

Analysis of a stochastic HIV model with cell-to-cell transmission and Ornstein-Uhlenbeck process

Qun Liu (✉ liuqun151608@163.com)

Northeast Normal University

Research Article

Keywords: HIV model, Cell-to-cell transmission, Ornstein-Uhlenbeck process, Stationary distribution, Probability density

Posted Date: September 6th, 2022

DOI: <https://doi.org/10.21203/rs.3.rs-2011526/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Analysis of a stochastic HIV model with cell-to-cell transmission and Ornstein-Uhlenbeck process

Qun Liu*

School of Mathematics and Statistics, Key Laboratory of Applied Statistics of MOE, Northeast Normal University, Changchun 130024, Jilin Province, P.R. China

Abstract In this paper, we establish and analyze a stochastic HIV model with both virus-to-cell and cell-to-cell transmissions and Ornstein-Uhlenbeck process, in which we suppose that the virus-to-cell infection rate and the cell-to-cell infection rate satisfy the Ornstein-Uhlenbeck process. Firstly, we validate that there exists a unique global solution to the stochastic model with any initial value. Then we adopt a stochastic Lyapunov function technique to develop sufficient criteria for the existence of a stationary distribution of positive solutions to the stochastic system, which reflects the strong persistence of all $CD4^+$ T cells and free viruses. In particular, under the same conditions as the existence of a stationary distribution, we obtain the specific form of the probability density around the quasi-chronic infection equilibrium of the stochastic system. Finally, numerical simulations are conducted to validate these analytical results. Our results suggest that the methods used in this paper can be applied to study other viral infection models in which the infected $CD4^+$ T cells are divided into latently infected and actively infected subgroups.

Keywords HIV model; Cell-to-cell transmission; Ornstein-Uhlenbeck process; Stationary distribution; Probability density.

1 Introduction

Acquired immunodeficiency syndrome (AIDS) has become a great threat not only to the society but also to the human health. According to the Global Progress Report on AIDS 2021, there were about 37.7 million people worldwide who had been infected with the Human Immunodeficiency Virus (HIV) in 2020 [1]. HIV primarily invades $CD4^+$ T lymphocytes cells or T-helper cells in the body of human being, which eventually leads to the deficiency of immune system against infections. Because of the immunodeficiency, human body will be susceptible to broad range of infectious diseases [2]. At this time, $CD4^+$ T cells play an important role in almost all adaptive immune responses because they can secrete some differentiation factors which are requisite for other cells in our immune system [3]. Therefore, in order to prevent and control HIV/AIDS effectively, people have taken some preventative measures in relation to the epidemics, such as the media and the media can convey positive messages related to the health which might change the behaviors of the people of unaware citizen.

Recently, using mathematical modeling to study the replication process and transmission dynamics of HIV infection has been a hot research issue in the field of epidemiology [4]. Earlier studies only focus on the healthy $CD4^+$ T cells, the infected $CD4^+$ T cells and the free virus particles, that is virus-to-cell infection [5, 6, 7, 8, 9, 10, 11]. However, the virus-to-cell infection is usually inefficient because target cells or donor cells often set up some specific obstacles to prevent the transmission of the virus-to-cell mode [12]. Many scholars have revealed that the virus can be also transmitted by the infected cells to target cells through direct contact [13, 14]. Recent experimental study illustrates that virus-to-cell infection is less effective than cell-to-cell transmission because many characteristics are more difficult to determine in the bloodstream than in tissue cultures. Thus, in order to establish a mathematical model to understand the pathogenesis

*Corresponding author at School of Mathematics and Statistics, Key Laboratory of Applied Statistics of MOE, Northeast Normal University, Changchun 130024, Jilin Province, P.R. China. E-mail address: liuqun151608@163.com (Q. Liu). Tel:+8653286983361.

of HIV infection, there are two approaches that should be incorporated: virus-to-cell infection and cell-to-cell transmission. In the past few decades, more and more researchers devoted to formulating suitable ordinary differential equations models with both the virus-to-cell infection and the cell-to-cell transmission to investigate and analyze the dynamic behaviors of HIV/AIDS [15, 16, 17, 18, 19, 20, 21]. In particular, Yang et al. [15] established an HIV model with $CD4^+$ T-cell proliferation, virus-to-cell infection and cell-to-cell transmission which is similar to the following system:

$$\begin{cases} \frac{dT(t)}{dt} = \lambda - \mu_1 T(t) + rT(t) \left(1 - \frac{T(t)}{T_{\max}}\right) - \beta_1 T(t)V(t) - \beta_2 T(t)I(t) \\ \frac{dI(t)}{dt} = \beta_1 T(t)V(t) + \beta_2 T(t)I(t) - \mu_2 I(t) - \alpha_1 I(t), \\ \frac{dV(t)}{dt} = kI(t) - \mu_3 V(t) - \alpha_2 V(t), \end{cases} \quad (1.1)$$

where T and I denote the concentrations of healthy $CD4^+$ T cells and infected $CD4^+$ T cells, respectively, V represents the concentration of virions. All parameters are assumed to be positive constants and their descriptions are given in Table 1.

Table 1: Summary of parameter meaning of system (1.1)

Parameters	Descriptions
λ	Recruitment rate of the healthy $CD4^+$ T cells
β_1	Virus-to-cell transmission rate
β_2	Cell-to-cell infection rate
μ_1	Death rate of the healthy $CD4^+$ T cells
μ_2	Death rate of the infected $CD4^+$ T cells
μ_3	Death rate of the virus particles
α_1	Remove rate of the infected $CD4^+$ T cells
α_2	Shedding rate of the free virus
r	Proliferation rate of the $CD4^+$ T cells
k	Average number of the virus releases
T_{\max}	Maximum capacity of the $CD4^+$ T cells

For system (1.1), the basic reproduction number is defined by

$$\mathcal{R}_0 = \frac{k\beta_1 T_0}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2)} + \frac{\beta_2 T_0}{\mu_2 + \alpha_1},$$

which is used to determine whether the disease occurs or not, where

$$T_0 = \frac{T_{\max}}{2r} \left[r - \mu_1 + \sqrt{(r - \mu_1)^2 + \frac{4r\lambda}{T_{\max}}} \right].$$

In addition, the dynamical behaviors of system (1.1) are as follows:

- If $\mathcal{R}_0 < 1$, the virus-free steady state $E_0 = (T_0, 0, 0)$ always exists and it is globally asymptotically stable in the invariant set Γ , where

$$\Gamma := \left\{ (T, I, V) \mid 0 < T + I \leq \frac{\bar{\lambda}}{\bar{\mu}}, 0 \leq V \leq \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} \right\},$$

and

$$\bar{\lambda} = \lambda + \frac{r}{T_{\max}} T_0^2, \quad \bar{\mu} = \min \left\{ \frac{\lambda}{T_0} + \frac{r}{T_{\max}} T_0, \mu_2 \right\}.$$

- If $\mathcal{R}_0 > 1$, then E_0 is unstable and there is also a unique chronic infection equilibrium $E^+ = (T^+, I^+, V^+)$ which is globally asymptotically stable provided that $\mu_1 > r(1 - \frac{T^+}{T_{\max}})$, where

$$T^+ = \frac{T_0}{\mathcal{R}_0}, \quad I^+ = \frac{(\mu_3 + \alpha_2)(\mathcal{R}_0 - 1) \left(\frac{\lambda}{T_0} + \frac{rT^+}{T_{\max}} \right)}{k\beta_1 + \beta_2(\mu_3 + \alpha_2)}, \quad V^+ = \frac{kI^+}{\mu_3 + \alpha_2}.$$

On the other hand, it is noticed that the system (1.1) is constructed under a constant environment. However, from the viewpoint of microscopic, the interference of random factor exists in the process of virus replication [22]. In order to take into account some crucial epidemiological factors such as, antiretroviral (ART) therapy, infection mechanism in heterogeneous environment, etc., many scholars have developed various stochastic differential equations (SDEs) models, specially stochastic ordinary differential equations models [22, 23, 24, 25, 26, 27] to study the pathogenesis and replication process of HIV/AIDS. For example, Lu et al. [22] analyzed the stationary distribution and probability density of a stochastic HIV model with cell-to-cell transmission. Djordjevic et al. [25] obtained sufficient conditions for extinction and persistence in mean of a stochastic SICA epidemic model for HIV transmission. Feng et al. [26] studied the asymptotic dynamics of a stochastic HIV-1 infection model with degenerate diffusion which are governed by a threshold parameter.

Up to now, there are several pathways to introduce stochastic perturbations in the deterministic models. One of the most popular pathways is to think that the parameters involved in the system satisfy the Ornstein-Uhlenbeck process which is an Itô process. Accordingly, in order to reveal the influence of environmental noise on the cell-free transmission rate β_1 and the cell-to-cell infection rate β_2 , we suppose that they are random variables involved in randomness and satisfy the following form:

$$\begin{aligned}d\beta_1(t) &= \rho_1[\bar{\beta}_1 - \beta_1(t)]dt + \sigma_1dB_1(t), \\d\beta_2(t) &= \rho_2[\bar{\beta}_2 - \beta_2(t)]dt + \sigma_2dB_2(t),\end{aligned}$$

where $\bar{\beta}_i$ are positive constants which measure the long-time mean levels of the infection rates β_i , $i = 1, 2$; ρ_i and σ_i are positive constants representing the speeds of reversion and the intensities of volatility, respectively, $i = 1, 2$; $B_i(t)$ are mutually independent standard Brownian motions defined on a complete probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathbb{P})$ with a filtration $\{\mathcal{F}_t\}_{t \geq 0}$ satisfying the usual conditions [28], $i = 1, 2$.

In view of Mao's monograph [28], it is easy to see that $\beta_i(t)$ have the following unique exact solutions:

$$\beta_i(t) = \bar{\beta}_i + (\beta_i(0) - \bar{\beta}_i)e^{-\rho_i t} + \sigma_i \int_0^t e^{-\rho_i(t-s)} dB_i(s), \quad i = 1, 2.$$

By direct calculation, the mathematical expectation and the variance of $\beta_i(t)$ over the interval $[0, t]$ are given as follows

$$\mathbb{E}[\beta_i(t)] = \bar{\beta}_i + (\beta_i(0) - \bar{\beta}_i)e^{-\rho_i t} \quad \text{and} \quad \text{Var}[\beta_i(t)] = \frac{\sigma_i^2}{2\rho_i}(1 - e^{-2\rho_i t}), \quad i = 1, 2,$$

respectively. Apparently, the limit distributions of the random variables $\beta_i(t)$ are $\mathbb{N}(\bar{\beta}_i, \sigma_i^2/2\rho_i)$, $i = 1, 2$.

In other words, the probability densities of the limit distributions are $\pi_i(x) = \frac{\sqrt{\rho_i}}{\sqrt{\pi}\sigma_i} e^{-\frac{\rho_i(x-\bar{\beta}_i)^2}{\sigma_i^2}}$, $i = 1, 2$. Moreover, it is obvious that $\lim_{t \rightarrow 0^+} \mathbb{E}[\beta_i(t)] = \beta_i(0)$ and $\lim_{t \rightarrow 0^+} \text{Var}[\beta_i(t)] = 0$, $i = 1, 2$. This implies that the modeling technique is biologically reasonable to simulate the random influences of crucial parameters in a within-host model. Motivated by the facts mentioned above, we establish the following stochastic HIV model with Ornstein-Uhlenbeck process:

$$\begin{cases} dT(t) = \left[\lambda - \mu_1 T(t) + rT(t) \left(1 - \frac{T(t)}{T_{\max}} \right) - \max\{\beta_1(t), 0\}T(t)V(t) - \max\{\beta_2(t), 0\}T(t)I(t) \right] dt, \\ dI(t) = [\max\{\beta_1(t), 0\}T(t)V(t) + \max\{\beta_2(t), 0\}T(t)I(t) - \mu_2 I(t) - \alpha_1 I(t)] dt, \\ dV(t) = [kI(t) - \mu_3 V(t) - \alpha_2 V(t)] dt, \\ d\beta_1(t) = \rho_1[\bar{\beta}_1 - \beta_1(t)]dt + \sigma_1 dB_1(t), \\ d\beta_2(t) = \rho_2[\bar{\beta}_2 - \beta_2(t)]dt + \sigma_2 dB_2(t). \end{cases} \quad (1.2)$$

Here we introduce the random variables $\max\{\beta_i(t), 0\}$ rather than $\beta_i(t)$ into the system (1.2) because $\max\{\beta_i(t), 0\}$ are nonnegative while $\beta_i(t)$ may be negative due to the features of the Ornstein-Uhlenbeck process, $i = 1, 2$. When we prove the existence of a stationary distribution of positive solutions to the system (1.2), the nonnegativity of the variables $\beta_i(t)$ is extremely significant, $i = 1, 2$. Based on this consideration, we develop the above system, that is, system (1.2).

Involving the stochastic model of HIV with Ornstein-Uhlenbeck process brings great difficulties and challenges to the theoretical analysis of the model because the Ornstein-Uhlenbeck process can lead to an increase in the dimensionality of the system. The main barrier is that how to construct suitable Lyapunov functions to study the existence of a stationary distribution theoretically since the previous method of

establishing Lyapunov function is no longer applicable to our model. We need to find a new method to construct some suitable Lyapunov functions and then verify the existence of a stationary distribution. In comparison with the existing literature, our main innovations and contributions of this paper are summarized as follows: (i) we adopt a novel method to establish some stochastic Lyapunov functions to obtain the existence of a stationary distribution, which can be seen as a kind of probability distribution with some variables from the viewpoint of stochastic process. (ii) Under the same conditions as the existence of a stationary distribution, we get the exact expression of the probability density, which is a function that describes the probability of the output value of the random variable around the quasi-chronic infection equilibrium of the system (1.2).

Throughout this paper, for the sake of convenience, we introduce the following notations:

$$\mathbb{R}_+^d = \{x = (x_1, \dots, x_d) \in \mathbb{R}^d : x_i > 0, 1 \leq i \leq d\} \text{ and } \overline{\mathbb{R}}_+^d = \{x = (x_1, \dots, x_d) \in \mathbb{R}^d : x_i \geq 0, 1 \leq i \leq d\},$$

$$x \vee y = \max\{x, y\} \text{ for any } x, y \in \mathbb{R}.$$

Denote by $C^2(\mathbb{R}^d; \overline{\mathbb{R}}_+)$ the family of all nonnegative functions $V(x)$ defined on \mathbb{R}^d such that they are continuously twice differentiable in x . Let \mathbf{I}_A be the indicator function of the set A . If G is a vector or matrix, we use the notation $\|G\|$ to denote its norm and its transpose is denoted by G^T . If G is an invertible matrix, we use the notation G^{-1} to represent its inverse matrix. If G is a square matrix, its determinant is represented by $|G|$. In addition, if \mathbb{H} and \mathbb{J} are two d -dimensional symmetric matrices, we define

$$\mathbb{H} \succeq \mathbb{J} : \mathbb{H} - \mathbb{J} \text{ is at least a semi-positive definite matrix.} \quad (1.3)$$

By (1.3), it is clear that the matrix \mathbb{H} is also positive definite if \mathbb{J} is a positive definite matrix.

The paper is organized as follows. In the next section, we validate that there exists a unique global solution to the system (1.2) with any initial value which is very important and necessary to analyze the dynamic behavior of a viral infection model. In Section 3, we adopt a novel method to construct some suitable Lyapunov functions to establish sufficient criteria for the existence of a stationary distribution, which indicates the strong persistence of all $CD4^+$ T cells and free viruses. In Section 4, we obtain the accurate expression of the probability density around the quasi-chronic infection equilibrium E^* of the system (1.2). In Section 5, numerical simulations are carried out to illustrate the analytical findings of this paper. Finally, a brief conclusion scope of the main results obtained in this paper is given.

2 Existence and uniqueness of the global solution

To study the transmission dynamics of a viral infection system, we should first ensure that the solution of the system is global. The following theorem is related to the existence and uniqueness of the global solution of system (1.2) with any initial value.

Theorem 2.1 *For any initial value $(T(0), I(0), V(0), \beta_1(0), \beta_2(0)) \in \mathbb{R}_+^3 \times \mathbb{R}^2$, there exists a unique global solution $(T(t), I(t), V(t), \beta_1(t), \beta_2(t))^T$ to system (1.2) on $t \geq 0$ and the solution will remain in $\mathbb{R}_+^3 \times \mathbb{R}^2$ almost surely (a.s.).*

Proof. Note that all the coefficients of system (1.2) satisfy the local Lipschitz conditions, then for any initial value $(T(0), I(0), V(0), \beta_1(0), \beta_2(0)) \in \mathbb{R}_+^3 \times \mathbb{R}^2$, there is a unique local solution $(T(t), I(t), V(t), \beta_1(t), \beta_2(t))^T$ on the interval $[0, \tau_e)$, where τ_e is an explosion time. Now we validate this solution is global, that is, to prove $\tau_e = \infty$ a.s. To this end, let $n_0 \geq 1$ be sufficiently large such that $T(0), I(0), V(0), e^{\beta_1(0)}$ and $e^{\beta_2(0)}$ all lie within the interval $[1/n_0, n_0]$. For each integer $n \geq n_0$, we define a stopping time by [28]

$$\tau_n = \inf \left\{ t \in [0, \tau_e) : \min\{T(t), I(t), V(t), e^{\beta_1(t)}, e^{\beta_2(t)}\} \leq \frac{1}{n} \text{ or } \max\{T(t), I(t), V(t), e^{\beta_1(t)}, e^{\beta_2(t)}\} \geq n \right\},$$

where throughout this paper we set $\inf \emptyset = \infty$ (here \emptyset means the empty set). It is clear that τ_n is increasing as $n \rightarrow \infty$. Denote by $\tau_\infty = \lim_{n \rightarrow \infty} \tau_n$, whence $\tau_\infty \leq \tau_e$ a.s. If $\tau_\infty = \infty$ a.s. is true, then $\tau_e = \infty$ a.s. and $(T(t), I(t), V(t), \beta_1(t), \beta_2(t))^T \in \mathbb{R}_+^3 \times \mathbb{R}^2$ a.s. for all $t \geq 0$. In other words, to confirm the proof we need to validate $\tau_\infty = \infty$ a.s. If this assertion is false, then there is a pair of constants $T > 0$ and $\epsilon \in (0, 1)$ such that

$$\mathbb{P}\{\tau_\infty \leq T\} > \epsilon.$$

As a consequence, there is an integer $n_1 \geq n_0$ such that

$$\mathbb{P}\{\tau_n \leq T\} \geq \epsilon, \quad \forall n \geq n_1.$$

Define a C^2 -function $\mathcal{U} : \mathbb{R}_+^3 \times \mathbb{R}^2 \rightarrow \overline{\mathbb{R}}_+$ by

$$\mathcal{U}(T, I, V, \beta_1, \beta_2) = (T - 1 - \ln T) + (I - 1 - \ln I) + (V - 1 - \ln V) + \frac{\beta_1^2}{2} + \frac{\beta_2^2}{2}.$$

It is noticed that the above function is nonnegative because of $u - 1 - \ln u \geq 0$ for any $u > 0$. Applying Itô's formula [28] to \mathcal{U} leads to that

$$d\mathcal{U}(T, I, V, \beta_1, \beta_2) = L\mathcal{U}(T, I, V, \beta_1, \beta_2)dt + \sigma_1\beta_1dB_1(t) + \sigma_2\beta_2dB_2(t),$$

where $L\mathcal{U} : \mathbb{R}_+^3 \times \mathbb{R}^2 \rightarrow \mathbb{R}$ is defined by

$$\begin{aligned} L\mathcal{U} = & \lambda - \mu_1T + rT \left(1 - \frac{T}{T_{\max}}\right) - \max\{\beta_1, 0\}TV - \max\{\beta_2, 0\}TI - \frac{\lambda}{T} + \mu_1 - r + \frac{r}{T_{\max}}T + \max\{\beta_1, 0\}V \\ & + \max\{\beta_2, 0\}I + \max\{\beta_1, 0\}TV + \max\{\beta_2, 0\}TI - \mu_2I - \alpha_1I - \frac{\max\{\beta_1, 0\}TV}{I} - \max\{\beta_2, 0\}T + \mu_2 \\ & + \alpha_1 + kI - \mu_3V - \alpha_2V - \frac{kI}{V} + \mu_3 + \alpha_2 + \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 - \rho_1\beta_1^2 - \rho_2\beta_2^2 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ \leq & \lambda + \mu_1 + \mu_2 + \mu_3 + \alpha_1 + \alpha_2 + rT + \frac{r}{T_{\max}}T + \max\{\beta_1, 0\}V + \max\{\beta_2, 0\}I + kI + \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 \\ & - \rho_1\beta_1^2 - \rho_2\beta_2^2 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ \leq & \lambda + \mu_1 + \mu_2 + \mu_3 + \alpha_1 + \alpha_2 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \left(r + \frac{r}{T_{\max}}\right)T + |\beta_1|V + |\beta_2|I + kI + \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 - \rho_1\beta_1^2 \\ & - \rho_2\beta_2^2. \end{aligned} \tag{2.1}$$

In addition, we have

$$\begin{aligned} d(T + I) &= \left[\lambda - \mu_1T + rT - \frac{r}{T_{\max}}T^2 - \mu_2I - \alpha_1I \right] dt \\ &\leq \left[\lambda + \frac{r}{T_{\max}}T_0^2 - \left(\frac{\lambda}{T_0} + \frac{r}{T_{\max}}T_0 \right)T - \mu_2I \right] dt \\ &\leq \left[\lambda + \frac{r}{T_{\max}}T_0^2 - \min \left\{ \frac{\lambda}{T_0} + \frac{r}{T_{\max}}T_0, \mu_2 \right\} (T + I) \right] dt \\ &= [\bar{\lambda} - \bar{\mu}(T + I)]dt, \end{aligned}$$

which implies that

$$T(t) + I(t) \leq \begin{cases} T(0) + I(0), & \text{if } T(0) + I(0) \geq \frac{\bar{\lambda}}{\bar{\mu}}, \\ \frac{\bar{\lambda}}{\bar{\mu}}, & \text{if } T(0) + I(0) < \frac{\bar{\lambda}}{\bar{\mu}} \end{cases} \leq K_1, \tag{2.2}$$

where

$$K_1 := \max \left\{ T(0) + I(0), \frac{\bar{\lambda}}{\bar{\mu}} \right\}.$$

According to the third equation of system (1.2), we obtain

$$\begin{aligned} dV &= (kI - \mu_3V - \alpha_2V)dt \\ &\leq (kI - \mu_3V)dt, \end{aligned}$$

and so

$$V(t) \leq \begin{cases} V(0), & \text{if } V(0) \geq \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}, \\ \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}, & \text{if } V(0) < \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} \end{cases} \leq K_2, \tag{2.3}$$

where

$$K_2 := \max \left\{ V(0), \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} \right\}.$$

Substituting (2.2) and (2.3) into (2.1) leads to that

$$\begin{aligned} LU &\leq \lambda + \mu_1 + \mu_2 + \mu_3 + \alpha_1 + \alpha_2 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \left(r + \frac{r}{T_{\max}} \right) K_1 + K_2 |\beta_1| + K_1 |\beta_2| + kK_1 + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 \\ &\quad - \rho_1 \beta_1^2 - \rho_2 \beta_2^2 \\ &\leq \lambda + \mu_1 + \mu_2 + \mu_3 + \alpha_1 + \alpha_2 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + \left(r + \frac{r}{T_{\max}} \right) K_1 + kK_1 + \sup_{\beta_1 \in \mathbb{R}} \{ -\rho_1 \beta_1^2 + K_2 |\beta_1| + \rho_1 \bar{\beta}_1 \beta_1 \} \\ &\quad + \sup_{\beta_2 \in \mathbb{R}} \{ -\rho_2 \beta_2^2 + K_1 |\beta_2| + \rho_2 \bar{\beta}_2 \beta_2 \} \\ &:= K_3. \end{aligned}$$

Here K_3 is a positive constant which is independent of the variables T , I , V , β_1 and β_2 . The rest of the proof is similar to that of Zhou et al. [29] and so it is omitted here. This completes the proof.

Remark 2.1 *By the proof of Theorem 2.1, we can get that if $T(0) + I(0) < \bar{\lambda}/\bar{\mu}$ and $V(0) < k\bar{\lambda}/(\bar{\mu}\mu_3)$, then the set*

$$\Xi = \left\{ (T, I, V, \beta_1, \beta_2)^T \in \mathbb{R}_+^3 \times \mathbb{R}^2 : T + I < \frac{\bar{\lambda}}{\bar{\mu}}, V < \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} \right\}$$

is positively invariant for the system (1.2).

Therefore, from now on, we always suppose that the initial value $(T(0), I(0), V(0), \beta_1(0), \beta_2(0))^T$ of the system (1.2) belongs to the set Ξ . This shows that the unique global solution $(T(t), I(t), V(t), \beta_1(t), \beta_2(t))^T$ to the system (1.2) will also belong to the set Ξ with probability one.

3 Existence of a stationary distribution

In this section, we pay attention to developing sufficient criteria for the existence of a stationary distribution which implies the strong persistence of healthy $CD4^+$ T cells, infected $CD4^+$ T cells and free viruses. We first give some theories about the existence of a stationary distribution (see Du et al. [30]).

For a homogeneous Markov process defined in \mathbb{R}^d which is described by the stochastic differential equation:

$$dX(t) = f(X(t))dt + g(X(t))dB(t), \quad (3.1)$$

with the initial value $X(0) \in \mathbb{R}^d$, where $B(t)$ is a d -dimensional Brownian motion defined on the complete probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathbb{P})$. In addition, $f : \mathbb{R}^d \rightarrow \mathbb{R}^d$ and $g : \mathbb{R}^d \rightarrow \mathbb{R}^{d \times m}$ are Borel measurable. The following lemma is related to the existence of a stationary distribution of system (1.2).

Lemma 3.1 *(See Theorem 2.2 in [30]). Suppose that there exists a bounded closed domain $\mathbb{A} \subset \mathbb{R}^d$ with a regular boundary Γ , for any initial value $X(0) \in \mathbb{R}^d$, if*

$$\liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{P}(s, X(s), \mathbb{A}) ds > 0 \text{ a.s.},$$

where $\mathbb{P}(s, X(s), \cdot)$ denotes the transition probability of $X(t)$. Then there exists a solution of system (3.1) which has the Feller property, and system (3.1) admits at least one stationary distribution $\pi(\cdot)$ on \mathbb{R}^d .

Theorem 3.1 *Assume that*

$$\mathcal{R}_0^S = \frac{k\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_1 \sqrt{\rho_1}}{\sigma_1}}^{\infty} \left(\frac{\sigma_1}{\sqrt{\rho_1}} x + \bar{\beta}_1 \right)^{\frac{1}{3}} e^{-x^2} dx \right)^3}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2) \left(\frac{\lambda}{T_0} + \frac{k\bar{\lambda}\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} + \frac{\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_2 \sqrt{\rho_2}}{\sigma_2}}^{\infty} \left(\frac{\sigma_2}{\sqrt{\rho_2}} x + \bar{\beta}_2 \right)^{\frac{1}{2}} e^{-x^2} dx \right)^2}{(\mu_2 + \alpha_1) \left(\frac{\lambda}{T_0} + \frac{k\bar{\lambda}\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} > 1,$$

then system (1.2) has at least one stationary distribution $\pi(\cdot)$ on $\mathbb{R}_+^3 \times \mathbb{R}^2$, where

$$\bar{\lambda} = \lambda + \frac{r}{T_{\max}} T_0^2, \quad \bar{\mu} = \min \left\{ \frac{\lambda}{T_0} + \frac{r}{T_{\max}} T_0, \mu_2 \right\}.$$

Proof. By Remark 2.1, it is easy to see that $(T(t), I(t), V(t), \beta_1(t), \beta_2(t))^T \in \Xi$ a.s. Thus, all the descriptions of \mathbb{R}^d in Lemma 3.1 should be modified as Ξ for the system (1.2). We divide the proof process into three steps: the first two steps are to find a nonnegative C^2 -function $\mathcal{W}(T, I, V, \beta_1, \beta_2)$ and a compact set $D \subset \Xi$ such that $L\mathcal{W} \leq -1$ for all $(T, I, V, \beta_1, \beta_2)^T \in \Xi \setminus D$, the last step is to validate the existence of a stationary distribution of system (1.2) by adopting Theorem 2.2 in Du et al. [30].

Step 1. (Construction of a nonnegative C^2 -function): Firstly, according to system (1.2), we have

$$L(-\ln T) = -\frac{\lambda}{T} + \mu_1 - r \left(1 - \frac{T}{T_{\max}}\right) + \max\{\beta_1, 0\}V + \max\{\beta_2, 0\}I, \quad (3.2)$$

$$L(-\ln I) = -\frac{\max\{\beta_1, 0\}TV}{I} - \max\{\beta_2, 0\}T + \mu_2 + \alpha_1, \quad (3.3)$$

$$L(-\ln V) = -\frac{kI}{V} + \mu_3 + \alpha_2, \quad (3.4)$$

and

$$L(V) = kI - \mu_3V - \alpha_2V. \quad (3.5)$$

In addition, it is noticed that

$$-(T - T_0)^2 = -(T - T_0)(T + T_1) + (T - T_0)(T_1 + T_0) \leq 0,$$

where T_0 and $-T_1$ are the roots of the quadratic equation

$$f(T) := \lambda + (r - \mu_1)T - \frac{r}{T_{\max}}T^2 = 0.$$

Accordingly

$$f(T) = -\frac{r}{T_{\max}}(T - T_0)(T + T_1) \leq -\frac{r}{T_{\max}}(T - T_0)(T_1 + T_0),$$

and so

$$L\left(\frac{T}{T_1 + T_0}\right) \leq \frac{f(T)}{T_1 + T_0} \leq -\frac{r}{T_{\max}}(T - T_0). \quad (3.6)$$

Define a function \mathcal{W}_1 which takes the form

$$\mathcal{W}_1(T, V) = -\ln T + \frac{\bar{\beta}_1}{\mu_3 + \alpha_2}V + \frac{T}{T_0 + T_1}.$$

In view of (3.2), (3.5) and (3.6), it is easy to obtain that

$$\begin{aligned} L\mathcal{W}_1 &\leq -\frac{\lambda}{T} + \mu_1 - r \left(1 - \frac{T}{T_{\max}}\right) + \max\{\beta_1, 0\}V + \max\{\beta_2, 0\}I + \frac{\bar{\beta}_1}{\mu_3 + \alpha_2}(kI - \mu_3V - \alpha_2V) - \frac{r}{T_{\max}}(T - T_0) \\ &\leq -\frac{\lambda}{T} + \mu_1 - r + \frac{r}{T_{\max}}T_0 + \bar{\beta}_1V + \bar{\beta}_2I + (\xi_1(t) \vee 0)V + (\xi_2(t) \vee 0)I + \frac{k\bar{\beta}_1}{\mu_3 + \alpha_2}I - \bar{\beta}_1V \\ &\leq -\frac{\lambda}{T} + \mu_1 - r + \frac{r}{T_{\max}}T_0 + \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2\right)I + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}(\xi_1(t) \vee 0) + \frac{\bar{\lambda}}{\bar{\mu}}(\xi_2(t) \vee 0) \\ &= -\frac{\lambda}{T} + \frac{\lambda}{T_0} + \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2\right)I + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}(\xi_1(t) \vee 0) + \frac{\bar{\lambda}}{\bar{\mu}}(\xi_2(t) \vee 0), \end{aligned} \quad (3.7)$$

where

$$\xi_1(t) = \beta_1(t) - \bar{\beta}_1, \quad \xi_2(t) = \beta_2(t) - \bar{\beta}_2.$$

Next, define

$$\mathcal{W}_2(T, I, V) = -\ln I + c_1\mathcal{W}_1(T, V) - c_2 \ln V + c_3\mathcal{W}_1(T, V),$$

where c_1 , c_2 and c_3 are positive constants which will be determined later. Then by (3.3), (3.4) and (3.7), we obtain

$$\begin{aligned}
LW_2 &\leq -\frac{\max\{\beta_1, 0\}TV}{I} - \max\{\beta_2, 0\}T + \mu_2 + \alpha_1 - \frac{c_1\lambda}{T} + \frac{c_1\lambda}{T_0} + c_1\left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2\right)I + \frac{c_1k\bar{\lambda}}{\bar{\mu}\mu_3}(\xi_1(t) \vee 0) \\
&\quad + \frac{c_1\bar{\lambda}}{\bar{\mu}}(\xi_2(t) \vee 0) - \frac{c_2kI}{V} + c_2(\mu_3 + \alpha_2) - \frac{c_3\lambda}{T} + \frac{c_3\lambda}{T_0} + c_3\left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2\right)I + \frac{c_3k\bar{\lambda}}{\bar{\mu}\mu_3}(\xi_1(t) \vee 0) \\
&\quad + \frac{c_3\bar{\lambda}}{\bar{\mu}}(\xi_2(t) \vee 0) \\
&\leq -3\sqrt[3]{c_1c_2k\lambda\bar{\beta}_1} - 2\sqrt{c_3\lambda\bar{\beta}_2} + \mu_2 + \alpha_1 + \frac{c_1\lambda}{T_0} + \frac{c_1k\bar{\lambda}}{\bar{\mu}\mu_3}(\xi_1(t) \vee 0) + \frac{c_1\bar{\lambda}}{\bar{\mu}}(\xi_2(t) \vee 0) + c_2(\mu_3 + \alpha_2) + \frac{c_3\lambda}{T_0} \\
&\quad + \frac{c_3k\bar{\lambda}}{\bar{\mu}\mu_3}(\xi_1(t) \vee 0) + \frac{c_3\bar{\lambda}}{\bar{\mu}}(\xi_2(t) \vee 0) + (c_1 + c_3)\left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2\right)I,
\end{aligned} \tag{3.8}$$

where

$$\tilde{\beta}_1(t) = \max\{\beta_1(t), 0\}, \quad \tilde{\beta}_2(t) = \max\{\beta_2(t), 0\}.$$

For the fourth and fifth equations of system (1.2), that is,

$$d\beta_i(t) = \rho_i[\bar{\beta}_i - \beta_i(t)]dt + \sigma_i dB_i(t), \quad i = 1, 2.$$

According to the references [31, 32, 33], we can obtain that $\beta_i(t)$ ($i = 1, 2$) have the ergodic property and they will weakly converge to the invariant density

$$\pi_i(x) = \frac{\sqrt{\rho_i}}{\sqrt{\pi}\sigma_i} e^{-\frac{\rho_i(x-\bar{\beta}_i)^2}{\sigma_i^2}}, \quad x \in \mathbb{R}, \quad i = 1, 2,$$

which together with the ergodic theorem [34], we obtain

$$\begin{aligned}
\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{3}} \pi_i(x) dx &= \int_0^{\infty} x^{\frac{1}{3}} \pi_i(x) dx \\
&= \int_0^{\infty} x^{\frac{1}{3}} \frac{\sqrt{\rho_i}}{\sqrt{\pi}\sigma_i} e^{-\frac{\rho_i(x-\bar{\beta}_i)^2}{\sigma_i^2}} dx \\
&= \frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_i\sqrt{\rho_i}}{\sigma_i}}^{\infty} \left(\frac{\sigma_i}{\sqrt{\rho_i}}y + \bar{\beta}_i\right)^{\frac{1}{3}} e^{-y^2} dy \quad \left(\text{let } y = \frac{\sqrt{\rho_i}(x-\bar{\beta}_i)}{\sigma_i}\right) \\
&= \frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_i\sqrt{\rho_i}}{\sigma_i}}^{\infty} \left(\frac{\sigma_i}{\sqrt{\rho_i}}x + \bar{\beta}_i\right)^{\frac{1}{3}} e^{-x^2} dx, \quad i = 1, 2,
\end{aligned} \tag{3.9}$$

and

$$\begin{aligned}
\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{2}} \pi_i(x) dx &= \int_0^{\infty} x^{\frac{1}{2}} \pi_i(x) dx \\
&= \int_0^{\infty} x^{\frac{1}{2}} \frac{\sqrt{\rho_i}}{\sqrt{\pi}\sigma_i} e^{-\frac{\rho_i(x-\bar{\beta}_i)^2}{\sigma_i^2}} dx \\
&= \frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_i\sqrt{\rho_i}}{\sigma_i}}^{\infty} \left(\frac{\sigma_i}{\sqrt{\rho_i}}x + \bar{\beta}_i\right)^{\frac{1}{2}} e^{-x^2} dx, \quad i = 1, 2.
\end{aligned} \tag{3.10}$$

Analogously, for the stochastic differential equations

$$d\xi_i(t) = -\rho_i\xi_i(t)dt + \sigma_i dB_i(t), \quad i = 1, 2.$$

It is easy to get that $\xi_i(t)$ ($i = 1, 2$) have the ergodic property and they will weakly converge to the invariant density

$$\tilde{\pi}_i(x) = \frac{\sqrt{\rho_i}}{\sqrt{\pi}\sigma_i} e^{-\frac{\rho_i x^2}{\sigma_i^2}}, \quad x \in \mathbb{R}, \quad i = 1, 2.$$

By the ergodic theorem, we have

$$\begin{aligned}
\int_{-\infty}^{\infty} (x \vee 0) \tilde{\pi}_i(x) dx &= \int_0^{\infty} x \tilde{\pi}_i(x) dx \\
&= \int_0^{\infty} x \frac{\sqrt{\rho_i}}{\sqrt{\pi} \sigma_i} e^{-\frac{\rho_i x^2}{\sigma_i^2}} dx \\
&= \frac{\sigma_i}{2\sqrt{\pi} \rho_i}, \quad i = 1, 2.
\end{aligned} \tag{3.11}$$

Substituting (3.9), (3.10) and (3.11) into (3.8) leads to that

$$\begin{aligned}
LW_2 &\leq -3\sqrt[3]{c_1 c_2 k \lambda \widehat{\beta}_1} - 2\sqrt{c_3 \lambda \widehat{\beta}_2} + \left(3\sqrt[3]{c_1 c_2 k \lambda \widehat{\beta}_1} - 3\sqrt[3]{c_1 c_2 k \lambda \widetilde{\beta}_1} \right) + \left(2\sqrt{c_3 \lambda \widehat{\beta}_2} - 2\sqrt{c_3 \lambda \widetilde{\beta}_2} \right) + \mu_2 + \alpha_1 \\
&+ c_1 \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right) + c_2 (\mu_3 + \alpha_2) + c_3 \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right) \\
&+ (c_1 + c_3) \left(\frac{k \bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I + \frac{k \bar{\lambda} (c_1 + c_3)}{\bar{\mu} \mu_3} \left(\xi_1(t) \vee 0 - \int_0^{\infty} x \tilde{\pi}_1(x) dx \right) \\
&+ \frac{\bar{\lambda} (c_1 + c_3)}{\bar{\mu}} \left(\xi_2(t) \vee 0 - \int_0^{\infty} x \tilde{\pi}_2(x) dx \right),
\end{aligned}$$

where

$$\begin{aligned}
\widehat{\beta}_1 &= \left(\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{3}} \pi_1(x) dx \right)^3 = \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_1 \sqrt{\rho_1}}{\sigma_1}}^{\infty} \left(\frac{\sigma_1}{\sqrt{\rho_1}} x + \bar{\beta}_1 \right)^{\frac{1}{3}} e^{-x^2} dx \right)^3, \\
\widehat{\beta}_2 &= \left(\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{2}} \pi_2(x) dx \right)^2 = \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_2 \sqrt{\rho_2}}{\sigma_2}}^{\infty} \left(\frac{\sigma_2}{\sqrt{\rho_2}} x + \bar{\beta}_2 \right)^{\frac{1}{2}} e^{-x^2} dx \right)^2.
\end{aligned}$$

Let

$$\begin{aligned}
c_1 \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right) &= c_2 (\mu_3 + \alpha_2) = \frac{k \lambda \widehat{\beta}_1}{(\mu_3 + \alpha_2) \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right)}, \\
c_3 \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right) &= \frac{\lambda \widehat{\beta}_2}{\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2}},
\end{aligned}$$

then we have

$$c_1 = \frac{k \lambda \widehat{\beta}_1}{(\mu_3 + \alpha_2) \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right)^2}, \quad c_2 = \frac{k \lambda \widehat{\beta}_1}{(\mu_3 + \alpha_2)^2 \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right)}, \quad c_3 = \frac{\lambda \widehat{\beta}_2}{\left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right)^2},$$

and hence

$$\begin{aligned}
LW_2 &\leq -\frac{k \lambda \widehat{\beta}_1}{(\mu_3 + \alpha_2) \left(\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2} \right)} - \frac{\lambda \widehat{\beta}_2}{\frac{\lambda}{T_0} + \frac{k \bar{\lambda} \sigma_1}{2\bar{\mu} \mu_3 \sqrt{\pi} \rho_1} + \frac{\bar{\lambda} \sigma_2}{2\bar{\mu} \sqrt{\pi} \rho_2}} + \left(3\sqrt[3]{c_1 c_2 k \lambda \widehat{\beta}_1} - 3\sqrt[3]{c_1 c_2 k \lambda \widetilde{\beta}_1} \right) \\
&+ \left(2\sqrt{c_3 \lambda \widehat{\beta}_2} - 2\sqrt{c_3 \lambda \widetilde{\beta}_2} \right) + \mu_2 + \alpha_1 + (c_1 + c_3) \left(\frac{k \bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I + \frac{k \bar{\lambda} (c_1 + c_3)}{\bar{\mu} \mu_3} \left(\xi_1(t) \vee 0 - \int_0^{\infty} x \tilde{\pi}_1(x) dx \right) \\
&+ \frac{\bar{\lambda} (c_1 + c_3)}{\bar{\mu}} \left(\xi_2(t) \vee 0 - \int_0^{\infty} x \tilde{\pi}_2(x) dx \right) \\
&:= -(\mu_2 + \alpha_1) (\mathcal{R}_0^S - 1) + (c_1 + c_3) \left(\frac{k \bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I + 3\sqrt[3]{c_1 c_2 k \lambda} \left(\sqrt[3]{\widehat{\beta}_1} - \sqrt[3]{\widetilde{\beta}_1} \right) + 2\sqrt{c_3 \lambda} \left(\sqrt{\widehat{\beta}_2} - \sqrt{\widetilde{\beta}_2} \right) \\
&+ \frac{k \bar{\lambda} (c_1 + c_3)}{\bar{\mu} \mu_3} \left(\xi_1(t) \vee 0 - \int_0^{\infty} x \tilde{\pi}_1(x) dx \right) + \frac{\bar{\lambda} (c_1 + c_3)}{\bar{\mu}} \left(\xi_2(t) \vee 0 - \int_0^{\infty} x \tilde{\pi}_2(x) dx \right),
\end{aligned} \tag{3.12}$$

where

$$\begin{aligned}\mathcal{R}_0^S &= \frac{k\lambda\widehat{\beta}_1}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2)\left(\frac{\lambda}{T_0} + \frac{k\bar{\lambda}\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}}\right)} + \frac{\lambda\widehat{\beta}_2}{(\mu_2 + \alpha_1)\left(\frac{\lambda}{T_0} + \frac{k\bar{\lambda}\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}}\right)} \\ &= \frac{k\lambda\left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_1\sqrt{\rho_1}}{\sigma_1}}^{\infty} \left(\frac{\sigma_1}{\sqrt{\rho_1}}x + \bar{\beta}_1\right)^{\frac{1}{3}} e^{-x^2} dx\right)^3}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2)\left(\frac{\lambda}{T_0} + \frac{k\bar{\lambda}\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}}\right)} + \frac{\lambda\left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_2\sqrt{\rho_2}}{\sigma_2}}^{\infty} \left(\frac{\sigma_2}{\sqrt{\rho_2}}x + \bar{\beta}_2\right)^{\frac{1}{2}} e^{-x^2} dx\right)^2}{(\mu_2 + \alpha_1)\left(\frac{\lambda}{T_0} + \frac{k\bar{\lambda}\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}}\right)}.\end{aligned}$$

Next, define

$$\mathcal{W}_3(T, I, V) = -\ln\left(\frac{\bar{\lambda}}{\bar{\mu}} - T - I\right) - \ln\left(\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V\right), \quad \mathcal{W}_4(\beta_1, \beta_2) = \frac{\beta_1^2}{2} + \frac{\beta_2^2}{2},$$

then applying Itô's formula [28] to \mathcal{W}_3 and \mathcal{W}_4 leads to that

$$\begin{aligned}L\mathcal{W}_3 &= \frac{\lambda - \mu_1 T + rT - \frac{r}{T_{\max}}T^2 - \mu_2 I - \alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} + \frac{kI - \mu_3 V - \alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} \\ &\leq \frac{\lambda + \frac{r}{T_{\max}}T_0^2 - \left(\frac{\lambda}{T_0} + \frac{r}{T_{\max}}T_0\right)T - \mu_2 I - \alpha_1 I}{\frac{\lambda}{\mu} - T - I} + \frac{kI - \mu_3 V - \alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} \\ &\leq \frac{\lambda + \frac{r}{T_{\max}}T_0^2 - \min\left\{\frac{\lambda}{T_0} + \frac{r}{T_{\max}}T_0, \mu_2\right\}(T + I) - \alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} + \frac{kI - \mu_3 V - \alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} \\ &\leq -\frac{\alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} - \frac{\alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} + \bar{\mu} + \mu_3,\end{aligned}\tag{3.13}$$

and

$$\begin{aligned}L\mathcal{W}_4 &= \rho_1\beta_1(\bar{\beta}_1 - \beta_1) + \rho_2\beta_2(\bar{\beta}_2 - \beta_2) + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &= \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 - \rho_1\beta_1^2 - \rho_2\beta_2^2 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2}.\end{aligned}\tag{3.14}$$

Define a C^2 -function $\bar{\mathcal{W}}(T, I, V, \beta_1, \beta_2) : \Xi \rightarrow \mathbb{R}$ as follows

$$\bar{\mathcal{W}}(T, I, V, \beta_1, \beta_2) = M\mathcal{W}_2(T, I, V) - \ln T - \ln V + \mathcal{W}_3(T, I, V) + \mathcal{W}_4(\beta_1, \beta_2),$$

where M is a sufficiently large positive constant satisfying the condition

$$-M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + K_4 \leq -2,\tag{3.15}$$

and

$$\begin{aligned}K_4 &:= \sup_{(\beta_1, \beta_2) \in \mathbb{R}^2} \left\{ -\frac{\rho_1}{2}\beta_1^2 - \frac{\rho_2}{2}\beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}|\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}}|\beta_2| + \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 \right\} + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} \\ &\quad + \frac{\sigma_2^2}{2} < \infty.\end{aligned}$$

In addition, it is noted that $\bar{\mathcal{W}}(T, I, V, \beta_1, \beta_2)$ is not only continuous, but also tends to ∞ as $(T, I, V, \beta_1, \beta_2)^T$ approaches the boundary of Ξ . As a consequence, it should be lower bounded and achieves this lower bound at a point $(T^0, I^0, V^0, \beta_1^0, \beta_2^0)^T$ in the interior of Ξ . Then a C^2 -function $\mathcal{W} : \Xi \rightarrow \mathbb{R}_+$ is defined by

$$\begin{aligned}\mathcal{W}(T, I, V, \beta_1, \beta_2) &= \bar{\mathcal{W}}(T, I, V, \beta_1, \beta_2) - \bar{\mathcal{W}}(T^0, I^0, V^0, \beta_1^0, \beta_2^0) \\ &= M\mathcal{W}_2(T, I, V) - \ln T - \ln V + \mathcal{W}_3(T, I, V) + \mathcal{W}_4(\beta_1, \beta_2) - \bar{\mathcal{W}}(T^0, I^0, V^0, \beta_1^0, \beta_2^0).\end{aligned}$$

According to (3.2), (3.4), (3.12), (3.13) and (3.14), we obtain

$$\begin{aligned}
LW &\leq -M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\lambda}{T} - \frac{kI}{V} - \frac{\alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} - \frac{\alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} - \rho_1 \beta_1^2 \\
&\quad - \rho_2 \beta_2^2 + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 + 3M \sqrt[3]{c_1 c_2 k \lambda} \left(\sqrt[3]{\widehat{\beta}_1} - \sqrt[3]{\widetilde{\beta}_1} \right) + \frac{Mk\bar{\lambda}(c_1 + c_3)}{\bar{\mu}\mu_3} \left(\xi_1(t) \vee 0 - \int_0^\infty x \tilde{\pi}_1(x) dx \right) \\
&\quad + 2M \sqrt{c_3 \lambda} \left(\sqrt{\widehat{\beta}_2} - \sqrt{\widetilde{\beta}_2} \right) + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\xi_2(t) \vee 0 - \int_0^\infty x \tilde{\pi}_2(x) dx \right) + \mu_1 + \frac{r}{T_{\max}} T + |\beta_1| V + |\beta_2| I \\
&\quad + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&\leq -M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\lambda}{T} - \frac{kI}{V} - \frac{\alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} - \frac{\alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} - \rho_1 \beta_1^2 \\
&\quad - \rho_2 \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 + 3M \sqrt[3]{c_1 c_2 k \lambda} \left(\sqrt[3]{\widehat{\beta}_1} - \sqrt[3]{\widetilde{\beta}_1} \right) + 2M \sqrt{c_3 \lambda} \left(\sqrt{\widehat{\beta}_2} - \sqrt{\widetilde{\beta}_2} \right) \\
&\quad + \frac{Mk\bar{\lambda}(c_1 + c_3)}{\bar{\mu}\mu_3} \left(\xi_1(t) \vee 0 - \int_0^\infty x \tilde{\pi}_1(x) dx \right) + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\xi_2(t) \vee 0 - \int_0^\infty x \tilde{\pi}_2(x) dx \right) + \mu_1 + 2\mu_3 \\
&\quad + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&:= G(T, I, V, \beta_1, \beta_2) + 3M \sqrt[3]{c_1 c_2 k \lambda} \left(\sqrt[3]{\widehat{\beta}_1} - \sqrt[3]{\widetilde{\beta}_1} \right) + \frac{Mk\bar{\lambda}(c_1 + c_3)}{\bar{\mu}\mu_3} \left(\xi_1(t) \vee 0 - \int_0^\infty x \tilde{\pi}_1(x) dx \right) \\
&\quad + 2M \sqrt{c_3 \lambda} \left(\sqrt{\widehat{\beta}_2} - \sqrt{\widetilde{\beta}_2} \right) + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\xi_2(t) \vee 0 - \int_0^\infty x \tilde{\pi}_2(x) dx \right), \tag{3.16}
\end{aligned}$$

where

$$\begin{aligned}
G(T, I, V, \beta_1, \beta_2) &= -M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\lambda}{T} - \frac{kI}{V} - \frac{\alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} - \frac{\alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} \\
&\quad - \rho_1 \beta_1^2 - \rho_2 \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} \\
&\quad + \frac{\sigma_2^2}{2}.
\end{aligned}$$

Step 2. (Construction of a compact set): Define a closed bounded set D_ϵ by

$$D_\epsilon = \left\{ (T, I, V, \beta_1, \beta_2)^T \in \Xi : T \geq \epsilon, I \geq \epsilon, V \geq \epsilon^2, T + I \leq \frac{\bar{\lambda}}{\bar{\mu}} - \epsilon^2, V \leq \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - \epsilon^3, |\beta_1| \leq \frac{1}{\epsilon}, |\beta_2| \leq \frac{1}{\epsilon} \right\},$$

where ϵ is a sufficiently small positive constant satisfying the following conditions

$$-\frac{\lambda}{\epsilon} + K_5 \leq -1, \tag{3.17}$$

$$\epsilon \leq \frac{1}{M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right)}, \tag{3.18}$$

$$-\frac{k}{\epsilon} + K_5 \leq -1, \tag{3.19}$$

$$-\frac{\alpha_1}{\epsilon} + K_5 \leq -1, \tag{3.20}$$

$$-\frac{\alpha_2}{\epsilon} + K_5 \leq -1, \tag{3.21}$$

$$-\frac{\rho_1}{2\epsilon^2} + K_5 \leq -1, \tag{3.22}$$

$$-\frac{\rho_2}{2\epsilon^2} + K_5 \leq -1. \quad (3.23)$$

Here K_5 is a positive constant explicitly given in the expression (3.25). Next, we can divide the set $\Xi \setminus D_\epsilon$ into the following seven subsets $D_{\epsilon,i}^c$, $i = 1, \dots, 7$, where

$$\begin{aligned} D_{\epsilon,1}^c &= \{(T, I, V, \beta_1, \beta_2)^T \in \Xi : T < \epsilon\}, \quad D_{\epsilon,2}^c = \{(T, I, V, \beta_1, \beta_2)^T \in \Xi : I < \epsilon\}, \\ D_{\epsilon,3}^c &= \{(T, I, V, \beta_1, \beta_2)^T \in \Xi : V < \epsilon^2, I \geq \epsilon\}, \quad D_{\epsilon,4}^c = \left\{ (T, I, V, \beta_1, \beta_2)^T \in \Xi : T + I > \frac{\bar{\lambda}}{\bar{\mu}} - \epsilon^2, I \geq \epsilon \right\}, \\ D_{\epsilon,5}^c &= \left\{ (T, I, V, \beta_1, \beta_2)^T \in \Xi : V > \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - \epsilon^3, V \geq \epsilon^2 \right\}, \quad D_{\epsilon,6}^c = \left\{ (T, I, V, \beta_1, \beta_2)^T \in \Xi : |\beta_1| > \frac{1}{\epsilon} \right\}, \\ D_{\epsilon,7}^c &= \left\{ (T, I, V, \beta_1, \beta_2)^T \in \Xi : |\beta_2| > \frac{1}{\epsilon} \right\}. \end{aligned}$$

Apparently, $\Xi \setminus D_\epsilon = \bigcup_{i=1}^7 D_{\epsilon,i}^c$. Next, we will show that $G(T, I, V, \beta_1, \beta_2) \leq -1$ on the region D_ϵ^c . That is to say, we need to show its satisfaction on the above seven sets.

Case 1. For any $(T, I, V, \beta_1, \beta_2)^T \in D_{\epsilon,1}^c$, by (3.16), we obtain

$$\begin{aligned} G(T, I, V, \beta_1, \beta_2) &\leq -\frac{\lambda}{T} + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 \\ &\quad + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &\leq -\frac{\lambda}{T} + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\lambda}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 \\ &\quad + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &\leq -\frac{\lambda}{T} + K_5 \\ &\leq -\frac{\lambda}{\epsilon} + K_5 \\ &\leq -1, \end{aligned} \quad (3.24)$$

which follows from (3.17) and

$$\begin{aligned} K_5 &:= \sup_{(\beta_1, \beta_2) \in \mathbb{R}^2} \left\{ -\frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 \right\} + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) \\ &\quad + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} < \infty. \end{aligned} \quad (3.25)$$

Case 2. For any $(T, I, V, \beta_1, \beta_2)^T \in D_{\epsilon,2}^c$, according to (3.16), we have

$$\begin{aligned} G(T, I, V, \beta_1, \beta_2) &\leq -M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| \\ &\quad + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &\leq -M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I + K_4 \\ &\leq -M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) \epsilon + K_4 \\ &\leq -2 + 1 \\ &= -1, \end{aligned} \quad (3.26)$$

which follows from (3.15) and (3.18) and

$$K_4 := \sup_{(\beta_1, \beta_2) \in \mathbb{R}^2} \left\{ -\frac{\rho_1}{2}\beta_1^2 - \frac{\rho_2}{2}\beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}|\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}}|\beta_2| + \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 \right\} + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} < \infty.$$

Case 3. For any $(T, I, V, \beta_1, \beta_2)^T \in D_{\epsilon,3}^c$, in view of (3.16), we have

$$\begin{aligned} G(T, I, V, \beta_1, \beta_2) &\leq -\frac{kI}{V} + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\rho_1}{2}\beta_1^2 - \frac{\rho_2}{2}\beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}|\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}}|\beta_2| + \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 \\ &\quad + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &\leq -\frac{kI}{V} + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) - \frac{\rho_1}{2}\beta_1^2 - \frac{\rho_2}{2}\beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}|\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}}|\beta_2| + \rho_1\bar{\beta}_1\beta_1 + \rho_2\bar{\beta}_2\beta_2 \\ &\quad + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &\leq -\frac{k\epsilon}{\epsilon^2} + K_5 \\ &= -\frac{k}{\epsilon} + K_5 \\ &\leq -1, \end{aligned} \tag{3.27}$$

which follows from (3.19).

Case 4. For any $(T, I, V, \beta_1, \beta_2)^T \in D_{\epsilon,4}^c$, from (3.16) it follows that

$$\begin{aligned} G(T, I, V, \beta_1, \beta_2) &\leq -\frac{\alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\rho_1}{2}\beta_1^2 - \frac{\rho_2}{2}\beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}|\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}}|\beta_2| + \rho_1\bar{\beta}_1\beta_1 \\ &\quad + \rho_2\bar{\beta}_2\beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &\leq -\frac{\alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) - \frac{\rho_1}{2}\beta_1^2 - \frac{\rho_2}{2}\beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3}|\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}}|\beta_2| + \rho_1\bar{\beta}_1\beta_1 \\ &\quad + \rho_2\bar{\beta}_2\beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\ &\leq -\frac{\alpha_1\epsilon}{\epsilon^2} + K_5 \\ &= -\frac{\alpha_1}{\epsilon} + K_5 \\ &\leq -1, \end{aligned} \tag{3.28}$$

which follows from (3.20).

Case 5. For any $(T, I, V, \beta_1, \beta_2)^T \in D_{\epsilon,5}^c$, according to (3.16), it is easy to see that

$$\begin{aligned}
G(T, I, V, \beta_1, \beta_2) &\leq -\frac{\alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 \\
&\quad + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&\leq -\frac{\alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 \\
&\quad + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&\leq -\frac{\alpha_2 \epsilon^2}{\epsilon^3} + K_5 \\
&= -\frac{\alpha_2}{\epsilon} + K_5 \\
&\leq -1,
\end{aligned} \tag{3.29}$$

which follows from (3.21).

Case 6. For any $(T, I, V, \beta_1, \beta_2)^T \in D_{\epsilon,6}^c$, by (3.16), it is clear that

$$\begin{aligned}
G(T, I, V, \beta_1, \beta_2) &\leq -\frac{\rho_1}{2} \beta_1^2 + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 \\
&\quad + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&\leq -\frac{\rho_1}{2} \beta_1^2 + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 \\
&\quad + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&\leq -\frac{\rho_1}{2\epsilon^2} + K_5 \\
&\leq -1,
\end{aligned} \tag{3.30}$$

which follows from (3.22).

Case 7. For any $(T, I, V, \beta_1, \beta_2)^T \in D_{\epsilon,7}^c$, in view of (3.16), it is easy to obtain that

$$\begin{aligned}
G(T, I, V, \beta_1, \beta_2) &\leq -\frac{\rho_2}{2} \beta_2^2 + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 \\
&\quad + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&\leq -\frac{\rho_2}{2} \beta_2^2 + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) - \frac{\rho_1}{2} \beta_1^2 - \frac{\rho_2}{2} \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 \\
&\quad + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} \\
&\leq -\frac{\rho_2}{2\epsilon^2} + K_5 \\
&\leq -1,
\end{aligned} \tag{3.31}$$

which follows from (3.23).

On the basis of (3.24), (3.26), (3.27), (3.28), (3.29), (3.30) and (3.31), we can easily conclude that there is an adequately small ϵ such that

$$G(T, I, V, \beta_1, \beta_2) \leq -1 \text{ for any } (T, I, V, \beta_1, \beta_2) \in \Xi \setminus D_\epsilon. \tag{3.32}$$

Let

$$K_6 := \sup_{(T, I, V, \beta_1, \beta_2) \in \mathbb{R}_+^3 \times \mathbb{R}^2} \left\{ -M(\mu_2 + \alpha_1)(\mathcal{R}_0^S - 1) + M(c_1 + c_3) \left(\frac{k\bar{\beta}_1}{\mu_3 + \alpha_2} + \bar{\beta}_2 \right) I - \frac{\lambda}{T} - \frac{kI}{V} - \frac{\alpha_1 I}{\frac{\bar{\lambda}}{\bar{\mu}} - T - I} \right. \\ \left. - \frac{\alpha_2 V}{\frac{k\bar{\lambda}}{\bar{\mu}\mu_3} - V} - \rho_1 \beta_1^2 - \rho_2 \beta_2^2 + \frac{k\bar{\lambda}}{\bar{\mu}\mu_3} |\beta_1| + \frac{\bar{\lambda}}{\bar{\mu}} |\beta_2| + \rho_1 \bar{\beta}_1 \beta_1 + \rho_2 \bar{\beta}_2 \beta_2 + \mu_1 + 2\mu_3 + \bar{\mu} + \alpha_2 + \frac{r\bar{\lambda}}{T_{\max}\bar{\mu}} + \frac{\sigma_1^2}{2} \right. \\ \left. + \frac{\sigma_2^2}{2} \right\}.$$

Then

$$G(T, I, V, \beta_1, \beta_2) \leq K_6 < \infty \text{ for any } (T, I, V, \beta_1, \beta_2) \in \mathbb{R}_+^3 \times \mathbb{R}^2. \quad (3.33)$$

Step 3. (Existence): For any initial value $(T(0), I(0), V(0), \beta_1(0), \beta_2(0)) \in \Xi$, integrating both sides of (3.16) from 0 to t and then taking the mathematical expectation, we get

$$0 \leq \frac{\mathbb{E}\mathcal{W}(T(t), I(t), V(t), \beta_1(t), \beta_2(t))}{t} \\ = \frac{\mathbb{E}\mathcal{W}(T(0), I(0), V(0), \beta_1(0), \beta_2(0))}{t} + \frac{1}{t} \int_0^t \mathbb{E}(L\mathcal{W}(T(s), I(s), V(s), \beta_1(s), \beta_2(s))) ds \\ \leq \frac{\mathbb{E}\mathcal{W}(T(0), I(0), V(0), \beta_1(0), \beta_2(0))}{t} + \frac{1}{t} \int_0^t \mathbb{E}(G(T(s), I(s), V(s), \beta_1(s), \beta_2(s))) ds \\ + 3M\sqrt[3]{c_1 c_2 k \bar{\lambda}} \mathbb{E} \left[\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{3}} \pi_1(x) dx - \frac{1}{t} \int_0^t (\beta_1(s) \vee 0)^{\frac{1}{3}} ds \right] \\ + 2M\sqrt{c_3 \bar{\lambda}} \mathbb{E} \left[\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{2}} \pi_2(x) dx - \frac{1}{t} \int_0^t (\beta_2(s) \vee 0)^{\frac{1}{2}} ds \right] + \frac{Mk\bar{\lambda}(c_1 + c_3)}{\bar{\mu}\mu_3} \mathbb{E} \left[\frac{1}{t} \int_0^t (\xi_1(s) \vee 0) ds - \int_0^{\infty} x \tilde{\pi}_1(x) dx \right] \\ + \frac{M\bar{\lambda}(c_1 + c_3)}{\bar{\mu}} \mathbb{E} \left[\frac{1}{t} \int_0^t (\xi_2(s) \vee 0) ds - \int_0^{\infty} x \tilde{\pi}_2(x) dx \right]. \quad (3.34)$$

According to the ergodicity of $\beta_i(t)$ and $\xi_i(t)$ ($i = 1, 2$) and the strong law of large numbers [35], we have

$$\lim_{t \rightarrow \infty} \mathbb{E} \left[\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{3}} \pi_1(x) dx - \frac{1}{t} \int_0^t (\beta_1(s) \vee 0)^{\frac{1}{3}} ds \right] = \mathbb{E} \left[\int_0^{\infty} x^{\frac{1}{3}} \pi_1(x) dx \right] - \int_0^{\infty} x^{\frac{1}{3}} \pi_1(x) dx = 0 \text{ a.s.}, \quad (3.35)$$

$$\lim_{t \rightarrow \infty} \mathbb{E} \left[\int_{-\infty}^{\infty} (x \vee 0)^{\frac{1}{2}} \pi_2(x) dx - \frac{1}{t} \int_0^t (\beta_2(s) \vee 0)^{\frac{1}{2}} ds \right] = \mathbb{E} \left[\int_0^{\infty} x^{\frac{1}{2}} \pi_2(x) dx \right] - \int_0^{\infty} x^{\frac{1}{2}} \pi_2(x) dx = 0 \text{ a.s.}, \quad (3.36)$$

$$\lim_{t \rightarrow \infty} \mathbb{E} \left[\frac{1}{t} \int_0^t (\xi_1(s) \vee 0) ds - \int_0^{\infty} x \tilde{\pi}_1(x) dx \right] = \mathbb{E} \left[\int_0^{\infty} x \tilde{\pi}_1(x) dx \right] - \int_0^{\infty} x \tilde{\pi}_1(x) dx = 0 \text{ a.s.}, \quad (3.37)$$

and

$$\lim_{t \rightarrow \infty} \mathbb{E} \left[\frac{1}{t} \int_0^t (\xi_2(s) \vee 0) ds - \int_0^{\infty} x \tilde{\pi}_2(x) dx \right] = \mathbb{E} \left[\int_0^{\infty} x \tilde{\pi}_2(x) dx \right] - \int_0^{\infty} x \tilde{\pi}_2(x) dx = 0 \text{ a.s.} \quad (3.38)$$

Taking the inferior limit on both sides of (3.34) and combining with (3.35), (3.36), (3.37) and (3.38), we obtain

$$0 \leq \liminf_{t \rightarrow \infty} \frac{\mathbb{E}\mathcal{W}(T(0), I(0), V(0), \beta_1(0), \beta_2(0))}{t} + \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{E}(G(T(s), I(s), V(s), \beta_1(s), \beta_2(s))) ds \\ = \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{E}(G(T(s), I(s), V(s), \beta_1(s), \beta_2(s))) ds \text{ a.s.} \quad (3.39)$$

In addition, in view of (3.32) and (3.33), we get

$$\begin{aligned}
& \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{E}(G(T(s), I(s), V(s), \beta_1(s), \beta_2(s))) ds \\
&= \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{E}(G(T(s), I(s), V(s), \beta_1(s), \beta_2(s))) \mathbf{1}_{\{(T(s), I(s), V(s), \beta_1(s), \beta_2(s)) \in D_\epsilon\}} ds \\
&+ \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{E}(G(T(s), I(s), V(s), \beta_1(s), \beta_2(s))) \mathbf{1}_{\{(T(s), I(s), V(s), \beta_1(s), \beta_2(s)) \in (\Xi \setminus D_\epsilon)\}} ds \\
&\leq K_6 \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbf{1}_{\{(T(s), I(s), V(s), \beta_1(s), \beta_2(s)) \in D_\epsilon\}} ds - \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbf{1}_{\{(T(s), I(s), V(s), \beta_1(s), \beta_2(s)) \in (\Xi \setminus D_\epsilon)\}} ds \\
&\leq -1 + (K_6 + 1) \liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbf{1}_{\{(T(s), I(s), V(s), \beta_1(s), \beta_2(s)) \in D_\epsilon\}} ds.
\end{aligned} \tag{3.40}$$

By (3.39) and (3.40), it is easy to conclude that

$$\liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbf{1}_{\{(T(s), I(s), V(s), \beta_1(s), \beta_2(s)) \in D_\epsilon\}} ds \geq \frac{1}{K_6 + 1} > 0 \text{ a.s.} \tag{3.41}$$

By the definition of event probability and Fatou's lemma [30], (3.41) is equivalent to the following form

$$\liminf_{t \rightarrow \infty} \frac{1}{t} \int_0^t \mathbb{P}(s, (T(s), I(s), V(s), \beta_1(s), \beta_2(s)), D_\epsilon) ds \geq \frac{1}{K_6 + 1} > 0 \text{ a.s.},$$

where $\mathbb{P}(t, (T, I, V, \beta_1, \beta_2), \mathbb{A})$ is the transition probability of $(T(t), I(t), V(t), \beta_1(t), \beta_2(t))$ belonging to the set \mathbb{A} . Thus, in view of Lemma 3.1, we obtain that system (1.2) has at least one stationary distribution $\pi(\cdot)$ on $\mathbb{R}_+^3 \times \mathbb{R}^2$, which has the Feller property. This completes the proof.

Remark 3.1 Actually, $\widehat{\beta}_i$ ($i = 1, 2$) can be regarded as anomalous integrals of parametric variables with respect to the intensities of volatility σ_i ($i = 1, 2$) and if σ_i ($i = 1, 2$) tend to zero, we obtain

$$\begin{aligned}
\lim_{\sigma_1 \rightarrow 0^+} \widehat{\beta}_1 &= \lim_{\sigma_1 \rightarrow 0^+} \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_1 \sqrt{\rho_1}}{\sigma_1}}^{\infty} \left(\frac{\sigma_1}{\sqrt{\rho_1}} x + \bar{\beta}_1 \right)^{\frac{1}{3}} e^{-x^2} dx \right)^3 \\
&= \left(\frac{1}{\sqrt{\pi}} \int_{-\infty}^{\infty} \bar{\beta}_1^{\frac{1}{3}} e^{-x^2} dx \right)^3 \\
&= \bar{\beta}_1, \\
\lim_{\sigma_2 \rightarrow 0^+} \widehat{\beta}_2 &= \lim_{\sigma_2 \rightarrow 0^+} \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_2 \sqrt{\rho_2}}{\sigma_2}}^{\infty} \left(\frac{\sigma_2}{\sqrt{\rho_2}} x + \bar{\beta}_2 \right)^{\frac{1}{2}} e^{-x^2} dx \right)^2 \\
&= \left(\frac{1}{\sqrt{\pi}} \int_{-\infty}^{\infty} \bar{\beta}_2^{\frac{1}{2}} e^{-x^2} dx \right)^2 \\
&= \bar{\beta}_2.
\end{aligned}$$

In this situation, we have

$$\begin{aligned}
& \lim_{\sigma_1 \rightarrow 0^+, \sigma_2 \rightarrow 0^+} \mathcal{R}_0^S \\
&= \lim_{\sigma_1 \rightarrow 0^+, \sigma_2 \rightarrow 0^+} \frac{k\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_1 \sqrt{\rho_1}}{\sigma_1}}^{\infty} \left(\frac{\sigma_1}{\sqrt{\rho_1}} x + \bar{\beta}_1 \right)^{\frac{1}{3}} e^{-x^2} dx \right)^3}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2) \left(\frac{\lambda}{T_0} + \frac{k\lambda\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} + \frac{\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_2 \sqrt{\rho_2}}{\sigma_2}}^{\infty} \left(\frac{\sigma_2}{\sqrt{\rho_2}} x + \bar{\beta}_2 \right)^{\frac{1}{2}} e^{-x^2} dx \right)^2}{(\mu_2 + \alpha_1) \left(\frac{\lambda}{T_0} + \frac{k\lambda\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} \\
&= \frac{k\bar{\beta}_1 T_0}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2)} + \frac{\bar{\beta}_2 T_0}{\mu_2 + \alpha_1} \\
&= \mathcal{R}_0.
\end{aligned}$$

Moreover, by the expressions of \mathcal{R}_0 and \mathcal{R}_0^S , we can conclude that $\mathcal{R}_0^S < \mathcal{R}_0$. Consequently, we generalize the results of the deterministic system (1.1).

4 Probability density for system (1.2)

In this section, we will focus on getting the explicit expression of the probability density of the distribution $\pi(\cdot)$. Mathematically, the existence of the probability density of system (1.2) is more in-depth and specific than that of the stationary distribution. Firstly, equivalent transformations of system (1.2) are given.

4.1. Equivalent transformations of system (1.2)

Firstly, we define a quasi-chronic infection equilibrium $E^* = (T^*, I^*, V^*, \beta_1^*, \beta_2^*)^T$ involved in stochasticity by the equations

$$\begin{cases} \lambda - \mu_1 T^* + r T^* \left(1 - \frac{T^*}{T_{\max}}\right) - \max\{\beta_1^*, 0\} T^* V^* - \max\{\beta_2^*, 0\} T^* I^* = 0, \\ \max\{\beta_1^*, 0\} T^* V^* + \max\{\beta_2^*, 0\} T^* I^* - \mu_2 I^* - \alpha_1 I^* = 0, \\ k I^* - \mu_3 V^* - \alpha_2 V^* = 0, \\ \rho_1 (\bar{\beta}_1 - \beta_1^*) = 0, \\ \rho_2 (\bar{\beta}_2 - \beta_2^*) = 0. \end{cases} \quad (4.1)$$

By solving Equation (4.1), we get that if $\mathcal{R}_0^S > 1$, then

$$T^* = T^+ > 0, \quad I^* = I^+ > 0, \quad V^* = V^+ > 0, \quad \beta_1^* = \bar{\beta}_1, \quad \beta_2^* = \bar{\beta}_2,$$

where T^+ , I^+ and V^+ are the same as in Section one.

Let $(x_1, x_2, x_3, x_4, x_5)^T = (T - T^*, I - I^*, V - V^*, \beta_1 - \beta_1^*, \beta_2 - \beta_2^*)^T$. According to the Itô's integral and system (1.2), the corresponding linearized system of (1.2) around E^* takes the form

$$\begin{cases} dx_1 = (-a_{11}x_1 - a_{12}x_2 - a_{13}x_3 - a_{14}x_4 - a_{15}x_5)dt, \\ dx_2 = (a_{21}x_1 - a_{22}x_2 + a_{23}x_3 + a_{24}x_4 + a_{25}x_5)dt, \\ dx_3 = (a_{32}x_2 - a_{33}x_3)dt, \\ dx_4 = -\rho_1 x_4 dt + \sigma_1 dB_1(t), \\ dx_5 = -\rho_2 x_5 dt + \sigma_2 dB_2(t), \end{cases} \quad (4.2)$$

where

$$a_{11} = \mu_1 - r + \frac{2r}{T_{\max}} T^* + \beta_1^* V^* + \beta_2^* I^* = \frac{\lambda}{T^*} + \frac{r}{T_{\max}} T^* > 0, \quad a_{12} = \beta_2^* T^* > 0, \quad a_{13} = \beta_1^* T^* > 0, \quad a_{14} = T^* V^* > 0,$$

$$a_{15} = T^* I^* > 0, \quad a_{21} = \beta_1^* V^* + \beta_2^* I^* > 0, \quad a_{22} = \mu_2 + \alpha_1 - \beta_2^* T^* = \frac{\beta_1^* T^* V^*}{I^*} > 0, \quad a_{23} = \beta_1^* T^* > 0, \quad a_{24} = T^* V^* > 0,$$

$$a_{25} = T^* I^* > 0, \quad a_{32} = k > 0, \quad a_{33} = \mu_3 + \alpha_2 > 0.$$

It is easy to see that $a_{13} = a_{23}$, $a_{14} = a_{24}$, $a_{15} = a_{25}$ and $a_{22}a_{33} > a_{23}a_{32}$.

Before introducing the corresponding probability density, we need to introduce a significant definition and two lemmas.

Definition 4.1 [36]. *The characteristic polynomial of the square matrix A_n is defined as $\varphi_{A_n}(\lambda) = \lambda^n + a_1 \lambda^{n-1} + \dots + a_{n-1} \lambda + a_n$, then A_n is called a Hurwitz matrix if and only if A_n has all negative real-part eigenvalues, i.e.,*

$$H_k = \begin{vmatrix} a_1 & a_3 & a_5 & \dots & a_{2k-1} \\ 1 & a_2 & a_4 & \dots & a_{2k-2} \\ 0 & a_1 & a_3 & \dots & a_{2k-3} \\ 0 & 1 & a_2 & \dots & a_{2k-4} \\ \dots & \dots & \dots & \dots & \dots \\ 0 & 0 & 0 & \dots & a_k \end{vmatrix} > 0, \quad k = 1, \dots, n,$$

where the complementary definition is $a_j = 0$, $j > n$. Additionally, the corresponding necessary conditions for A_n to be a Hurwitz matrix are as follows

$$(i) \ a_j > 0, \quad j = 1, \dots, n; \quad (ii) \ a_i a_{i+1} > a_{i-1} a_{i+2}, \quad i = 1, \dots, n-2, \quad a_0 = 1.$$

Lemma 4.1 [37]. For the algebraic equation $H_0^2 + A_0\Sigma_0 + \Sigma_0A_0^T = 0$, where $H_0 = \text{diag}(1, 0, 0, 0)$ and Σ_0 is a real symmetric matrix, and the standard matrix

$$A_0 = \begin{pmatrix} -\tau_1 & -\tau_2 & -\tau_3 & -\tau_4 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{pmatrix}.$$

If $\tau_1 > 0$, $\tau_3 > 0$, $\tau_4 > 0$ and $\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4 > 0$, then Σ_0 is a positive definite matrix, where

$$\Sigma_0 = \begin{pmatrix} \frac{\tau_2\tau_3 - \tau_1\tau_4}{2(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} & 0 & -\frac{\tau_3}{2(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} & 0 \\ 0 & \frac{\tau_3}{2(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} & 0 & -\frac{\tau_1}{2(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} \\ -\frac{\tau_3}{2(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} & 0 & \frac{\tau_1}{2(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} & 0 \\ 0 & -\frac{\tau_1}{2(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} & 0 & \frac{\tau_1\tau_2 - \tau_3}{2\tau_4(\tau_1\tau_2\tau_3 - \tau_3^2 - \tau_1^2\tau_4)} \end{pmatrix}.$$

Here A_0 in this form is called the standard R_1 matrix.

Lemma 4.2 [37]. For the algebraic equation $H_0^2 + \tilde{A}_0\Theta_0 + \Theta_0\tilde{A}_0^T = 0$, where $H_0 = \text{diag}(1, 0, 0, 0)$, Θ_0 is a real symmetric matrix, and the standard matrix

$$\tilde{A}_0 = \begin{pmatrix} -l_1 & -l_2 & -l_3 & -l_4 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & -a_{21} \end{pmatrix}.$$

If $l_1 > 0$, $l_3 > 0$ and $l_1l_2 - l_3 > 0$, then the matrix Θ_0 is semi-positive definite which takes the form

$$\Theta_0 = \begin{pmatrix} \frac{l_2}{2(l_1l_2 - l_3)} & 0 & -\frac{1}{2(l_1l_2 - l_3)} & 0 \\ 0 & \frac{1}{2(l_1l_2 - l_3)} & 0 & 0 \\ -\frac{1}{2(l_1l_2 - l_3)} & 0 & \frac{l_1}{2l_3(l_1l_2 - l_3)} & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}.$$

Here \tilde{A}_0 in this form is called the standard R_2 matrix.

4.2. Probability density of stationary distribution $\pi(\cdot)$

Theorem 4.1 Let $(T(t), I(t), V(t), \beta_1(t), \beta_2(t))^T$ be a solution of system (1.2) with the initial value $(T(0), I(0), V(0), \beta_1(0), \beta_2(0))^T \in \mathbb{R}_+^3 \times \mathbb{R}^2$. If $\mathcal{R}_0^S > 1$, then there exists a probability density of a multivariate normal distribution $\Phi(T, I, V, \beta_1, \beta_2)$ around the quasi-chronic infection equilibrium $(T^*, I^*, V^*, \beta_1^*, \beta_2^*)^T$, which takes the form

$$\Phi(T, I, V, \beta_1, \beta_2) = (2\pi)^{-\frac{5}{2}} |\Sigma|^{-\frac{1}{2}} e^{-\frac{1}{2}(T-T^*, I-I^*, V-V^*, \beta_1-\beta_1^*, \beta_2-\beta_2^*)\Sigma^{-1}(T-T^*, I-I^*, V-V^*, \beta_1-\beta_1^*, \beta_2-\beta_2^*)^T},$$

where Σ is a positive definite matrix, and the specific form of Σ is given as follows.

(1) If $p_1 = 0$, then

$$\Sigma = \bar{\xi}_1^2 (J_{10}J_9J_8J_2J_1)^{-1} \bar{\Theta}_0 [(J_{10}J_9J_8J_2J_1)^{-1}]^T + \bar{\xi}_2^2 (J_{20}J_{19}J_{18}J_{12}J_{11})^{-1} \bar{\Delta}_0 [(J_{20}J_{19}J_{18}J_{12}J_{11})^{-1}]^T.$$

(2) If $p_2 \neq 0$, then

$$\Sigma = \xi_1^2 (J_5J_4J_3J_2J_1)^{-1} \Sigma_{01} [(J_5J_4J_3J_2J_1)^{-1}]^T + \xi_2^2 (J_{15}J_{14}J_{13}J_{12}J_{11})^{-1} \Sigma_{02} [(J_{15}J_{14}J_{13}J_{12}J_{11})^{-1}]^T.$$

(3) If $p_2 = 0$, then

$$\Sigma = \tilde{\xi}_1^2 (J_7J_6J_3J_2J_1)^{-1} \tilde{\Theta}_0 [(J_7J_6J_3J_2J_1)^{-1}]^T + \tilde{\xi}_2^2 (J_{17}J_{16}J_{13}J_{12}J_{11})^{-1} \tilde{\Delta}_0 [(J_{17}J_{16}J_{13}J_{12}J_{11})^{-1}]^T,$$

where

$$\begin{aligned}
p_1 &= a_{12} + a_{21} + a_{22} - a_{11}, \quad p_2 = \frac{a_{32}(a_{21} + a_{33} - a_{11})}{p_1}, \quad \xi_1 = -a_{14}p_1p_2\sigma_1, \quad \xi_2 = -a_{15}p_1p_2\sigma_2, \quad \tilde{\xi}_1 = -a_{14}p_1\sigma_1, \\
\tilde{\xi}_2 &= -a_{15}p_1\sigma_2, \quad \bar{\xi}_1 = a_{14}a_{32}\sigma_1, \quad \bar{\xi}_2 = a_{15}a_{32}\sigma_2, \quad \tau_1 = a_{11} + a_{22} + a_{33}, \quad \tau_2 = a_{11}a_{22} + a_{11}a_{33} + a_{22}a_{33} + a_{12}a_{21} - a_{13}a_{32}, \\
\tau_3 &= a_{11}a_{22}a_{33} + a_{12}a_{21}a_{33} + a_{13}a_{21}a_{32} - a_{11}a_{13}a_{32}, \quad l_1 = a_{11} + a_{22}, \quad l_2 = a_{11}a_{22} + a_{12}a_{21} - a_{13}a_{32}, \\
\bar{l}_1 &= a_{21} + a_{22} + a_{33}, \quad \bar{l}_2 = a_{21}a_{33} + a_{22}a_{33} - a_{13}a_{32}, \quad \Sigma_{01}^* = 2(\rho_1^3 + \rho_1^2\tau_1 + \rho_1\tau_2 + \tau_3)(\tau_1\tau_2 - \tau_3), \\
\Sigma_{02}^* &= 2(\rho_2^3 + \rho_2^2\tau_1 + \rho_2\tau_2 + \tau_3)(\tau_1\tau_2 - \tau_3),
\end{aligned}$$

and

$$\begin{aligned}
J_1 &= \begin{pmatrix} 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_2 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_3 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & \frac{a_{32}}{p_1} & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \\
J_4 &= \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & p_1p_2 & -(a_{12} + a_{22} + a_{33})p_2 & a_{33}^2 & 0 \\ 0 & 0 & p_2 & -a_{33} & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_5 = \begin{pmatrix} -a_{14}p_1p_2 & -\tau_1 & -\tau_2 & -\tau_3 & -a_{15}p_1p_2 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \\
J_6 &= \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & p_1 & -(a_{12} + a_{22}) & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_8 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_9 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & -a_{32} & -a_{33} & a_{32} & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \\
J_7 &= \begin{pmatrix} -a_{14}p_1 & -(a_{11} + a_{22}) & -a_{11}a_{22} + a_{13}a_{32} - a_{12}a_{21} & -a_{13}p_1 & -a_{15}p_1 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_{11} = \begin{pmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \end{pmatrix}, \\
J_{10} &= \begin{pmatrix} a_{14}a_{32} & -(a_{21} + a_{22} + a_{33}) & a_{13}a_{32} - a_{21}a_{33} - a_{22}a_{33} & a_{21}a_{32} & a_{15}a_{32} \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_{12} = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \\
J_{13} &= J_3, \quad J_{14} = J_4, \quad J_{15} = \begin{pmatrix} -a_{15}p_1p_2 & -\tau_1 & -\tau_2 & -\tau_3 & -a_{14}p_1p_2 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_{16} = J_6, \\
J_{17} &= \begin{pmatrix} -a_{15}p_1 & -(a_{11} + a_{22}) & -a_{11}a_{22} + a_{13}a_{32} - a_{12}a_{21} & -a_{13}p_1 & -a_{14}p_1 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}, \quad J_{18} = J_8, \quad J_{19} = J_9, \\
J_{20} &= \begin{pmatrix} a_{15}a_{32} & -(a_{21} + a_{22} + a_{33}) & a_{13}a_{32} - a_{21}a_{33} - a_{22}a_{33} & a_{21}a_{32} & a_{14}a_{32} \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix},
\end{aligned}$$

$$\Sigma_{01} = \begin{pmatrix} \frac{\rho_1^2(\tau_1\tau_2 - \tau_3) + \tau_2(\rho_1\tau_2 + \tau_3)}{\Sigma_{01}^*} & 0 & -\frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & 0 \\ 0 & \frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & -\frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 \\ -\frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & \frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 & 0 \\ 0 & -\frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 & \frac{\rho_1\tau_1(\rho_1 + \tau_1) + \tau_1\tau_2 - \tau_3}{\rho_1\tau_3\Sigma_{01}^*} & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\Sigma_{02} = \begin{pmatrix} \frac{\rho_2^2(\tau_1\tau_2 - \tau_3) + \tau_2(\rho_2\tau_2 + \tau_3)}{\Sigma_{02}^*} & 0 & -\frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & 0 \\ 0 & \frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & -\frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 \\ -\frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & \frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 & 0 \\ 0 & -\frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 & \frac{\rho_2\tau_1(\rho_2 + \tau_1) + \tau_1\tau_2 - \tau_3}{\rho_2\tau_3\Sigma_{02}^*} & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\tilde{\Theta}_0 = \begin{pmatrix} \frac{\rho_1 l_1 + l_2}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & -\frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & 0 \\ 0 & \frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & 0 & 0 \\ -\frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & \frac{\rho_1 + l_1}{2\rho_1 l_1 l_2(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\bar{\Theta}_0 = \begin{pmatrix} \frac{\rho_1 \bar{l}_1 + \bar{l}_2}{2\bar{l}_1(\rho_1 \bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & -\frac{1}{2\bar{l}_1(\rho_1 \bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & 0 \\ 0 & \frac{1}{2\bar{l}_1(\rho_1 \bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & 0 & 0 \\ -\frac{1}{2\bar{l}_1(\rho_1 \bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & \frac{\rho_1 + \bar{l}_1}{2\rho_1 \bar{l}_1 \bar{l}_2(\rho_1 \bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\tilde{\Delta}_0 = \begin{pmatrix} \frac{\rho_2 l_1 + l_2}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & -\frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & 0 \\ 0 & \frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & 0 & 0 \\ -\frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & \frac{\rho_2 + l_1}{2\rho_2 l_1 l_2(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

$$\bar{\Delta}_0 = \begin{pmatrix} \frac{\rho_2 \bar{l}_1 + \bar{l}_2}{2\bar{l}_1(\rho_2 \bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & -\frac{1}{2\bar{l}_1(\rho_2 \bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & 0 \\ 0 & \frac{1}{2\bar{l}_1(\rho_2 \bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & 0 & 0 \\ -\frac{1}{2\bar{l}_1(\rho_2 \bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & \frac{\rho_2 + \bar{l}_1}{2\rho_2 \bar{l}_1 \bar{l}_2(\rho_2 \bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Proof. For the sake of simplicity, let $X = (x_1, x_2, x_3, x_4, x_5)^T$, $B(t) = (0, 0, 0, B_1(t), B_2(t))^T$,

$$A = \begin{pmatrix} -a_{11} & -a_{12} & -a_{13} & -a_{14} & -a_{15} \\ a_{21} & -a_{22} & a_{23} & a_{24} & a_{25} \\ 0 & a_{32} & -a_{33} & 0 & 0 \\ 0 & 0 & 0 & -\rho_1 & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix}, \quad H = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \sigma_1 & 0 \\ 0 & 0 & 0 & 0 & \sigma_2 \end{pmatrix}.$$

With these notations, system (4.2) can be rewritten into the following equivalent form

$$dX(t) = AX(t)dt + HdB(t). \quad (4.3)$$

In the light of the continuous Markov processes theory [38], system (4.3) has a unique probability density $\Phi(x_1, x_2, x_3, x_4, x_5, t)$, which is determined by the following five-dimensional Fokker-Planck equation

$$\frac{\partial}{\partial t}\Phi(X(t), t) + \frac{\partial}{\partial X(t)}[AX(t)\Phi(X(t), t)] - \frac{\sigma_1^2}{2} \frac{\partial^2}{\partial x_4^2}\Phi(X(t), t) - \frac{\sigma_2^2}{2} \frac{\partial^2}{\partial x_5^2}\Phi(X(t), t) = 0. \quad (4.4)$$

Next, we will give the accurate expression of the probability density by solving Equation (4.4). It is noticed that $\partial\Phi(X(t), t)/\partial t = 0$ under a stationary case, then (4.4) becomes

$$\begin{aligned} & \frac{\partial}{\partial x_1}[(-a_{11}x_1 - a_{12}x_2 - a_{13}x_3 - a_{14}x_4 - a_{15}x_5)\Phi] + \frac{\partial}{\partial x_2}[(a_{21}x_1 - a_{22}x_2 + a_{23}x_3 + a_{24}x_4 + a_{25}x_5)\Phi] \\ & + \frac{\partial}{\partial x_3}[(a_{32}x_2 - a_{33}x_3)\Phi] + \frac{\partial}{\partial x_4}(-\rho_1x_4\Phi) + \frac{\partial}{\partial x_5}(-\rho_2x_5\Phi) - \frac{\sigma_1^2}{2} \frac{\partial^2}{\partial x_4^2}\Phi - \frac{\sigma_2^2}{2} \frac{\partial^2}{\partial x_5^2}\Phi = 0. \end{aligned} \quad (4.5)$$

Because the diffusion matrix H is a constant matrix, then the probability density $\Phi(X)$ can be described by a normal distribution according to the work of Roozen [39], that is,

$$\Phi(X) = m \exp \left\{ -\frac{1}{2} X^T Q X \right\},$$

where Q is a real symmetric matrix and m is a positive constant satisfying the normalization condition $\int_{\mathbb{R}^5} \Phi(X) dX = 1$.

Substituting these results into (4.5), we obtain the constant $m = (2\pi)^{-\frac{5}{2}} |\Sigma|^{-\frac{1}{2}}$ and Q satisfies the following algebraic equation

$$QH^2Q + QA + A^TQ = 0. \quad (4.6)$$

If the matrix Q is positive definite and so it is invertible, we define $Q^{-1} = \Sigma$, then the algebraic equation (4.6) can be transformed into the following equivalent form

$$H^2 + A\Sigma + \Sigma A^T = 0. \quad (4.7)$$

In consideration of the finite independent superposition principle [38], (4.7) is equivalent to the sum of the following two algebraic sub-equations,

$$H_i^2 + A\Sigma_i + \Sigma_i A^T = 0, \quad i = 1, 2,$$

where $H_1^2 = \text{diag}(0, 0, 0, \sigma_1^2, 0)$, $H_2^2 = \text{diag}(0, 0, 0, 0, \sigma_2^2)$, and the symmetric matrices Σ_i ($i = 1, 2$) are their solutions, respectively. It is easy to see that $\Sigma = \Sigma_1 + \Sigma_2$ and $H^2 = H_1^2 + H_2^2$.

Denote by

$$A^{(3)} := \begin{pmatrix} -a_{11} & -a_{12} & -a_{13} \\ a_{21} & -a_{22} & a_{23} \\ 0 & a_{32} & -a_{33} \end{pmatrix}.$$

To validate that the matrix $A^{(3)}$ is a Hurwitz matrix, in view of Definition 4.1, we need to validate that all the eigenvalues of $A^{(3)}$ have negative real-parts. To this end, define the characteristic equation of $A^{(3)}$ by

$$\varphi_{A^{(3)}}(\lambda) = \lambda^3 + \tau_1\lambda^2 + \tau_2\lambda + \tau_3 = 0, \quad (4.8)$$

where

$$\tau_1 = a_{11} + a_{22} + a_{33}, \tau_2 = a_{11}a_{22} + a_{11}a_{33} + a_{22}a_{33} + a_{12}a_{21} - a_{13}a_{32}, \tau_3 = a_{11}a_{22}a_{33} + a_{12}a_{21}a_{33} + a_{13}a_{21}a_{32} - a_{11}a_{13}a_{32}.$$

On the basis of the expressions of T^* , I^* , V^* , we have

$$\tau_1 > 0, \tau_3 > a_{11}(a_{22}a_{33} - a_{23}a_{32}) > 0, \tau_1\tau_2 - \tau_3 > a_{11}(a_{11}a_{22} + a_{11}a_{33} + a_{12}a_{21} + a_{22}a_{33} + a_{22}^2 + a_{33}^2) > 0,$$

which shows that all the roots of the characteristic equation (4.8) have negative real-parts and hence the matrix $A^{(3)}$ is a Hurwitz matrix.

Now we are in the position to give the specific form of Σ and validate its positive definiteness. We realize it in two steps.

Step 1. Consider the algebraic equation

$$H_1^2 + A\Sigma_1 + \Sigma_1A^T = 0. \quad (4.9)$$

Define $A_1 = J_1AJ_1^{-1}$, where the ordering matrix J_1 takes the form

$$J_1 = \begin{pmatrix} 0 & 0 & 0 & 1 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Direct calculation leads to that

$$A_1 = \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 \\ -a_{14} & -a_{11} & -a_{12} & -a_{13} & -a_{15} \\ a_{24} & a_{21} & -a_{22} & a_{23} & a_{25} \\ 0 & 0 & a_{32} & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix}.$$

Define $A_2 = J_2A_1J_2^{-1}$, where the elimination matrix J_2 is given by

$$J_2 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Then we have

$$A_2 = \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 \\ -a_{14} & a_{12} - a_{11} & -a_{12} & -a_{13} & -a_{15} \\ 0 & p_1 & -(a_{12} + a_{22}) & 0 & 0 \\ 0 & -a_{32} & a_{32} & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix},$$

where

$$p_1 = a_{12} + a_{21} + a_{22} - a_{11}.$$

In the light of the value of p_1 , we will consider the following two cases:

(1) $p_1 \neq 0$; (2) $p_1 = 0$.

Case 1. If $p_1 \neq 0$, let $A_3 = J_3A_2J_3^{-1}$, where the elimination matrix J_3 takes the form

$$J_3 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & \frac{a_{32}}{p_1} & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Then it is easy to obtain that

$$A_3 = \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 \\ -a_{14} & a_{12} - a_{11} & \frac{a_{13}a_{32} - a_{12}p_1}{p_1} & -a_{13} & -a_{15} \\ 0 & p_1 & -(a_{12} + a_{22}) & 0 & 0 \\ 0 & 0 & p_2 & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix},$$

where

$$p_2 = \frac{a_{32}(a_{21} + a_{33} - a_{11})}{p_1}.$$

Based on the value of p_2 , we study the following two conditions

(i) $p_2 \neq 0$; (ii) $p_2 = 0$.

Case 1.1. If $p_2 \neq 0$, let $A_4 = J_4 A_3 J_4^{-1}$, where the standardized transformation matrix J_4 is given by

$$J_4 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & p_1 p_2 & -(a_{12} + a_{22} + a_{33})p_2 & a_{33}^2 & 0 \\ 0 & 0 & p_2 & -a_{33} & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix},$$

then

$$A_4 = \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 \\ -a_{14}p_1p_2 & -(a_{11} + a_{22} + a_{33}) & a_{4(23)} & a_{4(24)} & -a_{15}p_1p_2 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix},$$

where

$$a_{4(23)} = -\tau_2 = -(a_{11}a_{22} + a_{11}a_{33} + a_{22}a_{33} + a_{12}a_{21} - a_{13}a_{32}),$$

$$a_{4(24)} = -\tau_3 = -(a_{11}a_{22}a_{33} + a_{12}a_{21}a_{33} + a_{13}a_{21}a_{32} - a_{11}a_{13}a_{32}).$$

In addition, let $A_5 = J_5 A_4 J_5^{-1}$, where the standardized transformation matrix J_5 is given by

$$J_5 = \begin{pmatrix} -a_{14}p_1p_2 & -\tau_1 & -\tau_2 & -\tau_3 & -a_{15}p_1p_2 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

By simple computation, we have

$$A_5 = \begin{pmatrix} -(\tau_1 + \rho_1) & -(\tau_1\rho_1 + \tau_2) & -(\tau_2\rho_1 + \tau_3) & -\tau_3\rho_1 & a_{15}p_1p_2(\rho_2 - \rho_1) \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix}.$$

In addition, Equation (4.9) can be transformed into the following form

$$(J_5 J_4 J_3 J_2 J_1) H_1^2 (J_5 J_4 J_3 J_2 J_1)^T + A_5 (J_5 J_4 J_3 J_2 J_1) \Sigma_1 (J_5 J_4 J_3 J_2 J_1)^T + (J_5 J_4 J_3 J_2 J_1) \Sigma_1 (J_5 J_4 J_3 J_2 J_1)^T A_5^T = 0,$$

that is,

$$H_0^2 + A_5 \Sigma_{01} + \Sigma_{01} A_5^T = 0, \quad (4.10)$$

where $\Sigma_{01} = \xi_1^{-2}(J_5 J_4 J_3 J_2 J_1) \Sigma_1 (J_5 J_4 J_3 J_2 J_1)^T$ and $\xi_1 = -a_{14} p_1 p_2 \sigma_1$. By solving Equation (4.10), we obtain

$$\Sigma_{01} = \begin{pmatrix} \frac{\rho_1^2(\tau_1\tau_2 - \tau_3) + \tau_2(\rho_1\tau_2 + \tau_3)}{\Sigma_{01}^*} & 0 & -\frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & 0 \\ 0 & \frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & -\frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 \\ -\frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & \frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 & 0 \\ 0 & -\frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 & \frac{\rho_1\tau_1(\rho_1 + \tau_1) + \tau_1\tau_2 - \tau_3}{\rho_1\tau_3\Sigma_{01}^*} & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix},$$

where $\Sigma_{01}^* = 2(\rho_1^3 + \rho_1^2\tau_1 + \rho_1\tau_2 + \tau_3)(\tau_1\tau_2 - \tau_3)$.

It is noticed that the matrix Σ_{01} is positive semi-definite and its submatrix

$$\Sigma_{01}^{(4)} = \begin{pmatrix} \frac{\rho_1^2(\tau_1\tau_2 - \tau_3) + \tau_2(\rho_1\tau_2 + \tau_3)}{\Sigma_{01}^*} & 0 & -\frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 \\ 0 & \frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & -\frac{\rho_1 + \tau_1}{\Sigma_{01}^*} \\ -\frac{\rho_1\tau_2 + \tau_3}{\Sigma_{01}^*} & 0 & \frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 \\ 0 & -\frac{\rho_1 + \tau_1}{\Sigma_{01}^*} & 0 & \frac{\rho_1\tau_1(\rho_1 + \tau_1) + \tau_1\tau_2 - \tau_3}{\rho_1\tau_3\Sigma_{01}^*} \end{pmatrix}$$

is positive definite. Therefore, the matrix $\Sigma_1 = \xi_1^2(J_5 J_4 J_3 J_2 J_1)^{-1} \Sigma_{01} [(J_5 J_4 J_3 J_2 J_1)^{-1}]^T$ is also positive semi-definite and there exists a positive constant η_1 such that

$$\Sigma_1 \succeq \eta_1 \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Case 1.2. If $p_2 = 0$, let $A_6 = J_6 A_3 J_6^{-1}$, where the standardized transformation matrix J_6 is given by

$$J_6 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & p_1 & -(a_{12} + a_{22}) & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix},$$

then

$$A_6 = \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 \\ -a_{14}p_1 & -(a_{11} + a_{22}) & -a_{11}a_{22} + a_{13}a_{32} - a_{12}a_{21} & -a_{13}p_1 & -a_{15}p_1 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix}.$$

Next, define $A_7 = J_7 A_6 J_7^{-1}$, where the standardized transformation matrix J_7 takes the form

$$J_7 = \begin{pmatrix} -a_{14}p_1 & -(a_{11} + a_{22}) & -a_{11}a_{22} + a_{13}a_{32} - a_{12}a_{21} & -a_{13}p_1 & -a_{15}p_1 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Direct calculation gives that

$$A_7 = \begin{pmatrix} -(\rho_1 + l_1) & -(\rho_1 l_1 + l_2) & -\rho_1 l_2 & a_{13}p_1(a_{33} - \rho_1) & a_{15}p_1(\rho_2 - \rho_1) \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix},$$

where

$$l_1 = a_{11} + a_{22}, \quad l_2 = a_{11}a_{22} + a_{12}a_{21} - a_{13}a_{32}.$$

Similarly, Equation (4.9) can be rewritten into the following equivalent form

$$(J_7 J_6 J_3 J_2 J_1) H_1^2 (J_7 J_6 J_3 J_2 J_1)^T + A_7 (J_7 J_6 J_3 J_2 J_1) \Sigma_1 (J_7 J_6 J_3 J_2 J_1)^T + (J_7 J_6 J_3 J_2 J_1) \Sigma_1 (J_7 J_6 J_3 J_2 J_1)^T A_7^T = 0,$$

i.e.,

$$H_0^2 + A_7 \tilde{\Theta}_0 + \tilde{\Theta}_0 A_7^T = 0, \quad (4.11)$$

where $\tilde{\Theta}_0 = \tilde{\xi}_1^{-2} (J_7 J_6 J_3 J_2 J_1) \Sigma_1 (J_7 J_6 J_3 J_2 J_1)^T$ and $\tilde{\xi}_1 = -a_{14} p_1 \sigma_1$. By solving Equation (4.11), we have

$$\tilde{\Theta}_0 = \begin{pmatrix} \frac{\rho_1 l_1 + l_2}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & -\frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & 0 \\ 0 & \frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & 0 & 0 \\ -\frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & \frac{\rho_1 + l_1}{2\rho_1 l_1 l_2(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Apparently, the matrix $\tilde{\Theta}_0$ is positive semi-definite and its submatrix

$$\tilde{\Theta}_0^{(4)} = \begin{pmatrix} \frac{\rho_1 l_1 + l_2}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & -\frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 \\ 0 & \frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & 0 \\ -\frac{1}{2l_1(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 & \frac{\rho_1 + l_1}{2\rho_1 l_1 l_2(\rho_1 l_1 + l_2 + \rho_1^2)} & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

is positive semi-definite. Hence, the matrix $\Sigma_1 = \tilde{\xi}_1^2 (J_7 J_6 J_3 J_2 J_1)^{-1} \tilde{\Theta}_0 [(J_7 J_6 J_3 J_2 J_1)^{-1}]^T$ is also positive semi-definite and there exists a positive constant $\tilde{\eta}_1$ such that

$$\Sigma_1 \succeq \tilde{\eta}_1 \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Case 2. If $p_1 = 0$, i.e., $a_{12} + a_{21} + a_{22} - a_{11} = 0$, let $A_8 = J_8 A_2 J_8^{-1}$, where the ordering matrix J_8 is given by

$$J_8 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix},$$

then we have

$$A_8 = \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 \\ -a_{14} & a_{12} - a_{11} & -a_{13} & -a_{12} & -a_{15} \\ 0 & -a_{32} & -a_{33} & a_{32} & 0 \\ 0 & 0 & 0 & -(a_{12} + a_{22}) & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix}.$$

Next, define $A_9 = J_9 A_8 J_9^{-1}$, where the standardized transformation matrix J_9 takes the form

$$J_9 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & -a_{32} & -a_{33} & a_{32} & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

It is easy to calculate that

$$A_9 = \begin{pmatrix} -\rho_1 & 0 & 0 & 0 & 0 \\ a_{14}a_{32} & -(a_{21} + a_{22} + a_{33}) & a_{13}a_{32} - a_{21}a_{33} - a_{22}a_{33} & a_{21}a_{32} & a_{15}a_{32} \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -(a_{12} + a_{22}) & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix}.$$

Let $A_{10} = J_{10}A_9J_{10}^{-1}$, where the standardized transformation matrix J_{10} is given by

$$J_{10} = \begin{pmatrix} a_{14}a_{32} & -(a_{21} + a_{22} + a_{33}) & a_{13}a_{32} - a_{21}a_{33} - a_{22}a_{33} & a_{21}a_{32} & a_{15}a_{32} \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

It is easy to obtain that

$$A_{10} = \begin{pmatrix} -(\rho_1 + \bar{l}_1) & -(\rho_1\bar{l}_1 + \bar{l}_2) & -\rho_1\bar{l}_2 & a_{21}a_{32}(\rho_1 - a_{12} - a_{22}) & a_{15}a_{32}(\rho_1 - \rho_2) \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -(a_{12} + a_{22}) & 0 \\ 0 & 0 & 0 & 0 & -\rho_2 \end{pmatrix},$$

where

$$\bar{l}_1 = a_{21} + a_{22} + a_{33}, \quad \bar{l}_2 = a_{21}a_{33} + a_{22}a_{33} - a_{13}a_{32}.$$

Moreover, Equation (4.9) can be equivalently transformed into the following form

$$(J_{10}J_9J_8J_2J_1)H_1^2(J_{10}J_9J_8J_2J_1)^T + A_{10}(J_{10}J_9J_8J_2J_1)\Sigma_1(J_{10}J_9J_8J_2J_1)^T + (J_{10}J_9J_8J_2J_1)\Sigma_1(J_{10}J_9J_8J_2J_1)^T A_{10}^T = 0.$$

The above equation can be rewritten as the following equivalent form

$$H_0^2 + A_{10}\bar{\Theta}_0 + \bar{\Theta}_0A_{10}^T = 0, \quad (4.12)$$

where $H_0 = \text{diag}(1, 0, 0, 0, 0)$, $\bar{\Theta}_0 = \bar{\xi}_1^{-2}(J_{10}J_9J_8J_2J_1)\Sigma_1(J_{10}J_9J_8J_2J_1)^T$ and $\bar{\xi}_1 = a_{14}a_{32}\sigma_1$. By solving Equation (4.12), we obtain

$$\bar{\Theta}_0 = \begin{pmatrix} \frac{\rho_1\bar{l}_1 + \bar{l}_2}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & -\frac{1}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & 0 \\ 0 & \frac{1}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & 0 & 0 \\ -\frac{1}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & \frac{\rho_1 + \bar{l}_1}{2\rho_1\bar{l}_1\bar{l}_2(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Note that the matrix $\bar{\Theta}_0$ is positive semi-definite and its submatrix

$$\bar{\Theta}_0^{(4)} = \begin{pmatrix} \frac{\rho_1\bar{l}_1 + \bar{l}_2}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & -\frac{1}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 \\ 0 & \frac{1}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & 0 \\ -\frac{1}{2\bar{l}_1(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 & \frac{\rho_1 + \bar{l}_1}{2\rho_1\bar{l}_1\bar{l}_2(\rho_1\bar{l}_1 + \bar{l}_2 + \rho_1^2)} & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

is positive semi-definite. Thus, the matrix $\Sigma_1 = \bar{\xi}_1^2(J_{10}J_9J_8J_2J_1)^{-1}\bar{\Theta}_0[(J_{10}J_9J_8J_2J_1)^{-1}]^T$ is also positive semi-definite and there exists a positive constant $\bar{\eta}_1$ such that

$$\Sigma_1 \succeq \bar{\eta}_1 \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Step 2. Consider the algebraic equation

$$H_2^2 + A\Sigma_2 + \Sigma_2A^T = 0. \quad (4.13)$$

Let $A_{11} = J_{11}AJ_{11}^{-1}$, where the ordering matrix J_{11} takes the form

$$J_{11} = \begin{pmatrix} 0 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \end{pmatrix},$$

then we obtain

$$A_{11} = \begin{pmatrix} -\rho_2 & 0 & 0 & 0 & 0 \\ -a_{15} & -a_{11} & -a_{12} & -a_{13} & -a_{14} \\ a_{25} & a_{21} & -a_{22} & a_{23} & a_{24} \\ 0 & 0 & a_{32} & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix}.$$

Next, let $A_{12} = J_{12}A_{11}J_{12}^{-1}$, where the elimination matrix J_{12} is given by

$$J_{12} = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Then

$$A_{12} = \begin{pmatrix} -\rho_2 & 0 & 0 & 0 & 0 \\ -a_{15} & a_{12} - a_{11} & -a_{12} & -a_{13} & -a_{14} \\ 0 & p_1 & -(a_{12} + a_{22}) & 0 & 0 \\ 0 & -a_{32} & a_{32} & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix},$$

where

$$p_1 = a_{12} + a_{21} + a_{22} - a_{11}.$$

In view of the value of p_1 , we will study the following two cases:

(1) $p_1 \neq 0$; (2) $p_1 = 0$.

Case 1. If $p_1 \neq 0$, following the derivation process in Step 1, we define $A_{13} = J_{13}A_{12}J_{13}^{-1}$, where the elimination matrix J_{13} takes the form

$$J_{13} = J_3 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & \frac{a_{32}}{p_1} & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Then we compute that

$$A_{13} = \begin{pmatrix} -\rho_2 & 0 & 0 & 0 & 0 \\ -a_{15} & a_{12} - a_{11} & \frac{a_{13}a_{32} - a_{12}p_1}{p_1} & -a_{13} & -a_{14} \\ 0 & p_1 & -(a_{12} + a_{22}) & 0 & 0 \\ 0 & 0 & p_2 & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix},$$

where

$$p_2 = \frac{a_{32}(a_{21} + a_{33} - a_{11})}{p_1}.$$

On the basis of the value of p_2 , we consider the following two conditions

(i) $p_2 \neq 0$; (ii) $p_2 = 0$.

Case 1.1. If $p_2 \neq 0$, let $A_{14} = J_{14}A_{13}J_{14}^{-1}$, where the standardized transformation matrix J_{14} is given by

$$J_{14} = J_4 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & p_1p_2 & -(a_{12} + a_{22} + a_{33})p_2 & a_{33}^2 & 0 \\ 0 & 0 & p_2 & -a_{33} & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

We obtain that

$$A_{14} = \begin{pmatrix} -\rho_2 & 0 & 0 & 0 & 0 \\ -a_{15}p_1p_2 & -(a_{11} + a_{22} + a_{33}) & a_{14(23)} & a_{14(24)} & -a_{14}p_1p_2 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix},$$

where

$$a_{14(23)} = -\tau_2 = -(a_{11}a_{22} + a_{11}a_{33} + a_{22}a_{33} + a_{12}a_{21} - a_{13}a_{32}),$$

$$a_{14(24)} = -\tau_3 = -(a_{11}a_{22}a_{33} + a_{12}a_{21}a_{33} + a_{13}a_{21}a_{32} - a_{11}a_{13}a_{32}).$$

Next, define $A_{15} = J_{15}A_{14}J_{15}^{-1}$, where the standardized transformation matrix J_{15} takes the form

$$J_{15} = \begin{pmatrix} -a_{15}p_1p_2 & -\tau_1 & -\tau_2 & -\tau_3 & -a_{14}p_1p_2 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Then it is easy to see that

$$A_{15} = \begin{pmatrix} -(\rho_2 + \tau_1) & -(\rho_2\tau_1 + \tau_2) & -(\rho_2\tau_2 + \tau_3) & -\rho_2\tau_3 & a_{14}p_1p_2(\rho_1 - \rho_2) \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix}.$$

Thus, Equation (4.13) can be transformed into the following form

$$(J_{15}J_{14}J_{13}J_{12}J_{11})H_2^2(J_{15}J_{14}J_{13}J_{12}J_{11})^T + A_{15}(J_{15}J_{14}J_{13}J_{12}J_{11})\Sigma_2(J_{15}J_{14}J_{13}J_{12}J_{11})^T + (J_{15}J_{14}J_{13}J_{12}J_{11})\Sigma_2(J_{15}J_{14}J_{13}J_{12}J_{11})^T A_{15}^T = 0,$$

that is,

$$H_0^2 + A_{15}\Sigma_{02} + \Sigma_{02}A_{15}^T = 0, \quad (4.14)$$

where $\Sigma_{02} = \xi_2^{-2}(J_{15}J_{14}J_{13}J_{12}J_{11})\Sigma_2(J_{15}J_{14}J_{13}J_{12}J_{11})^T$ and $\xi_2 = -a_{15}p_1p_2\sigma_2$. By solving Equation (4.14), we have

$$\Sigma_{02} = \begin{pmatrix} \frac{\rho_2^2(\tau_1\tau_2 - \tau_3) + \tau_2(\rho_2\tau_2 + \tau_3)}{\Sigma_{02}^*} & 0 & -\frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & 0 \\ 0 & \frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & -\frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 \\ -\frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & \frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 & 0 \\ 0 & -\frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 & \frac{\rho_2\tau_1(\rho_2 + \tau_1) + \tau_1\tau_2 - \tau_3}{\rho_2\tau_3\Sigma_{02}^*} & 0 \\ 0 & 0 & 0 & \frac{\rho_2\tau_3\Sigma_{02}^*}{0} & 0 \end{pmatrix},$$

where $\Sigma_{02}^* = 2(\rho_2^3 + \rho_2^2\tau_1 + \rho_2\tau_2 + \tau_3)(\tau_1\tau_2 - \tau_3)$.

It is easy to conclude that the matrix Σ_{02} is positive semi-definite and its submatrix

$$\Sigma_{02}^{(4)} = \begin{pmatrix} \frac{\rho_2^2(\tau_1\tau_2 - \tau_3) + \tau_2(\rho_2\tau_2 + \tau_3)}{\Sigma_{02}^*} & 0 & -\frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 \\ 0 & \frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & -\frac{\rho_2 + \tau_1}{\Sigma_{02}^*} \\ -\frac{\rho_2\tau_2 + \tau_3}{\Sigma_{02}^*} & 0 & \frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 \\ 0 & -\frac{\rho_2 + \tau_1}{\Sigma_{02}^*} & 0 & \frac{\rho_2\tau_1(\rho_2 + \tau_1) + \tau_1\tau_2 - \tau_3}{\rho_2\tau_3\Sigma_{02}^*} \end{pmatrix}$$

is positive definite. Accordingly, the matrix $\Sigma_2 = \xi_2^2(J_{15}J_{14}J_{13}J_{12}J_{11})^{-1}\Sigma_{02}[(J_{15}J_{14}J_{13}J_{12}J_{11})^{-1}]^T$ is also positive semi-definite and there exists a positive constant η_2 such that

$$\Sigma_2 \succeq \eta_2 \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Case 1.2. If $p_2 = 0$, let $A_{16} = J_{16}A_{13}J_{16}^{-1}$, where the standardized transformation matrix J_{16} is given by

$$J_{16} = J_6 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & p_1 & -(a_{12} + a_{22}) & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix},$$

then

$$A_{16} = \begin{pmatrix} -\rho_2 & 0 & 0 & 0 & 0 \\ -a_{15}p_1 & -(a_{11} + a_{22}) & -a_{11}a_{22} + a_{13}a_{32} - a_{12}a_{21} & -a_{13}p_1 & -a_{14}p_1 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix}.$$

Next, define $A_{17} = J_{17}A_{16}J_{17}^{-1}$, where the standardized transformation matrix J_{17} takes the form

$$J_{17} = \begin{pmatrix} -a_{15}p_1 & -(a_{11} + a_{22}) & -a_{11}a_{22} + a_{13}a_{32} - a_{12}a_{21} & -a_{13}p_1 & -a_{14}p_1 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Direct calculation gives that

$$A_{17} = \begin{pmatrix} -(\rho_2 + l_1) & -(\rho_2 l_1 + l_2) & -\rho_2 l_2 & a_{13}p_1(a_{33} - \rho_2) & a_{14}p_1(\rho_1 - \rho_2) \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -a_{33} & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix},$$

where

$$l_1 = a_{11} + a_{22}, \quad l_2 = a_{11}a_{22} + a_{12}a_{21} - a_{13}a_{32}.$$

Similarly, Equation (4.13) can be rewritten into the following equivalent form

$$(J_{17}J_{16}J_{13}J_{12}J_{11})H_2^2(J_{17}J_{16}J_{13}J_{12}J_{11})^T + A_{17}(J_{17}J_{16}J_{13}J_{12}J_{11})\Sigma_2(J_{17}J_{16}J_{13}J_{12}J_{11})^T + (J_{17}J_{16}J_{13}J_{12}J_{11})\Sigma_2(J_{17}J_{16}J_{13}J_{12}J_{11})^T A_{17}^T = 0,$$

i.e.,

$$H_0^2 + A_{17}\tilde{\Delta}_0 + \tilde{\Delta}_0 A_{17}^T = 0, \quad (4.15)$$

where $\tilde{\Delta}_0 = \tilde{\xi}_2^{-2}(J_{17}J_{16}J_{13}J_{12}J_{11})\Sigma_2(J_{17}J_{16}J_{13}J_{12}J_{11})^T$ and $\tilde{\xi}_2 = -a_{15}p_1\sigma_2$. By solving Equation (4.15), we obtain

$$\tilde{\Delta}_0 = \begin{pmatrix} \frac{\rho_2 l_1 + l_2}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & -\frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & 0 \\ 0 & \frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & 0 & 0 \\ -\frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & \frac{\rho_2 + l_1}{2\rho_2 l_1 l_2(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

It is obvious that the matrix $\tilde{\Delta}_0$ is positive semi-definite and its submatrix

$$\tilde{\Delta}_0^{(4)} = \begin{pmatrix} \frac{\rho_2 l_1 + l_2}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & -\frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 \\ 0 & \frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & 0 \\ -\frac{1}{2l_1(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 & \frac{\rho_2 + l_1}{2\rho_2 l_1 l_2(\rho_2 l_1 + l_2 + \rho_2^2)} & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

is positive semi-definite. So the matrix $\Sigma_2 = \tilde{\xi}_2^2(J_{17}J_{16}J_{13}J_{12}J_{11})^{-1}\tilde{\Delta}_0[(J_{17}J_{16}J_{13}J_{12}J_{11})^{-1}]^T$ is also positive semi-definite and there exists a positive constant $\tilde{\eta}_2$ such that

$$\Sigma_2 \succeq \tilde{\eta}_2 \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Case 2. If $p_1 = 0$, i.e., $a_{12} + a_{21} + a_{22} - a_{11} = 0$, let $A_{18} = J_{18}A_{12}J_{18}^{-1}$, where the standardized transformation matrix J_{18} takes the form

$$J_{18} = J_8 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

By simple computation, we obtain

$$A_{18} = \begin{pmatrix} -\rho_2 & 0 & 0 & 0 & 0 \\ -a_{15} & a_{12} - a_{11} & -a_{13} & -a_{12} & -a_{14} \\ 0 & -a_{32} & -a_{33} & a_{32} & 0 \\ 0 & 0 & 0 & -(a_{12} + a_{22}) & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix}.$$

In addition, let $A_{19} = J_{19}A_{18}J_{19}^{-1}$, where the standardized transformation matrix J_{19} takes the form

$$J_{19} = J_9 = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & -a_{32} & -a_{33} & a_{32} & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Direct calculation leads to that

$$A_{19} = \begin{pmatrix} -\rho_2 & 0 & 0 & 0 & 0 & 0 \\ a_{15}a_{32} & -(a_{21} + a_{22} + a_{33}) & a_{13}a_{32} - a_{21}a_{33} - a_{22}a_{33} & a_{21}a_{32} & a_{14}a_{32} & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -(a_{12} + a_{22}) & 0 \\ 0 & 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix}.$$

Define $A_{20} = J_{20}A_{19}J_{20}^{-1}$, where the standardized transformation matrix J_{20} is given by

$$J_{20} = \begin{pmatrix} a_{15}a_{32} & -(a_{21} + a_{22} + a_{33}) & a_{13}a_{32} - a_{21}a_{33} - a_{22}a_{33} & a_{21}a_{32} & a_{14}a_{32} \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Then

$$A_{20} = \begin{pmatrix} -(\rho_2 + \bar{l}_1) & -(\rho_2\bar{l}_1 + \bar{l}_2) & -\rho_2\bar{l}_2 & a_{21}a_{32}(\rho_2 - a_{12} - a_{22}) & a_{14}a_{32}(\rho_2 - \rho_1) \\ 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -(a_{12} + a_{22}) & 0 \\ 0 & 0 & 0 & 0 & -\rho_1 \end{pmatrix},$$

where

$$\bar{l}_1 = a_{21} + a_{22} + a_{33}, \quad \bar{l}_2 = a_{21}a_{33} + a_{22}a_{33} - a_{13}a_{32}.$$

Similarly, Equation (4.13) can be transformed into the following equivalent form

$$(J_{20}J_{19}J_{18}J_{12}J_{11})H_2^2(J_{20}J_{19}J_{18}J_{12}J_{11})^T + A_{20}(J_{20}J_{19}J_{18}J_{12}J_{11})\Sigma_2(J_{20}J_{19}J_{18}J_{12}J_{11})^T + (J_{20}J_{19}J_{18}J_{12}J_{11})\Sigma_2(J_{20}J_{19}J_{18}J_{12}J_{11})^T A_{20}^T = 0,$$

that is,

$$H_0^2 + A_{20}\bar{\Delta}_0 + \bar{\Delta}_0A_{20}^T = 0, \quad (4.16)$$

where $\bar{\Delta}_0 = \bar{\xi}_2^{-2}(J_{20}J_{19}J_{18}J_{12}J_{11})\Sigma_2(J_{20}J_{19}J_{18}J_{12}J_{11})^T$ and $\bar{\xi}_2 = a_{15}a_{32}\sigma_2$. By solving Equation (4.16), we have

$$\bar{\Delta}_0 = \begin{pmatrix} \frac{\rho_2\bar{l}_1 + \bar{l}_2}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & -\frac{1}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & 0 \\ 0 & \frac{1}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & 0 & 0 \\ -\frac{1}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & \frac{\rho_2 + \bar{l}_1}{2\rho_2\bar{l}_1\bar{l}_2(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix}.$$

Clearly, the matrix $\bar{\Delta}_0$ is positive semi-definite and its submatrix

$$\bar{\Delta}_0^{(4)} = \begin{pmatrix} \frac{\rho_2\bar{l}_1 + \bar{l}_2}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & -\frac{1}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 \\ 0 & \frac{1}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & 0 \\ -\frac{1}{2\bar{l}_1(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 & \frac{\rho_2 + \bar{l}_1}{2\rho_2\bar{l}_1\bar{l}_2(\rho_2\bar{l}_1 + \bar{l}_2 + \rho_2^2)} & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

is positive semi-definite. So the matrix $\Sigma_2 = \bar{\xi}_2^2(J_{20}J_{19}J_{18}J_{12}J_{11})^{-1}\bar{\Delta}_0[(J_{20}J_{19}J_{18}J_{12}J_{11})^{-1}]^T$ is also positive semi-definite and there exists a positive constant $\bar{\eta}_2$ such that

$$\Sigma_2 \succeq \bar{\eta}_2 \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Now we validate the matrix $\Sigma = \Sigma_1 + \Sigma_2$ in Eq. (4.7) is positive definite. If $p_2 \neq 0$, then the covariance matrix

$$\begin{aligned} \Sigma &= \Sigma_1 + \Sigma_2 \\ &\succeq \eta_1 \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{pmatrix} + \eta_2 \begin{pmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \\ &\succeq (\eta_1 \wedge \eta_2) \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \end{pmatrix} \end{aligned}$$

is positive definite. Similarly, we can validate that under the other two cases, the covariance matrix Σ is also positive definite. Accordingly, we obtain that the stationary distribution $\pi(\cdot)$ around the quasi-chronic infection equilibrium $(T^*, I^*, V^*, \beta_1^*, \beta_2^*)^T$ follows a unique probability density $\Phi(T, I, V, \beta_1, \beta_2)$, which takes the form

$$\Phi(T, I, V, \beta_1, \beta_2) = (2\pi)^{-\frac{5}{2}} |\Sigma|^{-\frac{1}{2}} e^{-\frac{1}{2}(T-T^*, I-I^*, V-V^*, \beta_1-\beta_1^*, \beta_2-\beta_2^*)\Sigma^{-1}(T-T^*, I-I^*, V-V^*, \beta_1-\beta_1^*, \beta_2-\beta_2^*)^T},$$

where the specific form of Σ can be determined by the above discussion. This completes the proof.

5 Numerical simulations

In this section, we supply some numerical simulations to validate our theoretical results. For the stochastic system (1.2), we adopt the Milstein higher-order method mentioned in [40] and the discretization form of the stochastic system is as follows:

$$\begin{cases} T^{j+1} = T^j + \left[\lambda - \mu_1 T^j + r T^j \left(1 - \frac{T^j}{T_{\max}} \right) - \max\{\beta_1^j, 0\} T^j V^j - \max\{\beta_2^j, 0\} T^j I^j \right] \Delta t, \\ I^{j+1} = I^j + [\max\{\beta_1^j, 0\} T^j V^j + \max\{\beta_2^j, 0\} T^j I^j - (\mu_2 + \alpha_1) I^j] \Delta t, \\ V^{j+1} = V^j + [k I^j - (\mu_3 + \alpha_2) V^j] \Delta t, \\ \beta_1^{j+1} = \beta_1^j + \rho_1 (\bar{\beta}_1 - \beta_1^j) \Delta t + \sigma_1 \sqrt{\Delta t} \varepsilon_{1,j}, \\ \beta_2^{j+1} = \beta_2^j + \rho_2 (\bar{\beta}_2 - \beta_2^j) \Delta t + \sigma_2 \sqrt{\Delta t} \varepsilon_{2,j}, \end{cases} \quad (5.1)$$

where $(T^j, I^j, V^j, \beta_1^j, \beta_2^j)^T$ represents the corresponding value of the j th iteration of the equation (5.1). Δt is the time increment which is positive, σ_i^2 denote the intensities of white noises, $\varepsilon_{i,j}$ ($i = 1, 2; j = 1, \dots, n$) are mutually independent normal random variables following the distribution $N(0, 1)$. We choose actual parameter values from the published references, and all the values of biological parameters are given in Table 2.

Next, in view of numerical simulations, we mainly focus on validating two aspects:

- (i) there exists a stationary distribution of system (1.2) if the condition $\mathcal{R}_0^S > 1$ holds;
- (ii) the existence of the probability density.

Example 5.1. In order to get the existence of a stationary distribution numerically, we choose $\rho_1 = 0.5$, $\rho_2 = 0.5$, $\sigma_1 = 10^{-6}$, $\sigma_2 = 5 \times 10^{-5}$ and the other parameter values are presented in Table 2. By direct calculation, we obtain

$$\mathcal{R}_0^S = \frac{k\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_1 \sqrt{\rho_1}}{\sigma_1}}^{\frac{\sigma_1}{\sqrt{\rho_1}} x + \bar{\beta}_1} \frac{1}{3} e^{-x^2} dx \right)^3}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2) \left(\frac{\lambda}{T_0} + \frac{k\lambda\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\lambda\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} + \frac{\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_2 \sqrt{\rho_2}}{\sigma_2}}^{\frac{\sigma_2}{\sqrt{\rho_2}} x + \bar{\beta}_2} \frac{1}{2} e^{-x^2} dx \right)^2}{(\mu_2 + \alpha_1) \left(\frac{\lambda}{T_0} + \frac{k\lambda\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\lambda\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} \approx 2.524 > 1.$$

In other words, the conditions of Theorem 3.1 are satisfied. By Theorem 3.1, we obtain that system (1.2) has a stationary distribution $\pi(\cdot)$ which shows that all $CD4^+$ T cells and free viruses are persistent a.s. See Fig. 1.

Table 2: List of parameters

Parameters	Unit	Value	Source
λ	$\mu\text{l}^{-1}\text{day}^{-1}$	10	[41, 42]
μ_1	day^{-1}	0.1	[42, 43]
r	day^{-1}	0.1	[5, 41]
T_{\max}	μl^{-1}	1500	[41]
β_1	$\mu\text{l}\text{day}^{-1}$	1.3×10^{-5}	[8, 43]
β_2	$\mu\text{l}\text{day}^{-1}$	2×10^{-3}	[44]
μ_2	day^{-1}	0.5	[41, 43]
k	virions/cell	3000	[9, 10]
μ_3	day^{-1}	23	[11, 41, 42]
α_1	day^{-1}	0.01	Estimated
α_2	day^{-1}	0.02	Estimated

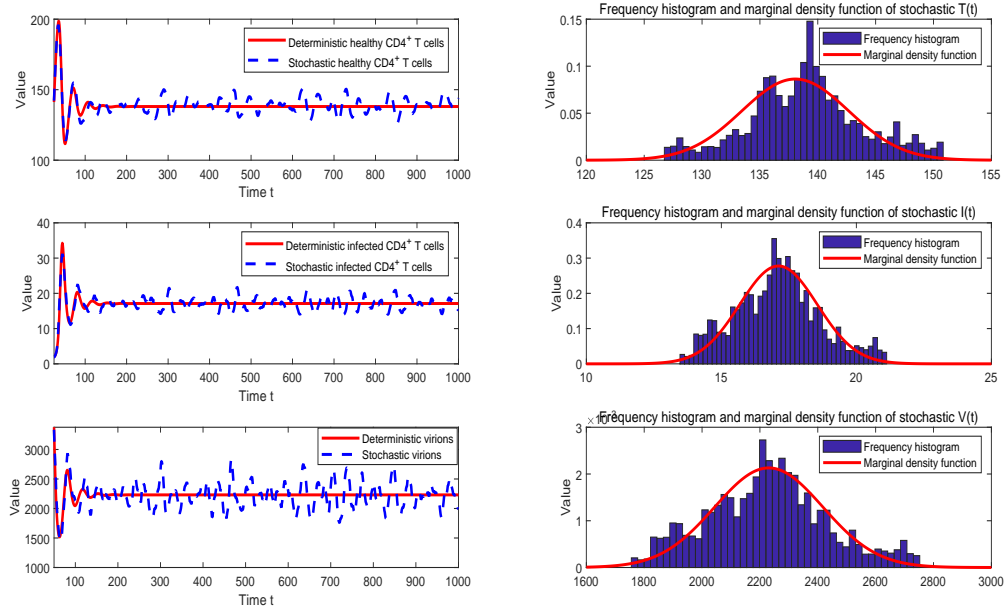


Fig. 1. The left column shows the time series diagrams of the healthy $CD4^+$ T cells, the infected $CD4^+$ T cells and the free viruses in the stochastic model (1.2) and their corresponding deterministic model (1.1) with $\rho_1 = 0.5$, $\rho_2 = 0.5$, $\sigma_1 = 10^{-6}$ and $\sigma_2 = 5 \times 10^{-5}$. The right column shows the marginal density functions and frequency histograms for T , I and V , respectively.

Example 5.2. To validate the existence of the probability density around the quasi-chronic infection equilibrium, we choose $\rho_1 = 0.5$, $\rho_2 = 0.5$, $\sigma_1 = 10^{-6}$, $\sigma_2 = 5 \times 10^{-5}$ and the other parameter values are presented in Table 2. Then we have $E^* = (T^*, I^*, V^*, \bar{\beta}_1, \bar{\beta}_2)^T = (138.0550, 17.1164, 2230.6402, 1.3 \times 10^{-5}, 2 \times 10^{-3})^T$ and

$$\mathcal{R}_0^S = \frac{k\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_1 \sqrt{\rho_1}}{\sigma_1}}^{\infty} \left(\frac{\sigma_1}{\sqrt{\rho_1}} x + \bar{\beta}_1 \right)^{\frac{1}{3}} e^{-x^2} dx \right)^3}{(\mu_2 + \alpha_1)(\mu_3 + \alpha_2) \left(\frac{\lambda}{T_0} + \frac{k\lambda\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} + \frac{\lambda \left(\frac{1}{\sqrt{\pi}} \int_{-\frac{\bar{\beta}_2 \sqrt{\rho_2}}{\sigma_2}}^{\infty} \left(\frac{\sigma_2}{\sqrt{\rho_2}} x + \bar{\beta}_2 \right)^{\frac{1}{2}} e^{-x^2} dx \right)^2}{(\mu_2 + \alpha_1) \left(\frac{\lambda}{T_0} + \frac{k\lambda\sigma_1}{2\bar{\mu}\mu_3\sqrt{\pi\rho_1}} + \frac{\bar{\lambda}\sigma_2}{2\bar{\mu}\sqrt{\pi\rho_2}} \right)} \approx 2.524 > 1.$$

That is to say, the conditions of Theorem 4.1 hold. So system (1.2) has a Gaussian probability density near the quasi-chronic infection equilibrium E^* . In addition, we obtain $p_2 = 140369.8291 > 0$. Hence, by the

second case of Theorem 4.1, it is easy to get the specific expression of the covariance matrix Σ ,

$$\begin{aligned} \Sigma &= \xi_1^2 (J_5 J_4 J_3 J_2 J_1)^{-1} \Sigma_{01} [(J_5 J_4 J_3 J_2 J_1)^{-1}]^T + \xi_2^2 (J_{15} J_{14} J_{13} J_{12} J_{11})^{-1} \Sigma_{02} [(J_{15} J_{14} J_{13} J_{12} J_{11})^{-1}]^T \\ &= \begin{pmatrix} 21.3617 & -2.7380 & -362.4600 & -9.5512 \times 10^{-7} & -0.00001832 \\ -2.73802 & 2.0658 & 269.1870 & 4.9024 \times 10^{-7} & 0.000009404 \\ -362.4600 & 269.1870 & 35080.9 & 0.00006253 & 0.001200 \\ -9.5512 \times 10^{-7} & 4.9024 \times 10^{-7} & 0.00006253 & 1.0 \times 10^{-12} & 0 \\ -0.00001832 & 0.000009404 & 0.001200 & 0 & 2.5 \times 10^{-9} \end{pmatrix}, \end{aligned}$$

and the corresponding probability density $\Phi(T, I, V, \beta_1, \beta_2)$ is given by

$$\begin{aligned} &\Phi(T, I, V, \beta_1, \beta_2) \\ &= (2\pi)^{-\frac{5}{2}} |\Sigma|^{-\frac{1}{2}} \exp \left\{ -\frac{1}{2} (T - 138.0550, I - 17.1164, V - 2230.6402, \beta_1 - 1.3 \times 10^{-5}, \beta_2 - 2 \times 10^{-3})^T \Sigma^{-1} \right. \\ &\quad \left. \times (T - 138.0550, I - 17.1164, V - 2230.6402, \beta_1 - 1.3 \times 10^{-5}, \beta_2 - 2 \times 10^{-3}) \right\} \\ &= 136249280.8326 \exp \left\{ -\frac{1}{2} (T - 138.0550, I - 17.1164, V - 2230.6402, \beta_1 - 1.3 \times 10^{-5}, \beta_2 - 2 \times 10^{-3})^T \Sigma^{-1} \right. \\ &\quad \left. \times (T - 138.0550, I - 17.1164, V - 2230.6402, \beta_1 - 1.3 \times 10^{-5}, \beta_2 - 2 \times 10^{-3}) \right\}. \end{aligned}$$

Thus, $\Phi(T, I, V, \beta_1, \beta_2)$ has the following five marginal probability densities

$$\begin{aligned} \frac{\partial \Phi}{\partial T} &= 0.08632e^{-0.02341(T-138.0550)^2}, \quad \frac{\partial \Phi}{\partial I} = 0.2776e^{-0.2420(I-17.1164)^2}, \quad \frac{\partial \Phi}{\partial V} = 0.002130e^{-0.00001425(V-2230.6402)^2}, \\ \frac{\partial \Phi}{\partial \beta_1} &= 398942.2804e^{-50000000000(\beta_1-1.3 \times 10^{-5})^2}, \quad \frac{\partial \Phi}{\partial \beta_2} = 7978.8456e^{-200000000(\beta_2-0.002)^2}. \end{aligned}$$

Fig. 2 illustrates this.

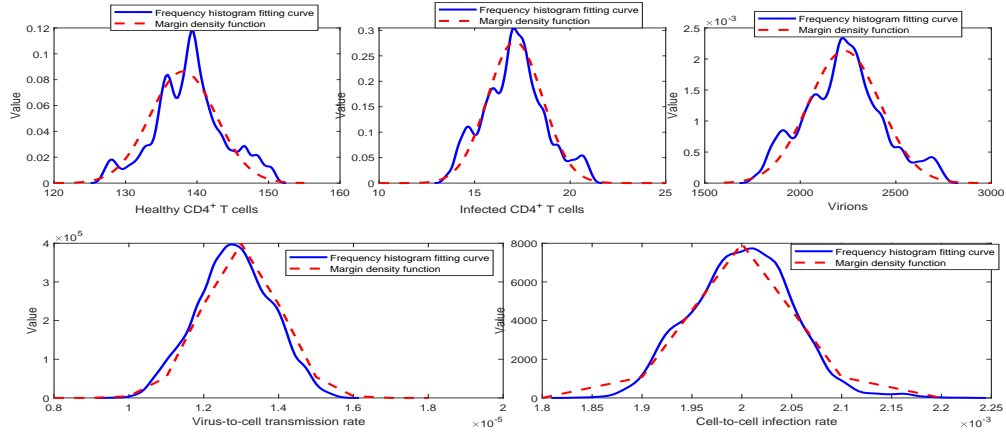


Fig. 2. Numerical simulations for: (i) the frequency histogram fitting density curves of T , I , V , β_1 and β_2 of system (1.2) with 50000, 50000 iteration points, respectively. (ii) The marginal probability densities of T , I , V , β_1 and β_2 of system (1.2). All of the parameter values are the same as in Fig. 1.

6 Conclusion

In this paper, based on both biological significance and mathematically reasonable hypotheses, we develop and analyze a stochastic HIV model with cell-to-cell transmission and Ornstein-Uhlenbeck process to describe the replication process and the pathogenesis of HIV infection in the population. Firstly, we validate that system (1.2) has a unique global solution with any given initial value. Then we adopt a novel method to

construct some suitable stochastic Lyapunov functions to establish sufficient criteria for the existence of a stationary distribution, which is a kind of probability distribution with some variables from the viewpoint of stochastic process. Especially, under the same conditions as the existence of a stationary distribution, we derive the accurate form of the probability density, which is a function that describes the probability of the output value of the random variable near the quasi-chronic infection equilibrium of system (1.2). Mathematically, the existence of a stationary distribution implies the weak stability in stochastic sense while the existence of the probability density of system (1.2) is more in-depth and specific than that of the stationary distribution. Biologically, the existence of a stationary distribution and probability density indicates the persistence and coexistence of all $CD4^+$ T cells and free viruses.

Numerically, on the basis of the actual parameter values in the existing literature, we get two important conclusions: (i) small environmental noise makes each population fluctuate extremely little which can still retain some stochastic weak stability to some extent; (ii) we obtain the specific form of the probability density around the quasi-chronic infection equilibrium E^* of system (1.2).

On the other hand, there are remain lots of significant topics deserve further consideration. For example, in this paper, we assume that the parameters β_1 and β_2 satisfy the Ornstein-Uhlenbeck process. It is interesting to assume that the other parameters involved in system (1.1) satisfy the Ornstein-Uhlenbeck process which may make the model fit the actual situation better. In addition, it is also significant to analyze the influences of other types of random perturbations (such as nonlinear perturbations, colored noise, Poisson jumps et al.) on HIV models. To our knowledge, there is little literature to study viral infection models with Lévy jumps or Poisson jumps since there are many barriers to deal with the corresponding Fokker-Planck equation in the discontinuous situation. This is because we lack appropriate mathematical methods and skills. These issues are expected to be resolved in the near future since the relevant work is now underway.

Acknowledgments

This work is supported by the National Natural Science Foundation of China (No.12001090) and the Fundamental Research Funds for the Central Universities of China (No.2412020QD024).

Availability of Data and Materials Data sharing is not applicable to this article as no datasets are generated or analyzed during the current study.

Conflict of interest The author declares that there is no conflict of interest.

References

- [1] The joint united nations program on HIV/AIDS, in: *Confronting Inequalities-Global AIDS Update 2021*, 2021.
- [2] P. Tamilalagan, S. Karthiga, P. Manivannan, Dynamics of fractional order HIV infection model with antibody and cytotoxic T-lymphocyte immune responses, *J. Comput. Appl. Math.* 382 (2021) 113064.
- [3] M. Kumar, S. Abbas, Global dynamics of an age-structured model for HIV viral dynamics with latently infected T cells, *Math. Comput. Simul.* 198 (2022) 237-252.
- [4] P. Wu, S. Zheng, Z. He, Evolution dynamics of a time-delayed reaction-diffusion HIV latent infection model with two strains and periodic therapies, *Nonlinear Anal.: RWA* 67 (2022) 103559.
- [5] P.De Leenheer, H.L. Smith, Virus dynamics: a global analysis, *SIAM J. Appl. Math.* 63 (2003) 1313-1327.
- [6] M.A. Nowak, R.M. May, *Virus Dynamics, Mathematical Principles of Immunology and Virology*, Oxford University, Oxford, 2000.
- [7] A.S. Perelson, P.W. Nelson, Mathematical analysis of HIV-1 dynamics in vivo, *SIAM Rev.* 41 (1999) 3-44.
- [8] A.S. Perelson, D.E. Kirschner, R. De Boer, Dynamics of HIV infection of $CD4^+$ T cells, *Math. Biosci.* 114 (1993) 81-125.
- [9] Y. Wang, Y. Zhou, F. Brauer, J. Heffernan, Viral dynamics model with CTL immune response incorporating antiretroviral therapy, *J. Math. Biol.* 67 (2013) 901-934.
- [10] Y. Wang, Y. Zhou, J. Wu, J. Heffernan, Oscillatory viral dynamics in a delayed HIV pathogenesis model, *Math. Biosci.* 219 (2009) 104-112.
- [11] B. Ramratnam, S. Bonhoeffer, J. Binley, A. Hurley, L. Zhang, J.E. Mittler, M. Markowitz, J.P. Moore, A.S. Perelson, D.D. Ho, Rapid production and clearance of HIV-1 and hepatitis c virus assessed by large volume plasma apheresis, *Lancet* 354 (1999) 1782-1785.

- [12] P. Zhong, L.M. Agosto, J.B. Munro, W. Mothes, Cell-to-cell transmission of viruses, *Curr. Opin. Virol.* 3 (2013) 44-50.
- [13] J. Feldmann, O. Schwartz, HIV-1 virological synapse: live imaging of transmission, *Viruses* 2 (2010) 1666-1680.
- [14] W. Hübner, G.P. McNerney, P. Chen, B.M. Dale, R.E. Gordon, F.Y.S. Chuang, X.D. Li, D.M. Asmuth, T. Huser, B.K. Chen, Quantitative 3d video microscopy of HIV transfer across T cell virological synapses, *Science* 323 (2009) 1743-1747.
- [15] Y. Yang, L. Zou, S. Ruan, Global dynamics of a delayed within-host viral infection model with both virus-to-cell and cell-to-cell transmissions, *Math. Biosci.* 270 (2015) 183-191.
- [16] N. Bai, R. Xu, Backward bifurcation and stability analysis in a within-host HIV model with both virus-to-cell infection and cell-to-cell transmission, and anti-retroviral therapy, *Math. Comput. Simul.* 200 (2022) 162-185.
- [17] T.K. Gharahasanlou, V. Roomi, Z. Hemmatzadeh, Global stability analysis of viral infection model with logistic growth rate, general incidence function and cellular immunity, *Math. Comput. Simul.* 194 (2022) 64-79.
- [18] X. Lai, X. Zou, Modeling cell-to-cell spread of HIV-1 with logistic target cell growth, *J. Math. Anal. Appl.* 426 (2015) 563-584.
- [19] X. Lai, X. Zou, Modeling HIV-1 virus dynamics with both virus-to-cell infection and cell-to-cell transmission, *SIAM J. Appl. Math.* 74 (2014) 898-917.
- [20] H. Shu, Y. Chen, L. Wang, Impacts of the virus-to-cell and cell-to-cell infection modes on viral dynamics, *J. Dyn. Differ. Equ.* 30 (2018) 1817-1836.
- [21] H. Yan, Y. Xiao, Q. Yan, X. Liu, Dynamics of an HIV-1 virus model with both virus-to-cell and cell-to-cell transmissions, general incidence rate, intracellular delay, and CTL immune responses, *Math. Method. Appl. Sci.* 42 (2018) 6385-6406.
- [22] M. Lu, Y. Wang, D. Jiang, Stationary distribution and probability density function analysis of a stochastic HIV model with cell-to-cell infection, *Appl. Math. Comput.* 410 (2021) 126483.
- [23] Q. Liu, D. Jiang, Dynamical behavior of a higher order stochastically perturbed HIV/AIDS model with differential infectivity and amelioration, *Chaos Soliton. Fract.* 141 (2020) 110333.
- [24] Y. Wang, K. Qi, D. Jiang, An HIV latent infection model with cell-to-cell transmission and stochastic perturbation, *Chaos Soliton. Fract.* 151 (2021) 111215.
- [25] J. Djordjevic, C.J. Silva, D.F.M. Torres, A stochastic SICA epidemic model for HIV transmission, *Appl. Math. Lett.* 84 (2018) 168-175.
- [26] F. Rao, J. Luo, Stochastic effects on an HIV/AIDS infection model with incomplete diagnosis, *Chaos Soliton. Fract.* 152 (2021) 111344.
- [27] T. Feng, Z. Qiu, X. Meng, L. Rong, Analysis of a stochastic HIV-1 infection model with degenerate diffusion, *Appl. Math. Comput.* 348 (2019) 437-455.
- [28] X. Mao, *Stochastic Differential Equations and their Applications*, Horwood Publishing, Chichester, 1997.
- [29] B. Zhou, D. Jiang, B. Han, T. Hayat, Threshold dynamics and density function of a stochastic epidemic model with media coverage and mean-reverting Ornstein-Uhlenbeck process, *Math. Comput. Simul.* 196 (2022) 15-44.
- [30] N.H. Du, G. Yin, Conditions for permanence and ergodicity of certain stochastic predator-prey models, *J. Appl. Prob.* 53 (2016) 187-202.
- [31] Y. Cai, J. Jiao, Z. Gui, Y. Liu, W. Wang, Environmental variability in a stochastic epidemic model, *Appl. Math. Comput.* 329 (2018) 210-226.
- [32] Y. Lin, D. Jiang, P. Xia, Long-time behavior of a stochastic SIR model, *Appl. Math. Comput.* 236 (2014) 1-9.
- [33] X. Zhang, R. Yuan, A stochastic chemostat model with mean-reverting Ornstein-Uhlenbeck process and Monod-Haldane response function, *Appl. Math. Comput.* 394 (2021) 125833.
- [34] A.Y. Kutoyants, *Statistical Inference for Ergodic Diffusion Processes*, Springer, London, 2003.
- [35] R. Lipster, A strong law of large numbers for local martingales, *Stochastics* 3 (1980) 217-228.

- [36] Z. Ma, Y. Zhou, C. Li, Qualitative and Stability Methods for Ordinary Differential Equations, Science Press, Beijing, 2015. (In Chinese).
- [37] B. Han, B. Zhou, D. Jiang, T. Hayat, A. Alsaedi, Stationary solution, extinction and density function for a high-dimensional stochastic SEI epidemic model with general distributed delay, *Appl. Math. Comput.* 405 (2021) 126236.
- [38] C.W. Gardiner, Handbook of Stochastic Methods for Physics, Chemistry and the Natural Sciences, Springer Berlin, 1983.
- [39] H. Roozen, An asymptotic solution to a two-dimensional exit problem arising in population dynamics, *SIAM J. Appl. Math.* 49 (1989) 1793-1810.
- [40] D.J. Higham, An algorithmic introduction to numerical simulation of stochastic differential equations, *SIAM Rev.* 43 (2001) 525-546.
- [41] R.V. Culshaw, S.G. Ruan, A delay-differential equation model of HIV infection of CD4⁺ T-cells, *Math. Biosci.* 165 (2000) 27-39.
- [42] P.W. Nelson, J.D. Murray, A.S. Perelson, A model of HIV-1 pathogenesis that includes an intracellular delay, *Math. Biosci.* 163 (2000) 201-215.
- [43] R.V. Culshaw, S.G. Ruan, R.J. Spiteri, Optimal HIV treatment by maximising immune response, *J. Math. Biol.* 48 (2004) 545-562.
- [44] N.H.A. Shamrani, A.M. Elaiw, H. Dutta, Stability of a delay-distributed HIV infection model with silent infected cell-to-cell spread and CTL-mediated immunity, *Math. Biosci. Eng.* 135 (2019) 134-136.