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DYNAMICAL BEHAVIORS OF A TUMOR-IMMUNE-VITAMIN MODEL WITH RANDOM PERTURBATION

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Abstract This paper mainly explores the stochastic behaviors of the interaction between tumor cells and immune cells when vitamins are added. First, it is shown that the stochastic tumor-immune-vitamin model has a unique global positive solution. Second, we obtain that the solution of our model is stochastically ultimately bounded, stochastically permanent, extinct and persistent in mean under some threshold conditions. Moreover, when the perturbation is weak, the stochastic model has a unique stationary distribution. Finally, numerical simulations are performed to verify the theoretical results.

Keywords Tumor-immune-vitamin model, stochastic process, extinction, persistence, stationary distribution.

MSC(2010) 60H10, 65C20.

1. Introduction

In recent years, with the improvement of medical level and medical devices, some major breakthroughs have been made in many areas of disease research. However, no effective treatment for cancer has yet been found. Traditional treatments cause great pain to cancer patients because of their severe side effects. For example, surgery can cause cancer to return or metastasize. Although radiotherapy or chemotherapy can kill cancer cells, healthy cells can also be greatly affected. As a result, scientists have begun to try immunotherapy to treat cancer, mainly by boosting immunity. For decades, mathematicians have proposed classical mathematical models of immunotherapy to study its dynamical properties [15, 17] in the hope of improving treatment methods. Suzuki [29] focused on the mathematical modeling at different stages of cancer development. Gerisch et al. [9] explored the approaches in the study of multiscale modeling in the life sciences, particularly in mechano and tumor biology. More and more scholars have discussed the tumor-immune model, for instance, see [7, 18, 23, 26, 27, 30, 32] and the references therein. A new deterministic tumor-immune model was proposed and analyzed by Li et al. [18]. They mainly studied the stability at its equilibrium point and carried out the bifurcation analysis. Recently, studies have shown that there is a close relationship between the nutrients (such as the A, B and D group vitamins) and the immune system, and

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proved that vitamins can enhance immunity, which can ensure the normal growth of cells (see [12–14]). Therefore, a tumor-immune-vitamin model was proposed by Alharbi and Rambely [2] as follows.

$$\begin{cases} dx(t) = (\sigma - \delta x + \dfrac{\rho x y}{m+y} - \mu x y + c_2 x v)dt, \\ dy(t) = (\alpha_1 y(1-\alpha_2 y) - \alpha_3 x y - c_1 y v)dt, \\ dv(t) = (k_1 - k_2 v)dt, \end{cases} \tag{1.1}$$

where $x(t)$ and $y(t)$ represent the population of immune cells and tumor cells respectively, $v(t)$ denotes vitamins and the significance of parameters in system (1.1) is shown in Table 1. Furthermore, the parameters of system (1.1) are positive and no bigger than one. The process of vitamin supplementation to assist the treatment of cancer is shown in Figure 1 below.

Table 1. The parameters and their interpretations in model (1.1)

Parameter	Description
σ	A constant source of immune cells produced daily in the human body
δ	Natural mortality rate of immune cells
ρ	Immune response rate
m	Threshold rate of the immune system
μ	The rate of suppression of immune cells
α_1	Growth limit of tumor cells
α_2	Reduction of tumors due to body deformation in dietary metabolisation
α_3	The rate of elimination of tumor cells by immune response
c_1	Effect of vitamins on tumor cells
c_2	Effect of vitamins on immune cells
k_1	Regular rate of vitamins provided by external environment
k_2	The rate at which cells absorb vitamins

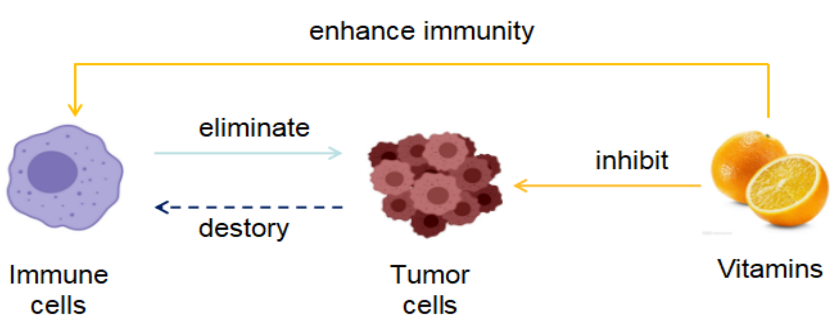

Figure 1. The process of vitamins assisting immunotherapy.

In fact, there are many factors that affect the growth of cancer cells, such as stress, mood, temperature, living habits and so on. It is then reasonable to believe that noise may lead to different therapeutic effects for different patients. In addition, stochastic models have been widely used to study biological and medical models (see [1, 10, 19, 20, 22, 28]). In particular, a growing number of scholars have been engaged in studying the mechanisms of tumor evolution in recent years. Li et al. [21] considered the dynamical behavior of a stochastic tumor-immune model. Their analysis has made a significant contribution to the understanding of the immunotherapy process. Krstić [16] analyzed the asymptotic stability of the stochastic tumor-immune model with time delay by using Lyapunov functions. Therefore, in order to study cancer in depth, it is inevitable to take into account the interference of the external environment, and we are in a position to consider stochastic perturbations. We assume that fluctuations mainly affect the parameters δ and α_1,

$$-\delta dt \to -\delta dt + \sigma_1 dB_1(t), \quad \alpha_1 dt \to \alpha_1 dt + \sigma_2 dB_2(t),$$

where σ_1 and σ_2 represent the intensity of white noises. $B_1(t)$ and $B_2(t)$ are mutually independent 1-dimensional Brown motion. Thus based on system (1.1), we derive the stochastic tumor-immune-vitamin system described as follows.

$$\begin{cases} dx(t) = (\sigma - \delta x + \dfrac{\rho xy}{m+y} - \mu xy + c_2 xv)dt + \sigma_1 x dB_1(t), \\ dy(t) = (\alpha_1 y(1 - \alpha_2 y) - \alpha_3 xy - c_1 yv)dt + \sigma_2 y dB_2(t), \\ dv(t) = (k_1 - k_2 v)dt, \end{cases} \tag{1.2}$$

with initial value $x(0) = x_0 > 0$ and $y(0) = y_0 > 0$. It is worth noting that the last equation is independent of the first two equations. Moreover, we deduce from the third equation that

$$v(t) = \frac{k_1}{k_2} + (v_0 - \frac{k_1}{k_2})e^{-k_2 t}. \tag{1.3}$$

Throughout the paper we assume that $v_0 > \frac{k_1}{k_2}$. Hence system (1.2) can be reduced to

$$\begin{cases} dx(t) = (\sigma - \delta x + \dfrac{\rho xy}{m+y} - \mu xy + c_2 xv)dt + \sigma_1 x dB_1(t), \\ dy(t) = (\alpha_1 y(1 - \alpha_2 y) - \alpha_3 xy - c_1 yv)dt + \sigma_2 y dB_2(t). \end{cases} \tag{1.4}$$

Compared with the stochastic tumor-immune system [21], vitamins are introduced into our model as a more effective treatment. Providing vitamins to immunotherapy patients has fewer side effects and is a more acceptable treatment for cancer patients. However, to the best of our knowledge, the stochastic tumor-immune-vitamin system has not been investigated so far. To fill this gap, we study the dynamical behavior of the stochastic tumor-immune-vitamin system. By choosing suitable Lyapunov functions, we get the existence of the unique global positive solution. And we derive the sufficient conditions for stochastic ultimate boundedness, stochastic permanence, persistence in mean, the existence of the unique invariant measure and extinction.

The rest of this paper is organized as follows. In Section 2, we introduce some notations that will be used throughout the paper. In Section 3, we obtain the existence and uniqueness of the global positive solution for the stochastic model.

In Section 4, we get a sufficient criterion for the stochastic ultimate boundedness of our model. In Section 5, we prove that the solution of system (1.4) is stochastically permanent. Sufficient conditions for the extinction of tumor cells are established in Section 6. In Section 7, we deduce that under certain conditions, our model is persistence in mean. In Section 8, we focus on the ergodicity of tumor and immune cells in system (1.4) which implies the permanence of cells. In addition, we demonstrate the theoretical results by numerical simulations. The last part ends with a conclusion.

2. Preliminaries

To explore the problem discussed above, firstly, we need to define some notations. Let $(\Omega, \mathcal{F}, \mathbb{P})$ be a complete probability space with a filtration $\{\mathcal{F}_t\}_{t\geq 0}$ satisfying the usual conditions. Let $\mathbb{E}$ represent the probability expectation with respect to $\mathbb{P}$. Let $\mathbb{N}_+ = \{1, 2, \cdots\}$ be the set of positive integers and $n,\ m \in \mathbb{N}_+$. $\mathbb{R}^n$ denotes the space of n-dimensional real column vectors and $\mathbb{R}^n_+$ is the set of n-dimensional real column vectors with positive elements, that is $\mathbb{R}^n_+ = \{x \in \mathbb{R}^n | x_i > 0, 1 \leq i \leq n\}$, and we have $\bar{\mathbb{R}}^n_+ = \{x \in \mathbb{R}^n | x_i \geq 0, 1 \leq i \leq n\}$. If $x \in \mathbb{R}^n$, then $|x|$ denotes its Euclidean norm. For a matrix $A \in \mathbb{R}^{n\times m}$, its transpose is denoted by A^T and its trace norm is defined by $|A| = \sqrt{\text{trace}(AA^T)}$. For any $a, b \in \mathbb{R}$, define $a \vee b = \max\{a, b\}$, and $a \wedge b = \min\{a, b\}$. Let $B_i(t)(i = 1, 2, \cdots, n)$ be mutually independent standard one-dimensional Brownian motions and adapted with respect to $\{\mathcal{F}_t\}_{t\geq 0}$. Define

$$[x]^+ = \begin{cases} x, & x \geq 0, \\ 0, & x < 0. \end{cases}$$

Moreover, we let $C^{1,2}(\bar{\mathbb{R}}_+ \times \mathbb{R}^2; \mathbb{R})$ be the family of all real-valued functions $V(t, x)$ defined on $\bar{\mathbb{R}}_+ \times \mathbb{R}^2$, which are continuously once differentiable in t and continuously twice differentiable in x. From the reference [24], we define the differential operator $\mathcal{L}$ associated with equation (1.4). If $\mathcal{L}$ acts on a function $V(t, x) \in C^{1,2}(\bar{\mathbb{R}}_+ \times \mathbb{R}^2; \mathbb{R})$, then

$$\begin{aligned} \mathcal{L}V(t,x,y) =& V_t(t,x,y) + V_x(t,x,y)\Big(\sigma - \delta x + \frac{\rho x y}{m+y} - \mu x y + c_2 x v\Big) + V_y(t,x,y) \\ & \times \Big(\alpha_1 y(1-\alpha_2 y) - \alpha_3 x y - c_1 y v\Big) + \frac{1}{2}\Big(V_{xx}(t,x)\sigma_1^2 x^2 + V_{yy}(t,x)\sigma_2^2 y^2\Big), \end{aligned}$$

where we set

$$\begin{aligned} &V_t(t,x,y) = \frac{\partial V}{\partial t}, \quad V_x(t,x,y) = \frac{\partial V}{\partial x}, \quad V_y(t,x,y) = \frac{\partial V}{\partial y}, \\ &V_{xx}(t,x,y) = \frac{\partial^2 V}{\partial x^2}, \quad V_{yy}(t,x,y) = \frac{\partial^2 V}{\partial y^2}. \end{aligned}$$

For convenience, define

$$\langle\langle f\rangle\rangle_t = \frac{\int_0^t f(s)ds}{t}, \quad f^* = \limsup_{t\to+\infty} f(t), \quad f_* = \liminf_{t\to+\infty} f(t).$$

3. Existence and uniqueness of global positive solution

In order to satisfy the biological significance, firstly, we need to ensure that the cancer model (1.4) has a unique global positive solution. Therefore, we present the proof in this section.

Theorem 3.1. *For any initial value* $(x_0, y_0) \in \mathbb{R}^2_+$*, system* (1.4) *has a unique global positive solution* $(x(t), y(t))$ *on* $t \geq 0$ *with probability one. That is to say,* $(x(t), y(t)) \in \mathbb{R}^2_+$ *for all* $t \geq 0$ *almost surely.*

Proof. For any given initial value $(x_0, y_0) \in \mathbb{R}^2_+$, it is obvious that the coefficients of system (1.4) are locally Lipschitz continuous. According to [25, Theorem 3.3.15], there exists a unique local solution $(x(t), y(t))$ on $t \in [0, \tau_e)$, where τ_e is the explosion time. To prove this solution is global, we need to show that $\tau_e = \infty$ a.s. Let $k_0 \in \mathbb{N}_+$ be sufficiently large so that $x_0 \in (\frac{1}{k_0}, k_0)$, $y_0 \in (\frac{1}{k_0}, k_0)$. For any $k \geq k_0$, $k \in \mathbb{N}_+$, define the following stopping time

$$\tau_k = \inf\Big\{t \in [0, \tau_e) : \min\{x(t), y(t)\} \leq \frac{1}{k} \text{ or } \max\{x(t), y(t)\} \geq k\Big\},$$

where $\emptyset$ denotes the empty set and $\inf \emptyset = \infty$. It is easy to see that τ_k is increasing as $k \to \infty$. We set $\tau_\infty = \lim_{k\to\infty} \tau_k$, then $\tau_\infty \leq \tau_e$ a.s. Exactly, we need to prove $\tau_\infty = \infty$ a.s. If this assertion is false, then there are two constants $T > 0$ and $\epsilon \in (0, 1)$ such that

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

Then, there is an integer $k_1 \geq k_0$ such that

$$\mathbb{P}\{\tau_k \leq T\} \geq \frac{\epsilon}{2}, \quad \text{for all } \ k \geq k_1. \tag{3.1}$$

Define $V : \mathbb{R}^2_+ \to \bar{\mathbb{R}}_+$ by

$$V(x, y) = (x + 1 - \ln x) + (y + 1 - \ln y).$$

By Itô's formula, we obtain

$$dV(x, y) = \mathcal{L}V(x, y)dt + \sigma_1(x - 1)dB_1(t) + \sigma_2(y - 1)dB_2(t). \tag{3.2}$$

For any $u > 0$, $u \leq 2(u + 1 - \ln u)$, we obtain that

$$\begin{aligned}
\mathcal{L}V(x,y) =&(1 - \frac{1}{x})\Big(\sigma - \delta x + \frac{\rho x y}{m + y} - \mu x y + c_2 x v\Big)\\
&+ (1 - \frac{1}{y})\Big(\alpha_1 y(1 - \alpha_2 y) - \alpha_3 x y - c_1 y v\Big) + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2}\\
=&\Big(\sigma + \delta + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + c_1 v\Big) + \Big(\frac{\rho y}{m+y} + c_2 v + \alpha_3\Big)x + (\mu + \alpha_1 + \alpha_1\alpha_2)y\\
&- \delta x - \frac{\sigma}{x} - c_2 v - \alpha_3 x y - c_1 y v - \mu x y - \frac{\rho y}{m + y} - \alpha_1\alpha_2 y^2 - \alpha_1\\
\leq&\Big(\sigma + \delta + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + c_1 v_0\Big) + (\rho + c_2 v_0 + \alpha_3)x + (\mu + \alpha_1 + \alpha_1\alpha_2)y
\end{aligned}$$

$$
\begin{aligned}
&\leq \Big(\sigma + \delta + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + c_1 v_0\Big) + 2(\rho + c_2 v_0 + \alpha_3)(x + 1 - \ln x) \\
&\quad + 2(\mu + \alpha_1 + \alpha_1\alpha_2)(y + 1 - \ln y) \\
&\leq v_1 + v_2 V(x, y),
\end{aligned}
$$

where

$$
v_1 = \sigma + \delta + \frac{\sigma_1^2}{2} + \frac{\sigma_2^2}{2} + c_1 v_0, \;\; v_2 = 2(\rho + c_2 v_0 + \alpha_3 + \mu + \alpha_1 + \alpha_1\alpha_2).
$$

Integrating both sides of (3.2) from 0 to $T \wedge \tau_k$ and taking expectations, by the Gronwall inequality we derive that

$$
\begin{aligned}
\mathbb{E}V(x(T\wedge\tau_k), y(T\wedge\tau_k)) &\leq V(x_0, y_0) + \mathbb{E}\int_0^{T\wedge\tau_k} \Big(v_1 + v_2 V(x(t), y(t))\Big)dt \\
&\leq V(x_0, y_0) + v_1 T + v_2 \mathbb{E}\int_0^{T\wedge\tau_k} V(x(t), y(t))dt \\
&= V(x_0, y_0) + v_1 T + v_2 \mathbb{E}\int_0^{T} I_{[[0,\tau_k]]}(t) V(x(t), y(t))dt \\
&\leq V(x_0, y_0) + v_1 T + v_2 \mathbb{E}\int_0^{T} V(x(t\wedge\tau_k), y(t\wedge\tau_k))dt \\
&= V(x_0, y_0) + v_1 T + v_2 \int_0^{T} \mathbb{E}V(x(t\wedge\tau_k), y(t\wedge\tau_k))dt \\
&\leq (V(x_0, y_0) + v_1 T)e^{v_2 T},
\end{aligned} \tag{3.3}
$$

where $I_A(\cdot)$ is the indicator function of a set A. Set $\Omega_k = \{\omega : \tau_k \leq T\}$ for $k \geq k_1$. Noting that for any $\omega \in \Omega_k$, there is at least one of $x(T\wedge\tau_k)$ and $y(T\wedge\tau_k)$ equals either k or $\dfrac{1}{k}$. It implies that for any $\omega \in \Omega_k$,

$$
V(x(T\wedge\tau_k), y(T\wedge\tau_k)) \geq (k + 1 - \ln k) \wedge (\frac{1}{k} + 1 + \ln k). \tag{3.4}
$$

In view of (3.1), (3.3) and (3.4), we have

$$
\begin{aligned}
(V(x_0, y_0) + v_1 T)e^{v_2 T} &\geq \mathbb{E}[V(x(T\wedge\tau_k), y(T\wedge\tau_k))] \\
&\geq \mathbb{E}[I_{\Omega_k}(\omega) V(x(T\wedge\tau_k), y(T\wedge\tau_k)] \\
&\geq \frac{\epsilon}{2}[(k + 1 - \ln k) \wedge (\frac{1}{k} + 1 + \ln k)].
\end{aligned} \tag{3.5}
$$

On the other hand, letting $k \to +\infty$ leads to $(k + 1 - \ln k) \wedge (\frac{1}{k} + 1 + \ln k) \to \infty$, then we get the contradiction

$$
\infty \leq (V(x_0, y_0) + v_1 T)e^{v_2 T} < \infty.
$$

Therefore, we obtain $\tau_\infty = \infty$ a.s. That is, system (1.4) has a unique global positive solution $(x(t), y(t)) \in \mathbb{R}_+^2$ with probability one for all $t \geq 0$. This proof is complete. $\square$

4. Stochastic ultimate boundedness

In order to prove that the solution of system (1.4) is stochastically ultimately bounded, firstly, we show the moment boundedness of the solution of system (1.4). Now we introduce an auxiliary process $\psi(t)$ as follows.

$$\begin{cases} d\psi(t) = \alpha_1\psi(t)(1-\alpha_2\psi(t))dt + \sigma_2\psi(t)dB_2(t), \\ \psi(0) = y_0 > 0, \end{cases} \tag{4.1}$$

where $B_2(t)$ is the Brown motion defined in (1.4). By utilizing the comparison theorem, one observes that $0 < y(t) \leq \psi(t)$, $t \geq 0$. The following result is taken from [3], we cite it as a lemma.

Lemma 4.1 (Lemma 2.1, [3]). *Let $\psi(t)$ be the solution of* (4.1). *Then it holds that for any $k > 1$,*

$$\mathbb{E}\psi^k(t) \leq \Big[\frac{1}{y_0}e^{-(\alpha_1+\frac{k-1}{2}\sigma_2{}^2)t} + \frac{2\alpha_1\alpha_2}{2\alpha_1+(k-1)\sigma_2{}^2}(1-e^{-(\alpha_1+\frac{k-1}{2}\sigma_2{}^2)t})\Big]^{-k}. \tag{4.2}$$

Therefore, we have

$$\limsup_{t\to+\infty}\mathbb{E}\psi^k(t) \leq j_k := \Big(\frac{2\alpha_1+(k-1)\sigma_2{}^2}{2\alpha_1\alpha_2}\Big)^k, \forall\ k > 1.$$

Now we investigate the properties of the moments of $y(t)$.

Theorem 4.1. *For any $k > 0$, there exists a positive constant $\hat{j_k}$ such that*

$$\limsup_{t\to+\infty}\mathbb{E}[y^k(t)] \leq \hat{j_k},$$

where $\hat{j_k}$ is defined by (4.3).

Proof. Since $0 < y(t) \leq \psi(t)$, for $k > 1$, by Lemma 4.1, we obtain

$$\limsup_{t\to+\infty}\mathbb{E}y^k(t) \leq \limsup_{t\to+\infty}\mathbb{E}\psi^k(t) \leq j_k.$$

For any $0 < k \leq 1$, using the *Hölder* inequality yields that

$$\limsup_{t\to+\infty}\mathbb{E}y^k(t) \leq \limsup_{t\to+\infty}[\mathbb{E}y^2(t)]^{\frac{k}{2}} \leq (j_2)^{\frac{k}{2}}.$$

Combining the above inequalities leads to the desired result for process $y(t)$ with

$$\hat{j_k} = \begin{cases} j_k, & k > 1, \\ (j_2)^{\frac{k}{2}}, & 0 < k \leq 1. \end{cases} \tag{4.3}$$

The proof is complete. □

Theorem 4.2. *If $1 + 2(\delta - c_2v_0)/\sigma_1^2 > 0$, for any $\theta \in (0, 1 + 2(\delta - c_2v_0)/\sigma_1^2)$, $c > [\frac{\rho}{m} - \mu]^+/\alpha_3$, then*

$$\limsup_{t\to+\infty}\mathbb{E}(1 + x(t) + cy(t))^\theta \leq F(c, \theta),$$

where $F(c, \theta)$ is a positive constant depending on c and θ, which is defined by (4.11) *below.*

Proof. Because the proof is complicated, we divide it into three steps.

Step 1. Define the function $f_1(y) = \rho y/(m+y) - (\mu + c\alpha_3)y$, for any $y \geq 0$,

$$f_1'(y) = \frac{-(\mu + c\alpha_3)y^2 - 2(\mu + c\alpha_3)my + (\rho - (\mu + c\alpha_3)m)m}{(m+y)^2}.$$

Let $f_1'(y) = 0$, and we derive two roots: $y_1 = -m - \sqrt{m\rho/(\mu + c\alpha_3)} < 0$, $y_2 = -m + \sqrt{m\rho/(\mu + c\alpha_3)}$. Using the condition $c > [\frac{\rho}{m} - \mu]^+/\alpha_3$, we obtain that $y_2 < 0$. Consequently, for any $y > 0$, we have $f_1'(y) < 0$ and

$$f_1(y) < f_1(0) = 0, \qquad \forall\ y > 0. \tag{4.4}$$

Choosing $\theta \in (0, 1 + 2(\delta - c_2 v_0)/\sigma_1^2)$, define

$$V_1(x,y) = (1 + x + cy)^\theta, \qquad \forall\ (x,y) \in \mathbb{R}_+^2.$$

Then we have that

$$\begin{aligned} \mathcal{L}V_1(x,y) =& \theta(1 + x + cy)^{\theta-1}(\sigma - \delta x + \frac{\rho xy}{m+y} - \mu xy + c_2 xv) + c\theta(1 + x + cy)^{\theta-1} \\ & \times[\alpha_1 y(1 - \alpha_2 y) - \alpha_3 xy - c_1 yv] + \frac{\theta(\theta-1)}{2}(1 + x + cy)^{\theta-2}(\sigma_1^2 x^2 + c^2\sigma_2^2 y^2). \end{aligned} \tag{4.5}$$

The condition $0 < \theta < 1 + 2(\delta - c_2 v_0)/\sigma_1^2$ implies $\delta - c_2 v_0 + (1-\theta)\sigma_1^2/2 > 0$. Choose a positive constant $\gamma := \gamma(\theta)$ sufficiently small such that

$$F_1(\theta) := \delta - c_2 v_0 + \frac{(1-\theta)\sigma_1^2}{2} - \frac{\gamma}{\theta} > 0.$$

By the Itô formula, we get

$$\begin{aligned} d[e^{\gamma t}V_1(x,y)] =& \mathcal{L}[e^{\gamma t}V_1(x,y)]dt + e^{\gamma t}\theta(1 + x + cy)^{\theta-1}\sigma_1 x dB_1(t) \\ & + e^{\gamma t}c\theta(1 + x + cy)^{\theta-1}\sigma_2 y dB_2(t). \end{aligned}$$

Integrating both sides of the above formula from 0 to t yields that

$$\begin{aligned} e^{\gamma t}V_1(x(t), y(t)) =& V_1(x_0, y_0) + \int_0^t \mathcal{L}[e^{\gamma s}V_1(x(s), y(s))]ds \\ & + \int_0^t [e^{\gamma s}\theta(1 + x(s) + cy(s))^{\theta-1}\sigma_1 x(s)]dB_1(s) \\ & + \int_0^t [e^{\gamma s}c\theta(1 + x(s) + cy(s))^{\theta-1}\sigma_2 y(s)]dB_2(s), \end{aligned}$$

and define

$$N_{v_1}(t) := e^{\gamma t}V_1(x(t), y(t)) - V_1(x_0, y_0) - \int_0^t \mathcal{L}[e^{\gamma s}V_1(x(s), y(s))]ds,$$

which is a local martingale. Combining (4.4) and (4.5) yields that

$$\begin{aligned}
\mathcal{L}[e^{\gamma t}V_1(x,y)] =& \gamma e^{\gamma t}(1+x+cy)^\theta + e^{\gamma t}\mathcal{L}(1+x+cy)^\theta \\
=&\theta e^{\gamma t}(1+x+cy)^{\theta-2}\bigg\{\Big[\frac{\rho y}{m+y}-(\mu+c\alpha_3)y-(\delta-c_2v+\frac{(1-\theta)\sigma_1^2}{2} \\
&-\frac{\gamma}{\theta})\Big]x^2+(\frac{\rho y}{m+y}-\delta+\sigma+c_2v+\frac{2\gamma}{\theta})x+\Big[-c(\mu+\alpha_1\alpha_2+\alpha_3 c)y^2 \\
&+(-\mu-\delta c+\frac{\rho c y}{m+y}+c_2cv-c\alpha_3+c\alpha_1-c_1cv+\frac{2c\gamma}{\theta})y\Big]x \\
&-c^2\alpha_1\alpha_2y^3+\Big(c^2\alpha_1-c\alpha_1\alpha_2-c^2c_1v+\frac{\gamma c^2}{\theta}+\frac{(\theta-1)}{2}\sigma_2^2c^2\Big)y^2 \\
&+c(\sigma+\alpha_1-c_1v+\frac{2\gamma}{\theta})y+\sigma+\frac{\gamma}{\theta}\bigg\} \qquad (4.6)\\
\le& \theta e^{\gamma t}(1+x+cy)^{\theta-2}\bigg\{\Big[-(\delta-c_2v_0+\frac{(1-\theta)\sigma_1^2}{2}-\frac{\gamma}{\theta})\Big]x^2 \\
&+(\rho+\sigma+c_2v_0+\frac{2\gamma}{\theta})x+\Big[-c(\mu+\alpha_1\alpha_2+\alpha_3c)y^2 \\
&+(\rho c+c_2cv_0+c\alpha_1+\frac{2c\gamma}{\theta})y\Big]x-c^2\alpha_1\alpha_2y^3+\Big(c^2\alpha_1+\frac{\gamma c^2}{\theta} \\
&+\frac{(\theta-1)c^2\sigma_2^2}{2}\Big)y^2+c(\sigma+\alpha_1+\frac{2\gamma}{\theta})y+\sigma+\frac{\gamma}{\theta}\bigg\} \\
\le& \theta e^{\gamma t}(1+x+cy)^{\theta-2}W(x,y),
\end{aligned}$$

where

$$\begin{aligned}
W(x,y) =& -F_1(\theta)x^2+F_2(c,\theta)x-c^2\alpha_1\alpha_2y^3+(c^2\alpha_1+\frac{\gamma c^2}{\theta}+\frac{(\theta-1)c^2\sigma_2^2}{2})y^2 \\
&+c(\sigma+\alpha_1+\frac{2\gamma}{\theta})y+\sigma+\frac{\gamma}{\theta}, \\
F_2(c,\theta)=&\sup_{y\in\mathbb{R}_+}\bigg\{-c(\mu+\alpha_1\alpha_2+\alpha_3c)y^2+(\rho c+c_2cv_0+c\alpha_1+\frac{2c\gamma}{\theta})y+\rho+\sigma+c_2v_0+\frac{2\gamma}{\theta}\bigg\}.
\end{aligned}$$

Because the coefficients of the highest-order term of x and y in $W(x,y)$ are negative respectively, we obtain

$$\lim_{x^2+y^2\to+\infty}(1+x+cy)^{\theta-2}W(x,y)=-\infty.$$

This together with the continuity of $(1+x+cy)^{\theta-2}W(x,y)$ on $\mathbb{R}_+^2$ implies that

$$F_3(c,\theta):=\theta\cdot\sup_{x,y\in\mathbb{R}_+}\big\{(1+x+cy)^{\theta-2}W(x,y)\big\}<+\infty. \qquad (4.7)$$

Therefore, from (4.6) and (4.7), we obtain

$$\mathcal{L}[e^{\gamma t}V_1(x,y)]\le F_3(c,\theta)e^{\gamma t}. \qquad (4.8)$$

Step 2. We will prove that

$$\mathbb{E}[e^{\gamma t}V_1(x(t),y(t))]=\mathbb{E}V_1(x_0,y_0)+\mathbb{E}\int_0^t\mathcal{L}[e^{\gamma s}V_1(x(s),y(s))]ds.$$

In fact, choose a sufficiently large constant n_0 such that x_0 and y_0 belong to $(1/n_0, n_0)$. For any constant $n \geq n_0$, we define the stopping time

$$\eta_n = \inf\Big\{t \geq 0 \mid \max\{x(t), y(t)\} \geq n\Big\}.$$

Considering η_n is monotonically increasing and therefore it has a limit. Denote $\lim_{n\to+\infty} \eta_n = \eta_\infty$. By the definition of τ_n and Theorem 3.1, we have $\eta_n \geq \tau_n$, and $\tau_\infty = \infty$ *a.s.*, hence $\eta_\infty = \infty$ *a.s.* Owing to the local martingale property, then $\mathbb{E}N_{v_1}(t \wedge \eta_n) = 0$. Namely, for any $t \geq 0$, one has

$$\mathbb{E}[e^{\gamma(t\wedge\eta_n)} V_1(x(t\wedge\eta_n), y(t\wedge\eta_n))] = \mathbb{E}V_1(x_0, y_0) + \mathbb{E}\int_0^{t\wedge\eta_n} \mathcal{L}[e^{\gamma s} V_1(x(s), y(s))]ds. \tag{4.9}$$

From (4.8) and the dominated convergence theorem, it then follows

$$\lim_{n\to+\infty} \mathbb{E}\int_0^{t\wedge\eta_n} \mathcal{L}[e^{\gamma s} V_1(x(s), y(s))]ds = \mathbb{E}\int_0^{t} \mathcal{L}[e^{\gamma s} V_1(x(s), y(s))]ds.$$

By the definition of η_n, it yields that $e^{\gamma(t\wedge\eta_n)}(1 + x(t\wedge\eta_n) + cy(t\wedge\eta_n))^\theta$ is monotonically increasing in n. Letting $n \to +\infty$ leads to

$$\lim_{n\to+\infty} e^{\gamma(t\wedge\eta_n)}(1 + x(t\wedge\eta_n) + cy(t\wedge\eta_n))^\theta = e^{\gamma t}(1 + x(t) + cy(t))^\theta \qquad a.s.$$

By the monotone convergence theorem, we derive that

$$\lim_{n\to+\infty} \mathbb{E}[e^{\gamma(t\wedge\eta_n)}(1 + x(t\wedge\eta_n) + cy(t\wedge\eta_n))^\theta] = \mathbb{E}[e^{\gamma t}(1 + x(t) + cy(t))^\theta].$$

Letting $n \to +\infty$ in (4.9) yields that

$$\mathbb{E}[e^{\gamma t} V_1(x(t), y(t))] = \mathbb{E}V_1(x_0, y_0) + \mathbb{E}\int_0^{t} \mathcal{L}[e^{\gamma s} V_1(x(s), y(s))]ds. \tag{4.10}$$

Step 3. Applying (4.8) and (4.10) implies that

$$\begin{aligned} e^{\gamma t}\mathbb{E}(1 + x(t) + cy(t))^\theta &\leq \mathbb{E}(1 + x_0 + cy_0)^\theta + \mathbb{E}\int_0^t F_3(c,\theta)e^{\gamma s}ds \\ &\leq \mathbb{E}(1 + x_0 + cy_0)^\theta + \frac{F_3(c,\theta)}{\gamma}e^{\gamma t}. \end{aligned}$$

Then

$$\mathbb{E}(1 + x(t) + cy(t))^\theta \leq \mathbb{E}[(1 + x_0 + cy_0)^\theta e^{-\gamma t}] + \frac{F_3(c,\theta)}{\gamma}.$$

Letting $t \to +\infty$ implies that

$$\limsup_{t\to+\infty} \mathbb{E}(1 + x(t) + cy(t))^\theta \leq \frac{F_3(c,\theta)}{\gamma} := F(c,\theta). \tag{4.11}$$

The proof is complete. $\square$

By virtue of the positivity of $y(t)$, we get the following corollary.

Corollary 4.1. If $1+2(\delta-c_2v_0)/\sigma_1^2>0$, for any $\theta\in(0,1+2(\delta-c_2v_0)/\sigma_1^2)$, $c>[\frac{\rho}{m}-\mu]^+/\alpha_3$, then

$$\limsup_{t\to+\infty}\mathbb{E}(1+x(t))^\theta\le F(c,\theta),$$

where $F(c,\theta)$ is defined by (4.11).

Definition 4.1 (Definition 3.1, [31])**.** The solution $X(t)=(x(t),y(t))$ of system (1.4) is said to be stochastically ultimately bounded if for any $\epsilon\in(0,1)$, there is a positive constant $\xi_1=\xi_1(\epsilon)$ such that for any initial value $X(0)=(x_0,y_0)\in\mathbb{R}_+^2$, the solution $X(t)$ of (1.4) has the property that

$$\limsup_{t\to+\infty}\mathbb{P}\left\{|X(t)|>\xi_1\right\}<\epsilon.$$

Making use of the asymptotic moment boundedness of $x(t)$ and $y(t)$, we can yield the stochastic ultimate boundedness of the solutions.

Theorem 4.3. *If $1+2(\delta-c_2v_0)/\sigma_1^2>0$, then for any $p\in(0,1+2(\delta-c_2v_0)/\sigma_1^2)$ and $(x_0,y_0)\in\mathbb{R}_+^2$, the solution $X(t)$ of system (1.4) is stochastically ultimately bounded.*

Proof. For any fixed $c=1+[\frac{\rho}{m}-\mu]^+/\alpha_3$ and $p\in(0,1+2(\delta-c_2v_0)/\sigma_1^2)$. From Theorem 4.1 and Corollary 4.1, one can see that $\limsup\limits_{t\to+\infty}\mathbb{E}y^p(t)\le\hat{j}_p$ and $\limsup\limits_{t\to+\infty}\mathbb{E}x^p(t)\le F(c,p)$. Using the inequality $|X(t)|^p\le 2^{\frac{p}{2}}(x^p(t)+y^p(t))$ yields that

$$\begin{aligned}\limsup_{t\to+\infty}\mathbb{E}|X(t)|^p&\le 2^{\frac{p}{2}}(\limsup_{t\to+\infty}\mathbb{E}x^p(t)+\limsup_{t\to+\infty}\mathbb{E}y^p(t))\\&\le 2^{\frac{p}{2}}[F(c,p)+\hat{j}_p]<+\infty.\end{aligned}$$

Denote $r(p)/2:=2^{\frac{p}{2}}[F(c,p)+\hat{j}_p]$, then for any $\epsilon>0$, there exists $\xi_1=(r(p)/\epsilon)^{\frac{1}{p}}$, applying the Chebyshev inequality implies that

$$\limsup_{t\to+\infty}\mathbb{P}\left\{|X(t)|>\xi_1\right\}\le\frac{\limsup\limits_{t\to+\infty}\mathbb{E}|X(t)|^p}{\xi_1^p}=\frac{\epsilon}{2}<\epsilon.$$

The proof is therefore complete. □

5. Stochastically permanent

In this section, we shall establish the sufficient condition ensuring that system (1.4) is stochastically permanent.

Definition 5.1 (Definition 4.1, [31])**.** System (1.4) is said to be stochastically permanent if for every $\epsilon\in(0,1)$, there is a pair of positive constants $\xi_1=\xi_1(\epsilon)$ and $\xi_2=\xi_2(\epsilon)$ such that for any initial value $X(0)=(x_0,y_0)\in\mathbb{R}_+^2$, the solution $X(t)=(x(t),y(t))$ has the properties that

$$\liminf_{t\to+\infty}\mathbb{P}\left\{|X(t)|\le\xi_1\right\}\ge 1-\epsilon,\quad \liminf_{t\to+\infty}\mathbb{P}\left\{|X(t)|\ge\xi_2\right\}\ge 1-\epsilon.$$

Theorem 5.1. *If $1 + 2(\delta - c_2 v_0)/\sigma_1^2 > 0$, for any initial value $(x_0, y_0) \in \mathbb{R}_+^2$, the solution of system* (1.4) *is stochastically permanent.*

Proof. First, we prove that for any $\epsilon > 0$, there exists $\xi_2 > 0$ such that

$$\liminf_{t\to+\infty} \mathbb{P}\left\{|X(t)| \geq \xi_2\right\} \geq 1 - \epsilon.$$

Define $\widetilde{V_1}(x, y) = x + y$, $(x, y) \in \mathbb{R}_2^+$. By the Itô formula, it follows that

$$\begin{aligned} d\widetilde{V_1}(x,y) = &\left[\sigma - \delta x + \frac{\rho x y}{m+y} - \mu x y + c_2 x v + \alpha_1 y(1 - \alpha_2 y) - \alpha_3 x y - c_1 y v\right] dt \\ &+ \sigma_1 x dB_1(t) + \sigma_2 y dB_2(t). \end{aligned}$$

Next, define $U(x,y) = \frac{1}{\widetilde{V_1}(x,y)}$. Applying the Itô formula, we get

$$\begin{aligned} dU(x,y) =& - U^2(x,y)(dx+dy) + U^3(x,y)[(dx)^2 + (dy)^2] \\ =& \mathcal{L}U(x,y)dt - U^2(x,y)(\sigma_1 x dB_1(t) + \sigma_2 y dB_2(t)), \end{aligned}$$

where

$$\begin{aligned} \mathcal{L}U(x,y) =& - U^2(x,y)\Big[\sigma - \delta x + \frac{\rho x y}{m+y} - \mu x y + c_2 x v + \alpha_1 y(1 - \alpha_2 y) \\ & - \alpha_3 x y - c_1 y v\Big] + U^3(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2]. \end{aligned} \tag{5.1}$$

For any fixed $p > 0$, define $\widetilde{V_2}(x,y) = (1 + U(x,y))^p$. Applying Itô's formula leads to

$$\begin{aligned} d\widetilde{V_2}(x,y) =& p(1+U(x,y))^{p-1} dU(x,y) + \frac{p(p-1)}{2}(1+U(x,y))^{p-2}[dU(x,y)]^2 \\ =& \mathcal{L}(1+U(x,y))^p dt - p(1+U(x,y))^{p-1}U^2(x,y)(\sigma_1 x dB_1(t) + \sigma_2 y dB_2(t)), \end{aligned}$$

where

$$\begin{aligned} \mathcal{L}(1+U(x,y))^p =& p(1+U(x,y))^{p-1}\mathcal{L}U(x,y) + \frac{p(p-1)}{2} U^4(x,y)(1+U(x,y))^{p-2} \\ & \times [(\sigma_1 x)^2 + (\sigma_2 y)^2]. \end{aligned}$$

For any $\gamma > 0$, define $\widetilde{V_3}(x,y) = e^{\gamma t}\widetilde{V_2}(x,y) = e^{\gamma t}(1+U(x,y))^p$. By the Itô formula, we derive that

$$\begin{aligned} d\widetilde{V_3}(x,y) =& \mathcal{L}[e^{\gamma t}(1+U(x,y))^p]dt - e^{\gamma t} p (1+U(x,y))^{p-1} U^2(x,y) \\ & \times (\sigma_1 x dB_1(t) + \sigma_2 y dB_2(t)), \end{aligned} \tag{5.2}$$

where

$$\begin{aligned} \mathcal{L}[e^{\gamma t}(1+U(x,y))^p] =& \gamma e^{\gamma t}(1+U(x,y))^p + e^{\gamma t}\mathcal{L}(1+U(x,y))^p \\ =& e^{\gamma t}(1+U(x,y))^{p-2}[\gamma(1+U(x,y))^2 + Q], \end{aligned}$$

and combining with (5.1) yields

$$
\begin{aligned}
Q =& p(1+U(x,y))\mathcal{L}U(x,y) + \frac{p(p-1)}{2}U^4(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2] \\
=& -pU^2(x,y)\Big[\sigma - \delta x + \frac{\rho xy}{m+y} - \mu xy + c_2 xv + \alpha_1 y(1-\alpha_2 y) - \alpha_3 xy - c_1 yv\Big] \\
& - pU^3(x,y)\Big[\sigma - \delta x + \frac{\rho xy}{m+y} - \mu xy + c_2 xv + \alpha_1 y(1-\alpha_2 y) - \alpha_3 xy - c_1 yv\Big] \\
& + pU^3(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2] + \frac{p(p+1)}{2}U^4(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2] \\
\leq& -p\sigma U^2(x,y) + \delta pxU^2(x,y) + (\mu+\alpha_3)pxyU^2(x,y) + \alpha_1\alpha_2 py^2U^2(x,y) \\
& + pc_1 yvU^2(x,y) + U(x,y)\Big[-p\sigma U^2(x,y) + \delta pxU^2(x,y) + (\mu+\alpha_3)pxyU^2(x,y) \\
& + \alpha_1\alpha_2 py^2U^2(x,y) + pc_1 yvU^2(x,y)\Big] + pU^3(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2] \\
& + \frac{p(p+1)}{2}U^4(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2].
\end{aligned}
$$

By the definition of $U(x,y)$, we obtain

$$
\begin{aligned}
& \delta pxU^2(x,y) \leq \delta(x+y)pU^2(x,y) = p\delta U(x,y), \\
& (\mu+\alpha_3)pxyU^2(x,y) \leq (\mu+\alpha_3)p\frac{(x+y)^2}{4}U^2(x,y) = \frac{(\mu+\alpha_3)p}{4}, \\
& \alpha_1\alpha_2 py^2U^2(x,y) \leq \alpha_1\alpha_2 p(x+y)^2U^2(x,y) = \alpha_1\alpha_2 p, \\
& pc_1 yvU^2(x,y) \leq pc_1 v_0(x+y)U^2(x,y) = pc_1 v_0 U(x,y), \\
& pU^3(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2] \leq \max\left\{\sigma_1^2, \sigma_2^2\right\} p(x+y)^2U^3(x,y) \\
& \qquad\qquad\qquad\qquad\qquad\quad = \max\left\{\sigma_1^2, \sigma_2^2\right\} pU(x,y), \\
& \frac{p(p+1)}{2}U^4(x,y)[(\sigma_1 x)^2 + (\sigma_2 y)^2] \leq \frac{p(p+1)}{2}\max\left\{\sigma_1^2, \sigma_2^2\right\}(x+y)^2U^4(x,y) \\
& \qquad\qquad\qquad\qquad\qquad\qquad\qquad\quad = \frac{p(p+1)}{2}\max\left\{\sigma_1^2, \sigma_2^2\right\}U^2(x,y).
\end{aligned}
$$

Consequently,

$$
\begin{aligned}
Q \leq & -p\sigma U^2(x,y) + \delta pU(x,y) + \frac{(\mu+\alpha_3)p}{4} + \alpha_1\alpha_2 p + pc_1 v_0 U(x,y) \\
& + U(x,y)\Big[-p\sigma U^2(x,y) + \delta pU(x,y) + \frac{(\mu+\alpha_3)p}{4} + \alpha_1\alpha_2 p + pc_1 v_0 U(x,y)\Big] \\
& + \max\left\{\sigma_1^2, \sigma_2^2\right\} pU(x,y) + \frac{p(p+1)}{2}\max\left\{\sigma_1^2, \sigma_2^2\right\}U^2(x,y) \\
= & -p\sigma U^3(x,y) + v_3 U^2(x,y) + v_4 U(x,y) + v_5,
\end{aligned}
$$

where $v_3 = -p\sigma + \delta p + pc_1 v_0 + \frac{p(p+1)}{2}\max\left\{\sigma_1^2, \sigma_2^2\right\}$, $v_4 = \delta p + pc_1 v_0 + \frac{(\mu+\alpha_3)p}{4} + p\alpha_1\alpha_2 + \max\left\{\sigma_1^2, \sigma_2^2\right\} p$ and $v_5 = \alpha_1\alpha_2 p + \frac{(\mu+\alpha_3)p}{4}$. Therefore,

$$
\begin{aligned}
\mathcal{L}[e^{\gamma t}(1+U(x,y))^p] \leq & e^{\gamma t}(1+U(x,y))^{p-2}[\gamma(1+U(x,y))^2 - p\sigma U^3(x,y) \\
& + v_3 U^2(x,y) + v_4 U(x,y) + v_5] \\
\leq & Ge^{\gamma t},
\end{aligned}
$$

where $G = \sup_{U\in\mathbb{R}_+}(1+U(x,y))^{p-2}[\gamma(1+U(x,y))^2 - p\sigma U^3(x,y) + v_3U^2(x,y) + v_4U(x,y) + v_5]$. Integrating both sides of (5.2) from 0 to t and taking expectations yields that

$$\begin{aligned}\mathbb{E}[e^{\gamma t}(1+U(x,y))^p] &= (1+U(x_0,y_0))^p + \mathbb{E}\int_0^t \mathcal{L}[e^{\gamma s}(1+U(x(s),y(s)))^p]ds \\ &\le (1+U(x_0,y_0))^p + \frac{G}{\gamma}e^{\gamma t}.\end{aligned}$$

This implies

$$\limsup_{t\to+\infty}\mathbb{E}U^p(x,y) \le \limsup_{t\to+\infty}\mathbb{E}(1+U(x,y))^p \le \frac{G}{\gamma}.$$

Let $X=(x,y)$, and we derive that

$$(x+y)^p \le 2^p(x^2+y^2)^{\frac{p}{2}} = 2^p|X|^p.$$

Hence

$$\limsup_{t\to+\infty}\mathbb{E}\frac{1}{|X(t)|^p} \le 2^p \limsup_{t\to+\infty}\mathbb{E}\frac{1}{(x+y)^p} \le 2^p\frac{G}{\gamma}.$$

Denote $H := 2^p\frac{G}{\gamma}$. By utilizing the Chebyshev inequality, then for any $\epsilon>0$, there exists $\xi_2 = (\epsilon/2H)^{\frac{1}{p}}$, such that

$$\mathbb{P}\{|X(t)|<\xi_2\} = \mathbb{P}\left\{|X(t)|^{-p} > \xi_2^{-p}\right\} \le \frac{\mathbb{E}|X(t)|^{-p}}{\xi_2^{-p}}.$$

Thus, we obtain

$$\limsup_{t\to+\infty}\mathbb{P}\{|X(t)|<\xi_2\} \le H\xi_2^p = \frac{\epsilon}{2} < \epsilon.$$

That is

$$\liminf_{t\to+\infty}\mathbb{P}\{|X(t)|\ge\xi_2\} \ge 1-\epsilon. \tag{5.3}$$

Due to the proof of Theorem 4.3, then for any $p\in(0,1+2(\delta-c_2v_0)/\sigma_1^2)$, and the above $\epsilon>0$, there exists $\xi_1>0$ such that

$$\limsup_{t\to+\infty}\mathbb{P}\{|X(t)|>\xi_1\} < \epsilon.$$

That is

$$\liminf_{t\to+\infty}\mathbb{P}\{|X(t)|\le\xi_1\} \ge 1-\epsilon. \tag{5.4}$$

The proof is complete. □

Applying the Milstein method in Higham [11] yields the discrete equation as follows

$$\begin{cases} x_{k+1} = x_k + \Big(\sigma - \delta x_k + \dfrac{\rho x_k y_k}{m+y_k} - \mu x_k y_k + c_2 x_k v_k\Big)\Delta t + \sigma_1 x_k\sqrt{\Delta t}b_{1,k} + \dfrac{\sigma_1^2}{2}x_k\Delta t(b_{1,k}^2-1), \\ y_{k+1} = y_k + \Big(\alpha_1 y_k(1-\alpha_2 y_k) - \alpha_3 x_k y_k - c_1 y_k v_k\Big)\Delta t + \sigma_2 y_k\sqrt{\Delta t}b_{2,k} + \dfrac{\sigma_2^2}{2}y_k\Delta t(b_{2,k}^2-1), \\ v_{k+1} = v_k + (k_1 - k_2 v_k)\Delta t. \end{cases}$$

Next, the numerical simulation is carried out to illustrate Theorem 5.1.

Example 5.1. The parameter values in the random model (1.4) are as follows: $\sigma = 0.2$, $\alpha_1 = 0.9$, $\alpha_2 = 0.4$, $\alpha_3 = 0.514$, $c_1 = 0.04$, $c_2 = 0.01$, $\mu = 0.1859$, $\rho = 0.4$, $m = 0.862$, $k_1 = 0.5463$, $k_2 = 0.9757$, $\delta = 0.7$, $\sigma_1 = 0.2$, $\sigma_2 = 0.09$ and $(x_0, y_0, v_0) = (1.22, 1, 0.7)$. Then

$$1 + \frac{2(\delta - c_2 v_0)}{\sigma_1^2} > 0.$$

The condition of Theorem 5.1 is satisfied. Figure 2 depicts that the path of $x(t)$ and $y(t)$ in the deterministic model (1.1) and the stochastic model (1.4), respectively. Figure 3 depicts the path of $|X(t)| = (x(t)+y(t))^{\frac{1}{2}}$ in system (1.4). Figure 4 depicts the path of $x(t)$, $y(t)$ and $v(t)$ in system (1.2). Therefore, this example verifies the theoretical result of Theorem 5.1.

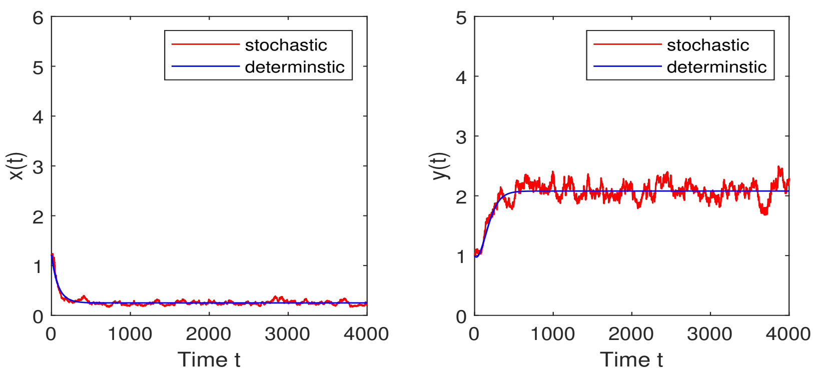

Figure 2. The path of $x(t)$ and $y(t)$ for the stochastic model (1.4) and the deterministic model (1.1).

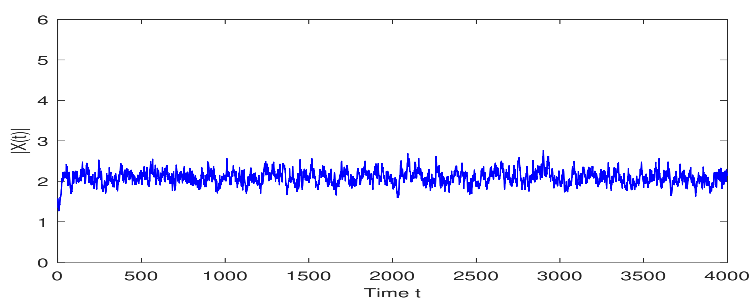

Figure 3. The path of $|X(t)|$ for the stochastic model (1.4), where $X(t) = (x(t), y(t))$.

6. Extinction

Lemma 6.1. *Considering the function* $f_2(y) = \frac{\rho y}{m+y} - \mu y$, $\forall\ y \geq 0$. *We have the following results.*

(i) *If* $\rho \leq m\mu$, *then* $f_2(y) < 0$, $\forall\ y > 0$.

(ii) *If* $\rho > m\mu$, *then* $f_2(y) \leq (\sqrt{\rho} - \sqrt{m\mu})^2$, $\forall\ y > 0$.

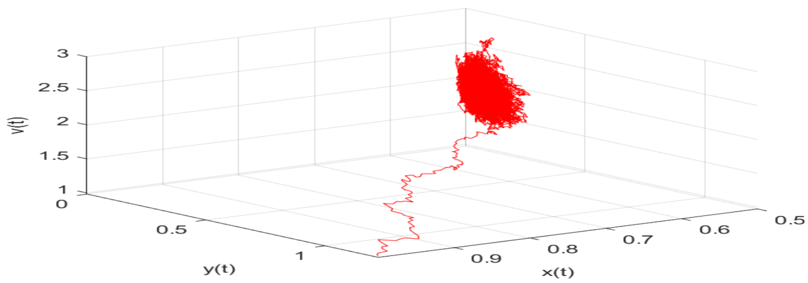

Figure 4. The path of $(x(t), y(t), v(t))$ for the stochastic model (1.2).

Next, we introduce a new auxiliary process $h(t)$ described by

$$\begin{cases} dh(t) = [\sigma - (\delta - \frac{c_2 k_1}{k_2})h(t)]dt + \sigma_1 h(t)dB_1(t), \\ h(0) = x_0 > 0. \end{cases} \tag{6.1}$$

If $\delta - c_2k_1/k_2 > 0$, by solving the Fokker-Planck equation (see details in [6]), the process $h(t)$ has a unique stationary distribution $\vartheta(\cdot)$ which is the inverse Gamma distribution with parameters

$$p_1 = \frac{2(\delta - c_2k_1/k_2)}{\sigma_1^2} + 1, \qquad q_1 = \frac{2\sigma}{\sigma_1^2}.$$

The probability density of $\vartheta(\cdot)$ is

$$f_1^*(x) = \frac{q_1^{p_1}}{\Gamma(p_1)} x^{-(p_1+1)} e^{-\frac{q_1}{x}}, \qquad x > 0.$$

For any $p > 0$, by the strong ergodicity we derive that

$$\lim_{t\to+\infty} \langle\langle h^p \rangle\rangle_t = \int_0^\infty x^p f_1^*(x)dx := \overline{M_p} \qquad a.s. \tag{6.2}$$

Particularly, if $p = 1$, then $\overline{M_1} = \sigma k_2/(k_2\delta - c_2k_1)$. Now we investigate the long-time behaviors of $x(t)$ and $y(t)$ when σ_2 is large sufficiently.

Theorem 6.1. *If $\zeta_1 := \sigma_2^2/2 - \alpha_1 > 0$ and $\delta - c_2k_1/k_2 > 0$, then*

$$\limsup_{t\to+\infty} \frac{\ln y(t)}{t} \le -\zeta_1 \qquad a.s.$$

and the distribution of $x(t)$ converges weakly to the measure $\vartheta(\cdot)$ as $t \to +\infty$.

Proof. Recall the auxiliary process $\psi(t)$ defined by (4.1). By the Itô formula, we have

$$d\ln\psi(t) = [\alpha_1 - \alpha_1\alpha_2\psi(t) - \frac{\sigma_2^2}{2}]dt + \sigma_2 dB_2(t).$$

Integrating both sides of the above formula from 0 to t and dividing both sides by t, we obtain

$$\frac{\ln\psi(t)}{t} - \frac{\ln\psi(0)}{t} \le \alpha_1 - \frac{\sigma_2^2}{2} + \frac{\sigma_2^2 B_2(t)}{t}. \tag{6.3}$$

By the strong law of large numbers, we have $\lim\limits_{t\to+\infty}\frac{B_2(t)}{t}=0$. Hence

$$\limsup_{t\to+\infty}\frac{\ln\psi(t)}{t}\leq\alpha_1-\frac{\sigma_2^2}{2}:=-\zeta_1.$$

Using the comparison theorem implies that

$$\limsup_{t\to+\infty}\frac{\ln y(t)}{t}\leq\limsup_{t\to+\infty}\frac{\ln\psi(t)}{t}\leq-\zeta_1\qquad a.s. \tag{6.4}$$

Consequently, tumor cells will become extinct exponentially with probability one. Next, we will reveal the permanence of effector cells when tumor cells tend to be extinct.

Case 1. If $\rho\leq m\mu$, by Lemma 6.1, we have $f_2(y)<0$. Furthermore,

$$\lim_{t\to+\infty}f_2(y(t))=0\qquad a.s.$$

Then for any $\epsilon>0$, there exists $T_1>0$, such that for any $t\geq T_1$,

$$-\epsilon\leq\frac{\rho y(t)}{m+y(t)}-\mu y(t)<0. \tag{6.5}$$

Because $v(t)=\frac{k_1}{k_2}+(v_0-\frac{k_1}{k_2})e^{-k_2t}$, thus $v(t)$ is monotonically decreasing and $\lim\limits_{t\to+\infty}v(t)=\frac{k_1}{k_2}$. This implies that for the above ϵ, there exists $T_2>0$ such that for any $t\geq T_2$, we have

$$\frac{k_1}{k_2}\leq v(t)\leq\frac{k_1}{k_2}+\epsilon. \tag{6.6}$$

Due to (6.5) and (6.6), denote $T_3=\max\{T_1,T_2\}$. If $t\geq T_3$, then

$$(\sigma-\delta x+c_2\frac{k_1}{k_2}x-\epsilon x)dt+\sigma_1xdB_1(t)\leq dx\leq(\sigma-\delta x+c_2\frac{k_1}{k_2}x+c_2\epsilon x)dt+\sigma_1xdB_1(t). \tag{6.7}$$

Letting $\epsilon\to0$ in (6.7), this yields that the distribution of $x(t)$ converges weakly to $\vartheta(\cdot)$.

Case 2. If $\rho>m\mu$, by Lemma 6.1, we obtain that there exists $y'>0$ such that for any $0\leq y\leq y'$, $f_2(y)>0$. Hence for the above ϵ, there exists $T_4>0$, such that if $t\geq T_4$, then

$$0<\frac{\rho y(t)}{m+y(t)}-\mu y(t)\leq\epsilon. \tag{6.8}$$

We denote $T_5=\max\{T_2,T_4\}$. If $t\geq T_5$, from (6.6) and (6.8) we can derive that

$$\begin{aligned}&(\sigma-\delta x+c_2\frac{k_1}{k_2}x)dt+\sigma_1xdB_1(t)\\ \leq&(\sigma-\delta x+\frac{\rho xy}{m+y}-\mu xy+c_2xv)dt+\sigma_1xdB_1(t)\\ \leq&(\sigma-\delta x+\epsilon x+c_2\frac{k_1}{k_2}x+c_2\epsilon x)dt+\sigma_1xdB_1(t).\end{aligned}$$

This is equivalent to

$$(\sigma - \delta x + c_2 \frac{k_1}{k_2} x)dt + \sigma_1 x dB_1(t) \leq dx \leq (\sigma - \delta x + \epsilon x + c_2 \frac{k_1}{k_2} x + c_2 \epsilon x)dt + \sigma_1 x dB_1(t). \tag{6.9}$$

Letting $\epsilon \to 0$ in (6.9), we can obtain that the distribution of $x(t)$ converges weakly to $\vartheta(\cdot)$. Above all when $t \to +\infty$, we arrive at the distribution of $x(t)$ converges weakly to the measure $\vartheta(\cdot)$. □

Example 6.1. We choose the parameter values in stochastic model (1.4) as follows: $\sigma = 0.7$, $\alpha_1 = 0.4426$, $\alpha_2 = 0.4$, $\alpha_3 = 0.514$, $c_1 = 0.5$, $c_2 = 0.3826$, $\mu = 0.1859$, $\rho = 0.7829$, $m = 0.862$, $k_1 = 0.5463$, $k_2 = 0.9757$, $\delta = 0.57$, $\sigma_1 = 0.1$, $\sigma_2 = 2$ and $(x_0, y_0, v_0) = (1.22, 1, 1)$. Then

$$\frac{\sigma_2}{2} - \alpha_1 = 1.5574 > 0, \ \delta - \frac{c_2 k_1}{k_2} \approx 0.3558 > 0.$$

The condition of Theorem 6.1 is satisfied, which shows that the tumor cells will become extinct. We draw the path of the solution of system (1.4) and its corresponding deterministic system respectively in Figure 5. It is easy to see from Figure 5 that the immune cells can survive while the cancer cells tend to zero. Moreover, it is worth noting that cancer cells in the random state decay significantly faster than those in the deterministic state. This suggests that vitamins do play an important role in the treatment of cancer. This, however, is not the only way. We also need other external methods to enable patients to recover more quickly.

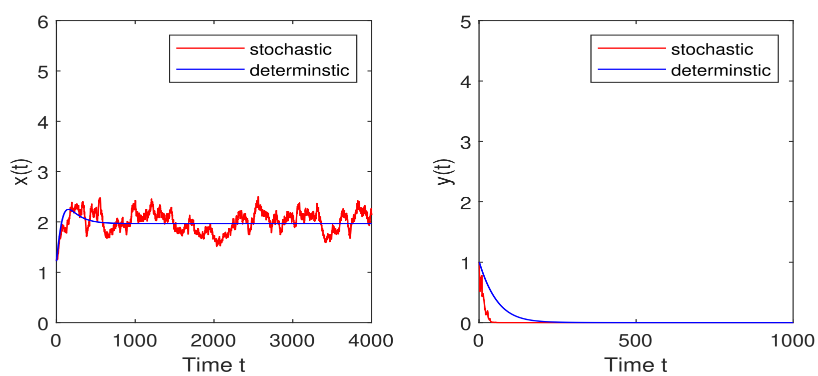

Figure 5. The path of $x(t)$ and $y(t)$ for the stochastic model (1.4) and the corresponding deterministic model (1.1).

7. Persistence in mean

In this section we discuss an important topic, namely persistence in mean [5]. Recall the auxiliary process $\psi(t)$, applying (6.4) yields that if $\alpha_1 < \frac{\sigma_2^2}{2}$, then $\limsup_{t \to +\infty} \psi(t) = 0$. Conversely, if $\alpha_1 > \frac{\sigma_2^2}{2}$, by solving the Fokker-Planck equation (see details in [8]), the process $\psi(t)$ has a unique stationary distribution $\pi(\cdot)$, with probability density $f_2^*(x) = \frac{b_1^{a_1}}{\Gamma(a_1)} x^{a_1 - 1} e^{-b_1 x}$, $x > 0$, where $a_1 = \frac{2\alpha_1}{\sigma_2^2} - 1$ and $b_1 = \frac{2\alpha_1 \alpha_2}{\sigma_2^2}$. We denote that

$\psi(t)$ obeys Gamma distribution $G(a_1, b_1)$. For any $p > 0$, by the strong ergodicity we get

$$\lim_{t\to+\infty} \langle\langle \psi^p \rangle\rangle_t = \int_0^\infty x^p f_2^*(x)dx := \overline{N_p} \qquad a.s. \tag{7.1}$$

Especially, if $p = 1$, we have $\overline{N_1} = (\alpha_1 - \frac{\sigma_2^2}{2})/(\alpha_1\alpha_2)$. Using the Itô formula implies

$$d\ln\psi(t) = \alpha_1(1 - \alpha_2\psi(t))dt + \sigma_2 dB_2(t) - \frac{\sigma_2^2}{2}dt.$$

Integrating both sides of the above formula from 0 to t, we have

$$\ln\psi(t) = \ln\psi(0) + \int_0^t \Big(\alpha_1 - \frac{\sigma_2^2}{2} - \alpha_1\alpha_2\psi(s)\Big)ds + \sigma_2 B_2(t).$$

Dividing both sides by t, from (7.1) and the strong law of large numbers we derive that

$$\lim_{t\to+\infty} \frac{\ln\psi(t)}{t} = 0.$$

Using the comparison theorem implies that

$$\limsup_{t\to+\infty} \frac{\ln y(t)}{t} \le 0 \qquad a.s. \tag{7.2}$$

Letting $r := \delta - c_2 v_0$ and $h := (\sqrt{\rho} - \sqrt{m\mu}) \vee 0$, by utilizing Lemma 6.1, one observes that $f_2(y) \le h^2$, $\forall\ y > 0$. We now introduce an auxiliary process $\varphi(t)$ described by

$$\begin{cases} d\varphi(t) = [\sigma - (r - h^2)\varphi(t)]dt + \sigma_1\varphi(t)dB_1(t), \\ \varphi(0) \ \ = x_0 > 0. \end{cases} \tag{7.3}$$

Similar to the process $h(t)$, we obtain $\varphi(t)$ has a unique stationary distribution, which is the inverse Gamma distribution with parameters $p_2 = 2(r - h^2)/\sigma_1^2 + 1$ and $q_2 = 2\sigma/\sigma_1^2$. The probability density of $\varphi(t)$ is

$$f_3^*(x) = \frac{q_2^{p_2}}{\Gamma(p_2)} x^{-(p_2+1)} e^{-\frac{q_2}{x}}, \qquad x > 0.$$

For any $p > 0$, by the strong ergodicity, we derive that

$$\lim_{t\to+\infty} \langle\langle \varphi^p \rangle\rangle_t = \int_0^\infty x^p f_3^*(x)dx := \overline{C_p} \qquad a.s. \tag{7.4}$$

In particular, when $p = 1$, we have $\overline{C_1} = \sigma/\big(r - h^2\big)$. The stationary distribution of $\varphi^{-1}(t)$ is the Gamma distribution with parameters p_2 and q_2 (see details in [8]), and

$$\lim_{t\to+\infty} \langle\langle \varphi^{-1} \rangle\rangle_t = \frac{2(r - h^2) + \sigma_1^2}{2\sigma} \qquad a.s. \tag{7.5}$$

Applying the Itô formula yields that

$$d\ln\varphi(t) = \Big(\frac{\sigma}{\varphi(t)} - (r - h^2)\Big)dt + \sigma_1 dB_1(t) - \frac{\sigma_1^2}{2}dt.$$

Integrating both sides of the above formula from 0 to t, we have

$$\ln\varphi(t) = \ln\varphi(0) + \int_0^t \Big(\frac{\sigma}{\varphi(s)} - r + h^2 - \frac{\sigma_1^2}{2}\Big)ds + \sigma_1 B_1(t).$$

Dividing both sides by t, by (7.5) and the strong law of large numbers, we derive that

$$\lim_{t\to+\infty} \frac{\ln\varphi(t)}{t} = 0.$$

Applying the comparison theorem implies that

$$\limsup_{t\to+\infty} \frac{\ln x(t)}{t} \le 0 \qquad a.s. \tag{7.6}$$

Next we will prove that under certain conditions $y(t)$ is persistence in mean.

Theorem 7.1. *If $r - h^2 > 0$ and $\alpha_1 - \sigma_2^2/2 - c_2 v_0 - \sigma\alpha_3/(r - h^2) > 0$, then*

$$\lambda_1 \le \langle\langle y\rangle\rangle_* \le \langle\langle y\rangle\rangle^* \le \lambda_2 \quad a.s.$$

where $\lambda_1 = \frac{1}{\alpha_1\alpha_2}(\alpha_1 - \frac{\sigma_2^2}{2} - c_2 v_0 - \frac{\sigma\alpha_3}{r-h^2})$ and $\lambda_2 = \frac{1}{\alpha_1\alpha_2}(\alpha_1 - \frac{\sigma_2^2}{2})$.

Proof. For any initial value $(x_0, y_0) \in \mathbb{R}_+^2$, by the Itô formula we have

$$d\ln y(t) =(\alpha_1(1-\alpha_2 y(t)) - \alpha_3 x(t) - c_1 v(t))dt + \sigma_2 dB_2(t) - \frac{\sigma_2^2}{2}dt.$$

Integrating both sides of the above formula from 0 to t, and dividing both sides by t, and since $0 < x(t) \le \varphi(t)$, we derive that

$$\frac{\ln y(t)}{t} \ge \frac{\ln y_0}{t} + \alpha_1 - \frac{\sigma_2^2}{2} - c_1 v_0 - \frac{\alpha_1\alpha_2}{t}\int_0^t y(s)ds - \frac{\alpha_3}{t}\int_0^t \varphi(s)ds + \frac{\sigma_2 B_2(t)}{t}.$$

Letting $t \to +\infty$, from (7.2) and (7.4) it follows that

$$\langle\langle y\rangle\rangle_* \ge \frac{1}{\alpha_1\alpha_2}(\alpha_1 - \frac{\sigma_2^2}{2} - c_1 v_0 - \frac{\sigma\alpha_3}{r-h^2}) \quad a.s.$$

Moreover, $0 < y(t) \le \psi(t)$, $\forall\, t \ge 0$. From (7.1), we obtain

$$\langle\langle y^p\rangle\rangle^* \le \langle\langle \psi^p\rangle\rangle^* := \overline{N_p} \quad a.s.$$

When $p = 1$, we have

$$\langle\langle y\rangle\rangle^* \le \langle\langle \psi\rangle\rangle^* = \frac{1}{\alpha_1\alpha_2}(\alpha_1 - \frac{\sigma_2^2}{2}) \qquad a.s.$$

Then we arrive at

$$\frac{1}{\alpha_1\alpha_2}(\alpha_1 - \frac{\sigma_2^2}{2} - c_1 v_0 - \frac{\sigma\alpha_3}{r-h^2}) \le \langle\langle y\rangle\rangle_* \le \langle\langle y\rangle\rangle^* \le \frac{1}{\alpha_1\alpha_2}(\alpha_1 - \frac{\sigma_2^2}{2}).$$

□

Now it is time for us to reveal a sufficient condition for $1/x(t)$ to be persistent in mean.

Theorem 7.2. *If $\alpha_1 > \sigma_2^2/2$, then*

$$\lambda_3 \leq \langle\langle x^{-1}\rangle\rangle_* \leq \langle\langle x^{-1}\rangle\rangle^* \leq \lambda_4 \quad a.s.$$

where $\lambda_3 = \frac{1}{\sigma}\left(\delta + \frac{\sigma_1^2}{2} - \rho - c_2 v_0\right) \vee 0$ *and* $\lambda_4 = \frac{1}{\sigma}\left[\frac{\mu(\alpha_1 - \sigma_2^2/2)}{\alpha_1\alpha_2} + \delta + \frac{\sigma_1^2}{2}\right]$.

Proof. Using the Itô formula, we derive that

$$d\ln x(t) = (\frac{\sigma}{x} - \delta + \frac{\rho y}{m+y} - \mu y + c_2 v - \frac{\sigma_1^2}{2})dt + \sigma_1 dB_1(t). \tag{7.7}$$

Integrating both sides of the above formula from 0 to t, we get

$$\begin{aligned} \ln x(t) \leq & \ \ln x_0 + \int_0^t \frac{\sigma}{x(s)}ds + (\rho + c_2 v_0 - \delta - \frac{\sigma_1^2}{2})t + \sigma_1 B_1(t) \\ = & \int_0^t \frac{\sigma}{x(s)}ds + Q_1(t), \end{aligned} \tag{7.8}$$

where $Q_1(t) = \ln x_0 + (\rho + c_2 v_0 - \delta - \frac{\sigma_1^2}{2})t + \sigma_1 B_1(t)$. By the strong law of large numbers we deduce that

$$\lim_{t\to+\infty} \frac{Q_1(t)}{t} = \rho + c_2 v_0 - \delta - \frac{\sigma_1^2}{2} \qquad a.s.$$

Hence, let $\Omega_1 \in \mathcal{F}$, and we have $\mathbb{P}(\Omega_1) = 1$. For any $\epsilon > 0$, any $\omega \in \Omega_1$, there exists $T_6 = T_6(\epsilon, \omega) > 0$, such that

$$\frac{Q_1(t)}{t} \leq \rho + c_2 v_0 - \delta - \frac{\sigma_1^2}{2} + \epsilon, \qquad \forall\ t \geq T_6.$$

Substituting the above formula into (7.8) yields that

$$\ln x(t) \leq (\rho + c_2 v_0 - \delta - \frac{\sigma_1^2}{2} + \epsilon)t + \int_0^t \frac{\sigma}{x(s)}ds. \tag{7.9}$$

Denote

$$z(t) := \int_0^t \frac{1}{x(s)}ds,\ \ m_1 := \rho + c_2 v_0 - \delta - \frac{\sigma_1^2}{2}.$$

Together with (7.9) we deduce that

$$e^{\sigma z(t)}\frac{dz(t)}{dt} \geq e^{-(m_1+\epsilon)t}, \qquad \forall\ t \geq T_6.$$

Integrating both sides of the above formula from T_6 to t, we derive that

$$\frac{1}{\sigma}(e^{\sigma z(t)} - e^{\sigma z(T_6)}) \geq -\frac{1}{m_1+\epsilon}(e^{-(m_1+\epsilon)t} - e^{-(m_1+\epsilon)T_6}), \qquad \forall\ t \geq T_6.$$

This is equivalent to

$$e^{\sigma z(t)} \geq e^{\sigma z(T_6)} - \frac{\sigma}{m_1+\epsilon}(e^{-(m_1+\epsilon)t} - e^{-(m_1+\epsilon)T_6}), \qquad \forall\ t \geq T_6.$$

Taking logarithms on both sides of the above formula, we have

$$z(t) \geq \frac{1}{\sigma} \ln \Big[e^{\sigma z(T_6)} - \frac{\sigma}{m_1+\epsilon}(e^{-(m_1+\epsilon)t} - e^{-(m_1+\epsilon)T_6}) \Big], \qquad \forall\ t \geq T_6.$$

Dividing both sides by t and letting $t \to +\infty$, and using $\mathrm{L}'\mathrm{Hopital}'\mathrm{s}$ rule we arrive at

$$\langle\langle x^{-1}\rangle\rangle_* \geq \frac{-(m_1+\epsilon)}{\sigma} \quad a.s.$$

Since ϵ is arbitrary, we obtain that

$$\langle\langle x^{-1}\rangle\rangle_* \geq \frac{-m_1}{\sigma} = \frac{\delta + \frac{\sigma_1^2}{2} - \rho - c_2 v_0}{\sigma} \quad a.s.$$

Due to the positivity of $x(t)$, one observes

$$\langle\langle x^{-1}\rangle\rangle_* \geq \frac{\delta + \frac{\sigma_1^2}{2} - \rho - c_2 v_0}{\sigma} \vee 0 \quad a.s. \tag{7.10}$$

On the other hand, for any initial value $(x_0, y_0) \in \mathbb{R}_+^2$, by utilizing $\psi(t)$, we have $0 < y(t) \leq \psi(t)$ *a.s.* Integrating both sides of (7.7) from 0 to t, and dividing both sides by t yields that

$$\frac{\ln x(t)}{t} \geq \frac{\ln x_0}{t} + \frac{1}{t}\int_0^t \frac{\sigma}{x(s)} ds - \frac{1}{t}\int_0^t \mu\psi(s) ds - (\delta + \frac{\sigma_1^2}{2}) + \frac{\sigma_1 B_1(t)}{t}.$$

From (7.1) and (7.6) it follows that

$$\langle\langle x^{-1}\rangle\rangle^* \leq \frac{1}{\sigma}\Big[\frac{\mu}{\alpha_1\alpha_2}(\alpha_1 - \frac{\sigma_2^2}{2}) + \delta + \frac{\sigma_1^2}{2}\Big] \quad a.s. \tag{7.11}$$

The proof is therefore complete. □

Example 7.1. We choose the parameter values in the stochastic model (1.4) as follows: $\sigma = 0.2$, $\alpha_1 = 0.9$, $\alpha_2 = 0.4$, $\alpha_3 = 0.514$, $c_1 = 0.04$, $c_2 = 0.01$, $\mu = 0.1859$, $\rho = 0.4$, $m = 0.862$, $k_1 = 0.5463$, $k_2 = 0.9757$, $\delta = 0.7$, $\sigma_1 = 0.2$, $\sigma_2 = 0.25$ and $(x_0, y_0, v_0) = (1.22, 1, 0.7)$, then

$$\begin{aligned} &\delta + \frac{\sigma_1^2}{2} - \rho - c_2 v_0 = 0.313 > 0,\ \alpha_1 - \frac{\sigma_2^2}{2} = 0.86875 > 0, \\ &r - h^2 \approx 0.6391 > 0,\ \alpha_1 - \frac{\sigma_2^2}{2} - c_2 v_0 - \frac{\sigma\alpha_3}{r - h^2} \approx 0.7009 > 0. \end{aligned}$$

Hence the conditions of Theorem 7.1 and Theorem 7.2 are satisfied. Figure 6 depicts the path of the time mean of $1/x(t)$ and $y(t)$ for the stochastic model (1.4), respectively.

8. Existence and uniqueness of invariant measure

Now we prove the existence and uniqueness of invariant measure of system (1.4) under weak noises.

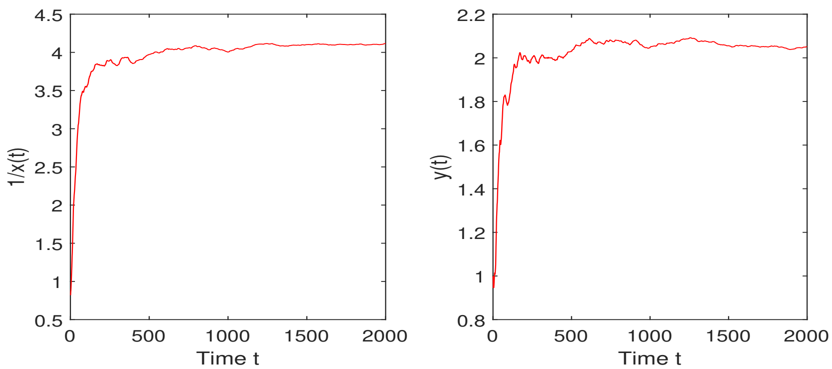

Figure 6. The path of the time mean of $1/x(t)$ and $y(t)$ for the stochastic model (1.4), respectively.

Theorem 8.1. *If $r > h^2$ and $\alpha_1 - \sigma_2^2/2 - c_1v_0 - \sigma/(r-h^2) > 0$, then the solution $(x(t), y(t))$ of system (1.4) has a unique invariant measure $\vartheta_1(\cdot)$ with support set $\mathbb{R}_+^2$.*

Proof. Denote $2\eta := (r-h^2)(\alpha_1 - \sigma_2^2/2 - c_1v_0) - \sigma$. If $r > h^2$ and $\alpha_1 - \sigma_2^2/2 - c_1v_0 - \sigma/(r-h^2) > 0$, we know that $\eta > 0$. Obviously, choose a constant c small sufficiently, such that

$$c(\delta + \sigma_1^2)^2 \leq \sigma\eta. \tag{8.1}$$

Define $U_1(x, y) : \mathbb{R}_+^2 \to \mathbb{R}_+$ by

$$U_1(x, y) = x + \frac{c}{x} + y^2 + (r-h^2)\ln(1 + \frac{1}{y}).$$

Computing $\mathcal{L}U_1(x, y)$ yields that

$$\begin{aligned}\mathcal{L}U_1(x, y) = \sigma &+ \frac{\rho xy}{m+y} - \mu xy - \delta x + c_2xv - c(\frac{\sigma}{x^2} + \frac{\rho y}{x(m+y)} - \frac{\mu y}{x} - \frac{\sigma_1^2 + \delta}{x} \\ &+ \frac{c_2v}{x}) + (\sigma_2^2 + 2\alpha_1)y^2 - 2\alpha_1\alpha_2y^3 - 2\alpha_3xy^2 - 2c_1vy^2 \\ &+ (r-h^2)\Big(\frac{-\sigma_2^2}{2(y+1)^2} - \frac{\alpha_1 - \alpha_3x - \sigma_2^2}{y+1} + \frac{\alpha_1\alpha_2y}{y+1} + \frac{c_1v}{y+1}\Big).\end{aligned}$$

Furthermore,

$$\frac{\mu y}{x} \leq \frac{\sigma}{2x^2} + \frac{\mu^2y^2}{2\sigma}.$$

Noting that Lemma 6.1, we have $f_2(y) \leq h^2$, $\forall\ y > 0$. By utilizing $r > h^2$, we deduce that

$$\begin{aligned}\mathcal{L}U_1(x, y) \leq [\sigma - (r-h^2)x] &- \frac{c\sigma}{2x^2} + \frac{c(\sigma_1^2 + \delta)}{x} + (2\alpha_1 + \sigma_2^2 + \frac{c\mu^2}{2\sigma})y^2 - 2\alpha_1\alpha_2y^3 \\ &+ (r-h^2)\Big(\frac{-\sigma_2^2}{2(y+1)^2} - \frac{\alpha_1 - \alpha_3x - \sigma_2^2}{y+1} + \frac{(\alpha_1\alpha_2 + c_1v_0)y}{y+1}\Big).\end{aligned}$$

One can see that

$$\lim_{x\to+\infty,\ y\to+\infty} \mathcal{L}U_1(x, y) = -\infty. \tag{8.2}$$

Then there exist positive constants G_x^1 and G_y^1 such that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad \forall\ x \ge G_x^1,\ y \ge G_y^1. \tag{8.3}$$

Besides, we see that

$$\lim_{x\to 0^+,\ y\to +\infty} \mathcal{L}U_1(x,y) = -\infty,$$

which implies that there exist positive constants $g_x^1 < G_x^1$ and $G_y^2 \ge G_y^1$ such that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad 0 < x \le g_x^1,\ y \ge G_y^2. \tag{8.4}$$

Moreover,

$$\lim_{y\to +\infty} \mathcal{L}U_1(x,y) = -\infty, \qquad g_x^1 < x < G_x^1,$$

which means that there exists a positive constant $G_y \ge G_y^2$ such that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad g_x^1 < x < G_x^1,\ y \ge G_y. \tag{8.5}$$

By (8.3), (8.4) and (8.5) we see that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad \forall\ x > 0,\ y \ge G_y. \tag{8.6}$$

Notice that

$$\lim_{x\to 0^+} \mathcal{L}U_1(x,y) = -\infty, \qquad 0 < y < G_y,$$

which implies that there exists a positive constant g_x such that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad 0 < x \le g_x,\ 0 < y < G_y. \tag{8.7}$$

Obviously,

$$\lim_{x\to +\infty,\ y\to 0^+} \mathcal{L}U_1(x,y) \le -2\eta,$$

we therefore derive that there exist positive constants $G_x^1 > g_x$ and $g_y^1 < G_y$ such that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad G_x^1 \le x,\ 0 < y < g_y^1. \tag{8.8}$$

Besides,

$$\lim_{x\to +\infty} \mathcal{L}U_1(x,y) = -\infty, \qquad g_y^1 < y < G_y,$$

hence, there exists a positive constant $G_x \ge G_x^1$ such that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad G_x \le x,\ g_y^1 < y < G_y. \tag{8.9}$$

Applying (8.8) and (8.9) leads to

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad G_x \le x,\ 0 < y < G_y. \tag{8.10}$$

It follows from (8.1) that for $x > 0$,

$$-\frac{c\sigma}{2x^2} + \frac{c(\sigma_1^2+\delta)}{x} = -\frac{c\sigma}{2}\Big(\frac{1}{x} - \frac{\delta+\sigma_1^2}{\sigma}\Big)^2 + \frac{c(\delta+\sigma_1^2)^2}{2\sigma} \le \frac{c(\delta+\sigma_1^2)^2}{2\sigma} \le \frac{\eta}{2}.$$

From the above inequality and the condition $0 < \alpha_3 < 1$, we have

$$\begin{aligned}\limsup_{y\to 0^+} \mathcal{L}U_1(x,y) &\le [\sigma - (r-h^2)x] - \frac{c\sigma}{2x^2} + \frac{c(\sigma_1^2+\delta)}{x} \\ &\quad + (r-h^2)\Big(\frac{\sigma_2^2}{2} - \alpha_1 + \alpha_3 x + c_1 v_0\Big) \\ &\le \sigma - \frac{c\sigma}{2x^2} + \frac{c(\sigma_1^2+\delta)}{x} + (r-h^2)\Big(\frac{\sigma_2^2}{2} - \alpha_1 + c_1 v_0\Big) \\ &\le -\frac{3\eta}{2}.\end{aligned}$$

Hence, there exists a positive constant $g_y < G_y$ such that

$$\mathcal{L}U_1(x,y) \le -\eta, \qquad 0 < x,\ 0 < y < g_y. \tag{8.11}$$

By (8.6), (8.7), (8.10) and (8.11), we obtain

$$\mathcal{L}U_1(x,y) \le -\eta, \tag{8.12}$$

where $(x,y) \notin D = \{(x,y) \in \mathbb{R}_+^2 : g_x < x < G_x,\ g_y < y < G_y\}$. And $(x(t),y(t))$ is positive recurrent with respect to D, that is $\mathbb{E}[\tau_D] < \infty$, where $\tau_D = \inf\{t > 0 : (x(t),y(t)) \in D\}$. Due to the nondegeneracy of the diffusion coefficient, we obtain that the solution $(x(t),y(t))$ of system (1.4) has a unique invariant measure $\vartheta_1(\cdot)$. From [4], we deduce that the support of the invariant measure $\vartheta_1(\cdot)$ is in $\mathbb{R}_+^2$. The proof is complete. $\square$

Example 8.1. Choose the parameters in model (1.4) as follows: $\sigma = 0.2$, $\alpha_1 = 0.9$, $\alpha_2 = 0.4$, $\alpha_3 = 0.514$, $c_1 = 0.04$, $c_2 = 0.01$, $\mu = 0.1859$, $\rho = 0.4$, $m = 0.862$, $k_1 = 0.5463$, $k_2 = 0.9757$, $\delta = 0.7$, $\sigma_1 = 0.4$, $\sigma_2 = 0.1$ and $(x_0, y_0, v_0) = (1.22, 1, 0.7)$, then

$$r - h^2 \approx 0.6391 > 0, \quad \alpha_1 - \frac{\sigma_2^2}{2} - c_1 v_0 - \frac{\sigma}{r-h^2} \approx 0.5541 > 0.$$

It follows from the conditions of Theorem 8.1. For the stochastic system (1.4), the frequency histograms of $x(t)$ and $y(t)$ are obtained in Figure 7, respectively.

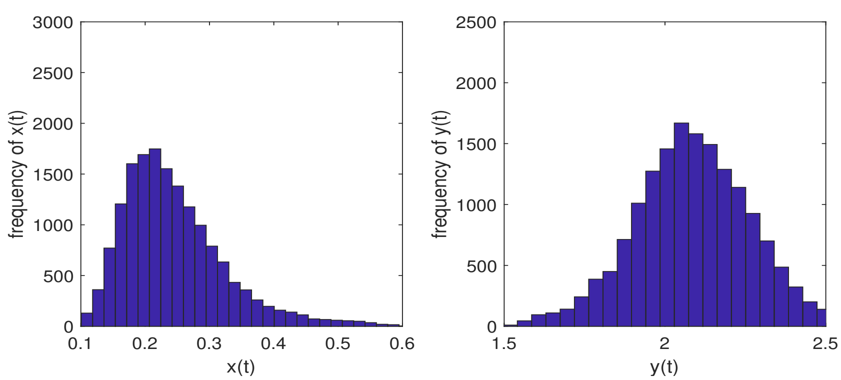

Figure 7. Frequency histograms of $x(t)$ and $y(t)$ for the stochastic system (1.4), respectively.

9. Conclusion

Because the formation and development of cancer is very complex, it can be affected by many factors. In this paper, we develop a stochastic tumor-immune-vitamin model. We focus on investigating its dynamical behavior. In order to satisfy the biological meaning, we show that the system has a unique globally positive solution. We obtain that the solution is stochastically ultimately bounded by proving the moment boundedness (see Theorem 4.3). Next, by constructing appropriate Lyapunov functions, we prove stochastic permanence of system (1.4), which implies long-term survival. Finally, we deduce that when the noise intensity is large enough, the cancer cells will become extinct, and the immune cells converge weakly to a unique stationary distribution. In contrast to adding vitamins to the treatment of cancer, we find by numerical simulation that the introduction of white noise causes cancer cells to die out more quickly, which is a novelty of this paper. By Theorem 8.1, the model has a unique two-dimensional stationary distribution when the noise intensity is small. This suggests that noise has an impact on the extinction and development of cancer cells. In this paper, we only give the sufficient conditions for the extinction of tumor cells.

In the future, we can further investigate the necessary and sufficient conditions for the extinction of tumor cells. In addition, we only consider the stochastic tumor-immune-vitamin model under white noise perturbation, and in fact we could also try to investigate the dynamical behaviors perturbed by colored noise.

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