



Research article

Stochastic dynamics and treatment strategies of an HIV infection model with quiescent cells, CTLs and antibody immune responses

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Abstract: In this paper, a stochastic human immunodeficiency virus (HIV) infection model incorporating quiescent cells, cytotoxic C lymphocytes (CTLs), and antibody immune responses is formulated. First, the existence and uniqueness of the global positive solutions to the model are proven, which guarantees the well-posedness and validity of the constructed dynamic system. Second, the existence of the ergodic stationary distribution is investigated by constructing suitable stochastic Lyapunov functions. Third, the sufficient conditions for virus elimination are derived. Furthermore, optimal control strategies consistent with clinical antiviral treatment regimens are proposed to achieve a trade-off between therapeutic efficacy and economic costs. To validate the theoretical results and further compare the practical performance of different intervention schemes, numerical simulations are implemented, including theoretical verification, parameter sensitivity analysis, and comprehensive cost-effectiveness assessment of various therapeutic strategies. This study systematically clarifies the dynamical evolutionary behaviors of stochastic HIV infection and the efficacy of different control measures. The findings not only enrich the theoretical research on stochastic HIV infection model but also provide solid theoretical support and quantitative guidance for the design, assessment, and optimal selection of clinical HIV treatment strategies.

Keywords: stochastic HIV infection model; ergodic stationary distribution; virus elimination; optimal control strategies

1. Introduction

Acquired immunodeficiency syndrome (AIDS) is a chronic infectious disease caused by human immunodeficiency virus (HIV) [1]. The virus primarily targets and destroys $CD4^+$ T cells, the key components among immune lymphocytes, thereby compromising the immune system's capacity to fend off external threats. After HIV invades the human body, the body mounts corresponding immune responses, which are mainly divided into humoral immunity and cellular immunity. Humoral immune

is also called the antibody-mediated immune. The cellular immune response is often called the cytotoxic T lymphocyte (CTL) immune response. According to the World Health Organization (WHO), in 2024, a total of 630,000 [490,000–820,000] people died from HIV-related causes worldwide. By the end of 2024, approximately 40.8 million [37.0–45.6 million] people were living with HIV globally, and around 1.3 million [1.0–1.7 million] people were newly infected [2].

To explore the pathogenesis of HIV infection and develop therapeutic strategies, numerous mathematical models have been established to characterize the interactive dynamics among the healthy $CD4^+$ T cells, the infected cells, the free virus and immune responses in vivo [3,4]. However, many earlier models only incorporate either the CTL immune response [5,6] or the antibody-mediated immune response [7] alone. The significance of studying antibody and CTL responses in the hepatitis C virus (HCV) infection model was clearly demonstrated in [8]. With this in mind, some researchers investigated the HIV infection models incorporating both CTL and antibody responses [9–11].

Quiescent $CD4^+$ T cells are a population of resting immune cells that do not mount active responses to infection yet serve as critical reservoirs for latent HIV. Upon immune stimulation, these cells can become activated and differentiate into activated $CD4^+$ T cells, which represent the primary cellular targets of HIV infection [12]. This activation process is of considerable biological significance, linking homeostatic immune regulation to infection susceptibility. Following subsidence of stimulatory signals, activated cells can either revert to the quiescent state or undergo apoptosis via physiological pathways including activation-induced cell death. Hence, it is essential to take quiescent $CD4^+$ T cells into account within the mathematical models [13], which is frequently overlooked in the vast majority of existing literatures.

Inspired by [8–11, 13], one can formulate the following HIV infection model to investigate the effects of quiescent cells, CTLs and antibody immune responses:

$$\left\{ \begin{array}{l} \frac{dQ(t)}{dt} = A + \rho T - \gamma Q - \mu_1 Q, \\ \frac{dT(t)}{dt} = \gamma Q - \rho T - \mu_2 T - \frac{\beta TV}{1 + kV}, \\ \frac{dI(t)}{dt} = \frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ, \\ \frac{dV(t)}{dt} = \eta I - \mu_4 V - q_1 VW, \\ \frac{dZ(t)}{dt} = p_2 IZ - \mu_5 Z, \\ \frac{dW(t)}{dt} = q_2 VW - \mu_6 W. \end{array} \right. \quad (1.1)$$

Here, Q , T , I , V , Z , and W represent the quiescent cells, uninfected $CD4^+$ T cells, infected $CD4^+$ T cells, free viruses, CTLs, and antibodies at time t , respectively. The biological meaning of all parameters is summarized in Table 1.

The viral immune response is inherently stochastic. Studies have shown that transcriptional bursting in HIV-1 acts as a major source of random noise, leading to high variability in early gene products, which causes HIV-1 gene expression levels to fluctuate instead of following a deterministic pattern [14]. Furthermore, stochastic effects exert profound impacts on disease dynamics [15]. Traditional ordinary differential equation models for infectious diseases cannot well capture the

Table 1. Parameters and their biological meanings in the model (1.2).

Parameter	Biological meaning
A	Constant input rate of quiescent cells Q
ρ	Conversion rate from activated cells T to quiescent cells Q
γ	Conversion rate from quiescent cells Q to activated cells T
μ_1	Mortality rate of quiescent cells Q
μ_2	Mortality rate of activated cells T
β	Viral infection rate
k	Saturation constant
μ_3	Mortality rate of infected cells I
p_1	Clearance rate of infected cells I mediated by CTLs
η	Production rate of virus V from infected cells I
μ_4	Mortality rate of virus V
q_1	Clearance rate of virus V mediated by antibody immune cells W
p_2	Proliferation rate of CTLs activated by infected cells I
μ_5	Mortality rate of CTLs Z
q_2	Proliferation rate of antibody immune cells W induced by virus V
μ_6	Mortality rate of antibody immune cells W

sustained viral production and sudden viral outbreaks observed in HIV infection. Because the mechanisms governing viral extinction and persistent infection depend on numerous factors that have not been fully elucidated, many scholars have developed stochastic models to explain complex dynamical behaviors [16–19]. For instance, Liu et al. [20] constructed a stochastic HIV model with distributed time delays and logistic growth.

Motivated by these considerations, we assume that the natural death rates of each compartment are perturbed by Gaussian white noise, that is,

$$\begin{aligned}
 -\mu_1 &\rightarrow -\mu_1 + \sigma_1 dB_1(t), \quad -\mu_2 \rightarrow -\mu_2 + \sigma_2 dB_2(t), \quad -\mu_3 \rightarrow -\mu_3 + \sigma_3 dB_3(t), \\
 -\mu_4 &\rightarrow -\mu_4 + \sigma_4 dB_4(t), \quad -\mu_5 \rightarrow -\mu_5 + \sigma_5 dB_5(t), \quad -\mu_6 \rightarrow -\mu_6 + \sigma_6 dB_6(t).
 \end{aligned}$$

Accordingly, the deterministic system (1.1) is extended to the following stochastic differential equation model:

$$\begin{cases}
 dQ(t) = [A + \rho T - \gamma Q - \mu_1 Q]dt + \sigma_1 Q dB_1(t), \\
 dT(t) = [\gamma Q - \rho T - \mu_2 T - \frac{\beta TV}{1 + kV}]dt + \sigma_2 T dB_2(t), \\
 dI(t) = [\frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ]dt + \sigma_3 I dB_3(t), \\
 dV(t) = [\eta I - \mu_4 V - q_1 VW]dt + \sigma_4 V dB_4(t), \\
 dZ(t) = [p_2 IZ - \mu_5 Z]dt + \sigma_5 Z dB_5(t), \\
 dW(t) = [q_2 VW - \mu_6 W]dt + \sigma_6 W dB_6(t).
 \end{cases} \quad (1.2)$$

Here, $B_i(t)$ denotes independent standard Brownian motions with $B_i(0) = 0$, and $\sigma_i^2 > 0$ represents the intensity of white noise for $i = 1, 2, 3, 4, 5, 6$. The biological meanings of the other parameters are the same as those in Model (1.1).

Although numerous studies have focused on HIV modeling, most existing stochastic models only consider either CTL immune response or antibody immune response in isolation and frequently neglect the critical role of resting cells. To fill this gap, the major innovations of this study are summarized as follows: (1) We construct for the first time an HIV dynamical model under stochastic perturbations, which incorporates resting cells, CTL immune response and antibody immune response simultaneously; (2) We design optimal control within the stochastic framework, and innovatively introduce cost-effectiveness analysis to quantitatively evaluate the actual therapeutic effects of different medication regimens under economic cost constraints, which is extremely rare in previous mathematical modeling studies.

This paper is organized as follows. The existence and uniqueness of the global positive solutions of Model (1.2) are verified in Section 2. The existence of its ergodic stationary distribution is discussed in Section 3. The conditions for virus elimination are investigated in Section 4. The optimal control strategies for the proposed system are developed in Section 5. Numerical simulations, including theoretical validation, parameter sensitivity analysis, and evaluation of therapeutic strategies are presented in Section 6. Finally, a comprehensive discussion is provided.

2. Existence and uniqueness of global positive solutions

Theorem 2.1. *For any initial value $X_0 = (Q(0), T(0), I(0), V(0), Z(0), W(0)) \in \mathbb{R}_+^6$, the model (1.2) admits a unique positive solution $(Q(t), T(t), I(t), V(t), Z(t), W(t))$ for all $t \geq 0$ that remains in $\mathbb{R}_+^6$ almost surely (a.s.), that is, for all $t \geq 0$, $(Q(t), T(t), I(t), V(t), Z(t), W(t)) \in \mathbb{R}_+^6$ a.s.*

Proof. For any initial value $(Q(0), T(0), I(0), V(0), Z(0), W(0)) \in \mathbb{R}_+^6$, because the coefficients of System (1.2) satisfy the local Lipschitz condition, System (1.2) possesses a unique local solution

$$(Q(t), T(t), I(t), V(t), Z(t), W(t)), \quad t \in [0, \tau_e),$$

where τ_e denotes the explosion time. To prove the global existence of the solution, it suffices to show that $\tau_e = \infty$ a.s. Let $k_0 \geq 1$ be sufficiently large such that

$$(Q(0), T(0), I(0), V(0), Z(0), W(0)) \in \mathbb{R}_+^6$$

is contained in the interval $[1/k_0, k_0]$. For each integer $k \geq k_0$, define the stopping time:

$$\tau_k = \inf \left\{ t \in [0, \tau_e) : Q(t) \notin \left(\frac{1}{k}, k\right) \text{ or } T(t) \notin \left(\frac{1}{k}, k\right) \text{ or } I(t) \notin \left(\frac{1}{k}, k\right) \right. \\ \left. \text{or } V(t) \notin \left(\frac{1}{k}, k\right) \text{ or } Z(t) \notin \left(\frac{1}{k}, k\right) \text{ or } W(t) \notin \left(\frac{1}{k}, k\right) \right\},$$

where $\inf \emptyset = \infty$ ($\emptyset$ denotes the empty set). Clearly, τ_k is increasing as $k \rightarrow \infty$. Set $\tau_\infty = \lim_{k \rightarrow \infty} \tau_k$; then, $\tau_\infty \leq \tau_e$ a.s. If $\tau_\infty = \infty$ holds almost surely, then $\tau_e = \infty$ a.s., which implies the global solution exists for any initial value $X_0 \in \mathbb{R}_+^6$ a.s. Therefore, it is sufficient to verify that $\tau_\infty = \infty$ a.s.

We now proceed by contradiction. Assume that there exist a constant $\mathcal{T} > 0$ and a constant $\epsilon \in (0, 1)$ such that $\mathbb{P}\{\tau_\infty \leq \mathcal{T}\} > \epsilon$. Then, there exists an integer $k_1 \geq k_0$ satisfying

$$\mathbb{P}\{\tau_k \leq \mathcal{T}\} \geq \epsilon \quad (2.1)$$

for all $k \geq k_1$.

Define a C^2 -function $U : \mathbb{R}_+^6 \rightarrow \mathbb{R}_+$ by

$$U(Q, T, I, V, Z, W) = (Q - 1 - \ln Q) + \left(T - a_1 - a_1 \ln \frac{T}{a_1}\right) + \left(I - a_2 - a_2 \ln \frac{I}{a_2}\right) \\ + \frac{\mu_3}{2\eta} \left(V - a_3 - a_3 \ln \frac{V}{a_3}\right) + a_4(Z - 1 - \ln Z) + a_5(W - 1 - \ln W),$$

where a_1, a_2, a_3, a_4, a_5 are undetermined coefficients. Note that $u - 1 - \ln u \geq 0$ for all $u > 0$, which guarantees the non-negativity of the function U .

Applying Itô's formula to the function U , we obtain

$$dU = LUdt + \sigma_1(Q - 1)dB_1(t) + \sigma_2(T - a_1)dB_2(t) + \sigma_3(I - a_2)dB_3(t) + \frac{\mu_3}{2\eta}\sigma_4(V - a_3)dB_4(t) \\ + \sigma_5a_4(Z - 1)dB_5(t) + \sigma_6a_5(W - 1)dB_6(t),$$

where

$$LU = (1 - \frac{1}{Q})(A + \rho T - \gamma Q - \mu_1 Q) + \frac{1}{2}\sigma_1^2 + (1 - \frac{a_1}{T})(\gamma Q - \rho T - \mu_2 T - \frac{\beta TV}{1 + kV}) \\ + \frac{1}{2}a_1\sigma_2^2 + (1 - \frac{a_2}{I})(\frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ) + \frac{1}{2}a_2\sigma_3^2 + \frac{\mu_3}{2\eta}(1 - \frac{a_3}{V})(\eta I - \mu_4 V - q_1 VW) \\ + \frac{\mu_3 a_3 \sigma_4^2}{4\eta} + a_4(1 - \frac{1}{Z})(p_2 IZ - \mu_5 Z) + \frac{1}{2}a_4\sigma_5^2 + a_5(1 - \frac{1}{W})(q_2 VW - \mu_6 W) + \frac{1}{2}a_5\sigma_6^2 \\ = A + \rho T - \gamma Q - \mu_1 Q - \frac{A}{Q} - \rho \frac{T}{Q} + \gamma + \mu_1 + \frac{1}{2}\sigma_1^2 + \gamma Q - \rho T - \mu_2 T - \frac{\beta TV}{1 + kV} - \frac{a_1 \gamma Q}{T} \\ + a_1 \rho + a_1 \mu_2 + \frac{a_1 \beta V}{1 + kV} + \frac{1}{2}a_1\sigma_2^2 + \frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ - \frac{a_2 \beta TV}{I(1 + kV)} + a_2 \mu_3 + a_2 p_1 Z \\ + \frac{1}{2}a_2\sigma_3^2 + \frac{\mu_3}{2}I - \frac{\mu_3 \mu_4}{2\eta}V - \frac{\mu_3 q_1}{2\eta}VW - \frac{\mu_3 a_3}{2V}I + \frac{\mu_3 a_3 \mu_4}{2\eta} + \frac{\mu_3 a_3 q_1}{2\eta}W + \frac{\mu_3 a_3 \sigma_4^2}{4\eta} + a_4 p_2 IZ \\ - a_4 \mu_5 Z - a_4 p_2 I + a_4 \mu_5 + \frac{1}{2}a_4\sigma_5^2 + a_5 q_2 VW - a_5 \mu_6 W - a_5 q_2 V + a_5 \mu_6 + \frac{1}{2}a_5\sigma_6^2 \\ \leq A + \gamma + \mu_1 + \frac{1}{2}\sigma_1^2 + a_1 \rho + a_1 \mu_2 + (a_1 \beta - \frac{\mu_3 \mu_4}{2\eta})V + \frac{1}{2}a_1\sigma_2^2 + a_2 \mu_3 + (a_2 p_1 - a_4 \mu_5)Z + \\ + \frac{1}{2}a_2\sigma_3^2 + \frac{\mu_3 a_3 \mu_4}{2\eta} + (\frac{\mu_3 a_3 q_1}{2\eta} - a_5 \mu_6)W + \frac{\mu_3 a_3 \sigma_4^2}{4\eta} + (a_4 p_2 - p_1)IZ + a_4 \mu_5 + \frac{1}{2}a_4\sigma_5^2 \\ + (a_5 q_2 - \frac{\mu_3 q_1}{2\eta})VW + a_5 \mu_6 + \frac{1}{2}a_5\sigma_6^2.$$

Choose

$$a_1 = \frac{\mu_3 \mu_4}{2\eta \beta}, \quad a_2 = \frac{\mu_5}{p_2}, \quad a_3 = \frac{\mu_6}{q_2}, \quad a_4 = \frac{p_1}{p_2}, \quad a_5 = \frac{\mu_3 q_1}{2\eta q_2}$$

to satisfy

$$a_1 \beta - \frac{\mu_3 \mu_4}{2\eta} = 0, \quad a_2 p_1 - a_4 \mu_5 = 0, \quad \frac{\mu_3 a_3 q_1}{2\eta} - a_5 \mu_6 = 0, \quad a_4 p_2 - p_1 = 0, \quad a_5 q_2 - \frac{\mu_3 q_1}{2\eta} = 0.$$

Hence,

$$LU \leq A + \gamma + \mu_1 + \frac{1}{2}\sigma_1^2 + a_1\rho + a_1\mu_2 + \frac{1}{2}a_1\sigma_2^2 + a_2\mu_3 + \frac{1}{2}a_2\sigma_3^2 + \frac{\mu_3a_3a_4}{2\eta} \\ + \frac{\mu_3a_3\sigma_4^2}{4\eta} + a_4\mu_5 + \frac{1}{2}a_4\sigma_5^2 + a_5\mu_6 + \frac{1}{2}a_5\sigma_6^2 \triangleq K.$$

Obviously, K is a positive constant. It thus follows that

$$dU \leq Kdt + \sigma_1(Q - 1)dB_1(t) + \sigma_2(T - a_1)dB_2(t) + \sigma_3(I - a_2)dB_3(t) \\ + \frac{\mu_3}{2\eta}\sigma_4(V - a_3)dB_4(t) + \sigma_4a_4(Z - 1)dB_5(t) + \sigma_6a_5(W - 1)dB_6(t). \quad (2.2)$$

Integrating both sides of (2.2) from 0 to $\tau_k \wedge \mathcal{T}$ and taking the expectation, we obtain

$$\mathbb{E}[U(Q(\tau_k \wedge \mathcal{T}), T(\tau_k \wedge \mathcal{T}), I(\tau_k \wedge \mathcal{T}), V(\tau_k \wedge \mathcal{T}), Z(\tau_k \wedge \mathcal{T}), W(\tau_k \wedge \mathcal{T}))] \\ \leq U(Q(0), T(0), I(0), V(0), Z(0), W(0)) + K\mathcal{T}. \quad (2.3)$$

Let $\Omega_k = \{\tau_k \leq \mathcal{T}\}$ for $k \geq k_1$. It follows from $\mathbb{P}\{\tau_k \leq \mathcal{T}\} \geq \epsilon$ that $\mathbb{P}(\Omega_k) \geq \epsilon$. Then, for each $\omega \in \Omega_k$, at least one of $Q(\tau_k, \omega)$, $T(\tau_k, \omega)$, $I(\tau_k, \omega)$, $V(\tau_k, \omega)$, $Z(\tau_k, \omega)$, $W(\tau_k, \omega)$ equals either k or $1/k$. Consequently,

$$U(Q(\tau_k, \mathcal{T}), T(\tau_k, \mathcal{T}), I(\tau_k, \mathcal{T}), V(\tau_k, \mathcal{T}), Z(\tau_k, \mathcal{T}), W(\tau_k, \mathcal{T})) \geq M_1,$$

where

$$M_1 = (k - 1 - \ln k) \wedge \left(\frac{1}{k} - 1 + \ln k\right) \wedge (k - a_1 - a_1 \ln \frac{k}{a_1}) \wedge \left(\frac{1}{k} - a_1 + a_1 \ln a_1 k\right) \\ \wedge (k - a_2 - a_2 \ln \frac{k}{a_2}) \wedge \left(\frac{1}{k} - a_2 + a_2 \ln a_2 k\right) \wedge \frac{\mu_3}{2\eta}(k - a_3 - a_3 \ln \frac{k}{a_3}) \\ \wedge \frac{\mu_3}{2\eta}\left(\frac{1}{k} - a_3 + a_3 \ln a_3 k\right) \wedge a_4(k - 1 - \ln k) \wedge a_4\left(\frac{1}{k} - 1 + \ln k\right) \\ \wedge a_5(k - 1 - \ln k) \wedge a_5\left(\frac{1}{k} - 1 + \ln k\right).$$

From (2.3), we have

$$U(Q(0), T(0), I(0), V(0), Z(0), W(0)) + K\mathcal{T} \\ \geq \mathbb{E}\left[\mathbf{1}_{\Omega_k} U(Q(\tau_k), T(\tau_k), I(\tau_k), V(\tau_k), Z(\tau_k), W(\tau_k))\right] \\ \geq \epsilon M_1,$$

where $\mathbf{1}_{\Omega_k}$ denotes the characteristic function of Ω_k . Taking $k \rightarrow \infty$, we derive

$$\infty > U(Q(0), T(0), I(0), V(0), Z(0), W(0)) + K\mathcal{T} = \infty,$$

which leads to a contradiction. Therefore, $\tau_\infty = \infty$ a.s., which implies that the solution of System (1.2) does not blow up in finite time with probability one. This completes the proof of the theorem. $\square$

3. Existence of ergodic stationary distribution

In this section, we investigate the existence of a unique ergodic stationary distribution for System (1.2). For the convenience of proof, we first define

$$\mathcal{R}_0^S = \frac{A\beta\eta\gamma^2\rho q_2}{k(\gamma + \mu_1 + \frac{1}{2}\sigma_1^2)(\rho + \mu_2 + \frac{\beta}{k} + \frac{1}{2}\sigma_2^2)(\mu_3 + \frac{1}{2}\sigma_3^2)(\mu_4 + \frac{1}{2}\sigma_4^2)(\frac{q_2}{k} + \mu_6 + \frac{1}{2}\sigma_6^2)}.$$

Biologically, $\mathcal{R}_0^S$ acts as the basic reproduction number of Model (1.2), and it governs the long-term persistence of infection in the presence of random noise. In $\mathcal{R}_0^S$, the terms $1/(\gamma + \mu_1 + \frac{1}{2}\sigma_1^2)$, $1/(\rho + \mu_2 + \frac{\beta}{k} + \frac{1}{2}\sigma_2^2)$, $1/(\mu_3 + \frac{1}{2}\sigma_3^2)$, $1/(\mu_4 + \frac{1}{2}\sigma_4^2)$, $1/(\frac{q_2}{k} + \mu_6 + \frac{1}{2}\sigma_6^2)$, represent the mean survival time of quiescent cells Q , the mean survival time of activated $CD4^+$ T cells T , the mean survival time of infected cells I , the mean survival time of free virus V , and the mean survival time of antibody immune response cells W under stochastic perturbations, respectively.

In the absence of noise ($\sigma_i = 0$), $\mathcal{R}_0^S$ reduces to:

$$\mathcal{R}_0 = \frac{A\beta\eta\gamma^2\rho q_2}{k(\gamma + \mu_1)^2(\rho + \mu_2 + \frac{\beta}{k})^2\mu_3\mu_4(\frac{q_2}{k} + \mu_6)}.$$

Obviously, $\mathcal{R}_0^S \leq \mathcal{R}_0$, which indicates that stochastic perturbations can “compress” the virus’s transmission potential. Even when the deterministic model predicts chronic infection, noise can induce viral extinction.

Let $X(t)$ be a regular time-homogeneous Markov process in $\mathbb{R}^d$ satisfying the stochastic differential equation

$$dX(t) = b(X)dt + \sum_{r=1}^k g_r(X)dB_r(t).$$

The diffusion matrix is defined as follows:

$$\tilde{A}(x) = (a_{ij}(x)), \quad a_{ij}(x) = \sum_{r=1}^k g_r^i(x)g_r^j(x).$$

Lemma 3.1. [21] *The Markov process $X(t)$ has a unique ergodic stationary distribution $\mu(\cdot)$ if there exists a bounded open domain $D \subset \mathbb{R}_+^d$ with regular boundary Γ such that the following hold:*

(A1) *There exists a positive constant $\tilde{M}$ such that*

$$\sum_{i,j=1}^d a_{ij}(x)\xi_i\xi_j \geq \tilde{M}|\xi|^2$$

for all $x \in D$ and $\xi \in \mathbb{R}_+^d$;

(A2) *There exists a non-negative C^2 -function $V(x)$ and a positive constant $\bar{C}$ satisfying*

$$LV(x) \leq -\bar{C}, \quad \forall x \in \mathbb{R}_+^d \setminus D.$$

Then, the Markov process $X(t)$ admits a unique ergodic stationary distribution μ , and

$$\mathbb{P}_x \left\{ \lim_{\mathcal{T} \rightarrow \infty} \frac{1}{\mathcal{T}} \int_0^{\mathcal{T}} f(X(t))dt = \int_D f(x)\mu(dx) \right\} = 1,$$

where $f(\cdot)$ is an integrable function with respect to the measure μ .

Theorem 3.1. If $\mathcal{R}_0^S > 1$, then for any initial value $(Q(0), T(0), I(0), V(0), Z(0), W(0)) \in \mathbb{R}_+^6$, System (1.2) admits a unique stationary distribution which is ergodic.

Proof. See Appendix. □

4. Virus elimination

Since the emergence of HIV, researchers have long aimed to achieve the ultimate eradication of the virus. Accordingly, studies on viral clearance can provide solid theoretical support for the prevention, control and comprehensive management of HIV epidemics. In the following sections, we analyze viral clearance dynamics. First, we introduce the necessary theorems and lemmas.

Theorem 4.1. [22] (Strong law of large numbers) Let $M = \{M_t\}_{t \geq 0}$ be a real-valued, continuous, local martingale with $M(0) = 0$. Then,

$$\lim_{t \rightarrow +\infty} \langle M, M \rangle_t = \infty \text{ a.s.} \implies \lim_{t \rightarrow +\infty} \frac{M_t}{\langle M, M \rangle_t} = 0 \text{ a.s.},$$

and

$$\limsup_{t \rightarrow +\infty} \frac{\langle M, M \rangle_t}{t} < \infty \text{ a.s.} \implies \lim_{t \rightarrow +\infty} \frac{M_t}{t} = 0 \text{ a.s.}$$

Lemma 4.1. (Non-negative submartingale convergence theorem) Let $\{A_t\}_{t \geq 0}$ and $\{U_t\}_{t \geq 0}$ be two continuous increasing processes with $A_0 = U_0 = 0$ a.s. Let $\{M_t\}_{t \geq 0}$ be a real-valued, continuous, local martingale satisfying $M_0 = 0$ a.s., and let ξ be a non-negative $\mathcal{F}_0$ -measurable random variable. Define

$$X_t = \xi + A_t - U_t + M_t, \quad \forall t \geq 0.$$

If X_t is nonnegative. Then

$$\left\{ \lim_{t \rightarrow \infty} A_t < \infty \right\} \subseteq \left\{ \lim_{t \rightarrow \infty} X_t \text{ exists and is finite} \right\} \cap \left\{ \lim_{t \rightarrow \infty} U_t < \infty \right\}.$$

Here, $B \subseteq D$ a.s. means that $\mathbb{P}(B \cap D^c) = 0$. In particular, if $\lim_{t \rightarrow \infty} A_t < \infty$ a.s., then for almost every $\omega \in \Omega$, the limit $\lim_{t \rightarrow \infty} X_t(\omega)$ exists and is finite, and $\lim_{t \rightarrow \infty} U_t < \infty$ holds a.s.

Theorem 4.2. Let $(Q(t), T(t), I(t), V(t), Z(t), W(t))$ be the solution of System (1.2) with the initial value $X_0 \in \mathbb{R}_+^6$. Then

$$\limsup_{t \rightarrow \infty} (Q(t) + T(t) + I(t) + \frac{\mu_3}{2\eta} V(t) + \frac{p_1}{p_2} Z(t) + \frac{\mu_3 q_1}{2\eta q_2} W(t)) < \infty \quad \text{a.s.}$$

Furthermore,

$$\begin{aligned} \lim_{t \rightarrow \infty} \frac{Q(t)}{t} &= 0, & \lim_{t \rightarrow \infty} \frac{T(t)}{t} &= 0, & \lim_{t \rightarrow \infty} \frac{I(t)}{t} &= 0, & \text{a.s.}, \\ \lim_{t \rightarrow \infty} \frac{V(t)}{t} &= 0, & \lim_{t \rightarrow \infty} \frac{Z(t)}{t} &= 0, & \lim_{t \rightarrow \infty} \frac{W(t)}{t} &= 0, & \text{a.s.}, \\ \lim_{t \rightarrow \infty} \frac{\ln Q(t)}{t} &= 0, & \lim_{t \rightarrow \infty} \frac{\ln T(t)}{t} &= 0, & \lim_{t \rightarrow \infty} \frac{\ln I(t)}{t} &= 0, & \text{a.s.}, \end{aligned}$$

$$\begin{aligned} \lim_{t \rightarrow \infty} \frac{\ln V(t)}{t} = 0, \quad \lim_{t \rightarrow \infty} \frac{\ln Z(t)}{t} = 0, \quad \lim_{t \rightarrow \infty} \frac{\ln W(t)}{t} = 0, \quad a.s., \\ \lim_{t \rightarrow \infty} \frac{\sigma_1 \int_0^t Q(s) dB_1(s)}{t} = 0, \quad \lim_{t \rightarrow \infty} \frac{\sigma_2 \int_0^t T(s) dB_2(s)}{t} = 0, \quad \lim_{t \rightarrow \infty} \frac{\sigma_3 \int_0^t I(s) dB_3(s)}{t} = 0, \quad a.s. \\ \lim_{t \rightarrow \infty} \frac{\sigma_4 \int_0^t V(s) dB_4(s)}{t} = 0, \quad \lim_{t \rightarrow \infty} \frac{\sigma_5 \int_0^t Z(s) dB_5(s)}{t} = 0, \quad \lim_{t \rightarrow \infty} \frac{\sigma_6 \int_0^t W(s) dB_6(s)}{t} = 0, \quad a.s. \end{aligned}$$

The proof is analogous to Lemma 2.1 in [23] and thus is omitted.

Theorem 4.3. For any initial value $X_0 = (Q(0), T(0), I(0), V(0), Z(0), W(0)) \in \mathbb{R}_+^6$, if $\mathcal{R}_1^S < 1$, any solution $X_t = (Q(t), T(t), I(t), V(t), Z(t), W(t)) \in \mathbb{R}_+^6$ of Model (1.2) satisfies

$$\limsup_{t \rightarrow \infty} \frac{1}{t} \ln \left[I(t) + \frac{\mu_3}{2\eta} V(t) \right] < 0 \quad a.s.$$

Furthermore, we obtain

$$\lim_{t \rightarrow \infty} I(t) = 0, \quad \lim_{t \rightarrow \infty} V(t) = 0,$$

where

$$\mathcal{R}_1^S = \frac{2\eta\beta A}{\mu_3(\mu_1 \wedge \mu_2) \left[\left(\frac{1}{2}\mu_3 \wedge \mu_4 \right) + \frac{\sigma_3^2 \sigma_4^2}{2(\sigma_3^2 + \sigma_4^2)} \right]}.$$

Proof. Applying Itô's formula to $\ln [I(t) + (\mu_3/2\eta)V(t)]$, we have

$$d \ln \left(I + \frac{\mu_3}{2\eta} V \right) = L \ln \left(I + \frac{\mu_3}{2\eta} V \right) dt + \frac{1}{I + \frac{\mu_3}{2\eta} V} (\sigma_3 I dB_3(t) + \frac{\mu_3}{2\eta} \sigma_4 V dB_4(t)), \quad (4.1)$$

where

$$L \ln \left(I + \frac{\mu_3}{2\eta} V \right) = J_1 - J_2.$$

Here

$$\begin{aligned} J_1 &= \frac{1}{I + \frac{\mu_3}{2\eta} V} \left(\frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ + \frac{\mu_3}{2} I - \frac{\mu_3 \mu_4}{2\eta} V - \frac{\mu_3 q_1}{2\eta} VW \right), \\ J_2 &= \frac{1}{2(I + \frac{\mu_3}{2\eta} V)^2} \left[(\sigma_3 I)^2 + \left(\frac{\mu_3}{2\eta} \sigma_4 V \right)^2 \right]. \end{aligned}$$

Simplifying J_1 , we obtain

$$\begin{aligned} J_1 &= \frac{1}{I + \frac{\mu_3}{2\eta} V} \left(\frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ + \frac{\mu_3}{2} I - \frac{\mu_3 \mu_4}{2\eta} V - \frac{\mu_3 q_1}{2\eta} VW \right) \\ &\leq \frac{2\eta}{2\eta I + \mu_3 V} \left(\beta TV - \frac{\mu_3}{2} I - \frac{\mu_3 \mu_4}{2\eta} V \right) \\ &\leq \frac{2\eta\beta T}{\mu_3} - \frac{2\eta}{2\eta I + \mu_3 V} \frac{\eta\mu_3 I + \mu_3 \mu_4 V}{2\eta} \\ &= \frac{2\eta\beta}{\mu_3} T - \frac{\frac{1}{2}\mu_3 2\eta I + \mu_3 \mu_4 V}{2\eta I + \mu_3 V} \\ &\leq \frac{2\eta\beta}{\mu_3} T - \left(\frac{1}{2}\mu_3 \wedge \mu_4 \right). \end{aligned}$$

Because

$$(I + \frac{\mu_3}{2\eta}V)^2 = (\sigma_3 I \frac{1}{\sigma_3} + \sigma_4 \frac{\mu_3}{2\eta} V \frac{1}{\sigma_4})^2 \leq \left[(\sigma_3 I)^2 + (\sigma_4 \frac{\mu_3}{2\eta} V)^2 \right] (\frac{1}{\sigma_3^2} + \frac{1}{\sigma_4^2}),$$

we have

$$J_2 \geq \frac{1}{2(\frac{1}{\sigma_3^2} + \frac{1}{\sigma_4^2})} = \frac{\sigma_3^2 \sigma_4^2}{2(\sigma_3^2 + \sigma_4^2)}.$$

Thereby,

$$L \ln(I + \frac{\mu_3}{2\eta}V) \leq \frac{2\eta\beta}{\mu_3}T - (\frac{1}{2}\mu_3 \wedge \mu_4) - \frac{\sigma_3^2 \sigma_4^2}{2(\sigma_3^2 + \sigma_4^2)}. \quad (4.2)$$

It follows from the first and second expressions of (1.2) that

$$\begin{aligned} d(Q + T) &\leq (A - \mu_1 Q - \mu_2 T)dt + \sigma_1 Q dB_1(t) + \sigma_2 T dB_2(t) \\ &\leq [A - (\mu_1 \wedge \mu_2)(Q + T)]dt + \sigma_1 Q dB_1(t) + \sigma_2 T dB_2(t). \end{aligned}$$

Integrating the above equation from 0 to t , together with Theorem 4.2, we get

$$\limsup_{t \rightarrow \infty} \langle Q + T \rangle \leq \frac{A}{\mu_1 \wedge \mu_2} \quad \text{a.s.}$$

Consequently,

$$\limsup_{t \rightarrow \infty} \langle T(t) \rangle \leq \frac{A}{\mu_1 \wedge \mu_2} \quad \text{a.s.}$$

Let

$$M_1(t) = \int_0^t \frac{\sigma_3 I}{I + \frac{\mu_3}{2\eta}V} dB_3(s), \quad M_2(t) = \int_0^t \frac{\sigma_4 \frac{\mu_3}{2\eta}V}{I + \frac{\mu_3}{2\eta}V} dB_4(s).$$

Obviously, $M_1(t)$ and $M_2(t)$ are continuous local martingales. Furthermore,

$$\begin{aligned} \langle M_1(t), M_1(t) \rangle &= \int_0^t \frac{(\sigma_3 I)^2}{(I + \frac{\mu_3}{2\eta}V)^2} dB_3(s) \leq \sigma_3^2 t, \\ \langle M_2(t), M_2(t) \rangle &= \int_0^t \frac{(\sigma_4 \frac{\mu_3}{2\eta}V)^2}{(I + \frac{\mu_3}{2\eta}V)^2} dB_4(s) \leq \sigma_4^2 t. \end{aligned}$$

Hence,

$$\limsup_{t \rightarrow \infty} \frac{\langle M_i(t), M_i(t) \rangle}{t} < \infty \quad (i = 1, 2) \quad \text{a.s.}$$

From Theorem 4.1, we can get

$$\lim_{t \rightarrow \infty} \frac{M_i(t)}{t} = 0 \quad (i = 1, 2) \quad \text{a.s.}$$

Integrating both sides of (4.1) from 0 to t and combining with (4.2), we obtain

$$\begin{aligned} &\ln(I(t) + \frac{\mu_3}{2\eta}V(t)) - \ln(I(0) + \frac{\mu_3}{2\eta}V(0)) \\ &\leq \int_0^t \left[\frac{2\eta\beta}{\mu_3}T(s) - (\frac{1}{2}\mu_3 \wedge \mu_4) - \frac{\sigma_3^2 \sigma_4^2}{2(\sigma_3^2 + \sigma_4^2)} \right] ds + M_1(t) + M_2(t). \end{aligned}$$

Dividing both sides of the above formula by t and taking the limit yields

$$\limsup_{t \rightarrow \infty} \frac{1}{t} \ln \left[I(t) + \frac{\mu_3}{2\eta} V(t) \right] \leq \frac{2\eta\beta A}{\mu_3(\mu_1 \wedge \mu_2)} - \left(\frac{1}{2} \mu_3 \wedge \mu_4 \right) - \frac{\sigma_3^2 \sigma_4^2}{2(\sigma_3^2 + \sigma_4^2)}.$$

□

5. Optimal control

In this section, we mainly investigate the optimal control problem of HIV treatment with two classes of antiviral drugs, namely reverse transcriptase inhibitors (RTIs) and protease inhibitors (PIs). Within a given treatment period, the administration strategies of RTIs and PIs are regulated to maximize the concentrations of uninfected $CD4^+$ T cells and CTLs while minimizing the therapeutic cost. The therapeutic cost includes actual drug expenses and adverse drug reactions. Based on System (1.2), the model is established as follows:

$$\begin{cases} dQ(t) = [A + \rho T - \gamma Q - \mu_1 Q]dt + \sigma_1 Q dB_1(t), \\ dT(t) = [\gamma Q - \rho T - \mu_2 T - (1 - u_1(t)) \frac{\beta TV}{1 + kV}]dt + \sigma_2 T dB_2(t), \\ dI(t) = [(1 - u_1(t)) \frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ]dt + \sigma_3 I dB_3(t), \\ dV(t) = [(1 - u_2(t)) \eta I - \mu_4 V - q_1 VW]dt + \sigma_4 V dB_4(t), \\ dZ(t) = [p_2 IZ - \mu_5 Z]dt + \sigma_5 Z dB_5(t), \\ dW(t) = [q_2 VW - \mu_6 W]dt + \sigma_6 W dB_6(t). \end{cases} \quad (5.1)$$

Here, $u_1(t)$ and $u_2(t)$ represent the effects of RTIs and PIs, respectively. $1 - u_1(t)$ denotes the efficacy of RTIs for suppressing viral proliferation, and $1 - u_2(t)$ denotes the efficacy of PIs for inhibiting viral maturation. Let

$$x(t) = [Q(t), T(t), I(t), V(t), Z(t), W(t)]^T, \quad u(t) = [u_1(t), u_2(t)]^T.$$

System (5.1) can be rewritten as

$$dx = f(x(t), u(t))dt + g(x(t))dB(t),$$

where the components of $f(x(t), u(t))$ are given by

$$\begin{cases} f_1(x, u) = A + \rho T - \gamma Q - \mu_1 Q, \\ f_2(x, u) = \gamma Q - \rho T - \mu_2 T - (1 - u_1) \frac{\beta TV}{1 + kV}, \\ f_3(x, u) = (1 - u_1) \frac{\beta TV}{1 + kV} - \mu_3 I - p_1 IZ, \\ f_4(x, u) = (1 - u_2) \eta I - \mu_4 V - q_1 VW, \\ f_5(x, u) = p_2 IZ - \mu_5 Z, \\ f_6(x, u) = q_2 VW - \mu_6 W \end{cases}$$

and

$$g(x(t)) = \begin{pmatrix} \sigma_1 Q & 0 & 0 & 0 & 0 & 0 \\ 0 & \sigma_2 T & 0 & 0 & 0 & 0 \\ 0 & 0 & \sigma_3 I & 0 & 0 & 0 \\ 0 & 0 & 0 & \sigma_4 V & 0 & 0 \\ 0 & 0 & 0 & 0 & \sigma_5 Z & 0 \\ 0 & 0 & 0 & 0 & 0 & \sigma_6 W \end{pmatrix}.$$

To solve for $u_1(t)$ and $u_2(t)$, we define the performance index J of the optimal control problem, and then

$$J(u) = \frac{1}{2} \mathbb{E} \left\{ \int_0^T \left[I + V + \frac{1}{2} (B_1 u_1^2 + B_2 u_2^2) \right] dt \right\},$$

where T denotes the terminal control time. The coefficients B_1, B_2 are positive constants. These two coefficients are the cost weighting parameters for RTIs and PIs, respectively, accounting for both direct pharmacotherapy costs and the health burden caused by drug-related adverse effects. A quadratic cost function is employed, supported by pharmacological and economic evidence. As drug dosage rises, marginal treatment costs, including additional pharmaceutical expenses and cumulative hepatorenal toxicity risk increase monotonically. This characteristic conforms to the classical pharmacological dose-toxicity relationship and the health-economic principle of rising marginal cost. Differences in the weighting coefficients between the two drug classes also reflect real-world disparities in their overall clinical treatment costs. To rule out the possibility that core findings rely on particular weight values, subsection 6.4 presents a robustness analysis for cost weights. Five control weight levels (2, 4, 6, 8, 10) are set to compare virus extinction time and nonextinction proportion among the three therapeutic strategies.

Consider the optimal control problem. The objective is to seek an optimal control $u^*(t) = (u_1^*(t), u_2^*(t))$ such that

$$J(u^*) = \inf_{u \in U} J(u), \quad \forall u \in U,$$

where U is an admissible control set

$$U = \left\{ u_i(t) \mid u_i(t) \in [0, u_i^{\max}], u_i(t) \in L^2[0, T], t \in [0, T], i = 1, 2 \right\},$$

with $0 < u_i^{\max} < 1$ for $i = 1, 2$. Based on the stochastic maximum principle, we construct the Hamiltonian function $Y(x, u, m, n)$ as follows:

$$Y(x, u, m, n) = \langle f(x, u), m \rangle - l(x, u) + \langle g(x), n \rangle,$$

where $\langle \cdot, \cdot \rangle$ denotes the Euclidean inner product. Moreover, $m = [m_1, m_2, m_3, m_4, m_5]^T$ and $n = [n_1, n_2, n_3, n_4, n_5]^T$ are adjoint variables.

Define the Hamiltonian function Y for the stochastic optimal control problem as follows:

$$\begin{aligned}
 Y = Y(x, u, m, n) = & L + \sum_{i=1}^6 m_i f_i(x(t), u(t)) + \sum_{i=1}^6 n_i g_i(x(t)) \\
 = & L + m_1 [A + \rho T - \gamma Q - \mu_1 Q] \\
 & + m_2 \left[\gamma Q - \rho T - \mu_2 T - (1 - u_1) \frac{\beta T V}{1 + k V} \right] \\
 & + m_3 \left[(1 - u_1) \frac{\beta T V}{1 + k V} - \mu_3 I - p_1 I Z \right] \\
 & + m_4 [(1 - u_2) \eta I - \mu_4 V - q_1 V W] \\
 & + m_5 [p_2 I Z - \mu_5 Z] + m_6 [q_2 V W - \mu_6 W] \\
 & + n_1 \sigma_1 Q + n_2 \sigma_2 T + n_3 \sigma_3 I + n_4 \sigma_4 V + n_5 \sigma_5 Z + n_6 \sigma_6 W,
 \end{aligned}$$

where L denotes the Lagrangian function:

$$L(I, V, u_1, u_2) = I + V + \frac{1}{2} (B_1 u_1^2 + B_2 u_2^2).$$

To find the optimal solution of Model (5.1), we apply the Pontryagin maximum principle and obtain the following result. If (x, u) is the optimal solution to the optimal control problem, then there exists a nontrivial vector function $m = [m_1, m_2, m_3, m_4, m_5]^T$ satisfying the following equations:

$$\begin{aligned}
 dx^*(t) &= \frac{\partial Y(x^*, u^*, m, n)}{\partial m} dt + g(x^*(t)) dW(t), \\
 dm^*(t) &= -\frac{\partial Y(x^*, u^*, m, n)}{\partial x} dt + n(t) dW(t), \\
 0 &= \frac{\partial Y(x^*, u^*, m, n)}{\partial u^*}.
 \end{aligned} \tag{5.2}$$

Next, substituting the Hamiltonian function Y into Eq (5.2), we obtain the following theorem concerning the optimal control.

Theorem 5.1. Suppose that the Model (5.1) admits a set of optimal controls $u^*(t) \in U$ and the corresponding optimal state solutions $(Q^*, T^*, I^*, V^*, Z^*, W^*)$. Then, there exist adjoint variables m_i ($i = 1, 2, 3, 4, 5, 6$) satisfying the following adjoint equations:

$$\begin{cases}
 \frac{dm_1}{dt} = m_1(\gamma + \mu_1) - m_2\gamma - n_1\sigma_1, \\
 \frac{dm_2}{dt} = -m_1\rho + m_2(\rho + \mu_2 + (1 - u_1)\frac{\beta V}{1 + kV}) - m_3(1 - u_1)\frac{\beta V}{1 + kV} - n_2\sigma_2, \\
 \frac{dm_3}{dt} = m_3(\mu_3 + p_1Z) - m_4(1 - u_2)\eta - m_5p_2Z - A_1 - n_3\sigma_3, \\
 \frac{dm_4}{dt} = m_2(1 - u_1)\frac{\beta T}{(1 + kV)^2} - m_3(1 - u_1)\frac{\beta T}{(1 + kV)^2} + m_4(\mu_4 + q_1W) \\
 \quad - m_6q_2W - A_2 - n_4\sigma_4, \\
 \frac{dm_5}{dt} = m_3p_1I + m_5(-p_2I + \mu_5) - n_5\sigma_5, \\
 \frac{dm_6}{dt} = m_4q_1V + m_6(-q_2V + \mu_6) - n_6\sigma_6.
 \end{cases} \tag{5.3}$$

The transversality conditions are

$$m_1(T) = m_2(T) = m_3(T) = m_4(T) = m_5(T) = m_6(T) = 0.$$

Consequently, the optimal control is determined:

$$\begin{aligned} u_1^* &= \max \left\{ \min \left\{ 1, \frac{(m_3 - m_2) \frac{\beta T^* V^*}{1 + k V^*}}{B_1} \right\}, 0 \right\}, \\ u_2^* &= \max \left\{ \min \left\{ 1, \frac{m_4 \eta I^*}{B_2} \right\}, 0 \right\}. \end{aligned} \quad (5.4)$$

Proof. To verify the above results, namely to derive the adjoint equations and transversality conditions, we next employ the Hamiltonian. Here, the adjoint System (5.3) is derived from the stochastic Pontryagin maximum principle. Let

$$Q = Q^*, \quad T = T^*, \quad I = I^*, \quad V = V^*, \quad Z = Z^*, \quad W = W^*.$$

By differentiating the Hamiltonian Y with respect to Q, T, I, V, Z, W , respectively, we obtain System (5.3). Considering the admissible control set U and solving the equations

$$\begin{aligned} \frac{\partial Y}{\partial u_1^*} &= B_1 u_1^* + m_2 \frac{\beta T^* V^*}{1 + k V^*} - m_3 \frac{\beta T^* V^*}{1 + k V^*} = 0, \\ \frac{\partial Y}{\partial u_2^*} &= B_2 u_2^* - m_4 \eta I^* = 0, \end{aligned}$$

we can derive the optimal control functions (5.4) presented above. This completes the proof of the theorem. $\square$

6. Numerical simulations

6.1. Theoretical verification

In this section, numerical simulations of Model (1.2) are carried out by using the mathematical software MATLAB R2024b to verify the theoretical results. Based on the Milstein method proposed by Higham [24], the following discrete equation is given:

$$\begin{cases} Q_{k+1} = Q_k + [A + \rho T_k - (\gamma + \mu_1) Q_k] \Delta t + \sigma_1 Q_k \sqrt{\Delta t} \phi_{1,k} + \frac{\sigma_1^2}{2} Q_k (\phi_{1,k}^2 - 1) \Delta t, \\ T_{k+1} = T_k + [\gamma Q_k - (\rho + \mu_2) T_k - \frac{\beta T_k V_k}{1 + k V_k}] \Delta t + \sigma_2 T_k \sqrt{\Delta t} \phi_{2,k} + \frac{\sigma_2^2}{2} T_k (\phi_{2,k}^2 - 1) \Delta t, \\ I_{k+1} = I_k + [\frac{\beta T_k V_k}{1 + k V_k} - (\mu_3 + p_1 Z_k) I_k] \Delta t + \sigma_3 I_k \sqrt{\Delta t} \phi_{3,k} + \frac{\sigma_3^2}{2} I_k (\phi_{3,k}^2 - 1) \Delta t, \\ V_{k+1} = V_k + [\eta I_k - (\mu_4 + q_1 W_k) V_k] \Delta t + \sigma_4 V_k \sqrt{\Delta t} \phi_{4,k} + \frac{\sigma_4^2}{2} V_k (\phi_{4,k}^2 - 1) \Delta t, \\ Z_{k+1} = Z_k + (p_2 I_k - \mu_5) Z_k \Delta t + \sigma_5 Z_k \sqrt{\Delta t} \phi_{5,k} + \frac{\sigma_5^2}{2} Z_k (\phi_{5,k}^2 - 1) \Delta t, \\ W_{k+1} = W_k + (q_2 V_k - \mu_6) W_k \Delta t + \sigma_6 W_k \sqrt{\Delta t} \phi_{6,k} + \frac{\sigma_6^2}{2} W_k (\phi_{6,k}^2 - 1) \Delta t, \end{cases} \quad (6.1)$$

where $\phi_{1,k}, \phi_{2,k}, \phi_{3,k}, \phi_{4,k}, \phi_{5,k}, \phi_{6,k}$ ($k = 1, 2, \dots, n$) are mutually independent Gaussian random variables following the standard normal distribution $N(0, 1)$, and $\Delta t > 0$ denotes the time step increment.

Case 1. With initial values $(Q(0), T(0), I(0), V(0), Z(0), W(0)) = (50, 20, 10, 5, 1, 1)$; parameters given in Table 2; and noise intensities $\sigma_1 = \sigma_2 = \sigma_3 = \sigma_4 = \sigma_5 = \sigma_6 = 0.1$, Figure 1 shows the solution trajectories of Model (1.2), which confirms that the system has a stationary distribution. We obtain the basic reproduction number $\mathcal{R}_0^S \approx 3.13 > 1$. This satisfies the conditions of Theorem 3.1 and implies that System (1.2) admits a unique stationary distribution. With all other parameters kept fixed, and $\sigma_1 = \sigma_2 = \sigma_3 = \sigma_4 = \sigma_5 = \sigma_6 = 0$, we obtain the trajectories of the corresponding deterministic counterpart (Figure 1).

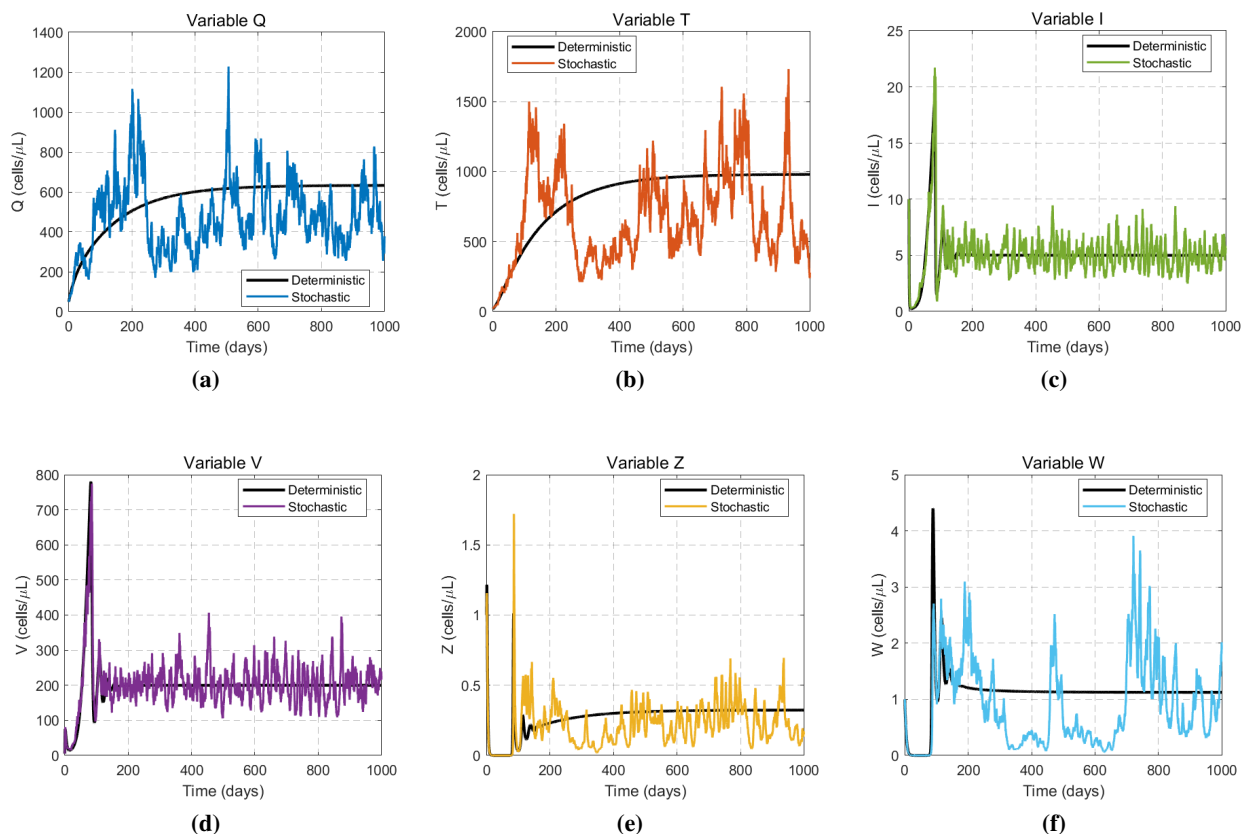


Figure 1. These trajectories represent the dynamics of the stochastic model (1.2) with noise intensity $\sigma_i = 0.1$ and its corresponding deterministic model.

To uncover the unique effects of stochastic perturbations on HIV infection dynamics, we carried out comparative numerical experiments with three noise intensity levels, whose results are presented in Figures 1–3, while fixing all deterministic parameters. Numerical results indicate that weak noise yields sample paths close to the deterministic solution, with mild fluctuations in viral load and cell populations. Increasing noise intensity gives rise to pronounced random oscillations of state variables. Notably, strong noise can induce stochastic viral extinction even when $\mathcal{R}_0^S > 1$, a behavior absent in the deterministic counterpart. From Figures 1–3, our results show that noise intensities σ_i are the most influential determinants of viral clearance. This highlights the distinct dynamical features captured by the stochastic model compared with its counterpart based on classical derivatives.

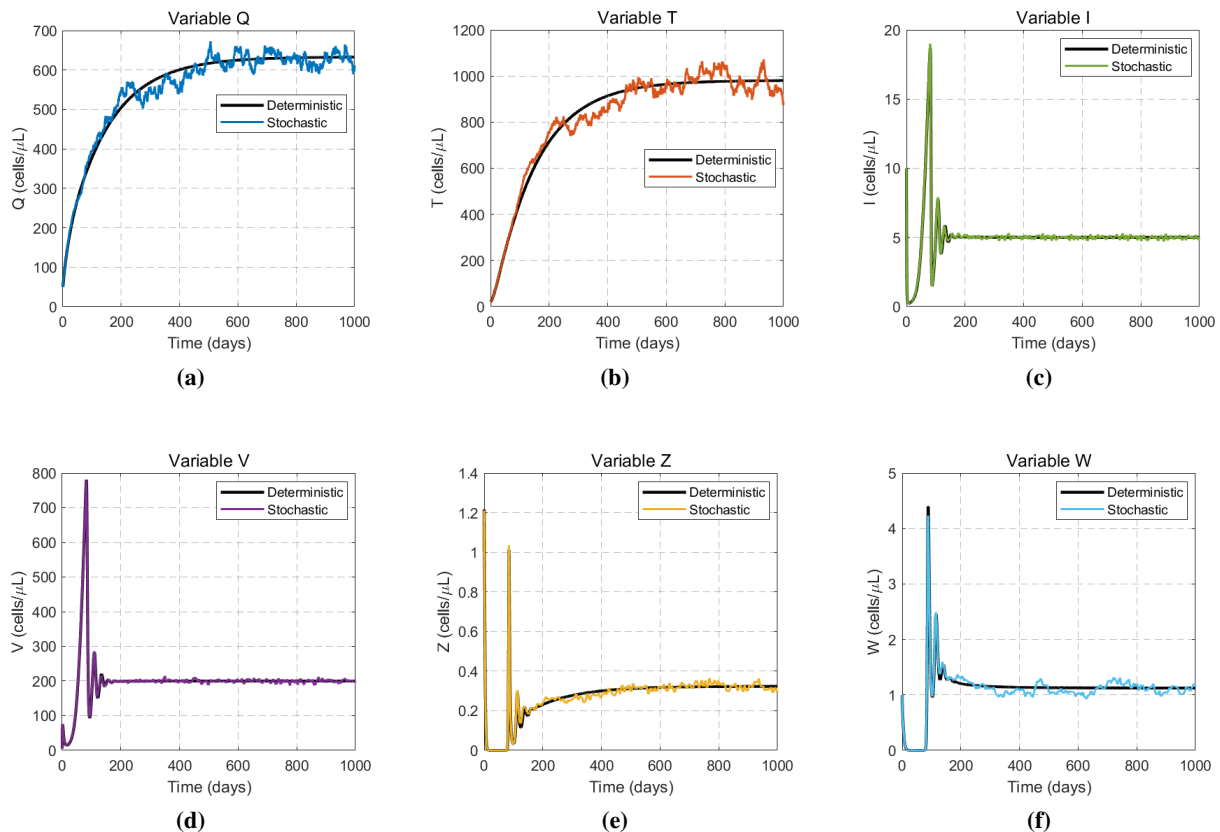


Figure 2. These trajectories represent the dynamics of the stochastic model (1.2) with noise intensity $\sigma_i = 0.01$ and its corresponding deterministic model.

As proposed by Tan et al. [25], the viral threshold is defined as:

$$V_{\text{thr}} := \frac{20 \text{ copies}}{\text{ml}} \times \frac{1 \text{ ml}}{1000 \mu\text{l}} = 0.02 \text{ copies}/\mu\text{l}.$$

Here, viral suppression is defined by the condition $V(t) < 0.02 \text{ copies}/\mu\text{l}$, which serves as a surrogate for almost sure viral extinction. This setting accounts for the limitation of clinical assays, which cannot distinguish true viral eradication from undetectable low-level viremia.

Due to environmental stochasticity, viral load fluctuates across multiple orders of magnitude, which compresses low-viremia data visually on linear scales. Logarithmic scaling is thus preferred to capture the complete dynamic range [26]. Although some trajectories show transient viral rebounds, this does not conflict with the theoretical almost sure extinction. Sustained median viral loads below V_{thr} reliably indicate virologic quiescence [26].

The median trajectory reliably reflects the main temporal trend, and quantile bands effectively quantify the variability among individual trajectories. Accordingly, Figures 4 and 5 present median viral load trajectories along with the corresponding uncertainty intervals obtained from 1000 stochastic simulations, including the interquartile range (25%–75%) and the full-range interval (5%–95%). These visualizations clearly demonstrate how environmental noise modulates infection dynamics at different intensity levels.

Table 2. Parameter values of Model (1.2).

Parameter	Value	Source	Parameter	Value	Source
A	$10 \mu\text{l}^{-1}d^{-1}$	[25]	ρ	$0.017 \mu\text{l}^{-1}d^{-1}$	[13]
γ	$0.042 \mu\text{l}^{-1}d^{-1}$	[13]	μ_1	$0.00014 d^{-1}$	[29]
μ_2	$0.0085 d^{-1}$	[13] [30]	β	$2.4 \times 10^{-5} \mu\text{l}^{-1}d^{-1}$	[25]
k	$0.01 \mu\text{l}^{-1}d^{-1}$	Assumption	μ_3	$0.01 d^{-1}$	[27]
p_1	$0.94 \mu\text{l}^{-1}d^{-1}$	[27]	η	$11.349 \mu\text{l}^{-1}d^{-1}$	[28]
μ_4	$0.25 d^{-1}$	[27]	q_1	$0.03 \mu\text{l}^{-1}d^{-1}$	[27]
p_2	$0.1 \mu\text{l}^{-1}d^{-1}$	[27]	μ_5	$0.5 d^{-1}$	[28]
q_2	$0.0015 \mu\text{l}^{-1}d^{-1}$	[27]	μ_6	$0.3 d^{-1}$	Assumption

Table 3. Parameter values of Model (1.2).

Parameter	Value	Source	Parameter	Value	Source
A	$10 \mu\text{l}^{-1}d^{-1}$	[25]	ρ	$0.017 \mu\text{l}^{-1}d^{-1}$	[13]
γ	$0.042 \mu\text{l}^{-1}d^{-1}$	[13]	μ_1	$0.2 d^{-1}$	Assumption
μ_2	$0.2 d^{-1}$	Assumption	β	$2.4 \times 10^{-5} \mu\text{l}^{-1}d^{-1}$	[25]
k	$0.01 \mu\text{l}^{-1}d^{-1}$	Assumption	μ_3	$0.3 d^{-1}$	Assumption
p_1	$0.94 \mu\text{l}^{-1}d^{-1}$	[27]	η	$11.349 \mu\text{l}^{-1}d^{-1}$	[28]
μ_4	$0.25 d^{-1}$	[27]	q_1	$0.03 \mu\text{l}^{-1}d^{-1}$	[27]
p_2	$0.1 \mu\text{l}^{-1}d^{-1}$	[27]	μ_5	$0.5 d^{-1}$	[28]
q_2	$0.0015 \mu\text{l}^{-1}d^{-1}$	[27]	μ_6	$0.3 d^{-1}$	Assumption

Case 2. Set $\beta = 2.4 \times 10^{-6}$, $\mu_1 = 0.014$, and $\mu_3 = 0.3$, with all other parameters taken from Table 2. Figure 4 plots the solution trajectories of the stochastic system (1.2), confirming complete viral elimination. We obtain $\mathcal{R}_1^S \approx 0.81 < 1$, which is consistent with the hypotheses of Theorem 4.3. As further observed in Figure 4, higher noise levels accelerate viral extinction.

Case 3. Using the parameter values listed in Table 2 and setting $\sigma_i = 0.1$ (consistent with the parameter setup in Case 1), Figure 5(a) presents the solution trajectories of the stochastic system (1.2), which indicates persistent infection. Here, we obtain $\mathcal{R}_0^S \approx 3.13 > 1$, satisfying the conditions of Theorem 3.1 and implying that System (1.2) admits a unique stationary distribution. With all other parameters kept fixed, we plot Figure 5(b),(c) for $\sigma_i = 0.6$ and $\sigma_i = 0.7$, respectively, where viral extinction occurs. These results show that moderate and strong environmental noise can lead to viral elimination and that higher noise intensity reduces the time required for viral eradication.

6.2. Sensitivity analysis

To further explore how different parameters affect HIV infection, we perform a sensitivity analysis in this section. We calculate the partial rank correlation coefficients (PRCC) of $\mathcal{R}_1^S$, and the results are presented in Figure 6. Several parameters show significant impacts on $\mathcal{R}_1^S$, namely $\eta, \beta, A, \mu_1, \mu_2$, and μ_3 . Here, η, β , and A are positively correlated with $\mathcal{R}_1^S$, whereas μ_1, μ_2 , and μ_3 show negative correlations.

Subsequently, we investigate the combined effects of every pair of parameters in System (1.2) on the threshold $\mathcal{R}_1^S$. The ezmesh plots are produced using MATLAB R2024b, as illustrated in Figure 7.

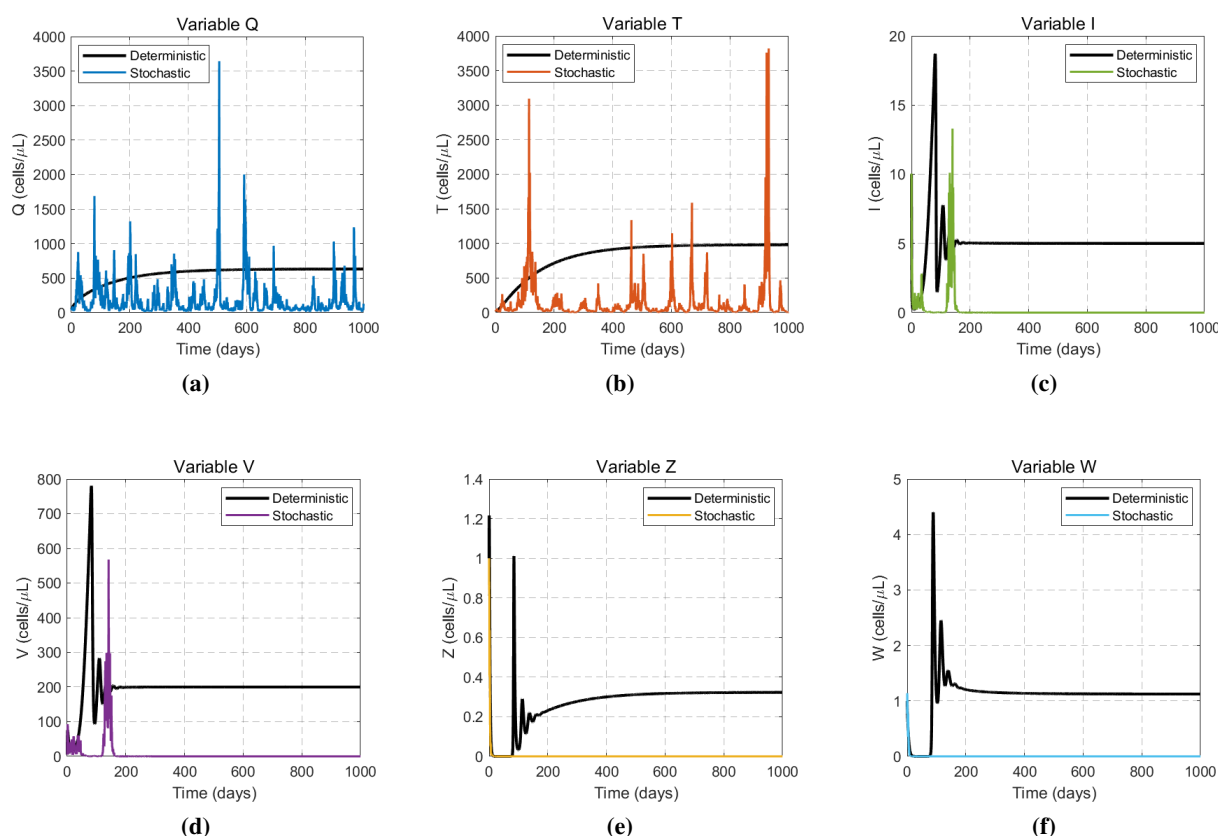


Figure 3. These trajectories represent the dynamics of the stochastic model (1.2) with noise intensity $\sigma_i = 0.5$ and its corresponding deterministic model.

The results indicate that $\mathcal{R}_1^S$ declines as the infection rate β and virus production rate η decrease (Figure 7(a)); $\mathcal{R}_1^S$ decreases as η decreases and the virus mortality rate μ_4 rises (Figure 7(b)). Increases in both noise intensity σ_3 and μ_4 lead to a reduction in $\mathcal{R}_1^S$ (Figure 7(c)); similarly, decreasing β and raising μ_4 lowers $\mathcal{R}_1^S$ (Figure 7(d)).

Figure 8 shows the time series of viral load V for different values of β , η , μ_4 , σ_4 , ρ , and γ , where $\sigma_i = 0.3$ and all other parameters are kept fixed (see Table 3). We can see that despite changes to these parameters, the virus eventually dies out in all scenarios, with only the extinction time differing. The main findings are summarized below:

(1) Reducing the infection rate β and virus production rate η shortens the viral extinction time. Likewise, raising the virus mortality rate μ_4 and noise intensity σ_4 also speeds up viral extinction.

(2) Although ρ and γ do not appear in the analytical expression for $\mathcal{R}_1^S$, the results indicate that decreasing γ and increasing ρ can accelerate viral extinction. Accordingly, such parameter adjustments lead to a larger population of quiescent cells in Model (1.2).

6.3. Treatment strategies

This section explores HIV treatment strategies from two complementary perspectives. Subsection 6.3.1 uses forward simulations to characterize the stochastic dynamics of three therapeutic

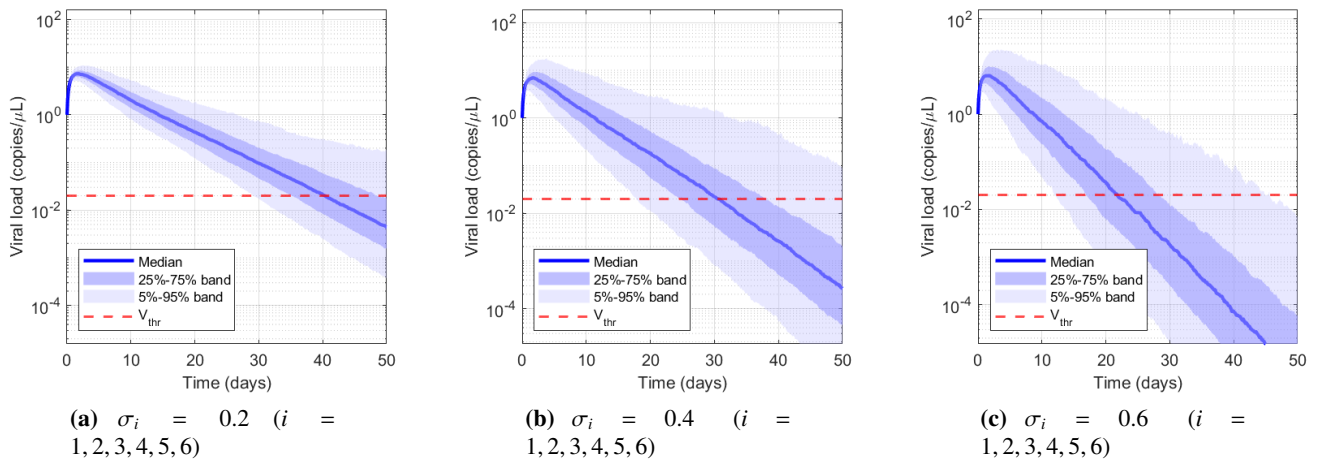


Figure 4. Effects of varying noise intensities on viral elimination.

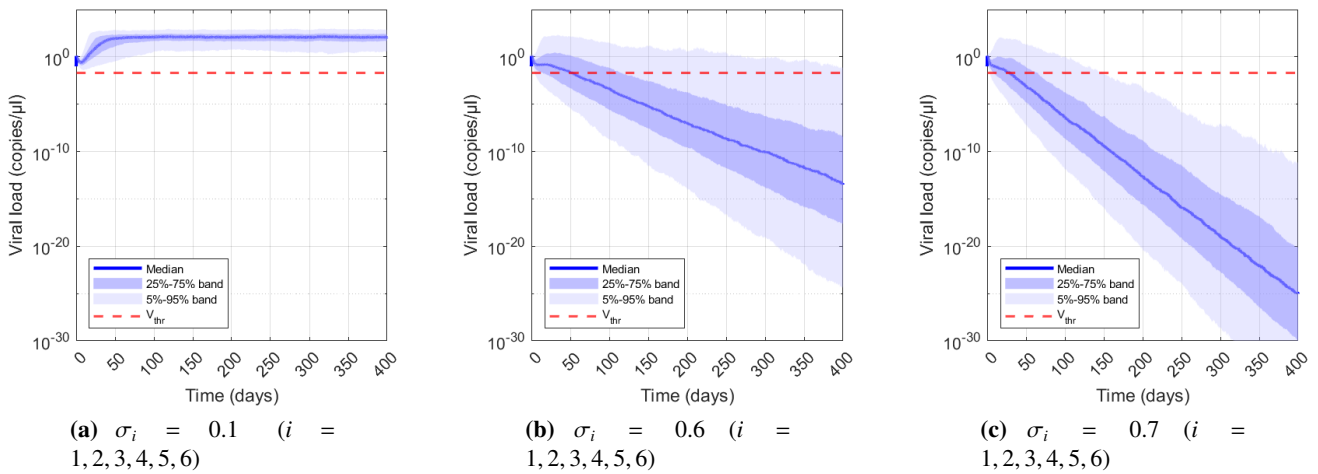


Figure 5. The effect on viruses with the increase of noise intensity.

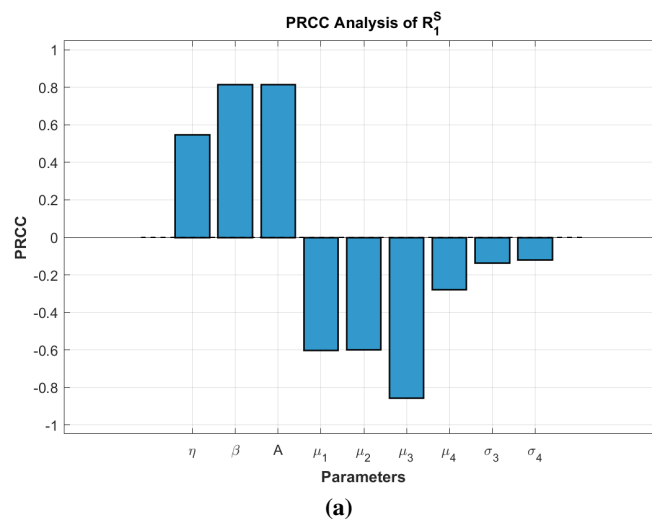


Figure 6. Sensitivity analysis of the threshold $\mathcal{R}_1^S$.

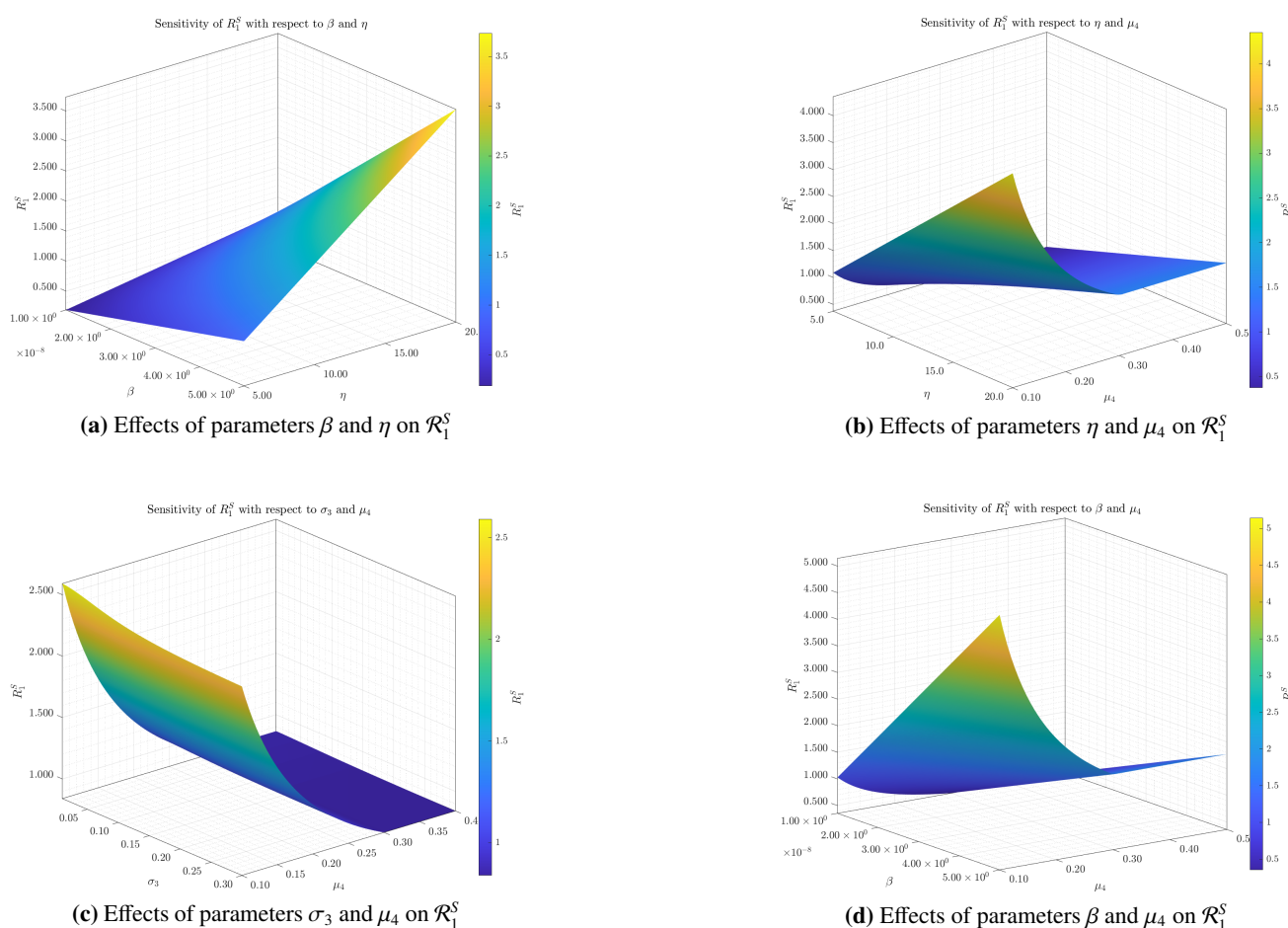


Figure 7. Sensitivity analysis of $\mathcal{R}_1^S$ with respect to various parameter combinations.

regimens (single RTI therapy, single PI therapy, combined therapy) under constant drug efficacy, and evaluates their respective control performance. In Subsection 6.3.2, we adopt backward optimization to implement stochastic optimal control and derive time-varying optimal dosing strategies.

6.3.1. Antiviral therapy

This subsection investigates the kinetic effects of monotherapy and combination therapy using RTIs and PIs on HIV dynamics under stochastic environmental perturbations. The following dynamical system is formulated through mathematical modeling of pharmacotherapy:

$$\begin{cases} dQ(t) = [A + \rho T - \gamma Q - \mu_1 Q]dt + \sigma_1 Q dB_1(t), \\ dT(t) = [\gamma Q - \rho T - \mu_2 T - (1 - \epsilon_{RT}) \frac{\beta TV}{1+kV}]dt + \sigma_2 T dB_2(t), \\ dI(t) = [(1 - \epsilon_{RT}) \frac{\beta TV}{1+kV} - \mu_3 I - p_1 IZ]dt + \sigma_3 I dB_3(t), \\ dV(t) = [(1 - \epsilon_{PI}) \eta I - \mu_4 V - q_1 VW]dt + \sigma_4 V dB_4(t), \\ dZ(t) = [p_2 IZ - \mu_5 Z]dt + \sigma_5 Z dB_5(t), \\ dW(t) = [q_2 VW - \mu_6 W]dt + \sigma_6 W dB_6(t), \end{cases} \quad (6.2)$$

where ϵ_{RT} denotes the efficacy of RTIs, and ϵ_{PI} denotes the efficacy of PIs.

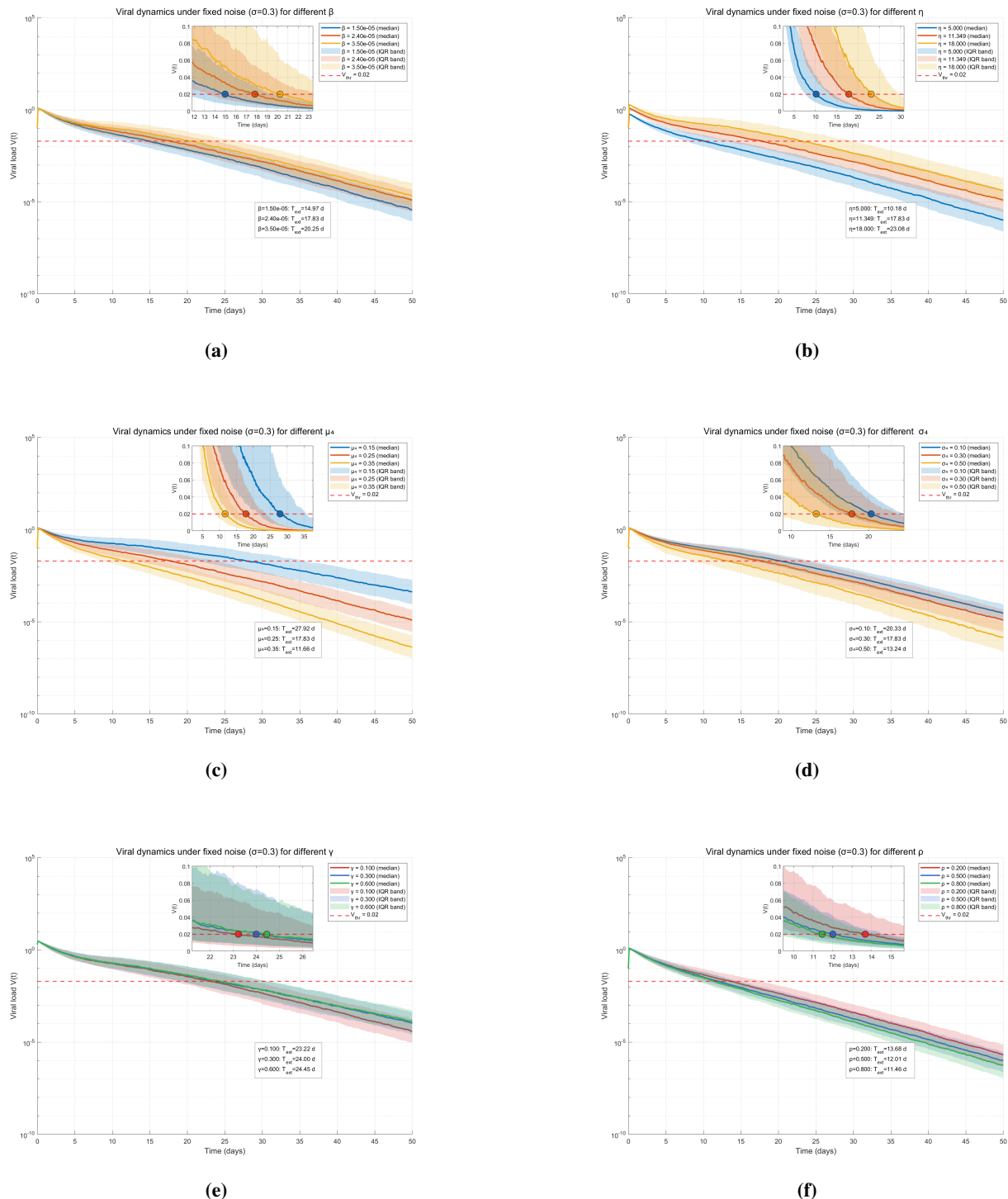


Figure 8. Effects of different values of the same parameter on the extinction time of the virus.

Figure 9 displays the median viral load trajectories obtained from 1000 stochastic simulations under varying noise intensities and therapeutic regimens, where $\mu_6 = 0.6$, and all remaining parameters follow the values in Table 2. The key conclusions are listed below:

(1) Low noise (Figure 9(a),(b)): Under the deterministic framework, PI monotherapy ($\epsilon_{RT} = 0, \epsilon_{PI} = 0.7$) suppresses viral load far more effectively than RTI monotherapy ($\epsilon_{RT} = 0.7, \epsilon_{PI} = 0$). Combination antiretroviral therapy (cART) achieves the strongest overall inhibitory effect.

(2) Moderately high noise (Figure 9(c)): PI monotherapy remains superior to RTI monotherapy. Furthermore, under intense stochastic perturbations, cART can reduce viral load below the detection limit and achieve suppression close to functional cure.

These simulation results reveal that distinct therapeutic strategies have divergent therapeutic potentials under fixed drug efficacy coefficients, with combination therapy showing prominent advantages. In real clinical practice, however, drug efficacy can be dynamically modulated. Accordingly, an optimal control model is constructed in the subsequent section to derive time-dependent optimal medication schedules.

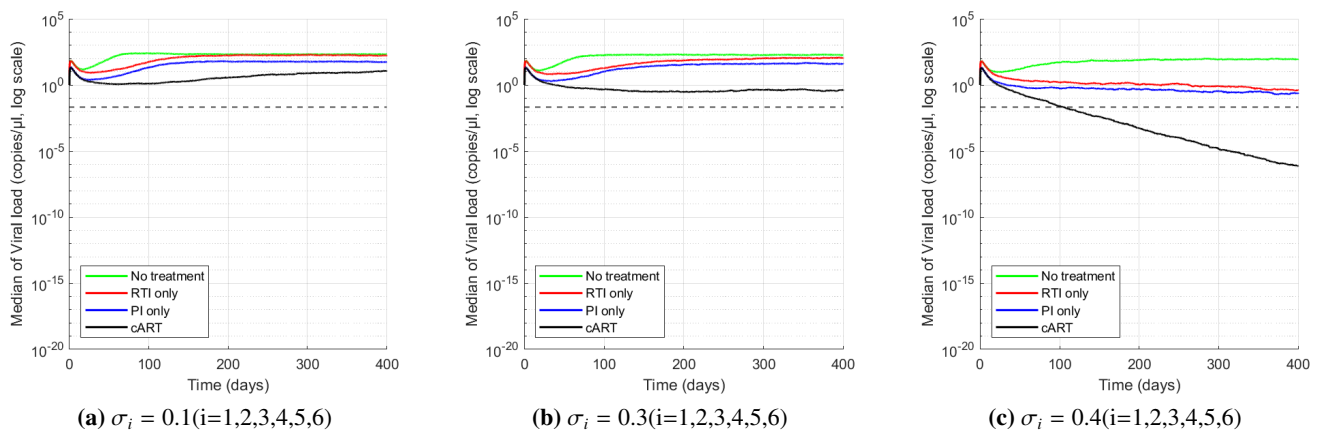


Figure 9. Viral load dynamics under different treatment strategies in Model (6.2).

6.3.2. Implementation and comparison of control strategies

We conduct numerical simulations with 1000 sample paths using the fourth-order Runge-Kutta scheme to verify the derived optimal control results. The control horizon is set to 400 days; noise intensities are fixed at $\sigma_1 = \sigma_2 = \sigma_3 = \sigma_4 = \sigma_5 = \sigma_6 = 0.1$, and $\mu_3 = 0.3$; and all remaining parameters are taken from Table 2. The numerical outcomes are shown in Figures 10–12. Further comparisons and analyses of the performance of different control strategies are provided below.

Strategy 1 (RTI monotherapy): Figure 10 shows the optimal control trajectories and viral load dynamics when only RTIs are administered. As seen in Figure 10(a), the median curve of the optimal control input $u_1^*(t)$ begins at a relatively low level and increases gradually. This indicates that a higher RTI dosage is needed in the early stage of treatment, followed by a gradual dose reduction. Figure 10(b) shows that compared with the uncontrolled scenario, this treatment lowers the median viral load and achieves viral clearance on day 48 for the first time. These results confirm that RTI monotherapy can suppress viral proliferation.

Strategy 2 (PI monotherapy). Figure 11 presents the numerical results when only PIs are administered. The temporal profile of $u_2^*(t)$ (Figure 11(a)) is opposite to that of $u_1^*(t)$ in Strategy 1: The drug intensity starts at a high level and decreases steadily throughout treatment. PI monotherapy

achieves viral clearance on day 34, earlier than RTI monotherapy.

Strategy 3 (RTI/PI combination therapy): It can be observed from Figure 12 that the combined regimen yields a shorter viral clearance duration than RTI monotherapy and a much faster decline in viral load than PI monotherapy, which demonstrates that combination antiretroviral treatment achieves faster and more potent viral suppression. Overall, this combined strategy leads to the most substantial and sustained reduction in viral load, confirming that the synergistic effect of the two classes of drugs suppresses viral load more efficiently and accelerates viral clearance.

Compared with the simulations with fixed drug efficacy in Subsection 6.3.1, the optimal control results in this subsection suggest that dynamic adjustment of drug dosage enables viral clearance even under monotherapy via optimized administration protocols. This conclusion theoretically highlights the clinical significance of individualized medication regimens. In summary, Subsection 6.3.1 elaborates the merits of static fixed-dose combination therapy, and Subsection 6.3.2 reflects the advantages of dynamically optimized dosing. Complementing one another, these two parts provide comprehensive theoretical guidance for HIV clinical treatment under stochastic environments.

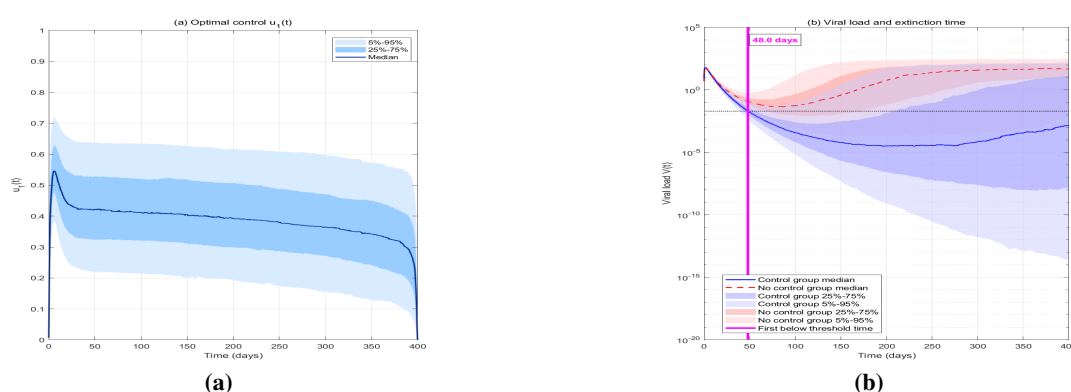


Figure 10. Efficacy of monotherapy with RTIs.

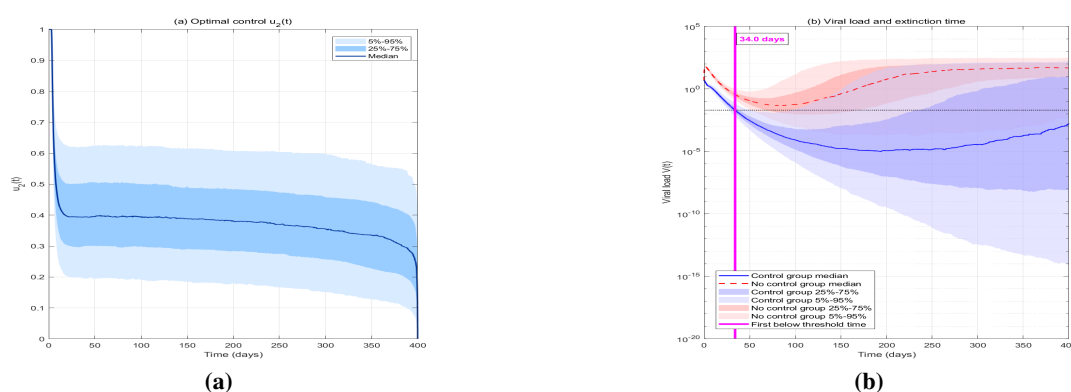


Figure 11. Efficacy of monotherapy with PIs.

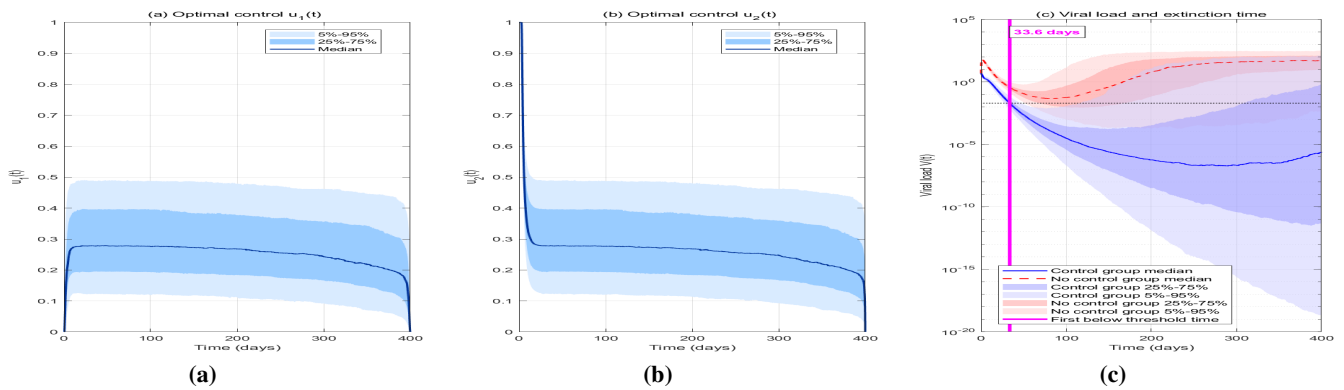


Figure 12. Therapeutic efficacy of the combined action of RTIs and PIs.

6.4. Cost-effectiveness analysis of different control strategies

To comprehensively evaluate the cost-effectiveness of the proposed strategies, we examine their viral extinction time distributions under various cost constraints. Simulations are carried out with $\rho = 0.8$ (an elevated conversion rate from quiescent to activated cells), and all other parameters are specified in Table 2. Figure 13 presents boxplots from 1000 Monte Carlo runs for the three schemes, illustrating how cost affects viral containment. Median extinction times and nonextinction proportions are summarized in Tables 4 and 5 as supplementary data, respectively.

Table 4. Median extinction time comparison of strategies across varying cost weights.

Cost weight	Strategy 1	Strategy 2	Strategy 3
2	48.85	35.1	33.65
4	53.8	38.9	36.2
6	57.8	40.9	37.4
8	59.95	42.2	38.15
10	62.5	43	39.35

Table 5. Comparison of nonextinction proportions for each strategy under different cost weights (%).

Cost weight	Strategy 1	Strategy 2	Strategy 3
2	9.2	5.7	3.7
4	11.9	7.7	4.6
6	14.4	9.4	5.1
8	15.5	10	5.8
10	16.8	10.6	6.3

Under Strategy 1, the median extinction time rises gradually from 48.85 days to 62.5 days with increasing cost weight (Table 4) and remains at a high level. The boxplots in Figure 13(a) shift noticeably upward, accompanied by a high nonextinction proportion (Table 5). This indicates that

Strategy 1 is sensitive to cost and is only applicable to low-cost scenarios. By contrast, Strategy 2 yields a much shorter median extinction time and maintains satisfactory performance even under high-cost settings. It exhibits low cost sensitivity and far fewer nonextinction cases, confirming that PIs outperform RTIs. Strategy 3 achieves the shortest viral eradication time and the lowest nonextinction proportion across all cost configurations. The virus can therefore be nearly eradicated in most cases, making this strategy the optimal choice with well-balanced therapeutic and economic benefits.

In summary, as shown in Figure 13 and Tables 4 and 5, Strategy 3 achieves the shortest extinction time across all cost settings, Strategy 2 delivers moderate performance, and Strategy 1 has the poorest efficacy. A higher cost weight prolongs extinction time for all three schemes, though their degrees of cost sensitivity differ substantially. Notably, the combination therapy adopted in Strategy 3 maintains strong efficacy even under tight budget constraints, which provides valuable references for clinical treatment planning.

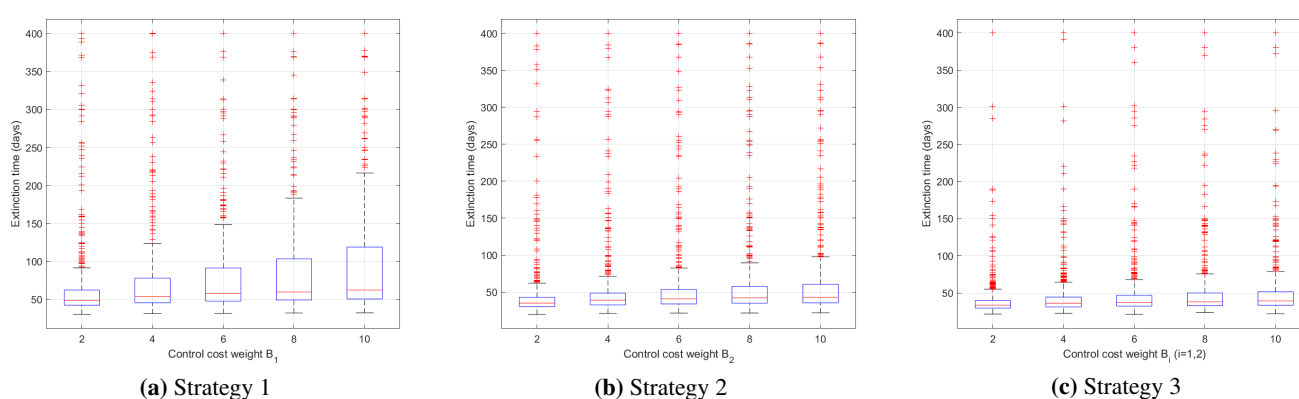


Figure 13. Distributions of extinction times for the three strategies under different cost weights. (a) $B_1 = 2, 4, 6, 8, 10$; (b) $B_2 = 2, 4, 6, 8, 10$; (c) $B_1 = B_2 = 2, 4, 6, 8, 10$.

7. Conclusions

In this paper, we construct a novel stochastic HIV model incorporating quiescent cells, as well as CTL and antibody immune responses. We investigate the model's dynamical characteristics and optimal intervention strategies, including theoretical analysis, dynamical mechanism analysis, optimal control design, and numerical assessments. Our findings advance the theoretical framework of stochastic viral dynamics and provide efficient quantitative tools alongside practical clinical insights to evaluate the cost-effectiveness of HIV antiviral therapies.

We derive three key mathematical results for the stochastic system (1.2). First, Theorem 2.1 gives the existence and uniqueness of the global positive solution by virtue of the local Lipschitz condition and a properly constructed Lyapunov function, which guarantees the well-posedness of the model. Second, Theorem 3.1 confirms the existence of a unique ergodic stationary distribution whenever the stochastic basic reproduction number $\mathcal{R}_0^S > 1$, describing the long-term persistence of HIV infection subject to environmental noise. Third, Theorem 4.3 yields a sufficient condition for almost sure viral extinction when $\mathcal{R}_1^S < 1$, which serves as a quantitative indicator for successful therapy. Notably, the

thresholds $\mathcal{R}_0^S$ and $\mathcal{R}_1^S$ differ structurally from their deterministic counterparts: They contain noise driven correction terms (e.g., $+1/2\sigma_i^2$ in denominators). These terms mathematically reveal that environmental fluctuations can intrinsically reduce viral reproductive potential, a property not observed in conventional deterministic models.

To discretize the stochastic system, we adopt the Milstein scheme [24]. It possesses a strong convergence order of 1.0, outperforming the Euler-Maruyama method, whose strong convergence order is only 0.5. Such high order accuracy is essential for our six-dimensional model driven by multiplicative noise, as it produces trustworthy sample trajectories and captures key statistical quantities (including stationary distributions and extinction times) within extensive Monte Carlo simulations with 1000 independent realizations. Numerical simulations consistently confirm our theoretical threshold predictions for all considered parameter settings. Figures 1–3 illustrate a transition from chronic persistence to stochastic extinction governed by noise intensity. The results confirm that $\mathcal{R}_0^S > 1$ is a necessary yet insufficient condition for sustained infection, as strong stochastic perturbations may override deterministic forecasts. Sensitivity analysis (Figures 6 and 7) further highlights critical therapeutic targets. Parameters β (infection rate) and η (virus production rate) impose the most pronounced positive effects on $\mathcal{R}_1^S$, whereas μ_3 (infected cell death rate) yields the dominant negative effect. These findings provide quantitative support for the better efficacy of PIs relative to RTIs, which can be seen from the comparison between Figures 10 and 11.

We design three clinically feasible intervention strategies: RTI monotherapy (Strategy 1), PI monotherapy (Strategy 2), and RTI/PI combination therapy (Strategy 3). Figures 9–12 uncover a practically meaningful difference: Fixed-dose monotherapy cannot eliminate virus, whereas dynamically optimized monotherapy may realize viral clearance when RTIs are initiated at day 48 and PIs at day 34. Among all considered cost weight levels (2, 4, 6, 8, 10), optimal-control-based combination therapy produces the shortest extinction time and the smallest nonextinction fraction. In detail, Strategy 1 exhibits strong cost sensitivity and is applicable merely to low budget cases; Strategy 2 possesses weaker cost dependence and delivers more steady treatment outcomes; Strategy 3 surpasses both monotherapies for every cost weight setting and attains a favorable trade-off between therapeutic effectiveness and cost efficiency. Taken together, these results indicate that stochastic optimal control informed by the dual threshold framework can provide robust, cost-adaptive references for HIV clinical treatment.

Notwithstanding its theoretical strengths and satisfactory numerical performance, the present model possesses several noteworthy limitations that deserve explicit discussion. Only cell-free virus to cell infection is taken into account, whereas direct cell-to-cell transmission a highly efficient infection route within lymphoid tissues is excluded, which may lead to an underestimation of viral persistence. Quiescent cells are treated solely as susceptible targets. The generation of latent viral reservoirs together with the stochastic reactivation of latent proviruses, key obstacles toward achieving a functional cure, are absent from the current model. The optimal control setup ignores the generation of drug resistant viral strains under selective pressure and fails to account for cumulative hepatorenal toxicity induced by prolonged antiretroviral administration. Accordingly, its utility for designing long-term therapeutic schedules is restricted.

To address the aforementioned limitations, we propose specific feasible follow up research directions grouped into theoretical mathematical extensions and clinical application expansions.

For theoretical mathematical extensions, first, stochastic delayed dynamics will be introduced.

Intracellular viral replication delays and immune response delays will be added to Model (1.2). Using delayed stochastic differential equations, we can investigate how time lags and environmental noise jointly affect stability transitions, stationary distributions and extinction thresholds. Second, dual transmission pathway modeling will integrate direct cell-to-cell infection alongside cell-free infection. A new stochastic basic reproduction number will be derived to quantify each pathway's contribution to viral persistence under stochastic disturbances. In terms of clinical application expansions, we will build compartments for latent reservoirs to simulate “shock and kill” functional cure strategies. A multistrain stochastic model will characterize evolutionary competition between wild-type and drug-resistant HIV strains to optimize combination therapy. The cost functional will incorporate cumulative drug toxicity to balance antiviral efficacy, economic costs, and safety for long-term treatment. Furthermore, patient heterogeneous parameter distributions will replace population averaged parameters to establish individualized optimal control for personalized HIV clinical management. We leave these tasks for future work.

Author contributions

L.Y. Zuo: Writing - original draft, Software; X.Y. Zhou: Supervision, Methodology, Writing - review & editing; X.Y. Shi: Methodology, Funding acquisition, Writing - review & editing.

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Use of AI tools declaration

The authors declare they have not used artificial intelligence (AI) tools in the creation of this article.

Conflict of interest

The authors declare there are no conflicts of interest.

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Appendix

Proof of Theorem 3.1.

Proof. To prove Theorem 3.1, we need to verify the Conditions (A1) and (A2) in Lemma 3.1. We first verify Condition (A1). The diffusion matrix of System (1.2) is given by

$$\tilde{\mathbf{A}}(x) = \text{diag}(\sigma_1^2 Q^2, \sigma_2^2 T^2, \sigma_3^2 I^2, \sigma_4^2 V^2, \sigma_5^2 Z^2, \sigma_5^2 W^2).$$

Clearly, we can choose a positive constant

$$\tilde{M} = \min_{(Q,T,I,V,Z,W) \in D_\epsilon \subset \mathbb{R}_+^6} \{\sigma_1^2 Q^2, \sigma_2^2 T^2, \sigma_3^2 I^2, \sigma_4^2 V^2, \sigma_5^2 Z^2, \sigma_6^2 W^2\},$$

such that for any $(Q, T, I, V, Z, W) \in D_\epsilon$ and $\xi = (\xi_1, \xi_2, \dots, \xi_5, \xi_6) \in \mathbb{R}_+^6$,

$$\begin{aligned} \sum_{i,j=1}^6 a_{ij}(Q, T, I, V, Z, W) \xi_i \xi_j &= \sigma_1^2 Q^2 \xi_1^2 + \sigma_2^2 T^2 \xi_2^2 + \sigma_3^2 I^2 \xi_3^2 + \sigma_4^2 V^2 \xi_4^2 + \sigma_5^2 Z^2 \xi_5^2 + \sigma_6^2 W^2 \xi_6^2 \\ &\geq \tilde{M} |\xi|^2. \end{aligned}$$

Here, D_ϵ is a bounded domain whose specific range will be given later. Hence, Condition **(A1)** holds. We next prove that Condition **(A2)** is satisfied.

Step 1. Define a function $U_1 \in C^2(\mathbb{R}_+^6; \mathbb{R})$ as

$$U_1 = -\ln I - c_1 \ln Q - 2c_2 \ln T - c_3 \ln V - c_4 \ln Z - \frac{k}{q_2} c_5 \ln W,$$

where c_i ($i = 1, 2, 3, 4, 5, 6$) are positive constants, which we choose as follows:

$$\begin{aligned} c_1 &= \frac{\mu_3 + \frac{1}{2}\sigma_3^2}{\gamma + \mu_1 + \frac{1}{2}\sigma_1^2}, \quad c_2 = \frac{\mu_3 + \frac{1}{2}\sigma_3^2}{\rho + \mu_2 + \frac{\beta}{k} + \frac{1}{2}\sigma_2^2}, \\ c_3 &= \frac{\mu_3 + \frac{1}{2}\sigma_3^2}{\mu_4 + \frac{1}{2}\sigma_4^2}, \quad c_4 = \frac{\mu_3 + \frac{1}{2}\sigma_3^2}{\mu_5 + \frac{1}{2}\sigma_5^2}, \quad c_5 = \frac{q_2(\mu_3 + \frac{1}{2}\sigma_3^2)}{k(\frac{q_2}{k} + \mu_6 + \frac{1}{2}\sigma_6^2)}. \end{aligned}$$

By virtue of the Itô's formula, we have

$$L(-\ln Q) = -\frac{A}{Q} - \rho \frac{T}{Q} + \gamma + \mu_1 + \frac{1}{2}\sigma_1^2, \quad (\text{A.1})$$

$$L(-\ln T) = -\gamma \frac{Q}{T} + \rho + \mu_2 + \frac{\beta V}{1 + kV} + \frac{1}{2}\sigma_2^2, \quad (\text{A.2})$$

$$L(-\ln I) = -\frac{\beta TV}{(1 + kV)I} + \mu_3 + p_1 Z + \frac{1}{2}\sigma_3^2, \quad (\text{A.3})$$

$$L(-\ln V) = -\eta \frac{I}{V} + \mu_4 + q_1 W + \frac{1}{2}\sigma_4^2, \quad (\text{A.4})$$

$$L(-\ln Z) = -p_2 I + \mu_5 + \frac{1}{2}\sigma_5^2, \quad (\text{A.5})$$

$$L(-\ln W) = -q_2 V + \mu_6 + \frac{1}{2}\sigma_6^2. \quad (\text{A.6})$$

Therefore, combining (A.1) to (A.6), we obtain

$$\begin{aligned} LU_1 &= -\frac{\beta TV}{(1 + kV)I} + \mu_3 + p_1 Z + \frac{1}{2}\sigma_3^2 - c_1 \frac{A}{Q} - c_1 \rho \frac{T}{Q} + c_1 \left(\gamma + \mu_1 + \frac{1}{2}\sigma_1^2 \right) \\ &\quad - 2c_2 \gamma \frac{Q}{T} + 2c_2 \left(\rho + \mu_2 + \frac{1}{2}\sigma_2^2 \right) + 2c_2 \frac{\beta V}{1 + kV} - c_3 \eta \frac{I}{V} + c_3 \left(\mu_4 + \frac{1}{2}\sigma_4^2 \right) \end{aligned}$$

$$\begin{aligned}
& + c_3 q_1 W - c_4 p_2 I + c_4 \left(\mu_5 + \frac{1}{2} \sigma_5^2 \right) - c_5 k V + \frac{k}{q_2} c_5 \left(\mu_6 + \frac{1}{2} \sigma_6^2 \right) \\
& \leq -\frac{\beta T V}{(1+kV)I} - c_1 \frac{A}{Q} - c_1 \rho \frac{T}{Q} - c_2 \gamma \frac{Q}{T} - c_2 \gamma \frac{Q}{T} - c_3 \eta \frac{I}{V} - c_5 (1+kV) \\
& \quad + p_1 Z + c_3 q_1 W + \mu_3 + \frac{1}{2} \sigma_3^2 + c_1 \left(\gamma + \mu_1 + \frac{1}{2} \sigma_1^2 \right) + 2c_2 \left(\rho + \mu_2 + \frac{1}{2} \sigma_2^2 + \frac{\beta}{k} \right) \\
& \quad + c_3 \left(\mu_4 + \frac{1}{2} \sigma_4^2 \right) + c_4 \left(\mu_5 + \frac{1}{2} \sigma_5^2 \right) + \frac{k}{q_2} c_5 \left(\mu_6 + \frac{1}{2} \sigma_6^2 + \frac{q_2}{k} \right) \\
& \leq -7 \sqrt[7]{A \beta \eta \gamma^2 \rho c_1^2 c_2^2 c_3 c_5} + p_1 Z + c_3 q_1 W + \mu_3 + \frac{1}{2} \sigma_3^2 + c_1 \left(\gamma + \mu_1 + \frac{1}{2} \sigma_1^2 \right) \\
& \quad + 2c_2 \left(\rho + \mu_2 + \frac{1}{2} \sigma_2^2 + \frac{\beta}{k} \right) + c_3 \left(\mu_4 + \frac{1}{2} \sigma_4^2 \right) + c_4 \left(\mu_5 + \frac{1}{2} \sigma_5^2 \right) + \frac{k}{q_2} c_5 \left(\mu_6 + \frac{1}{2} \sigma_6^2 + \frac{q_2}{k} \right) \\
& = -7 \left(\mu_3 + \frac{1}{2} \sigma_3^2 \right) \left(\sqrt[7]{R_0^S} - 1 \right) + p_1 Z + c_3 q_1 W \\
& = -7\lambda + p_1 Z + c_3 q_1 W,
\end{aligned} \tag{A.7}$$

where $\lambda = \left(\mu_3 + \frac{1}{2} \sigma_3^2 \right) \left(\sqrt[7]{R_0^S} - 1 \right)$. Because $R_0^S > 1$, it follows that $\lambda > 0$.

Step 2. Define a function $U_2 \in C^2(\mathbb{R}_+^6; \mathbb{R})$ as

$$\begin{aligned}
U_2 &= M U_1 - \ln Q - \ln T - \ln V - \frac{1}{I} + \frac{1}{I} + \frac{1}{1+\theta} \left(Q + T + I + \frac{\mu_3}{2\eta} V + \frac{p_1}{2p_2} Z + \frac{\mu_3 q_1}{4\eta q_2} W \right)^{\theta+1} \\
&= M U_1 + \bar{U}_2 + \bar{U}_3,
\end{aligned}$$

where

$$\begin{aligned}
\bar{U}_2 &= -\ln Q - \ln T - \ln V - \frac{1}{I} + \frac{1}{I}, \\
\bar{U}_3 &= \frac{1}{1+\theta} \left(Q + T + I + \frac{\mu_3}{2\eta} V + \frac{p_1}{2p_2} Z + \frac{\mu_3 q_1}{4\eta q_2} W \right)^{\theta+1},
\end{aligned}$$

θ satisfies

$$\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 > \frac{\theta}{2} (\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2 \vee \sigma_5^2 \vee \sigma_6^2),$$

and where M is a positive constant satisfying

$$-7\lambda M + E \wedge F \leq -2,$$

with E and F to be determined later.

Similarly, from (A.1)–(A.6), we derive that

$$\begin{aligned}
L \bar{U}_2 &= L \left(-\ln Q - \ln T - \ln V - \frac{1}{I} + \frac{1}{I} \right) \\
&= -\frac{A}{Q} - \rho \frac{T}{Q} + \gamma + \mu_1 + \frac{1}{2} \sigma_1^2 - \gamma \frac{Q}{T} + \rho + \mu_2 + \frac{\beta V}{1+kV} + \frac{1}{2} \sigma_2^2 - \eta \frac{I}{V} + \mu_4 \\
&\quad + q_1 W + \frac{1}{2} \sigma_4^2 + \frac{\beta T V}{(1+kV)I^2} - \frac{\mu_3}{I} - \frac{p_1 Z}{I} - \frac{\beta T V}{(1+kV)I^2} + \frac{\mu_3}{I} + \frac{p_1 Z}{I}
\end{aligned}$$

$$\begin{aligned} &\leq -\frac{A}{Q} - \rho \frac{T}{Q} - \gamma \frac{Q}{T} - \eta \frac{I}{V} - \frac{\mu_3}{I} + q_1 W + \frac{\mu_3}{I} + \gamma + \mu_1 + \frac{1}{2} \sigma_1^2 + \rho + \mu_2 \\ &\quad + \frac{\beta}{k} + \frac{1}{2} \sigma_2^2 + \mu_4 + \frac{1}{2} \sigma_4^2 \end{aligned} \quad (\text{A.8})$$

and

$$\begin{aligned} L\bar{U}_3 &= L \left(\frac{1}{1+\theta} \left(Q + T + I + \frac{\mu_3}{2\eta} V + \frac{p_1}{2p_2} Z + \frac{\mu_3 q_1}{4\eta q_2} W \right)^{\theta+1} \right) \\ &= Y^\theta \left(A - \mu_1 Q - \mu_2 T - \mu_3 I - p_1 IZ + \frac{\mu_3}{2} I - \frac{\mu_3 \mu_4}{2\eta} V - \frac{\mu_3 q_1}{2\eta} VW + \frac{p_1}{2} IZ \right. \\ &\quad \left. - \frac{p_1 \mu_5}{2q_2} Z + \frac{\mu_3 q_1}{4\eta} VW - \frac{\mu_3 q_1 \mu_6}{4\eta q_2} W \right) + \frac{\theta}{2} Y^{\theta-1} \left[\sigma_1^2 Q^2 + \sigma_2^2 T^2 + \sigma_3^2 I^2 + \left(\frac{\mu_3}{2\eta} V \right)^2 \sigma_4^2 \right. \\ &\quad \left. + \left(\frac{p_1}{2p_2} Z \right)^2 \sigma_5^2 + \left(\frac{\mu_3 q_1}{4\eta q_2} W \right)^2 \sigma_6^2 \right] \\ &\leq \left[A - \left(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 \right) Y \right] Y^\theta + \frac{\theta}{2} \bar{\sigma}^2 Y^{\theta+1} \\ &= AY^\theta - \left(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 \right) Y^{\theta+1} + \frac{\theta}{2} \bar{\sigma}^2 Y^{\theta+1} \\ &\leq B - \frac{1}{2} Y^{\theta+1} \left[\left(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 \right) - \frac{\theta}{2} \bar{\sigma}^2 \right] \\ &\leq B - \frac{1}{2} \left[\left(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 \right) - \frac{\theta}{2} \bar{\sigma}^2 \right] (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} \\ &\quad + \left(\frac{\mu_3}{2\eta} V \right)^{\theta+1} + \left(\frac{p_1}{2p_2} Z \right)^{\theta+1} + \left(\frac{\mu_3 q_1}{4\eta q_2} W \right)^{\theta+1}), \end{aligned} \quad (\text{A.9})$$

where

$$\begin{aligned} Y &= Q + T + I + \frac{\mu_3}{2\eta} V + \frac{p_1}{2p_2} Z + \frac{\mu_3 q_1}{4\eta q_2} W, \bar{\sigma} = \max\{\sigma_1, \sigma_2, \sigma_3, \sigma_4, \sigma_5, \sigma_6\}, \\ B &= \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} \left\{ AY^\theta - \frac{1}{2} Y^{\theta+1} \left[\left(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 \right) - \frac{\theta}{2} \bar{\sigma}^2 \right] \right\}. \end{aligned}$$

Step 3. In view of the monotonicity of the function $f(x) = ax^{1+\theta} - b \ln x$ ($a, b > 0$, $x > 0$) and the continuity of U_2 , it follows that U_2 attains its minimum at a unique point $(\bar{Q}, \bar{T}, \bar{I}, \bar{V}, \bar{Z}, \bar{W})$ in the interior of $\mathbb{R}_+^6$.

Define a non-negative function $\bar{U} \in C^2(\mathbb{R}_+^6; \mathbb{R}_+)$ as follows:

$$\bar{U}(Q, T, I, V, Z, W) = U_2(Q, T, I, V, Z, W) - U_2(\bar{Q}, \bar{T}, \bar{I}, \bar{V}, \bar{Z}, \bar{W}).$$

Clearly, as $\|(Q, T, I, V, Z, W)\| \rightarrow \infty$, we have $\bar{U}(Q, T, I, V, Z, W) \rightarrow \infty$, where $\|\cdot\|$ denotes the Euclidean norm.

From (A.7) to (A.9), we obtain

$$\begin{aligned} L\bar{U} &= MLU_1 + L\bar{U}_2 + L\bar{U}_3 \\ &\leq -7M\lambda + M(p_1 Z + c_3 q_1 W) - \frac{A}{Q} - \rho \frac{T}{Q} - \gamma \frac{Q}{T} - \eta \frac{I}{V} - \frac{\mu_3}{I} - \frac{1}{2} \left[\left(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 \right) \right. \\ &\quad \left. - \frac{\theta}{2} \bar{\sigma}^2 \right] (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + \left(\frac{\mu_3}{2\eta} V \right)^{\theta+1} + \left(\frac{p_1}{2p_2} Z \right)^{\theta+1} + \left(\frac{\mu_3 q_1}{4\eta q_2} W \right)^{\theta+1}) + C, \end{aligned}$$

where

$$C = q_1 W + \frac{\mu_3}{I} + \gamma + \mu_1 + \frac{1}{2}\sigma_1^2 + \rho + \mu_2 + \frac{\beta}{k} + \frac{1}{2}\sigma_2^2 + \mu_4 + \frac{1}{2}\sigma_4^2 + B.$$

Consider the following bounded closed set:

$$D_\epsilon = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : \epsilon < Q < \frac{1}{\epsilon}, \epsilon^2 < T < \frac{1}{\epsilon^2}, \epsilon < I < \frac{1}{\epsilon}, \\ \epsilon^2 < V < \frac{1}{\epsilon^2}, \epsilon < Z < \frac{1}{\epsilon}, \epsilon < W < \frac{1}{\epsilon}\},$$

where $0 < \epsilon < 1$ is a sufficiently small constant satisfying the following conditions:

$$\frac{1}{\epsilon} \geq (1 + D) \cdot \max \left\{ \frac{1}{A}, 1, \frac{1}{\mu_3}, \frac{1}{\eta} \right\}, \quad (\text{A.10})$$

$$Mp_1\epsilon \leq 1, \quad (\text{A.11})$$

$$Mc_3q_1\epsilon \leq 1, \quad (\text{A.12})$$

$$-\frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \frac{1}{\epsilon^{\theta+1}} + G \leq -1, \quad (\text{A.13})$$

$$-\frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \frac{1}{\epsilon^{2(\theta+1)}} + H \leq -1, \quad (\text{A.14})$$

$$-\frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \frac{1}{\epsilon^{\theta+1}} + L \leq -1, \quad (\text{A.15})$$

$$-\frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \left(\frac{\mu_3}{2\eta} \right)^{\theta+1} \frac{1}{\epsilon^{2(\theta+1)}} + N \leq -1, \quad (\text{A.16})$$

$$-\frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \left(\frac{p_1}{2p_2} \right)^{\theta+1} \frac{1}{\epsilon^{\theta+1}} + O \leq -1, \quad (\text{A.17})$$

$$-\frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \left(\frac{\mu_3 q_1}{4\eta q_2} \right)^{\theta+1} \frac{1}{\epsilon^{\theta+1}} + P \leq -1, \quad (\text{A.18})$$

where D, E, F, G, H, L, N, O , and P are positive constants, which will be explicitly given in expressions (A.19) to (A.27).

For convenience, we divide $\mathbb{R}_+^6 \setminus D_\epsilon$ into the following twelve regions:

$$D_1 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : 0 < Q < \epsilon\},$$

$$D_2 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : 0 < T < \epsilon^2, Q \geq \epsilon\},$$

$$D_3 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : 0 < I < \epsilon\},$$

$$D_4 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : 0 < V < \epsilon^2, I \geq \epsilon\},$$

$$D_5 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : 0 < Z < \epsilon\},$$

$$D_6 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : 0 < W < \epsilon\},$$

$$D_7 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : Q > \frac{1}{\epsilon}\},$$

$$D_8 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : T > \frac{1}{\epsilon^2}\},$$

$$D_9 = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : I > \frac{1}{\epsilon}\},$$

$$D_{10} = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : V > \frac{1}{\epsilon^2}\},$$

$$D_{11} = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : Z > \frac{1}{\epsilon}\},$$

$$D_{12} = \{(Q, T, I, V, Z, W) \in \mathbb{R}_+^6 : W > \frac{1}{\epsilon}\}.$$

Clearly,

$$\mathbb{R}_+^6 \setminus D_\epsilon = D_1 \cup D_2 \cup D_3 \cup D_4 \cup D_5 \cup D_6 \cup D_7 \cup D_8 \cup D_9 \cup D_{10} \cup D_{11} \cup D_{12}.$$

Next, we prove that $L\bar{U} \leq -1$ holds on $\mathbb{R}_+^6 \setminus D_\epsilon$.

Case 1. If $(Q, T, I, V, Z, W) \in D_1$, we have

$$\begin{aligned} L\bar{U} &\leq M(p_1Z + c_3q_1W) - \frac{A}{Q} - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\ &\quad - \frac{\theta}{2}\bar{\sigma}^2](Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\ &\leq -\frac{A}{Q} + D \\ &\leq -\frac{A}{\epsilon} + D, \end{aligned}$$

where

$$\begin{aligned} D = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} &\left\{ M(p_1Z + c_3q_1W) - \frac{1}{2} \left[\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6 - \frac{\theta}{2}\bar{\sigma}^2 \right] \cdot \right. \\ &\left. (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \end{aligned} \quad (\text{A.19})$$

It follows from Condition (A.10) that $L\bar{U} \leq -1$.

Case 2. If $(Q, T, I, V, Z, W) \in D_2$, we have

$$L\bar{U} \leq -\frac{Q}{T} + D \leq -\frac{1}{\epsilon} + D.$$

It follows from Condition (A.10) that $L\bar{U} \leq -1$.

Case 3. If $(Q, T, I, V, Z, W) \in D_3$, we have

$$L\bar{U} \leq -\frac{\mu_3}{I} + D \leq -\frac{\mu_3}{\epsilon} + D.$$

It follows from Condition (A.10) that $L\bar{U} \leq -1$.

Case 4. If $(Q, T, I, V, Z, W) \in D_4$, we have

$$L\bar{U} \leq -\eta \frac{I}{V} + D \leq -\frac{\eta}{\epsilon} + D.$$

It follows from Condition (A.10) that $L\bar{U} \leq -1$.

Case 5. If $(Q, T, I, V, Z, W) \in D_5$, we have

$$\begin{aligned} L\bar{U} &\leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\ &\quad - \frac{\theta}{2}\bar{\sigma}^2](Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\ &\leq -7M\lambda + Mp_1Z + E \\ &\leq -2 + Mp_1\epsilon. \end{aligned}$$

It follows from Condition (A.11) that $L\bar{U} \leq -1$, where

$$E = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} \left\{ Mc_3q_1W - \frac{1}{2} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \right. \\ \left. (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \quad (\text{A.20})$$

Case 6. If $(Q, T, I, V, Z, W) \in D_6$, we have

$$L\bar{U} \leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\ - \frac{\theta}{2} \bar{\sigma}^2](Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\ \leq -7M\lambda + Mc_3q_1W + F \\ \leq -2 + Mc_3q_1\epsilon.$$

It follows from Condition (A.12) that $L\bar{U} \leq -1$, where

$$F = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} \left\{ Mp_1Z - \frac{1}{2} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \right. \\ \left. (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \quad (\text{A.21})$$

Case 7. If $(Q, T, I, V, Z, W) \in D_7$, we have

$$L\bar{U} \leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2]Q^{\theta+1} \\ - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2]Q^{\theta+1} - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\ - \frac{\theta}{2} \bar{\sigma}^2](T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\ \leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2]Q^{\theta+1} + G \\ \leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2] \frac{1}{\epsilon^{\theta+1}} + G.$$

From (A.13), we can get $L\bar{U} \leq -1$, where

$$G = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} \left\{ M(p_1Z + c_3q_1W) - \frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] Q^{\theta+1} \right. \\ \left. - \frac{1}{2} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2} \bar{\sigma}^2 \right] \cdot \right. \\ \left. (T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \quad (\text{A.22})$$

Case 8. If $(Q, T, I, V, Z, W) \in D_8$, we have

$$\begin{aligned}
 L\bar{U} &\leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]T^{\theta+1} \\
 &\quad - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]T^{\theta+1} - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\
 &\quad - \frac{\theta}{2}\bar{\sigma}^2](Q^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]T^{\theta+1} + H \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]\frac{1}{\epsilon^{2(\theta+1)}} + H.
 \end{aligned}$$

It follows from Condition (A.14) that $L\bar{U} \leq -1$, where

$$\begin{aligned}
 H = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} &\left\{ M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]T^{\theta+1} \right. \\
 &\quad \left. - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2] \right. \\
 &\quad \left. (Q^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \quad (A.23)
 \end{aligned}$$

Case 9. If $(Q, T, I, V, Z, W) \in D_9$, we have

$$\begin{aligned}
 L\bar{U} &\leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]I^{\theta+1} \\
 &\quad - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]I^{\theta+1} - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\
 &\quad - \frac{\theta}{2}\bar{\sigma}^2](Q^{\theta+1} + T^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]I^{\theta+1} + L \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]\frac{1}{\epsilon^{\theta+1}} + L.
 \end{aligned}$$

It follows from Condition (A.15) that $L\bar{U} \leq -1$, where

$$\begin{aligned}
 L = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} &\left\{ M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2]I^{\theta+1} \right. \\
 &\quad \left. - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2] \right. \\
 &\quad \left. (Q^{\theta+1} + T^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \quad (A.24)
 \end{aligned}$$

Case 10. If $(Q, T, I, V, Z, W) \in D_{10}$, we have

$$\begin{aligned}
 L\bar{U} &\leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3}{2\eta}V)^{\theta+1} \\
 &\quad - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3}{2\eta}V)^{\theta+1} - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\
 &\quad - \frac{\theta}{2}\bar{\sigma}^2](Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3}{2\eta}V)^{\theta+1} + N \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3}{2\eta})^{\theta+1} \frac{1}{\epsilon^{2(\theta+1)}} + N.
 \end{aligned}$$

It follows from Condition (A.16) that $L\bar{U} \leq -1$, where

$$\begin{aligned}
 N = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} &\left\{ M(p_1Z + c_3q_1W) - \frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2 \right] (\frac{\mu_3}{2\eta}V)^{\theta+1} \right. \\
 &\quad \left. - \frac{1}{2} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2 \right] \right. \\
 &\quad \left. (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \quad (\text{A.25})
 \end{aligned}$$

Case 11. If $(Q, T, I, V, Z, W) \in D_{11}$, we have

$$\begin{aligned}
 L\bar{U} &\leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{p_1}{2p_2}Z)^{\theta+1} \\
 &\quad - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{p_1}{2p_2}Z)^{\theta+1} - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\
 &\quad - \frac{\theta}{2}\bar{\sigma}^2](Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{p_1}{2p_2}Z)^{\theta+1} + O \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{p_1}{2p_2})^{\theta+1} \frac{1}{\epsilon^{\theta+1}} + O.
 \end{aligned}$$

It follows from Condition (A.17) that $L\bar{U} \leq -1$, where

$$\begin{aligned}
 O = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} &\left\{ M(p_1Z + c_3q_1W) - \frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2 \right] (\frac{p_1}{2p_2}Z)^{\theta+1} \right. \\
 &\quad \left. - \frac{1}{2} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2 \right] \right. \\
 &\quad \left. (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1}) + C \right\}. \quad (\text{A.26})
 \end{aligned}$$

Case 12. If $(Q, T, I, V, Z, W) \in D_{12}$, we have

$$\begin{aligned}
 L\bar{U} &\leq -7M\lambda + M(p_1Z + c_3q_1W) - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1} \\
 &\quad - \frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1} - \frac{1}{2}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) \\
 &\quad - \frac{\theta}{2}\bar{\sigma}^2](Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1}) + C \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1} + P \\
 &\leq -\frac{1}{4}[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2](\frac{\mu_3q_1}{4\eta q_2})^{\theta+1} \frac{1}{\epsilon^{\theta+1}} + P.
 \end{aligned}$$

In view of Condition (A.18), we have $L\bar{U} \leq -1$, where

$$\begin{aligned}
 P = \sup_{(Q,T,I,V,Z,W) \in \mathbb{R}_+^6} &\left\{ M(p_1Z + c_3q_1W) - \frac{1}{4} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2 \right] (\frac{\mu_3q_1}{4\eta q_2}W)^{\theta+1} \right. \\
 &\quad \left. - \frac{1}{2} \left[(\mu_1 \wedge \mu_2 \wedge \frac{\mu_3}{2} \wedge \mu_4 \wedge \mu_5 \wedge \mu_6) - \frac{\theta}{2}\bar{\sigma}^2 \right] \right. \\
 &\quad \left. (Q^{\theta+1} + T^{\theta+1} + I^{\theta+1} + (\frac{\mu_3}{2\eta}V)^{\theta+1} + (\frac{p_1}{2p_2}Z)^{\theta+1}) + C \right\}.
 \end{aligned} \tag{A.27}$$

Therefore, Conditions (A1) and (A2) in Lemma 3.1 are both satisfied. Consequently, System (1.2) is ergodic and admits a unique stationary distribution. $\square$



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