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Dynamics of a stochastic tuberculosis model with antibiotic resistance

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ABSTRACT

In this paper, we study a stochastic tuberculosis model with antibiotic resistance. By constructing a suitable stochastic Lyapunov function, we establish sufficient conditions for the existence and uniqueness of an ergodic stationary distribution of the positive solutions to the model. Moreover, we obtain sufficient conditions for extinction of the disease. The existence of a stationary distribution implies stochastic weak stability.

1. Introduction

In recent years, mathematical models have been regarded as a powerful tool in understanding the dynamic spread of tuberculosis (TB) (see e.g. [1–7]) and it has been one of the most major public health problems facing society today. Tuberculosis is a bacterial disease with about one third of the world human population as its reservoir (see e.g. [8,9]) and it remains the leading cause of death by an infectious disease in the world. As we know, tuberculosis is caused by Mycobacterium tuberculosis. The disease is most commonly transmitted from a person suffering from infectious tuberculosis to other persons by infected droplets created when the person with active TB coughs or sneezes.

Antibiotic resistance in pathogenic bacteria can be defined microbiologically or clinically. Microbiological resistance is the presence of a genetically determined resistance mechanism, categorizing the pathogen as resistant or susceptible based on the application of a set cut-off in a phenotypic laboratory text while clinical resistance is a level of antimicrobial activity that is correlated with a high likelihood of therapeutic failure [10]. Antibiotics resistance has accompanied with the introduction of antibiotics since shortly after penicillin was introduced [11]. Due to continuous evolution of new species, multi-antibiotic resistant bacteria has been considered as serious threat to public health and these bacterial strains have already presented in different bacteria species and resulting in increased patient mortality [12]. As we know, incomplete treatment of patients with infectious TB can not only lead to relapse but also to the development of antibiotic resistant TB. Due to its sociological importance, the study of the spread of TB using mathematical models has received much attention (see e.g. [3–5,13]). Especially, Castillo-Chavez and Feng [3] formulated one-strain transmission model to study the dynamics of TB. Their model takes the following form

$$\begin{cases} \dfrac{dS}{dt} = \Lambda - \dfrac{\beta cSI}{N} - \mu S, \\ \dfrac{dL}{dt} = \dfrac{\beta cSI}{N} - (\mu + k + r_1)L + \dfrac{\beta' cTI}{N}, \\ \dfrac{dI}{dt} = kL - (\mu + d)I - r_2 I, \\ \dfrac{dT}{dt} = r_1 L + r_2 I - \dfrac{\beta' cTI}{N} - \mu T, \\ N = S + L + I + T, \end{cases} \tag{1.1}$$

where the host population is divided into the following epidemiological class or subgroups: Susceptibles (S), Latent (L, infected but not infectious), Infectious (I) and (effectively) Treated (T) individuals, N denotes the total population, Λ denotes the recruitment rate; β and β' are rate of transmission that susceptible and treated

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individuals become infected by one infectious individual per contact per unit of time, respectively; c denotes the per-capita contact rate; μ represents the per-capita natural death rate of S, L, I and T, respectively; k is the rate at which an individual leaves the latent class by becoming infectious; d denotes the per-capita disease induced death rate, r_1 and r_2 denote per-capita treatment rates. The parameters involved in system (1.1) are positive constants. The basic reproduction number for system (1.1) is $\mathscr{R}_0 = (\frac{\beta c}{\mu+d+r_2})(\frac{k}{\mu+k+r_1})$ which determines the epidemic occurs or not. If $\mathscr{R}_0 < 1$, system (1.1) has a unique disease-free equilibrium $E^0 = (S^0, 0, 0, 0) = (\frac{\Lambda}{\mu}, 0, 0, 0)$ and it is globally asymptotically stable in the invariant set Γ. While if $\mathscr{R}_0 > 1$, then model (1.1) has two possible equilibria, i.e., the disease-free equilibrium E^0 and the unique positive endemic equilibrium $E^* = (S^*, L^*, I^*, T^*)$, E^0 is unstable and E^* is locally asymptotically stable, where $\Gamma = \{(S, L, I, T) : S > 0, L > 0, I > 0, T > 0, S + L + I + T \le \frac{\Lambda}{\mu}\}$. These results can be found in the literature [3].

Moreover, in an ecosystem, epidemic models are always affected by the environmental noise (see e.g. [14–18]). For human disease related epidemics, the nature of epidemic growth and spread is random due to the unpredictability in person-to-person contacts [19]. Hence the variability and randomness of the environment is fed through the state of the epidemic [20]. In epidemic dynamics, stochastic models may be a more appropriate way of modeling epidemics in many circumstances (see e.g. [21–24]). For instance, stochastic models are able to take care of randomness of infectious contacts occurring in the latent and infectious periods [25]. It also has been shown that some stochastic epidemic models can provide an additional degree of realism in comparison with their deterministic counterparts (see e.g. [14,26–28]). Particularly, Allee et al. [14] revealed that stochastic model should suit the question of disease extinction better. Herwaarden et al. [26] suggested that an endemic equilibrium in a deterministic model can disappear in its corresponding stochastic system due to stochastic fluctuations. And Näsell [27] formulated stochastic models to show that some stochastic models are a better approach to describe epidemics for a large range of realistic parameter values in comparison with their deterministic counterparts.

There exist different approaches to introduce stochastic perturbations into the model, both from a mathematical and biological perspective [28,29]. In this paper, our approach to include stochastic perturbations is similar to that of Imhof and Walcher [16]. Here we assume that stochastic perturbations are of the white noise type which are proportional to S, L, I and T, influenced on the $\frac{dS}{dt}$, $\frac{dL}{dt}$, $\frac{dI}{dt}$ and $\frac{dT}{dt}$ in (1.1). Then corresponding to system (1.1), the stochastic version can be expressed as follows

$$\begin{cases} dS = \left[\Lambda - \dfrac{\beta cSI}{N} - \mu S\right]dt + \sigma_1 S dB_1(t), \\ dL = \left[\dfrac{\beta cSI}{N} - (\mu + k + r_1)L + \dfrac{\beta' cTI}{N}\right]dt + \sigma_2 L dB_2(t), \\ dI = [kL - (\mu + d)I - r_2 I]dt + \sigma_3 I dB_3(t), \\ dT = \left[r_1 L + r_2 I - \dfrac{\beta' cTI}{N} - \mu T\right]dt + \sigma_4 T dB_4(t), \end{cases} \tag{1.2}$$

where $B_i(t)$ are mutually independent standard Brownian motions with $B_i(0) = 0$, $\sigma_i^2 > 0$ denote the intensities of the white noise, $i = 1, 2, 3, 4$.

This paper is organized as follows. In Section 2, we give some known results, definition and lemma which will be used in the following analysis. In Section 3, we show that there exists a unique global positive solution of system (1.2). In Section 4, we prove that there is a unique ergodic stationary distribution of the positive solutions to system (1.2) under certain condition. In Section 5, we establish sufficient conditions for extinction of the disease. Finally, concluding remarks and future directions are provided to end this paper.

2. Preliminaries

In this section, we shall present some known results, definition and lemma which will be used later. Throughout this paper, unless otherwise specified, let $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\ge 0}, \mathbb{P})$ be a complete probability space with a filtration $\{\mathcal{F}_t\}_{t\ge 0}$ satisfying the usual conditions (i.e., it is increasing and right continuous while $\mathcal{F}_0$ contains all $\mathbb{P}$-null sets) and we also let $B_i(t)$ be defined on the complete probability space, $i = 1, 2, 3, 4$. We introduce the following notations:

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

$$\overline{\mathbb{R}}^d_+ = \{x = (x_1, \dots, x_d) \in \mathbb{R}^d : x_i \ge 0, 1 \le i \le d\}.$$

Then we give some basic theory in stochastic differential equations which is introduced in [15].

In general, consider the d-dimensional stochastic differential equation

$$dX(t) = f(X(t))dt + g(X(t))dB(t) \text{ for } t \ge t_0, \tag{2.1}$$

with the initial value $X(0) = X_0 \in \mathbb{R}^d$. $B(t)$ denotes a d-dimensional standard Brownian motion defined on the complete probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\ge 0}, \mathbb{P})$. 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. The differential operator L of Eq. (2.1) is defined by [15]

$$L = \sum_{i=1}^{d} f_i(X, t)\frac{\partial}{\partial X_i} + \frac{1}{2}\sum_{i,j=1}^{d}[g^T(X, t)g(X, t)]_{ij}\frac{\partial^2}{\partial X_i \partial X_j}.$$

If L acts on a function $V \in C^2(\mathbb{R}^d; \overline{\mathbb{R}}_+)$, then

$$LV(X) = V_X(X)f(X) + \frac{1}{2}\text{trace}[g^T(X)V_{XX}(X)g(X)],$$

where $V_X = (\frac{\partial V}{\partial X_1}, \dots, \frac{\partial V}{\partial X_d})$, $V_{XX} = (\frac{\partial^2 V}{\partial X_i \partial X_j})_{d\times d}$. According to Itô's formula [15], if $X(t) \in \mathbb{R}^d$, then

$$dV(X(t)) = LV(X(t))dt + V_X(X(t))g(X(t))dB(t).$$

Definition 2.1 [30]. The transition probability function $P(s, x, t, A)$ is said to be time-homogeneous (and the corresponding Markov process is called time-homogeneous) if the function $P(s, x, t + s, A)$ is independent of s, where $0 \le s \le t$, $x \in \mathbb{R}^d$ and $A \in \mathcal{B}$ and $\mathcal{B}$ denotes the σ-algebra of Borel sets in $\mathbb{R}^d$.

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

$$dX(t) = f(X(t))dt + g(X(t))dB(t).$$

The diffusion matrix of the process $X(t)$ is defined as follows

$$A(x) = (a_{ij}(x)), \quad a_{ij}(x) = g^i(x)g^j(x).$$

Lemma 2.1 *[30]. The Markov process $X(t)$ has a unique ergodic stationary distribution $\pi(\cdot)$ if there exists a bounded open domain $D \subset \mathbb{R}^d$ with regular boundary Γ, having the following properties:*

A_1: there is a positive number M such that $\sum_{i,j=1}^{d} a_{ij}(x)\xi_i\xi_j \ge M|\xi|^2$, $x \in D$, $\xi \in \mathbb{R}^d$.

A_2: there exists a nonnegative C^2-function V such that LV is negative for any $\mathbb{R}^d \setminus D$.

3. Existence and uniqueness of the positive solution

To study the dynamical behavior of a tuberculosis model, the first concern is whether the solution is global and positive. The following result is regarded to the existence and uniqueness of the

global positive solution, which is a prerequisite for investigating the long-time behavior of model (1.2).

Theorem 3.1. *For any initial value $(S_0, L_0, I_0, T_0) \in \mathbb{R}^4_+$, there is a unique positive solution $(S(t), L(t), I(t), T(t))$ of system (1.2) on $t \geq 0$ and the solution will remain in $\mathbb{R}^4_+$ with probability one.*

Proof. Since the coefficients of system (1.2) satisfy the local Lipschitz condition, then for any initial value $(S_0, L_0, I_0, T_0) \in \mathbb{R}^4_+$ there is a unique local solution $(S(t), L(t), I(t), T(t))$ on $[0, \tau_e)$, where τ_e is the explosion time [15]. To prove this solution is global, we only need to verify that $\tau_e = \infty$ a.s. To this end, let $n_0 > 0$ be sufficiently large such that S_0, L_0, I_0 and T_0 all lie within the interval $[\frac{1}{n_0}, n_0]$. For each integer $n > n_0$, define the following stopping time [15]

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

where throughout this paper, we set $\inf\emptyset = \infty$ (as usual $\emptyset$ denotes the empty set). It is easy to see that τ_n is increasing as $n \to \infty$. Let $\tau_\infty = \lim_{n\to\infty} \tau_n$, then $\tau_\infty \leq \tau_e$ a.s. Next, we need to prove $\tau_\infty = \infty$ a.s. If this assertion is false, there is a constant $\widetilde{T} > 0$ and an $\epsilon \in (0, 1)$ such that $\mathbb{P}\{\tau_\infty \leq \widetilde{T}\} > \epsilon$. As a result, there is an integer $n_1 \geq n_0$ such that

$$\mathbb{P}\{\tau_n \leq \widetilde{T}\} \geq \epsilon, \ \ n \geq n_1. \tag{3.1}$$

Define a C^2-function $V : \mathbb{R}^4_+ \to \mathbb{R}_+$ by

$$V(S, L, I, T) = (S - 1 - \ln S) + (L - 1 - \ln L) + (I - 1 - \ln I) + (T - 1 - \ln T).$$

The nonnegativity of this function can be seen from

$$u - 1 - \ln u \geq 0, \ \ \forall u > 0.$$

Making use of Itô's formula to V, we obtain

$$dV = LV(S, L, I, T)dt + \sigma_1(S-1)dB_1(t) + \sigma_2(L-1)dB_2(t) + \sigma_3(I-1)dB_3(t) + \sigma_4(T-1)dB_4(t),$$

where $LV : \mathbb{R}^4_+ \to \mathbb{R}$ is defined by

$$\begin{aligned} LV &= \Big(1 - \frac{1}{S}\Big)\Big(\Lambda - \frac{\beta cSI}{N} - \mu S\Big) + \Big(1 - \frac{1}{L}\Big) \\ &\quad \times \Big(\frac{\beta cSI}{N} - (\mu + k + r_1)L + \frac{\beta' cTI}{N}\Big) + \Big(1 - \frac{1}{I}\Big) \\ &\quad \times (kL - (\mu + d + r_2)I) + \Big(1 - \frac{1}{T}\Big)\Big(r_1 L + r_2 I - \frac{\beta' cTI}{N} - \mu T\Big) \\ &\quad + \frac{\sigma_1^2 + \sigma_2^2 + \sigma_3^2 + \sigma_4^2}{2} \\ &= \Lambda + 4\mu + k + d + r_1 + r_2 - \mu(S + L + I + T) - dI \\ &\quad + \frac{\beta cI}{S+L+I+T} + \frac{\beta' cI}{S+L+I+T} - \frac{\beta cSI}{L(S+L+I+T)} \\ &\quad - \frac{\beta' cTI}{L(S+L+I+T)} - \frac{\Lambda}{S} - \frac{kL}{I} - \frac{r_1 L}{T} - \frac{r_2 I}{T} + \frac{\sigma_1^2+\sigma_2^2+\sigma_3^2+\sigma_4^2}{2} \\ &< \Lambda + 4\mu + k + d + r_1 + r_2 + c(\beta + \beta') + \frac{\sigma_1^2+\sigma_2^2+\sigma_3^2+\sigma_4^2}{2} \\ &:= K, \end{aligned}$$

where K is a positive constant. Hence

$$dV(S, L, I, T) \leq Kdt + \sigma_1(S-1)dB_1(t) + \sigma_2(L-1)dB_2(t) + \sigma_3(I-1)dB_3(t) + \sigma_4(T-1)dB_4(t). \tag{3.2}$$

Integrating the both sides of (3.2) from 0 to $\tau_n \wedge \widetilde{T} = \min\{\tau_n, \widetilde{T}\}$ and then taking the expectation lead to

$$\begin{aligned} &\mathbb{E}V(S(\tau_n \wedge \widetilde{T}), L(\tau_n \wedge \widetilde{T}), I(\tau_n \wedge \widetilde{T}), T(\tau_n \wedge \widetilde{T})) \\ &\quad \leq V(S(0), L(0), I(0), T(0)) + K\mathbb{E}(\tau_n \wedge \widetilde{T}). \end{aligned}$$

Thus

$$\begin{aligned} &\mathbb{E}V(S(\tau_n \wedge \widetilde{T}), L(\tau_n \wedge \widetilde{T}), I(\tau_n \wedge \widetilde{T}), T(\tau_n \wedge \widetilde{T})) \\ &\quad \leq V(S(0), L(0), I(0), T(0)) + K\widetilde{T}. \end{aligned} \tag{3.3}$$

Let $\Omega_n = \{\omega \in \Omega : \tau_n = \tau_n(\omega) \leq T\}$ for $n \geq n_1$ and according to (3.1), we get $\mathbb{P}(\Omega_n) \geq \epsilon$. Note that for every $\omega \in \Omega_n$, there exists $S(\tau_n, \omega)$ or $L(\tau_n, \omega)$ or $I(\tau_n, \omega)$ or $T(\tau_n, \omega)$ equals either n or $\frac{1}{n}$. Consequently, $V(S(\tau_n, \omega), L(\tau_n, \omega), I(\tau_n, \omega), T(\tau_n, \omega))$ is no less than either

$$n - 1 - \ln n \text{ or } \frac{1}{n} - 1 - \ln\frac{1}{n} = \frac{1}{n} - 1 + \ln n.$$

Therefore, we obtain

$$\begin{aligned} &V(S(\tau_n, \omega), L(\tau_n, \omega), I(\tau_n, \omega), T(\tau_n, \omega)) \\ &\quad \geq (n - 1 - \ln n) \wedge \Big(\frac{1}{n} - 1 + \ln n\Big). \end{aligned}$$

According to (3.3), one can get that

$$\begin{aligned} &V(S(0), L(0), I(0), T(0)) + K\widetilde{T} \\ &\quad \geq \mathbb{E}[1_{\Omega_n(\omega)} V(S(\tau_n, \omega), L(\tau_n, \omega), I(\tau_n, \omega), T(\tau_n, \omega))] \\ &\quad \geq \epsilon(n - 1 - \ln n) \wedge \Big(\frac{1}{n} - 1 + \ln n\Big), \end{aligned}$$

where 1_{Ω_n} denotes the indicator function of Ω_n. Letting $n \to \infty$ leads to the contradiction

$$\infty > V(S(0), L(0), I(0), T(0)) + K\widetilde{T} = \infty,$$

and hence we must have $\tau_\infty = \infty$ a.s. This completes the proof. □

4. Stationary distribution and ergodicity

In this section, based on Has'minskii's theory [30], we establish sufficient conditions for the existence and uniqueness of an ergodic stationary distribution, which reveals that the disease will persist.

Theorem 4.1. *Assume that $R_0^S > 1$, then for any initial value $(S_0, L_0, I_0, T_0) \in \mathbb{R}^4_+$, system (1.2) has a unique stationary distribution $\pi(\cdot)$ and it has the ergodic property, where $R_0^S = \frac{\beta ck\mu}{(\mu+\frac{\sigma_1^2}{2})(\mu+k+r_1+\frac{\sigma_2^2}{2})(\mu+d+r_2+\frac{\sigma_3^2}{2})}$.*

Proof. In order to prove Theorem 4.1, it suffices to validate conditions A_1 and A_2 of Lemma 2.1. Now we prove the condition A_1. The diffusion matrix of system (1.2) is given by

$$A = \begin{pmatrix} \sigma_1^2 S^2 & 0 & 0 & 0 \\ 0 & \sigma_2^2 L^2 & 0 & 0 \\ 0 & 0 & \sigma_3^2 I^2 & 0 \\ 0 & 0 & 0 & \sigma_4^2 T^2 \end{pmatrix}.$$

Choosing $M = \min_{(S,L,I,T)\in\overline{D}\subset\mathbb{R}^4_+}\{\sigma_1^2 S^2, \sigma_2^2 L^2, \sigma_3^2 I^2, \sigma_4^2 T^2\}$, one can get that

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

where $\overline{D} = [\frac{1}{k}, k] \times [\frac{1}{k}, k] \times [\frac{1}{k}, k] \times [\frac{1}{k}, k]$, then the condition A_1 of Lemma 2.1 holds.

In view of system (1.2), we define

$$V_1(S, L, I, T) = -\ln S - c_1 \ln L - c_2 \ln I + c_3(S + L + I + T),$$

where c_1, c_2, c_3 are positive constants to be determined later. Making use of Itô's formula, we get

$$\begin{aligned}
LV_1 &= -\frac{\Lambda}{S} - \frac{c_1\beta cSI}{LN} - \frac{c_2kL}{I} - c_3\mu N + \mu + \frac{\sigma_1^2}{2} \\
&\quad + c_1\Big(\mu + k + r_1 + \frac{\sigma_2^2}{2}\Big) + c_2\Big(\mu + d + r_2 + \frac{\sigma_3^2}{2}\Big) \\
&\quad + c_3\Lambda + \frac{\beta cI}{N} - \frac{c_1\beta' cTI}{LN} \\
&\le -2\sqrt{\frac{c_2\Lambda kL}{SI}} - 2\sqrt{\frac{c_1c_3\beta c\mu SI}{L}} + \mu + \frac{\sigma_1^2}{2} \\
&\quad + c_1\Big(\mu + k + r_1 + \frac{\sigma_2^2}{2}\Big) + c_2\Big(\mu + d + r_2 + \frac{\sigma_3^2}{2}\Big) \\
&\quad + c_3\Lambda + \frac{\beta cI}{N} \\
&\le -4\sqrt[4]{c_1c_2c_3\beta\Lambda ck\mu} + \mu + \frac{\sigma_1^2}{2} + c_1\Big(\mu + k + r_1 + \frac{\sigma_2^2}{2}\Big) \\
&\quad + c_2\Big(\mu + d + r_2 + \frac{\sigma_3^2}{2}\Big) + c_3\Lambda + \frac{\beta cI}{N},
\end{aligned}$$

where in the first and second inequalities, we have used the fact that $a + b \ge 2\sqrt{ab}$ for $\forall a, b > 0$. Let

$$c_1\Big(\mu + k + r_1 + \frac{\sigma_2^2}{2}\Big) = c_2\Big(\mu + d + r_2 + \frac{\sigma_3^2}{2}\Big) = c_3\Lambda = \mu + \frac{\sigma_1^2}{2},$$

then we have

$$c_1 = \frac{\mu + \frac{\sigma_1^2}{2}}{\Big(\mu + k + r_1 + \frac{\sigma_2^2}{2}\Big)},\ c_2 = \frac{\mu + \frac{\sigma_1^2}{2}}{\Big(\mu + d + r_2 + \frac{\sigma_3^2}{2}\Big)},\ c_3 = \frac{\mu + \frac{\sigma_1^2}{2}}{\Lambda}.$$

Hence

$$\begin{aligned}
LV_1 &\le -4\sqrt[4]{\frac{(\mu + \frac{\sigma_1^2}{2})^3\beta ck\mu}{(\mu + k + r_1 + \frac{\sigma_2^2}{2})(\mu + d + r_2 + \frac{\sigma_3^2}{2})}} + 4\Big(\mu + \frac{\sigma_1^2}{2}\Big) + \frac{\beta cI}{N} \\
&= -4\Big(\mu + \frac{\sigma_1^2}{2}\Big)\left[\sqrt[4]{\frac{\beta ck\mu}{\Big(\mu + \frac{\sigma_1^2}{2}\Big)\Big(\mu + k + r_1 + \frac{\sigma_2^2}{2}\Big)\Big(\mu + d + r_2 + \frac{\sigma_3^2}{2}\Big)}} - 1\right] \\
&\quad + \frac{\beta cI}{N} \\
&= -4\Big(\mu + \frac{\sigma_1^2}{2}\Big)\Big[(R_0^S)^{\frac{1}{4}} - 1\Big] + \frac{\beta cI}{N} \\
&:= -\lambda + \frac{\beta cI}{N},
\end{aligned} \tag{4.1}$$

where

$$\lambda = 4\Big(\mu + \frac{\sigma_1^2}{2}\Big)[(R_0^S)^{\frac{1}{4}} - 1] > 0.$$

Constructing a C^2-function $Q : \mathbb{R}_+^4 \to \mathbb{R}$ in the following form

$$\begin{aligned}
Q(S, L, I, T) &= MV_1(S, L, I, T) + V_2(S, L, I, T) + V_3(S) + V_4(L) \\
&\quad + V_5(T) + V_6(S, L, I, T),
\end{aligned}$$

where $V_2(S, L, I, T) = \frac{1}{\theta+1}(S + L + I + T)^{\theta+1}$, $V_3(S) = -\ln S$, $V_4(L) = -\ln L$, $V_5(T) = -\ln T$, $V_6(S, L, I, T) = (S + L + I + T)$, θ is a constant satisfying $0 < \theta < \frac{2\mu}{\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2}$ and $M > 0$ is a sufficiently large number satisfying the following condition

$$-M\lambda + C \le -2, \tag{4.2}$$

where

$$\begin{aligned}
B = \sup_{(S,L,I,T)\in\mathbb{R}_+^4} &\Big\{\Lambda(S+L+I+T)^\theta - \frac{1}{2}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\times (S + L + I + T)^{\theta+1}\Big\} < \infty
\end{aligned}$$

and

$$C = \Lambda + B + 3\mu + c(\beta + \beta') + k + r_1 + \frac{\sigma_1^2 + \sigma_2^2 + \sigma_4^2}{2}.$$

Moreover, $Q(S, L, I, T)$ is not only continuous, but also tends to ∞ as (S, L, I, T) approaches the boundary of $\mathbb{R}_+^4$ and as $\|(S, L, I, T)\| \to \infty$, where $\|\cdot\|$ denotes the Euclidean norm of a point in $\mathbb{R}_+^4$. Therefore, it must be lower bounded and achieve this lower bound at a point $(\bar{S}_0, \bar{L}_0, \bar{I}_0, \bar{T}_0)$ in the interior of $\mathbb{R}_+^4$. Then we can define a nonnegative C^2-function $V : \mathbb{R}_+^4 \to \mathbb{R}_+ \cup \{0\}$ as follows

$$\begin{aligned}
V(S, L, I, T) &= Q(S, L, I, T) - Q(\bar{S}_0, \bar{L}_0, \bar{I}_0, \bar{T}_0) \\
&= MV_1 + V_2 + V_3 + V_4 + V_5 + V_6 - Q(\bar{S}_0, \bar{L}_0, \bar{I}_0, \bar{T}_0).
\end{aligned}$$

Applying Itô's formula, we obtain

$$\begin{aligned}
LV_2 &= (S + L + I + T)^\theta[\Lambda - \mu S - \mu L - (\mu + d)I - \mu T] \\
&\quad + \frac{\theta}{2}(S + L + I + T)^{\theta-1}(\sigma_1^2S^2 + \sigma_2^2L^2 + \sigma_3^2I^2 + \sigma_4^2T^2) \\
&\le (S + L + I + T)^\theta[\Lambda - \mu(S + L + I + T)] \\
&\quad + \frac{\theta}{2}(S + L + I + T)^{\theta+1}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2) \\
&= \Lambda(S + L + I + T)^\theta - \Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\quad \times (S + L + I + T)^{\theta+1} \\
&\le B - \frac{1}{2}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big](S + L + I + T)^{\theta+1} \\
&\le B - \frac{1}{2}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\quad \times (S^{\theta+1} + L^{\theta+1} + I^{\theta+1} + T^{\theta+1})
\end{aligned} \tag{4.3}$$

where

$$\begin{aligned}
B = \sup_{(S,L,I,T)\in\mathbb{R}_+^4} &\Big\{\Lambda(S+L+I+T)^\theta - \frac{1}{2}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\times (S + L + I + T)^{\theta+1}\Big\} < \infty.
\end{aligned}$$

We can also obtain that

$$\begin{aligned}
LV_3 &= -\frac{\Lambda}{S} + \frac{\beta cI}{S + L + I + T} + \mu + \frac{\sigma_1^2}{2} \\
&\le -\frac{\Lambda}{S} + \beta c + \mu + \frac{\sigma_1^2}{2},
\end{aligned} \tag{4.4}$$

$$\begin{aligned}
LV_4 &= -\frac{\beta cSI}{L(S + L + I + T)} - \frac{\beta' cTI}{L(S + L + I + T)} + \mu + k + r_1 + \frac{\sigma_2^2}{2} \\
&\le -\frac{\beta cSI}{L(S + L + I + T)} + \mu + k + r_1 + \frac{\sigma_2^2}{2},
\end{aligned} \tag{4.5}$$

$$\begin{aligned}
LV_5 &= -\frac{r_1L}{T} - \frac{r_2I}{T} + \frac{\beta' cI}{S + L + I + T} + \mu + \frac{\sigma_4^2}{2} \\
&\le -\frac{r_2I}{T} + \beta' c + \mu + \frac{\sigma_4^2}{2}
\end{aligned} \tag{4.6}$$

and

$$\begin{aligned}
LV_6 &= \Lambda - \mu(S + L + I + T) - dI \\
&\le \Lambda - \mu(S + L + I + T).
\end{aligned} \tag{4.7}$$

Therefore, in view of (4.1), (4.3)–(4.7), we have

$$\begin{aligned}
LV &\le -M\lambda + \frac{M\beta cI}{S+L+I+T} - \frac{\beta cSI}{L(S+L+I+T)} \\
&\quad - \frac{1}{2}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big](S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) \\
&\quad - \mu(S+L+I+T) - \frac{\Lambda}{S} - \frac{r_2 I}{T} + \Lambda + B + 3\mu + c(\beta+\beta') \\
&\quad + k + r_1 + \frac{\sigma_1^2+\sigma_2^2+\sigma_4^2}{2} \\
&\le -M\lambda + \frac{M\beta cI}{S+L+I+T} - \frac{1}{2}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\quad \times (S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) - 2\Big(\frac{\beta c\mu SI}{L}\Big)^{\frac{1}{2}} - \frac{\Lambda}{S} - \frac{r_2 I}{T} \\
&\quad + \Lambda + B + 3\mu + c(\beta+\beta') + k + r_1 + \frac{\sigma_1^2+\sigma_2^2+\sigma_4^2}{2} \\
&= -M\lambda + \frac{M\beta cI}{S+L+I+T} - \frac{\Lambda}{S} - 2\Big(\frac{\beta c\mu SI}{L}\Big)^{\frac{1}{2}} - \frac{r_2 I}{T} \\
&\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big](S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) \\
&\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big](S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) \\
&\quad + \Lambda + B + 3\mu + c(\beta+\beta') + k + r_1 + \frac{\sigma_1^2+\sigma_2^2+\sigma_4^2}{2} \\
&\le -M\lambda + \frac{M\beta cI}{S+L+I+T} - \frac{\Lambda}{S} - 2\Big(\frac{\beta c\mu SI}{L}\Big)^{\frac{1}{2}} - \frac{r_2 I}{T} \\
&\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big](S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) \\
&\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big](S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) + C,
\end{aligned} \tag{4.8}$$

where

$$C = \Lambda + B + 3\mu + c(\beta+\beta') + k + r_1 + \frac{\sigma_1^2+\sigma_2^2+\sigma_4^2}{2}.$$

Now we are in the position to construct a compact subset D such that the condition A_2 of Lemma 2.1 holds. Define a bounded closed set as follows

$$D = \Big\{(S,L,I,T) \in \mathbb{R}_+^4 : \epsilon \le S \le \frac{1}{\epsilon}, \epsilon^2 \le I \le \frac{1}{\epsilon^2}, \epsilon^4 \le L \le \frac{1}{\epsilon^4}, \epsilon^3 \le T \le \frac{1}{\epsilon^3}\Big\},$$

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

$$-\frac{\Lambda}{\epsilon} + F \le -1, \tag{4.9}$$

$$0 < \epsilon < \frac{1}{M\beta c}, \tag{4.10}$$

$$-2\Big(\frac{\beta c\mu}{\epsilon}\Big)^{\frac{1}{2}} + F \le -1, \tag{4.11}$$

$$-\frac{r_2}{\epsilon} + F \le -1, \tag{4.12}$$

$$-\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{\theta+1}} + F \le -1, \tag{4.13}$$

$$-\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{2(\theta+1)}} + F \le -1, \tag{4.14}$$

$$-\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{4(\theta+1)}} + F \le -1, \tag{4.15}$$

$$-\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{3(\theta+1)}} + F \le -1, \tag{4.16}$$

where F is a positive constant which will be given explicitly in expression (4.18). For convenience, we can divide $\mathbb{R}_+^4 \setminus D$ into eight domains,

$$D_1 = \{(S,L,I,T) \in \mathbb{R}_+^4 : 0 < S < \epsilon\},$$
$$D_2 = \{(S,L,I,T) \in \mathbb{R}_+^4 : 0 < I < \epsilon^2, S \ge \epsilon\},$$
$$D_3 = \{(S,L,I,T) \in \mathbb{R}_+^4 : 0 < L < \epsilon^4, S \ge \epsilon, I \ge \epsilon^2\},$$
$$D_4 = \{(S,L,I,T) \in \mathbb{R}_+^4 : 0 < T < \epsilon^3, I \ge \epsilon^2\},$$

$$D_5 = \Big\{(S,L,I,T) \in \mathbb{R}_+^4 : S > \frac{1}{\epsilon}\Big\},\ D_6 = \Big\{(S,L,I,T) \in \mathbb{R}_+^4 : I > \frac{1}{\epsilon^2}\Big\},$$

$$D_7 = \Big\{(S,L,I,T) \in \mathbb{R}_+^4 : L > \frac{1}{\epsilon^4}\Big\},\ D_8 = \Big\{(S,L,I,T) \in \mathbb{R}_+^4 : T > \frac{1}{\epsilon^3}\Big\}.$$

Obviously, $D^c = D_1 \cup D_2 \cup D_3 \cup D_4 \cup D_5 \cup D_6 \cup D_7 \cup D_8$. Next, we prove that $LV(S,L,I,T) \le -1$ for any $(S,L,I,T) \in D^c$, which is equivalent to proving it on the above eight domains, respectively.

Case 1. If $(S,L,I,T) \in D_1$, in view of (4.8), one can see that

$$\begin{aligned}
LV &\le -\frac{\Lambda}{S} + \frac{M\beta cI}{S+L+I+T} - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\quad \times (S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) + C \\
&\le -\frac{\Lambda}{S} + F \le -\frac{\Lambda}{\epsilon} + F \le -1,
\end{aligned} \tag{4.17}$$

which follows from (4.9) and

$$\begin{aligned}
F = \sup_{(S,L,I,T)\in\mathbb{R}_+^4} \Big\{ &\frac{M\beta cI}{S+L+I+T} - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\times (S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) + C\Big\}.
\end{aligned} \tag{4.18}$$

Case 2. If $(S,L,I,T) \in D_2$, according to (4.8), we get

$$\begin{aligned}
LV &\le -M\lambda + \frac{M\beta cI}{S+L+I+T} + C \\
&\le -M\lambda + \frac{M\beta cI}{S} + C < -M\lambda + \frac{M\beta c\epsilon^2}{\epsilon} + C \\
&= -M\lambda + M\beta c\epsilon + C < -1,
\end{aligned} \tag{4.19}$$

which follows from (4.2) and (4.10).

Case 3. If $(S,L,I,T) \in D_3$, by (4.8), one can obtain that

$$\begin{aligned}
LV &\le -2\Big(\frac{\beta c\mu SI}{L}\Big)^{\frac{1}{2}} + \frac{M\beta cI}{S+L+I+T} \\
&\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\
&\quad \times (S^{\theta+1}+L^{\theta+1}+I^{\theta+1}+T^{\theta+1}) + C \\
&\le -2\Big(\frac{\beta c\mu SI}{L}\Big)^{\frac{1}{2}} + F < -2\Big(\frac{\beta c\mu\epsilon^3}{\epsilon^4}\Big)^{\frac{1}{2}} + F \\
&= -2\Big(\frac{\beta c\mu}{\epsilon}\Big)^{\frac{1}{2}} + F \\
&\le -1,
\end{aligned} \tag{4.20}$$

which follows from (4.11).

Case 4. If $(S, L, I, T) \in D_4$, in view of (4.8), we have

$$\begin{aligned} LV &\le -\frac{r_2 I}{T} + \frac{M\beta cI}{S+L+I+T} - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\ &\quad \times (S^{\theta+1} + L^{\theta+1} + I^{\theta+1} + T^{\theta+1}) + C \\ &\le -\frac{r_2 I}{T} + F < -\frac{r_2\epsilon^2}{\epsilon^3} + F \\ &= -\frac{r_2}{\epsilon} + F \\ &\le -1, \end{aligned} \tag{4.21}$$

which follows from (4.12).

Case 5. If $(S, L, I, T) \in D_5$, from (4.8), we obtain

$$\begin{aligned} LV &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]S^{\theta+1} + \frac{M\beta cI}{S+L+I+T} \\ &\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\ &\quad \times (S^{\theta+1} + L^{\theta+1} + I^{\theta+1} + T^{\theta+1}) + C \\ &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]S^{\theta+1} + F \\ &\quad < -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{\theta+1}} + F \\ &\le -1, \end{aligned} \tag{4.22}$$

which follows from (4.13).

Case 6. If $(S, L, I, T) \in D_6$, according to (4.8), one can obtain that

$$\begin{aligned} LV &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]I^{\theta+1} + \frac{M\beta cI}{S+L+I+T} \\ &\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\ &\quad \times (S^{\theta+1} + L^{\theta+1} + I^{\theta+1} + T^{\theta+1}) + C \\ &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]I^{\theta+1} + F \\ &\quad < -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{2(\theta+1)}} + F \\ &\le -1, \end{aligned} \tag{4.23}$$

which follows from (4.14).

Case 7. If $(S, L, I, T) \in D_7$, by (4.8), we derive

$$\begin{aligned} LV &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]L^{\theta+1} + \frac{M\beta cI}{S+L+I+T} \\ &\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\ &\quad \times (S^{\theta+1} + L^{\theta+1} + I^{\theta+1} + T^{\theta+1}) + C \\ &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]L^{\theta+1} + F \\ &\quad < -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{4(\theta+1)}} + F \\ &\le -1, \end{aligned} \tag{4.24}$$

which follows from (4.15).

Case 8. If $(S, L, I, T) \in D_8$, from (4.8), we have

$$\begin{aligned} LV &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]T^{\theta+1} + \frac{M\beta cI}{S+L+I+T} \\ &\quad - \frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big] \\ &\quad \times (S^{\theta+1} + L^{\theta+1} + I^{\theta+1} + T^{\theta+1}) + C \\ &\le -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]T^{\theta+1} + F \\ &\quad < -\frac{1}{4}\Big[\mu - \frac{\theta}{2}(\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2)\Big]\frac{1}{\epsilon^{3(\theta+1)}} + F \\ &\le -1, \end{aligned} \tag{4.25}$$

which follows from (4.16).

Obviously, from (4.17), (4.19)–(4.25), we can obtain that for a sufficiently small ϵ,

$$LV(S, L, I, T) \le -1, \quad \forall (S, L, I, T) \in \mathbb{R}^4_+ \setminus D.$$

Hence the condition A_2 of Lemma 2.1 holds. It follows from Lemma 2.1 that system (1.2) is ergodic and has a unique stationary distribution $\pi(\cdot)$. This completes the proof. □

5. Extinction of the disease

In this section, we shall establish sufficient conditions for extinction of the disease in the stochastic system (1.2).

Lemma 5.1. *Let $(S(t), L(t), I(t), T(t))$ be the solution of system (1.2) with any initial value $(S_0, L_0, I_0, T_0) \in \mathbb{R}^4_+$. Then*

$$\lim_{t\to\infty} \frac{S(t) + L(t) + I(t) + T(t)}{t} = 0 \ a.s. \tag{5.1}$$

Moreover, if $\mu > \frac{\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2}{2}$, then

$$\begin{aligned} &\lim_{t\to\infty} \frac{1}{t}\int_0^t S(u)dB_1(u) = 0, \lim_{t\to\infty} \frac{1}{t}\int_0^t L(u)dB_2(u) = 0, \\ &\lim_{t\to\infty} \frac{1}{t}\int_0^t I(u)dB_3(u) = 0, \lim_{t\to\infty} \frac{1}{t}\int_0^t T(u)dB_4(u) = 0 \ a.s. \end{aligned} \tag{5.2}$$

We can prove Lemma 5.1 by using the same approaches as that in Lemmas 2.1 and 2.2 of [31] and so we omit it here.

Theorem 5.1. *Let $(S(t), L(t), I(t), T(t))$ be the solution of system (1.2) with any initial value $(S_0, L_0, I_0, T_0) \in \mathbb{R}^4_+$. If $\widehat{R}_0^S < 1$ and $\mu > \frac{\sigma_1^2 \vee \sigma_2^2 \vee \sigma_3^2 \vee \sigma_4^2}{2}$, then the solution $(S(t), L(t), I(t), T(t))$ of system (1.2) satisfies*

$$\begin{aligned} &\limsup_{t\to\infty} \frac{\ln(k(L(t) + T(t)) + (\mu + k)I(t))}{t} \\ &\quad \le \frac{\beta ck}{\mu + k} - \frac{1}{4}\Big\{(2\mu + 2d + \sigma_3^2) \wedge \Big[\frac{\sigma_2^2}{2} \wedge \Big(\mu + \frac{\sigma_4^2}{2}\Big)\Big]\Big\} < 0 \ a.s. \end{aligned}$$

and the distribution of $S(t)$ converges weakly to the measure which has the density

$$f_*(x) = Cx^{-2}x^{-\frac{2\mu}{\sigma_1^2}} e^{-\frac{2\Lambda}{\sigma_1^2 x}},$$

where $\widehat{R}_0^S = \frac{4\beta ck(\mu+k)}{(2\mu+2d+\sigma_3^2)\wedge[\frac{\sigma_2^2}{2}\wedge(\mu+\frac{\sigma_4^2}{2})]}$ *and* $C = \Big[(\frac{2\Lambda}{\sigma_1^2})^{-\frac{2\mu+\sigma_1^2}{\sigma_1^2}} \Gamma(\frac{2\mu+\sigma_1^2}{\sigma_1^2})\Big]^{-1}$.

Proof. Since for any initial value $(S_0, L_0, I_0, T_0) \in \mathbb{R}^4_+$, the solution of system (1.2) is positive, we get

$$dS \le (\Lambda - \mu S)dt + \sigma_1 S dB_1(t).$$

Consider the following 1-dimensional stochastic differential equation

$$d\widetilde{U} = (\Lambda - \mu\widetilde{U})dt + \sigma_1\widetilde{U}dB_1(t). \tag{5.3}$$

It is easy to check that Eq. (5.3) has a stationary solution $\hat{U}(t)$ which has the density $f_*(x) = Cx^{-2}x^{-\frac{2\mu}{\sigma_1^2}} e^{-\frac{2\Lambda}{\sigma_1^2 x}}$, where $C =$

$\left[\left(\frac{2\Lambda}{\sigma_1^2}\right)^{-\frac{2\mu+\sigma_1^2}{\sigma_1^2}}\Gamma\left(\frac{2\mu+\sigma_1^2}{\sigma_1^2}\right)\right]^{-1}$. From the ergodic theorem it follows that

$$\lim_{t\to\infty}\frac{1}{t}\int_0^t S(s)ds=\int_0^\infty xf_*(x)dx \ a.s. \tag{5.4}$$

From SDE (5.3), by direct calculation, we have

$$\int_0^\infty xf_*(x)dx=\mathbb{E}(\widetilde{U}(t))=\frac{\Lambda}{\mu}.$$

Let $\widetilde{u}(t)$ be the solution of SDE (5.3) with the initial value $\widetilde{U}(0)=S(0)>0$, then applying the comparison theorem for stochastic differential equation [32], we obtain

$$S(t)\le\widetilde{U}(t) \ a.s. \tag{5.5}$$

In addition, let $P(t)=k(L(t)+T(t))+(\mu+k)I(t)$. Applying Itô's formula to differentiate $\ln P$ leads to

$$\begin{aligned}
d\ln P(t)=&\left\{\frac{\frac{\beta ckS(t)I(t)}{S(t)+L(t)+I(t)+T(t)}-((\mu+k)(\mu+d)+\mu r_2)I(t)-\mu kT(t)}{k(L(t)+T(t))+(\mu+k)I(t)}\right.\\
&\left.-\frac{k^2\sigma_2^2L^2(t)+k^2\sigma_4^2T^2(t)+(\mu+k)^2\sigma_3^2I^2(t)}{2[k(L(t)+T(t))+(\mu+k)I(t)]^2}\right\}dt\\
&+\frac{k\sigma_2L(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_2(t)\\
&+\frac{k\sigma_4T(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_4(t)\\
&+\frac{(\mu+k)\sigma_3I(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_3(t)\\
\le&\frac{\beta ck}{\mu+k}dt-\frac{1}{[k(L(t)+T(t))+(\mu+k)I(t)]^2}\\
&\times\left\{\left[(\mu+k)^2(\mu+d)+\frac{(\mu+k)^2}{2}\sigma_3^2\right]I^2(t)\right.\\
&\left.+k^2\left[\frac{\sigma_2^2}{2}L^2(t)+\left(\mu+\frac{\sigma_4^2}{2}\right)T^2(t)\right]\right\}dt\\
&+\frac{k\sigma_2L(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_2(t)\\
&+\frac{k\sigma_4T(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_4(t)\\
&+\frac{(\mu+k)\sigma_3I(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_3(t)\\
\le&\frac{\beta ck}{\mu+k}dt-\frac{1}{4}\left\{(2\mu+2d+\sigma_3^2)\wedge\left[\frac{\sigma_2^2}{2}\wedge\left(\mu+\frac{\sigma_4^2}{2}\right)\right]\right\}dt\\
&+\frac{k\sigma_2L(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_2(t)\\
&+\frac{k\sigma_4T(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_4(t)\\
&+\frac{(\mu+k)\sigma_3I(t)}{k(L(t)+T(t))+(\mu+k)I(t)}dB_3(t).
\end{aligned}\tag{5.6}$$

Integrating (5.6) from 0 to t and then dividing by t on both sides, we have

$$\begin{aligned}
&\frac{\ln P(t)}{t}-\frac{\ln P(0)}{t}\\
&\le\frac{\beta ck}{\mu+k}-\frac{1}{4}\left\{(2\mu+2d+\sigma_3^2)\wedge\left[\frac{\sigma_2^2}{2}\wedge\left(\mu+\frac{\sigma_4^2}{2}\right)\right]\right\}\\
&\quad+\frac{k\sigma_2}{t}\int_0^t\frac{L(s)}{k(L(s)+T(s))+(\mu+k)I(s)}dB_2(s)\\
&\quad+\frac{k\sigma_4}{t}\int_0^t\frac{T(s)}{k(L(s)+T(s))+(\mu+k)I(s)}dB_4(s)\\
&\quad+\frac{(\mu+k)\sigma_3}{t}\int_0^t\frac{I(s)}{k(L(s)+T(s))+(\mu+k)I(s)}dB_3(s).
\end{aligned}\tag{5.7}$$

Taking the superior limit on both sides of (5.7) and combining with (5.1), (5.2) and noting that $\widehat{R}_0^S<1$, one can see that

$$\begin{aligned}
&\limsup_{t\to\infty}\frac{\ln P(t)}{t}\\
&\le\frac{\beta ck}{\mu+k}-\frac{1}{4}\left\{(2\mu+2d+\sigma_3^2)\wedge\left[\frac{\sigma_2^2}{2}\wedge\left(\mu+\frac{\sigma_4^2}{2}\right)\right]\right\}<0 \ a.s.,
\end{aligned}$$

which implies that

$$\lim_{t\to\infty}L(t)=0,\ \lim_{t\to\infty}I(t)=0 \text{ and } \lim_{t\to\infty}T(t)=0 \ a.s.$$

Therefore, for any small $\epsilon>0$ there are t_0 and a set $\Omega_\epsilon\subset\Omega$ such that $\mathbb{P}(\Omega_\epsilon)>1-\epsilon$ and $\beta cSI\le\epsilon S$ for $t\ge t_0$ and $\omega\in\Omega_\epsilon$. Now from

$$\begin{aligned}
&\left(\Lambda-\frac{\epsilon S}{S+L+I+T}-\mu S\right)dt+\sigma_1SdB_1(t)\\
&\le dS\le(\Lambda-\mu S)dt+\sigma_1SdB_1(t),
\end{aligned}$$

(5.4) and (5.5), it follows that the distribution of the process $S(t)$ converges to the measure with the density f_*. This completes the proof. □

6. Concluding remarks and future directions

In the present paper, we investigate the dynamical behavior of a stochastic tuberculosis model with antibiotic resistance. By constructing a suitable stochastic Lyapunov function, we establish sufficient conditions for the existence of a unique ergodic stationary distribution of the positive solutions to model (1.2). Furthermore, we also establish sufficient conditions for extinction of the disease. Our results reveal some interesting facts: the smaller white noise can ensure the existence of a unique ergodic stationary distribution which implies the persistence of the disease while the larger white noise can lead to the extinction of the disease.

Some interesting topics deserve further consideration. On the one hand, one may propose some more realistic but complex models, such as considering the effects of impulsive perturbations on system (1.2). The motivation for investigating this is that discontinuity is a common phenomenon and many real phenomena are generally discontinuous, and the most interesting thing concerning the tuberculosis model is its discontinuous properties in time [33]. On the other hand, it is interesting to introduce the colored noise, such as continuous-time Markov chain, into model (1.2). The motivation is that the dynamics of TB may suffer sudden-environmental changes, e.g. temperature, humidity, etc. Frequently, the switching among different environments is memoryless and the waiting time for the next switch is exponentially distributed, then the sudden-environmental changes can be modeled by a continuous-time Markov chain (see e.g. [34–36]). It is also interesting to study more complex tuberculosis models, for example, two-strain TB model. When one studies these problems, new Lyapunov functions need to be constructed and the method of constructing Lyapunov function developed in this paper can be referred. Moreover, our model (1.2) is similar to some existing SEIR, SEI or SIRS models and our model is based on ordinary differential equations, it has some drawbacks in that it neglects the local characteristics of the spreading process and it does not include variable susceptibility of individuals [37]. Specifically, it fails to capture spatial and temporal variations in the risk of transmission of infection. To solve these problems, one can use Agent Based Models (ABM) which can reflect the heterogeneity of real surroundings by giving due consideration to individual properties and raising spatial and time discrete

models of dynamical systems [38]. We leave these investigations for our future work.

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