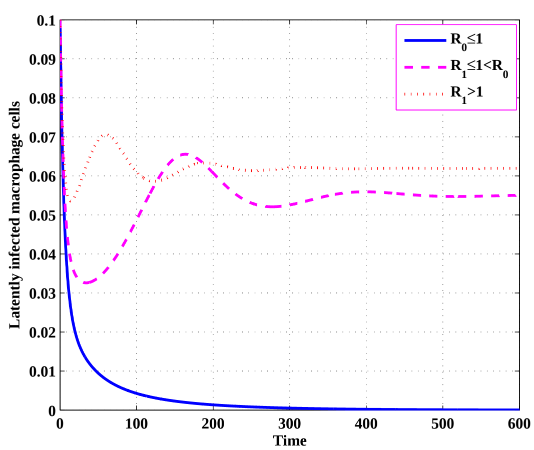


Figure 5: The evolution of latently infected macrophage cells for model (51)-(55).

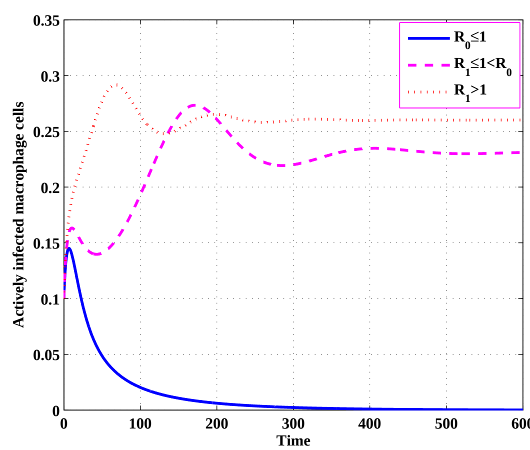


Figure 6: The evolution of actively infected macrophage cells for model (51)-(55).

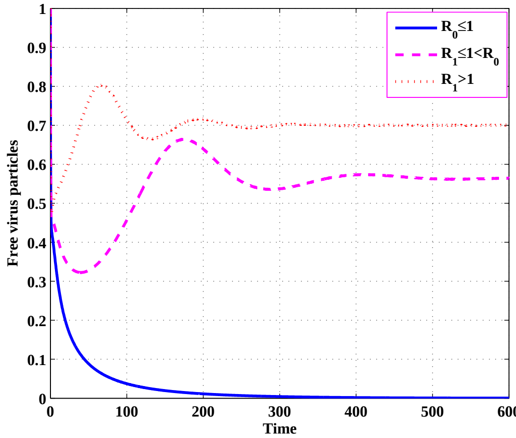


Figure 7: The evolution of free virus particles for model (51)-(55).

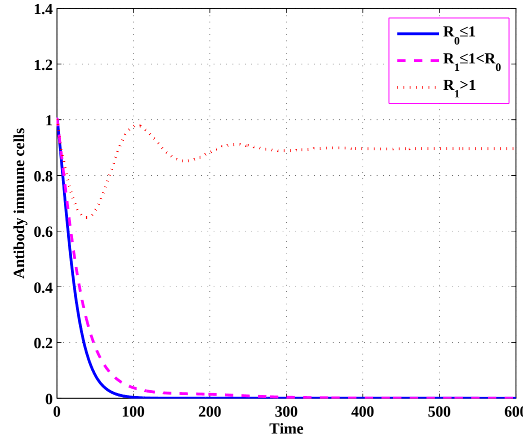


Figure 8: The evolution of antibody immune cells for model (51)-(55).

## 7 Acknowledgment

This article was funded by the Deanship of Scientific Research (DSR), King Abdulaziz University, Jeddah. The authors, therefore, acknowledge with thanks DSR technical and financial support.

## References

[1] M. A. Nowak and R. M. May, "Virus dynamics: Mathematical Principles of Immunology and Virology", *Oxford Uni., Oxford*, 2000.

[2] A. S. Perelson and P. W. Nelson, "Mathematical analysis of HIV-1 dynamics in vivo", *SIAM Rev.*, vol. **41,** pp. 3-44**,** 1999.

[3] A. M. Elaiw and A. M. Shehata, "Stability and feedback stabilization of HIV infection model with two classes of target cells", *Discrete Dyn. Nat. Soc.*,vol. **20**, 2012.

[4] A. M. Elaiw, and N. A. Almuallem, "Global properties of delayed-HIV dynamics models with differential drug efficacy in co-circulating target cells", *Appl. Math. Comput.*, vol. **265**, 1067-1089, 2015.

[5] A. M. Elaiw, and N. A. Almuallem, "Global dynamics of delay-distributed HIV infection models with differential drug efficacy in cocirculating target cells", *Math. Method Appl. Sci.*, vol. **39,** 4-31, 2016.

[6] A. M. Elaiw, I. A. Hassanien, and S. A. Azoz, "Global stability of HIV infection models with intracellular delays", *J. Korean Math. Soc.*, vol. **49**(4), 779-794, 2012.

[7] D. S. Callaway and A. S. Perelson, "HIV-1 infection and low steady state viral loads", *Bull. Math. Biol.*, vol. **64,** pp. 29-64, 2002.

[8] L. Wang, M.Y. Li, "Mathematical analysis of the global dynamics of a model for HIV infection of $CD4^+$ T cells", *Math. Biosc.*, vol. **200(1)**, pp. 44-57, 2006.

[9] Y. Zhao, D. T. Dimitrov, H. Liu and Y. Kuang, "Mathematical insights in evaluating state dependent e ectiveness of HIV prevention interventions", *Bull. Math. Biol.*, vol. 75, pp. 649-675, 2013.

[10] A.M. Elaiw, and S.A. Azoz, "Global properties of a class of HIV infection models with Beddington-DeAngelis functional response", *Math. Method Appl. Sci.*, vol. **36**, pp. 383-394, 2013.

[11] S. A. Gourley, Y. Kuang and J. D. Nagy, "Dynamics of a delay differential equation model of hepatitis B virus infection", *J. Biol. Dyn.*, vol. **2,** pp. 140-153, 2008.

[12] S. Eikenberry, S. Hews, J. D. Nagy and Y. Kuang, "The dynamics of a delay model of HBV infection with logistic hepatocyte growth", *Math. Biosc. Eng.*, vol. **6,** pp. 283-299, 2009.

[13] J. Li, K. Wang, Y. Yang, "Dynamical behaviors of an HBV infection model with logistic hepatocyte growth", *Math. Comput. Modelling*, vol. **54,** pp. 704-711, 2011.

[14] R. Qesmi, J. Wu, J. Wu and J.M. Heffernan, "Influence of backward bifurcation in a model of hepatitis B and C viruses", *Math. Biosci.*, vol. **224,** pp. 118–125, 2010.

[15] A. U. Neumann, N. P. Lam, H. Dahari, D. R. Gretch, T. E. Wiley, T. J, Layden and A. S. Perelson, "Hepatitis C viral dynamics in vivo and the antiviral efficacy of interferon-alpha therapy", *Science*, vol. **282,** pp. 103-107, 1998.

[16] M. Y. Li and H. Shu, "Global dynamics of a mathematical model for HTLV-I infection of CD4+ T cells with delayed CTL response", *Nonlinear Anal. Real World Appl.*, vol. **13,** pp. 1080-1092, 2012.

[17] P. Tanvi, G. Gujarati, and G. Ambika, "Virus antibody dynamics in primary and secondary dengue infections", *J. Math. Biol.*, vol. **69**, pp 1773-1800, 2014.

[18] J. A. Deans and S. Cohen, "Immunology of malaria", *Ann.Rev.Microbiol.*, vol. **37,** pp. 25-49, 1983.

[19] A. Murase, T. Sasaki and T. Kajiwara, "Stability analysis of pathogen-immune interaction dynamics", *J. Math. Biol.*, vol. **51,** pp. 247-267, 2005.

[20] W. Dominik, R. M. May and M. A. Nowak, "The role of antigen-independent persistence of memory cytotoxic T lymphocytes", *Int. Immunol.*, vol. **12 (4)**, pp. 467–477, 2000.

[21] S. Wang and D. Zou, "Global stability of in host viral models with humoral immunity and intracellular delays", *J. Appl. Math. Mod.*, vol. **36,** pp. 1313-1322, 2012.

[22] A. M. Elaiw and N. H. AlShameani, Global stability of humoral immunity virus dynamics models with nonlinear infection rate and removal, *Nonlinear Anal. Real World Appl.*, vol. **26**, pp. 161-190, 2015.

[23] T. Wang, Z. Hu, F. Liao and Wanbiao, "Global stability analysis for delayed virus infection model with general incidence rate and humoral immunity", *Math. Comput. Simulation*, vol. **89,** pp. 13-22, 2013.

[24] M. A . Obaid and A.M. Elaiw, "Stability of virus infection models with antibodies and chronically infected cells", *Abstr. Appl. Anal*, 2014**.**

[25] A. S. Perelson, P. Essunger, Y. Cao et al., "Decay characteristics of HIV-1- infected compartments during combination therapy", *Nature*, vol. **387(6629)**, pp. 188–191, 1997.

[26] A. M. Elaiw, " Global threshold dynamics in humoral immunity viral infection models including an eclipse stage of infected cells" *J. Korean Soc. Ind. Appl. Math.*, vol. **19** 137-170, 2015.

[27] J. K. Hale and S. Verduyn Lunel, "Introduction to functional differential equations", *Springer-Verlag, NewYork*, 1993.