Stability analysis of general humoral immunity HIV dynamics models with discrete delays and HAART

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Abstract

We investigate a general HIV infection model with three types of infected cells: latently infected cells, long-lived productively infected cells, and short-lived productively infected cells. We consider two kinds of target cells: CD4+ T cells and macrophages. We incorporate three discrete time delays into the model. Moreover, we consider the effect of humoral immunity on the dynamical behavior of the HIV. The HIV-target incidence rate, production/proliferation, and removal rates of the cells and HIV are represented by general nonlinear functions. We show that the solutions of the proposed model are nonnegative and ultimately bounded. We derive two threshold parameters which determine the stability of the three steady states of the model. Using Lyapunov functionals, we established the global stability of the steady states of the model. The theoretical results are confirmed by numerical simulations.

Keywords: HIV infection, global stability, humoral immune response, latency, viral reservoirs.

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1. Introduction

During the last decades several mathematical models have been proposed with the aim to understand the dynamics of HIV in the human body [1, 3–8, 10–12, 14, 16–18, 20–25, 27, 28, 30–33, 35–37, 39]. The basic and pioneering model describing the HIV dynamics is due Nowak and Bangham [33]. The model contains three compartments: uninfected CD4+ T cells (s), infected cells (y), and free HIV particles (p):

\[
\begin{align*}
\dot{s}(t) &= \rho - \delta s(t) - \lambda s(t)p(t), \\
\dot{y}(t) &= \lambda s(t)p(t) - \eta y(t), \\
\dot{p}(t) &= N \eta y(t) - gp(t),
\end{align*}
\]

(1.1)

where \(\rho, \delta,\) and \(\lambda\) represent the production, death, and infection rates of the uninfected CD4+ T cells, respectively; \(\eta\) and \(g\) are the death rate constants of the infected cells and free HIV, respectively; \(N\) is the...
average number of HIV particles generated in the lifetime of the infected cells. A lot of considerations have been added that aim to get the best representation of the HIV infection. Most notably is latent HIV reservoirs which serve as a major barrier in curing HIV infection. In despite of antiretroviral therapy limits significantly the level of HIV in the blood, there still a low viral load due to ongoing latently infected cells reservoir reactivation. Variant models have been developed to study the dynamics of HIV in the presence of latent reservoirs (see, e.g., [2, 9, 13, 15, 29]).

In a very recent work Elaiw et al. [19] have modified model (1.1) by considering: (i) three types of infected cells, latently infected cells (w), short-lived productively infected cells (y), and long-lived productively infected cells (u); (ii) three types of time delays; (iii) antibody immune response (x); (iv) general nonlinear functions for the HIV-target incidence rate, production/proliferation and removal rates of the cells and HIV; and (v) highly active antiretroviral therapy (HAART) which combine both reverse transcriptase inhibitor and protease inhibitor. The model presented in [19] is given by:

\[
\begin{align*}
\dot{s}(t) &= \pi(s(t)) - (1 - \epsilon_1)\lambda_i X_i(s(t), p(t)), \\
\dot{w}(t) &= (1 - \epsilon_1)\lambda_2 e^{-\mu_1\tau_1}X(s(t - \tau_1), p(t - \tau_1)) - (\alpha + \beta)\psi_1(w(t)), \\
\dot{y}(t) &= (1 - \epsilon_1)\lambda_2 e^{-\mu_2\tau_2}X(s(t - \tau_2), p(t - \tau_2)) + \alpha\psi_1(w(t)) - \eta\psi_2(y(t)), \\
\dot{u}(t) &= (1 - \epsilon_1)\lambda_2 e^{-\mu_3\tau_3}X(s(t - \tau_3), p(t - \tau_3)) - \nu_3\psi_3(u(t)), \\
\dot{p}(t) &= (1 - \epsilon_2)N_3\psi_2(y(t)) + (1 - \epsilon_2)\lambda_4 p(t) - \mu\psi_4(p(t)) \psi_5(x(t)), \\
\dot{x}(t) &= \eta_4\psi_4(p(t)) \psi_5(x(t)) - \omega\psi_5(x(t)).
\end{align*}
\]

Parameter \(\tau_1\) is the time between viral entry and latent infection (i.e., the integration of viral DNA into cell’s DNA has finished), while \(\tau_2\) and \(\tau_3\) are the times between viral entry and viral production from short-lived productively infected and long-lived productively infected cells, respectively. The factor \(e^{-\mu_i\tau_j}\), \(j = 1, 2, 3\) accounts for the loss of target cells during the delay period of length \(\tau_j\), where \(\mu_i > 0\) is constant. The model incorporates reverse transcriptase inhibitor (RTI) with efficacy \(\epsilon_1\) and protease inhibitor (PI) with efficacy \(\epsilon_2\), where \(\epsilon_1, \epsilon_2 \in [0, 1]\). \(\chi, \pi, \psi_i, j = 1, \ldots, 5\) are general nonlinear functions.

Model (1.2) has considered the interaction of the HIV with one class of target cells, CD4\(^+\) T cells. It has been reported in [34] that the HIV can infect both the CD4\(^+\) T cells and macrophages. To have more accurate HIV dynamics model the interaction between the HIV with the macrophages have to be considered. The aim of this paper is to propose and analyze an HIV infection model which improves model (1.2) by taking into account two classes of target cells, CD4\(^+\) T cells and macrophages. We propose the following model:

\[
\begin{align*}
\dot{s}_i(t) &= \pi_i(s_i(t)) - \lambda_i X_i(s_i(t), p(t)), \\
\dot{w}_i(t) &= \lambda_i e^{-\mu_i\tau_1}X_i(s_i(t - \tau_1), p(t - \tau_1)) - (\alpha_i + \beta_i)\psi_1(w_i(t)), \\
\dot{y}_i(t) &= \lambda_i e^{-\mu_i\tau_2}X_i(s_i(t - \tau_2), p(t - \tau_2)) + \alpha_i\psi_1(w_i(t)) - \eta_i\psi_2(y_i(t)), \\
\dot{u}_i(t) &= \lambda_i e^{-\mu_i\tau_3}X_i(s_i(t - \tau_3), p(t - \tau_3)) - \nu_i\psi_3(u_i(t)), \\
\dot{p}(t) &= \sum_{i=1}^{2} \left( N_1\eta_i e^{-\mu_i\tau_4}\psi_2(y_i(t - \tau_4)) + M_i\psi_4(p(t)) \psi_5(x(t)) - \eta_4\psi_4(p(t)) \psi_5(x(t)) \right), \\
\dot{x}(t) &= \eta_4\psi_4(p(t)) \psi_5(x(t)) - \omega\psi_5(x(t)),
\end{align*}
\]

where \(i = 1\) for the CD4\(^+\) T cells and \(i = 2\) for the macrophages. We have \(\lambda_{m_1} = (1 - \epsilon_1)\lambda_{m_1}, \lambda_{m_2} = (1 - \epsilon_2)\lambda_{m_2}, m = 1, 2, 3, N_1 = (1 - \epsilon_2)N_1, M_1 = (1 - \epsilon_2)M_1, N_2 = (1 - \epsilon_2)N_2, M_2 = (1 - \epsilon_2)M_2, \lambda = \lambda_1 + \lambda_2 + \lambda_3\) and \(\epsilon_1, \epsilon_2 \in (0, 1)\). The parameters \(\tau_4\) and \(\tau_5\) represent the time necessary for producing new infectious viruses from the short-lived productively infected and long-lived productively infected cells, respectively. All the parameters are positive.

Functions \(X_i, \pi_i, \psi_i, j = 1, \ldots, 4, i = 1, 2\), are continuously differentiable and satisfy the following hypotheses:
H1 (i) there exists $s_i^0$ such that $\pi_i(s_i^0) = 0$, $\pi_i(s_i) > 0$ for $s_i \in [0, s_i^0]$;
(ii) $\pi'_i(s_i) < 0$ for $s_i \in (0, \infty)$;
(iii) there are $b_i > 0$ and $\overline{b}_i > 0$ such that $\pi_i(s_i) \leq b_i - \overline{b}_i s_i$ for $s_i \in [0, \infty)$;
H2 (i) $\chi_i(s_i, p) > 0$ and $\chi_i(0, p) = \chi_i(s_i, 0) = 0$ for $s_i, p \in (0, \infty)$;
(ii) $\frac{\partial \chi_i(s_i, p)}{\partial s_i} > 0$ and $\frac{\partial \chi_i(s_i, p)}{\partial p} > 0$ for all $s_i, p \in (0, \infty)$;
(iii) $\frac{d}{ds_i} \left( \frac{\partial \chi_i(s_i, p)}{\partial p} \right) > 0$ for $s_i \in (0, \infty)$;
H3 (i) $\psi_{ij}(\eta) > 0$ for $\eta \in (0, \infty)$, $\psi_{ij}(0) = 0$, $j = 1, \ldots, 4, i = 1, 2$;
(ii) $\psi_{ij}'(\eta) > 0$, $\psi_{ij}''(\eta) > 0$ for $\eta \in (0, \infty)$, $j = 1, 2, 3, i = 1, 2, \psi_{ij}(\eta) > 0$ for $\eta \in [0, \infty)$;
(iii) there are $\alpha_{ij} > 0$, $j = 1, \ldots, 4, i = 1, 2$, such that $\psi_{ij}(\eta) \geq \alpha_{ij} \eta$ for $\eta \in [0, \infty)$;
H4 $\frac{\chi_i(s_i, p)}{\psi_{41}(p)}$ is decreasing function w.r.t $p$ for $p \in (0, \infty)$.

Remark 1.1. From H1-H4 we have

$$\left( \frac{\chi_i(s_i, p)}{\psi_{41}(p)} \right) \left( \frac{\chi_i(s_i, p')}{\psi_{41}(p')} \right) \left( \frac{\chi_i(s_i, p)}{\psi_{41}(p)} \right) \leq 0,$$

which gives

$$\left( \frac{\chi_i(s_i, p)}{\psi_{41}(p)} \right) \left( \frac{\chi_i(s_i, p')}{\psi_{41}(p')} \right) \left( \frac{\chi_i(s_i, p)}{\psi_{41}(p)} \right) \leq 0.$$

We consider system (1.3) with the initial conditions:

$$s_1(t) = \varphi_1(t), \quad s_2(t) = \varphi_2(t), \quad w_1(t) = \varphi_3(t), \quad w_2(t) = \varphi_4(t), \quad y_1(t) = \varphi_5(t),$$
$$y_2(t) = \varphi_6(t), \quad u_1(t) = \varphi_7(t), \quad u_2(t) = \varphi_8(t), \quad p(t) = \varphi_9(t), \quad x(t) = \varphi_{10}(t),$$

for $t \in [-\sigma, 0]$, $\sigma = \max(\tau_{11}, \tau_{12}, \tau_{21}, \tau_{22}, \tau_{31}, \tau_{32}, \tau_{41}, \tau_{42}, \tau_{51}, \tau_{52})$, and denote by $C$ the Banach space of continuous functions mapping the interval $[-\sigma, 0]$ into $\mathbb{R}_{\geq 0}$ and $(\varphi_1(\theta), \ldots, \varphi_{10}(\theta)) \in C\left([-\sigma, 0], \mathbb{R}_{\geq 0}^5\right)$. Then, the uniqueness of the solution for $t > 0$ is guaranteed [26].

1.1. Preliminaries

Lemma 1.2. Let hypotheses H1-H3 be valid, then the solutions of system (1.3) is non-negative and ultimately bounded.

Proof. Let us write system (1.3) in matrix form $\dot{k}(t) = L(k(t))$, where $k = (s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x)^T$, $L = (L_1, L_2, \ldots, L_{10})^T$ and

$$L(k(t)) = \begin{pmatrix}
L_1(k(t)) \\
L_2(k(t)) \\
\vdots \\
L_{10}(k(t))
\end{pmatrix}.$$

Let

$$L = \begin{pmatrix}
\pi_1(s_1(t)) - \lambda_1 \chi_1(s_1(t), p(t)) \\
\pi_2(s_2(t)) - \lambda_2 \chi_2(s_2(t), p(t)) \\
\lambda_{11} e^{-\mu_{11}(t) \tau_{11}} \chi_1(s_1(t - \tau_{11}), p(t - \tau_{11})) - (\alpha_1 + \beta_1) \psi_{11}(w_1(t)) \\
\lambda_{12} e^{-\mu_{12}(t) \tau_{12}} \chi_2(s_2(t - \tau_{12}), p(t - \tau_{12})) - (\alpha_2 + \beta_2) \psi_{12}(w_2(t)) \\
\lambda_{21} e^{-\mu_{21}(t) \tau_{21}} \chi_1(s_1(t - \tau_{21}), p(t - \tau_{21})) + \alpha_1 \psi_{11}(w_1(t)) - \eta_1 \psi_{21}(y_1(t)) \\
\lambda_{22} e^{-\mu_{22}(t) \tau_{22}} \chi_2(s_2(t - \tau_{22}), p(t - \tau_{22})) + \alpha_2 \psi_{12}(w_2(t)) - \eta_2 \psi_{22}(y_2(t)) \\
\lambda_{31} e^{-\mu_{31}(t) \tau_{31}} \chi_1(s_1(t - \tau_{31}), p(t - \tau_{31})) - \nu_1 \psi_{31}(u_1(t)) \\
\lambda_{32} e^{-\mu_{32}(t) \tau_{32}} \chi_2(s_2(t - \tau_{32}), p(t - \tau_{32})) - \nu_2 \psi_{32}(u_2(t)) \\
\sum_{i=1}^{2} (N_i \eta_i e^{-\mu_{41}(t) \tau_{41}} \psi_{21}(y_1(t - \tau_{41})) + M_i \psi_i e^{-\mu_{41}(t) \tau_{51}} \psi_{31}(u_1(t - \tau_{51}))) - g \psi_{41}(p(t)) \\
- \mu \psi_{41}(p(t)) \psi_{42}(x(t)) \\
\tau \psi_{41}(p(t)) \psi_{42}(x(t)) - \omega \psi_{42}(x(t))
\end{pmatrix}.$$
We have

\[ L_j (k(t)) \big|_{k(t) \in \mathbb{R}^{n_j}} \geq 0, \quad j = 1, \ldots, 10. \]

Using lemma 2 in [38], the solutions of system (1.3) with the initial states (1.4) satisfy \( k(t) \in \mathbb{R}^{10}_{\geq 0} \) for all \( t \geq 0 \). The non-negativity of the model’s solution implies that \( \lim_{t \to \infty} \sup_{s_1} s_1(t) \leq M_{1L} \), where \( M_{1L} = \frac{b_1}{b_1} \). Let

\[
T_i(t) = N_i e^{-\mu_i \tau_i} s_i(t - \tau_i) + N_i e^{-\mu_i \tau_2} s_i(t - \tau_2) + M_i e^{-\mu_i \tau_3} s_i(t - \tau_3)
\]

\[
+ N_i w_i(t) + N_i y_i(t) + M_i u_i(t),
\]

then

\[
\dot{T}_i(t) = N_i e^{-\mu_i \tau_i} \left[ \pi_i(s_i(t - \tau_i)) - \lambda_i \chi_i(s_i(t - \tau_i), p(t - \tau_i)) \right]
\]

\[
+ N_i e^{-\mu_i \tau_2} \left[ \pi_i(s_i(t - \tau_2)) - \lambda_i \chi_i(s_i(t - \tau_2), p(t - \tau_2)) \right]
\]

\[
+ M_i e^{-\mu_i \tau_3} \left[ \pi_i(s_i(t - \tau_3)) - \lambda_i \chi_i(s_i(t - \tau_3), p(t - \tau_3)) \right]
\]

\[
+ N_i \left[ \lambda_i e^{-\mu_i \tau_1} \chi_i(s_i(t - \tau_1), p(t - \tau_1)) - (\alpha_i + \beta_i) \psi_1(w_i(t)) \right]
\]

\[
+ N_i \left[ \lambda_i e^{-\mu_i \tau_2} \chi_i(s_i(t - \tau_2), p(t - \tau_2)) + \alpha_i \psi_1(w_i(t)) - \eta_i \psi_2(y_i(t)) \right]
\]

\[
+ M_i \left[ \lambda_i e^{-\mu_i \tau_3} \chi_i(s_i(t - \tau_3), p(t - \tau_3)) - \gamma_i \psi_3(u_i(t)) \right]
\]

\[
\leq N_i e^{-\mu_i \tau_1} \left[ b_1 - b_i s_i(t - \tau_1) \right] + N_i e^{-\mu_i \tau_2} \left[ b_1 - b_i s_i(t - \tau_2) \right]
\]

\[
+ M_i e^{-\mu_i \tau_3} \left[ b_1 - b_i s_i(t - \tau_3) \right] - N_i \beta_i \alpha_1 \psi_1(t) - N_i \eta_i \alpha_2 \psi_1(y_i(t)) - M_i \gamma_i \alpha_3 \psi_3(u_i(t))
\]

\[
\leq b_1 \left( N_i e^{-\mu_i \tau_1} + N_i e^{-\mu_i \tau_2} + M_i e^{-\mu_i \tau_3} \right) - \sigma_i \left[ N_i e^{-\mu_i \tau_1} s_i(t - \tau_1) + N_i e^{-\mu_i \tau_2} s_i(t - \tau_2) + N_i e^{-\mu_i \tau_3} s_i(t - \tau_3) \right] + N_i w_i(t) + N_i y_i(t) + M_i u_i(t)
\]

\[
\leq b_1 \left( 2N_i + M_i \right) - \sigma_i T_i(t),
\]

where \( \sigma_i = \min(\beta_i \alpha_1, \eta_i \alpha_2, \gamma_i \alpha_3) \). Then \( \lim_{t \to \infty} \sup_{s_1} T_i(t) \leq \frac{b_1 (2N_i + M_i)}{\sigma_i} \). The non-negativity of the system’s variables implies that

\[
\lim_{t \to \infty} \sup_{s_1} w_i(t) \leq \frac{b_1 (2N_i + M_2)}{N_i \sigma_i} = M_{2L},
\]

\[
\lim_{t \to \infty} \sup_{s_1} y_i(t) \leq \frac{b_1 (2N_i + M_1)}{N_i \sigma_i} = M_{2L},
\]

\[
\lim_{t \to \infty} \sup_{s_1} u_i(t) \leq \frac{b_1 (2N_i + M_3)}{M_i \sigma_i} = M_{3L}.
\]

Moreover, we let \( T_3(t) = p(t) + \frac{w_3(t)}{x(t)} \). Then

\[
\dot{T}_3 = \sum_{i=1}^{2} \left( N_i \eta_i e^{-\mu_i \tau_1} \psi_2(y_i(t - \tau_i)) + M_i \gamma_i e^{-\mu_i \tau_3} \psi_3(u_i(t - \tau_3)) \right) - g \psi_1(p) - \frac{\mu \omega}{r} \psi_2(x)
\]

\[
\leq \sum_{i=1}^{2} \left( N_i \eta_i e^{-\mu_i \tau_1} \psi_2(M_2) + M_i \gamma_i e^{-\mu_i \tau_3} \psi_3(M_3) \right) - g \psi_1(p) - \frac{\mu \omega}{r} \psi_2(x)
\]

\[
\leq \sum_{i=1}^{2} \left( N_i \eta_i \psi_2(M_2) + M_i \gamma_i \psi_3(M_3) \right) - \sigma_3 T_3(t),
\]

where \( \sigma_3 = \min(g \alpha_4, \omega \alpha_4) \). Hence,

\[
\lim_{t \to \infty} \sup_{s_1} T_3(t) \leq \sum_{i=1}^{2} \left( N_i \eta_i \psi_2(M_2) + M_i \gamma_i \psi_3(M_3) \right) \sigma_3 = M_{4L}.
\]
The steady state of (1.3) satisfies the following equations:

\[ \lim_{t \to \infty} \sup_{x(t)} \leq M_{41}, \]
\[ \lim_{t \to \infty} \sup_{x(t)} \leq \frac{rM_{41}}{\mu} = M_{42}. \]

Therefore, \( s_i(t) \), \( w_i(t) \), \( y_i(t) \), \( u_i(t) \), \( p(t) \), and \( x(t) \) are ultimately bounded.

According to Lemma 1.2, we can show that the region
\[
\Omega = \{ (s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x) \in C^1 : \|s_i\| \leq M_{11}, \|w_i\| \leq M_{21}, \|y_i\| \leq M_{21}, \|u_i\| \leq M_{31}, \|p\| \leq M_{41}, \|x\| \leq M_{42} \}
\]
is positively invariant with respect to system (1.3).

### 1.2. Steady states

We define the basic reproduction number \( R_0 \) of system (1.3) as follows:

\[ R_0 = \sum_{i=1}^{2} \frac{\rho_i}{\psi_{41}(x, 0)} \frac{\partial \chi_i(s_i, 0)}{\partial p}. \]

The steady state of (1.3) satisfies the following equations:

\[ 0 = \pi_1(s_1) - \lambda_1 x(t, s_1, p), \]
\[ 0 = \lambda_1 e^{-\mu_1 \tau_1} x(t, s_1, p) - (\alpha_1 + \beta_1) \psi_1(w_1), \]
\[ 0 = \lambda_2 e^{-\mu_2 \tau_2} x(t, s_1, p) + \alpha_1 \psi_1(w_1) - \eta_1 \psi_2(y_1), \]
\[ 0 = \lambda_3 e^{-\mu_3 \tau_3} x(t, s_1, p) - \nu_1 \psi_3(u_1), \]
\[ 0 = \sum_{i=1}^{2} \left( \psi_i(y_1, w_1) + M_i \psi_i e^{-\mu_i \tau_i} \psi_3(u_1) - g \psi_{41}(p) - \mu \psi_{41}(p)^2 \psi_{42}(x), \right) \]
\[ 0 = r \psi_{41}(p) \psi_{42}(x) - \omega \psi_{42}(x). \]

From Eq. (1.10) we have two possible solutions: \( \psi_{42}(x) = 0 \) and \( \psi_{41}(p) = \omega / r \). The first possibility \( \psi_{42}(x) = 0 \) implies that \( x = 0 \). H3 implies that \( \psi_j^{-1}, j = 1, \ldots, 4, i = 1, 2 \), exists, strictly increasing and \( \psi_j^{-1}(0) = 0 \). Let us define

\[ \Delta_1(s_1) = \psi_1^{-1} \left( \frac{\lambda_1 e^{-\mu_1 \tau_1} + \alpha_1 + \beta_1}{\lambda_1 (\alpha_1 + \beta_1)} \pi_1(s_1) \right), \]
\[ \Delta_2(s_1) = \psi_2^{-1} \left( \frac{\lambda_2 e^{-\mu_2 \tau_2} + \alpha_1 \beta_1}{\lambda_2 \eta_1 (\alpha_1 + \beta_1)} \pi_1(s_1) \right), \]
\[ \Delta_3(s_1) = \psi_3^{-1} \left( \frac{\lambda_3 e^{-\mu_3 \tau_3} + \alpha_1 + \beta_1}{\lambda_3 \nu_1 (\alpha_1 + \beta_1)} \pi_1(s_1) \right), \]
\[ \Delta_4(s_1) = \psi_4^{-1} \left( \sum_{i=1}^{2} \frac{\rho_i}{\lambda_i} \pi_i(s_i) \right), \]

where \( \rho_i = \sum_{i=1}^{2} N_i e^{-\mu_i \tau_i} (\alpha_1 \lambda_1 e^{-\mu_1 \tau_1} + (\alpha_1 + \beta_1) \lambda_2 e^{-\mu_2 \tau_2} + M_i e^{-\mu_3 \tau_3} \lambda_3 (\alpha_1 + \beta_1)) \). It follows from Eqs. (1.5)-(1.9) that:

\[ w_i = \Delta_1(s_i), \quad y_i = \Delta_2(s_i), \quad u_i = \Delta_3(s_i), \quad p = \Delta_4(s_i). \]

Obviously, \( \Delta_1(s_i), \Delta_2(s_i), \Delta_3(s_i), \Delta_4(s_i) > 0 \) for \( s_i \in [0, s_i^0] \) and \( \Delta_1(s_i^0) = \Delta_2(s_i^0) = \Delta_3(s_i^0) = \Delta_4(s_i^0) = 0 \), i = 1, 2. From Eqs. (1.5), (1.11), and (1.12) we obtain

\[ \sum_{i=1}^{2} \rho_i \chi_i(s_i, \Delta_4(s_i)) - \psi_4(\Delta_4(s_i)) = 0. \]

Eq. (1.13) has two possible solutions, \( \Delta_4 = 0 \) and \( \Delta_4 \neq 0 \). The solution \( \Delta_4 = 0 \) implies \( s_i = s_i^0 \) which gives the infection-free steady state \( \Pi_0(s_1^0, s_2^0, 0, 0, 0, 0, 0, 0, 0, 0) \). The other solution \( \Delta_4 \neq 0 \) admits
a humoral-inactivated infection steady state \( \Pi_1(\bar{s}_1, \bar{s}_2, \bar{w}_1, \bar{w}_2, \bar{\gamma}_1, \bar{\gamma}_2, \bar{u}_1, \bar{u}_2, \bar{p}, 0) \) where the coordinates satisfy the equalities:

\[
\begin{align*}
\tau_0(\bar{s}_1) &= \chi_1(\bar{s}_1, \bar{p}), \\
\lambda_{11} e^{-\mu_{11}(\bar{x}_1)} &= (\alpha_1 + \beta_1) \psi_{11}(\bar{w}_1), \\
\eta_{1} \psi_{21}(\bar{\gamma}_1) &= \lambda_{21} e^{-\mu_{21}(\bar{x}_1)} + \alpha_1 \psi_{11}(\bar{w}_1), \\
\psi_{21}(\bar{u}_1) &= \lambda_{31} e^{-\mu_{31}(\bar{x}_1)} \\
\psi_{41}(\bar{p}) &= \sum_{i=1}^{2} \left( \frac{2}{\sigma_i} \right) \left( N_i \eta_{1} e^{-\mu_{11}(\bar{x}_1)} \psi_{21}(\bar{\gamma}_1) + M_i \eta_{1} e^{-\mu_{11}(\bar{x}_1)} \psi_{31}(\bar{u}_1) \right).
\end{align*}
\] (1.14)

The other solution of Eq. (1.10) is \( \psi_{41}(\bar{p}) = \frac{\omega}{\tau} \), which yields \( \bar{p} = \psi_{41}^{-1} \left( \frac{\omega}{\tau} \right) > 0 \). Substitute \( p = \bar{p} \) in Eq. (1.5) and let \( \Delta_1(s_i) = \pi_1(s_i) - \chi_1(s_i, \bar{p}) = 0 \). According to H1 and H2, \( \Delta_1(0) = \pi_1(0) > 0 \) and \( \Delta_1(s_0^p) = -\chi_1(s_0^p, \bar{p}) < 0 \). Thus, there exists a unique \( \bar{s}_1 \in (0, s_0^p) \) such that \( \Delta_1(\bar{s}_1) = 0 \). It follows from Eqs. (1.9) and (1.12) that

\[
\bar{w}_1 = \Delta_1(\bar{s}_1) > 0, \quad \bar{\gamma}_1 = \Delta_2(\bar{s}_1) > 0, \quad \bar{u}_1 = \Delta_3(\bar{s}_1) > 0,
\]

\[
\bar{p} = \psi_{41}^{-1} \left( \frac{\omega}{\tau} \right) > 0, \quad \bar{x} = \psi_{42}^{-1} \left( \frac{g}{\mu} \left( \sum_{i=1}^{2} \rho_i \chi_i(\bar{s}_i, \bar{p}) \psi_{41}(\bar{p}) - 1 \right) \right).
\]

Thus, \( \bar{x} > 0 \) when \( \sum_{i=1}^{2} \rho_i \frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})} > 1 \). Now we define the humoral immune response activation number as follows:

\[
R_1 = \sum_{i=1}^{2} \rho_i \frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})}.
\]

If \( R_1 > 1 \), then \( \bar{x} = \psi_{42}^{-1} \left( \frac{g}{\mu} (R_1 - 1) \right) > 0 \), and there exists a humoral-activated infection steady state \( \Pi_2(\bar{s}_1, \bar{s}_2, \bar{w}_1, \bar{w}_2, \bar{\gamma}_1, \bar{\gamma}_2, \bar{u}_1, \bar{u}_2, \bar{p}, \bar{x}) \). Clearly, from H2 and H4, we have

\[
R_1 = \sum_{i=1}^{2} \rho_i \frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})} \leq \sum_{i=1}^{2} \lim_{\bar{p} \to 0^+} \rho_i \frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})} \leq \sum_{i=1}^{2} \frac{\rho_i}{\psi_{41}^{(0)}(\bar{p})} \frac{\partial \chi_i(\bar{s}_i, 0)}{\partial \bar{p}} \leq \sum_{i=1}^{2} \frac{\rho_i}{\psi_{41}^{(0)}(\bar{p})} \frac{\partial \chi_i(\bar{s}_i, 0)}{\partial \bar{p}} = R_0.
\]

We will use the following equalities throughout the paper:

\[
\begin{align*}
\ln \left( \frac{\chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{11}(\bar{w}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{11}(\bar{w}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{21}(\bar{\gamma}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{21}(\bar{\gamma}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{31}(\bar{u}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{31}(\bar{u}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{41}(\bar{p}) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{41}(\bar{p}) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{11}(\bar{w}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{11}(\bar{w}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\psi_{21}(\bar{\gamma}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{21}(\bar{\gamma}_1) \chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{31}(\bar{u}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{31}(\bar{u}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\psi_{41}(\bar{p}) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{41}(\bar{p}) \chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{11}(\bar{w}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{11}(\bar{w}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\psi_{21}(\bar{\gamma}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{21}(\bar{\gamma}_1) \chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{31}(\bar{u}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{31}(\bar{u}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right), \\
\ln \left( \frac{\psi_{41}(\bar{p}) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{41}(\bar{p}) \chi_i(s_i, p)} \right) &= \ln \left( \frac{\psi_{11}(\bar{w}_1) \chi_i(s_i(t - \tau_i), p(t - \tau_i))}{\psi_{11}(\bar{w}_1) \chi_i(s_i, p)} \right) + \ln \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, p)} \right).
\]

(1.15)
2. Global properties

The following theorems investigate the global stability of the steady states of system (1.3).

Let us denote $\{s_i(t), w_i(t), y_1(t), u_1(t), p(t), x(t)\}$.

Theorem 2.1. If $R_0 \leq 1$ and hypotheses H1-H4 are valid, then $\Pi_0$ is GAS.

Proof. Define a Lyapunov functional $V_0(s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x)$ as:

$$
V_0 = \sum_{i=1}^{2} \rho_i \left[ s_i - s_0 - \int_{s_i}^{s_0} \lim_{p \to 0^+} \frac{M_i(s_i^0, p)}{M_i(\eta, p)} \, d\eta + \ell_1 s_i + \ell_2 y_i + \ell_3 u_i \\
+ \ell_1 \lambda_{11} \int_{0}^{\tau_1} e^{-\mu \tau_1} \chi_i(s_i(t - \theta), p(t - \theta)) \, d\theta + \ell_2 \lambda_{21} \int_{0}^{\tau_2} e^{-\mu \tau_2} \chi_i(s_i(t - \theta), p(t - \theta)) \, d\theta \\
+ \ell_3 \lambda_{31} \int_{0}^{\tau_3} e^{-\mu \tau_3} \chi_i(s_i(t - \theta), p(t - \theta)) \, d\theta + \ell_4 y_i \\
+ \ell_5 \psi_i \int_{0}^{\tau_5} e^{-\mu \tau_5} \psi_3(u_i(t - \theta)) \, d\theta \right] + \ell_{61} p + \ell_{62} x,
$$

where $\lambda_1, \ldots, \lambda_5, \ell_{61}, \ell_{62}$ satisfy the following equations:

$$
\begin{align*}
\lambda_1 &= \lambda_{11} \ell_1 e^{-\mu \tau_1} + \lambda_{21} \ell_2 e^{-\mu \tau_2} + \lambda_{31} \ell_3 e^{-\mu \tau_3}, \\
\lambda_2 &= \ell_4 e^{-\mu \tau_4}, \\
\lambda_3 &= \ell_5 e^{-\mu \tau_5}, \\
\rho_1 \ell_4 &= N_1 \ell_6, \\
\rho_1 \ell_5 &= M_1 \ell_6, \\
\mu \ell_6 &= \tau \ell_6.
\end{align*}
$$

The solution of Eqs. (2.1) is given by

$$
\begin{align*}
\ell_{11} &= \frac{\alpha_i N_1 \lambda_{11} e^{-\mu \tau_1}}{\rho_1 g}, \\
\ell_{21} &= \frac{N_1 \lambda_{11} e^{-\mu \tau_1}}{\rho_1 g}, \\
\ell_{31} &= \frac{M_1 \lambda_{11} e^{-\mu \tau_5}}{\rho_1 g}, \\
\ell_{41} &= \frac{N_1 \lambda_{11}}{\rho_1 g}, \\
\ell_{51} &= \frac{M_1 \lambda_{11}}{\rho_1 g}, \\
\ell_{61} &= \frac{\lambda_{11}}{g}, \\
\ell_{62} &= \frac{\mu \lambda_{11}}{g}.
\end{align*}
$$

Clearly, $V_0(s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x) > 0$ for all $s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x > 0$ and $V_0(s_1^0, s_2^0, 0, 0, 0, 0, 0, 0, 0, 0) = 0$. We calculate $\frac{dV_0}{dt}$ along the trajectories of (1.3) as:

$$
\frac{dV_0}{dt} = \sum_{i=1}^{2} \rho_i \left[ \left(1 - \lim_{p \to 0^+} \frac{M_i(s_i, p)}{M_i(\eta, p)}\right) (\pi_i(s_i) - \lambda_1 \chi_i(s_i, p)) \\
+ \ell_{11} (\lambda_{11} e^{-\mu \tau_1} \chi_i(s_i(t - \tau_{11}), p(t - \tau_{11})) - (\alpha_i + \beta_i) \psi_1(w_i)) \\
+ \ell_{21} (\lambda_{21} e^{-\mu \tau_2} \chi_i(s_i(t - \tau_{21}), p(t - \tau_{21})) + \alpha \psi_1(w_i) - \eta \psi_2(y_i)) \\
+ \ell_{31} (\lambda_{31} e^{-\mu \tau_3} \chi_i(s_i(t - \tau_{31}), p(t - \tau_{31})) - \psi_3(u_i)) \\
+ \ell_{41} (\lambda_{41} e^{-\mu \tau_4} (\psi_2(y_i) - \psi_3(u_i(t - \tau_4))) \\
+ \ell_{51} \psi_i e^{-\mu \tau_5} (\psi_3(u_i(t - \tau_5))) \\
+ \ell_{61} \psi_1 e^{-\mu \tau_4} (\psi_2(y_i(t - \tau_4))) + M_1 \psi_1 e^{-\mu \tau_5} (\psi_3(u_i(t - \tau_5))) \\
- \ell_{61} \psi_4(p) - \ell_{61} \mu \psi_4(p) \psi_4(x) + \ell_{62} \tau \psi_4(p) \psi_4(x) - \omega \psi_4(x) \right]
$$

(2.2)
Collecting terms of Eq. (2.2) and using \( \tau(s_i^0) = 0 \), we obtain
\[
\frac{dV_o}{dt} = \sum_{i=1}^{2} \rho_i \left( \tau_i(s_i) - \tau_i(s_i^0) \right) \left( 1 - \lim_{p \to 0^+} \frac{\chi_i(s_i^0, p)}{\chi_i(s_i, p)} \right) \\
+ \sum_{i=1}^{2} \rho_i \lambda_i \left( \lim_{p \to 0^+} \frac{\chi_i(s_i^0, p)}{\chi_i(s_i, p)} - \ell_{61} g \psi_{41}(p) - \ell_{62} \omega \psi_{42}(x) \right) \\
\leq \sum_{i=1}^{2} \rho_i \left( \tau_i(s_i) - \tau_i(s_i^0) \right) \left( 1 - \lim_{p \to 0^+} \frac{\chi_i(s_i^0, p)}{\chi_i(s_i, p)} \right) \\
+ \left( \sum_{i=1}^{2} \rho_i \lambda_i \lim_{p \to 0^+} \frac{\chi_i(s_i^0, p)}{\psi_{41}(p)} \right) \left( \lim_{p \to 0^+} \frac{\chi_i(s_i^0, p)}{\chi_i(s_i, p)} - \ell_{61} g \right) \psi_{41}(p) - \ell_{62} \omega \psi_{42}(x) \\
= \sum_{i=1}^{2} \rho_i \left( \tau_i(s_i) - \tau_i(s_i^0) \right) \left( 1 - \frac{\partial \chi_i(s_i^0, 0)}{\partial p} \right) \\
+ \ell_{61} g \left( \sum_{i=1}^{2} \rho_i \lambda_i \left( \frac{\partial \chi_i}{\partial p} (0) - 1 \right) \psi_{41}(p) - \ell_{62} \omega \psi_{42}(x) \right) \\
= \sum_{i=1}^{2} \rho_i \left( \tau_i(s_i) - \tau_i(s_i^0) \right) \left( 1 - \frac{\partial \chi_i(s_i^0, 0)}{\partial p} \right) + \ell_{61} g (R_0 - 1) \psi_{41}(p) - \ell_{62} \omega \psi_{42}(x).
\]
By H1 and H2, we obtain
\[
(\tau_i(s_i) - \tau_i(s_i^0)) \left( 1 - \frac{\partial \chi_i(s_i^0, 0)}{\partial p} \right) \leq 0.
\]
Therefore, if \( R_0 \leq 1 \), then \( \frac{dV_o}{dt} \leq 0 \) for \( s_i, p, x \in (0, \infty) \). Clearly, \( \frac{dV_o}{dt} = 0 \) at \( \Pi_0 \). Applying LIP, we get that \( \Pi_0 \) is GAS.

**Lemma 2.2.** If \( R_0 > 1 \) and hypotheses H1-H4 are valid, then
\[
\text{sgn}(R_1 - 1) = \text{sgn}(\bar{p} - \bar{p}) = \text{sgn}(\bar{s}_i - \bar{s}_i).
\]

**Proof.** Using hypotheses H1 and H2, for \( \bar{s}_i, \bar{s}_i, \bar{p}, \bar{p} > 0 \), we get
\[
(\bar{s}_i - \bar{s}_i)(\tau_i(\bar{s}_i) - \tau_i(\bar{s}_i)) > 0, \\
(\bar{s}_i - \bar{s}_i)(\chi_i(\bar{s}_i, \bar{p}) - \chi_i(\bar{s}_i, \bar{p})) > 0, \\
(\bar{p} - \bar{p})(\chi_i(\bar{s}_i, \bar{p}) - \chi_i(\bar{s}_i, \bar{p})) > 0,
\]
and from hypothesis H4, we obtain
\[
(\bar{p} - \bar{p}) (\frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})} - \frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})}) > 0.
\]
First, we show that \( \text{sgn}(\bar{p} - \bar{p}) = \text{sgn}(\bar{s}_i - \bar{s}_i) \). Suppose that \( \text{sgn}(\bar{p} - \bar{p}) = \text{sgn}(\bar{s}_i - \bar{s}_i) \). Using the steady state conditions of H1 and H2, we obtain
\[
\tau_i(\bar{s}_i) - \tau_i(\bar{s}_i) = \lambda_i [\chi_i(\bar{s}_i, \bar{p}) - \chi_i(\bar{s}_i, \bar{p})] = \lambda_i [(\chi_i(\bar{s}_i, \bar{p}) - \chi_i(\bar{s}_i, \bar{p})) + (\chi_i(\bar{s}_i, \bar{p}) - \chi_i(\bar{s}_i, \bar{p}))].
\]
Therefore, from the inequalities (2.3)-(2.5) we obtain \( \text{sgn}(\bar{s}_i - \bar{s}_i) = \text{sgn}(\bar{s}_i - \bar{s}_i) \), which is a contradiction; hence, \( \text{sgn}(\bar{p} - \bar{p}) = \text{sgn}(\bar{s}_i - \bar{s}_i) \). Using Eqs. (1.14) and the definition of \( R_1 \), we get
\[
R_1 - 1 = \sum_{i=1}^{2} \rho_i \left( \frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})} - \frac{\chi_i(\bar{s}_i, \bar{p})}{\psi_{41}(\bar{p})} \right) = \sum_{i=1}^{2} \rho_i \left[ \frac{1}{\psi_{41}(\bar{p})} (\chi_i(\bar{s}_i, \bar{p}) - \chi_i(\bar{s}_i, \bar{p})) + \chi_i(\bar{s}_i, \bar{p}) - \chi_i(\bar{s}_i, \bar{p}) \right].
\]
Thus, from inequalities (2.4) and (2.6) we obtain \( \text{sgn}(R_1 - 1) = \text{sgn}(\bar{p} - \bar{p}). \)

**Theorem 2.3.** Suppose that hypotheses H1-H4 are valid, \( \Pi_1 \) exists, and \( R_1 \leq 1 \), then \( \Pi_1 \) is GAS.
Proof. Let $V_i (s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x)$ as

$$V_i = \sum_{i=1}^{2} p_i \left[ s_i - s_i - \int_{s_i}^{s_i} \frac{\chi_i(s_i, \tilde{p})}{\chi_i(s_i, p)} d\eta + \ell_{t_3} \left( w_i - \tilde{w}_i - \int_{\tilde{w}_i}^{w_i} \frac{\psi_{31}(\tilde{w}_i)}{\psi_{31}(\eta)} d\eta \right) \right]$$

$$+ \ell_{t_2} \left( y_i - \tilde{y}_i - \int_{\tilde{y}_i}^{y_i} \frac{\psi_{21}(\tilde{y}_i)}{\psi_{21}(\eta)} d\eta \right) + \ell_{t_1} \left( u_i - \tilde{u}_i - \int_{\tilde{u}_i}^{u_i} \frac{\psi_{31}(\tilde{u}_i)}{\psi_{31}(\eta)} d\eta \right)$$

$$+ \ell_{t_1} \lambda_{t_1} \chi_i(s_i, \tilde{p}) e^{-\mu_{t_1} \tau_{t_1}} \frac{\chi_i(s_i (t - \theta), p (t - \theta))}{\chi_i(s_i, p)} d\theta$$

$$+ \ell_{t_2} \lambda_{t_2} \chi_i(s_i, \tilde{p}) e^{-\mu_{t_2} \tau_{t_2}} \frac{\chi_i(s_i (t - \theta), p (t - \theta))}{\chi_i(s_i, p)} d\theta$$

$$+ \ell_{t_3} \lambda_{t_3} \chi_i(s_i, \tilde{p}) e^{-\mu_{t_3} \tau_{t_3}} \frac{\chi_i(s_i (t - \theta), p (t - \theta))}{\chi_i(s_i, p)} d\theta$$

$$+ \ell_{t_4} \eta_i \psi_{21}(\tilde{y}_i) e^{-\mu_{t_4} \tau_{t_4}} \frac{\psi_{21}(y_i (t - \theta))}{\psi_{21}(\tilde{y}_i)} d\theta$$

$$+ \ell_{t_5} \gamma_i \psi_{21}(\tilde{u}_i) e^{-\mu_{t_5} \tau_{t_5}} \frac{\psi_{31}(u_i (t - \theta))}{\psi_{31}(\tilde{u}_i)} d\theta + \ell_{t_6} \left( p - \tilde{p} - \int_{\tilde{p}}^{p} \frac{\psi_{41}(\tilde{p})}{\psi_{41}(\eta)} d\eta \right) + \ell_{t_2} x.$$
Collecting terms of Eq. (2.7) and applying \( \pi_i(\tilde{s}_i) = \lambda_i \chi_i(\tilde{s}_i, \tilde{p}) \) we get

\[
\frac{dV_i}{dt} = \sum_{i=1}^{2} \rho_i \left[ \pi_i(s_i) - \pi_i(\tilde{s}_i) \left( 1 - \frac{X_i(s_i, p)}{X_i(s_i, \tilde{p})} \right) + \lambda_i \chi_i(\tilde{s}_i, \tilde{p}) \left( 1 - \frac{X_i(s_i, \tilde{p})}{X_i(s_i, p)} \right) \right]
\]

From the conditions of the steady state \( \Pi_1: \)

\[
(\alpha_i + \beta_i)\psi_{1i}(\tilde{w}_i) = \lambda_i e^{-\mu_i \tau_i} \chi_i(\tilde{s}_i, \tilde{p}), \quad \psi_{2i}(\tilde{g}_i) = (\ell_1 \lambda_1 e^{-\mu_i \tau_i} + \ell_2 \lambda_2 e^{-\mu_2 \tau_2}) \chi_i(\tilde{s}_i, \tilde{p}),
\]

\[
\nu_i \psi_{3i}(\tilde{u}_i) = \lambda_i e^{-\mu_i \tau_3} \chi_i(\tilde{s}_i, \tilde{p}), \quad \ell_6 g \psi_{4i}(\tilde{p}) = \sum_{i=1}^{2} \rho_i \lambda_i \chi_i(\tilde{s}_i, \tilde{p}),
\]

we get

\[
\frac{dV_i}{dt} = \sum_{i=1}^{2} \rho_i \left[ \pi_i(s_i) - \pi_i(\tilde{s}_i) \left( 1 - \frac{X_i(s_i, p)}{X_i(s_i, \tilde{p})} \right) + \lambda_i \chi_i(\tilde{s}_i, \tilde{p}) \left( 1 - \frac{X_i(s_i, \tilde{p})}{X_i(s_i, p)} \right) \right]
\]
\[ + \ell_3 \lambda_3 e^{-\mu_3 \tau_1 \chi_1(s_1, \bar{p})} - \ell_3 \lambda_3 X_1(s_1, \bar{p}) e^{-\mu_3 \tau_3 \chi_1(s_1(t-\tau_3), p(t-\tau_3))} \psi_{31}(\bar{u}_1) / \chi_1(s_1, \bar{p}) \psi_{31}(u_1) \]

\[ + \ell_1 \lambda_1 X_1(s_1, \bar{p}) e^{-\mu_1 \tau_1 \chi_1(s_1, \bar{p})} \left( \chi_1(s_1(t-\tau_1), p(t-\tau_1)) / \chi_1(s_1, \bar{p}) \right) \]

\[ + \ell_2 \lambda_2 X_1(s_1, \bar{p}) e^{-\mu_2 \tau_2 \chi_1(s_1, \bar{p})} \left( \chi_1(s_1(t-\tau_2), p(t-\tau_2)) / \chi_1(s_1, \bar{p}) \right) \]

\[ + \ell_3 \lambda_3 X_1(s_1, \bar{p}) e^{-\mu_3 \tau_3 \chi_1(s_1, \bar{p})} \left( \chi_1(s_1(t-\tau_3), p(t-\tau_3)) / \chi_1(s_1, \bar{p}) \right) \]

\[ + (\ell_1 \lambda_1 e^{-\mu_1 \tau_1 \chi_1(s_1, \bar{p})} + \ell_2 \lambda_2 e^{-\mu_2 \tau_2 \chi_1(s_1, \bar{p})}) \chi_1(s_1, \bar{p}) \psi_{31}(u_1(t-\tau_5)) / \psi_{31}(u_1) \]

\[ + \ell_3 \lambda_3 e^{-\mu_3 \tau_3 \chi_1(s_1, \bar{p})} \psi_{31}(u_1(t-\tau_5)) / \psi_{31}(u_1) \] \[ + \sum_{i=1}^{2} \rho_i \lambda_i X_1(s_i, \bar{p}) \]

\[ - \sum_{i=1}^{2} \rho_i (\ell_1 \lambda_1 e^{-\mu_1 \tau_1 \chi_1(s_i, \bar{p})} + \ell_2 \lambda_2 e^{-\mu_2 \tau_2 \chi_1(s_i, \bar{p})}) \chi_1(s_i, \bar{p}) \psi_{31}(u_i(t-\tau_5)) / \psi_{31}(u_i) \psi_{41}(p) / \psi_{21}(y_1) \psi_{41}(p) \]

\[ - r \ell_2 \left( \psi_{41}(p) - \frac{w}{r} \right) \psi_{42}(x). \]

Using the equalities (1.15) with \( s_i = s_i, \nu_1 = \nu_1, y_i = y_i, u_i = u_i \) and \( \bar{p} = \bar{p} \), we can obtain

\[
\frac{dV_i}{dt} = \sum_{i=1}^{2} \rho_i \left[ (\pi_i(s_i) - \pi_i(s_i)) \left( 1 - \frac{\chi_i(s_i, \bar{p})}{\chi_i(s_i, \bar{p})} \right) \right] ^{2}
\]

\[ + \lambda_1 X_1(s, \bar{p}) \left( \frac{\chi_1(s, \bar{p})}{\chi_1(s, \bar{p})} - \frac{\psi_{41}(p)}{\psi_{41}(p)} - 1 \right) \psi_{41}(p) \chi_1(s, \bar{p}) \]

\[ - \lambda_2 X_1(s, \bar{p}) \left( \frac{\psi_{41}(p)}{\psi_{41}(p)} \chi_1(s, \bar{p}) - 1 - \ln \left( \frac{\chi_1(s, \bar{p})}{\chi_1(s, \bar{p})} \right) \right) \]

\[ - \lambda_3 X_1(s, \bar{p}) \left( \frac{\psi_{41}(p)}{\psi_{41}(p)} \chi_1(s, \bar{p}) - 1 - \ln \left( \frac{\chi_1(s, \bar{p})}{\chi_1(s, \bar{p})} \right) \right) \]

\[ - \ell_1 \lambda_1 e^{-\mu_1 \tau_1 \chi_1(s_i, \bar{p})} \left( \psi_{31}(u_i(t-\tau_5)) \chi_1(s_i(t-\tau_5), p(t-\tau_5)) / \psi_{31}(u_i) \chi_1(s_i, \bar{p}) \right) \]

\[ - 1 - \ln \left( \frac{\psi_{31}(w_i) \chi_1(s_i(t-\tau_5), p(t-\tau_5)) / \psi_{31}(u_i) \chi_1(s_i, \bar{p})}{\psi_{31}(w_i) \chi_1(s_i, \bar{p})} \right) \]

\[ - \ell_2 \lambda_2 e^{-\mu_2 \tau_2 \chi_1(s_i, \bar{p})} \left( \psi_{21}(y_i) \chi_1(s_i(t-\tau_5), p(t-\tau_5)) / \psi_{21}(y_i) \chi_1(s_i, \bar{p}) \right) \]

\[ - 1 - \ln \left( \frac{\psi_{21}(y_i) \chi_1(s_i(t-\tau_5), p(t-\tau_5)) / \psi_{21}(y_i) \chi_1(s_i, \bar{p})}{\psi_{21}(y_i) \chi_1(s_i, \bar{p})} \right) \]

\[ - \ell_3 \lambda_3 e^{-\mu_3 \tau_3 \chi_1(s_i, \bar{p})} \left( \psi_{31}(u_i(t-\tau_5)) \chi_1(s_i(t-\tau_5), p(t-\tau_5)) / \psi_{31}(u_i) \chi_1(s_i, \bar{p}) \right) \]

\[ - 1 - \ln \left( \frac{\psi_{31}(u_i(t-\tau_5)) \chi_1(s_i(t-\tau_5), p(t-\tau_5)) / \psi_{31}(u_i) \chi_1(s_i, \bar{p})}{\psi_{31}(u_i) \chi_1(s_i, \bar{p})} \right) \]

\[ - \ell_1 \lambda_1 e^{-\mu_1 \tau_1 \chi_1(s_i, \bar{p})} \left( \psi_{31}(u_i) \chi_1(s_i(t-\tau_3), p(t-\tau_3)) / \psi_{31}(u_i) \chi_1(s_i, \bar{p}) \right) \]

\[ - 1 - \ln \left( \frac{\psi_{31}(u_i) \chi_1(s_i(t-\tau_3), p(t-\tau_3)) / \psi_{31}(u_i) \chi_1(s_i, \bar{p})}{\psi_{31}(u_i) \chi_1(s_i, \bar{p})} \right) \]

\[ - (\ell_1 \lambda_1 e^{-\mu_1 \tau_1 \chi_1(s_i, \bar{p})} + \ell_2 \lambda_2 e^{-\mu_2 \tau_2 \chi_1(s_i, \bar{p})}) \chi_1(s_i, \bar{p}) \left( \psi_{21}(y_i(t-\tau_5)) / \psi_{21}(y_i) \psi_{41}(p) \right) \]

\[ - 1 - \ln \left( \frac{\psi_{21}(y_i(t-\tau_5)) / \psi_{21}(y_i) \psi_{41}(p)}{\psi_{21}(y_i) \psi_{41}(p)} \right) \]

\[ - \ell_3 \lambda_3 e^{-\mu_3 \tau_3 \chi_1(s_i, \bar{p})} \left( \psi_{31}(u_i(t-\tau_5)) \psi_{41}(p) / \psi_{31}(u_i) \psi_{41}(p) \right) - 1 \]

\[ - 1 - \ln \left( \frac{\psi_{31}(u_i(t-\tau_5)) \psi_{41}(p) / \psi_{31}(u_i) \psi_{41}(p)}{\psi_{31}(u_i) \psi_{41}(p)} \right) \]

\[ + r \ell_2 \left( \psi_{41}(p) - \psi_{41}(p) \right) \psi_{42}(x). \]
Eq. (2.8) becomes:

\[
\frac{dV_1}{dt} = \sum_{i=1}^{2} \rho_i \left[ (\pi_i(s_i) - \pi_i(\tilde{s}_i)) \left( 1 - \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \right) + \lambda_i \chi_i(s_i, p) \left( \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} - \psi_{41}(\tilde{p}) \right) \left( 1 - \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \right) \right]
\]

\[
- \lambda_i \chi_i(s_i, p) \left( \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} + F \left( \frac{\psi_{41}(p)}{\psi_{41}(\tilde{p})} \chi_i(s_i, p) \right) \right) - \ell_{11} \lambda_i e^{-\mu_{11}} \chi_i(s_i, p) F \left( \frac{\psi_{21}(\tilde{y}_i)}{\psi_{21}(y_i)} \psi_{11}(\tilde{w}_i) \right)
\]

\[
- \ell_{11} \chi_i(s_i, p) e^{-\mu_{11}} F \left( \psi_{11}(\tilde{w}_i) \chi_i(s_i, p) \right) \psi_{11}(\tilde{w}_i) \chi_i(s_i, p) \psi_{11}(\tilde{w}_i)
\]

H1, H2, H4, Remark 1.1, Lemma 2.2, and the condition R1 \( \leq 1 \) imply that

\[
(\pi_i(s_i) - \pi_i(\tilde{s}_i)) \left( 1 - \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \right) \leq 0, \quad \left( \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} - \psi_{41}(\tilde{p}) \right) \left( 1 - \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \right) \leq 0, \quad \psi_{41}(\tilde{p}) - \psi_{41}(\tilde{p}) \leq 0.
\]

It follows that, for all \( s_i, y_i, p, x > 0 \), we have \( \frac{dV_i}{dt} \leq 0 \) and \( \frac{dV_i}{dt} = 0 \) at \( \Pi_1 \). By LIP, \( \Pi_1 \) is GAS.

**Theorem 2.4.** If \( R_1 > 1 \) and hypotheses H1–H4 are valid, then \( \Pi_2 \) is GAS.

**Proof.** Define \( V_2(s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x) \) as

\[
V_2 = \sum_{i=1}^{2} \rho_i \left[ s_i - \tilde{s}_i - \int_{s_i}^{\tilde{s}_i} \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \, d\eta + \ell_{11} \left( w_i - \tilde{w}_i - \int_{\tilde{w}_i}^{w_i} \psi_{11}(\tilde{w}_i) \psi_{11}(\eta) \, d\eta \right) \right]
\]

\[
+ \ell_{11} \lambda_{11} \chi_i(s_i, p) \int_{0}^{\tau_{11}} e^{-\mu_{11} \theta} \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \, d\theta
\]

\[
+ \ell_{21} \lambda_{21} \chi_i(s_i, p) \int_{0}^{\tau_{21}} e^{-\mu_{21} \theta} \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \, d\theta
\]

\[
+ \ell_{31} \lambda_{31} \chi_i(s_i, p) \int_{0}^{\tau_{31}} e^{-\mu_{31} \theta} \frac{\chi_i(s_i, p)}{\chi_i(\tilde{s}_i, p)} \, d\theta
\]

\[
+ \ell_{41} \lambda_{41} \psi_{21}(\tilde{y}_i) \int_{0}^{\tau_{41}} e^{-\mu_{41} \theta} \frac{\psi_{21}(y_i)}{\psi_{21}(\tilde{y}_i)} \, d\theta + \ell_{51} \lambda_{51} \psi_{31}(\tilde{u}_i) \int_{0}^{\tau_{51}} e^{-\mu_{51} \theta} \frac{\psi_{31}(u_i)}{\psi_{31}(\tilde{u}_i)} \, d\theta
\]

\[
+ \ell_{61} \left( p - \tilde{p} - \frac{\psi_{41}(\tilde{p})}{\psi_{41}(\tilde{p})} \, d\eta \right) + \ell_{62} \left( x - \tilde{x} - \int_{\tilde{x}}^{x} \frac{\psi_{42}(\tilde{x})}{\psi_{42}(\tilde{x})} \, d\eta \right).
\]
Note that, $V_2(s_1, s_2, w_1, w_2, y_2, y_2, u_2, p, x > 0$ for all $s_1, s_2, w_1, w_2, y_1, y_2, p, x > 0$ and $V_2(\bar{s}_1, \bar{s}_2, \bar{w}_1, \bar{w}_2, \bar{y}_1, \bar{y}_2, \bar{u}_1, \bar{u}_2, \bar{p}, \bar{x}) = 0$. Calculating $\frac{dV_2}{dt}$ along the solutions of model (1.3), we get

$$
\frac{dV_2}{dt} = \sum_{i=1}^{2} p_i \left[ \left( 1 - \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, \bar{p})} \right) \left( \tau_i(s_i) - \lambda_i(s_i, p) \right) \right]
$$

$$
+ \ell_1 \left( 1 - \frac{\psi_1(\bar{w}_1)}{\psi_1(w_1)} \right) \left( \lambda_1 e^{-\mu_{1}^{s_1} s_1(t - \tau_{11}), p \left( t - \tau_{11} \right)} \right) - \left( \alpha_i + \beta_i \right) \psi_1(w_1)
$$

$$
+ \ell_2 \left( 1 - \frac{\psi_2(\bar{y}_1)}{\psi_2(y_1)} \right) \left( \lambda_2 e^{-\mu_{21}^{s_2} s_2(t - \tau_{21}), p \left( t - \tau_{21} \right)} + \alpha_2 \psi_2(w_1) + \eta_1 \psi_2(y_1) \right)
$$

$$
+ \ell_3 \left( 1 - \frac{\psi_3(\bar{u}_1)}{\psi_3(u_1)} \right) \left( \lambda_3 e^{-\mu_{31}^{s_3} s_3(t - \tau_{31}), p \left( t - \tau_{31} \right)} - \gamma_1 \psi_3(u_1) \right)
$$

$$
+ \ell_1 \lambda_1 e^{-\mu_{11}^{s_1} s_1(t - \tau_{11}), p \left( t - \tau_{11} \right)} \left( \chi_i(s_i, p) - \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \chi_i(\bar{s}_i, \bar{p}) \ell_1 \lambda_1 e^{-\mu_{11}^{s_1} s_1(t - \tau_{11}), p \left( t - \tau_{11} \right)} \left( \chi_i(s_i, p) \right)
$$

$$
+ \ell_2 \lambda_2 e^{-\mu_{21}^{s_2} s_2(t - \tau_{21}), p \left( t - \tau_{21} \right)} \left( \chi_i(s_i, p) - \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \chi_i(\bar{s}_i, \bar{p}) \ell_2 \lambda_2 e^{-\mu_{21}^{s_2} s_2(t - \tau_{21}), p \left( t - \tau_{21} \right)} \left( \chi_i(s_i, p) \right)
$$

$$
+ \ell_3 \lambda_3 e^{-\mu_{31}^{s_3} s_3(t - \tau_{31}), p \left( t - \tau_{31} \right)} \left( \chi_i(s_i, p) - \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \chi_i(\bar{s}_i, \bar{p}) \ell_3 \lambda_3 e^{-\mu_{31}^{s_3} s_3(t - \tau_{31}), p \left( t - \tau_{31} \right)} \left( \chi_i(s_i, p) \right)
$$

$$
\text{(2.9)}
$$

Collecting terms of Eq. (2.9) and applying $\tau_1(s_i) = \lambda_1 \chi_i(s_i, \bar{p})$, we get

$$
\frac{dV_2}{dt} = \sum_{i=1}^{2} p_i \left[ \left( 1 - \frac{\chi_i(\bar{s}_i, \bar{p})}{\chi_i(s_i, \bar{p})} \right) \left( \tau_i(s_i) - \lambda_i(s_i, p) \right) \right]
$$

$$
- \ell_1 \lambda_1 e^{-\mu_{11}^{s_1} s_1(t - \tau_{11}), p \left( t - \tau_{11} \right)} \left( \chi_i(s_i, \bar{p}) \right) \left( \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \chi_i(\bar{s}_i, \bar{p}) \ell_1 \lambda_1 e^{-\mu_{11}^{s_1} s_1(t - \tau_{11}), p \left( t - \tau_{11} \right)} \left( \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \ell_2 \lambda_2 e^{-\mu_{21}^{s_2} s_2(t - \tau_{21}), p \left( t - \tau_{21} \right)} \left( \chi_i(s_i, \bar{p}) \right) \left( \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \chi_i(\bar{s}_i, \bar{p}) \ell_2 \lambda_2 e^{-\mu_{21}^{s_2} s_2(t - \tau_{21}), p \left( t - \tau_{21} \right)} \left( \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \ell_3 \lambda_3 e^{-\mu_{31}^{s_3} s_3(t - \tau_{31}), p \left( t - \tau_{31} \right)} \left( \chi_i(s_i, \bar{p}) \right) \left( \chi_i(s_i, \bar{p}) \right)
$$

$$
- \alpha \ell_2 \left( \psi_{11}(w_1) \psi_{21}(y_1) \psi_{31}(u_1) \right) \left( \chi_i(s_i, \bar{p}) \right) \left( \chi_i(s_i, \bar{p}) \right)
$$

$$
- \ell_3 \lambda_3 e^{-\mu_{31}^{s_3} s_3(t - \tau_{31}), p \left( t - \tau_{31} \right)} \left( \chi_i(s_i, \bar{p}) \right) \left( \chi_i(s_i, \bar{p}) \right)
$$

$$
+ \ell_2 \lambda_2 \chi_i(\bar{s}_i, \bar{p}) e^{-\mu_{21}^{s_2} s_2(t - \tau_{21}), p \left( t - \tau_{21} \right)} \left( \chi_i(s_i, \bar{p}) \right) \left( \chi_i(s_i, \bar{p}) \right)
$$

\[
\begin{align*}
&+ \ell_{3i} \lambda_{3i} \chi_{i}(\bar{s}_{i}, \bar{p}) e^{-\mu_{3i} \tau_{3i}} \ln \left( \frac{\chi_{i}(s_{i}(t - \tau_{3i}), p(t - \tau_{3i}))}{\chi_{i}(s_{i}, p)} \right) \\
&+ \ell_{4i} \eta_{i} \psi_{2i}(\bar{y}_{i}) e^{-\mu_{4i} \tau_{4i}} \ln \left( \frac{\psi_{2i}(y_{i}(t - \tau_{4i}))}{\psi_{2i}(y_{i})} \right) \\
&+ \ell_{5i} \nu_{i} \psi_{3i}(\bar{u}_{i}) e^{-\mu_{5i} \tau_{5i}} \ln \left( \frac{\psi_{3i}(u_{i}(t - \tau_{5i}))}{\psi_{3i}(u_{i})} \right) = -\ell_{6i} g\psi_{4i}(p) \\
&+ \ell_{6i} g\psi_{4i}(p) - \ell_{6i} \sum_{i=1}^{2} N_{ii} e^{-\mu_{4i} \tau_{4i}} \psi_{2i}(y_{i}(t - \tau_{4i})) \psi_{4i}(p) \\
&- \ell_{6i} \omega_{i} \psi_{4i}(x) + \ell_{6i} \omega_{i} \psi_{4i}(x) - \tau_{l}\ell_{6i} \psi_{4i}(p) \psi_{42}(\bar{x}).
\end{align*}
\]

Using the state conditions for $\Pi_{2}$:

\[
\begin{align*}
\alpha_{i} + \beta_{i} \psi_{1i} (\bar{w}_{i}) &= \lambda_{1i} e^{-\mu_{1i} \tau_{1i}} \chi_{i}(\bar{s}_{i}, \bar{p}), \\
\ell_{2i} \eta_{i} \psi_{2i}(\bar{y}_{i}) &= (\ell_{1i} \lambda_{1i} e^{-\mu_{1i} \tau_{1i}} + \ell_{2i} \lambda_{2i} e^{-\mu_{2i} \tau_{2i}}) \chi_{i}(\bar{s}_{i}, \bar{p}), \\
\nu_{i} \psi_{3i}(\bar{u}_{i}) &= \lambda_{3i} e^{-\mu_{3i} \tau_{3i}} \chi_{i}(\bar{s}_{i}, \bar{p}), \\
\ell_{6i} g\psi_{4i}(p) &= \sum_{i=1}^{2} \rho_{i} \lambda_{i} \chi_{i}(\bar{s}_{i}, \bar{p}) - \mu_{6i} \psi_{4i}(p) \psi_{42}(\bar{x}),
\end{align*}
\]

we obtain

\[
\begin{align*}
\frac{dV_{2}}{dt} &= \sum_{i=1}^{2} \rho_{i} \left[ (\tau_{1i}(s_{i}) - \tau_{1i}(\bar{s}_{i})) \left( 1 - \frac{\chi_{i}(\bar{s}_{i}, \bar{p})}{\chi_{i}(s_{i}, \bar{p})} \right) \\
&+ \lambda_{1i} \chi_{i}(\bar{s}_{i}, \bar{p}) \left( 1 - \frac{\chi_{i}(\bar{s}_{i}, \bar{p})}{\chi_{i}(s_{i}, \bar{p})} \right) + \lambda_{1i} \chi_{i}(\bar{s}_{i}, \bar{p}) \left( \frac{\chi_{i}(s_{i}, \bar{p})}{\chi_{i}(s_{i}, \bar{p})} - \frac{\psi_{4i}(p)}{\psi_{4i}(p)} \right) \right] \\
&+ \ell_{1i} \lambda_{11} e^{-\mu_{1i} \tau_{1i}} \chi_{i}(\bar{s}_{i}, \bar{p}) - \ell_{1i} \lambda_{11} \chi_{i}(\bar{s}_{i}, \bar{p}) e^{-\mu_{1i} \tau_{1i}} \chi_{i}(s_{i}(t - \tau_{1i}), p(t - \tau_{1i})) \psi_{1i}(\bar{y}_{i}) \\
&- \ell_{2i} \lambda_{21} \chi_{i}(\bar{s}_{i}, \bar{p}) e^{-\mu_{2i} \tau_{2i}} \chi_{i}(s_{i}(t - \tau_{2i}), p(t - \tau_{2i})) \psi_{2i}(\bar{y}_{i}) \\
&- \ell_{1i} \lambda_{11} e^{-\mu_{1i} \tau_{1i}} \chi_{i}(\bar{s}_{i}, \bar{p}) \frac{\psi_{2i}(\bar{y}_{i}) \psi_{4i}(\bar{w}_{i})}{\psi_{2i}(y_{i}) \psi_{4i}(\bar{w}_{i})} + (\ell_{1i} \lambda_{11} e^{-\mu_{1i} \tau_{1i}} + \ell_{2i} \lambda_{21} e^{-\mu_{2i} \tau_{2i}}) \chi_{i}(\bar{s}_{i}, \bar{p}) \\
&+ \ell_{3i} \lambda_{31} e^{-\mu_{3i} \tau_{3i}} \chi_{i}(\bar{s}_{i}, \bar{p}) - \ell_{3i} \lambda_{31} \chi_{i}(\bar{s}_{i}, \bar{p}) e^{-\mu_{3i} \tau_{3i}} \chi_{i}(s_{i}(t - \tau_{3i}), p(t - \tau_{3i})) \psi_{3i}(\bar{u}_{i}) \\
&+ \ell_{1i} \lambda_{11} \chi_{i}(\bar{s}_{i}, \bar{p}) e^{-\mu_{1i} \tau_{1i}} \ln \left( \frac{\chi_{i}(s_{i}(t - \tau_{1i}), p(t - \tau_{1i}))}{\chi_{i}(s_{i}, p)} \right) \\
&+ \ell_{2i} \lambda_{21} \chi_{i}(\bar{s}_{i}, \bar{p}) e^{-\mu_{2i} \tau_{2i}} \ln \left( \frac{\chi_{i}(s_{i}(t - \tau_{2i}), p(t - \tau_{2i}))}{\chi_{i}(s_{i}, p)} \right) \\
&+ \ell_{3i} \lambda_{31} \chi_{i}(\bar{s}_{i}, \bar{p}) e^{-\mu_{3i} \tau_{3i}} \ln \left( \frac{\chi_{i}(s_{i}(t - \tau_{3i}), p(t - \tau_{3i}))}{\chi_{i}(s_{i}, p)} \right) \\
&+ (\ell_{1i} \lambda_{11} e^{-\mu_{1i} \tau_{1i}} + \ell_{2i} \lambda_{21} e^{-\mu_{2i} \tau_{2i}}) \chi_{i}(\bar{s}_{i}, \bar{p}) \ln \left( \frac{\psi_{2i}(y_{i}(t - \tau_{4i}))}{\psi_{2i}(y_{i})} \right) \\
&+ \ell_{3i} \lambda_{31} e^{-\mu_{3i} \tau_{3i}} \chi_{i}(\bar{s}_{i}, \bar{p}) \ln \left( \frac{\psi_{3i}(u_{i}(t - \tau_{5i}))}{\psi_{3i}(u_{i})} \right) + \sum_{i=1}^{2} \rho_{i} \lambda_{i} \chi_{i}(\bar{s}_{i}, \bar{p})
\end{align*}
\]
\[-\sum_{i=1}^{2} \rho_i (\ell_1 \lambda_1 e^{-\mu_1 \tau_{1i}} + \ell_2 \lambda_2 e^{-\mu_2 \tau_{2i}})X_i(\bar{s}_i, \bar{\rho}) \frac{\psi_{2i}(y_i (t - \tau_{4i}))\psi_{4i}(\bar{p})}{\psi_{2i}(y_i)\psi_{4i}(p)} \]

\[-\sum_{i=1}^{2} \rho_i \ell_3 \lambda_3 e^{-\mu_3 \tau_{3i}}X_i(\bar{s}_i, \bar{\rho}) \frac{\psi_{3i}(u_i (t - \tau_{5i}))\psi_{4i}(\bar{p})}{\psi_{3i}(u_i)\psi_{4i}(p)}.\]

By the equalities (1.15) with \(\bar{s}_i = s_i, \bar{\lambda}_i = \lambda_i, \bar{\rho}_i = \rho_i, \bar{u}_i = u_i,\) and \(\bar{\rho} = \bar{\rho},\) we can get

\[
\frac{dV_2}{dt} = \sum_{i=1}^{2} \rho_i \left[ \left( \tau_i(s_i, \rho) - \tau_i(\bar{s}_i, \bar{\rho}) \right) \left( 1 - \frac{X_i(s_i, \rho)}{X_i(s_i, \bar{\rho})} \right) \right]
\]

\[
+ \lambda_i X_i(\bar{s}_i, \bar{\rho}) \left( \frac{X_i(s_i, \rho)}{X_i(\bar{s}_i, \bar{\rho})} - \psi_{4i}(p) \frac{\psi_{4i}(\bar{p})}{\psi_{4i}(p)} - 1 + \psi_{4i}(p) X_i(s_i, \rho) \right)
\]

\[
- \lambda_i X_i(s_i, \rho) \left( X_i(s_i, \rho) - 1 - \ln \left( X_i(s_i, \rho) \right) \right)
\]

\[
- \lambda_i X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{4i}(p) X_i(s_i, \rho) - 1 - \ln \left( \psi_{4i}(p) X_i(s_i, \rho) \right) \right)
\]

\[
- \ell_1 \lambda_1 X_i(\bar{s}_i, \bar{\rho}) e^{-\mu_1 \tau_{1i}} \left( \psi_{1i}(w_i) X_i(s_i (t - \tau_{1i}), p (t - \tau_{1i})) \psi_{1i}(w_i) X_i(s_i, \rho) \right)
\]

\[
- 1 - \ln \left( \psi_{1i}(w_i) X_i(s_i (t - \tau_{1i}), p (t - \tau_{1i})) \psi_{1i}(w_i) X_i(s_i, \rho) \right)
\]

\[
- \ell_2 \lambda_2 X_i(\bar{s}_i, \bar{\rho}) e^{-\mu_2 \tau_{2i}} \left( \psi_{2i}(y_i) X_i(s_i (t - \tau_{2i}), p (t - \tau_{2i})) \psi_{2i}(y_i) X_i(s_i, \rho) \right)
\]

\[
- 1 - \ln \left( \psi_{2i}(y_i) X_i(s_i (t - \tau_{2i}), p (t - \tau_{2i})) \psi_{2i}(y_i) X_i(s_i, \rho) \right)
\]

\[
- \ell_3 \lambda_3 X_i(\bar{s}_i, \bar{\rho}) e^{-\mu_3 \tau_{3i}} \left( \psi_{3i}(u_i) X_i(s_i (t - \tau_{3i}), p (t - \tau_{3i})) \psi_{3i}(u_i) X_i(s_i, \rho) \right)
\]

\[
- 1 - \ln \left( \psi_{3i}(u_i) X_i(s_i (t - \tau_{3i}), p (t - \tau_{3i})) \psi_{3i}(u_i) X_i(s_i, \rho) \right)
\]

\[
- \ell_1 \lambda_1 e^{-\mu_1 \tau_{1i}} X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{1i}(w_i) \psi_{1i}(w_i) - 1 - \ln \left( \psi_{1i}(w_i) \psi_{1i}(w_i) \right) \right)
\]

\[
- \left( \ell_1 \lambda_1 e^{-\mu_1 \tau_{1i}} + \ell_2 \lambda_2 e^{-\mu_2 \tau_{2i}} \right) X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{2i}(y_i) (t - \tau_{4i}) \psi_{4i}(p) \psi_{2i}(y_i) \psi_{4i}(p) \right)
\]

\[
- 1 - \ln \left( \psi_{2i}(y_i) (t - \tau_{4i}) \psi_{4i}(p) \psi_{2i}(y_i) \psi_{4i}(p) \right)
\]

\[
- \ell_3 \lambda_3 e^{-\mu_3 \tau_{3i}} X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{3i}(u_i) (t - \tau_{5i}) \psi_{4i}(p) \psi_{3i}(u_i) \psi_{4i}(p) \right)
\]

\[
- 1 - \ln \left( \psi_{3i}(u_i) (t - \tau_{5i}) \psi_{4i}(p) \psi_{3i}(u_i) \psi_{4i}(p) \right)
\]

Eq. (2.10) becomes

\[
\frac{dV_2}{dt} = \sum_{i=1}^{2} \rho_i \left[ \left( \tau_i(s_i, \rho) - \tau_i(\bar{s}_i, \bar{\rho}) \right) \left( 1 - \frac{X_i(s_i, \rho)}{X_i(s_i, \bar{\rho})} \right) \right]
\]

\[
+ \lambda_i X_i(\bar{s}_i, \bar{\rho}) \left( \frac{X_i(s_i, \rho)}{X_i(\bar{s}_i, \bar{\rho})} - \psi_{4i}(p) \frac{\psi_{4i}(\bar{p})}{\psi_{4i}(p)} - 1 + \psi_{4i}(p) X_i(s_i, \rho) \right)
\]

\[
- \lambda_i X_i(s_i, \rho) \left( X_i(s_i, \rho) - 1 - \ln \left( X_i(s_i, \rho) \right) \right)
\]

\[
- \lambda_i X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{4i}(p) X_i(s_i, \rho) - 1 - \ln \left( \psi_{4i}(p) X_i(s_i, \rho) \right) \right)
\]

\[
- \ell_1 \lambda_1 e^{-\mu_1 \tau_{1i}} X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{1i}(w_i) X_i(s_i (t - \tau_{1i}), p (t - \tau_{1i})) \psi_{1i}(w_i) X_i(s_i, \rho) \right)
\]

\[
- \left( \ell_1 \lambda_1 e^{-\mu_1 \tau_{1i}} + \ell_2 \lambda_2 e^{-\mu_2 \tau_{2i}} \right) X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{2i}(y_i) (t - \tau_{4i}) \psi_{4i}(p) \psi_{2i}(y_i) \psi_{4i}(p) \right)
\]

\[
- 1 - \ln \left( \psi_{2i}(y_i) (t - \tau_{4i}) \psi_{4i}(p) \psi_{2i}(y_i) \psi_{4i}(p) \right)
\]

\[
- \ell_3 \lambda_3 e^{-\mu_3 \tau_{3i}} X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{3i}(u_i) (t - \tau_{5i}) \psi_{4i}(p) \psi_{3i}(u_i) \psi_{4i}(p) \right)
\]

\[
- 1 - \ln \left( \psi_{3i}(u_i) (t - \tau_{5i}) \psi_{4i}(p) \psi_{3i}(u_i) \psi_{4i}(p) \right)
\]

\[
- \ell_1 \lambda_1 e^{-\mu_1 \tau_{1i}} X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{1i}(w_i) \psi_{1i}(w_i) - 1 - \ln \left( \psi_{1i}(w_i) \psi_{1i}(w_i) \right) \right)
\]

\[
- \left( \ell_1 \lambda_1 e^{-\mu_1 \tau_{1i}} + \ell_2 \lambda_2 e^{-\mu_2 \tau_{2i}} \right) X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{2i}(y_i) (t - \tau_{4i}) \psi_{4i}(p) \psi_{2i}(y_i) \psi_{4i}(p) \right)
\]

\[
- 1 - \ln \left( \psi_{2i}(y_i) (t - \tau_{4i}) \psi_{4i}(p) \psi_{2i}(y_i) \psi_{4i}(p) \right)
\]

\[
- \ell_3 \lambda_3 e^{-\mu_3 \tau_{3i}} X_i(\bar{s}_i, \bar{\rho}) \left( \psi_{3i}(u_i) (t - \tau_{5i}) \psi_{4i}(p) \psi_{3i}(u_i) \psi_{4i}(p) \right)
\]

\[
- 1 - \ln \left( \psi_{3i}(u_i) (t - \tau_{5i}) \psi_{4i}(p) \psi_{3i}(u_i) \psi_{4i}(p) \right)
\]
First we verify hypotheses H1-H4 for the chosen forms, then we solve the system using MATLAB. Clearly, according to H1, H2, and H4 we get $\frac{dV_1}{dt} \leq 0$ and $\frac{dV_2}{dt} = 0$ at $\Pi_2$. LIP implies that $\Pi_2$ is GAS.

3. Numerical simulations

We now perform some computer simulations on the following application:

\[
\begin{align*}
\dot{s}_1 (t) &= \rho_1 - \delta_1 s_1 (t) + B s_1 (t) \left( 1 - \frac{s_1 (t)}{s_{\text{max}}} \right) - \left( \ell_1 \lambda_1 e^{-\mu_1 t} + \ell_2 \lambda_2 e^{-\mu_2 t} \right) X_1 (s, p) F \left( \frac{\psi_{11} (y_1 (t - \tau_{41})) \psi_{41} (p)}{\psi_{11} (y_1) \psi_{41} (p)} \right), \\
\dot{s}_2 (t) &= \rho_2 - \delta_2 s_2 (t) - \left( 1 - f \ell_1 \right) \lambda_2 s_2 (t) p(t), \\
\dot{w}_1 (t) &= \left( 1 - \varepsilon_1 \lambda_1 e^{-\mu_1 t} s_1 (t - \tau_{11}) p(t - \tau_{11}) \right) - (\alpha_1 + \beta_1) w_1 (t), \\
\dot{w}_2 (t) &= \left( 1 - f \ell_1 \right) \lambda_2 e^{-\mu_2 t} s_2 (t - \tau_{12}) p(t - \tau_{12}) - (\alpha_2 + \beta_2) w_2 (t), \\
\dot{y}_1 (t) &= \left( 1 - \varepsilon_1 \lambda_1 e^{-\mu_1 t} s_1 (t - \tau_{21}) p(t - \tau_{21}) \right) + \alpha_1 w_1 (t) - \eta_1 y_1 (t), \\
\dot{y}_2 (t) &= \left( 1 - f \ell_1 \right) \lambda_2 e^{-\mu_2 t} s_2 (t - \tau_{22}) p(t - \tau_{22}) - \alpha_2 w_2 (t) - \eta_2 y_2 (t), \\
\dot{u}_1 (t) &= \left( 1 - \varepsilon_1 \lambda_1 e^{-\mu_1 t} s_1 (t - \tau_{31}) p(t - \tau_{31}) \right) - \nu_1 u_1 (t), \\
\dot{u}_2 (t) &= \left( 1 - f \ell_1 \right) \lambda_2 e^{-\mu_2 t} s_2 (t - \tau_{32}) p(t - \tau_{32}) - \nu_2 u_2 (t), \\
\dot{p} (t) &= (1 - \varepsilon_2) \overline{N} \eta_1 e^{-\mu_1 t} y_1 (t - \tau_{41}) + (1 - \varepsilon_2) \overline{N} \eta_2 e^{-\mu_2 t} \tau_{41} y_2 (t - \tau_{42}) + (1 - \varepsilon_2) \overline{N} \epsilon_1 e^{-\mu_1 t} s_1 (t - \tau_{51}) + (1 - \varepsilon_2) \overline{N} \epsilon_2 e^{-\mu_2 t} s_2 (t - \tau_{52}) - gp(t) - \mu p(t) x(t), \\
\dot{x} (t) &= rp(t) x(t) - wx(t), \\
\end{align*}
\]

where $B < \delta_1$. In this application, we consider the following specific forms of the general functions:

\[
\begin{align*}
\pi_1 (s_1 (t)) &= \rho_1 - \delta_1 s_1 (t) + B s_1 (t) \left( 1 - \frac{s_1 (t)}{s_{\text{max}}} \right), \\
\pi_2 (s_2 (t)) &= \rho_2 - \delta_2 s_2 (t), \\
\chi_1 (s_1 (t), p (t)) &= \frac{s_1 (t) p (t)}{1 + \delta_1 p (t)}, \\
\psi_{j1} (0) &= 0, \quad j = 1, \ldots, 4, \quad i = 1, 2.
\end{align*}
\]

First we verify hypotheses H1-H4 for the chosen forms, then we solve the system using MATLAB. Clearly, $\pi_i (0) = \rho_i > 0$ and $\pi_i (s_i^0) = 0$, where

\[
s_1^0 = \frac{s_{\text{max}}}{2B} \left( B - \delta_1 + \sqrt{(B - \delta_1)^2 + \frac{4 \rho_1 B}{s_{\text{max}}}} \right), \quad s_2^0 = \frac{\rho_2}{\delta_2}.
\]

We have

\[
\pi_1' (s_1) = -\delta_1 + B - \frac{2Bs_1}{s_{\text{max}}} < 0, \quad \pi_2' (s_2) = -\delta_2 < 0.
\]

Clearly, $\pi_i (s_i) > 0$ for $s_i \in [0, s_i^0]$ and

\[
\pi_1 (s_1) = \rho_1 - (\delta_1 - B) s_1 - B \frac{s_1^2}{s_{\text{max}}} \leq \rho_1 - (\delta_1 - B) s_1, \quad \pi_2 (s_2) = \rho_2 - \delta_2 s_2.
\]
Then H1 is satisfied. We also have \( \chi_i(s_l, p) > 0, \chi_i(0, p) = \chi(s_l, 0) = 0 \) for \( s_l, p \in (0, \infty) \), and

\[
\frac{\partial \chi_i(s_l, p)}{\partial s_l} = \frac{p}{(1 + \theta_1 p)^{\gamma}}, \quad \frac{\partial \chi_i(s_l, p)}{\partial p} = \frac{s_l}{(1 + \theta_1 p)^{\gamma}}, \quad \frac{\partial \chi_i(s_l, 0)}{\partial p} = s_l.
\]

Then, \( \frac{\partial \chi_i(s_l, p)}{\partial s_l} > 0, \frac{\partial \chi_i(s_l, p)}{\partial p} > 0, \) and \( \frac{\partial \chi_i(s_l, 0)}{\partial p} > 0 \) for all \( s_l, p \in (0, \infty) \). Therefore, H1 is satisfied. In addition

\[
\left( \frac{\partial \chi_i(s_l, 0)}{\partial p} \right)' = 1 > 0 \text{ for all } s_l > 0.
\]

It follows that, H2 is satisfied. Clearly H3 holds true. Moreover,

\[
\frac{\partial}{\partial p} \left( \frac{\chi_i(s_l, p)}{\psi_4(l)} \right) = -\frac{\theta_1 s}{(1 + \theta_1 p)^2} < 0.
\]

Therefore, H4 holds true and Theorems 2.1, 2.3, and 2.4 are applicable. The parameters \( R_0 \) and \( R_1 \) for this application are given by:

\[
R_0 = \sum_{i=1}^2 \left\{ \frac{[N_i A_i e^{-\mu_i \tau_i}] + M_i \lambda_3 i e^{-\mu_3 \tau_3} (\alpha_i + \beta_i) e^{-\mu_3 \tau_3}}{g(\alpha_i + \beta_i)} \right\}_0 s_l^0,
\]

\[
R_1 = \sum_{i=1}^2 \left\{ \frac{[N_i A_i e^{-\mu_i \tau_i}] + M_i \lambda_3 i e^{-\mu_3 \tau_3} (\alpha_i + \beta_i) e^{-\mu_3 \tau_3}}{g(\alpha_i + \beta_i)} \right\}_1 s_l^1 \frac{1}{1 + \theta_1 p}.
\]

\[
A_i = \alpha_i \lambda_1 i e^{-\mu_i \tau_i} + (\alpha_i + \beta_i) A_2 i e^{-\mu_2 \tau_2}.
\]

**Remark 3.1.** There are several forms of the general function \( \chi_i(s_l, p) \) where H1-H4 can be satisfied such as:

(i) Holling-type incidence \( \chi_i(s_l, p) = \frac{s_l^0 p}{1 + \theta_1 s_l} \);

(ii) Beddington-DeAngelis incidence \( \chi_i(s_l, p) = \frac{s_l^0 p}{1 + \theta_1 s_l + \theta_2 p} \);

(iii) Crowley-Martin incidence \( \chi_i(s_l, p) = \frac{s_l^0 p}{(1 + \theta_1 s_l)(1 + \theta_2 p)} \);

(iv) Hill-type incidence \( \chi_i(s_l, p) = \frac{s_l^0 p}{\theta_1 s_l + \theta_2 p} \).

Now we are ready to perform some numerical simulations for system (3.1). The data of system (3.1) are provided in Table 1. We let \( \tau_{m1} = \tau, \mu_{m1} = \mu, i = 1,2, \lambda_{m2} = 0.000625, \) and \( \lambda_{m2} = 0.000625, m = 1,2,3. \)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
<th>Parameter</th>
<th>Value</th>
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<tr>
<td>( \rho_1 )</td>
<td>10</td>
<td>( \rho_2 )</td>
<td>0.03198</td>
<td>( \eta_1 )</td>
<td>0.36</td>
<td>( \eta_2 )</td>
<td>0.03</td>
</tr>
<tr>
<td>( \delta_1 )</td>
<td>0.01</td>
<td>( \delta_2 )</td>
<td>0.005</td>
<td>( \nu_1 )</td>
<td>0.031</td>
<td>( \nu_2 )</td>
<td>0.01</td>
</tr>
<tr>
<td>( B )</td>
<td>0.0001</td>
<td>( x_{\text{max}} )</td>
<td>1200</td>
<td>( g )</td>
<td>3</td>
<td>( \mu )</td>
<td>0.5</td>
</tr>
<tr>
<td>( \alpha_1 )</td>
<td>0.2</td>
<td>( \alpha_2 )</td>
<td>0.01</td>
<td>( \omega )</td>
<td>0.1</td>
<td>( \mu_{\text{e}} )</td>
<td>1</td>
</tr>
<tr>
<td>( \beta_1 )</td>
<td>0.02</td>
<td>( \beta_2 )</td>
<td>0.002</td>
<td>( f )</td>
<td>0.5</td>
<td>( h )</td>
<td>0.5</td>
</tr>
<tr>
<td>( \theta_1 )</td>
<td>0.01</td>
<td>( \theta_2 )</td>
<td>0.002</td>
<td>( N_1 )</td>
<td>20</td>
<td>( N_2 )</td>
<td>5</td>
</tr>
<tr>
<td>( M_1 )</td>
<td>6</td>
<td>( M_2 )</td>
<td>1</td>
<td>( \varepsilon_1, \varepsilon_2 )</td>
<td>varied</td>
<td>( \tau, \tau )</td>
<td>varied</td>
</tr>
</tbody>
</table>

**3.1. Stability of the steady states of the system**

To discuss our global results, we choose three different initial conditions:

IC1: \( (s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x)(0) = (900, 6, 2, 0.02, 3, 0.02, 15, 0.02, 2, 3); \)

IC2: \( (s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x)(0) = (700, 5, 4, 0.08, 5, 0.06, 25, 0.1, 5, 5); \)

IC3: \( (s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x)(0) = (500, 4, 6, 0.15, 6.5, 0.1, 40, 0.2, 7, 8); \)
Let us address three cases for the parameters $\varepsilon_1, \varepsilon_2, \tau$, and $r$.

**Case (I):** Choose $\varepsilon_1 = 0.6, \varepsilon_2 = 0.8, \tau = 1.0$, and $r = 0.009$, which gives $R_0 = 0.1232 < 1$ and $R_1 = 0.0635 < 1$. Therefore, based on Theorem 2.1, the uninfected steady state $\Pi_0$ is GAS. As we can see from Figures 1-10 that, the concentrations of the uninfected CD4$^+$ T cells and macrophages are increased and approached their normal value before infection, that are, $s_1^0 = 1001.7, s_2^0 = 6.4$; while concentrations of the other compartments converge to zero for all the three initial conditions. As a result, the HIV is removed from the plasma.

**Case (II):** We take $\varepsilon_1 = 0.1, \varepsilon_2 = 0.2, \tau = 0.5$, and $r = 0.009$. For these values, $R_1 = 0.8910 < 1 < R_0 = 2.6577$. Consequently, based on Theorem 2.3, the humoral-inactivated infection steady state $\Pi_1$ is GAS. Figures 1-10 confirm that the numerical results support the theoretical results presented in Theorem 2.3. It can be observed that, the variables of the model eventually converge to $\Pi_1 = (443.186, 4.960, 5.143, 0.121, 6.0, 0.089, 36.497, 0.145, 8.088, 0.0)$ for all the three initial conditions. This case corresponds to a chronic HIV infection in the absence of humoral immune response.

**Case (III):** $\varepsilon_1 = 0.1, \varepsilon_2 = 0.2, \tau = 0.5$, and $r = 0.08$. Then, we calculate $R_0 = 2.6577 > 1$ and $R_1 = 2.1744 > 1$. According to Theorem 2.4, the humoral-activated infection steady state $\Pi_2$ is GAS. We can see from Figures 1-10 that, there is a consistency between the numerical results and theoretical results of Theorem 2.4. The states of the system converge to $\Pi_2 = (829.705, 6.118, 1.589, 0.023, 1.853, 0.017, 11.273, 0.028, 1.25, 5.99$) for all the three initial conditions. In this case the humoral immune response is activated and can control the disease.

### 3.2. Effect of the time delay on the stability of the system

Choosing $\varepsilon_1 = \varepsilon_2 = 0$ and $r = 0.08$, the initial conditions are considered to be $(s_1, s_2, w_1, w_2, y_1, y_2, u_1, u_2, p, x) (0) = (850, 6.2, 2, 0.01, 1.5, 0.01, 10, 0.015, 1.7)$. Figures 11-20 and Table 2 show the effect of the time delay parameter $\tau$ on the stability of $\Pi_0, \Pi_1$, and $\Pi_2$. Clearly, the parameter $\tau$ has similar effect as the drug efficacies parameters $\varepsilon_1$ and $\varepsilon_2$.

<table>
<thead>
<tr>
<th>$\tau$</th>
<th>steady states</th>
<th>$R_0$</th>
<th>$R_1$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>$\Pi_2 = (814.16, 6.11, 2.86, 0.04, 3.33, 0.03, 20.27, 0.05, 1.25, 38.42)$</td>
<td>9.22</td>
<td>7.40</td>
</tr>
<tr>
<td>0.5</td>
<td>$\Pi_2 = (814.16, 6.11, 1.73, 0.024, 2.02, 0.02, 12.29, 0.03, 1.25, 10.34)$</td>
<td>3.69</td>
<td>2.96</td>
</tr>
<tr>
<td>1.0</td>
<td>$\Pi_2 = (814.28, 6.11, 1.05, 1.23, 1.19, 0.011, 7.45, 0.02, 1.25, 0.01)$</td>
<td>1.54</td>
<td>1.24</td>
</tr>
<tr>
<td>1.1</td>
<td>$\Pi_1 = (981.43, 6.37, 0.10, 0.00, 0.12, 0.00, 0.73, 0.00, 0.11, 0)$</td>
<td>1.3</td>
<td>1.04</td>
</tr>
<tr>
<td>1.2</td>
<td>$\Pi_0 = (1001.7, 6.4, 0, 0, 0, 0, 0, 0, 0, 0)$</td>
<td>1.1</td>
<td>0.88</td>
</tr>
<tr>
<td>1.5</td>
<td>$\Pi_0 = (1001.7, 6.4, 0, 0, 0, 0, 0, 0, 0, 0)$</td>
<td>0.68</td>
<td>0.54</td>
</tr>
</tbody>
</table>

![Figure 1: The concentration of uninfected CD4$^+$ T cells.](image1)

![Figure 2: The concentration of uninfected macrophages.](image2)
Figure 3: The concentration of latently infected CD4$^+$ T cells.

Figure 4: The concentration of latently infected macrophages.

Figure 5: The concentration of short-lived productively infected CD4$^+$ T cells.

Figure 6: The concentration of short-lived productively infected macrophages.

Figure 7: The concentration of long-lived productively infected CD4$^+$ T cells.

Figure 8: The concentration of long-lived productively infected macrophages.
Figure 9: The concentration of free virus particles.

Figure 10: The concentration of B cells.

Figure 11: The concentration of uninfected CD4\(^+\) T cells.

Figure 12: The concentration of uninfected macrophages.

Figure 13: The concentration of latently infected CD4\(^+\) T cells.

Figure 14: The concentration of latently infected macrophages.
Figure 15: The concentration of short-lived productively infected CD4$^+$ T cells.

Figure 16: The concentration of short-lived productively infected macrophages.

Figure 17: The concentration of long-lived productively infected CD4$^+$ T cells.

Figure 18: The concentration of long-lived productively infected macrophages.

Figure 19: The concentration of free virus particles.

Figure 20: The concentration of B cells.
References


