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Stability of discrete-time HIV dynamics models with long-lived chronically infected cells

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Abstract

This paper studies the global dynamics for discrete-time HIV infection models. The models integrate both long-lived chronically infected and short-lived infected cells. The HIV-susceptible incidence rate is taken as bilinear, saturation and general function. We discretize the continuous-time models by using nonstandard finite difference scheme. The positivity and boundedness of solutions are established. The basic reproduction number is derived. By using Lyapunov method, we prove the global stability of the models. Numerical simulations are presented to illustrate our theoretical results.

Keywords: HIV infection, short-lived infected cells, long-lived infected cells, global stability, Lyapunov function.

2010 MSC: 34D20, 34D23, 37N25, 92B05.

1. Introduction

Human immunodeficiency virus (HIV) destroys the human immune system by attacking the $CD4^+$ T cells. Modeling within host dynamics of HIV has attracted the interest of several researchers (see, e.g., [1–3, 6–14, 19, 23, 26, 27, 32–34, 40, 41, 47]). The basic HIV dynamics model is given by [33]:

$$\dot{s} = \beta - \delta s - \bar{k}sp, \qquad \dot{z} = \bar{k}sp - dz, \qquad \dot{p} = N_z dz - cp,$$

where s, z and p are the concentrations of susceptible (uninfected) $CD4^+$ T cells, infected cells, and free HIV particles, respectively. Parameters β, δ, and $\bar{k}$ represent the rate of birth, death, and infection of the susceptible cells, respectively. The parameters d and c are the death rate constants of the infected cells and free HIV particles, respectively. N_z is the average number of HIV particles produced in the lifetime of the infected cell.

Antiretroviral drug therapies such as reverse transcriptase inhibitors (RTI) and protease inhibitors (PI) can significantly reduce the level of HIV in the blood. However, there still is a low viral load due to the

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presence of long-lived chronically infected cells. Callaway and Perelson [1] have proposed the following HIV dynamics model with both short-lived infected and long-lived chronically infected cells:

$$\dot{s} = \beta - \delta s - (1-\epsilon)\,\bar{k}sp, \tag{1.1}$$
$$\dot{z} = (1-\alpha)\,(1-\epsilon)\,\bar{k}sp - dz, \tag{1.2}$$
$$\dot{u} = \alpha\,(1-\epsilon)\,\bar{k}sp - au, \tag{1.3}$$
$$\dot{p} = N_z dz + N_u au - cp, \tag{1.4}$$

where z and u are the concentrations of short-lived infected cells and long-lived chronically infected cells. A fraction $(1-\alpha)$ and α with $0 < \alpha < 1$ are the probabilities that, upon infection, susceptible cell will become either short-lived infected or chronically infected. The parameter a is the death rate constant of the chronically infected cells. N_u is the average number of HIV particles produced in the lifetime of the chronically infected cells. The chronically infected cells produce much smaller amounts of HIV than the short-lived infected cells and die at a much slower rate [1]. The RTI drug efficacy is denoted by ϵ and $0 \leqslant \epsilon \leqslant 1$.

Model (1.1)-(1.4) 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 [30] 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. NSFD has been used to investigate the global stability of equilibria of the corresponding continuous time models in epidemiology [4, 5, 16, 18, 28, 39] and virology [17, 20–22, 24, 29, 35, 36, 41–46, 48].

In this paper, our target is to study a class of discrete time HIV infection models with both short-lived infected and long-lived chronically infected cells. We study the qualitative behavior of the models with different forms of the infection rate. We investigate global stability of the equilibria of the models using Lyapunov method.

2. Discrete-time model

Discretizing system (1.1)-(1.4) using NSFD method as in [30] and [31] we obtain

$$s_{n+1} - s_n = \beta - \delta s_{n+1} - ks_{n+1}p_n, \tag{2.1}$$
$$z_{n+1} - z_n = (1-\alpha)ks_{n+1}p_n - dz_{n+1}, \tag{2.2}$$
$$u_{n+1} - u_n = \alpha ks_{n+1}p_n - au_{n+1}, \tag{2.3}$$
$$p_{n+1} - p_n = N_z dz_{n+1} + N_u au_{n+1} - cp_{n+1}, \tag{2.4}$$

where, $k = (1-\epsilon)\,\bar{k}$ and $n \in \mathbb{N} = \{0, 1, 2, \ldots\}$. We consider the initial conditions:

$$(s_0, z_0, u_0, p_0) \in \mathbb{R}^4_+ = \{(s, z, u, p) \mid s > 0, z > 0, u > 0, p > 0\}. \tag{2.5}$$

2.1. Preliminaries

Let us consider the region

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

where $N_1 = \frac{\beta}{\xi}$, $N_2 = \frac{(N_z\lambda + N_u a)}{c} N_1$ and $\xi = \min\{\delta, d, a\}$.

Lemma 2.1. *Any solution* (s_n, z_n, u_n, p_n) *of model* (2.1)-(2.4) *with initial condition* (2.5) *is positive and ultimately bounded.*

Proof. From Eqs. (2.1)-(2.4) we obtain

$$\begin{aligned} s_{n+1} &= \frac{\beta + s_n}{1+\delta+kp_n}, \\ z_{n+1} &= \frac{z_n}{1+d} + \frac{(1-\alpha)k(\beta+s_n)p_n}{(1+d)(1+\delta+kp_n)}, \\ u_{n+1} &= \frac{u_n}{1+a} + \frac{\alpha k(\beta+s_n)p_n}{(1+a)(1+\delta+kp_n)}, \\ p_{n+1} &= \frac{p_n}{1+c} + \frac{N_z d}{1+c}\left(\frac{z_n}{1+d} + \frac{(1-\alpha)k(\beta+s_n)p_n}{(1+d)(1+\delta+kp_n)}\right) + \frac{N_u a}{1+c}\left(\frac{u_n}{1+a} + \frac{\alpha k(\beta+s_n)p_n}{(1+a)(1+\delta+kp_n)}\right). \end{aligned}$$

Since all parameters in (2.1)-(2.4) and the initial condition (2.5) are positive, then by induction we get $s_n > 0$, $z_n > 0$, $u_n > 0$ and $p_n > 0$ for all $n \in \mathbb{N}$.

Define a sequence M_n as:

$$M_n = s_n + z_n + u_n.$$

Then

$$M_{n+1} = M_n + \beta - \delta s_{n+1} - d z_{n+1} - a u_{n+1} \leqslant M_n + \beta - \xi M_{n+1},$$

Hence

$$M_{n+1} \leqslant \frac{M_n}{1+\xi} + \frac{\beta}{1+\xi}.$$

According Lemma 2.2 in [36] we obtain

$$M_n \leqslant \left(\frac{1}{1+\xi}\right)^n M_0 + \frac{\beta}{\xi}\left[1 - \left(\frac{1}{1+\xi}\right)^n\right].$$

Consequently, $\lim_{n\to\infty} \sup M_n \leqslant N_1$, $\lim_{n\to\infty} \sup s_n \leqslant N_1$, $\lim_{n\to\infty} \sup z_n \leqslant N_1$, $\lim_{n\to\infty} \sup u_n \leqslant N_1$. We have

$$p_{n+1} - p_n = N_z d z_{n+1} + N_u a u_{n+1} - c p_{n+1} \leqslant (N_z d + N_u a)\,\frac{\beta}{\xi} - c p_{n+1},$$

Hence

$$p_{n+1} \leqslant \frac{p_n}{1+c} + \frac{(N_z d + N_u a)}{(1+c)}\frac{\beta}{\xi} = \frac{p_n}{1+c} + \frac{(N_z d + N_u a)}{(1+c)} N_1.$$

By induction

$$p_n \leqslant \left(\frac{1}{1+c}\right)^n p_0 + \frac{(N_z \lambda + N_u a)\,\beta}{c\xi}\left[1 - \left(\frac{1}{1+c}\right)^n\right].$$

Consequently, $\lim_{n\to\infty} \sup p_n \leqslant N_2$. Therefore, the solution (s_n, z_n, u_n, p_n) converges to Γ_1 as $n \to \infty$. □

System (2.1)-(2.4) has two equilibria,

(i) HIV-free equilibrium $Q^0(s^0, 0, 0, 0)$, where $s^0 = \beta/\delta$;
(ii) persistent HIV equilibrium $Q^*(s^*, z^*, u^*, p^*)$, where

$$s^* = \frac{s^0}{\mathcal{R}_0}, \qquad z^* = \frac{\beta(1-\alpha)}{d\mathcal{R}_0}(\mathcal{R}_0 - 1), \qquad u^* = \frac{\alpha\beta}{a\mathcal{R}_0}(\mathcal{R}_0 - 1), \qquad p^* = \frac{\delta}{k}(\mathcal{R}_0 - 1).$$

Clearly, Q^* exists only when $\mathcal{R}_0 > 1$, where $\mathcal{R}_0$ is basic reproduction number and is given by:

$$\mathcal{R}_0 = \frac{k\beta}{\delta c}\left(N_z(1-\alpha) + \alpha N_u\right). \tag{2.6}$$

2.2. Global Stability

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

$$\ln x \leqslant x - 1. \tag{2.7}$$

Theorem 2.2. *If $\mathcal{R}_0 \leqslant 1$, then Q^0 is globally asymptotically stable.*

Proof. Construct a discrete Lyapunov function $L_n(s_n, z_n, u_n, p_n)$ as:

$$L_n = s^0 G\left(\frac{s_n}{s^0}\right) + \eta_1 z_n + \eta_2 u_n + \eta_3 (1+c) p_n,$$

where $\eta_i, i = 1, 2, 3$ are positive constants to be determined below. Hence, $L_n > 0$ for all $s_n > 0$, $z_n > 0$, $u_n > 0$ and $p_n > 0$. In addition, $L_n = 0$ if and only if $s_n = s^0$, $z_n = 0$, $u_n = 0$ and $p_n = 0$. Computing the difference $\Delta L_n = L_{n+1} - L_n$, as:

$$\begin{aligned}\Delta L_n &= s^0 G\left(\frac{s_{n+1}}{s^0}\right) + \eta_1 z_{n+1} + \eta_2 u_{n+1} + \eta_3 (1+c) p_{n+1} - \left[s^0 G\left(\frac{s_n}{s^0}\right) + \eta_1 z_n + \eta_2 u_n + \eta_3 (1+c) p_n\right] \\ &= s^0 \left(\frac{s_{n+1}}{s^0} - \frac{s_n}{s^0} + \ln \frac{s_n}{s_{n+1}}\right) + \eta_1 (z_{n+1} - z_n) + \eta_2 (u_{n+1} - u_n) + \eta_3 (1+c)(p_{n+1} - p_n).\end{aligned}$$

Using inequality (2.7), we have

$$\begin{aligned}\Delta L_n &\leqslant s_{n+1} - s_n + s^0 \left(\frac{s_n}{s_{n+1}} - 1\right) + \eta_1 (z_{n+1} - z_n) + \eta_2 (u_{n+1} - u_n) + \eta_3 (1+c)(p_{n+1} - p_n) \\ &= \left(1 - \frac{s^0}{s_{n+1}}\right)(s_{n+1} - s_n) + \eta_1 (z_{n+1} - z_n) + \eta_2 (u_{n+1} - u_n) + \eta_3 (1+c)(p_{n+1} - p_n).\end{aligned}$$

From Eqs. (2.1)-(2.4), we have

$$\begin{aligned}\Delta L_n \leqslant &\left(1 - \frac{s^0}{s_{n+1}}\right)(\beta - \delta s_{n+1} - k s_{n+1} p_n) + \eta_1((1-\alpha) k s_{n+1} p_n - d z_{n+1}) \\ &+ \eta_2(\alpha k s_{n+1} p_n - a u_{n+1}) + \eta_3(N_z d z_{n+1} + N_u a u_{n+1} - c p_{n+1}) + \eta_3 c (p_{n+1} - p_n).\end{aligned}$$

Let $\eta_i, i = 1, 2, 3$, be chosen such as

$$(1-\alpha)\eta_1 + \alpha\eta_2 = 1, \qquad N_z \eta_3 - \eta_1 = 0, \qquad N_u \eta_3 - \eta_2 = 0. \tag{2.8}$$

The solution of (2.8) is given by

$$\eta_1 = \frac{N_z}{\alpha N_u + (1-\alpha) N_z}, \qquad \eta_2 = \frac{N_u}{\alpha N_u + (1-\alpha) N_z}, \qquad \eta_3 = \frac{1}{\alpha N_u + (1-\alpha) N_z}. \tag{2.9}$$

The values of $\eta_i, i = 1, 2, 3$, given by (2.9) will be used thought the paper. Then

$$\begin{aligned}\Delta L_n &\leqslant \left(1 - \frac{s^0}{s_{n+1}}\right)(\beta - \delta s_{n+1}) + k s^0 p_n - \eta_3 c p_n \\ &= \frac{-\delta}{s_{n+1}}(s_{n+1} - s^0)^2 + \left(k s^0 - \eta_3 c\right) p_n \\ &= \frac{-\delta}{s_{n+1}}(s_{n+1} - s^0)^2 + \eta_3 c \left(\frac{k s^0 (\alpha N_u + (1-\alpha) N_z)}{c} - 1\right) p_n \\ &= \frac{-\delta}{s_{n+1}}(s_{n+1} - s^0)^2 + \eta_3 c (\mathcal{R}_0 - 1) p_n.\end{aligned}$$

Hence, for $\mathcal{R}_0 \leqslant 1$, we have $\Delta L_n \leqslant 0$ for all $n \geqslant 0$, hence L_n is a monotone decreasing sequence. we have $L_n \geqslant 0$, then there is a limit $\lim_{n\to\infty} L_n \geqslant 0$. Therefore, $\lim_{n\to\infty} \Delta L_n = 0$, which implies that $\lim_{n\to\infty} s_{n+1} = s^0$ and $\lim_{n\to\infty} (\mathcal{R}_0 - 1)p_n = 0$. For the case $\mathcal{R}_0 < 1$, we have $\lim_{n\to\infty} s_{n+1} = s^0$ and $\lim_{n\to\infty} p_n = 0$. From Eqs. (2.2)-(2.4), we obtain $\lim_{n\to\infty} z_n = 0$ and $\lim_{n\to\infty} u_n = 0$. For the case $\mathcal{R}_0 = 1$, we have $\lim_{n\to\infty} s_{n+1} = s^0$. From Eqs. (2.2)-(2.4), we obtain $\lim_{n\to\infty} p_n = 0$, $\lim_{n\to\infty} u_n = 0$ and $\lim_{n\to\infty} z_n = 0$. Hence, in the case $\mathcal{R}_0 \leqslant 1$, the HIV-free equilibrium Q^0 is globally asymptotically stable. □

Theorem 2.3. *If $\mathcal{R}_0 > 1$, then Q^* is globally asymptotically stable.*

Proof. Define

$$U_n(s_n, z_n, u_n, p_n) = s^* G\left(\frac{s_n}{s^*}\right) + \eta_1 z^* G\left(\frac{z_n}{z^*}\right) + \eta_2 u^* G\left(\frac{u_n}{u^*}\right) + (1+c)\eta_3 p^* G\left(\frac{p_n}{p^*}\right),$$

where $\eta_i, i = 1,2,3$ are given by Eq. (2.9). Clearly, $U_n(s_n, z_n, u_n, p_n) > 0$ for all $s_n, z_n, u_n, p_n > 0$ and $U_n(s^*, z^*, u^*, p^*) = 0$. Computing $\Delta U_n = U_{n+1} - U_n$ as:

$$\begin{aligned}
\Delta U_n &= s^* G\left(\frac{s_{n+1}}{s^*}\right) + \eta_1 z^* G\left(\frac{z_{n+1}}{z^*}\right) + \eta_2 u^* G\left(\frac{u_{n+1}}{u^*}\right) + (1+c)\eta_3 p^* G\left(\frac{p_{n+1}}{p^*}\right) \\
&\quad - \left[s^* G\left(\frac{s_n}{s^*}\right) + \eta_1 z^* G\left(\frac{z_n}{z^*}\right) + \eta_2 u^* G\left(\frac{u_n}{u^*}\right) + (1+c)\eta_3 p^* G\left(\frac{p_n}{p^*}\right)\right] \\
&= s^*\left(\frac{s_{n+1}}{s^*} - \frac{s_n}{s^*} + \ln\frac{s_n}{s_{n+1}}\right) + \eta_1 z^*\left(\frac{z_{n+1}}{z^*} - \frac{z_n}{z^*} + \ln\frac{z_n}{z_{n+1}}\right) + \eta_2 u^*\left(\frac{u_{n+1}}{u^*} - \frac{u_n}{u^*} + \ln\frac{u_n}{u_{n+1}}\right) \\
&\quad + \eta_3 p^*\left(\frac{p_{n+1}}{p^*} - \frac{p_n}{p^*} + \ln\frac{p_n}{p_{n+1}}\right) + c\eta_3 p^*\left[G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right].
\end{aligned}$$

Using inequality (2.7), we get

$$\begin{aligned}
\Delta U_n &\leqslant s^*\left(\frac{s_{n+1} - s_n}{s^*} + \frac{s_n}{s_{n+1}} - 1\right) + \eta_1 z^*\left(\frac{z_{n+1} - z_n}{z^*} + \frac{z_n}{z_{n+1}} - 1\right) + \eta_2 u^*\left(\frac{u_{n+1} - u_n}{u^*} + \frac{u_n}{u_{n+1}} - 1\right) \\
&\quad + \eta_3 p^*\left(\frac{p_{n+1} - p_n}{p^*} + \frac{p_n}{p_{n+1}} - 1\right) + c\eta_3 p^*\left[G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right] \\
&= \left(1 - \frac{s^*}{s_{n+1}}\right)(s_{n+1} - s_n) + \eta_1\left(1 - \frac{z^*}{z_{n+1}}\right)(z_{n+1} - z_n) + \eta_2\left(1 - \frac{u^*}{u_{n+1}}\right)(u_{n+1} - u_n) \\
&\quad + \eta_3\left(1 - \frac{p^*}{p_{n+1}}\right)(p_{n+1} - p_n) + c\eta_3 p^*\left[G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right].
\end{aligned}$$

From Eqs. (2.1)-(2.4), we have

$$\begin{aligned}
\Delta U_n &\leqslant \left(1 - \frac{s^*}{s_{n+1}}\right)(\beta - \delta s_{n+1} - k s_{n+1} p_n) + \eta_1\left(1 - \frac{z^*}{z_{n+1}}\right)((1-\alpha)k s_{n+1} p_n - d z_{n+1}) \\
&\quad + \eta_2\left(1 - \frac{u^*}{u_{n+1}}\right)(\alpha k s_{n+1} p_n - a u_{n+1}) + \eta_3\left(1 - \frac{p^*}{p_{n+1}}\right)(N_z d z_{n+1} + N_u a u_{n+1} - c p_{n+1}) \\
&\quad + c\eta_3 p^*\left[G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right].
\end{aligned}$$

Since $\beta = \delta s^* + k s^* p^*$, then

$$\Delta U_n \leqslant \left(1 - \frac{s^*}{s_{n+1}}\right)(\delta s^* + k s^* p^* - \delta s_{n+1} - k s_{n+1} p_n) + \eta_1\left(1 - \frac{z^*}{z_{n+1}}\right)((1-\alpha)k s_{n+1} p_n - d z_{n+1})$$

$$
\begin{aligned}
&+\eta_2\left(1-\frac{u^*}{u_{n+1}}\right)(\alpha k s_{n+1}p_n - a u_{n+1}) + \eta_3\left(1-\frac{p^*}{p_{n+1}}\right)(N_z d z_{n+1} + N_u a u_{n+1} - c p_{n+1}) \\
&+ c\eta_3 p^*\left[\frac{p_{n+1}}{p^*} - \frac{p_n}{p^*} + \ln\frac{p_n}{p_{n+1}}\right] \\
=&\left(1-\frac{s^*}{s_{n+1}}\right)(\delta s^* - \delta s_{n+1}) + \left(1-\frac{s^*}{s_{n+1}}\right) k s^* p^* + k s^* p_n - \eta_1\frac{z^*}{z_{n+1}}(1-\alpha)k s_{n+1}p_n + \eta_1 d z^* \\
&- \eta_2\frac{u^*}{u_{n+1}}\alpha k s_{n+1}p_n + \eta_2 a u^* - \eta_3\frac{p^*}{p_{n+1}}(N_z d z_{n+1} + N_u a u_{n+1}) + c\eta_3 p^* + c\eta_3 p^*\left(-\frac{p_n}{p^*} + \ln\frac{p_n}{p_{n+1}}\right).
\end{aligned}
$$

Using the conditions of Q^*

$$
(1-\alpha)k s^* p^* = d z^*, \qquad \alpha k s^* p^* = a u^*, \qquad N_z d z^* + N_u a u^* = c p^*,
$$

we get

$$
k s^* p^* = \eta_1 d z^* + \eta_2 a u^* = \eta_3 c p^*,
$$

and

$$
\begin{aligned}
\Delta U_n \leqslant& \frac{-\delta}{s_{n+1}}(s_{n+1}-s^*)^2 + \left(1-\frac{s^*}{s_{n+1}}\right)(\eta_1 d z^* + \eta_2 a u^*) - \eta_1(1-\alpha)k s^* p^* \frac{s_{n+1}p_n z^*}{s^* p^* z_{n+1}} \\
&+ \eta_1 d z^* - \eta_2 \alpha k s^* p^* \frac{s_{n+1}p_n u^*}{s^* p^* u_{n+1}} + a\eta_2 u^* - \eta_3 N_z d z^* \frac{z_{n+1}p^*}{z^* p_{n+1}} - \eta_3 N_u a u^* \frac{u_{n+1}p^*}{u^* p_{n+1}} \\
&+ c\eta_3 p^* + c\eta_3 p^* \ln\frac{p_n}{p_{n+1}} \\
=& \frac{-\delta}{s_{n+1}}(s_{n+1}-s^*)^2 + \left(1-\frac{s^*}{s_{n+1}}\right)(\eta_1 d z^* + \eta_2 a u^*) - \eta_1 d z^* \frac{s_{n+1}p_n z^*}{s^* p^* z_{n+1}} + \eta_1 d z^* \\
&- \eta_2 a u^* \frac{s_{n+1}p_n u^*}{s^* p^* u_{n+1}} + a\eta_2 u^* - \eta_1 d z^* \frac{z_{n+1}p^*}{z^* p_{n+1}} - \eta_2 a u^* \frac{u_{n+1}p^*}{u^* p_{n+1}} + \eta_1 d z^* + \eta_2 a u^* \\
&+ (\eta_1 d z^* + \eta_2 a u^*)\ln\frac{p_n}{p_{n+1}} \\
=& \frac{-\delta}{s_{n+1}}(s_{n+1}-s^*)^2 + \eta_1 d z^*\left(3 - \frac{s^*}{s_{n+1}} - \frac{s_{n+1}p_n z^*}{s^* p^* z_{n+1}} - \frac{z_{n+1}p^*}{z^* p_{n+1}} + \ln\frac{p_n}{p_{n+1}}\right) \\
&+ \eta_2 a u^*\left(3 - \frac{s^*}{s_{n+1}} - \frac{s_{n+1}p_n u^*}{s^* p^* u_{n+1}} - \frac{u_{n+1}p^*}{u^* p_{n+1}} + \ln\frac{p_n}{p_{n+1}}\right), \\
\Delta U_n \leqslant& \frac{-\delta}{s_{n+1}}(s_{n+1}-s^*)^2 - \eta_1 d z^*\left[G\left(\frac{s^*}{s_{n+1}}\right) + G\left(\frac{s_{n+1}p_n z^*}{s^* p^* z_{n+1}}\right) + G\left(\frac{z_{n+1}p^*}{z^* p_{n+1}}\right)\right] \\
&- \eta_2 a u^*\left[G\left(\frac{s^*}{s_{n+1}}\right) + G\left(\frac{s_{n+1}p_n u^*}{s^* p^* u_{n+1}}\right) + G\left(\frac{u_{n+1}p^*}{u^* p_{n+1}}\right)\right].
\end{aligned}
$$

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 $\lim_{n\to\infty} s_n = s^*$, $\lim_{n\to\infty} z_n = z^*$, $\lim_{n\to\infty} u_n = u^*$ and $\lim_{n\to\infty} p_n = p^*$. □

3. Model with saturated incidence

It has been reported in [37, 38] that HIV dynamics model with saturated incidence is more accurate in case of high concentration of the HIV particles. Thus we consider the following model:

$$
\dot{s} = \beta - \delta s - \frac{ksp}{1+\mu p}, \qquad \dot{z} = \frac{(1-\alpha)ksp}{1+\mu p} - dz, \qquad \dot{u} = \frac{\alpha ksp}{1+\mu p} - au, \qquad \dot{p} = N_z dz + N_u au - cp,
$$

where μ is the saturation constant. Using the NSFD method we obtain

$$
s_{n+1} - s_n = \beta - \delta s_{n+1} - \frac{k s_{n+1} p_n}{1+\mu p_n}, \tag{3.1}
$$

$$z_{n+1} - z_n = \frac{(1-\alpha)ks_{n+1}p_n}{1+\mu p_n} - dz_{n+1}, \tag{3.2}$$

$$u_{n+1} - u_n = \frac{\alpha ks_{n+1}p_n}{1+\mu p_n} - au_{n+1}, \tag{3.3}$$

$$p_{n+1} - p_n = N_z dz_{n+1} + N_u au_{n+1} - cp_{n+1}. \tag{3.4}$$

Now we study the basic and global properties of model (3.1)-(3.4).

3.1. Preliminaries

Lemma 3.1. *Any solution* (s_n, z_n, u_n, p_n) *of model* (3.1)-(3.4) *with initial conditions* (2.5) *is positive and ultimately bounded.*

Proof. From Eqs. (3.1)-(3.4) we obtain

$$\begin{aligned}
s_{n+1} &= \frac{(\beta+s_n)(1+\mu p_n)}{1+\delta+(\mu(1+\delta)+k)p_n},\\
z_{n+1} &= \frac{z_n}{1+d} + \frac{(1-\alpha)kp_n(\beta+s_n)}{(1+d)\left(1+\delta+(\mu(1+\delta)+k)p_n\right)},\\
u_{n+1} &= \frac{u_n}{1+a} + \frac{\alpha kp_n(\beta+s_n)}{(1+a)\left(1+\delta+(\mu(1+\delta)+k)p_n\right)},\\
p_{n+1} &= \frac{p_n}{1+c} + \frac{N_z d}{1+c}\left(\frac{z_n}{1+d} + \frac{(1-\alpha)kp_n(\beta+s_n)}{(1+d)\left(1+\delta+(\mu(1+\delta)+k)p_n\right)}\right)\\
&\quad + \frac{N_c a}{1+c}\left(\frac{u_n}{1+a} + \frac{\alpha kp_n(\beta+s_n)}{(1+a)\left(1+\delta+(\mu(1+\delta)+k)p_n\right)}\right).
\end{aligned}$$

The solution of (3.1)-(3.4) with initial (2.5) satisfies $s_n > 0, z_n > 0, u_n > 0$ and $p_n > 0$. The boundedness of solutions of model (3.1)-(3.4) is similar to the proof of Lemma 2.1. □

System (3.1)-(3.4) has two equilibria,

(i) HIV-free equilibrium $Q^0(s^0, 0, 0, 0)$ where $s^0 = \beta/\delta$;
(ii) persistent HIV equilibrium $Q^*(s^*, z^*, u^*, p^*)$, where

$$s^* = \frac{\mu\beta\left[N_z(1-\alpha)+\alpha N_u\right]+c}{(k+\delta\mu)\left[N_z(1-\alpha)+\alpha N_u\right]}, \qquad z^* = \frac{(1-\alpha)c\delta}{d\,(k+\delta\mu)\left[N_z(1-\alpha)+\alpha N_u\right]}(\mathcal{R}_0-1),$$

$$u^* = \frac{\alpha c\delta}{a\,(k+\delta\mu)\left[N_z(1-\alpha)+\alpha N_u\right]}(\mathcal{R}_0-1), \qquad p^* = \frac{\delta}{k+\delta\mu}(\mathcal{R}_0-1),$$

where $\mathcal{R}_0$ is given by Eq. (2.6).

3.2. Global Stability

Theorem 3.2. *If* $\mathcal{R}_0 \leqslant 1$, *then* Q^0 *is globally asymptotically stable.*

Proof. Construct a discrete Lyapunov function $L_n(s_n, z_n, u_n, p_n)$ as:

$$L_n = s^0 G\left(\frac{s_n}{s^0}\right) + \eta_1 z_n + \eta_2 u_n + \eta_3(1+c)p_n,$$

where $\eta_i, i = 1, 2, 3$ are given by Eq. (2.9). Hence, $L_n \geqslant 0$ for all $s_n > 0$, $z_n > 0$, $u_n > 0$ and $p_n > 0$. In addition, $L_n = 0$ if and only if $s_n = s^0$, $z_n = 0$, $u_n = 0$ and $p_n = 0$. Computing the difference $\Delta L_n = L_{n+1} - L_n$ as:

$$\Delta L_n = s^0 G\left(\frac{s_{n+1}}{s^0}\right) + \eta_1 z_{n+1} + \eta_2 u_{n+1} + \eta_3(1+c)p_{n+1} - \left[s^0 G\left(\frac{s_n}{s^0}\right) + \eta_1 z_n + \eta_2 u_n + \eta_3(1+c)p_n\right]$$

$$= s^0\left(\frac{s_{n+1}}{s^0}-\frac{s_n}{s^0}+\ln\frac{s_n}{s_{+1}}\right)+\eta_1\left(z_{n+1}-z_n\right)+\eta_2\left(u_{n+1}-u_n\right)+\eta_3(1+c)\left(p_{n+1}-p_n\right).$$

Using inequality (2.7), we have

$$\begin{aligned}\Delta L_n &\leqslant s_{n+1}-s_n+s^0\left(\frac{s_n}{s_{n+1}}-1\right)+\eta_1\left(z_{n+1}-z_n\right)+\eta_2\left(u_{n+1}-u_n\right)+\eta_3(1+c)\left(p_{n+1}-p_n\right)\\ &=\left(1-\frac{s^0}{s_{n+1}}\right)\left(s_{n+1}-s_n\right)+\eta_1\left(z_{n+1}-z_n\right)+\eta_2\left(u_{n+1}-u_n\right)+\eta_3(1+c)\left(p_{n+1}-p_n\right).\end{aligned}$$

From Eqs. (3.1)-(3.4), we have

$$\begin{aligned}\Delta L_n \leqslant& \left(1-\frac{s^0}{s_{n+1}}\right)\left(\beta-\delta s_{n+1}-\frac{ks_{n+1}p_n}{1+\mu p_n}\right)+\eta_1\left(\frac{(1-\alpha)ks_{n+1}p_n}{1+\mu p_n}-dz_{n+1}\right)\\ &+\eta_2\left(\frac{\alpha ks_{n+1}p_n}{1+\mu p_n}-au_{n+1}\right)+\eta_3\left(N_z dz_{n+1}+N_u au_{n+1}-cp_{n+1}\right)+\eta_3 c\left(p_{n+1}-p_n\right)\\ =&\left(1-\frac{s^0}{s_{n+1}}\right)\left(\beta-\delta s_{n+1}\right)+\frac{ks_0p_n}{1+\mu p_n}-\eta_3 cp_n\\ =&\frac{-\delta}{s_{n+1}}\left(s_{n+1}-s^0\right)^2+\left(\frac{ks_0p_n}{1+\mu p_n}-\frac{c}{N_z(1-\alpha)+\alpha N_u}\right)p_n\\ =&\frac{-\delta}{s_{n+1}}\left(s_{n+1}-s^0\right)^2+\frac{c}{N_z(1-\alpha)+\alpha N_u}\left(\frac{\left(N_z(1-\alpha)+\alpha N_u\right)ks_0}{c\left(1+\mu p_n\right)}-1\right)p_n\\ =&\frac{-\delta}{s_{n+1}}\left(s_{n+1}-s^0\right)^2+\eta_3 c\left(\frac{\mathcal{R}_0}{1+\mu p_n}-1\right)p_n\\ =&\frac{-\delta}{s_{n+1}}\left(s_{n+1}-s^0\right)^2+\eta_3 c\left(\mathcal{R}_0-\frac{\mathcal{R}_0\mu p_n}{1+\mu p_n}-1\right)p_n\\ =&\frac{-\delta}{s_{n+1}}\left(s_{n+1}-s^0\right)^2-\eta_3 c\frac{\mathcal{R}_0\mu p_n^2}{1+\mu p_n}+\eta_3 c\left(\mathcal{R}_0-1\right)p_n.\end{aligned}$$

Hence, for $\mathcal{R}_0 \leqslant 1$, we have $\Delta L_n \leqslant 0$ for all $n \geqslant 0$. This yields that L_n is a monotone decreasing sequence. The proof can be completed similar to that of Theorem 2.2. □

Theorem 3.3. *If $\mathcal{R}_0 > 1$, then Q^* is globally asymptotically stable.*

Proof. Let us consider

$$U_n(s_n,z_n,u_n,p_n)=s^*G\left(\frac{s_n}{s^*}\right)+\eta_1 z^*G\left(\frac{z_n}{z^*}\right)+\eta_2 u^*G\left(\frac{u_n}{u^*}\right)+\eta_3(1+c)p^*G\left(\frac{p_n}{p^*}\right).$$

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

$$\begin{aligned}\Delta U_n =& s^*G\left(\frac{s_{n+1}}{s^*}\right)+\eta_1 z^*G\left(\frac{z_{n+1}}{z^*}\right)+\eta_2 u^*G\left(\frac{u_{n+1}}{u^*}\right)+\eta_3(1+c)p^*G\left(\frac{p_{n+1}}{p^*}\right)\\ &-\left[s^*G\left(\frac{s_n}{s^*}\right)+\eta_1 z^*G\left(\frac{z_n}{z^*}\right)+\eta_2 u^*G\left(\frac{u_n}{u^*}\right)+\eta_3(1+c)p^*G\left(\frac{p_n}{p^*}\right)\right]\\ =& s^*\left(\frac{s_{n+1}}{s^*}-\frac{s_n}{s^*}+\ln\frac{s_n}{s_{n+1}}\right)+\eta_1 z^*\left(\frac{z_{n+1}}{z^*}-\frac{z_n}{z^*}+\ln\frac{z_n}{z_{n+1}}\right)+\eta_2 u^*\left(\frac{u_{n+1}}{u^*}-\frac{u_n}{u^*}+\ln\frac{u_n}{u_{n+1}}\right)\\ &+\eta_3 p^*\left(\frac{p_{n+1}}{p^*}-\frac{p_n}{p^*}+\ln\frac{p_n}{p_{n+1}}\right)+\eta_3 cp^*\left[G\left(\frac{p_{n+1}}{p^*}\right)-G\left(\frac{p_n}{p^*}\right)\right].\end{aligned}$$

Using inequality (2.7), we get

$$\begin{aligned}\Delta U_n &\leqslant s^*\left(\frac{s_{n+1}-s_n}{s^*}+\frac{s_n}{s_{n+1}}-1\right)+\eta_1 z^*\left(\frac{z_{n+1}-z_n}{z^*}+\frac{z_n}{z_{n+1}}-1\right)+\eta_2 u^*\left(\frac{u_{n+1}-u_n}{u^*}+\frac{u_n}{u_{n+1}}-1\right)\\&\quad+\eta_3 p^*\left(\frac{p_{n+1}-p_n}{p^*}+\frac{p_n}{p_{n+1}}-1\right)+\eta_3 cp^*\left[G\left(\frac{p_{n+1}}{p^*}\right)-G\left(\frac{p_n}{p^*}\right)\right]\\&=\left(1-\frac{s^*}{s_{n+1}}\right)(s_{n+1}-s_n)+\eta_1\left(1-\frac{z^*}{z_{n+1}}\right)(z_{n+1}-z_n)+\eta_2\left(1-\frac{u^*}{u_{n+1}}\right)(u_{n+1}-u_n)\\&\quad+\eta_3\left(1-\frac{p^*}{p_{n+1}}\right)(p_{n+1}-p_n)+\eta_3 cp^*\left[G\left(\frac{p_{n+1}}{p^*}\right)-G\left(\frac{p_n}{p^*}\right)\right].\end{aligned}$$

From Eqs. (3.1)-(3.4), we have

$$\begin{aligned}\Delta U_n &\leqslant \left(1-\frac{s^*}{s_{n+1}}\right)\left(\beta-\delta s_{n+1}-\frac{ks_{n+1}p_n}{1+\mu p_n}\right)+\eta_1\left(1-\frac{z^*}{z_{n+1}}\right)\left(\frac{(1-\alpha)ks_{n+1}p_n}{1+\mu p_n}-dz_{n+1}\right)\\&\quad+\eta_2\left(1-\frac{u^*}{u_{n+1}}\right)\left(\frac{\alpha ks_{n+1}p_n}{1+\mu p_n}-au_{n+1}\right)+\eta_3\left(1-\frac{p^*}{p_{n+1}}\right)(N_z dz_{n+1}+N_u au_{n+1}-cp_{n+1})\\&\quad+\eta_3 cp^*\left(\frac{p_{n+1}}{p^*}-\frac{p_n}{p^*}+\ln\frac{p_n}{p_{n+1}}\right)\\&=\left(1-\frac{s^*}{s_{n+1}}\right)(\beta-\delta s_{n+1})+\frac{ks^*p_n}{1+\mu p_n}-\eta_1\frac{z^*}{z_{n+1}}\frac{(1-\alpha)ks_{n+1}p_n}{1+\mu p_n}+\eta_1 dz^*\\&\quad-\eta_2\frac{u^*}{u_{n+1}}\frac{\alpha ks_{n+1}p_n}{1+\mu p_n}+\eta_2 au^*-\eta_3\frac{p^*}{p_{n+1}}(N_z dz_{n+1}+N_u au_{n+1})+\eta_3 cp^*+\eta_3 cp^*\left(-\frac{p_n}{p^*}+\ln\frac{p_n}{p_{n+1}}\right).\end{aligned}$$

Using the conditions of Q^*

$$\beta=\delta s^*+\frac{ks^*p^*}{1+\mu p^*},\qquad \frac{(1-\alpha)ks^*p^*}{1+\mu p^*}=dz^*,\qquad \frac{\alpha ks^*p^*}{1+\mu p^*}=au^*,\qquad cp^*=N_z dz^*+N_u au^*,$$

we get

$$\frac{ks^*p^*}{1+\mu p^*}=\eta_1 dz^*+\eta_2 au^*=\eta_3 cp^*,$$

and

$$\begin{aligned}\Delta U_n &\leqslant \left(1-\frac{s^*}{s_{n+1}}\right)\left(\delta s^*+\frac{ks^*p^*}{1+\mu p^*}-\delta s_{n+1}\right)+\frac{ks^*p_n}{1+\mu p_n}-\eta_1\frac{(1-\alpha)ks^*p^*}{1+\mu p^*}\frac{s_{n+1}p_n z^*(1+\mu p^*)}{s^*p^*z_{n+1}(1+\mu p_n)}\\&\quad+\eta_1 dz^*-\eta_2\frac{\alpha ks^*p^*}{1+\mu p^*}\frac{s_{n+1}p_n u^*(1+\mu p^*)}{s^*p^*u_{n+1}(1+\mu p_n)}+\eta_2 au^*-\eta_1 dz^*\frac{p^*z_{n+1}}{p_{n+1}z^*}-\eta_2 au^*\frac{p^*u_{n+1}}{p_{n+1}u^*}+\eta_3 cp^*\\&\quad+\eta_3 cp^*\left(-\frac{p_n}{p^*}+\ln\frac{p_n}{p_{n+1}}\right)\\&=\left(1-\frac{s^*}{s_{n+1}}\right)(\delta s^*-\delta s_{n+1})+\frac{ks^*p^*}{1+\mu p^*}\left(1-\frac{s^*}{s_{n+1}}\right)+\frac{ks^*p^*}{1+\mu p^*}\frac{p_n(1+\mu p^*)}{p^*(1+\mu p_n)}\\&\quad-\eta_1 dz^*\frac{s_{n+1}p_n z^*(1+\mu p^*)}{s^*p^*z_{n+1}(1+\mu p_n)}+\eta_1 dz^*-\eta_2 au^*\frac{s_{n+1}p_n u^*(1+\mu p^*)}{s^*p^*u_{n+1}(1+\mu p_n)}+\eta_2 au^*-\eta_1 dz^*\frac{z_{n+1}p^*}{z^*p_{n+1}}\\&\quad-\eta_2 au^*\frac{u_{n+1}p^*}{u^*p_{n+1}}+\eta_1 dz^*+\eta_2 au^*+\frac{ks^*p^*}{1+\mu p^*}\left(-\frac{p_n}{p^*}+\ln\frac{p_n}{p_{n+1}}\right)\\&=\frac{-\delta}{s_{n+1}}(s_{n+1}-s^*)^2+\frac{ks^*p^*}{1+\mu p^*}\left(-1+\frac{p_n(1+\mu p^*)}{p^*(1+\mu p_n)}-\frac{p_n}{p*}+\frac{1+\mu p_n}{1+\mu p^*}\right)\\&\quad+\eta_1 dz^*\left[4-\frac{s^*}{s_{n+1}}-\frac{s_{n+1}p_n z^*(1+\mu p^*)}{s^*p^*z_{n+1}(1+\mu p_n)}-\frac{z_{n+1}p^*}{z^*p_{n+1}}-\frac{1+\mu p_n}{1+\mu p^*}+\ln\frac{p_n}{p_{n+1}}\right]\end{aligned}$$

$$+\eta_2 a u^* \left[4 - \frac{s^*}{s_{n+1}} - \frac{s_{n+1} p_n u^* (1+\mu p^*)}{s^* p^* u_{n+1} (1+\mu p_n)} - \frac{u_{n+1} p^*}{u^* p_{n+1}} - \frac{1+\mu p_n}{1+\mu p^*} + \ln \frac{p_n}{p_{n+1}}\right].$$

We have

$$-1 + \frac{p_n (1+\mu p^*)}{p^* (1+\mu p_n)} - \frac{p_n}{p*} + \frac{1+\mu p_n}{1+\mu p^*} = -\frac{\mu (p_n - p^*)^2}{p^*(1+\mu p^*)(1+\mu p_n)}.$$

Then

$$\begin{aligned}\Delta U_n \leqslant & \frac{-\delta}{s_{n+1}}(s_{n+1}-s^*)^2 - \frac{k s^* p^*}{1+\mu p^*}\left(\frac{\mu (p_n - p^*)^2}{p^*(1+\mu p^*)(1+\mu p_n)}\right) \\ & - \eta_1 d z^* \left[G\left(\frac{s^*}{s_{n+1}}\right) + G\left(\frac{s_{n+1} p_n z^*}{s^* p^* z_{n+1}}\frac{(1+\mu p^*)}{(1+\mu p_n)}\right) + G\left(\frac{z_{n+1} p^*}{z^* p_{n+1}}\right) + G\left(\frac{1+\mu p_n}{1+\mu p^*}\right)\right] \\ & - \eta_2 a u^* \left[G\left(\frac{s^*}{s_{n+1}}\right) + G\left(\frac{s_{n+1} p_n u^*}{s^* p^* u_{n+1}}\frac{(1+\mu p^*)}{(1+\mu p_n)}\right) + G\left(\frac{u_{n+1} p^*}{u^* p_{n+1}}\right) + G\left(\frac{1+\mu p_n}{1+\mu p^*}\right)\right].\end{aligned}$$

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

4. Model with general incidence

In this section, we assume that the incidence rate is given by $f(s,p)$, where f is a general function.

$$\dot{s} = \beta - \delta s - f(s,p), \qquad \dot{z} = (1-\alpha) f(s,p) - dz, \qquad \dot{u} = \alpha f(s,p) - au, \qquad \dot{p} = N_z dz + N_u au - cp.$$

Using the NSFD method we get

$$\begin{aligned} s_{n+1} - s_n &= \beta - \delta s_{n+1} - f(s_{n+1}, p_n), & (4.1)\\ z_{n+1} - z_n &= (1-\alpha) f(s_{n+1}, p_n) - d z_{n+1}, & (4.2)\\ u_{n+1} - u_n &= \alpha f(s_{n+1}, p_n) - a u_{n+1}, & (4.3)\\ p_{n+1} - p_n &= N_z d z_{n+1} + N_u a u_{n+1} - c p_{n+1}. & (4.4)\end{aligned}$$

4.1. Preliminaries

The function $f(s,p)$ is assumed to satisfy the following conditions:

(A1) $f(s,p) > 0$, and $f(0,p) = f(s,0) = 0$ for all $s > 0$, $p > 0$;
(A2) $\frac{\partial f(s,p)}{\partial s} > 0$, $\frac{\partial f(s,p)}{\partial p} > 0$, $\frac{\partial f(s,0)}{\partial p} > 0$ for all $s > 0$, $p > 0$;
(A3) $\frac{d}{ds}\left(\frac{\partial f(s,0)}{\partial p}\right) > 0$ for all $s > 0$;
(A4) $\frac{f(s,p)}{p}$ is decreasing with respect to p for all $p > 0$.

Lemma 4.1. *Any solution* (s_n, z_n, u_n, p_n) *of model* (4.1)-(4.4) *with initial conditions* (2.5) *is positive and ultimately bounded.*

Proof. From Eqs. (4.1)-(4.4) we obtain

$$\begin{aligned} s_{n+1} &= \frac{s_n + \beta - f(s_{n+1}, p_n)}{1+\delta}, & \\ z_{n+1} &= \frac{z_n + (1-\alpha) f(s_{n+1}, p_n)}{1+d}, & (4.5)\\ u_{n+1} &= \frac{u_n + \alpha f(s_{n+1}, p_n)}{1+a}, & (4.6)\end{aligned}$$

$$p_{n+1} = \frac{p_n + N_z d z_{n+1} + N_u a u_{n+1}}{1+c}. \tag{4.7}$$

When $n = 0$ we prove that (s_1, z_1, u_1, p_1) exists and is positive. From Eq. (4.1) we have

$$(1+\delta)\, s_1 - s_0 - \beta + f(s_1, p_0) = 0.$$

Let φ be defined as:

$$\varphi(s_1) = (1+\delta)\, s_1 - s_0 - \beta + f(s_1, p_0) = 0, \qquad \varphi(0) = -s_0 - \beta < 0, \qquad \lim_{s_1 \to \infty} \varphi(s_1) = \infty.$$

From Assumption (A2), φ is a strictly increasing function in s_1. Hence, there exists a unique $s_1 > 0$ such that $\varphi(s_1) = 0$. From Eqs. (4.5)-(4.7) we have $z_1 > 0$, $u_1 > 0$ and $p_1 > 0$. Therefore, by using the induction, we obtain $s_n > 0$, $z_n > 0$, $u_n > 0$ and $p_n > 0$ for all $n \geqslant 0$. The boundedness of solutions can be shown similar to Lemma 2.1. □

Lemma 4.2. *For model* (4.1)-(4.4) *let* (A1)-(A2) *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 $Q(s, z, u, p)$ be any equilibrium of model (4.1)-(4.4) satisfying

$$\beta - \delta s - f(s,p) = 0, \tag{4.8}$$
$$(1-\alpha) f(s,p) - dz = 0, \tag{4.9}$$
$$\alpha f(s,p) - au = 0, \tag{4.10}$$
$$N_z dz + N_u au - cp = 0. \tag{4.11}$$

From Eqs. (4.8)-(4.10) we have

$$z = \frac{(1-\alpha) f(s,p)}{d}, \qquad u = \frac{\alpha f(s,p)}{a}, \qquad f(s,p) = \beta - \delta s. \tag{4.12}$$

Substituting from Eq. (4.12) into Eq. (4.11) we get

$$(N_z(1-\alpha) + N_u \alpha)\, f(s,p) - cp = 0. \tag{4.13}$$

From Assumption (A1), we have $p = 0$ is a solution of (4.13). Therefore, $s = s^0$, $z = 0$ and $u = 0$ which leads to the HIV-free equilibrium $Q^0(s^0, 0, 0, 0)$ where $s^0 = \frac{\beta}{\delta}$. If $p \neq 0$, then, from Eqs. (4.12), (4.13), we obtain

$$p = \frac{\gamma f(s,p)}{c} = \frac{\gamma(\beta - \delta s)}{c}, \qquad s = s^0 - \frac{pc}{\gamma\delta},$$

where, $\gamma = N_z(1-\alpha) + N_u \alpha$. Then, Eq. (4.13) becomes

$$\gamma f\left(s^0 - \frac{c}{\gamma\delta} p, p\right) - cp = 0.$$

Let a function ψ_1 be defined as:

$$\psi_1(p) = \gamma f\left(s^0 - \frac{c}{\gamma\delta} p, p\right) - cp = 0.$$

From Assumption (A1), we have $\psi_1(0) = 0$, and $\psi_1(\bar{p}) = -c\bar{p} < 0$, where $\bar{p} = \frac{\gamma\beta}{c} > 0$. Moreover,

$$\psi_1'(0) = \gamma \frac{\partial f(s^0, 0)}{\partial p} - c = c\left(\frac{\gamma}{c} \frac{\partial f(s^0, 0)}{\partial p} - 1\right).$$

Therefore, $\psi'(0) > 0$ if the following condition is satisfied

$$\frac{\gamma}{c}\frac{\partial f(s^0,0)}{\partial p} > 1. \tag{4.14}$$

It follows that, if condition (4.14) is satisfied, then there exists $p^* \in (0,\bar{p})$ such that $\psi(p^*) = 0$. Hence, we can define the basic reproduction number of system (4.1)-(4.4) as:

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

Moreover, let $p = p^*$ in Eq. (4.8) we get

$$\beta - \delta s - f(s,p^*) = 0.$$

Let us define

$$\psi_2(s) = \beta - \delta s - f(s,p^*).$$

We have $\psi_2(0) = \beta > 0$ and $\psi_2(s^0) = -f(s^0,p^*) < 0$. Since $f(s,p)$ is strictly decreasing with respect to s, then $\psi_1(s)$ is strictly decreasing with respect to s. Hence, there exists a unique $s^* \in (0,s^0)$ such that $\psi_1(s^*) = 0$. From Eq. (4.12) and Assumption (A1) we have

$$z^* = \frac{(1-\alpha)f(s^*,p^*)}{d} > 0, \qquad u^* = \frac{\alpha f(s^*,p^*)}{a} > 0.$$

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

4.2. Global stability

Theorem 4.3. *Suppose that $\mathcal{R}_0 \leqslant 1$, then Q^0 of system (4.1)-(4.4) is globally asymptotically stable.*

Proof. Define

$$L_n = s_n - s^0 - \int_{s^0}^{s_n} \lim_{p\to 0^+}\frac{f(s^0,p)}{f(\tau,p)}d\tau + \eta_1 z_n + \eta_2 u_n + \eta_3(1+c)p_n.$$

Hence, $L_n > 0$ for all s_n, z_n, u_n, $p_n > 0$ and $L_n = 0$ if and only if $s_n = s^0$, $z_n = 0$, $u_n = 0$ and $p_n = 0$. Computing the difference $\Delta L_n = L_{n+1} - L_n$ as:

$$\begin{aligned}\Delta L_n &= s_{n+1} - s^0 - \int_{s^0}^{s_{n+1}} \lim_{p\to 0^+}\frac{f(s^0,p)}{f(\tau,p)}d\tau + \eta_1 z_{n+1} + \eta_2 u_{n+1} + \eta_3(1+c)p_{n+1}\\ &\quad - \left[s_n - s^0 - \int_{s^0}^{s_n} \lim_{p\to 0^+}\frac{f(s^0,p)}{f(\tau,p)}d\tau + \eta_1 z_n + \eta_2 u_n + \eta_3(1+c)p_n\right]\\ &= s_{n+1} - s_n - \int_{s_n}^{s_{n+1}} \lim_{p\to 0^+}\frac{f(s^0,p)}{f(\tau,p)}d\tau + \eta_1(z_{n+1}-z_n) + \eta_2(u_{n+1}-u_n) + \eta_3(1+c)(p_{n+1}-p_n).\end{aligned}$$

Using Lemma 3.1 in [22], we get

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

Hence

$$\Delta L_n \leqslant \left(1 - \lim_{p\to 0^+}\frac{f(s^0,p)}{f(s_{n+1},p)}\right)(s_{n+1}-s_n) + \eta_1(z_{n+1}-z_n) + \eta_2(u_{n+1}-u_n) + \eta_3(1+c)(p_{n+1}-p_n).$$

From Eqs. (4.1)-(4.4), we have

$$\Delta L_n \leqslant \left(1-\lim_{p\to 0}\frac{f(s^0,p)}{f(s_{n+1},p)}\right)(\beta-\delta s_{n+1}-f(s_{n+1},p_n))+\eta_1\left((1-\alpha)f(s_{n+1},p_n)-dz_{n+1}\right)$$
$$+\eta_2\left(\alpha f(s_{n+1},p_n)-au_{n+1}\right)+\eta_3\left(N_z dz_{n+1}+N_u au_{n+1}-cp_{n+1}\right)+\eta_3 c\left(p_{n+1}-p_n\right). \quad (4.15)$$

Collecting terms of Eq (4.15) and using $s^0=\frac{\beta}{\delta}$, we obtain

$$\begin{aligned}\Delta L_n &\leqslant \delta s^0\left(1-\frac{s_{n+1}}{s^0}\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}f(s_{n+1},p_n)-\eta_3 cp_n\\ &=\delta s^0\left(1-\frac{s_{n+1}}{s^0}\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\left(\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\frac{f(s_{n+1},p_n)}{p_n}-\eta_3 c\right)p_n.\end{aligned}$$

From Assumption (A4) we have

$$\begin{aligned}\frac{f(s_{n+1},p_n)}{p_n} &\leqslant \lim_{p\to 0^+}\frac{f(s_{n+1},p)}{p}\\ &=\frac{\partial f(s_{n+1},0)}{\partial p},\end{aligned}$$

then, we get

$$\begin{aligned}&=\delta s^0\left(1-\frac{s_{n+1}}{s^0}\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\left(\frac{\partial f(s^0,0)}{\partial p}-\eta_3 c\right)p_n\\ &=\delta s^0\left(1-\frac{s_{n+1}}{s^0}\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\eta_3 c\left(\frac{\gamma}{c}\frac{\partial f(s^0,0)}{\partial p}-1\right)p_n\\ &=\delta s^0\left(1-\frac{s_{n+1}}{s^0}\right)\left(1-\frac{\partial f(s^0,0)/\partial p}{\partial f(s_{n+1},0)/\partial p}\right)+\eta_3 c\left(\mathcal{R}_0-1\right)p_n.\end{aligned}$$

From Assumption (A3) we have

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

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 $\lim_{n\to\infty}p_n=0$. then we get $\lim_{n\to\infty}z_n=0$ and $\lim_{n\to\infty}u_n=0$;
- if $\mathcal{R}_0=1$, then by using $\lim_{n\to\infty}s_n=s^0$ and from Eq. (4.1), 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, $\lim_{n\to\infty}p_n=0$.

By the aforementioned discussion, we deduce that the largest compact invariant set in $\{(s_n,z_n,u_n,p_n)|(\Delta L_n)=0\}$ is the just the singleton Q^0. Therefore, Q^0 is globally asymptotically stable by the LaSalle's invariance principle [15, 25]. □

Remark 4.4. Assumptions (A2) and (A4) imply that

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

which yields

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

Theorem 4.5. *Suppose that $\mathcal{R}_0 > 1$, then Q^* of system (4.1)-(4.4) is globally asymptotically stable.*

Proof. Consider

$$U_n(s_n, z_n, u_n, p_n) = s_n - s^* - \int_{s^*}^{s_n} \frac{f(s^*, p^*)}{f(\tau, p^*)} d\tau + \eta_1 z^* G\left(\frac{z_n}{z^*}\right) + \eta_2 u^* G\left(\frac{u_n}{u^*}\right) + \eta_3(1+c)p^* G\left(\frac{p_n}{p^*}\right).$$

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

$$\begin{aligned}
\Delta U_n &= s_{n+1} - s^* - \int_{s^*}^{s_{n+1}} \frac{f(s^*, p^*)}{f(\tau, p^*)} d\tau + \eta_1 z^* G\left(\frac{z_{n+1}}{z^*}\right) + \eta_2 u^* G\left(\frac{u_{n+1}}{u^*}\right) + \eta_3(1+c)p^* G\left(\frac{p_{n+1}}{p^*}\right) \\
&\quad - \left[s_n - s^* - \int_{s^*}^{s_n} \frac{f(s^*, p^*)}{f(\tau, p^*)} d\tau + \eta_1 z^* G\left(\frac{z_n}{z^*}\right) + \eta_2 u^* G\left(\frac{u_n}{u^*}\right) + \eta_3(1+c)p^* G\left(\frac{p_n}{p^*}\right)\right] \\
&= s_{n+1} - s_n - \int_{s_n}^{s_{n+1}} \frac{f(s^*, p^*)}{f(\tau, p^*)} d\tau + \eta_1 z^* \left[G\left(\frac{z_{n+1}}{z^*}\right) - G\left(\frac{z_n}{z^*}\right)\right] + \eta_2 u^* \left[G\left(\frac{u_{n+1}}{u^*}\right) - G\left(\frac{u_n}{u^*}\right)\right] \\
&\quad + \eta_3(1+c)p^* \left[G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right].
\end{aligned}$$

From Lemma 3.1 in [22], we have

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

Then

$$\begin{aligned}
\Delta U_n &\leqslant \left(1 - \frac{f(s^*, p^*)}{f(s_{n+1}, p^*)}\right)(s_{n+1} - s_n) + \eta_1 z^* \left(\frac{z_{n+1}}{z^*} - \frac{z_n}{z^*} + \ln\frac{z_n}{z_{n+1}}\right) + \eta_2 u^* \left(\frac{u_{n+1}}{u^*} - \frac{u_n}{u^*} + \ln\frac{u_n}{u_{n+1}}\right) \\
&\quad + \eta_3 p^* \left(\frac{p_{n+1}}{p^*} - \frac{p_n}{p^*} + \ln\frac{p_n}{p_{n+1}}\right) + \eta_3 c p^* \left[G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right].
\end{aligned}$$

Using inequality (2.7), we get

$$\begin{aligned}
\Delta U_n &\leqslant \left(1 - \frac{f(s^*, p^*)}{f(s_{n+1}, p^*)}\right)(s_{n+1} - s_n) + \eta_1\left(z_{n+1} - z_n + z^*\left(\frac{z_n}{z_{n+1}} - 1\right)\right) \\
&\quad + \eta_2\left(u_{n+1} - u_n + u^*\left(\frac{u_n}{u_{n+1}} - 1\right)\right) \\
&\quad + \eta_3\left(p_{n+1} - p_n + p^*\left(\frac{p_n}{p_{n+1}} - 1\right)\right) + \eta_3 c p^*\left(G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right) \\
&= \left(1 - \frac{f(s^*, p^*)}{f(s_{n+1}, p^*)}\right)(s_{n+1} - s_n) + \eta_1\left(1 - \frac{z^*}{z_{n+1}}\right)(z_{n+1} - z_n) + \eta_2\left(1 - \frac{u^*}{u_{n+1}}\right)(u_{n+1} - u_n) \\
&\quad + \eta_3\left(1 - \frac{p^*}{p_{n+1}}\right)(p_{n+1} - p_n) + \eta_3 c p^*\left(G\left(\frac{p_{n+1}}{p^*}\right) - G\left(\frac{p_n}{p^*}\right)\right).
\end{aligned}$$

From Eqs. (4.1)-(4.4), we have

$$\begin{aligned}
\Delta U_n &\leqslant \left(1 - \frac{f(s^*, p^*)}{f(s_{n+1}, p^*)}\right)(\beta - \delta s_{n+1} - f(s_{n+1}, p_n)) + \eta_1\left(1 - \frac{z^*}{z_{n+1}}\right)((1-\alpha)f(s_{n+1}, p_n) - d z_{n+1}) \\
&\quad + \eta_2\left(1 - \frac{u^*}{u_{n+1}}\right)(\alpha f(s_{n+1}, p_n) - a u_{n+1}) + \eta_3\left(1 - \frac{p^*}{p_{n+1}}\right)(N_z d z_{n+1} + N_u a u_{n+1} - c p_{n+1}) \\
&\quad + \eta_3 c (p_{n+1} - p_n) + \eta_3 c p^* \ln\frac{p_n}{p_{n+1}}
\end{aligned}$$

$$= \left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(\beta-\delta s_{n+1})+\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}f(s_{n+1},p_n)-\eta_1\frac{z^*}{z_{n+1}}(1-\alpha)f(s_{n+1},p_n)+\eta_1 dz^*$$
$$-\eta_2\frac{u^*}{u_{n+1}}\alpha f(s_{n+1},p_n)+\eta_2 au^*-\eta_3\frac{p^*}{p_{n+1}}(N_z dz_{n+1}+N_u au_{n+1})+\eta_3 cp^*-\eta_3 cp_n+\eta_3 cp^*\ln\frac{p_n}{p_{n+1}}.$$

Using the conditions of Q^*,

$$\beta=\delta s^*+f(s^*,p^*),\qquad (1-\alpha)f(s^*,p^*)=dz^*,\qquad \alpha f(s^*,p^*)=au^*,\qquad N_z dz^*+N_u au^*=cp^*,$$

we get

$$f(s^*,p^*)=\eta_1 dz^*+\eta_2 au^*=\eta_3 cp^*$$

and

$$\Delta U_n\leqslant\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)(\delta s^*+f(s^*,p^*)-\delta s_{n+1})+\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}f(s_{n+1},p_n)$$
$$-\eta_1(1-\alpha)f(s^*,p^*)\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{z^*}{z_{n+1}}+\eta_1 dz^*-\eta_2\alpha f(s^*,p^*)\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{u^*}{u_{n+1}}+\eta_2 au^*$$
$$-\eta_1 dz^*\frac{z_{n+1}p^*}{z^*p_{n+1}}-\eta_2 au^*\frac{u_{n+1}p^*}{u^*p_{n+1}}+\eta_1 dz^*+\eta_2 au^*-f(s^*,p^*)\frac{p_n}{p_*}+\eta_3 cp^*\ln\frac{p_n}{p_{n+1}}$$
$$=\delta s^*\left(1-\frac{s_{n+1}}{s^*}\right)\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)+(\eta_1 dz^*+\eta_2 au^*)\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)+f(s^*,p^*)\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)}$$
$$-\eta_1 dz^*\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{z^*}{z_{n+1}}+\eta_1 dz^*-\eta_2 au^*\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{u^*}{u_{n+1}}+\eta_2 au^*$$
$$-\eta_1 dz^*\frac{z_{n+1}p^*}{z^*p_{n+1}}-\eta_2 au^*\frac{u_{n+1}p^*}{u^*p_{n+1}}+\eta_1 dz^*+\eta_2 au^*-f(s^*,p^*)\frac{p_n}{p_*}+\eta_3 cp^*\ln\frac{p_n}{p_{n+1}},$$

$$\Delta U_n\leqslant\delta s^*\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)\left(1-\frac{s_{n+1}}{s^*}\right)+f(s^*,p^*)\left[-1+\frac{p_n f(s_{n+1},p^*)}{p^*f(s_{n+1},p_n)}+\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)}-\frac{p_n}{p^*}\right]$$
$$+\eta_1 dz^*\left[4-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}-\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{z^*}{z_{n+1}}-\frac{z_{n+1}p^*}{z^*p_{n+1}}-\frac{p_n f(s_{n+1},p^*)}{p^*f(s_{n+1},p_n)}+\ln\frac{p_n}{p_{n+1}}\right]$$
$$+\eta_2 au^*\left[4-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}-\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{u^*}{u_{n+1}}-\frac{u_{n+1}p^*}{u^*p_{n+1}}-\frac{p_n f(s_{n+1},p^*)}{p^*f(s_{n+1},p_n)}+\ln\frac{p_n}{p_{n+1}}\right]$$
$$=\delta s^*\left(1-\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)\left(1-\frac{s_{n+1}}{s^*}\right)+f(s^*,p^*)\left[-1+\frac{p_n f(s_{n+1},p^*)}{p^*f(s_{n+1},p_n)}+\frac{f(s_{n+1},p_n)}{f(s_{n+1},p^*)}-\frac{p_n}{p^*}\right]$$
$$-\eta_1 dz^*\left[G\left(\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)+G\left(\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{z^*}{z_{n+1}}\right)+G\left(\frac{z_{n+1}p^*}{z^*p_{n+1}}\right)+G\left(\frac{p_n f(s_{n+1},p^*)}{p^*f(s_{n+1},p_n)}\right)\right]$$
$$-\eta_2 au^*\left[G\left(\frac{f(s^*,p^*)}{f(s_{n+1},p^*)}\right)+G\left(\frac{f(s_{n+1},p_n)}{f(s^*,p^*)}\frac{u^*}{u_{n+1}}\right)+G\left(\frac{u_{n+1}p^*}{u^*p_{n+1}}\right)+G\left(\frac{p_n f(s_{n+1},p^*)}{p^*f(s_{n+1},p_n)}\right)\right].$$

Because $f(s,p)$ is strictly increasing with respect to s, we obtain that

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

Based on Remark 4.4, we have

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

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 $\lim_{n\to\infty}s_n=s^*$, $\lim_{n\to\infty}z_n=z^*$, $\lim_{n\to\infty}u_n=u^*$ and $\lim_{n\to\infty}p_n=p^*$. □

5. Numerical simulations

We perform our simulation by choosing Crowly Martin incidence rate

$$f(s,p)=\frac{ksp}{(1+\lambda s)(1+\theta p)},$$

where $\lambda>0$ and $\theta>0$. Therefore, system (4.1)-(4.4) becomes

$$s_{n+1}-s_n=\beta-\delta s_{n+1}-\frac{(1-\epsilon)\bar{k}s_{n+1}p_n}{(1+\lambda s_{n+1})(1+\theta p_n)}, \tag{5.1}$$

$$z_{n+1}-z_n=\frac{(1-\alpha)(1-\epsilon)\bar{k}s_{n+1}p_n}{(1+\lambda s_{n+1})(1+\theta p_n)}-dz_{n+1}, \tag{5.2}$$

$$u_{n+1}-u_n=\frac{\alpha\bar{k}s_{n+1}p_n}{(1+\lambda s_{n+1})(1+\theta p_n)}-au_{n+1}, \tag{5.3}$$

$$p_{n+1}-p_n=N_z dz_{n+1}+N_u au_{n+1}-cp_{n+1}. \tag{5.4}$$

For this system, the basic reproduction number is given by

$$\mathcal{R}_0=\frac{\gamma(1-\epsilon)\bar{k}s^0}{c(1+\lambda s^0)}.$$

We verify the assumptions (A1)-(A4) as:

$$\begin{aligned}
f(s,p)&=\frac{(1-\epsilon)\bar{k}sp}{(1+\lambda s)(1+\theta p)}>0,\ \text{and } f(0,p)=f(s,0)=0 \text{ for all } s>0, p>0,\\
\frac{\partial f(s,p)}{\partial s}&=\frac{(1-\epsilon)\bar{k}p}{(1+\theta p)(1+\lambda s)^2}>0 \text{ for all } s>0,\ \text{and } p>0,\\
\frac{\partial f(s,p)}{\partial p}&=\frac{(1-\epsilon)\bar{k}s}{(1+\lambda s)(1+\theta p)^2} \text{ for all } s>0,\ \text{and } p>0,\\
\frac{\partial f(s,0)}{\partial p}&=\frac{(1-\epsilon)\bar{k}s}{1+\lambda s}>0 \text{ for all } s>0,\\
\frac{d}{ds}\left(\frac{\partial f(s,0)}{\partial p}\right)&=\frac{(1-\epsilon)\bar{k}}{(1+\lambda s)^2}>0 \text{ for all } s>0,\\
\frac{d}{dp}\left(\frac{f(s,p)}{p}\right)&=\frac{-\theta(1-\epsilon)\bar{k}s}{(1+\lambda s)(1+\theta p)^2}<0 \text{ for all } s>0,\ \text{and } p>0.
\end{aligned}$$

Then, function $f(s,p)$ satisfies Assumptions (A1)-(A4) and hence Theorems 4.3 and 4.5 are applicable for such function.

Remark 5.1. We note that Assumptions (A1)-(A4) can also be satisfied for other types of the incidence rate function such as: Beddington-DeAngelis incidence $f(s,p)=\frac{ksp}{1+\lambda s+\theta p}$ and Hill-type incidence $f(s,p)=\frac{ks^m p}{\lambda^m+s^m}$, $m>0$.

The numerical simulations for system (5.1)-(5.4) will be conducted using the following data: $\beta=10$, $\delta=0.01$, $\alpha=0.5$, $d=0.3$, $a=0.25$, $c=2$, $N_z=10$, $N_u=5$, $\lambda=0.0001$ and $\theta=0.0001$. The other parameters will be chosen as bellow.

Let us consider the initial values

IV1: $s(0)=800$, $w(0)=10$, $u(0)=20$, $p(0)=20$,

IV2: $s(0)=600$, $w(0)=2$, $u(0)=15$, $p(0)=15$,

IV3: $s(0)=400$, $w(0)=5$, $u(0)=10$, $p(0)=10$.

Case (I) Effect of $\bar{k}$ of stability of equilibria:

We choose $\epsilon=0.5$ and $\bar{k}$ is varied as:

(i) $\bar{k} = 0.0001$. This yields $\mathcal{R}_0 = 0.1705 < 1$. Figures 1-4 show that, the concentration of susceptible cells increases and tends to the value $s^0 = 1000$. In addition, the concentrations of long-lived infected cells, short-lived infected cells and free HIV decrease and tend to zero for the initial values IV1-IV3. This shows that Q^0 is globally asymptotically stable and Theorem 4.3 is valid.

(ii) $\bar{k} = 0.001$. With this value we obtain $\mathcal{R}_0 = 1.7045 > 1$. Figures 1-4 show that for the initial values IV1-IV3, the solutions of the system tend to the equilibrium $Q^* = (564.4143, 7.2953, 8.7541, 16.4141)$. Therefore, Q^* exists and it is globally asymptotically stable. This validate the result of Theorem 4.5.

Case (II) Effect of the drug efficacy ϵ on the HIV dynamics:

For this case, we take IV2 and choose the value $\bar{k} = 0.001$ and ϵ is varied. Figures 5-8 and Table 1 show the effect of drug efficacy ϵ on the stability of the system. We observe that, as ϵ is increased, the infection rate is decreased, then, the concentration of the susceptible cells are increased, while the concentrations of the long-lived infected cells, short-lived infected cells and free HIV particles are decreased. In addition

(i) if $\epsilon < 0.70666$, then Q^* is globally asymptotically stable;

(ii) if $\epsilon \geqslant 0.70666$, then Q^0 is globally asymptotically stable.

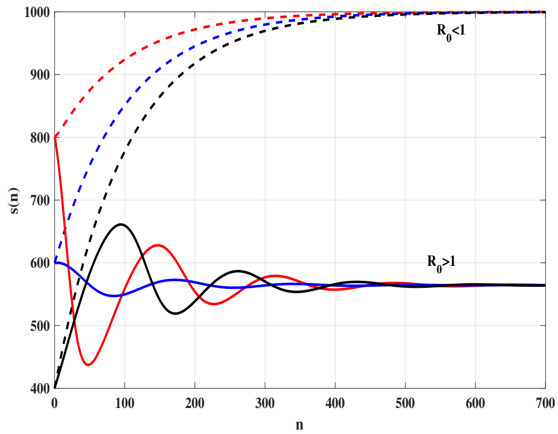

Figure 1: The simulation of susceptible cells of system (5.1)-(5.4) for Case (I).

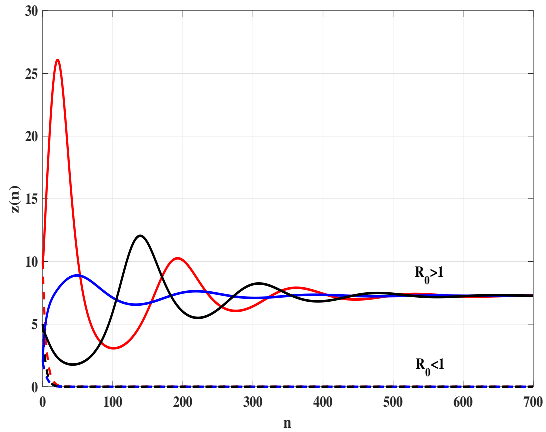

Figure 2: The simulation of short-lived infected cells of system (5.1)-(5.4) for Case (I).

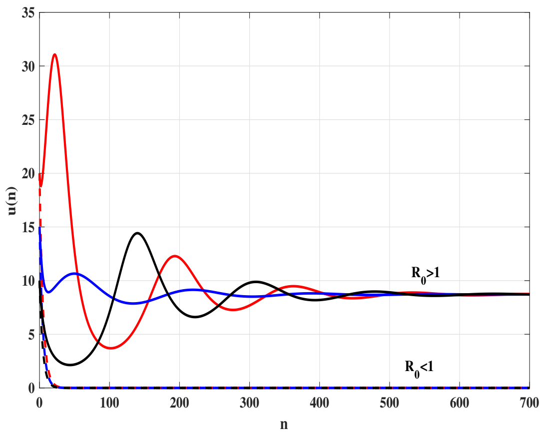

Figure 3: The simulation of long-lived infected cells of system (5.1)-(5.4) for Case (I).

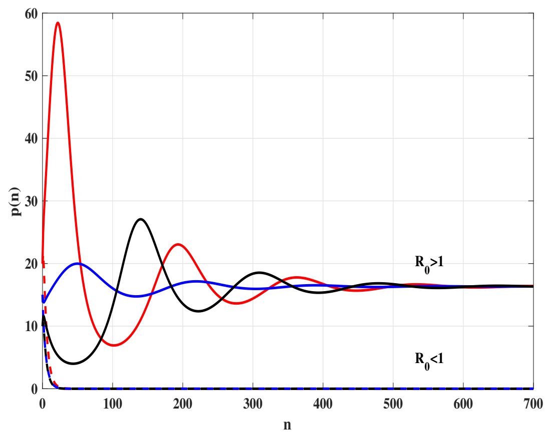

Figure 4: The simulation of pathogens of system (5.1)-(5.4) for Case (I).

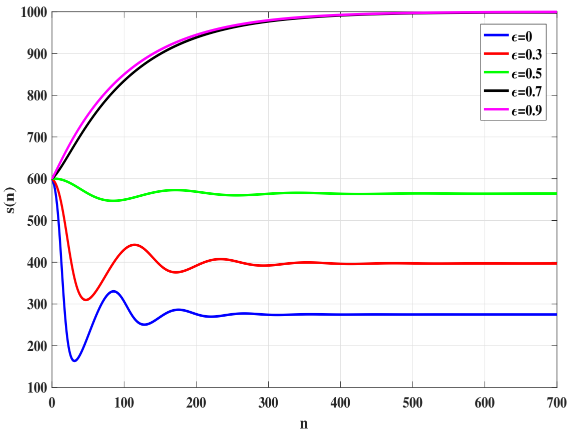

Figure 5: The simulation of susceptible cells of system (5.1)-(5.4) for Case (II).

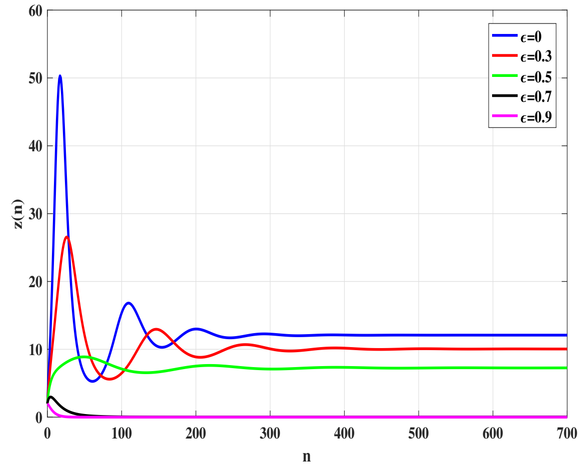

Figure 6: The simulation of short-lived infected cells of system (5.1)-(5.4) for Case (II).

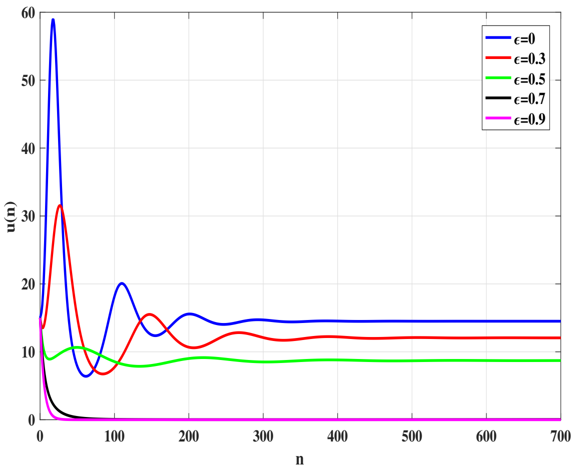

Figure 7: The simulation of long-lived infected cells of system (5.1)-(5.4) for Case (II).

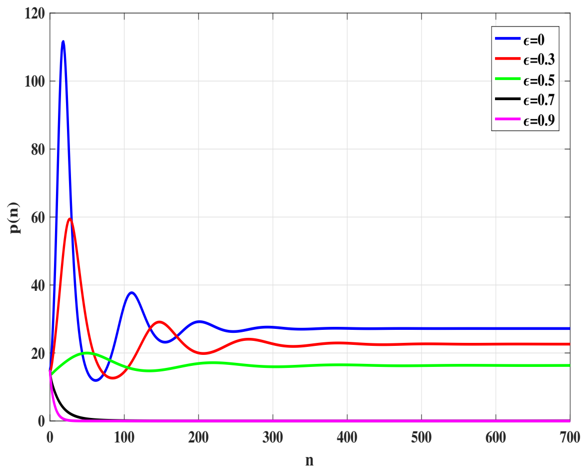

Figure 8: The simulation of pathogens of system (5.1)-(5.4) for Case (II).

Table 1: The values of $\mathcal{R}_0$ for system (5.1)-(5.4) with different values of ϵ.

ϵ	Equilibria	$\mathcal{R}_0$
0	Q^*	3.4091
0.3	Q^*	2.3864
0.5	Q^*	1.7045
0.7	Q^*	1.0227
0.70666	Q^0	1
0.8	Q^0	0.6818
0.9	Q^0	0.3409

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