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Stability of a general discrete-time HIV dynamics model with three categories of infected CD4$^+$ T-cells and multiple time delays

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Abstract

In this paper, we construct delayed HIV dynamics models with impairment of B-cell functions. Two forms of the incidence rate have been considered, bilinear and general. Three types of infected cells and five-time delays have been incorporated into the models. The well-posedness of the models is justified. The models admit two equilibria which are determined by the basic reproduction number R_0. The global stability of each equilibrium is proven by utilizing the Lyapunov function and LaSalle's invariance principle. The theoretical results are illustrated by numerical simulations.

Keywords: HIV infection, latent reservoirs, time delay, global stability, Lyapunov function, discrete time model.

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1. Introduction

During the last decades, biologists and mathematicians have interested in constructing mathematical models which describe the dynamics of human immunodeficiency virus (HIV) in the human body (see, e.g., [2, 3, 8, 10, 14, 17, 24, 25, 31, 39]). The basic HIV dynamics model which has been proposed by Nowak and Bangham [24] contains three compartments, the HIV (p), uninfected CD4$^+$ T cells (s) and infected CD4$^+$ T cells (z). Highly active anti-retroviral therapy (HAART) can suppress HIV replication to a low level but cannot eradicate the virus. An important reason is that HIV provirus can reside in latently infected CD4$^+$ T cells [32]. Latently infected CD4$^+$ T cells live long, but can be activated to produce virus by relevant antigens. It has been reported in [2] that there are three classes of infected CD4$^+$ T cells, (i) short lived productively infected cells which live short and produce large numbers of HIV, (ii) long lived productively infected cells which live long and produce small numbers of HIV particles, and (iii) latently infected cells which contain the viruses but not producing it until they activated.

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Callaway and Perelson [2] have extended the basic model by taking into consideration three classes of infected cells: (i) latently infected cells (w), (ii) short-lived infected (z), and (iii) long-lived chronically infected cells (u):

$$\dot{s}(t) = \beta - \delta s(t) - (k_1 + k_2 + k_3)s(t)p(t), \tag{1.1}$$
$$\dot{w}(t) = k_1 s(t)p(t) - (\alpha + m)w(t), \tag{1.2}$$
$$\dot{z}(t) = k_2 s(t)p(t) + mw(t) - dz(t), \tag{1.3}$$
$$\dot{u}(t) = k_3 s(t)p(t) - au(t), \tag{1.4}$$
$$\dot{p}(t) = N_z dz(t) + N_u au(t) - cp(t), \tag{1.5}$$

where $k_1 + k_2 + k_3$ represents the HIV-susceptible infection rate constant. The parameters α, d, a, c denote the death rate constants of the compartments w, z, u, and p, respectively; N_z and N_u are the average number of HIV particles produced in the lifetime of the compartments z and u, respectively; m is the activation rate constant of w.

A major shortcoming of model (1.1)-(1.5) is the assumption that cells produce viruses immediately after they are infected. It is commonly observed that in many biological processes, time delay is inevitable. For HIV-1 infection, it roughly takes about 1 day for a newly infected cell to become productive and then to be able to produce new HIV particles [5]. Therefore, mathematicians have frequently used different types of delay to make the HIV dynamics models more realistic [28].

Model (1.1)-(1.5) has been described by system of nonlinear ODEs, but the exact analytical solution of the model is unknown. Therefore, a discretization can be used to obtain discrete-time model which is an approximation of the exact one. Further, the use of digital computers in performing simulations necessitated the investigation of discrete-time systems. Furthermore, it is important to note that scientists often collect the data and analyze the results at discrete times. One of the very important task is to choose a discretization scheme which preserves the properties of the corresponding continuous time model. In 1994 Mickens [22] has introduced nonstandard finite difference (NSFD) scheme for solving differential equations. It has been proven that NSFD can preserve the main properties of several types of continuous time models. The main advantage of NSFD approach is that the essential qualitative features of the mathematical model such as equilibria, positivity, boundedness and global behaviors of solutions are preserved independently of the chosen step-size [19]. NSFD has been used to investigate the global stability of equilibria of the corresponding continuous time models in virology [6, 7, 15, 19, 20, 27, 31, 34–38, 40].

In this paper, our target is to study a general discrete time HIV infection model with three categories of infected cells, w, z and u and discrete time delays. The model is obtained by discretizing system (1.1)-(1.5) using NSFD. It is considering that the incidence rate and production/removal rate of the HIV particles and cells are given by general functions. We investigate the global stability of the equilibria of the model using Lyapunov method.

2. The model

In this section, we propose a general nonlinear HIV model as:

$$\dot{s}(t) = \pi(s(t)) - (k_1 + k_2 + k_3) f(s(t), p(t)), \tag{2.1}$$
$$\dot{w}(t) = k_1 e^{-\mu_1 \tau_1} f(s(t-\tau_1), p(t-\tau_1)) - (\alpha + m) g_1(w(t)), \tag{2.2}$$
$$\dot{z}(t) = k_2 e^{-\mu_2 \tau_2} f(s(t-\tau_2), p(t-\tau_2)) + m g_1(w(t)) - d g_2(z(t)), \tag{2.3}$$
$$\dot{u}(t) = k_3 e^{-\mu_3 \tau_3} f(s(t-\tau_3), p(t-\tau_3)) - a g_3(u(t)), \tag{2.4}$$
$$\dot{p}(t) = N_z e^{-\mu_4 \tau_4} d g_2(z(t-\tau_4)) + N_u e^{-\mu_5 \tau_5} a g_3(u(t-\tau_5)) - c g_4(p(t)). \tag{2.5}$$

We assume that the infected cells contact the susceptible cells at times $t-\tau_1$, $t-\tau_2$ and $t-\tau_3$, respectively, become latently infected and actively infected at time t, where τ_1, τ_2 and τ_3 are positive constants. The immature pathogens produced from short-lived and long-lived infected cells at time $t-\tau_4$ and $t-\tau_5$, respectively, are assumed to be matured at time t. Moreover, $e^{-\mu_j\tau_j}$, $j=1,\dots,5$ is the probability of the cells and pathogens survival during the delay periods, where μ_1, μ_2, μ_3, μ_4 and, μ_5 are positive constants. Functions π, f and g_i, $i=1,\dots,4$ are general functions and are assumed to satisfy the following conditions [9, 17]:

(A1) (i) there exists $s^0>0$ such that $\pi\left(s^0\right)=0$, $\pi(s)>0$ for $s\in\left[0,s^0\right)$;
(ii) $\pi'(s)<0$ for all $s>0$;
(iii) there are $b>0$ and $\bar{b}>0$ such that $\pi(s)\leqslant b-\bar{b}s$ for all $s\geqslant 0$;

(A2) (i) $f(s,p)>0$ and $f(0,p)=f(s,0)=0$ for all $s>0$, $p>0$;
(ii) $\frac{\partial f(s,p)}{\partial s}>0$, $\frac{\partial f(s,p)}{\partial p}>0$, $\frac{\partial f(s,0)}{\partial p}>0$ for all $s>0$, $p>0$;
(iii) $\frac{d}{ds}\left(\frac{\partial f(s,0)}{\partial p}\right)>0$ for all $s>0$;

(A3) (i) $g_j(\rho)>0$ for $\rho>0$, $g_j(0)=0$, $j=1,\dots,4$;
(ii) $g_j'(\rho)>0$ for $\rho>0$, $j=1,2,3$ and $g_4'(\rho)>0$ for $\rho\geqslant 0$;
(iii) there are $\upsilon_j>0$, $j=1,\dots,4$ such that $g_j(\rho)\geqslant \upsilon_j\rho$ for $\rho\geqslant 0$;

(A4) $\frac{\partial}{\partial p}\left(\frac{f(s,p)}{g_4(p)}\right)\leqslant 0$ for all $s>0$, $p>0$.

Discretizing system (2.1)-(2.5) using NSFD method [22] we obtain

$$\frac{s_{n+1}-s_n}{h}=\pi\left(s_{n+1}\right)-kf\left(s_{n+1},p_n\right), \tag{2.6}$$
$$\frac{w_{n+1}-w_n}{h}=k_1e^{-\mu_1\tau_1}f\left(s_{n-m_1+1},p_{n-m_1}\right)-(\alpha+m)g_1\left(w_{n+1}\right), \tag{2.7}$$
$$\frac{z_{n+1}-z_n}{h}=k_2e^{-\mu_2\tau_2}f\left(s_{n-m_2+1},p_{n-m_2}\right)+mg_1\left(w_{n+1}\right)-dg_2\left(z_{n+1}\right), \tag{2.8}$$
$$\frac{u_{n+1}-u_n}{h}=k_3e^{-\mu_3\tau_3}f\left(s_{n-m_3+1},p_{n-m_3}\right)-ag_3\left(u_{n+1}\right), \tag{2.9}$$
$$\frac{p_{n+1}-p_n}{h}=N_ze^{-\mu_4\tau_4}dg_2\left(z_{n-m_4+1}\right)+N_ue^{-\mu_5\tau_5}ag_3\left(u_{n-m_5+1}\right)-cg_4\left(p_{n+1}\right), \tag{2.10}$$

where $n\in\mathbb{N}=\{0,1,2,\dots\}$, $h>0$ is the time step size and (s_n,w_n,z_n,u_n,p_n) are the approximations of the solution $(s(t_n),w(t_n),z(t_n),u(t_n),p(t_n))$ of system (2.1)-(2.5) at the discrete time points $t_n=nh$. Assume that there exist integers $m_i\in\mathbb{N}$, $i=1,\dots,5$ with $\tau_i=hm_i$.

The initial conditions of system (2.6)-(2.10) are

$$s_\kappa=\psi_\kappa^1\geqslant 0,\ w_\kappa=\psi_\kappa^2\geqslant 0,\ z_\kappa=\psi_\kappa^3\geqslant 0,\ u_\kappa=\psi_\kappa^4\geqslant 0,\ p_\kappa=\psi_\kappa^5\geqslant 0,\ \text{ for all } \kappa=-\bar{m},-\bar{m}+1,\dots,0, \tag{2.11}$$

where $\bar{m}=\max\{m_1,m_2,m_3,m_4,m_5\}$ and $\psi_0^i>0$, $i=1,\dots,5$.

The basic reproduction number for model (2.6)-(2.10) is defined as

$$R_0=\frac{\rho\left[\omega_1\nu M_1e^{-\theta_1\tau_1-\theta_4\tau_4}+(\zeta+\nu)\left(\omega_2M_1e^{-\theta_2\tau_2-\theta_4\tau_4}+\omega_3M_2e^{-\theta_3\tau_3-\theta_5\tau_5}\right)\right]}{\xi\gamma(\zeta+\nu)}.$$

2.1. Preliminaries

Let us consider the region

$$\Gamma_1=\{(s,w,z,u,p):0<s,w,z,u<N_1,0<p<N_2\},$$

where $N_1=\frac{b}{\xi}$, $N_2=\frac{N_zdg_2(N_1)+N_uag_3(N_1)}{c\upsilon_4}$ and $\xi=\min\left\{\bar{b},\alpha\upsilon_1,d\upsilon_2,a\upsilon_3\right\}$.

Lemma 2.1. *Any solution* (s_n,w_n,z_n,u_n,p_n) *of model* (2.6)-(2.10) *with initial conditions* (2.11) *is positive and ultimately bounded.*

Proof. When $n = 0$ we prove that $(s_1, w_1, z_1, u_1, p_1)$ exists and is positive. From Eq. (2.6) we have

$$s_1 - s_0 + h\left[-\pi(s_1) + kf(s_1, p_0)\right] = 0.$$

Let $\varphi_1(s)$ be defined as:

$$\varphi_1(s) = s - s_0 + h\left[-\pi(s) + kf(s, p_0)\right] = 0.$$

According to A1-A2 we have φ_1 is a strictly increasing function in s and

$$\varphi_1(0) = -s_0 - h\pi(0) < 0, \quad \lim_{s\to\infty} \varphi_1(s) = \infty.$$

Hence, there exists a unique $s_1 > 0$ such that $\varphi_1(s_1) = 0$. From Eqs. (2.7) we have

$$w_1 - w_0 + h\left[(\alpha + m)\, g_1(w_1) - k_1 e^{-\mu_1\tau_1} f(s_{-m_1+1}, p_{-m_1})\right] = 0.$$

Let $\varphi_2(w)$ be defined as:

$$\varphi_2(w) = w - w_0 + h\left[(\alpha + m)\, g_1(w) - k_1 e^{-\mu_1\tau_1} f(s_{-m_1+1}, p_{-m_1})\right] = 0.$$

Based on A2-A3 we have φ_2 is a strictly increasing function in w, and

$$\varphi_2(0) = -w_0 - hk_1 e^{-\mu_1\tau_1} f(s_{-m_1+1}, p_{-m_1}) < 0, \quad \lim_{w\to\infty} \varphi_2(w) = \infty.$$

Hence, there exists a unique $w_1 \in (0, \infty)$ such that $\varphi_2(w_1) = 0$. From Eqs. (2.8) we have

$$z_1 - z_0 + h\left[dg_2(z_1) - mg_1(w_1) - k_2 e^{-\mu_2\tau_2} f(s_{-m_2+1}, p_{-m_2})\right] = 0.$$

Let $\varphi_3(z)$ be defined as:

$$\varphi_3(z) = z - z_0 + h\left[dg_2(z) - mg_1(w_1) - k_2 e^{-\mu_2\tau_2} f(s_{-m_2+1}, p_{-m_2})\right] = 0.$$

Based on A2-A3 we have φ_3 is a strictly increasing function in z. Moreover,

$$\varphi_3(0) = -z_0 - hmg_1(w_1) - hk_2 e^{-\mu_2\tau_2} f(s_{-m_2+1}, p_{-m_2}) < 0, \quad \lim_{z\to\infty} \varphi_3(z) = \infty.$$

Hence, there exists a unique $z_1 \in (0, \infty)$ such that $\varphi_3(z_1) = 0$.

Similarly, one can easily show from Eqs. (2.9)-(2.10) that $u_1 \in (0, \infty)$ and $p_1 \in (0, \infty)$. Therefore, by using the induction, we obtain $s_n > 0$, $w_n > 0$, $z_n > 0$, $u_n > 0$ and $p_n > 0$ for all $n \geqslant 0$.

Now we investigate the boundedness of solution. From Eq. (2.6) we have

$$\frac{s_{n+1} - s_n}{h} \leqslant \pi(s_{n+1}) \leqslant b - \bar{b}s_{n+1}.$$

Hence

$$s_{n+1} \leqslant \frac{hb}{1 + h\bar{b}} + \frac{s_n}{1 + h\bar{b}}.$$

By Lemma 2.2 in [29] we have

$$s_n \leqslant \left(\frac{1}{1 + h\bar{b}}\right)^n s_0 + \frac{b}{\bar{b}}\left[1 - \left(\frac{1}{1 + h\bar{b}}\right)^n\right],$$

which implies that $\lim_{n\to\infty} \sup s_n \leqslant b/\bar{b} \leqslant N_1$. Define

$$\Omega_n = e^{-\mu_1\tau_1} s_{n-m_1} + e^{-\mu_2\tau_2} s_{n-m_2} + e^{-\mu_3\tau_3} s_{n-m_3} + w_n + z_n + u_n.$$

Then

$$\begin{aligned}\Omega_{n+1}-\Omega_n &= e^{-\mu_1\tau_1}\left(s_{n-m_1+1}-s_{n-m_1}\right)+e^{-\mu_2\tau_2}\left(s_{n-m_2+1}-s_{n-m_2}\right)\\ &\quad+e^{-\mu_3\tau_3}\left(s_{n-m_3+1}-s_{n-m_3}\right)+w_{n+1}-w_n+z_{n+1}-z_n+u_{n+1}-u_n\\ &= h\left\{e^{-\mu_1\tau_1}\left[\pi\left(s_{n-m_1+1}\right)-kf\left(s_{n-m_1+1},p_{n-m_1}\right)\right]\right.\\ &\quad+e^{-\mu_2\tau_2}\left[\pi\left(s_{n-m_2+1}\right)-kf\left(s_{n-m_2+1},p_{n-m_2}\right)\right]\\ &\quad+e^{-\mu_3\tau_3}\left[\pi\left(s_{n-m_3+1}\right)-kf\left(s_{n-m_3+1},p_{n-m_3}\right)\right]\\ &\quad+k_1e^{-\mu_1\tau_1}f\left(s_{n-m_1+1},p_{n-m_1}\right)-(\alpha+m)g_1\left(w_{n+1}\right)\\ &\quad+k_2e^{-\mu_2\tau_2}f\left(s_{n-m_2+1},p_{n-m_2}\right)+mg_1\left(w_{n+1}\right)-dg_2\left(z_{n+1}\right)\\ &\quad\left.+k_3e^{-\mu_3\tau_3}f\left(s_{n-m_3+1},p_{n-m_3}\right)-ag_3\left(u_{n+1}\right)\right\}.\end{aligned}$$

Since $k_i<k$, $i=1,2,3$ then

$$\begin{aligned}\Omega_{n+1}-\Omega_n \leqslant h&\left\{e^{-\mu_1\tau_1}\pi\left(s_{n-m_1+1}\right)+e^{-\mu_2\tau_2}\pi\left(s_{n-m_2+1}\right)+e^{-\mu_3\tau_3}\pi\left(s_{n-m_3+1}\right)\right.\\ &\left.-\alpha g_1\left(w_{n+1}\right)-dg_2\left(z_{n+1}\right)-ag_3\left(u_{n+1}\right)\right\}.\end{aligned}$$

According to A1-A3 we have

$$\begin{aligned}\Omega_{n+1}-\Omega_n &\leqslant h\left\{e^{-\mu_1\tau_1}\left(b-\bar{b}s_{n-m_1+1}\right)+e^{-\mu_2\tau_2}\left(b-\bar{b}s_{n-m_2+1}\right)\right.\\ &\quad\left.+e^{-\mu_3\tau_3}\left(b-\bar{b}s_{n-m_3+1}\right)-\alpha\upsilon_1w_{n+1}-d\upsilon_2z_{n+1}-a\upsilon_3u_{n+1}\right\}\\ &\leqslant hb-h\xi\left\{e^{-\mu_1\tau_1}s_{n-m_1+1}+e^{-\mu_2\tau_2}s_{n-m_2+1}+e^{-\mu_3\tau_3}s_{n-m_3+1}\right.\\ &\quad\left.+w_{n+1}+z_{n+1}+u_{n+1}\right\}=hb-h\xi\Omega_{n+1}.\end{aligned}$$

Hence

$$\Omega_{n+1}\leqslant\frac{\Omega_n}{1+h\xi}+\frac{hb}{1+h\xi}.$$

By Lemma 2.2 in [29] we have

$$\Omega_n\leqslant\left(\frac{1}{1+h\xi}\right)^n\Omega_0+\frac{b}{\xi}\left[1-\left(\frac{1}{1+h\xi}\right)^n\right].$$

Consequently, $\lim\limits_{n\to\infty}\sup\Omega_n\leqslant N_1$, and then $\lim\limits_{n\to\infty}\sup w_n\leqslant N_1$, $\lim\limits_{n\to\infty}\sup z_n\leqslant N_1$ and $\lim\limits_{n\to\infty}\sup u_n\leqslant N_1$. Thus, for any $\rho_1>0$ and $\rho_2>0$, there exist integer numbers ν_{ρ_1} and ν_{ρ_2}, respectively, such that $z_n\leqslant N_1+\rho_1$ for $n\geqslant\nu_{\rho_1}$ and $u_n\leqslant N_1+\rho_2$ for $n\geqslant\nu_{\rho_2}$. From Eq. (2.10), we have

$$\begin{aligned}\frac{p_{n+1}-p_n}{h}&=N_ze^{-\mu_4\tau_4}dg_2\left(z_{n-m_4+1}\right)+N_ue^{-\mu_5\tau_5}ag_3\left(u_{n-m_5+1}\right)-cg_4\left(p_{n+1}\right)\\ &\leqslant N_zdg_2\left(N_1+\rho_1\right)+N_uag_3\left(N_1+\rho_2\right)-c\upsilon_4p_{n+1}.\end{aligned}$$

Hence

$$p_{n+1}\leqslant\frac{p_n}{1+hc\upsilon_4}+\frac{h\left(N_zdg_2\left(N_1+\rho_1\right)+N_uag_3\left(N_1+\rho_2\right)\right)}{1+hc\upsilon_4}.$$

By induction we get

$$p_n\leqslant\left(\frac{1}{1+hc\upsilon_4}\right)^np_0+\frac{N_zdg_2\left(N_1+\rho_1\right)+N_uag_3\left(N_1+\rho_2\right)}{c\upsilon_4}\left[1-\left(\frac{1}{1+hc\upsilon_4}\right)^n\right]$$

for $n\geqslant\max\{\nu_{\rho_1}+m_4,\nu_{\rho_2}+m_5\}$, then $\lim\limits_{n\to\infty}\sup p_n\leqslant\frac{N_zdg_2(N_1+\rho_1)+N_uag_3(N_1+\rho_2)}{c\upsilon_4}$. The arbitrariness of ρ_1 and ρ_2 yields that $\lim\limits_{n\to\infty}\sup p_n\leqslant\frac{N_zdg_2(N_1)+N_uag_3(N_1)}{c\upsilon_4}=N_2$. Therefore, the solution (s_n,w_n,z_n,u_n,p_n) converges to Γ_1 as $n\to\infty$. □

Lemma 2.2. *For model* (2.6)-(2.10) *let* (A1)-(A3) *hold true, then there exists a threshold parameter* $\mathcal{R}_0 > 0$ *such that*

(i) *if* $\mathcal{R}_0 \leqslant 1$, *then there exists only an HIV-free equilibrium* Q^0*;*
(ii) *if* $\mathcal{R}_0 > 1$, *then there exist two equilibria,* Q^0 *and a persistent HIV equilibrium* Q^*.

Proof. Let $Q(s, w, z, u, p)$ be any equilibrium of model (2.6)-(2.10) satisfying

$$\pi(s) - kf(s, p) = 0, \tag{2.12}$$

$$k_1 e^{-\mu_1\tau_1} f(s, p) - (\alpha + m)\, g_1(w) = 0, \tag{2.13}$$

$$k_2 e^{-\mu_2\tau_2} f(s, p) + m g_1(w) - d g_2(z) = 0, \tag{2.14}$$

$$k_3 e^{-\mu_3\tau_3} f(s, p) - a g_3(u) = 0, \tag{2.15}$$

$$N_z e^{-\mu_4\tau_4} d g_2(z) + N_u e^{-\mu_5\tau_5} a g_3(u) - c g_4(p) = 0. \tag{2.16}$$

From Eqs. (2.12)-(2.16) we have

$$\begin{aligned} w &= g_1^{-1}\left(\frac{k_1 e^{-\mu_1\tau_1}}{k(\alpha+m)}\pi(s)\right), \quad z = g_2^{-1}\left(\frac{\left(m k_1 e^{-\mu_1\tau_1} + (\alpha+m) k_2 e^{-\mu_2\tau_2}\right)}{dk(\alpha+m)}\pi(s)\right), \\ u &= g_3^{-1}\left(\frac{k_3 e^{-\mu_3\tau_3}}{ak}\pi(s)\right), \quad p = g_4^{-1}\left(\frac{\gamma}{k}\pi(s)\right). \end{aligned} \tag{2.17}$$

where

$$\gamma = \frac{N_z e^{-\mu_4\tau_4}\left(m k_1 e^{-\mu_1\tau_1} + (\alpha+m) k_2 e^{-\mu_2\tau_2}\right) + (\alpha+m) N_u k_3 e^{-\mu_3\tau_3 - \mu_5\tau_5}}{c(\alpha+m)}.$$

Let us define

$$w = \vartheta(s), \quad z = \psi(s), \quad u = \mu(s), \quad p = \ell(s). \tag{2.18}$$

Obviously, $\vartheta(s), \psi(s), \mu(s), \ell(s) > 0$ for $s \in [0, s^0)$ and $\vartheta(s^0) = \psi(s^0) = \mu(s^0) = \ell(s^0) = 0$. From Eqs. (2.12), (2.17), and (2.18) we obtain

$$\gamma f(s, \ell(s)) - g_4(\ell(s)) = 0. \tag{2.19}$$

Eq. (2.19) admits a solution $s = s^0$ which yields the HIV-free equilibrium $Q^0(s^0, 0, 0, 0, 0)$. Let

$$\Psi(s) = \gamma f(s, \ell(s)) - g_4(\ell(s)) = 0.$$

From Assumptions (A2) and (A3), $\Psi(0) = -g_4(\ell(0)) < 0$ and $\Psi(s^0) = 0$. Moreover,

$$\Psi'(s^0) = \gamma\left[\frac{\partial f(s^0, 0)}{\partial s} + \ell'(s^0)\frac{\partial f(s^0, 0)}{\partial p}\right] - g_4'(0)\,\ell'(s^0).$$

We note from Assumption (A2) that $\frac{\partial f(s^0,0)}{\partial s} = 0$. Then,

$$\Psi'(s^0) = \ell'(s^0)\, g_4'(0)\left(\frac{\gamma}{g_4'(0)}\frac{\partial f(s^0, 0)}{\partial p} - 1\right).$$

From Eqs. (2.17)-(2.18), we get

$$\Psi'(s^0) = \frac{\gamma\pi'(s^0)}{k}\left(\frac{\gamma}{g_4'(0)}\frac{\partial f(s^0, 0)}{\partial p} - 1\right).$$

Therefore, from Assumption (A1), we have $\pi'(s^0) < 0$. Therefore, if $\frac{\gamma}{g_4'(0)}\frac{\partial f(s^0,0)}{\partial p} > 1$, then $\Psi'(s^0) < 0$ and there exists $s^* \in (0, s^0)$ such that $\Psi(s^*) = 0$. Assumptions (A1)-(A3) imply that

$$w^* = \vartheta(s^*) > 0, \quad z^* = \psi(s^*) > 0, \quad u^* = \mu(s^*) > 0, \quad p^* = \ell(s^*).$$

It means that, a persistent-HIV equilibrium $Q^*(s^*, w^*, z^*, u^*, p^*)$ exists when $\frac{\gamma}{g_4'(0)} \frac{\partial f(s^0,0)}{\partial p} > 1$. Hence, we can define the basic reproduction number of system (2.6)-(2.10) as:

$$\mathcal{R}_0 = \frac{\gamma}{g_4'(0)} \frac{\partial f(s^0, 0)}{\partial p}.$$

This shows that if $\mathcal{R}_0 > 1$, then there exists a persistent-HIV equilibrium $Q^*(s^*, w^*, z^*, u^*, p^*)$. □

2.2. Global stability

We define the function $G(x) \geqslant 0$ as $G(x) = x - \ln x - 1$. Hence,

$$\ln x \leqslant x - 1. \tag{2.20}$$

Theorem 2.3. *Suppose that Assumptions* (A1)-(A4) *hold and* $\mathcal{R}_0 \leqslant 1$, *then* Q^0 *of system* (2.6)-(2.10) *is globally asymptotically stable.*

Proof. Consider a Lyapunov functional

$$\begin{aligned} L_n = {} & \frac{1}{h}\left[s_n - s^0 - \int_{s^0}^{s_n} \lim_{p \to 0^+} \frac{f(s^0, p)}{f(\tau, p)} d\tau + \eta_1 w_n + \eta_2 z_n + \eta_3 u_n + \eta_4 p_n + h\eta_4 c g_4(p_n)\right] \\ & + \eta_1 k_1 e^{-\mu_1 \tau_1} \sum_{j=n-m_1}^{n-1} f(s_{j+1}, p_j) + \eta_2 k_2 e^{-\mu_2 \tau_2} \sum_{j=n-m_2}^{n-1} f(s_{j+1}, p_j) + \eta_3 k_3 e^{-\mu_3 \tau_3} \sum_{j=n-m_3}^{n-1} f(s_{j+1}, p_j) \\ & + \eta_2 d \sum_{j=n-m_4}^{n-1} g_2(z_{j+1}) + \eta_3 a \sum_{j=n-m_5}^{n-1} g_3(u_{j+1}). \end{aligned}$$

Hence, $L_n > 0$ for all s_n, w_n, z_n, u_n, $p_n > 0$ and $L_n = 0$ if and only if $s_n = s^0$, $w_n = 0$, $z_n = 0$, $u_n = 0$ and $p_n = 0$. Let $\eta_i, i = 1, 2, 3, 4$, be chosen such as:

$$\begin{aligned} k_1\eta_1 e^{-\mu_1\tau_1} + k_2\eta_2 e^{-\mu_2\tau_2} + k_3\eta_3 e^{-\mu_3\tau_3} = k, \qquad & (\alpha + m)\eta_1 = m\eta_2, \\ \eta_2 = N_z e^{-\mu_4\tau_4}\eta_4, \qquad & \eta_3 = N_u e^{-\mu_5\tau_5}\eta_4. \end{aligned} \tag{2.21}$$

The solution of system (2.21) is given by

$$\eta_1 = \frac{m N_z e^{-\mu_4\tau_4} k}{(\alpha + m)\gamma c}, \qquad \eta_2 = \frac{N_z e^{-\mu_4\tau_4} k}{\gamma c}, \qquad \eta_3 = \frac{N_u e^{-\mu_5\tau_5} k}{\gamma c}, \qquad \eta_4 = \frac{k}{\gamma c}.$$

Compute the difference $\Delta L_n = L_{n+1} - L_n$ as:

$$\begin{aligned} \Delta L_n = {} & \frac{1}{h}\left[s_{n+1} - s^0 - \int_{s^0}^{s_{n+1}} \lim_{p \to 0^+} \frac{f(s^0, p)}{f(\tau, p)} d\tau + \eta_1 w_{n+1} + \eta_2 z_{n+1} + \eta_3 u_{n+1} + \eta_4 p_{n+1} + h\eta_4 c g_4(p_{n+1})\right] \\ & + \eta_1 k_1 e^{-\mu_1\tau_1} \sum_{j=n-m_1+1}^{n} f(s_{j+1}, p_j) + \eta_2 k_2 e^{-\mu_2\tau_2} \sum_{j=n-m_2+1}^{n} f(s_{j+1}, p_j) \\ & + \eta_3 k_3 e^{-\mu_3\tau_3} \sum_{j=n-m_3+1}^{n} f(s_{j+1}, p_j) + \eta_2 d \sum_{j=n-m_4+1}^{n} g_2(z_{j+1}) + \eta_3 a \sum_{j=n-m_5+1}^{n} g_3(u_{j+1}) \\ & - \frac{1}{h}\left[s_n - s^0 - \int_{s^0}^{s_n} \lim_{p \to 0^+} \frac{f(s^0, p)}{f(\tau, p)} d\tau + \eta_1 w_n + \eta_2 z_n + \eta_3 u_n + \eta_4 p_n + h\eta_4 c g_4(p_n)\right] \\ & - \eta_1 k_1 e^{-\mu_1\tau_1} \sum_{j=n-m_1}^{n-1} f(s_{j+1}, p_j) - \eta_2 k_2 e^{-\mu_2\tau_2} \sum_{j=n-m_2}^{n-1} f(s_{j+1}, p_j) - \eta_3 k_3 e^{-\mu_3\tau_3} \sum_{j=n-m_3}^{n-1} f(s_{j+1}, p_j) \end{aligned}$$

$$
\begin{aligned}
&-\eta_2 d \sum_{j=n-m_4}^{n-1} g_2\left(z_{j+1}\right)-\eta_3 a \sum_{j=n-m_5}^{n-1} g_3\left(u_{j+1}\right) \\
=&\frac{1}{h}\left[s_{n+1}-s_n-\int_{s_n}^{s_{n+1}} \lim_{p\to 0^+}\frac{f(s^0,p)}{f(\tau,p)} d\tau+\eta_1\left(w_{n+1}-w_n\right)+\eta_2\left(z_{n+1}-z_n\right)+\eta_3\left(u_{n+1}-u_n\right)\right. \\
&\left.+\eta_4\left(p_{n+1}-p_n\right)+h\eta_4 c\left(g_4\left(p_{n+1}\right)-g_4\left(p_n\right)\right)\right] \\
&+\eta_1 k_1 e^{-\mu_1\tau_1}\left(\sum_{j=n-m_1+1}^{n} f\left(s_{j+1}, p_j\right)-\sum_{j=n-m_1}^{n-1} f\left(s_{j+1}, p_j\right)\right) \\
&+\eta_2 k_2 e^{-\mu_2\tau_2}\left(\sum_{j=n-m_2+1}^{n} f\left(s_{j+1}, p_j\right)-\sum_{j=n-m_2}^{n-1} f\left(s_{j+1}, p_j\right)\right) \\
&+\eta_3 k_3 e^{-\mu_3\tau_3}\left(\sum_{j=n-m_3+1}^{n} f\left(s_{j+1}, p_j\right)-\sum_{j=n-m_3}^{n-1} f\left(s_{j+1}, p_j\right)\right) \\
&+\eta_2 d\left(\sum_{j=n-m_4+1}^{n} g_2\left(z_{j+1}\right)-\sum_{j=n-m_4}^{n-1} g_2\left(z_{j+1}\right)\right)+\eta_3 a\left(\sum_{j=n-m_5+1}^{n} g_3\left(u_{j+1}\right)-\sum_{j=n-m_5}^{n-1} g_3\left(u_{j+1}\right)\right).
\end{aligned}
$$

Using Lemma 3.1 in [16], we get

$$
\lim_{p\to 0^+}\frac{f(s^0,p)}{f(s_{n+1},p)}\left(s_{n+1}-s_n\right) \leqslant \int_{s_n}^{s_{n+1}} \lim_{p\to 0^+}\frac{f(s^0,p)}{f(\tau,p)} d\tau \leqslant \lim_{p\to 0^+}\frac{f(s^0,p)}{f(s_n,p)}\left(s_{n+1}-s_n\right).
$$

Hence

$$
\begin{aligned}
\Delta L_n \leqslant& \frac{1}{h}\left[\left(1-\lim_{p\to 0^+}\frac{f(s^0,p)}{f(s_{n+1},p)}\right)\left(s_{n+1}-s_n\right)+\eta_1\left(w_{n+1}-w_n\right)+\eta_2\left(z_{n+1}-z_n\right)\right. \\
&\left.+\eta_3\left(u_{n+1}-u_n\right)+\eta_4\left(p_{n+1}-p_n\right)+h\eta_4 c\left(g_4\left(p_{n+1}\right)-g_4\left(p_n\right)\right)\right] \\
&+\eta_1 k_1 e^{-\mu_1\tau_1}\left(f\left(s_{n+1}, p_n\right)-f\left(s_{n-m_1+1}, p_{n-m_1}\right)\right) \\
&+\eta_2 k_2 e^{-\mu_2\tau_2}\left(f\left(s_{n+1}, p_n\right)-f\left(s_{n-m_2+1}, p_{n-m_2}\right)\right) \\
&+\eta_3 k_3 e^{-\mu_3\tau_3}\left(f\left(s_{n+1}, p_n\right)-f\left(s_{n-m_3+1}, p_{n-m_3}\right)\right) \\
&+\eta_2 d\left(g_2\left(z_{n+1}\right)-g_2\left(z_{n-m_4+1}\right)\right)+\eta_3 a\left(g_3\left(u_{n+1}\right)-g_3\left(u_{n-m_5+1}\right)\right).
\end{aligned}
$$

From Eqs. (2.6)-(2.10), we have

$$
\begin{aligned}
\Delta L_n \leqslant& \left(1-\lim_{p\to 0^+}\frac{f(s^0,p)}{f(s_{n+1},p)}\right)\left(\pi\left(s_{n+1}\right)-k f(s_{n+1}, p_n)\right) \\
&+\eta_1\left(k_1 e^{-\mu_1\tau_1} f(s_{n-m_1+1}, p_{n-m_1})-(\alpha+m) g_1\left(w_{n+1}\right)\right) \\
&+\eta_2\left(k_2 e^{-\mu_2\tau_2} f(s_{n-m_2+1}, p_{n-m_2})+m g_1\left(w_{n+1}\right)-d g_2\left(z_{n+1}\right)\right) \\
&+\eta_3\left(k_3 e^{-\mu_3\tau_3} f(s_{n-m_3+1}, p_{n-m_3})-a g_3\left(u_{n+1}\right)\right) \\
&+\eta_4\left(N_z e^{-\mu_4\tau_4} d g_2\left(z_{n-m_4+1}\right)+N_u e^{-\mu_5\tau_5} a g_3\left(u_{n-m_5+1}\right)-c g_4\left(p_{n+1}\right)\right)+\eta_4 c\left(g_4\left(p_{n+1}\right)-g_4\left(p_n\right)\right) \\
&+\eta_1 k_1 e^{-\mu_1\tau_1}\left(f\left(s_{n+1}, p_n\right)-f\left(s_{n-m_1+1}, p_{n-m_1}\right)\right) \\
&+\eta_2 k_2 e^{-\mu_2\tau_2}\left(f\left(s_{n+1}, p_n\right)-f\left(s_{n-m_2+1}, p_{n-m_2}\right)\right) \\
&+\eta_3 k_3 e^{-\mu_3\tau_3}\left(f\left(s_{n+1}, p_n\right)-f\left(s_{n-m_3+1}, p_{n-m_3}\right)\right) \\
&+\eta_2 d\left(g_2\left(z_{n+1}\right)-g_2\left(z_{n-m_4+1}\right)\right)+\eta_3 a\left(g_3\left(u_{n+1}\right)-g_3\left(u_{n-m_5+1}\right)\right) \\
=& \left(1-\lim_{p\to 0^+}\frac{f(s^0,p)}{f(s_{n+1},p)}\right)\pi\left(s_{n+1}\right)+\lim_{p\to 0^+}\frac{f(s^0,p)}{f(s_{n+1},p)} k f(s_{n+1}, p_n)-\eta_4 c g_4\left(p_n\right).
\end{aligned}
$$

Using $\pi\left(s^0\right)=0$, we obtain

$$\begin{aligned}\Delta L_n &\leqslant \left(\pi\left(s_{n+1}\right)-\pi\left(s^0\right)\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}kf(s_{n+1},p_n)-\eta_4 c g_4\left(p_n\right)\\ &=\left(\pi\left(s_{n+1}\right)-\pi\left(s^0\right)\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\eta_4 c\left(\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\frac{\gamma f(s_{n+1},p_n)}{g_4\left(p_n\right)}-1\right)g_4\left(p_n\right).\end{aligned}$$

From Assumption (A4) we have

$$\frac{f(s_{n+1},p_n)}{g_4\left(p_n\right)}\leqslant\lim_{p\to 0^+}\frac{f(s_{n+1},p)}{g_4\left(p\right)}=\frac{\partial f(s_{n+1},0)/\partial p}{g_4'\left(0\right)}.$$

Then, we get

$$\begin{aligned}\Delta L_n &\leqslant \left(\pi\left(s_{n+1}\right)-\pi\left(s^0\right)\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\eta_4 c\left(\gamma\frac{\partial f(s^0,0)/\partial p}{g_4'\left(0\right)}-1\right)g_4\left(p_n\right)\\ &=\left(\pi\left(s_{n+1}\right)-\pi\left(s^0\right)\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\eta_4 c\left(\frac{\gamma}{g_4'\left(0\right)}\frac{\partial f(s^0,0)}{\partial p}-1\right)g_4\left(p_n\right)\\ &=\left(\pi\left(s_{n+1}\right)-\pi\left(s^0\right)\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\eta_4 c\left(\mathcal{R}_0-1\right)g_4\left(p_n\right).\end{aligned}$$

From Assumptions (A1) and (A2) we have

$$\left(\pi\left(s_{n+1}\right)-\pi\left(s^0\right)\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)\leqslant 0.$$

Hence, if $\mathcal{R}_0\leqslant 1$, we have $\Delta L_n\leqslant 0$ for all $n\geqslant 0$. Obviously, $\Delta L_n=0$ if and only if $s_n=s^0$ and $(\mathcal{R}_0-1)p_n=0$. We discuss two cases:

- If $\mathcal{R}_0<1$, then $\lim\limits_{n\to\infty}p_n=0$, then we get from Eqs. (2.7)-(2.9); $\lim\limits_{n\to\infty}w_n=0$, $\lim\limits_{n\to\infty}z_n=0$ and $\lim\limits_{n\to\infty}u_n=0$.
- If $\mathcal{R}_0=1$, then by using $\lim\limits_{n\to\infty}s_n=s^0$ and from Eq. (2.6), we obtain $f(s^0,p_n)=0$. Because $s^0>0$, we have $f(s^0,p_n)>f(0,p_n)=0$ (use Assumptions (A1) and (A2)). Thus, $\lim\limits_{n\to\infty}p_n=0$. Therefore, Q^0 is globally asymptotically stable. □

Remark 2.4. Assumptions (A2)-(A4) imply that

$$\left(\frac{f(s,p)}{g_4(p)}-\frac{f(s,p^*)}{g_4\left(p^*\right)}\right)\left(f(s,p)-f(s,p^*)\right)\leqslant 0,$$

which yields

$$\left(\frac{f(s,p)}{f(s,p^*)}-\frac{g_4\left(p\right)}{g_4\left(p^*\right)}\right)\left(1-\frac{f(s,p^*)}{f(s,p)}\right)\leqslant 0.$$

Theorem 2.5. *Suppose that Assumptions* (A1)-(A4) *hold and* $\mathcal{R}_0>1$, *then* Q^* *of system* (2.6)-(2.10) *is globally asymptotically stable.*

Proof. Consider

$$\begin{aligned}U_n(s_n,w_n,z_n,u_n,p_n)=\frac{1}{h}\Bigg[&s_n-s^*-\int_{s^*}^{s_n}\frac{f(s^*,p^*)}{f(\tau,p^*)}d\tau+\eta_1\left(w_n-w^*-\int_{w^*}^{w_n}\frac{g_1(w^*)}{g_1(\tau)}d\tau\right)\\ &+\eta_2\left(z_n-z^*-\int_{z^*}^{z_n}\frac{g_2(z^*)}{g_2(\tau)}d\tau\right)+\eta_3\left(u_n-u^*-\int_{u^*}^{u_n}\frac{g_3(u^*)}{g_3(\tau)}d\tau\right)\end{aligned}$$

$$
\begin{aligned}
&+\eta_4\left(p_n-p^*-\int_{p^*}^{p_n}\frac{g_4(p^*)}{g_4(\tau)}d\tau\right)+h\eta_4 c g_4(p^*)G\left(\frac{g_4\left(p_n\right)}{g_4(p^*)}\right)\Bigg]\\
&+\eta_1 k_1 e^{-\mu_1\tau_1}f\left(s^*,p^*\right)\sum_{j=n-m_1}^{n-1}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)\\
&+\eta_2 k_2 e^{-\mu_2\tau_2}f\left(s^*,p^*\right)\sum_{j=n-m_2}^{n-1}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)\\
&+\eta_3 k_3 e^{-\mu_3\tau_3}f\left(s^*,p^*\right)\sum_{j=n-m_3}^{n-1}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)\\
&+\eta_2 d g_2\left(z^*\right)\sum_{j=n-m_4}^{n-1}G\left(\frac{g_2\left(z_{j+1}\right)}{g_2\left(z^*\right)}\right)+\eta_3 a g_3\left(u^*\right)\sum_{j=n-m_5}^{n-1}G\left(\frac{g_3\left(u_{j+1}\right)}{g_3\left(u^*\right)}\right).
\end{aligned}
$$

Clearly, $U_n(s_n,w_n,z_n,u_n,p_n)>0$ for all $s_n,w_n,z_n,u_n,p_n>0$ and $U_n(s^*,w^*,z^*,u^*,p^*)=0$. Computing $\Delta U_n=U_{n+1}-U_n$ as:

$$
\begin{aligned}
\Delta U_n=&\frac{1}{h}\Bigg[s_{n+1}-s^*-\int_{s^*}^{s_{n+1}}\frac{f(s^*,p^*)}{f(\tau,p^*)}d\tau+\eta_1\left(w_{n+1}-w^*-\int_{w^*}^{w_{n+1}}\frac{g_1(w^*)}{g_1(\tau)}d\tau\right)\\
&+\eta_2\left(z_{n+1}-z^*-\int_{z^*}^{z_{n+1}}\frac{g_2(z^*)}{g_2(\tau)}d\tau\right)+\eta_3\left(u_{n+1}-u^*-\int_{u^*}^{u_{n+1}}\frac{g_3(u^*)}{g_3(\tau)}d\tau\right)\\
&+\eta_4\left(p_{n+1}-p^*-\int_{p^*}^{p_n+1}\frac{g_4(p^*)}{g_4(\tau)}d\tau\right)+h\eta_4 c g_4(p^*)G\left(\frac{g_4\left(p_{n+1}\right)}{g_4(p^*)}\right)\Bigg]\\
&+\eta_1 k_1 e^{-\mu_1\tau_1}f\left(s^*,p^*\right)\sum_{j=n-m_1+1}^{n}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)\\
&+\eta_2 k_2 e^{-\mu_2\tau_2}f\left(s^*,p^*\right)\sum_{j=n-m_2+1}^{n}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)\\
&+\eta_3 k_3 e^{-\mu_3\tau_3}f\left(s^*,p^*\right)\sum_{j=n-m_3+1}^{n}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)+\eta_2 d g_2\left(z^*\right)\sum_{j=n-m_4+1}^{n}G\left(\frac{g_2\left(z_{j+1}\right)}{g_2\left(z^*\right)}\right)\\
&+\eta_3 a g_3\left(u^*\right)\sum_{j=n-m_5+1}^{n}G\left(\frac{g_3\left(u_{j+1}\right)}{g_3\left(u^*\right)}\right)\\
&-\frac{1}{h}\Bigg[s_n-s^*-\int_{s^*}^{s_n}\frac{f(s^*,p^*)}{f(\tau,p^*)}d\tau+\eta_1\left(w_n-w^*-\int_{w^*}^{w_n}\frac{g_1(w^*)}{g_1(\tau)}d\tau\right)\\
&+\eta_2\left(z_n-z^*-\int_{z^*}^{z_n}\frac{g_2(z^*)}{g_2(\tau)}d\tau\right)+\eta_3\left(u_n-u^*-\int_{u^*}^{u_n}\frac{g_3(u^*)}{g_3(\tau)}d\tau\right)\\
&+\eta_4\left(p_n-p^*-\int_{p^*}^{p_n}\frac{g_4(p^*)}{g_4(\tau)}d\tau\right)+h\eta_4 c g_4(p^*)G\left(\frac{g_4\left(p_n\right)}{g_4(p^*)}\right)\Bigg]\\
&-\eta_1 k_1 e^{-\mu_1\tau_1}f\left(s^*,p^*\right)\sum_{j=n-m_1}^{n-1}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)-\eta_2 k_2 e^{-\mu_2\tau_2}f\left(s^*,p^*\right)\sum_{j=n-m_2}^{n-1}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)\\
&-\eta_3 k_3 e^{-\mu_3\tau_3}f\left(s^*,p^*\right)\sum_{j=n-m_3}^{n-1}G\left(\frac{f\left(s_{j+1},p_j\right)}{f\left(s^*,p^*\right)}\right)-\eta_2 d g_2\left(z^*\right)\sum_{j=n-m_4}^{n-1}G\left(\frac{g_2\left(z_{j+1}\right)}{g_2\left(z^*\right)}\right)
\end{aligned}
$$

$$-\eta_3 a g_3(u^*)\sum_{j=n-m_5}^{n-1} G\left(\frac{g_3(u_{j+1})}{g_3(u^*)}\right),$$

$$\begin{aligned}\Delta U_n =& \frac{1}{h}\left[s_{n+1}-s_n-\int_{s_n}^{s_{n+1}}\frac{f(s^*,p^*)}{f(\tau,p^*)}d\tau+\eta_1\left(w_{n+1}-w_n-\int_{w_n}^{w_{n+1}}\frac{g_1(w^*)}{g_1(\tau)}d\tau\right)\right.\\ &+\eta_2\left(z_{n+1}-z_n-\int_{z_n}^{z_{n+1}}\frac{g_2(z^*)}{g_2(\tau)}d\tau\right)+\eta_3\left(u_{n+1}-u_n-\int_{u_n}^{u_{n+1}}\frac{g_3(u^*)}{g_3(\tau)}d\tau\right)\\ &\left.+\eta_4\left(p_{n+1}-p_n-\int_{p_n}^{p_{n+1}}\frac{g_4(p^*)}{g_4(\tau)}d\tau\right)+h\eta_4 c g_4(p^*)\left(G\left(\frac{g_4(p_{n+1})}{g_4(p^*)}\right)-G\left(\frac{g_4(p_n)}{g_4(p^*)}\right)\right)\right]\\ &+\eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*)\left[\sum_{j=n-m_1+1}^{n} G\left(\frac{f(s_{j+1},p_j)}{f(s^*,p^*)}\right)-\sum_{j=n-m_1}^{n-1} G\left(\frac{f(s_{j+1},p_j)}{f(s^*,p^*)}\right)\right]\\ &+\eta_2 k_2 e^{-\mu_2\tau_2} f(s^*,p^*)\left[\sum_{j=n-m_2+1}^{n} G\left(\frac{f(s_{j+1},p_j)}{f(s^*,p^*)}\right)-\sum_{j=n-m_2}^{n-1} G\left(\frac{f(s_{j+1},p_j)}{f(s^*,p^*)}\right)\right]\\ &+\eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\left[\sum_{j=n-m_3+1}^{n} G\left(\frac{f(s_{j+1},p_j)}{f(s^*,p^*)}\right)-\sum_{j=n-m_3}^{n-1} G\left(\frac{f(s_{j+1},p_j)}{f(s^*,p^*)}\right)\right]\\ &+\eta_2 d g_2(z^*)\left[\sum_{j=n-m_4+1}^{n} G\left(\frac{g_2(z_{j+1})}{g_2(z^*)}\right)-\sum_{j=n-m_4}^{n-1} G\left(\frac{g_2(z_{j+1})}{g_2(z^*)}\right)\right]\\ &+\eta_3 a g_3(u^*)\left[\sum_{j=n-m_5+1}^{n} G\left(\frac{g_3(u_{j+1})}{g_3(u^*)}\right)-\sum_{j=n-m_5}^{n-1} G\left(\frac{g_3(u_{j+1})}{g_3(u^*)}\right)\right].\end{aligned}$$

From Lemma 3.1 in [16], we have

$$\left(1-\frac{f(s^*,p^*)}{f(s_n,p^*)}\right)(s_{n+1}-s_n)\leqslant s_{n+1}-s_n-\int_{s_n}^{s_{n+1}}\frac{f(s^*,p^*)}{f(\tau,p^*)}d\tau\leqslant\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(s_{n+1}-s_n),$$
$$\left(1-\frac{g_i(\rho^*)}{g_i(\rho_n)}\right)(\rho_{n+1}-\rho_n)\leqslant \rho_{n+1}-\rho_n-\int_{\rho_n}^{\rho_{n+1}}\frac{g_i(\rho^*)}{g_i(\tau)}d\tau\leqslant\left(1-\frac{g_i(\rho^*)}{g_i(\rho_{n+1})}\right)(\rho_{n+1}-\rho_n),$$

$i=1,\dots,4$. Then

$$\begin{aligned}\Delta U_n \leqslant& \frac{1}{h}\left[\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(s_{n+1}-s_n)+\eta_1\left(1-\frac{g_1(w^*)}{g_1(w_{n+1})}\right)(w_{n+1}-w_n)\right.\\ &+\eta_2\left(1-\frac{g_2(z^*)}{g_2(z_{n+1})}\right)(z_{n+1}-z_n)+\eta_3\left(1-\frac{g_3(u^*)}{g_3(u_{n+1})}\right)(u_{n+1}-u_n)\\ &\left.+\eta_4\left(1-\frac{g_4(p^*)}{g_4(p_{n+1})}\right)(p_{n+1}-p_n)+h\eta_4 c g_4(p^*)\left(\frac{g_4(p_{n+1})}{g_4(p^*)}-\frac{g_4(p_n)}{g_4(p^*)}+\ln\left(\frac{g_4(p_n)}{g_4(p_{n+1})}\right)\right)\right]\\ &+\eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*)\left[\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}-\frac{f(s_{n-m_1+1},p_{n-m_1})}{f(s^*,p^*)}+\ln\left(\frac{f(s_{n-m_1+1},p_{n-m_1})}{f(s_{n+1},p_n)}\right)\right]\\ &+\eta_2 k_2 e^{-\mu_2\tau_2} f(s^*,p^*)\left[\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}-\frac{f(s_{n-m_2+1},p_{n-m_2})}{f(s^*,p^*)}+\ln\left(\frac{f(s_{n-m_2+1},p_{n-m_2})}{f(s_{n+1},p_n)}\right)\right]\\ &+\eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\left[\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}-\frac{f(s_{n-m_3+1},p_{n-m_3})}{f(s^*,p^*)}+\ln\left(\frac{f(s_{n-m_3+1},p_{n-m_3})}{f(s_{n+1},p_n)}\right)\right]\\ &+\eta_2 d g_2(z^*)\left[\frac{g_2(z_{n+1})}{g_2(z^*)}-\frac{g_2(z_{n-m_4+1})}{g_2(z^*)}+\ln\left(\frac{g_2(z_{n-m_4+1})}{g_2(z_{n+1})}\right)\right]\end{aligned}$$

$$+\eta_3 a g_3(u^*)\left[\frac{g_3(u_{n+1})}{g_3(u^*)}-\frac{g_3(u_{n-m_5+1})}{g_3(u^*)}+\ln\left(\frac{g_3(u_{n-m_5+1})}{g_3(u_{n+1})}\right)\right].$$

From Eqs. (2.6)-(2.10), we have

$$\begin{aligned}
\Delta U_n \leqslant{} & \left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(\pi(s_{n+1})-kf(s_{n+1},p_n)) \\
&+\eta_1\left(1-\frac{g_1(w^*)}{g_1(w_{n+1})}\right)\left(k_1e^{-\mu_1\tau_1}f(s_{n-m_1+1},p_{n-m_1})-(\alpha+m)\,g_1(w_{n+1})\right) \\
&+\eta_2\left(1-\frac{g_2(z^*)}{g_2(z_{n+1})}\right)\left(k_2e^{-\mu_2\tau_2}f(s_{n-m_2+1},p_{n-m_2})+mg_1(w_{n+1})-dg_2(z_{n+1})\right) \\
&+\eta_3\left(1-\frac{g_3(u^*)}{g_3(u_{n+1})}\right)\left(k_3e^{-\mu_3\tau_3}f(s_{n-m_3+1},p_{n-m_3})-ag_3(u_{n+1})\right) \\
&+\eta_4\left(1-\frac{g_4(p^*)}{g_4(p_{n+1})}\right)\left(N_ze^{-\mu_4\tau_4}dg_2(z_{n-m_4+1})+N_ue^{-\mu_5\tau_5}ag_3(u_{n-m_5+1})-cg_4(p_{n+1})\right) \\
&+\eta_4 c\left(g_4(p_{n+1})-g_4(p_n)+g_4(p^*)\ln\left(\frac{g_4(p_n)}{g_4(p_{n+1})}\right)\right) \\
&+\eta_1k_1e^{-\mu_1\tau_1}f(s^*,p^*)\left[\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}-\frac{f(s_{n-m_1+1},p_{n-m_1})}{f(s^*,p^*)}+\ln\left(\frac{f(s_{n-m_1+1},p_{n-m_1})}{f(s_{n+1},p_n)}\right)\right] \\
&+\eta_2k_2e^{-\mu_2\tau_2}f(s^*,p^*)\left[\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}-\frac{f(s_{n-m_2+1},p_{n-m_2})}{f(s^*,p^*)}+\ln\left(\frac{f(s_{n-m_2+1},p_{n-m_2})}{f(s_{n+1},p_n)}\right)\right] \\
&+\eta_3k_3e^{-\mu_3\tau_3}f(s^*,p^*)\left[\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}-\frac{f(s_{n-m_3+1},p_{n-m_3})}{f(s^*,p^*)}+\ln\left(\frac{f(s_{n-m_3+1},p_{n-m_3})}{f(s_{n+1},p_n)}\right)\right] \\
&+\eta_2 dg_2(z^*)\left[\frac{g_2(z_{n+1})}{g_2(z^*)}-\frac{g_2(z_{n-m_4+1})}{g_2(z^*)}+\ln\left(\frac{g_2(z_{n-m_4+1})}{g_2(z_{n+1})}\right)\right] \\
&+\eta_3 ag_3(u^*)\left[\frac{g_3(u_{n+1})}{g_3(u^*)}-\frac{g_3(u_{n-m_5+1})}{g_3(u^*)}+\ln\left(\frac{g_3(u_{n-m_5+1})}{g_3(u_{n+1})}\right)\right],
\end{aligned}$$

$$\begin{aligned}
\Delta U_n \leqslant{} & \left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(\pi(s_{n+1})-\pi(s^*))+\pi(s^*)\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right) \\
&+\frac{kf(s^*,p^*)}{f(s_{n+1},p^*)}f(s_{n+1},p_n)-\eta_1k_1e^{-\mu_1\tau_1}\frac{g_1(w^*)}{g_1(w_{n+1})}f(s_{n-m_1+1},p_{n-m_1})+\eta_1(\alpha+m)\,g_1(w^*) \\
&-\eta_2k_2e^{-\mu_2\tau_2}\frac{g_2(z^*)}{g_2(z_{n+1})}f(s_{n-m_2+1},p_{n-m_2})-\eta_2 m\frac{g_2(z^*)}{g_2(z_{n+1})}g_1(w_{n+1})+\eta_2dg_2(z^*) \\
&-\eta_3k_3e^{-\mu_3\tau_3}\frac{g_3(u^*)}{g_3(u_{n+1})}f(s_{n-m_3+1},p_{n-m_3})+\eta_3ag_3(u^*)-\eta_4dN_ze^{-\mu_4\tau_4}\frac{g_4(p^*)}{g_4(p_{n+1})}g_2(z_{n-m_4+1}) \\
&-\eta_4aN_ue^{-\mu_5\tau_5}\frac{g_4(p^*)}{g_4(p_{n+1})}g_3(u_{n-m_5+1})+\eta_4cg_4(p^*)-\eta_4cg_4(p_n)+\eta_4cg_4(p^*)\ln\left(\frac{g_4(p_n)}{g_4(p_{n+1})}\right) \\
&+\eta_1k_1e^{-\mu_1\tau_1}f(s^*,p^*)\ln\left(\frac{f(s_{n-m_1+1},p_{n-m_1})}{f(s_{n+1},p_n)}\right)+\eta_2k_2e^{-\mu_2\tau_2}f(s^*,p^*)\ln\left(\frac{f(s_{n-m_2+1},p_{n-m_2})}{f(s_{n+1},p_n)}\right) \\
&+\eta_3k_3e^{-\mu_3\tau_3}f(s^*,p^*)\ln\left(\frac{f(s_{n-m_3+1},p_{n-m_3})}{f(s_{n+1},p_n)}\right)+\eta_2dg_2(z^*)\ln\left(\frac{g_2(z_{n-m_4+1})}{g_2(z_{n+1})}\right) \\
&+\eta_3ag_3(u^*)\ln\left(\frac{g_3(u_{n-m_5+1})}{g_3(u_{n+1})}\right).
\end{aligned}$$

Using the conditions of Q^*

$$\pi(s^*)=kf(s^*,p^*),$$

$$\begin{aligned} k_1 e^{-\mu_1\tau_1} f(s^*,p^*) &= (\alpha+m) g_1(w^*),\\ k_2 e^{-\mu_2\tau_2} f(s^*,p^*) + m g_1(w^*) &= d g_2(z^*),\\ k_3 e^{-\mu_3\tau_3} f(s^*,p^*) &= a g_3(u^*),\\ N_z e^{-\mu_4\tau_4} d g_2(z^*) + N_u e^{-\mu_5\tau_5} a g_3(u^*) &= c g_4(p^*), \end{aligned}$$

we get

$$\begin{aligned} k f(s^*,p^*) &= \eta_2 d g_2(z^*) + \eta_3 a g_3(u^*) = \eta_4 c g_4(p^*),\\ \left(\eta_1 k_1 e^{-\mu_1\tau_1} + \eta_2 k_2 e^{-\mu_2\tau_2}\right) f(s^*,p^*) &= \eta_2 d g_2(z^*), \end{aligned}$$

and

$$\begin{aligned} \Delta U_n \leqslant{}& \left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(\pi(s_{n+1})-\pi(s^*)) + k f(s^*,p^*)\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)\\ &+ k f(s^*,p^*)\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)} - \eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*)\frac{f\left(s_{n-m_1+1},p_{n-m_1}\right) g_1(w^*)}{f(s^*,p^*) g_1(w_{n+1})}\\ &+ \eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*) - \eta_2 k_2 e^{-\mu_2\tau_2} f(s^*,p^*)\frac{f\left(s_{n-m_2+1},p_{n-m_2}\right) g_2(z^*)}{f(s^*,p^*) g_2(z_{n+1})}\\ &- \eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*)\frac{g_2(z^*) g_1(w_{n+1})}{g_2(z_{n+1}) g_1(w^*)} + \left(\eta_1 k_1 e^{-\mu_1\tau_1} + \eta_2 k_2 e^{-\mu_2\tau_2}\right) f(s^*,p^*)\\ &- \eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\frac{f\left(s_{n-m_3+1},p_{n-m_3}\right) g_3(u^*)}{f(s^*,p^*) g_3(u_{n+1})} + \eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\\ &- \left(\eta_1 k_1 e^{-\mu_1\tau_1} + \eta_2 k_2 e^{-\mu_2\tau_2}\right) f(s^*,p^*)\frac{g_4(p^*) g_2\left(z_{n-m_4+1}\right)}{g_4(p_{n+1}) g_2(z^*)}\\ &- \eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\frac{g_4(p^*) g_3\left(u_{n-m_5+1}\right)}{g_4(p_{n+1}) g_3(u^*)} + k f(s^*,p^*) - k f(s^*,p^*)\frac{g_4(p_n)}{g_4(p^*)}\\ &+ k f(s^*,p^*)\ln\left(\frac{g_4(p_n)}{g_4(p_{n+1})}\right) + \eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*)\ln\left(\frac{f\left(s_{n-m_1+1},p_{n-m_1}\right)}{f(s_{n+1},p_n)}\right)\\ &+ \eta_2 k_2 e^{-\mu_2\tau_2} f(s^*,p^*)\ln\left(\frac{f\left(s_{n-m_2+1},p_{n-m_2}\right)}{f(s_{n+1},p_n)}\right) + \eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\ln\left(\frac{f\left(s_{n-m_3+1},p_{n-m_3}\right)}{f(s_{n+1},p_n)}\right)\\ &+ \left(\eta_1 k_1 e^{-\mu_1\tau_1} + \eta_2 k_2 e^{-\mu_2\tau_2}\right) f(s^*,p^*)\ln\left(\frac{g_2\left(z_{n-m_4+1}\right)}{g_2(z_{n+1})}\right)\\ &+ \eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\ln\left(\frac{g_3\left(u_{n-m_5+1}\right)}{g_3(u_{n+1})}\right)\\ ={}& \left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(\pi(s_{n+1})-\pi(s^*))\\ &+ \eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*)\left[5-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)} - \frac{f\left(s_{n-m_1+1},p_{n-m_1}\right) g_1(w^*)}{f(s^*,p^*) g_1(w_{n+1})} - \frac{g_2(z^*) g_1(w_{n+1})}{g_2(z_{n+1}) g_1(w^*)}\right.\\ &\left.-\frac{g_4(p^*) g_2\left(z_{n-m_4+1}\right)}{g_4(p_{n+1}) g_2(z^*)} - \frac{g_4(p_n) f(s_{n+1},p^*)}{g_4(p^*) f(s_{n+1},p_n)} + \ln\left(\frac{g_4(p_n) f\left(s_{n-m_1+1},p_{n-m_1}\right) g_2\left(z_{n-m_4+1}\right)}{g_4(p_{n+1}) f(s_{n+1},p_n) g_2(z_{n+1})}\right)\right]\\ &+ \eta_2 k_2 e^{-\mu_2\tau_2} f(s^*,p^*)\left[4-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)} - \frac{f\left(s_{n-m_2+1},p_{n-m_2}\right) g_2(z^*)}{f(s^*,p^*) g_2(z_{n+1})} - \frac{g_4(p^*) g_2\left(z_{n-m_4+1}\right)}{g_4(p_{n+1}) g_2(z^*)}\right.\\ &\left.-\frac{g_4(p_n) f(s_{n+1},p^*)}{g_4(p^*) f(s_{n+1},p_n)} + \ln\left(\frac{g_4(p_n) f\left(s_{n-m_2+1},p_{n-m_2}\right) g_2\left(z_{n-m_4+1}\right)}{g_4(p_{n+1}) f(s_{n+1},p_n) g_2(z_{n+1})}\right)\right] \end{aligned}$$

$$
\begin{aligned}
&+\eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\left[4-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}-\frac{f(s_{n-m_3+1},p_{n-m_3})g_3(u^*)}{f(s^*,p^*)g_3(u_{n+1})}-\frac{g_4(p^*)g_3\left(u_{n-m_5+1}\right)}{g_4(p_{n+1})g_3(u^*)}\right.\\
&\left.-\frac{g_4\left(p_n\right)f(s_{n+1},p^*)}{g_4\left(p^*\right)f(s_{n+1},p_n)}+\ln\left(\frac{g_4\left(p_n\right)f(s_{n-m_3+1},p_{n-m_3})g_3\left(u_{n-m_5+1}\right)}{g_4\left(p_{n+1}\right)f(s_{n+1},p_n)g_3(u_{n+1})}\right)\right]\\
&+kf(s^*,p^*)\left[-1+\frac{g_4\left(p_n\right)f(s_{n+1},p^*)}{g_4\left(p^*\right)f(s_{n+1},p_n)}+\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)}-\frac{g_4\left(p_n\right)}{g_4(p^*)}\right],
\end{aligned}
$$

$$
\begin{aligned}
\Delta U_n \leqslant{}& \left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)\left(\pi\left(s_{n+1}\right)-\pi\left(s^*\right)\right)-\eta_1 k_1 e^{-\mu_1\tau_1} f(s^*,p^*)\left[G\left(\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)\right.\\
&+G\left(\frac{f(s_{n-m_1+1},p_{n-m_1})g_1(w^*)}{f(s^*,p^*)g_1(w_{n+1})}\right)+G\left(\frac{g_2(z^*)g_1\left(w_{n+1}\right)}{g_2(z_{n+1})g_1(w^*)}\right)+G\left(\frac{g_4(p^*)g_2\left(z_{n-m_4+1}\right)}{g_4(p_{n+1})g_2(z^*)}\right)\\
&\left.+G\left(\frac{g_4\left(p_n\right)f(s_{n+1},p^*)}{g_4\left(p^*\right)f(s_{n+1},p_n)}\right)\right]\\
&-\eta_2 k_2 e^{-\mu_2\tau_2} f(s^*,p^*)\left[G\left(\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)+G\left(\frac{f(s_{n-m_2+1},p_{n-m_2})g_2(z^*)}{f(s^*,p^*)g_2(z_{n+1})}\right)\right.\\
&\left.+G\left(\frac{g_4(p^*)g_2\left(z_{n-m_4+1}\right)}{g_4(p_{n+1})g_2(z^*)}\right)+G\left(\frac{g_4\left(p_n\right)f(s_{n+1},p^*)}{g_4\left(p^*\right)f(s_{n+1},p_n)}\right)\right]\\
&-\eta_3 k_3 e^{-\mu_3\tau_3} f(s^*,p^*)\left[G\left(\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)+G\left(\frac{f(s_{n-m_3+1},p_{n-m_3})g_3(u^*)}{f(s^*,p^*)g_3(u_{n+1})}\right)\right.\\
&\left.+G\left(\frac{g_4(p^*)g_3\left(u_{n-m_5+1}\right)}{g_4(p_{n+1})g_3(u^*)}\right)+G\left(\frac{g_4\left(p_n\right)f(s_{n+1},p^*)}{g_4\left(p^*\right)f(s_{n+1},p_n)}\right)\right]\\
&+kf(s^*,p^*)\left[-1+\frac{g_4\left(p_n\right)f(s_{n+1},p^*)}{g_4\left(p^*\right)f(s_{n+1},p_n)}+\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)}-\frac{g_4\left(p_n\right)}{g_4(p^*)}\right].
\end{aligned}
$$

Assumptions (A1), (A2), and (A4) imply that

$$\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)\left(\pi\left(s_{n+1}\right)-\pi\left(s^*\right)\right)\leqslant 0.$$

Based on the Remark 2.4, we have

$$-1+\frac{g_4\left(p_n\right)f(s_{n+1},p^*)}{g_4\left(p^*\right)f(s_{n+1},p_n)}+\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)}-\frac{g_4\left(p_n\right)}{g_4(p^*)}=\left(1-\frac{f(s_{n+1},p^*)}{f(s_{n+1},p_n)}\right)\left(\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)}-\frac{g_4\left(p_n\right)}{g_4\left(p^*\right)}\right)\leqslant 0.$$

Thus, U_n is monotone decreasing sequence. Because $U_n \geqslant 0$, there is a limit $\lim_{n\to\infty} U_n \geqslant 0$. Therefore, $\lim_{n\to\infty} \Delta U_n = 0$, which implies that $\lim_{n\to\infty} s_n = s^*$, $\lim_{n\to\infty} w_n = w^*$, $\lim_{n\to\infty} z_n = z^*$, $\lim_{n\to\infty} u_n = u^*$ and $\lim_{n\to\infty} p_n = p^*$. □

Remark 2.6. We outline some different forms of the general functions presented in model (2.6)-(2.10) and satisfy Assumptions (A1)-(A4).

- Intrinsic growth rate function $\pi(s)$: Linear form $\pi(s) = \beta - \delta s$ [24], Logistic growth form $\pi(s) = \beta - \delta s + rs\left(1-\frac{s}{s_{max}}\right)$ [4], where the parameter $r > 0$ is the maximum proliferation rate of susceptible cells. The parameter $s_{max} > 0$ is the maximum level of susceptible cells concentration in the body. If the concentration arrives at s_{max}, it should decreases. Moreover, it can be assumed that $r < \delta$

- Incidence rate function $f(s,p)$: Bilinear incidence κsp [24], Saturated incidence $\frac{\kappa sp}{1+\eta p}$ [30], Beddington-DeAngelis incidence $\frac{\kappa sp}{1+\eta p+\varpi s}$, [18], Crowley-Martin incidence $\frac{\kappa sp}{(1+\eta p)(1+\varpi s)}$ [33], and Hill-type incidence $\frac{\kappa s^m p}{\zeta^m+s^m}$ [1], where κ, η, ϖ, ζ, and m are positive constants.

- Function $g_i(\rho)$: Linear $g_i(\rho) = \upsilon_j \rho$ [12, 24], Quadratic $g_i(\rho) = \upsilon_i\rho + \overline{\upsilon}_i\rho^2$ where υ_i and $\overline{\upsilon}_i$ are positive constants.

3. Numerical simulations

We perform our simulation by choosing the following functions

$$\pi(s) = \beta - \delta s, \qquad f(s,p) = \frac{sp}{r+s}, \qquad g_j(\rho) = \rho\ , j = 1,\dots,4, \tag{3.1}$$

where $r > 0$. System (2.6)-(2.10) becomes

$$\frac{s_{n+1}-s_n}{h} = \beta - \delta s_{n+1} - k\frac{s_{n+1}p_n}{r+s_{n+1}}, \tag{3.2}$$

$$\frac{w_{n+1}-w_n}{h} = k_1 e^{-\mu_1\tau_1}\frac{s_{n-m_1+1}p_{n-m_1}}{r+s_{n-m_1+1}} - (\alpha+m)w_{n+1}, \tag{3.3}$$

$$\frac{z_{n+1}-z_n}{h} = k_2 e^{-\mu_2\tau_2}\frac{s_{n-m_2+1}p_{n-m_2}}{r+s_{n-m_2+1}} + mw_{n+1} - dz_{n+1}, \tag{3.4}$$

$$\frac{u_{n+1}-u_n}{h} = k_3 e^{-\mu_3\tau_3}\frac{s_{n-m_3+1}p_{n-m_3}}{r+s_{n-m_3+1}} - au_{n+1}, \tag{3.5}$$

$$\frac{p_{n+1}-p_n}{h} = N_z e^{-\mu_4\tau_4} dz_{n-m_4+1} + N_u e^{-\mu_5\tau_5} au_{n-m_5+1} - cp_{n+1}. \tag{3.6}$$

For this system, the basic reproduction number is given by

$$\mathcal{R}_0 = \frac{\gamma\beta}{r\delta+\beta}.$$

We show that the functions given by (3.1) will satisfy assumptions (A1)-(A4). We have $\pi(0) = \beta > 0$, $\pi(s^0) = 0$ and $\pi'(s) = -\delta < 0$. It follows that, $\pi(s) > 0$ for all $s \in [0, s^0)$. Moreover, (A1) (iii) is satisfied with $b = \beta$ and $\bar{b} = \delta$. Thus, (A1) is satisfied. We also have

$$\begin{aligned}
f(s,p) &= \frac{sp}{r+s} > 0, \text{ and } f(0,p) = f(s,0) = 0 \text{ for all } s > 0, p > 0,\\
\frac{\partial f(s,p)}{\partial s} &= \frac{rp}{(r+s)^2} > 0 \text{ for all } s > 0, \text{ and } p > 0,\\
\frac{\partial f(s,p)}{\partial p} &= \frac{s}{r+s} > 0 \text{ for all } s > 0, \text{ and } p > 0,\\
\frac{\partial f(s,0)}{\partial p} &= \frac{s}{r+s} > 0, \text{ for all } s > 0,\\
\frac{d}{ds}\left(\frac{\partial f(s,0)}{\partial p}\right) &= \frac{r}{(r+s)^2} > 0, \text{ for all } s > 0.
\end{aligned}$$

Therefore, Assumption (A2) is satisfied. Moreover, We have $g_j(\rho) = \rho > 0$ for all $\rho > 0$ and $g_j(0) = 0$, $j = 1,\dots,4$. We also have, $g_j'(\rho) = 1 > 0$, $j = 1,\dots,4$ for all $\rho \geqslant 0$. Then Assumption (A3) is satisfied, where $\upsilon_j = 1$, $j = 1,\dots,4$. Finally, we have

$$\frac{\partial}{\partial p}\left(\frac{f(s,p)}{g_4(p)}\right) = 0, \text{ for all } s > 0, \text{ and } p > 0.$$

Therefore, Assumption (A4) hold true and hence Theorems 2.3 and 2.5 are applicable.

We use the following data: $\alpha = 0.4$, $\beta = 10$, $\delta = 0.01$, $d = 0.2$, $a = 0.1$, $c = 6$, $m = 0.2$, $r = 50$, $h = 0.1$ $k_i = 0.02$ $(i = 1,2,3)$ and $\mu_i = 0.5$ $(i = 1,\dots,5)$. The other parameters will be chosen below. Let us consider the initial values

1V1: $\psi_\kappa^1 = 600$, $\psi_\kappa^2 = 7$, $\psi_\kappa^3 = 15$, $\psi_\kappa^4 = 50$, $\psi_\kappa^5 = 70$;
2V2: $\psi_\kappa^1 = 400$, $\psi_\kappa^2 = 4$, $\psi_\kappa^3 = 10$, $\psi_\kappa^4 = 30$, $\psi_\kappa^5 = 50$;

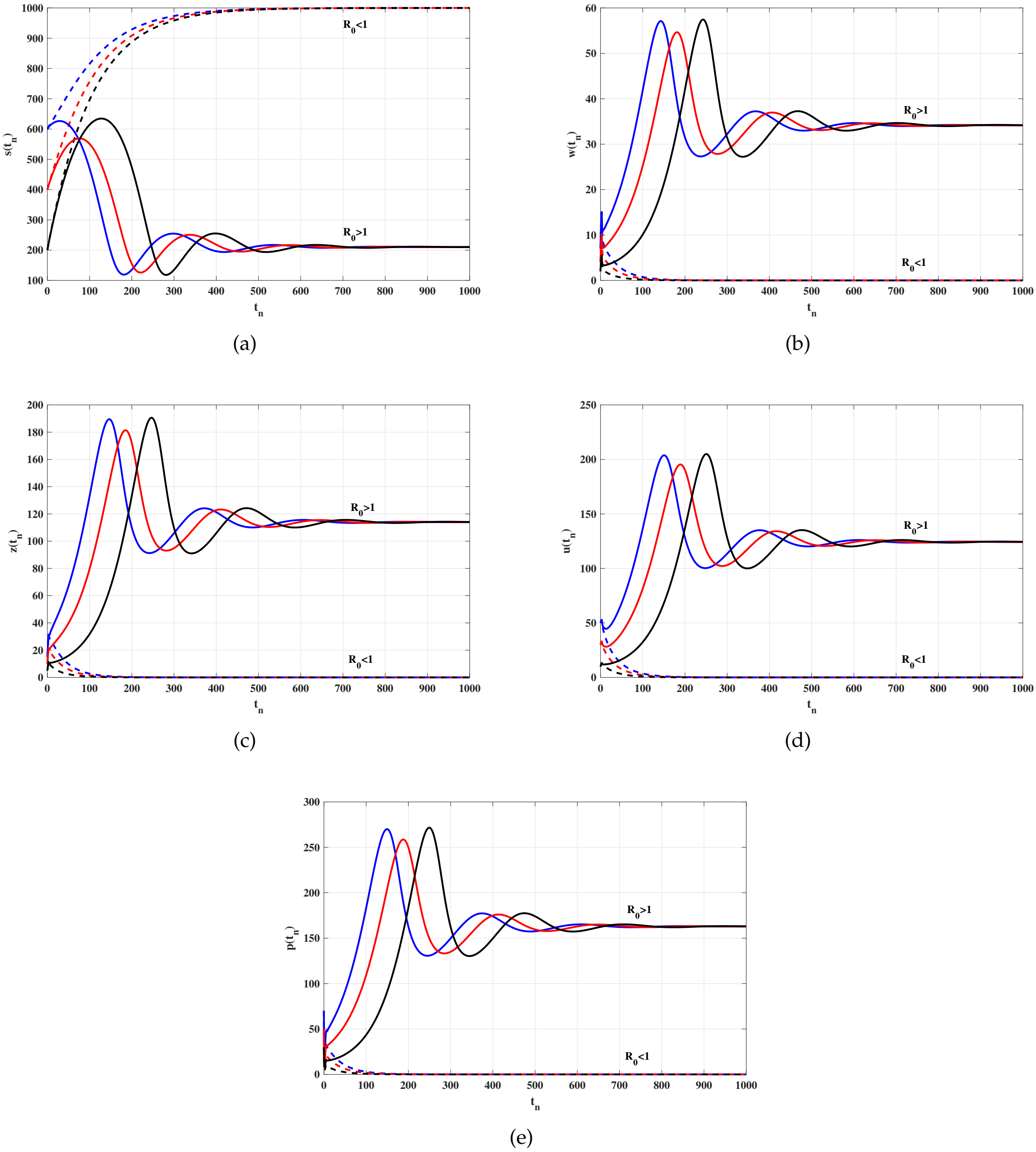

Figure 1: The simulation of trajectories of system (3.2)-(3.6) for Case (1).

3V3: $\psi_{\kappa}^{1} = 200$, $\psi_{\kappa}^{2} = 2$, $\psi_{\kappa}^{3} = 5$, $\psi_{\kappa}^{4} = 10$, $\psi_{\kappa}^{5} = 30$, $\kappa = -\bar{m}, -\bar{m}+1, \ldots, 0$.

Case(1): Effect of N_z, N_u of stability of equilibria

We choose $\tau_1 = 0.5$, $\tau_2 = 1$, $\tau_3 = 1.5$, $\tau_4 = 2$, $\tau_5 = 3$, and N_z, N_u are varied as:

(i) $N_z = 60$, $N_u = 50$. This yields $\mathcal{R}_0 = 0.7742 < 1$. Figure 1 shows that, the concentration of susceptible cells increases and tends to the value $s^0 = 1000$. In addition, the concentrations of infected cells and free HIV particles decrease and tend to zero for the initial values IV1-IV3. This shows that Q^0 is globally asymptotically stable and Theorem 2.3 is valid.

(ii) $N_z = 100$, $N_u = 50$. With these values we obtain $\mathcal{R}_0 = 1.1788 > 1$. Figure 1 shows that for the initial values IV1-IV3, the solutions of the system tend to the equilibrium $Q^* = (209.8434, 34.1801, 114.0590,$

124.4370, 163.0208). Therefore, Q^* exists and it is globally asymptotically stable. This validates the result of Theorem 2.5.

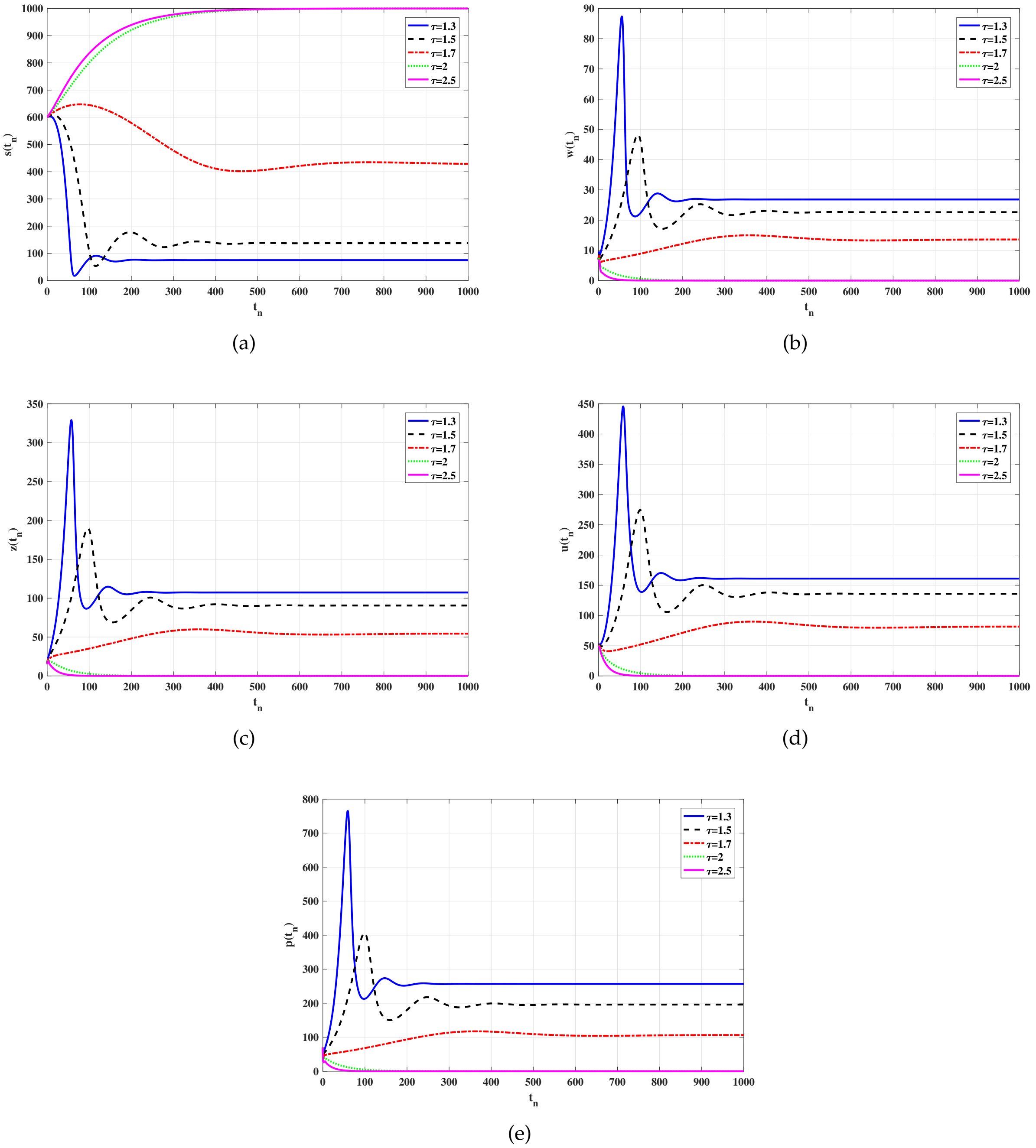

Figure 2: The simulation of trajectories of system (3.2)-(3.6) for Case (2).

Case(2): Effect of time delay on the pathogen dynamics

We fix the values $N_z = 100$, $N_u = 50$ and simulate the system with initial IV1 and different values of $\tau = \tau_1 = \tau_2 = \tau_3$. In Figure 2 we show the effect of the delay parameter τ on the the stability of the equilibria. We observe that the concentration of the susceptible cells is increased, while the concentrations of infected cells and free pathogens are decreased as τ is increased. Let us write $\mathcal{R}_0$ as:

$$\mathcal{R}_0(\tau) = \frac{\beta\left[N_z e^{-\mu_4\tau}\left(mk_1e^{-\mu_1\tau} + (\alpha+m)\,k_2e^{-\mu_2\tau}\right) + (\alpha+m)\,N_u k_3 e^{-(\mu_3+\mu_5)\tau}\right]}{c\,(\alpha+m)\,(r\delta+\beta)}.$$

Clearly, $\mathcal{R}_0$ is a decreasing function of τ. Let τ_c be such that $\mathcal{R}_0(\tau_c) = 1$. Using the values of the parameters we get $\tau_c = 1.7613$. From Figure 2 and Table 1 we can see that

(i) if $0 \leqslant \tau < \tau_c$, then Q^* exists and it is globally asymptotically stable;

(ii) if $\tau \geqslant \tau_c$, then Q^0 is globally asymptotically stable.

Table 1: The values of $\mathcal{R}_0$ for system (3.2)-(3.6) with different values of τ.

τ	Equilibria	$\mathcal{R}_0$
0	Q^*	5.8201
0.5	Q^*	3.5301
1	Q^*	2.1411
1.3	Q^*	1.5862
1.5	Q^*	1.2986
1.7	Q^*	1.0632
1.7613	Q^0	1
2	Q^0	0.7877
2.5	Q^0	0.4777

4. Conclusion

In this paper, we have proposed and analyzed a general discrete-time HIV infection model with time delays. We have considered three types of infected cells, latently infected cells, short-lived infected cells and long lived infected cells. The production and clearance rates of the cells and pathogens as well as the infection rate are given by general nonlinear functions which satisfy a set of conditions. The discrete-time model is obtained by discretizing the continuous-time one by using nonstandard finite difference scheme. We have determined the basic reproduction number $\mathcal{R}_0$. We have proven the positivity and boundedness of the solutions of the models. Using Lyapunov method, we have established the global stability of the two equilibria of the model. We have proven that if $\mathcal{R}_0 \leqslant 1$, then the HIV-free equilibrium Q^0 is globally asymptotically stable and if $R_0 > 1$, then the persistent HIV equilibrium Q^* exists and is globally asymptotically stable. We have presented an example and performed some numerical simulations to support our theoretical results. Moreover, we have demonstrated that the time delay plays a similar role as the treatment in clearing the HIV particles.

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