Research Article

A Stochastic HIV Infection Model with Latent Infection and Antiretroviral Therapy

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Recent studies have demonstrated that the latent infection is a major obstacle to the viral elimination in HIV infection process. In this paper, we formulate a stochastic HIV infection model to include both latent infection and combination drug therapies. We derive that the model solution is unique and positive, and the solution is global. By constructing appropriate stochastic Lyapunov functions, the existence of an ergodic stationary distribution is obtained when the critical condition is greater than one. Furthermore, through rigorous analysis and deduction, the extinction of the virus is established under certain conditions. Numerical simulations are performed to show that small intensity of white noises can maintain the existence of a stationary distribution, while large intensity of white noises is beneficial to the extinction of the virus.

1. Introduction

More and more mathematical models have been developed to reflect the dynamics mechanism of HIV virus. The classical HIV virus model is based on three-dimensional ordinary differential equations, which contains the target T-cells population, infected T-cells population, and virions [1–3]. With the progress of HIV drug treatment, some researchers have investigated the effects of drug therapies on model behaviors [4–7]. The commonly used highly active antiretroviral therapy (HAART) is combined by reverse transcriptase inhibitors and protease inhibitors. Reverse transcriptase inhibitors can inhibit the activity of reverse transcriptase and prevent the formation of provirus during the virus infection; protease inhibitors can block the virus infection of new target T-cells. Unfortunately, the current drug treatment can not eradicate the virus thoroughly. With the development of cell and molecular biology, it has been discovered that the existence of latent infection is a major obstacle to clear the virus [8, 9].

In recent years, mathematical models with the inclusion of latent infected T-cells have been developed to investigate the model behaviors [10–15]. However, all these models are deterministic model, and the effect of stochastic fluctuation

factor is not considered. Actually, HIV transcription is an inherent random process and produces strong random fluctuations in the HIV gene products [16–18]. Thus, by experimental data, it has been proved that these random factors seriously affect the evolution of HIV virus during the protease inhibitor therapy [16]. Moreover, Weinberger et al. have demonstrated that stochastic fluctuation could play an important role in delaying HIV transactivation and contributing to latency [19]. Therefore, it is necessary to consider stochastic fluctuation in HIV virus model, which will be more appropriate to reflect the virus infection process.

Recently, the stochastic differential equation models of infectious diseases [20–25] have been greatly developed, but the stochastic differential equation model of the virus dynamic model has just been developed. The classic three-dimensional stochastic model is studied in the earlier literatures [26–29], then the virus stochastic model with target T-cell logistic growth and CTL immune response is also developed in the last two years [30, 31]. However, all these models did not consider the latent infection mechanism. Conway and Coombs have formulated a stochastic model of latent infected T-cells [32], but they neither include the target T-cell logistic growth nor analyze the model dynamics

theoretically. In this paper, we will formulate an HIV model with latent infection, healthy T-cell logistic growth, antiretroviral therapy, and random perturbations.

The organization of this paper is as follows. In Section 2, we construct our stochastic model and give the existence and uniqueness of the global positive solution. By constructing suitable stochastic Lyapunov functions, the existence of a unique ergodic stationary distribution is derived in Section 3. In Section 4, the sufficient conditions for the extinction of the virus are obtained, and numerical simulations are also employed to show how the white noises affect the model behaviors in Section 5. We summarize our results and give future work finally.

2. Model and Preliminaries

For deterministic model, Wang et al. [14] have studied the following HIV model with latent infection, T-cell logistic growth, and antiretroviral therapy,

$$\begin{aligned} \frac{d}{dt}T(t) &= \lambda - d_T T + rT \left(1 - \frac{T}{T_{\max}}\right) - (1 - n_{rt})kVT, \\ \frac{d}{dt}L(t) &= \eta(1 - n_{rt})kVT - d_L L - aL, \\ \frac{d}{dt}I(t) &= (1 - \eta)(1 - n_{rt})kVT - \delta I + aL, \\ \frac{d}{dt}V(t) &= (1 - n_p)N\delta I - cV. \end{aligned} \quad (1)$$

Here, $T(t)$, $L(t)$, and $I(t)$ represent the concentrations of healthy T-cells, latent infected T-cells, and actively infected T-cells at time t , respectively. $V(t)$ denote the infectious viral particles at time t . Parameter λ is a constant input rate, r is the logistic growth rate, and $T_{\max}$ is the maximum capacity of the number of healthy T-cells in the blood. k is the infection rate between healthy T-cells and infectious virus, η is the fraction of infections leading to latency, and a is the activated rate. Parameters d_T , d_L , δ , and c are the death rates of the healthy T-cells, latently infected T-cells, actively infected T-cells, and infectious virions, respectively. N is the burst size of one productively infected T-cell. n_{rt} and n_p denote the drug efficacy of reverse transcriptase inhibitors and protease inhibitors ($0 \leq n_{rt} < 1$ and $0 \leq n_p < 1$), respectively.

Wang et al. in literature [14] have analyzed the theoretical results of system (1). System (1) always has an uninfected equilibrium E_0 ($T_0, 0, 0, 0$), where

$$T_0 = \frac{T_{\max}}{2r} \left[r - d_T + \sqrt{(r - d_T)^2 + \frac{4r\lambda}{T_{\max}}} \right], \quad (2)$$

and the basic reproduction number is

$$\mathcal{R}_0 = \frac{kNT_0(1 - n_{rt})(1 - n_p)[a + (1 - \eta)d_L]}{c(a + d_L)}. \quad (3)$$

When $\mathcal{R}_0 > 1$, only one infected equilibrium $\bar{E}$ ($\bar{T}, \bar{L}, \bar{I}, \bar{V}$) exists. Wang et al. have obtained the following theoretical results of system (1):

- (I) If $\mathcal{R}_0 < 1$, the uninfected equilibrium E_0 is globally asymptotically stable.
- (II) If $\mathcal{R}_0 > 1$, then the infected equilibrium $\bar{E}$ is locally asymptotically stable under certain condition, and the uninfected equilibrium E_0 is unstable.

In this paper, considering random fluctuation during HIV infection process [16–19], we follow the assumptions of previous literatures [26–31] and assume that the parameters $-d_T$, $-d_L$, $-\delta$, and $-c$ are perturbed by the white noise type. In other words, $-d_T \rightarrow -d_T + \sigma_1 \dot{B}_1(t)$, $-d_L \rightarrow -d_L + \sigma_2 \dot{B}_2(t)$, $-\delta \rightarrow -\delta + \sigma_3 \dot{B}_3(t)$, and $-c \rightarrow -c + \sigma_4 \dot{B}_4(t)$. Thus,

$$\begin{aligned} -d_T dt &\rightarrow -d_T dt + \sigma_1 dB_1(t), \\ -d_L dt &\rightarrow -d_L dt + \sigma_2 dB_2(t), \\ -\delta dt &\rightarrow -\delta dt + \sigma_3 dB_3(t), \\ -c dt &\rightarrow -c dt + \sigma_4 dB_4(t), \end{aligned} \quad (4)$$

where $B_i(t)$ are independent standard Brownian motions with $B_i(0) = 0$ and $\sigma_i^2 > 0$ denote the intensities of the white noise, $i = 1, 2, 3, 4$. Then, system (1) with white noises can be written as

$$\begin{aligned} dT(t) &= \left[\lambda - d_T T + rT \left(1 - \frac{T}{T_{\max}}\right) - (1 - n_{rt})kVT \right] dt \\ &\quad + \sigma_1 T dB_1(t), \\ dL(t) &= [\eta(1 - n_{rt})kVT - d_L L - aL] dt + \sigma_2 L dB_2(t), \\ dI(t) &= [(1 - \eta)(1 - n_{rt})kVT - \delta I + aL] dt \\ &\quad + \sigma_3 I dB_3(t), \\ dV(t) &= [(1 - n_p)N\delta I - cV] dt + \sigma_4 V dB_4(t). \end{aligned} \quad (5)$$

In the following of this paper, we assume $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathbb{P})$ be a complete probability space with a filtration $\{\mathcal{F}_t\}_{t \geq 0}$ satisfying the usual conditions (i.e., it is increasing and right continuous while $\mathcal{F}_0$ contains all $\mathbb{P}$ -null sets), and $B_i(t)$ ($i = 1, 2, 3, 4$) are defined on this complete probability space. We also let $\mathbb{R}_+^4 = \{x = (x_1, x_2, x_3, x_4) \in \mathbb{R}^4: x_i > 0, i = 1, 2, 3, 4\}$.

For convenience, we use symbol $a \wedge b$ to represent $\min\{a, b\}$ and use symbol $a \vee b$ to represent $\max\{a, b\}$. We further denote the following notations:

$$\begin{aligned} \bar{k} &:= (1 - n_{rt})k, \\ \bar{N} &:= (1 - n_p)N. \end{aligned} \quad (6)$$

Based on the theory of Mao [33] and the article of Mao et al. [34], we show the existence and uniqueness of the solution of system (5) in the following theorem.

Theorem 1. For any initial value $(T(0), L(0), I(0), V(0)) \in \mathbb{R}_+^4$ in system (5), there exists a unique positive solution $(T(t), L(t), I(t), V(t))$ and the solution will be contained in $\mathbb{R}_+^4$ with probability one, namely, $(T(t), L(t), I(t), V(t)) \in \mathbb{R}_+^4$ for all $t \geq 0$ almost surely (a.s.).

Proof. All the coefficients of system (5) are locally Lipschitz continuous, by the theory of stochastic differential equation [33], so we obtain that there exists a unique maximum local solution $(T(t), L(t), I(t), V(t))$ on $t \in [0, \tau_e]$, where τ_e is the explosion time.

We show the solution is global in the following; namely, we should derive that $\tau_e = \infty$ a.s. Otherwise, it is supposed that there is a finite time so that the solution $(T(t), L(t), I(t), V(t))$ can not explode to infinity. Let $n_0 > 0$ be big enough so that $T(0), L(0), I(0)$ and $V(0)$ are all on the interval $[1/n_0, n_0]$. For each integer $n \geq n_0$, the stopping time is defined as follows:

$$\tau_n = \inf \left\{ t \in [0, \tau_e) : \min \{T(t), L(t), I(t), V(t)\} \leq \frac{1}{n} \text{ or } \max \{T(t), L(t), I(t), V(t)\} \geq n \right\}, \quad (7)$$

and we let $\inf \emptyset = \infty$ (commonly, $\emptyset$ = the empty set). It is obvious that τ_n increases with $n \rightarrow \infty$. We denote $\tau_\infty = \lim_{n \rightarrow \infty} \tau_n$, then $\tau_\infty \leq \tau_e$ a.s.

(i) If $\tau_\infty = \infty$ is satisfied a.s., then $\tau_e = \infty$ a.s., so $(T(t), L(t), I(t), V(t)) \in \mathbb{R}_+^4$ a.s. for all $t \geq 0$.

(ii) Otherwise, we assume that there exists a pair of constants $\tilde{t} > 0$ and $\epsilon \in (0, 1)$ such that $\mathbb{P}\{\tau_\infty \leq \tilde{t}\} > \epsilon$. So, there exists an integer $n_1 \geq n_0$ that makes $\mathbb{P}\{\tau_\infty \leq \tilde{t}\} \geq \epsilon$ for all $n \geq n_1$ valid.

Define a C^2 -function $W: \mathbb{R}_+^4 \rightarrow \mathbb{R}_+$,

$$W(T, L, I, V) = \left(T - b - b \ln \frac{T}{b} \right) + (L - 1 - \ln L) + (I - 1 - \ln I) + \frac{1}{2N} (V - 1 - \ln V), \quad (8)$$

where b is a positive constant to be determined. Employing Itô's formula [33] to W yields

$$\begin{aligned} dW(T, L, I, V) &= LW(T, L, I, V) dt \\ &+ \sigma_1 (T - b) dB_1(t) \\ &+ \sigma_2 (L - 1) dB_2(t) \\ &+ \sigma_3 (I - 1) dB_3(t) \\ &+ \frac{\sigma_4}{2N} (V - 1) dB_4(t), \end{aligned} \quad (9)$$

and $LW: \mathbb{R}_+^4 \rightarrow \mathbb{R}_+$ is defined by

$$\begin{aligned} LW(T, L, I, V) &= \lambda - d_T T + rT \left(1 - \frac{T}{T_{\max}} \right) - d_L L - \frac{\delta}{2N} I \\ &- \frac{c}{2N} V - b \left[\frac{\lambda}{T} - d_T + r \left(1 - \frac{T}{T_{\max}} \right) - \bar{k} V \right] \\ &- \left(\frac{\eta \bar{k} VT}{L} - d_L - a \right) \\ &- \left[\frac{(1 - \eta) \bar{k} VT}{I} - \delta + a \frac{L}{I} \right] - \frac{1}{2N} \left(\frac{\bar{N} \delta I}{V} - c \right) \\ &+ \frac{1}{2} b \sigma_1^2 + \frac{1}{2} \sigma_2^2 + \frac{1}{2} \sigma_3^2 + \frac{1}{4N} \sigma_4^2 \\ &= -\frac{rT^2}{T_{\max}} + \left(r - d_T + \frac{br}{T_{\max}} \right) T - d_L L - \frac{\delta}{2N} I \\ &- \frac{b\lambda}{T} - \frac{\eta \bar{k} VT}{L} - \frac{(1 - \eta) \bar{k} VT}{I} - a \frac{L}{I} \\ &+ \left(b\bar{k} - \frac{c}{2N} \right) V + K \leq \left(b\bar{k} - \frac{c}{2N} \right) V + K. \end{aligned} \quad (10)$$

Here, we use the notation $K = \lambda + a + d_L + \delta + c/2N + bd_T + (1/2)b\sigma_1^2 + (1/2)\sigma_2^2 + (1/2)\sigma_3^2 + (1/4N)\sigma_4^2$, and we choose the constant $0 < b \leq c/2\bar{k}N$, such that $b\bar{k} - c/2N \leq 0$, so

$$LW(T, L, I, V) \leq K. \quad (11)$$

The rest of the proof is similar to Theorem 2.2 in literature [34]. At the end, we deduce that $\tau_\infty = \infty$. This completes the proof. $\square$

3. Stationary Distribution

Our main concern of this paper is to investigate whether the random fluctuations could affect the model dynamic behavior or not. According to the theory of Hasminskii [35] in the Appendix, we prove the existence of a unique ergodic stationary distribution, which means the survival of the virus population in the future.

Define the critical condition

$$\mathcal{R}_0^s = \frac{\lambda \bar{k} N \delta [a + (1 - \eta)(d_L + (1/2)\sigma_2^2)]}{(\lambda/T_0 + (1/2)\sigma_1^2)(d_L + a + (1/2)\sigma_2^2)(\delta + (1/2)\sigma_3^2)(c + (1/2)\sigma_4^2)}, \quad (12)$$

and denote $\sigma^2 = \sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2$.

Theorem 2. When $\mathcal{R}_0^s > 1$, system (5) has a unique ergodic stationary distribution $\pi(\cdot)$.

Proof. According to Lemma A.1 in the Appendix, we divide it into two steps to prove our conclusion. Now, we prove the validity of condition (A1) in Lemma A.1. The diffusion matrix of system (5) is

$$A = \begin{bmatrix} \sigma_1^2 T^2 & 0 & 0 & 0 \\ 0 & \sigma_2^2 L^2 & 0 & 0 \\ 0 & 0 & \sigma_3^2 I^2 & 0 \\ 0 & 0 & 0 & \sigma_4^2 V^2 \end{bmatrix}. \quad (13)$$

Choose $R = \min_{(T,L,I,V) \in \bar{D}_1 \subset \mathbb{R}_+^4} \{\sigma_1^2 T^2, \sigma_2^2 L^2, \sigma_3^2 I^2, \sigma_4^2 V^2\}$; we have

$$\begin{aligned} \sum_{i,j=1}^4 a_{ij}(T, L, I, V) \xi_i \xi_j &= \sigma_1^2 T^2 \xi_1^2 + \sigma_2^2 L^2 \xi_2^2 + \sigma_3^2 I^2 \xi_3^2 \\ &\quad + \sigma_4^2 V^2 \xi_4^2 \geq \sigma^2 |\xi|^2, \\ (T, L, I, V) &\in \bar{D}_s, \quad \xi = (\xi_1, \xi_2, \xi_3, \xi_4) \in \mathbb{R}_+^4, \end{aligned} \quad (14)$$

where $\bar{D}_1 = [1/l, l] \times [1/l, l] \times [1/l, l] \times [1/l, l]$ and l is a sufficiently large integer, then condition (A1) in Lemma A.1 is satisfied.

In the following, we illustrate the establishment of condition (A2) in Lemma A.1 in the Appendix. Denote

$$f(T) = \lambda + (r - d_T)T - \frac{r}{T_{\max}} T^2, \quad (15)$$

and f is a quadratic function with respect to T . Suppose T_0 and $-T_1$ are the two roots of $f(T) = 0$, then

$$f(T) = -\frac{r}{T_{\max}} (T - T_0)(T + T_1). \quad (16)$$

Since $-(T - T_0)^2 = -(T - T_0)(T + T_1) + (T - T_0)(T_0 + T_1) \leq 0$, then $(T - T_0)(T + T_1) \geq (T - T_0)(T_0 + T_1)$, and

$$\begin{aligned} f(T) &= -\frac{r}{T_{\max}} (T - T_0)(T + T_1) \\ &\leq -\frac{r}{T_{\max}} (T - T_0)(T_0 + T_1). \end{aligned} \quad (17)$$

We define a C^2 -function $W_1: \mathbb{R}_+^4 \rightarrow \mathbb{R}$,

$$W_1 = \frac{T}{T_0 + T_1} - \ln T, \quad (18)$$

and then,

$$\begin{aligned} LW_1 &= \frac{1}{T_0 + T_1} (f(T) - kVT) - \frac{\lambda}{T} + d_T \\ &\quad - r \left(1 - \frac{T}{T_{\max}}\right) + \bar{k}V + \frac{1}{2}\sigma_1^2 \\ &\leq \frac{f(T)}{T_0 + T_1} - \frac{\lambda}{T} + d_T - r + \frac{rT}{T_{\max}} + \bar{k}V + \frac{1}{2}\sigma_1^2 \\ &\leq -\frac{r}{T_{\max}} (T - T_0) - \frac{\lambda}{T} + d_T - r + \frac{rT}{T_{\max}} + \bar{k}V \\ &\quad + \frac{1}{2}\sigma_1^2 \leq -\frac{\lambda}{T} + \frac{\lambda}{T_0} + \bar{k}V + \frac{1}{2}\sigma_1^2. \end{aligned} \quad (19)$$

Here, we use the equality $d_T - r + rT_0/T_{\max} = \lambda/T_0$.

We construct a C^2 -function $U_1: \mathbb{R}_+^4 \rightarrow \mathbb{R}$,

$$\begin{aligned} U_1 &= -\ln I + (c_1 + d_1) \left(\frac{T}{T_0 + T_1} - \ln T \right) \\ &\quad - (c_2 + d_2) \ln V - d_3 \ln L, \end{aligned} \quad (20)$$

where c_1, c_2, d_1, d_2 , and d_3 are positive constants which will be confirmed later. Applying Itô's formula [33] to U_1 and using inequality (19) yield

$$\begin{aligned} LU_1 &\leq - \left[\frac{(1-\eta)\bar{k}TV}{I} + c_1 \frac{\lambda}{T} + c_2 \frac{\bar{N}\delta I}{V} \right] \\ &\quad - \left(\frac{aL}{I} + d_1 \frac{\lambda}{T} + d_2 \frac{\bar{N}\delta I}{V} + d_3 \frac{\eta\bar{k}VT}{L} \right) \\ &\quad + (c_1 + d_1) \left(\frac{\lambda}{T_0} + \frac{1}{2}\sigma_1^2 + \bar{k}V \right) \\ &\quad + (c_2 + d_2) \left(c + \frac{1}{2}\sigma_4^2 \right) + d_3 \left(d_L + a + \frac{1}{2}\sigma_2^2 \right) \\ &\quad + \left(\delta + \frac{1}{2}\sigma_3^2 \right) \\ &\leq -3\sqrt[3]{c_1 c_2 (1-\eta) \lambda \bar{k} \bar{N} \delta} + c_1 \left(\frac{\lambda}{T_0} + \frac{1}{2}\sigma_1^2 \right) \\ &\quad + c_2 \left(c + \frac{1}{2}\sigma_4^2 \right) - 4\sqrt[4]{d_1 d_2 d_3 a \lambda \eta \bar{k} \bar{N} \delta} \\ &\quad + d_1 \left(\frac{\lambda}{T_0} + \frac{1}{2}\sigma_1^2 \right) + d_2 \left(c + \frac{1}{2}\sigma_4^2 \right) \\ &\quad + d_3 \left(d_L + a + \frac{1}{2}\sigma_2^2 \right) + \left(\delta + \frac{1}{2}\sigma_3^2 \right) \\ &\quad + (c_1 + d_1) \bar{k}V. \end{aligned} \quad (21)$$

Let

$$\begin{aligned}
 c_1 \left(\frac{\lambda}{T_0} + \frac{1}{2} \sigma_1^2 \right) &= c_2 \left(c + \frac{1}{2} \sigma_4^2 \right) \\
 &= \frac{(1-\eta) \lambda \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2) (c + (1/2) \sigma_4^2)}, \\
 d_1 \left(\frac{\lambda}{T_0} + \frac{1}{2} \sigma_1^2 \right) &= d_2 \left(c + \frac{1}{2} \sigma_4^2 \right) = d_3 \left(d_L + a + \frac{1}{2} \sigma_2^2 \right) \\
 &= \frac{a \lambda \eta \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2) (d_L + a + (1/2) \sigma_2^2) (c + (1/2) \sigma_4^2)}.
 \end{aligned} \quad (22)$$

We calculate that

$$\begin{aligned}
 c_1 &= \frac{(1-\eta) \lambda \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2)^2 (c + (1/2) \sigma_4^2)}, \\
 c_2 &= \frac{(1-\eta) \lambda \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2) (c + (1/2) \sigma_4^2)^2}, \\
 d_1 &= \frac{a \lambda \eta \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2)^2 (d_L + a + (1/2) \sigma_2^2) (c + (1/2) \sigma_4^2)}, \\
 d_2 &= \frac{a \lambda \eta \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2) (d_L + a + (1/2) \sigma_2^2) (c + (1/2) \sigma_4^2)^2}, \\
 d_3 &= \frac{a \lambda \eta \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2) (d_L + a + (1/2) \sigma_2^2)^2 (c + (1/2) \sigma_4^2)}.
 \end{aligned} \quad (23)$$

Hence,

$$\begin{aligned}
 LU_1 &\leq -\frac{(1-\eta) \lambda \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2) (c + (1/2) \sigma_4^2)} \\
 &\quad - \frac{a \lambda \eta \bar{k} \bar{N} \delta}{(\lambda/T_0 + (1/2) \sigma_1^2) (d_L + a + (1/2) \sigma_2^2) (c + (1/2) \sigma_4^2)} \\
 &\quad + \left(\delta + \frac{1}{2} \sigma_3^2 \right) + (c_1 + d_1) \bar{k} V \\
 &= -\frac{\lambda \bar{k} \bar{N} \delta [a + (1-\eta) (d_L + (1/2) \sigma_2^2)]}{(\lambda/T_0 + (1/2) \sigma_1^2) (d_L + a + (1/2) \sigma_2^2) (c + (1/2) \sigma_4^2)} \\
 &\quad + \left(\delta + \frac{1}{2} \sigma_3^2 \right) + (c_1 + d_1) \bar{k} V \\
 &= -\left(\delta + \frac{1}{2} \sigma_3^2 \right) (\mathcal{R}_0^s - 1) + (c_1 + d_1) \bar{k} V := -H + BV,
 \end{aligned} \quad (24)$$

where $\mathcal{R}_0^s$ is defined in (12) and

$$\begin{aligned}
 H &= \left(\delta + \frac{1}{2} \sigma_3^2 \right) (\mathcal{R}_0^s - 1), \\
 B &= (c_1 + d_1) \bar{k}.
 \end{aligned} \quad (25)$$

Define a C^2 -function $U: \mathbb{R}_+^4 \rightarrow \mathbb{R}$, in the following form:

$$\begin{aligned}
 U(T, L, I, V) &= MU_1 - \ln T - \ln L - \ln I \\
 &\quad + \frac{1}{1+\theta} \left(T + L + I + \frac{V}{2N} \right)^{1+\theta} \\
 &:= MU_1 + U_2 + U_3 + U_4 + U_5,
 \end{aligned} \quad (26)$$

where $0 < \theta < \min\{1, (2d_L \wedge \delta \wedge 2c)/2\sigma^2\}$. Select an appropriate constant $M > 0$ to meet the following requirement:

$$-MH + C \leq -2, \quad (27)$$

where

$$\begin{aligned}
 C &= \sup_{(T,L,I,V) \in \mathbb{R}_+^4} \left\{ -\frac{r}{2T_{\max}} T^{2+\theta} - \frac{d_L}{2} L^{1+\theta} - \frac{\delta}{4} I^{1+\theta} \right. \\
 &\quad \left. - \frac{c}{2} \left(\frac{V}{2N} \right)^{1+\theta} + \frac{rT}{T_{\max}} + E + d_T + d_L + a + \delta \right. \\
 &\quad \left. + \frac{1}{2} \sigma_1^2 + \frac{1}{2} \sigma_2^2 + \frac{1}{2} \sigma_3^2 \right\} < \infty.
 \end{aligned} \quad (28)$$

It is obvious to get that

$$\liminf_{n \rightarrow \infty, (T,L,I,V) \in \mathbb{R}_+^4 \setminus U_n} U(T, L, I, V) = +\infty, \quad (29)$$

where $U_n = (1/n, n) \times (1/n, n) \times (1/n, n) \times (1/n, n)$ and $U(T, L, I, V)$ is a continuous function. So, $U(T, L, I, V)$ should have a minimum point $(\bar{T}_0, \bar{L}_0, \bar{I}_0, \bar{V}_0)$ in the interior of $\mathbb{R}_+^4$. Therefore, we formulate the following nonnegative C^2 -function $\bar{U}: \mathbb{R}_+^4 \rightarrow \mathbb{R}_+$:

$$\bar{U}(T, L, I, V) = U(T, L, I, V) - U(\bar{T}_0, \bar{L}_0, \bar{I}_0, \bar{V}_0). \quad (30)$$

According to Itô formula,

$$\begin{aligned}
 LU_2 &= -\frac{\lambda}{T} + d_T - r \left(1 - \frac{T}{T_{\max}} \right) + \bar{k} V + \frac{1}{2} \sigma_1^2, \\
 LU_3 &= -\frac{\eta \bar{k} T V}{L} + \delta_L + a + \frac{1}{2} \sigma_2^2, \\
 LU_4 &= -\frac{(1-\eta) \bar{k} T V}{I} + \delta - a \frac{L}{I} + \frac{1}{2} \sigma_3^2, \\
 LU_5 &= \left(T + L + I + \frac{V}{2N} \right)^\theta \\
 &\quad \cdot \left[\lambda - d_T T + r T \left(1 - \frac{T}{T_{\max}} \right) - d_L L - \frac{\delta I}{2} - \frac{cV}{2N} \right] \\
 &\quad + \frac{\theta}{2} \left(T + L + I + \frac{V}{2N} \right)^{\theta-1} \\
 &\quad \cdot \left[\sigma_1^2 T^2 + \sigma_2^2 L^2 + \sigma_3^2 I^2 + \sigma_4^2 \left(\frac{V}{2N} \right)^2 \right]
 \end{aligned}$$

$$\begin{aligned}
& \leq \left(T + L + I + \frac{V}{2N} \right)^\theta \\
& \cdot \left(\lambda + rT - \frac{rT^2}{T_{\max}} - d_L L - \frac{\delta I}{2} - \frac{cV}{2N} \right) \\
& + \frac{\theta}{2} (\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2) \left(T + L + I + \frac{V}{2N} \right)^{\theta-1} \\
& \cdot \left[T^2 + L^2 + I^2 + \left(\frac{V}{2N} \right)^2 \right] \leq (\lambda + rT) \\
& \cdot \left(T + L + I + \frac{V}{2N} \right)^\theta - \frac{r}{T_{\max}} T^{2+\theta} - d_L L^{1+\theta} - \frac{\delta}{2} \\
& \cdot I^{1+\theta} - c \left(\frac{V}{2N} \right)^{1+\theta} + \frac{\theta}{2} \\
& \cdot \sigma^2 \left[T^{1+\theta} + L^{1+\theta} + I^{1+\theta} + \left(\frac{V}{2N} \right)^{1+\theta} \right] \leq -\frac{r}{2T_{\max}} \\
& \cdot T^{2+\theta} - \frac{d_L}{2} L^{1+\theta} - \frac{\delta}{4} I^{1+\theta} - \frac{c}{2} \left(\frac{V}{2N} \right)^{1+\theta} + E,
\end{aligned} \tag{31}$$

where

$$\begin{aligned}
E = & \sup_{(T,L,I,V) \in \mathbb{R}_+^4} \left\{ -\frac{r}{2T_{\max}} T^{2+\theta} - \frac{d_L}{2} L^{1+\theta} - \frac{\delta}{4} I^{1+\theta} \right. \\
& - \frac{c}{2} \left(\frac{V}{2N} \right)^{1+\theta} \\
& + \frac{\theta}{2} \sigma^2 \left[T^{1+\theta} + L^{1+\theta} + I^{1+\theta} + \left(\frac{V}{2N} \right)^{1+\theta} \right] \\
& \left. + (\lambda + rT) \left(T + L + I + \frac{V}{2N} \right)^\theta \right\} < \infty.
\end{aligned} \tag{32}$$

According to inequalities (24) and (31), we obtain that

$$\begin{aligned}
L\bar{U} \leq & -MH + (MB + \bar{k})V - \frac{\lambda}{T} + \frac{rT}{T_{\max}} - \frac{\eta \bar{k} TV}{L} \\
& - \frac{(1-\eta) \bar{k} VT}{I} - \frac{r}{2T_{\max}} T^{2+\theta} - \frac{d_L}{2} L^{1+\theta} \\
& - \frac{\delta}{4} I^{1+\theta} - \frac{c}{2} \left(\frac{V}{2N} \right)^{1+\theta} + E + d_T + d_L + a + \delta \\
& + \frac{1}{2} \sigma_1^2 + \frac{1}{2} \sigma_2^2 + \frac{1}{2} \sigma_3^2.
\end{aligned} \tag{33}$$

Next, we define a compact subset D_ε which satisfies condition (A2) in Lemma A.1. Define the following bounded closed set:

$$\begin{aligned}
D_\varepsilon = & \left\{ \varepsilon \leq T \leq \frac{1}{\varepsilon}, \varepsilon^3 \leq L \leq \frac{1}{\varepsilon^3}, \varepsilon^3 \leq I \leq \frac{1}{\varepsilon^3}, \varepsilon \leq V \right. \\
& \left. \leq \frac{1}{\varepsilon} \right\},
\end{aligned} \tag{34}$$

where ε is a small enough constant. In set $\mathbb{R}_+^4 \setminus D_\varepsilon$, we further select ε sufficiently small which satisfies the following conditions:

$$-MH + (MB + \bar{k})\varepsilon + C \leq -1, \tag{35}$$

$$-\frac{\lambda}{\varepsilon} + F \leq -1, \tag{36}$$

$$-\frac{\eta \bar{k}}{\varepsilon} + F \leq -1, \tag{37}$$

$$-\frac{(1-\eta) \bar{k}}{\varepsilon} + F \leq -1, \tag{38}$$

$$-\frac{c}{4(2N\varepsilon)^{1+\theta}} + F \leq -1, \tag{39}$$

$$-\frac{r}{4\varepsilon^{2+\theta} T_{\max}} + F \leq -1, \tag{40}$$

$$-\frac{d_L}{4\varepsilon^{3(1+\theta)}} + F \leq -1, \tag{41}$$

$$-\frac{\delta}{8\varepsilon^{3(1+\theta)}} + F \leq -1, \tag{42}$$

where

$$\begin{aligned}
F = & \sup_{(T,L,I,V) \in \mathbb{R}_+^4} \left\{ -\frac{r}{4T_{\max}} T^{2+\theta} - \frac{d_L}{4} L^{1+\theta} - \frac{\delta}{8} I^{1+\theta} \right. \\
& - \frac{c}{4} \left(\frac{V}{2N} \right)^{1+\theta} + (MB + \bar{k})V + \frac{rT}{T_{\max}} + E + d_T \\
& \left. + d_L + a + \delta + \frac{1}{2} \sigma_1^2 + \frac{1}{2} \sigma_2^2 + \frac{1}{2} \sigma_3^2 \right\} < \infty.
\end{aligned} \tag{43}$$

Set $\mathbb{R}_+^4 \setminus D_\varepsilon$ is divided into the following eight domains:

$$\begin{aligned}
D_1 &= \{(T, L, I, V) \in \mathbb{R}_+^4, 0 < V < \varepsilon\}, \\
D_2 &= \{(T, L, I, V) \in \mathbb{R}_+^4, 0 < T < \varepsilon\}, \\
D_3 &= \{(T, L, I, V) \in \mathbb{R}_+^4, 0 < L < \varepsilon^3, T \geq \varepsilon, V \geq \varepsilon\}, \\
D_4 &= \{(T, L, I, V) \in \mathbb{R}_+^4, 0 < I < \varepsilon^3, T \geq \varepsilon, V \geq \varepsilon\}, \\
D_5 &= \{(T, L, I, V) \in \mathbb{R}_+^4, V > \frac{1}{\varepsilon}\}, \\
D_6 &= \{(T, L, I, V) \in \mathbb{R}_+^4, T > \frac{1}{\varepsilon}\}, \\
D_7 &= \{(T, L, I, V) \in \mathbb{R}_+^4, L > \frac{1}{\varepsilon^3}\}, \\
D_8 &= \{(T, L, I, V) \in \mathbb{R}_+^4, I > \frac{1}{\varepsilon^3}\}.
\end{aligned} \tag{44}$$

Obviously, $D_\varepsilon^c = D_1 \cup D_2 \cup D_3 \cup D_4 \cup D_5 \cup D_6 \cup D_7 \cup D_8$.

Case 1. If $(T, L, I, V) \in D_1$,

$$\begin{aligned}
L\bar{U} &\leq -MH + (MB + \bar{k})V + \frac{rT}{T_{\max}} - \frac{r}{2T_{\max}}T^{2+\theta} \\
&\quad - \frac{d_L}{2}L^{1+\theta} - \frac{\delta}{4}I^{1+\theta} - \frac{c}{2}\left(\frac{V}{2N}\right)^{1+\theta} + E + d_T \\
&\quad + d_L + a + \delta + \frac{1}{2}\sigma_1^2 + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \\
&\leq -MH + (MB + \bar{k})\varepsilon + C.
\end{aligned} \tag{45}$$

Based on condition (35), it indicates that $L\bar{U} \leq -1$ for any $(T, L, I, V) \in D_1$.

Case 2. If $(T, L, I, V) \in D_2$,

$$\begin{aligned}
L\bar{U} &\leq -\frac{\lambda}{T} + (MB + \bar{k})V + \frac{rT}{T_{\max}} - \frac{r}{4T_{\max}}T^{2+\theta} \\
&\quad - \frac{d_L}{4}L^{1+\theta} - \frac{\delta}{8}I^{1+\theta} - \frac{c}{4}\left(\frac{V}{2N}\right)^{1+\theta} + E + d_T \\
&\quad + d_L + a + \delta + \frac{1}{2}\sigma_1^2 + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \leq -\frac{\lambda}{T} + F \\
&\leq -\frac{\lambda}{\varepsilon} + F.
\end{aligned} \tag{46}$$

In view of (36), we get $L\bar{U} \leq -1$ for any $(T, L, I, V) \in D_2$.

Case 3. If $(T, L, I, V) \in D_3$,

$$\begin{aligned}
L\bar{U} &\leq -\frac{\eta\bar{k}TV}{L} + (MB + \bar{k})V + \frac{rT}{T_{\max}} - \frac{r}{4T_{\max}}T^{2+\theta} \\
&\quad - \frac{d_L}{4}L^{1+\theta} - \frac{\delta}{8}I^{1+\theta} - \frac{c}{4}\left(\frac{V}{2N}\right)^{1+\theta} + E + d_T \\
&\quad + d_L + a + \delta + \frac{1}{2}\sigma_1^2 + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \\
&\leq -\frac{\eta\bar{k}TV}{L} + F \leq -\frac{\eta\bar{k}}{\varepsilon} + F.
\end{aligned} \tag{47}$$

According to (37), we obtain that $L\bar{U} \leq -1$ for any $(T, L, I, V) \in D_3$.

Case 4. If $(T, L, I, V) \in D_4$,

$$\begin{aligned}
L\bar{U} &\leq -\frac{(1-\eta)\bar{k}VT}{I} + (MB + \bar{k})V + \frac{rT}{T_{\max}} \\
&\quad - \frac{r}{4T_{\max}}T^{2+\theta} - \frac{d_L}{4}L^{1+\theta} - \frac{\delta}{8}I^{1+\theta} \\
&\quad - \frac{c}{4}\left(\frac{V}{2N}\right)^{1+\theta} + E + d_T + d_L + a + \delta + \frac{1}{2}\sigma_1^2 \\
&\quad + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \leq -\frac{(1-\eta)\bar{k}VT}{I} + F \\
&\leq -\frac{(1-\eta)\bar{k}}{\varepsilon} + F.
\end{aligned} \tag{48}$$

From condition (38), we deduce that $L\bar{U} \leq -1$ for any $(T, L, I, V) \in D_4$.

Case 5. If $(T, L, I, V) \in D_5$,

$$\begin{aligned}
L\bar{U} &\leq -\frac{c}{2}\left(\frac{V}{2N}\right)^{1+\theta} + (MB + \bar{k})V + \frac{rT}{T_{\max}} \\
&\quad - \frac{r}{4T_{\max}}T^{2+\theta} - \frac{d_L}{4}L^{1+\theta} - \frac{\delta}{8}I^{1+\theta} + E + d_T \\
&\quad + d_L + a + \delta + \frac{1}{2}\sigma_1^2 + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \\
&\leq -\frac{c}{4}\left(\frac{V}{2N}\right)^{1+\theta} + F \leq -\frac{c}{4(2N\varepsilon)^{1+\theta}} + F.
\end{aligned} \tag{49}$$

In view of (39), we obtain that $L\bar{U} \leq -1$ for any $(T, L, I, V) \in D_5$.

Case 6. If $(T, L, I, V) \in D_6$,

$$\begin{aligned}
L\bar{U} &\leq -\frac{r}{2T_{\max}}T^{2+\theta} + (MB + \bar{k})V + \frac{rT}{T_{\max}} - \frac{d_L}{4}L^{1+\theta} \\
&\quad - \frac{\delta}{8}I^{1+\theta} - \frac{c}{4}\left(\frac{V}{2N}\right)^{1+\theta} + E + d_T + d_L + a + \delta \\
&\quad + \frac{1}{2}\sigma_1^2 + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \leq -\frac{r}{4T_{\max}}T^{2+\theta} + F \\
&\leq -\frac{r}{4\varepsilon^{2+\theta}T_{\max}} + F.
\end{aligned} \tag{50}$$

By condition (40), we conclude that $L\bar{U} \leq -1$ for all $(T, L, I, V) \in D_6$.

Case 7. If $(T, L, I, V) \in D_7$,

$$\begin{aligned}
L\bar{U} &\leq -\frac{d_L}{2}L^{1+\theta} + (MB + \bar{k})V + \frac{rT}{T_{\max}} - \frac{r}{4T_{\max}}T^{2+\theta} \\
&\quad - \frac{\delta}{8}I^{1+\theta} - \frac{c}{4}\left(\frac{V}{2N}\right)^{1+\theta} + E + d_T + d_L + a + \delta \\
&\quad + \frac{1}{2}\sigma_1^2 + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \leq -\frac{d_L}{4}L^{1+\theta} + F \\
&\leq -\frac{d_L}{4\varepsilon^{3(1+\theta)}} + F.
\end{aligned} \tag{51}$$

It derives that $L\bar{U} \leq -1$ for any $(T, L, I, V) \in D_7$ if condition (41) is satisfied.

Case 8. If $(T, L, I, V) \in D_8$,

$$\begin{aligned}
L\bar{U} &\leq -\frac{\delta}{4}I^{1+\theta} + (MB + \bar{k})V + \frac{rT}{T_{\max}} - \frac{r}{4T_{\max}}T^{2+\theta} \\
&\quad - \frac{d_L}{4}L^{1+\theta} - \frac{c}{4}\left(\frac{V}{2N}\right)^{1+\theta} + E + d_T + d_L + a
\end{aligned}$$

$$\begin{aligned}
& + \delta + \frac{1}{2}\sigma_1^2 + \frac{1}{2}\sigma_2^2 + \frac{1}{2}\sigma_3^2 \leq -\frac{\delta}{8}I^{1+\theta} + F \\
& \leq -\frac{\delta}{8\varepsilon^{3(1+\theta)}} + F.
\end{aligned} \tag{52}$$

By condition (42), it is obvious to get that $\bar{L}\bar{U} \leq -1$ for any $(T, L, I, V) \in D_8$. Clearly, from (45)–(52), there exists a sufficiently small ε , such that

$$\bar{L}\bar{U} \leq -1 \quad \forall (T, L, I, V) \in D_\varepsilon^c. \tag{53}$$

By Lemma A.1 in the Appendix, we obtain that system (5) is ergodic and has a unique stationary distribution. This completes the proof. $\square$

Remark 3. For system (5), if there is no white noise, that is, $\sigma_1 = \sigma_2 = \sigma_3 = \sigma_4 = 0$, then the critical condition $\mathcal{R}_0^s$ is the basic reproduction number $\mathcal{R}_0$ of its corresponding deterministic model (1). It indicates that the existence of the stationary distribution of our stochastic model is a generalization of its corresponding deterministic model to the stability of the infected equilibrium.

4. Extinction

Theorem 4. For any initial value $(T(0), L(0), I(0), V(0)) \in \mathbb{R}_+^4$, one assumes $(T(t), L(t), I(t), V(t))$ be the solution of system (5). If $r - d_T > \sigma_1^2/2$, then for almost $\omega \in \Omega$, the solution $(T(t), L(t), I(t), V(t))$ of system (5) is

$$\begin{aligned}
& \limsup_{t \rightarrow \infty} \frac{1}{t} \ln \left(\frac{\sqrt{\mathcal{R}_0}}{d_L + a} L(t) + \frac{\sqrt{\mathcal{R}_0}}{a} I(t) + \frac{\mathcal{R}_0}{aN} V(t) \right) \\
& \leq \phi, \quad a.s.,
\end{aligned} \tag{54}$$

where $\phi = \min\{d_L + a, \delta, c\}(\sqrt{\mathcal{R}_0} - 1)\mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} + \max\{d_L + a, \delta, c\}(\sqrt{\mathcal{R}_0} - 1)\mathbf{I}_{\{\mathcal{R}_0 > 1\}} + (c\sqrt{\mathcal{R}_0}/T_0) \int_0^\infty |x - T_0| \mu(x) dx - (1/2)(\sigma_2^{-2} + \sigma_3^{-2} + \sigma_4^{-2})^{-1}$, and the distribution of $T(t)$ converges weakly to a measure which has the invariant density

$$\begin{aligned}
\mu(x) &= Qx^{-2+2(r-d_T)/\sigma_1^2} \exp \left\{ -\frac{2}{\sigma_1^2} \left(\frac{\lambda}{x} + \frac{rx}{T_{\max}} \right) \right\}, \\
& x \in (0, \infty),
\end{aligned} \tag{55}$$

where Q is a constant such that $\int_0^\infty \mu(x) dx = 1$. If $\phi < 0$, then L, I and V will be eliminated with probability one; namely,

$$\begin{aligned}
& \lim_{t \rightarrow \infty} L(t) = 0, \\
& \lim_{t \rightarrow \infty} I(t) = 0, \\
& \lim_{t \rightarrow \infty} V(t) = 0,
\end{aligned} \tag{56}$$

a.s.

Proof. Firstly, we can obtain that the solution of system (5) is positive for any given positive initial value from Theorem 1.

Consider the following auxiliary stochastic differential equation:

$$\begin{aligned}
dx(t) &= \left[\lambda - d_T x(t) + rx(t) \left(1 - \frac{x(t)}{T_{\max}} \right) \right] dt \\
&+ \sigma_1 x(t) dB_1(t).
\end{aligned} \tag{57}$$

For the initial value $x(0) = T(0) > 0$ of system (57), denote $x(t)$ as its solution. Following the proof process in Theorem 3.1 of article [31], by the law of large numbers theorem [36], it is easy to get that $x(t)$ has the ergodic property with the invariant density

$$\begin{aligned}
\mu(x) &= Qx^{-2+2(r-d_T)/\sigma_1^2} \exp \left\{ -\frac{2}{\sigma_1^2} \left(\frac{\lambda}{x} + \frac{rx}{T_{\max}} \right) \right\}, \\
& x \in (0, \infty),
\end{aligned} \tag{58}$$

where Q is a constant such that $\int_0^\infty \mu(x) dx = 1$. It then follows that

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t x(s) ds = \int_0^\infty x \mu(x) dx \quad a.s. \tag{59}$$

By the comparison theorem of one-dimensional stochastic differential equation [37], we obtain that

$$T(t) \leq x(t) \quad \forall t \geq 0 \text{ a.s.} \tag{60}$$

Next, we denote a matrix

$$F = \begin{bmatrix} 0 & 0 & \frac{\eta \bar{k} T_0}{(d_L + a)} \\ \frac{a}{\delta} & 0 & \frac{(1-\eta) \bar{k} T_0}{\delta} \\ 0 & \frac{\bar{N} \delta}{c} & 0 \end{bmatrix}. \tag{61}$$

It is easy to obtain that there must be a left eigenvector (v_1, v_2, v_3) of matrix F corresponding to the value $\sqrt{\mathcal{R}_0}$ [38], such that

$$(v_1, v_2, v_3) F = \sqrt{\mathcal{R}_0} (v_1, v_2, v_3), \tag{62}$$

where $(v_1, v_2, v_3) = (\sqrt{\mathcal{R}_0}, \delta \sqrt{\mathcal{R}_0}/a, c \mathcal{R}_0/a \bar{N})$.

Define a C^2 -function $G: \mathbb{R}_+^4 \rightarrow \mathbb{R}$,

$$G(L, I, V) = \alpha_1 L + \alpha_2 I + \alpha_3 V, \tag{63}$$

where $\alpha_1 = v_1/(d_L + a)$, $\alpha_2 = v_2/\delta$, $\alpha_3 = v_3/c$. By applying Itô's formula, it yields

$$\begin{aligned}
d(\ln G) &= L(\ln G) dt + \frac{1}{G} [\alpha_1 \sigma_2 L dB_2(t) \\
&+ \alpha_2 \sigma_3 I dB_3(t) + \alpha_3 \sigma_4 V dB_4(t)],
\end{aligned} \tag{64}$$

where

$$\begin{aligned}
 L(\ln G) &= \frac{\alpha_1}{G} (\eta \bar{k} TV - d_L L - a) \\
 &\quad + \frac{\alpha_2}{G} [(1 - \eta) \bar{k} TV - \delta I + aL] \\
 &\quad + \frac{\alpha_3}{G} (\bar{N} \delta I - cV) - \frac{\alpha_1^2 \sigma_2^2 L^2}{2G^2} - \frac{\alpha_2^2 \sigma_3^2 I^2}{2G^2} \\
 &\quad - \frac{\alpha_3^2 \sigma_4^2 V^2}{2G^2} \\
 &:= J - \frac{\alpha_1^2 \sigma_2^2 L^2}{2G^2} - \frac{\alpha_2^2 \sigma_3^2 I^2}{2G^2} - \frac{\alpha_3^2 \sigma_4^2 V^2}{2G^2}.
 \end{aligned} \quad (65)$$

We have

$$\begin{aligned}
 G^2 &= \left(\alpha_1 \sigma_2 L \frac{1}{\sigma_2} + \alpha_2 \sigma_3 I \frac{1}{\sigma_3} + \alpha_3 \sigma_4 V \frac{1}{\sigma_4} \right)^2 \\
 &\leq (\alpha_1^2 \sigma_2^2 L^2 + \alpha_2^2 \sigma_3^2 I^2 + \alpha_3^2 \sigma_4^2 V^2) \left(\frac{1}{\sigma_2^2} + \frac{1}{\sigma_3^2} + \frac{1}{\sigma_4^2} \right).
 \end{aligned} \quad (66)$$

Moreover, by using (60), we get

$$\begin{aligned}
 J &= \frac{\alpha_1}{G} (\eta \bar{k} TV - d_L L - a) + \frac{\alpha_2}{G} [(1 - \eta) \bar{k} TV - \delta I \\
 &\quad + aL] + \frac{\alpha_3}{G} (\bar{N} \delta I - cV) \leq \frac{\alpha_1}{G} \eta \bar{k} (x - T_0) V \\
 &\quad + \frac{\alpha_1}{G} (\eta \bar{k} T_0 V - d_L L - a) + \frac{\alpha_2}{G} (1 - \eta) \bar{k} (x - T_0) V \\
 &\quad + \frac{\alpha_2}{G} [(1 - \eta) \bar{k} T_0 V - \delta I + aL] + \frac{\alpha_3}{G} (\bar{N} \delta I - cV) \\
 &\leq \frac{\bar{k}}{\alpha_3} [\alpha_1 \eta + \alpha_2 (1 - \eta)] |x - T_0| \\
 &\quad + \frac{1}{G} \left\{ \frac{v_1}{d_L + a} (\eta \bar{k} T_0 V - d_L L - a) \right. \\
 &\quad \left. + \frac{v_2}{\delta} [(1 - \eta) \bar{k} x V - \delta I + aL] + \frac{v_3}{c} (\bar{N} \delta I - cV) \right\} \\
 &= \frac{\bar{k}}{\alpha_3} [\alpha_1 \eta + \alpha_2 (1 - \eta)] |x - T_0| + \frac{1}{G} (v_1, v_2, v_3) \\
 &\quad \cdot [F(L, I, V)^T - (L, I, V)^T] = \frac{\bar{k}}{\alpha_3} [\alpha_1 \eta \\
 &\quad + \alpha_2 (1 - \eta)] |x - T_0| + \frac{1}{G} \left(\sqrt{\mathcal{R}_0} - 1 \right) (v_1 L + v_2 I \\
 &\quad + v_3 V) = \frac{\bar{k}}{\alpha_3} [\alpha_1 \eta + \alpha_2 (1 - \eta)] |x - T_0| \\
 &\quad + \frac{1}{G} \left(\sqrt{\mathcal{R}_0} - 1 \right) [\alpha_1 (d_L + a) L + \delta \alpha_2 I + c \alpha_3 V] \\
 &\leq \frac{\bar{k}}{\alpha_3} [\alpha_1 \eta + \alpha_2 (1 - \eta)] |x - T_0|
 \end{aligned}$$

$$\begin{aligned}
 &+ \min \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} \\
 &+ \max \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 > 1\}}.
 \end{aligned} \quad (67)$$

By (66) and (67), we obtain that

$$\begin{aligned}
 L(\ln G) &\leq \min \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} \\
 &\quad + \max \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 > 1\}} \\
 &\quad + \frac{\bar{k}}{\alpha_3} [\alpha_1 \eta + \alpha_2 (1 - \eta)] |x - T_0| \\
 &\quad - \frac{1}{2} (\sigma_2^{-2} + \sigma_3^{-2} + \sigma_4^{-2})^{-1}.
 \end{aligned} \quad (68)$$

From (64), we further derive that

$$\begin{aligned}
 d(\ln G) &\leq \left\{ \min \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} \right. \\
 &\quad + \max \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 > 1\}} \\
 &\quad + \frac{\bar{k}}{\alpha_3} [\alpha_1 \eta + \alpha_2 (1 - \eta)] |x - T_0| \\
 &\quad \left. - \frac{1}{2} (\sigma_2^{-2} + \sigma_3^{-2} + \sigma_4^{-2})^{-1} \right\} dt \\
 &\quad + \frac{1}{G} [\alpha_1 \sigma_2 L dB_2(t) + \alpha_2 \sigma_3 I dB_3(t) \\
 &\quad + \alpha_3 \sigma_4 V dB_4(t)].
 \end{aligned} \quad (69)$$

Integrate (69) from 0 to t , and divide by t on both sides, then

$$\begin{aligned}
 \frac{\ln G(t)}{t} &\leq \frac{\ln G(0)}{t} \\
 &\quad + \min \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} \\
 &\quad + \max \{d_L + a, \delta, c\} \times \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 > 1\}} \\
 &\quad + \frac{\bar{k} [\alpha_1 \eta + \alpha_2 (1 - \eta)]}{\alpha_3 t} \int_0^t |x(s) - T_0| ds \\
 &\quad - \frac{1}{2} (\sigma_2^{-2} + \sigma_3^{-2} + \sigma_4^{-2})^{-1} \\
 &\quad + \frac{1}{t} \int_0^t \frac{\alpha_1 \sigma_2 L(s)}{G(s)} dB_2(s) \\
 &\quad + \frac{1}{t} \int_0^t \frac{\alpha_2 \sigma_3 I(s)}{G(s)} dB_3(s) \\
 &\quad + \frac{1}{t} \int_0^t \frac{\alpha_3 \sigma_4 V(s)}{G(s)} dB_4(s)
 \end{aligned}$$

$$\begin{aligned}
&= \frac{\ln G(0)}{t} \\
&+ \min \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} \\
&+ \max \{d_L + a, \delta, c\} \times \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 > 1\}} \\
&+ \frac{\bar{k} [\alpha_1 \eta + \alpha_2 (1 - \eta)]}{\alpha_3 t} \int_0^t |x(s) - T_0| ds \\
&- \frac{1}{2} (\sigma_2^{-2} + \sigma_3^{-2} + \sigma_4^{-2})^{-1} + \frac{M_1(t)}{t} \\
&+ \frac{M_2(t)}{t} + \frac{M_3(t)}{t},
\end{aligned} \tag{70}$$

where

$$\begin{aligned}
M_1(t) &= \int_0^t \frac{\alpha_1 \sigma_2 L(s)}{G(s)} dB_2(s), \\
M_2(t) &= \int_0^t \frac{\alpha_2 \sigma_3 I(s)}{G(s)} dB_3(s), \\
M_3(t) &= \int_0^t \frac{\alpha_3 \sigma_4 V(s)}{G(s)} dB_4(s).
\end{aligned} \tag{71}$$

$M_1(t)$, $M_2(t)$, and $M_3(t)$ are local martingales whose quadratic variations are $\langle M_1, M_1 \rangle_t = \sigma_2^2 \int_0^t (\alpha_1 L(s)/G(s)) ds \leq \sigma_2^2 t$, $\langle M_2, M_2 \rangle_t = \sigma_3^2 \int_0^t (\alpha_2 I(s)/G(s)) ds \leq \sigma_3^2 t$, and $\langle M_3, M_3 \rangle_t = \sigma_4^2 \int_0^t (\alpha_3 V(s)/G(s)) ds \leq \sigma_4^2 t$. According to the strong law of large numbers for local martingale [33], we can obtain that

$$\lim_{t \rightarrow \infty} \frac{M_i(t)}{t} = 0 \quad \text{a.s., } i = 1, 2, 3. \tag{72}$$

Because $x(t)$ is ergodic and $\int_0^\infty x\mu(x)dx < \infty$,

$$\lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t |x(s) - T_0| ds = \int_0^\infty |x - T_0| \mu(x) dx < \infty. \tag{73}$$

Taking the superior limit on both sides of (70) and combining with (72) and (73) yield

$$\begin{aligned}
&\limsup_{t \rightarrow \infty} \frac{\ln G(t)}{t} \\
&\leq \min \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} \\
&+ \max \{d_L + a, \delta, c\} \times \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 > 1\}} \\
&+ \frac{\bar{k} [\alpha_1 \eta + \alpha_2 (1 - \eta)]}{\alpha_3} \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t |x(s) - T_0| ds \\
&- \frac{1}{2} (\sigma_2^{-2} + \sigma_3^{-2} + \sigma_4^{-2})^{-1}
\end{aligned}$$

$$\begin{aligned}
&= \min \{d_L + a, \delta, c\} \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 \leq 1\}} \\
&+ \max \{d_L + a, \delta, c\} \times \left(\sqrt{\mathcal{R}_0} - 1 \right) \mathbf{I}_{\{\mathcal{R}_0 > 1\}} \\
&+ \frac{c\sqrt{\mathcal{R}_0}}{T_0} \int_0^\infty |x - T_0| \mu(x) dx \\
&- \frac{1}{2} (\sigma_2^{-2} + \sigma_3^{-2} + \sigma_4^{-2})^{-1} := \phi \quad \text{a.s.,}
\end{aligned} \tag{74}$$

which is the required assertion. In particular, if $\phi < 0$, then it derives that

$$\begin{aligned}
\lim_{t \rightarrow \infty} \frac{\ln L(t)}{t} &= 0, \\
\lim_{t \rightarrow \infty} \frac{\ln I(t)}{t} &= 0, \\
\lim_{t \rightarrow \infty} \frac{\ln V(t)}{t} &= 0 \\
&\text{a.s.;}
\end{aligned} \tag{75}$$

therefore, $\lim_{t \rightarrow \infty} L(t) = 0$, $\lim_{t \rightarrow \infty} I(t) = 0$, and $\lim_{t \rightarrow \infty} V(t) = 0$ a.s. In other words, the populations L , I , and V will tend to zero exponentially with probability one. This completes the proof. $\square$

5. Numerical Simulations

The numerical simulation is performed to investigate the effect of the white noises on model dynamical behavior. Applying Milstein's higher order method [39], system (5) can be rewritten as the following discrete form:

$$\begin{aligned}
T_{m+1} &= T_m \\
&+ \left[\lambda - dT_m - rT_m \left(1 - \frac{T}{T_{\max}} \right) - \bar{k}V_m T_m \right] \Delta t \\
&+ \sigma_1 T_m \sqrt{\Delta t} \varphi_{1m} + 0.5\sigma_1^2 T_m (\Delta t \varphi_{1m}^2 - \Delta t), \\
L_{m+1} &= L_m + (\eta \bar{k} V_m T_m - d_L L_m + a L_m) \Delta t \\
&+ \sigma_2 L_m \sqrt{\Delta t} \varphi_{2m} + 0.5\sigma_2^2 L_m (\Delta t \varphi_{2m}^2 - \Delta t), \\
I_{m+1} &= I_m + [(1 - \eta) \bar{k} V_m T_m - \delta I_m + a L_m] \Delta t \\
&+ \sigma_3 I_m \sqrt{\Delta t} \varphi_{3m} + 0.5\sigma_3^2 I_m (\Delta t \varphi_{3m}^2 - \Delta t),
\end{aligned}$$

$$\begin{aligned}
V_{m+1} &= V_m + \left(\bar{N} \delta T_m^* - c V_m \right) \Delta t + \sigma_4 V_m \sqrt{\Delta t} \varphi_{4m} \\
&\quad + 0.5 \sigma_4^2 V_m \left(\Delta t \varphi_{4m}^2 - \Delta t \right),
\end{aligned} \tag{76}$$

where $\varphi_{1m}, \varphi_{2m}, \varphi_{3m}$, and φ_{4m} , $m = 1, 2, \dots, n$, are the m th realization of four independent Gaussian random variables with distribution $N(0, 1)$, and the time step $\Delta t = 0.01$.

In order to examine the effect of the white noises on model behavior numerically, we choose the same parameter values as the deterministic model (1). For the source of the parameter values, see literature [14] for detail.

$$\begin{aligned}
\lambda &= 10 \mu l^{-1} \text{ day}^{-1}, \\
d_T &= 0.03 \text{ day}^{-1}, \\
r &= 0.1 \text{ day}^{-1} \\
T_{\max} &= 1500 \mu l^{-1}, \\
k &= 0.0001 \mu l^{-1} \text{ day}^{-1}, \\
\eta &= 0.02, \\
d_L &= 0.001 \text{ day}^{-1}, \\
a &= 0.1 \text{ day}^{-1}, \\
\delta &= 1 \text{ day}^{-1}, \\
N &= 1000 \text{ virions/cell}, \\
c &= 20 \text{ day}^{-1}, \\
n_{rt} &= 0.4, \\
n_p &= 0.5,
\end{aligned} \tag{77}$$

and the white noises $\sigma_1 = \sigma_2 = \sigma_3 = 0.08$, $\sigma_4 = 0.4$. For this set of parameters, we have the critical condition $\mathcal{R}_0^s = 1.2726 > 1$, and system (5) has a unique stationary distribution (Theorem 2 is satisfied). For its corresponding deterministic model (1), the basic reproduction number $\mathcal{R}_0 = 1.7657 > 1$, and the unique infected equilibrium is locally asymptotically stable (result (II) in Section 2 is satisfied). When $\mathcal{R}_0^s > 1$, Figure 1 shows that the unique stationary distribution occurs (see Figures 1(a) and 1(c)), and the corresponding distributions of total T-cells population (the sum of the healthy T-cell T , the latently infected T-cells L , and the actively infected T-cells I) and virus population are also given (see Figures 1(b) and 1(d)).

We further choose the white noises $\sigma_1 = \sigma_2 = \sigma_3 = 0.3$, $\sigma_4 = 1.5$, and all the other parameters are the same as the above. We calculate that $\mathcal{R}_0^s = 0.2524 < 1$, and Theorem 2 does not hold. In Figure 2, we can see that the virus can be eradicated for the stochastic model (5), while the virus is prevalent for the deterministic model (1). From Figures 1 and 2, we examine that the existence of stationary distribution can

be maintained if the white noises are small, and the virus can be eradicated if the white noises are big enough.

6. Conclusions

We have studied a stochastic HIV infection model with latent infection, target T-cells logistic growth, and antiretroviral therapy. The critical condition $\mathcal{R}_0^s$ of the stochastic model which is related to its corresponding deterministic model is derived. We obtain the existence of the unique stationary distribution when the critical condition is bigger than one. Moreover, the sufficient condition which is dependent on the basic reproduction number is obtained for the extinction of the virus. Numerically, we investigate that small fluctuations can be helpful to the persistence of the virus, while large fluctuations can be beneficial to the extinction of the virus.

For the special case, if the target T-cells logistic growth is not considered in our stochastic model, then system (5) can be rewritten as the following:

$$\begin{aligned}
dT(t) &= [\lambda - d_T T - (1 - n_{rt}) kVT] dt + \sigma_1 T dB_1(t), \\
dL(t) &= [\eta(1 - n_{rt}) kVT - d_L L - aL] dt \\
&\quad + \sigma_2 L dB_2(t), \\
dI(t) &= [(1 - \eta)(1 - n_{rt}) kVT - \delta I + aL] dt \\
&\quad + \sigma_3 I dB_3(t), \\
dV(t) &= [(1 - n_p) N \delta I - cV] dt + \sigma_4 V dB_4(t).
\end{aligned} \tag{78}$$

Model (78) is the corresponding stochastic model of the deterministic HIV basic latent infection model in literature [10–12], and our theoretical analysis results can also be established for this model. When there are no drug therapies in system (5), that is, $n_{rt} = n_p = 0$, then our theoretical results are also satisfied.

In the process of virus infection, cytotoxic T lymphocyte (CTL) is the main immune cell in-host, which can limit the replication of virus in the body and determine the viral load [2, 40]. Wang et al. in article [31] have considered the CTL immune response in HIV stochastic model; therefore, a stochastic HIV model with latent infection and CTL immune response will be our future work. In addition, under the influence of environment, the stochastic perturbation is not always treated as a constant but a periodic behavior [41]; thus HIV latent infection model regarding periodic perturbation is also our research work in the future.

Appendix

In order to prove the existence of the stationary distribution, we should introduce the theory of Has'minskii [35].

Let $X(t)$ be usual time-homogeneous Markov process in $\mathbb{R}^l$, and $X(t)$ satisfies the following stochastic differential equation:

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

FIGURE 1: The solution of stochastic model (5) and its histogram with white noises $\sigma_1 = \sigma_2 = \sigma_3 = 0.08$ and $\sigma_4 = 0.4$. The black lines are the solutions of total T-cells and virus populations of stochastic model (5), and the red lines are the solutions of their deterministic model, respectively.

The definition of the diffusion matrix is as follows:

$$A(x) = (a_{ij}(x)), \quad a_{ij}(x) = \sum_{r=1}^k g_r^i(x) g_r^j(x), \quad (\text{A.2})$$

where $X(t)$ is nonsingular.

Lemma A.1. *It is assumed that there is a bounded open domain $U \subset \mathbb{R}^l$ with a regular boundary Γ , which has the following properties:*

(A1) *there is a positive number E that makes $\sum_{i,j=1}^l a_{ij}(x) \xi_i \xi_j \geq R|\xi|^2$ satisfied, for $x \in U$ and $\xi \in \mathbb{R}^l$, where R is a constant;*

(A2) *there is a nonnegative C^2 -function U that makes LU negative for any $\mathbb{R}^l \setminus D$, then*

$$\mathbb{P} \left\{ \lim_{t \rightarrow \infty} \frac{1}{t} \int_0^t f(X(s)) ds = \int_{\mathbb{R}^l} f(x) \pi(dx) \right\} = 1 \quad (\text{A.3})$$

for all $x \in \mathbb{R}^l$, where π is the stationary distribution of the Markov process $X(t)$ and $f(x)$ is an integrable function of measure π . Then, the Markov process $X(t)$ has a unique ergodic stationary distribution $\pi(\cdot)$.

Data Availability

The data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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FIGURE 2: The virus can be eradicated for the stochastic model (5) when the white noises $\sigma_1 = \sigma_2 = \sigma_3 = 0.3$ and $\sigma_4 = 1.5$, while the virus is prevalent for its corresponding deterministic model.

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