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Research article

The ACE2 receptor protein-mediated SARS-CoV-2 infection: dynamic properties of a novel delayed stochastic system

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Abstract: We investigated the dynamic effect of stochastic environmental fluctuations on the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus infection system with time delay and mediations by the angiotensin-converting enzyme 2 (ACE2) receptor protein. First, we discussed the existence and uniqueness of global positive solutions as well as the stochastic ultimate boundedness of the stochastic SARS-CoV-2 model. Second, the asymptotic properties of stochastic time-delay system were investigated by constructing a number of appropriate Lyapunov functions and applying differential inequality techniques. These properties indicated a positive relationship between the strength of oscillations and the intensity of environmental fluctuations, and this launched the properties of a deterministic system. When the random disturbance was relatively large, the disease went extinct. When the random disturbance was relatively small and $R_0 < 1$, the disease could become extinct. Conversely, when the random disturbance was smaller and $R_0 > 1$, then it would oscillate around the disease enduring equilibrium. At last, a series of numerical simulations were carried out to show how the SARS-CoV-2 system was affected by the intensity of environmental fluctuations and time delay.

Keywords: stochastic environmental fluctuations; SARS-CoV-2 system; Lyapunov functional; time delay; asymptotic properties
Mathematics Subject Classification: 37H10, 60H10

1. Introduction

During the development of human society, the outbreak of various infectious diseases and epidemics has brought great economic losses and harmful to human well-being, and therefore infectious diseases have always attracted widespread attention and research. Epidemiology [1–3] is a scientific discipline that specializes in the research of the transmission, occurrence, distribution, and control of disease in populations [4, 5]. Using epidemiological studies, one can gain an improved comprehension of the pathophysiology, modes of transmission, and influencing variables of diseases, which can aid in disease prevention and control [6, 7].

Since the end of 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) due to novel coronavirus infection has spread rapidly worldwide, bringing great challenges to human society. SARS-CoV-2 is a single-stranded RNA virus that undergoes genetic mutations during replication due to factors such as its replication mechanism and genome structure. As a result, multiple mutated strains emerged [8, 9], such as, the B.1.1.7 (Alpha) mutated strain detected in the UK in September 2020 [10]. In December 2020, a variant strain B.1.351 (Beta) was detected in South Africa [11–13]. The P.1 (Gamma) variant detected in Brazil in January 2021 was strongly drug-resistant. The B.1.617.2 (Delta) variant strain was detected in the UK in March 2021 [9, 12, 14]. The Omicron mutant was detected in Botswana in November 2021, and it is the most mutated strain of the new library virus so far [15–17]. These five variants are called "variants of concern".

Normally, the process of SARS-CoV-2 virus incursion into cells is a multifaceted interaction. First, the free SARS-CoV-2 virus combines with the receptor angiotensin-converting enzyme 2 (ACE2) on the target cell via the hook protein (S protein), which binds to the cell surface. Second, once the virus binds to the surface of the target cell, its fusion protein undergoes a conformational change that results in the virus fusing with the target cell membrane. This allows the viral genetic material (RNA) to enter the target cytoplasm. Finally, after the viral RNA enters the cytoplasm, it will utilize the target cell's biosynthetic machinery to replicate itself and produce new viral particles. These new viral particles gradually accumulate within the cell and are eventually released to continue infecting other cells. Among the steps involved in viral replication are transcription, translation, genome replication, and assembly. Blocking any of these stages in the process may prevent viral replication and provide selective targets for vaccines and drugs to act on. For example, hepatitis C virus particles invade regular cells by combining with target cell receptors via the E2 proteins [18]. SARS-CoV-2 enters target cells by combining with ACE2 receptors on target cells [19].

In recent decades, the development of mathematical models have provided powerful tools and methods for epidemiological research, allowing us to more accurately understand the transmission patterns of epidemics, predict the development trends of epidemics, and guide the development of appropriate prevention and control strategies [20]. In 1996, Perelson et al. [21] developed a fundamental model that includes free viruses, uninfected cells, and infected cells to study the interaction between host cells and replicating viruses. A brief mathematical model of free viruses, antibodies, uninfected cells, and infected cells was considered by Murase et al. [22]. For example, literature [23, 24] investigated the effectiveness of existing vaccines in controlling the SARS-CoV-2 virus. References [25–28] studied the kinetics of SARS-CoV-2 and its strains.

On the one hand, the infection process of viruses and cells is a complex and dynamic process that is usually not completed in a short period of time. For a virus, such as SARS-CoV-2, the infection process involves multiple links, from the entry of the virus into the target cell to the replication and spread of the virus, each of which requires a certain time delay. Therefore, the affect of time delay on the SARS-CoV-2 system needs to be considered. In recent years, a number of infectious disease models with time delays have been proposed [29, 30]. In 2023, Lv and Ma [30] established the system SARA-CoV-2 with time delay as follows:

$$\begin{cases} \dfrac{\mathrm{d}U(t)}{\mathrm{d}t} = \lambda - \beta v(t) f(D(t))U(t) - d_1 U(t), \\ \dfrac{\mathrm{d}I(t)}{\mathrm{d}t} = e^{-d_2\omega}\beta v(t-\omega) f(D(t-\omega)U(t-\omega)) - d_2 I(t), \\ \dfrac{\mathrm{d}v(t)}{\mathrm{d}t} = d_2 N I(t) - c_1 v(t), \\ \dfrac{\mathrm{d}D(t)}{\mathrm{d}t} = \lambda_1 - k\beta v(t) f(D(t))D(t) - c_2 D(t), \end{cases} \tag{1.1}$$

where $U(t)$, $I(t)$, $v(t)$, and $D(t)$ represent the densities of uninfected target celles, infected target cells, free viruses, and ACE2 receptors carried by uninfected target cells at time t, respectively. λ and d_1 are the proliferation and mortality rates of uninfected target cells, respectively. The free virus fuses with uninfected target cells mediated by the ACE2 receptor, leading to a reduction of uninfected target cell numbers $\beta v(t) f(D(t))U(t)$, in which β denotes the rate constant for free virus infection of uninfected target cells, and $f(D(t))$ denotes the probability that the virus successfully enters the target cell under ACE2 receptor mediation. Normally, $f(D(t))$ is defined as a Hill function:

$$f(D) = \frac{D^n}{D_1^n + D^n},$$

in which the Hill coefficient is denoted by $n > 0$, and D_1 denotes the half-saturation constant. It goes to show that $f(D(t)) \sim (0, 1)$. Let $f(D)$ be a continuously differentiable function that strictly monotonically increases on $[0, +\infty)$ and fulfills $f(0) = 0$. The term $e^{-d_2\omega}\beta v(t-\omega) f(D(t-\omega)U(t-\omega)$ represents the value added by infected cells, and d_2 denotes the mortality rate of infected target cells. The time delay is denoted by the constant ω, and the term $e^{-d_2\omega}$ denotes the survival probability of infected cells after time ω [4, 31]. $d_2 N I(t)$ denotes the amount of virus released from dead infected target cells, and the integer N is positive. Viruses degrade at a rate of c_1. λ_1 and c_2 represent proliferation and mortality rates of ACE2 receptor, respectively. The term $\beta v(t) f(D(t))U(t)$ refers to the reduction in the number of uninfected target cells resulting from free virus, and $D(t)/U(t)$ is the average amount of ACE2 receptors that are carried by per uninfected target cell. Therefore, the reduction of ACE2 receptors resulting from the reduction of non-infected target cells denotes

$$k\beta v(t) f(D(t))U(t) \times D(t)/U(t) = k\beta v(t) f(D(t))D(t),$$

in which k is a constant ratio. It is assumed that every parameter is a positive constant.

From [32], the next generation matrix method is used to calculate that the system (1.1) has one basic reproduction number

$$R_0 = \frac{e^{-d_2\omega}\beta N\lambda}{c_1 d_1} f\left(\frac{\lambda_1}{c_2}\right),$$

which has a number of properties, as follows:

(1) System (1.1) possesses a disease-free equilibrium point

$$E_0 = \left(\frac{\lambda}{d_1}, 0, 0, \frac{\lambda_1}{c_2}\right)$$

when $R_0 < 1$, and this point is globally asymptotically stable.

(2) System (1.1) possesses an endemic disease equilibrium point

$$E^* = (U^*, I^*, v^*, D^*)$$

when $R_0 > 1$, and this point is globally asymptotically stable.

On the other hand, some epidemiologic models usually consider the impact of environmental variables like precipitation, temperature, and relative humidity when exploring disease transmission [33, 34]. These factors in the environment may have a great influence on the viability, speed of spread, and range of transmission of pathogens. Therefore, during the infection process of the SARS-CoV-2 virus, it is inevitable that it will be affected by various environmental noises, which may have a great impact on the whole system. Generally, white noise, as a major environmental disturbance, is a noise consisting of zero-mean random signals of various frequencies. It is a continuous disturbance that can simulate various small or medium level fluctuations in the environment. Moreover these fluctuations have relatively little effect on the intrinsic cell growth rate. Therefore, revealing how environmental white noise disturbs and effects the SARA-CoV-2 system has great practical significance. Stochastic models with white noise interference have been constructed and investigated by numerous academics in the last few years. The reader is referred to the literature [35–41] and references contained therein. For example, Omamea et al. [41] proposed a SARS-CoV-2 bivariate stochastic model, and investigated the global asymptotic stability of the equilibrium point as well as the threshold conditions for disease extinction and ergodic stationary distribution.

Here, we consider the effect of stochastic environmental fluctuations on target cells, which leads to the following stochastic SARA-CoV-2 system with time delay

$$\begin{cases} \mathrm{d}U(t) = [\lambda - \beta v(t) f(D(t))U(t) - d_1 U(t)]\mathrm{d}t + \sigma_1 U(t)\mathrm{d}B_1(t), \\ \mathrm{d}I(t) = [e^{-d_2\omega}\beta v(t-\omega) f(D(t-\omega))U(t-\omega) - d_2 I(t)]\mathrm{d}t + \sigma_2 I(t)\mathrm{d}B_2(t), \\ \mathrm{d}v(t) = [d_2 N I(t) - c_1 v(t)]\mathrm{d}t, \\ \mathrm{d}D(t) = [\lambda_1 - k\beta v(t) f(D(t))D(t) - c_2 D(t)]\mathrm{d}t, \end{cases} \tag{1.2}$$

where $B_i(t)$ $(i = 1, 2)$ is standard Brownian motions independent of each other and $B_i(0) = 0$. And $\sigma_i^2 \geq 0$ $(i = 1, 2)$ is the intensity of white noise.

Our objective next is to investigate how stochastic disturbances in system (1.2) affect the global asymptotic stability of the equilibrium point that determines system (1.1).

The initial conditions of system (1.2) are

$$\begin{cases} U(\xi) = \Phi_1(\xi), \quad I(\xi) = \Phi_2(\xi), \\ v(\xi) = \Phi_3(\xi), \quad D(\xi) = \Phi_4(\xi), \\ \Phi_i(\xi) \geq 0, \quad \xi \in [-\omega, 0], \quad i = 1, 2, 3, 4, \\ (\Phi_1, \Phi_2, \Phi_3, \Phi_4) \in C, \end{cases} \tag{1.3}$$

here C stands for the Banach space $C\left([-\omega, 0]\ ,\ \mathbb{R}_+^4\right)$ of continuous functions mapping the interval $[-\omega, 0]$ into $\mathbb{R}_+^4$ and

$$\mathbb{R}_+^4 = \left\{y = (y_1, y_2, y_3, y_4) \in \mathbb{R}_+^4,\ \ y_i > 0,\ \ i = 1, 2, 3, 4\right\}.$$

We further assume, on the basis of biological significance, that

$$\Phi_i(\xi) > 0,\ \ (i = 1, 2, 3, 4).$$

Following is an arrangement of the remaining of the contents of the paper. In Section 2, we demonstrate that the stochastic system is stochastically ultimately bounded and has a global positive solution. In Section 3, by building a number of appropriate Lyapunov functions and utilizing differential inequality techniques, we investigate the long-term asymptotic properties of the stochastic system with time delay. Finally, we give some numerical simulations and discuss the conclusions.

2. Preliminary

2.1. Global positive solution

Lemma 2.1. *([42], Itô's formula) For a more detailed explanation of Itô's formula, see [42]. The following are the main formulas applied.*

$$dV(X(t), t) = V_t(X(t), t) + V_X\left(X(t), t\right) F(t) + \frac{1}{2} trace\left[G^T(t) V_{XX}(X(t), t) G(t)\right] dt + V_X(X(t), t) G(t) dB(t),$$

then by the diffusion operator

$$LV : \mathbb{R}^n \times \mathbb{R}_+ \to \mathbb{R}$$

and

$$LV(X(t), t) = V_t(X(t), t) + V_X\left(X(t), t\right) F(t) + \frac{1}{2} trace\left[G^T(t) V_{XX}(X(t), t) G(t)\right],$$

the another pxpression for Itô's formula is

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

Theorem 2.1. *There is a unique positive solution $(U(t), I(t), v(t), D(t)) \in \mathbb{R}_+^4$ to system (1.2) at $t \geq 0$ for any given initial value (1.3), and the solution will stay in $\mathbb{R}_+^4$ with a probability of one (a.s.).*

Proof. Due to the fact that the coefficients of the system (1.2) fulfill the local Lipschitz conditions, then for any given initial condition (1.3), there exists a unique local solution $(U(t), I(t), v(t), D(t))$ on $t \in [0, \omega_e)$, in which ω_e is the time of explosion. We merely have to prove that $\omega_e = \infty$ to guarantee that this solution is global. We will not go into the details here and can refer to the literature [29]. Construct a C^2-function V: $\mathbb{R}_+^4 \to \mathbb{R}_+$ by

$$\begin{aligned} V(U, I, v, D) =& e^{-d_2\omega} U + (I - 1 - \ln I) + \frac{1}{N}\left(v - c_1 - c_1 \ln \frac{v}{c_1}\right) + \frac{1}{k} e^{-d_2\omega} D \\ &+ e^{-d_2\omega} \int_{t-\omega}^{t} \beta v(\theta) f(D(\theta)) U(\theta) \mathrm{d}\theta. \end{aligned}$$

Application of Itô's formula yields

$$\mathrm{d}V = LV\mathrm{d}t + e^{-d_2\omega}\sigma_1 U\mathrm{d}B_1(t) + \sigma_2(I-1)\mathrm{d}B_2(t),$$

where

$$\begin{aligned}
LV =& e^{-d_2\omega}\left[\lambda - \beta v f(D)U - d_1 U\right] + \left(1-\frac{1}{I}\right)\left[e^{-d_2\omega}\beta v(t-\omega) f(D(t-\omega))U(t-\omega) - d_2 I\right] + \frac{1}{2}\sigma_2^2 \\
&+ \frac{1}{N}\left(1-\frac{c_1}{v}\right)(d_2NI - c_1 v) + \frac{1}{k}e^{-d_2\omega}\left[\lambda_1 - k\beta v f(D)D - c_2 D\right] + e^{-d_2\omega}\beta v f(D)U \\
&- e^{-d_2\omega}\beta v(t-\omega) f(D(t-\omega))U(t-\omega) \\
\le& d_2 + e^{-d_2\omega}\left(\lambda + \frac{\lambda_1}{k}\right) + \frac{c_1^2}{N} + \frac{1}{2}\sigma_2^2 \\
:=& M,
\end{aligned}$$

where M is a non-negative constant. The proof of the rest is given in [28] and will not be repeated here. □

2.2. Stochastically ultimate boundedness

Definition 2.1. *([43]) Assume that the solution of system (1.2) with initially value (1.3) is* $(U(t), I(t), v(t), D(t))$. *If there is a constant* $\Gamma = \Gamma(\alpha) > 0$ *for any* $\alpha \in (0, 1)$, *and the solution of system (1.2) satisfies*

$$\limsup_{t\to\infty} \mathbb{P}\{|U(t), I(t), v(t), D(t)| \le \Gamma\} \ge 1-\alpha,$$

then the system (1.2) is stochastically ultimately bounded.

Theorem 2.2. *The solution* $(U(t), I(t), v(t), D(t))$ *of the system (1.2) is stochastically ultimate bounded for any initial value (1.3).*

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

$$V(U, I, v, D) = e^{-d_2\omega}U + I + \frac{1}{2N}v + e^{-d_2\omega}D.$$

Applying Itô's formula gets

$$\mathrm{d}V = LV\mathrm{d}t + e^{-d_2\omega}\sigma_1 U\mathrm{d}B_1(t) + \sigma_2 I\mathrm{d}B_2(t),$$

where

$$\begin{aligned}
LV =& e^{-d_2\omega}\left[\lambda - \beta v f(D)U - d_1 U\right] + \left[e^{-d_2\omega}\beta v(t-\omega) f(D(t-\omega))U(t-\omega) - d_2 I\right] + \frac{1}{2N}(d_2NI - c_1 v) \\
&+ e^{-d_2\omega}\left[\lambda_1 - k\beta v f(D)D - c_2 D\right] \\
\le& e^{-d_2\omega}\lambda - H_0\left[e^{-d_2\omega}U + I + \frac{1}{2N}v + e^{-d_2\omega}D\right] - e^{-d_2\omega}\beta\left[v f(D)U - v(t-\omega) f(D(t-\omega)U(t-\omega)\right] \\
&+ e^{-d_2\omega}\lambda_1 - e^{-d_2\omega}k\beta v f(D)D
\end{aligned}$$

$$
\begin{aligned}
&\leq e^{-d_2\omega}(\lambda+\lambda_1)-H_0\left[e^{-d_2\omega}U+I+\frac{1}{2N}v+e^{-d_2\omega}D\right]\\
&\quad -e^{-d_2\omega}\beta\left[vf(D)U-v(t-\omega)f(D(t-\omega))U(t-\omega)\right]\\
&=e^{-d_2\omega}(\lambda+\lambda_1)-H_0V-e^{-d_2\omega}\beta\left[vf(D)U-v(t-\omega)f(D(t-\omega))U(t-\omega)\right],
\end{aligned}
$$

where

$$
H_0=\min\left\{d_1,\frac{d_2}{2},c_1,c_2\right\},
$$

then,

$$
\begin{aligned}
\mathrm{d}V\leq&\left[e^{-d_2\omega}(\lambda+\lambda_1)-H_0V\right]\mathrm{d}t-e^{-d_2\omega}\beta\left[vf(D)U-v(t-\omega)f(D(t-\omega))U(t-\omega)\right]\mathrm{d}t\\
&+e^{-d_2\omega}\sigma_1U\mathrm{d}B_1(t)+\sigma_2I\mathrm{d}B_2(t).
\end{aligned}
$$

Applying Itô's formula to $e^{H_0t}V$ yields

$$
\begin{aligned}
\mathrm{d}e^{H_0t}V=&e^{H_0t}\left(\mathrm{d}V+H_0V\mathrm{d}t\right)\\
\leq&e^{H_0t}\left[e^{-d_2\omega}(\lambda+\lambda_1)-H_0V\right]\mathrm{d}t-e^{H_0t}e^{-d_2\omega}\beta\left[vf(D)U-v(t-\omega)f(D(t-\omega))U(t-\omega)\right]\mathrm{d}t\\
&+e^{H_0t}\left[e^{-d_2\omega}\sigma_1U\mathrm{d}B_1(t)+\sigma_2I\mathrm{d}B_2(t)\right]+e^{H_0t}H_0V\mathrm{d}t\\
=&e^{H_0t}e^{-d_2\omega}(\lambda+\lambda_1)\mathrm{d}t-e^{H_0t}e^{-d_2\omega}\beta[vf(D)U-v(t-\omega)f(D(t-\omega))U(t-\omega)]\mathrm{d}t\\
&+e^{H_0t}[e^{-d_2\omega}\sigma_1U\mathrm{d}B_1(t)+\sigma_2I\mathrm{d}B_2(t)].
\end{aligned}
$$

Taking the expectation for either side of the above inequality results in

$$
\begin{aligned}
e^{H_0t}\mathbb{E}V(U(t),I(t),v(t),D(t))\leq&V(U(0),I(0),v(0),D(0))+\frac{e^{-d_2\omega}(\lambda+\lambda_1)}{H_0}\left(e^{H_0t}-1\right)\\
&-e^{-d_2\omega}\beta\mathbb{E}\int_0^t e^{H_0(s+\omega)}v(s)f(D(s))U(s)\mathrm{d}s\\
&+e^{-d_2\omega}\beta\mathbb{E}\int_{-\omega}^{t-\omega} e^{H_0(s+\omega)}v(s)f(D(s))U(s)\mathrm{d}s\\
\leq&V(U(0),I(0),v(0),D(0))+\frac{e^{-d_2\omega}(\lambda+\lambda_1)}{H_0}\left(e^{H_0t}-1\right)\\
&+e^{-d_2\omega}\beta\int_{-\omega}^{0} e^{H_0(s+\omega)}v(s)f(D(s))U(s)\mathrm{d}s,
\end{aligned}
$$

Taking the upper limit of the above inequality, one has

$$
\limsup_{t\to\infty}\mathbb{E}V(U(t),I(t),v(t),D(t))\leq\frac{e^{-d_2\omega}(\lambda+\lambda_1)}{H_0}.
$$

So,

$$
\limsup_{t\to\infty}\mathbb{E}V(U(t)+I(t)+v(t)+D(t))\leq\frac{1}{h}\limsup_{t\to\infty}\mathbb{E}V(U(t),I(t),v(t),D(t))\leq\frac{e^{-d_2\omega}(\lambda+\lambda_1)}{H_0h},
$$

where

$$h = \min\left\{e^{-d_2\omega}, 1, \frac{1}{2N}\right\}.$$

Therefore, for any $\alpha > 0$, set

$$\Gamma = \frac{\lambda + \lambda_1}{e^{d_2\omega} H_0 h\alpha},$$

application of Chebyshev's inequality leads to

$$\mathbb{P}\{|U(t), I(t), v(t), D(t)| > \Gamma\} \leq \frac{\mathbb{E}|U(t) + I(t) + v(t) + D(t)|}{\Gamma}.$$

Hence,

$$\limsup_{t\to\infty} \mathbb{P}\{|U(t), I(t), v(t), D(t)| > \Gamma\} \leq \alpha.$$

This implies

$$\limsup_{t\to\infty} \mathbb{P}\{|U(t), I(t), v(t), D(t)| \leq \Gamma\} \geq 1 - \alpha.$$

□

3. Main results

The asymptotic properties of the stochastic system (1.2) near the disease-free equilibrium E_0 and the endemic equilibrium E^* are examined in this subsection.

Definition 3.1. *Suppose* $(U(t), I(t), v(t), D(t))$ *is the solution of system (1.2) with initial conditions (1.3), and*

$$\bar{E} = (\bar{U}, \bar{I}, \bar{v}, \bar{D})$$

is an equilibrium point of the corresponding deterministic system (1.1). If there exists a constant $\Lambda > 0$ *that makes the following equation hold true*

$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t \left[(U(s) - \bar{U})^2 + (I(s) - \bar{I})^2 + (v(s) - \bar{v})^2 + (D(s) - \bar{D})^2\right] ds \leq \Lambda \quad a.s.,$$

then we claim that the solution of the system (1.2) will oscillate around the equilibrium point $\bar{E} = (\bar{U}, \bar{I}, \bar{v}, \bar{D})$ *of its deterministic system (1.1).*

Lemma 3.1. *([34]) The Young inequality is specified as follows*

$$|m|^x\, |n|^y \leq \varepsilon\, |m|^{(x+y)} + \frac{y}{x+y}\left[\frac{x}{\varepsilon(x+y)}\right]^{\frac{x}{y}} |n|^{(x+y)}, \quad \forall m, n \in \mathbb{R}, \quad \forall x, y, \varepsilon > 0.$$

3.1. Asymptotic properties near the E_0

System (1.1) has a globally asymptotically stable equilibrium point

$$E_0 = \left(\frac{\lambda}{d_1}, 0, 0, \frac{\lambda_1}{c_2}\right),$$

when $R_0 < 1$. The asymptotic characteristics of the system (1.2) solution in the vicinity of E_0 are investigated in this subsection.

Theorem 3.1. *Suppose $(U(t), I(t), v(t), D(t))$ is the solution of the system (1.2) with the initial conditions (1.3). If*

$$R_0 < 1 \text{ and } \sigma_i^2 < d_i, \ (i = 1, 2)$$

are valid, then,

$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t \left(U(s) - \frac{\lambda}{d_1}\right)^2 ds \le \frac{\lambda^2\sigma_1^2}{(d_1 - \sigma_1^2)d_1^2}, \quad a.s.,$$
$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t I^2(s)ds \le \Phi_1, \quad a.s.,$$
$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t v^2(s)ds \le \frac{2N^2\gamma_1}{c_1}, \quad a.s.,$$
$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t f'(\xi)\left(D(s) - \frac{\lambda_1}{c_2}\right)^2 ds \le \frac{k\lambda_1\sigma_1^2}{2c_2^2}, \quad a.s.,$$

where

$$\Phi_1 = e^{-2d_2\omega}\frac{(d_1 + d_2)^2\lambda^2\sigma_1^2}{(d_1 - \sigma_1^2)(d_2 - \sigma_2^2)d_1^2 d_2},$$
$$\gamma_1 = e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{(d_1 - \sigma_1^2)d_1^2}\left(1 + 2d_1 + c_1 + \frac{d_1^2}{c_1}\right) + \left(\frac{d_1^2}{4} + c_1 + \frac{\sigma_2^2}{2}\right)\Phi_1.$$

Proof. Define

$$V_1 = \frac{1}{2}\left(U - \frac{\lambda}{d_1}\right)^2.$$

Applying Itô's formula, one has

$$\mathrm{d}V_1 = LV_1\mathrm{d}t + \sigma_1 U\left(U - \frac{\lambda}{d_1}\right)\mathrm{d}B_1(t),$$

where

$$LV_1 = \left(U - \frac{\lambda}{d_1}\right)[\lambda - \beta v f(D)U - d_1 U] + \frac{1}{2}\sigma_1^2 U^2$$
$$= -d_1\left(U - \frac{\lambda}{d_1}\right)^2 + \left(U - \frac{\lambda}{d_1}\right)\left[-\beta v f(D)\left(U - \frac{\lambda}{d_1}\right) - \frac{\lambda}{d_1}\beta v f(D)\right] + \frac{1}{2}\sigma_1^2 U^2$$

$$\leq -d_1\left(U-\frac{\lambda}{d_1}\right)^2-\beta v f(D)\frac{\lambda}{d_1}\left(U-\frac{\lambda}{d_1}\right)+\sigma_1^2\left(U-\frac{\lambda}{d_1}\right)^2+\sigma_1^2\frac{\lambda^2}{d_1^2}$$
$$=-(d_1-\sigma_1^2)\left(U-\frac{\lambda}{d_1}\right)^2-\beta v f(D)\frac{\lambda}{d_1}\left(U-\frac{\lambda}{d_1}\right)+\sigma_1^2\frac{\lambda^2}{d_1^2}.$$

Define

$$V_2 = I(t+\omega)+d_2\int_t^{t+\omega} I(s)\mathrm{d}s.$$

Applying Itô's formula leads to

$$\mathrm{d}V_2 = LV_2\mathrm{d}t+\sigma_2 I\mathrm{d}B_2(t),$$

where

$$\begin{aligned}
LV_2 &= e^{-d_2\omega}\beta v f(D)U-d_2I(t+\omega)+d_2I(t+\omega)-d_2I(t)\\
&= e^{-d_2\omega}\beta v f(D)\left(U-\frac{\lambda}{d_1}\right)+e^{-d_2\omega}\beta v f(D)\frac{\lambda}{d_1}-d_2I\\
&= e^{-d_2\omega}\beta v f(D)\left(U-\frac{\lambda}{d_1}\right)+d_2I\left(\frac{e^{-d_2\omega}\beta v f(D)\lambda}{d_1d_2I}-1\right)\\
&= e^{-d_2\omega}\beta v f(D)\left(U-\frac{\lambda}{d_1}\right)+d_2I\left(\frac{e^{-d_2\omega}\beta f(D)N\lambda}{c_1d_1}-1\right)\\
&\leq e^{-d_2\omega}\beta v f(D)\left(U-\frac{\lambda}{d_1}\right)+d_2I\left(\frac{e^{-d_2\omega}\beta N\lambda}{c_1d_1}f(\frac{\lambda_1}{c_2})-1\right)\\
&\leq e^{-d_2\omega}\beta v f(D)\left(U-\frac{\lambda}{d_1}\right).
\end{aligned}$$

Define

$$V_3 = e^{-d_2\omega}V_1+\frac{\lambda}{d_1}V_2.$$

It is easy to get that

$$LV_3 \leq -e^{-d_2\omega}(d_1-\sigma_1^2)\left(U-\frac{\lambda}{d_1}\right)^2+e^{-d_2\omega}\frac{\lambda^2\sigma_1^2}{d_1^2}. \tag{3.1}$$

Taking the expected yield after integrating each side of Eq (3.1) from 0 to t

$$\mathbb{E}V_3(t)-\mathbb{E}V_3(0)\leq -e^{-d_2\omega}(d_1-\sigma_1^2)\mathbb{E}\int_0^t\left(U(s)-\frac{\lambda}{d_1}\right)^2\mathrm{d}s+e^{-d_2\omega}\frac{\lambda^2\sigma_1^2}{d_1^2}t. \tag{3.2}$$

Taking the upper limit yield after dividing both sides of (3.2) by t

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t\left(U(s)-\frac{\lambda}{d_1}\right)^2\mathrm{d}s\leq\frac{\lambda^2\sigma_1^2}{(d_1-\sigma_1^2)d_1^2},\quad a.s.$$

Moreover, define

$$V_4 = \frac{1}{2}\left[e^{-d_2\omega}\left(U - \frac{\lambda}{d_1}\right) + I(t+\omega)\right]^2,$$

then

$$\begin{aligned}
LV_4 =& \left[e^{-d_2\omega}\left(U - \frac{\lambda}{d_1}\right) + I(t+\omega)\right]\left[e^{-d_2\omega}(\lambda - d_1U) - d_2I(t+\omega)\right] + \frac{1}{2}e^{-2d_2\omega}\sigma_1^2U^2 + \frac{1}{2}\sigma_2^2I^2(t+\omega)\\
=& -\left[e^{-d_2\omega}\left(U - \frac{\lambda}{d_1}\right) + I(t+\omega)\right]\left[e^{-d_2\omega}d_1\left(U - \frac{\lambda}{d_1}\right) + d_2I(t+\omega)\right] + \frac{1}{2}e^{-2d_2\omega}\sigma_1^2U^2 + \frac{1}{2}\sigma_2^2I^2(t+\omega)\\
=& - e^{-2d_2\omega}d_1\left(U - \frac{\lambda}{d_1}\right)^2 - d_2I^2(t+\omega) - e^{-d_2\omega}(d_1+d_2)\left(U - \frac{\lambda}{d_1}\right)I(t+\omega)\\
&+ \frac{1}{2}e^{-2d_2\omega}\sigma_1^2U^2 + \frac{1}{2}\sigma_2^2I^2(t+\omega)\\
\le& - e^{-2d_2\omega}d_1\left(U - \frac{\lambda}{d_1}\right)^2 - d_2I^2(t+\omega) + \frac{d_2}{2}I^2(t+\omega) + e^{-2d_2\omega}\frac{(d_1+d_2)^2}{2d_2}\left(U - \frac{\lambda}{d_1}\right)^2\\
&+ e^{-2d_2\omega}\sigma_1^2\left(U - \frac{\lambda}{d_1}\right)^2 + e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{d_1^2} + \frac{1}{2}\sigma_2^2I^2(t+\omega)\\
=& e^{-2d_2\omega}\left(\frac{d_1^2+d_2^2}{2d_2} + \sigma_1^2\right)\left(U - \frac{\lambda}{d_1}\right)^2 - \frac{1}{2}(d_2 - \sigma_2^2)I^2(t+\omega) + e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{d_1^2},
\end{aligned}$$

where the Young inequality is utilized in the inequality above

$$-e^{-d_2\omega}(d_1+d_2)\left(U - \frac{\lambda}{d_1}\right)I(t+\omega) \le \frac{d_2}{2}I^2(t+\omega) + e^{-2d_2\omega}\frac{(d_1+d_2)^2}{2d_2}\left(U - \frac{\lambda}{d_1}\right)^2.$$

Define

$$V_5 = e^{-d_2\omega}\left[\frac{d_1^2+d_2^2}{2d_2(d_1-\sigma_1^2)} + \frac{\sigma_1^2}{d_1-\sigma_1^2}\right]V_3 + V_4 + \frac{1}{2}(d_2 - \sigma_2^2)\int_t^{t+\omega} I^2(s)\mathrm{d}s,$$

then,

$$LV_5 \le -\frac{1}{2}(d_2 - \sigma_2^2)I^2 + e^{-2d_2\omega}\frac{(d_1+d_2)^2\lambda^2\sigma_1^2}{2(d_1-\sigma_1^2)d_1^2d_2}. \tag{3.3}$$

Taking the expected yield after integrating each side of Eq (3.3) from 0 to t

$$\mathbb{E}V_5(t) - \mathbb{E}V_5(0) \le -\frac{1}{2}(d_2 - \sigma_2^2)\mathbb{E}\int_0^t I^2(s)\mathrm{d}s + e^{-2d_2\omega}\frac{(d_1+d_2)^2\lambda^2\sigma_1^2}{2(d_1-\sigma_1^2)d_1^2d_2}t. \tag{3.4}$$

Taking the upper limit yield after dividing both sides of (3.4) by t

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t I^2(s)\mathrm{d}s \le e^{-2d_2\omega}\frac{(d_1+d_2)^2\lambda^2\sigma_1^2}{(d_1-\sigma_1^2)(d_2-\sigma_2^2)d_1^2d_2} = \Phi_1, \quad a.s.$$

Define

$$V_6 = \frac{1}{2}\left[e^{-d_2\omega}\left(U - \frac{\lambda}{d_1}\right) + I(t+\omega) + \frac{1}{N}v(t+\omega)\right]^2,$$

then,

$$\begin{aligned}
LV_6 =& \left[e^{-d_2\omega}(U - \frac{\lambda}{d_1}) + I(t+\omega) + \frac{1}{N}v(t+\omega)\right]\left[e^{-d_2\omega}(\lambda - d_1U) - c_1v(t+\omega)\right] + \frac{1}{2}e^{-2d_2\omega}\sigma_1^2U^2 + \frac{1}{2}\sigma_2^2I^2(t+\omega)\\
\leq& -e^{-2d_2\omega}(d_1 - \sigma_1^2)\left(U - \frac{\lambda}{d_1}\right)^2 - e^{-d_2\omega}d_1\left(U - \frac{\lambda}{d_1}\right)I(t+\omega) - e^{-d_2\omega}\frac{(d_1+c_1)}{N}\left(U - \frac{\lambda}{d_1}\right)v(t+\omega)\\
&- \frac{c_1}{N}I(t+\omega)v(t+\omega) - \frac{c_1}{N^2}v^2(t+\omega) + \frac{1}{2}\sigma_2^2I^2(t+\omega) + e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{d_1^2}\\
\leq& -e^{-2d_2\omega}(d_1 - \sigma_1^2)\left(U - \frac{\lambda}{d_1}\right)^2 + e^{-2d_2\omega}\left(U - \frac{\lambda}{d_1}\right)^2 + \frac{d_1^2}{4}I^2(t+\omega) + e^{-2d_2\omega}\frac{(d_1+c_1)^2}{c_1}\left(U - \frac{\lambda}{d_1}\right)^2\\
&+ \frac{c_1}{4N^2}v^2(t+\omega) + c_1I^2(t+\omega) + \frac{c_1}{4N^2}v^2(t+\omega) - \frac{c_1}{N^2}v^2(t+\omega) + \frac{1}{2}\sigma_2^2I^2(t+\omega) + e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{d_1^2}\\
=& e^{-2d_2\omega}\left(1 + d_1 + c_1 + \frac{d_1^2}{c_1} + \sigma_1^2\right)\left(U - \frac{\lambda}{d_1}\right)^2 + \left(\frac{d_1^2}{4} + c_1 + \frac{\sigma_2^2}{2}\right)I^2(t+\omega) - \frac{c_1}{2N^2}v^2(t+\omega) + e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{d_1^2},
\end{aligned}$$

whereby we employ the Young inequality in the inequality above

$$\begin{cases}
-e^{-d_2\omega}d_1\left(U - \frac{\lambda}{d_1}\right)I(t+\omega) \leq e^{-2d_2\omega}\left(U - \frac{\lambda}{d_1}\right)^2 + \frac{d_1^2}{4}I^2(t+\omega),\\
-e^{-d_2\omega}\frac{(d_1+c_1)}{N}\left(U - \frac{\lambda}{d_1}\right)v(t+\omega) \leq e^{-2d_2\omega}\frac{(d_1+c_1)^2}{c_1}\left(U - \frac{\lambda}{d_1}\right)^2 + \frac{c_1}{4N^2}v^2(t+\omega),\\
-\frac{c_1}{N}I(t+\omega)v(t+\omega) \leq c_1I^2(t+\omega) + \frac{c_1}{4N^2}v^2(t+\omega),
\end{cases}$$

and the inequality $(a+b)^2 \leq 2a^2 + 2b^2$ for any $a, b \in \mathbb{R}_+$.

Define

$$V_7 = e^{-d_2\omega}p_1V_3 + h_1V_4 + V_6 + \frac{c_1}{2N^2}\int_t^{t+\omega} v^2(s)\mathrm{d}s,$$

where

$$\begin{aligned}
p_1 &= \frac{1}{d_1 - \sigma_1^2}\left[\left(1 + d_1 + c_1 + \frac{d_1^2}{c_1} + \sigma_1^2\right) + h_1\left(\frac{d_1^2 + d_2^2}{2d_2} + \sigma_1^2\right)\right],\\
h_1 &= \frac{2}{d_2 - \sigma_2^2}\left(\frac{d_1^2}{4} + c_1 + \frac{\sigma_2^2}{2}\right).
\end{aligned}$$

Therefore,

$$\begin{aligned}
LV_7 &\leq -\frac{c_1}{2N^2}v^2 + e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{(d_1 - \sigma_1^2)d_1^2}(1 + 2d_1 + c_1 + \frac{d_1^2}{c_1}) + (\frac{d_1^2}{4} + c_1 + \frac{\sigma_2^2}{2})\Phi_1\\
&= -\frac{c_1}{2N^2}v^2 + \gamma_1,
\end{aligned} \tag{3.5}$$

where

$$\gamma_1 = e^{-2d_2\omega}\frac{\lambda^2\sigma_1^2}{(d_1-\sigma_1^2)d_1^2}\left(1+2d_1+c_1+\frac{d_1^2}{c_1}\right)+\left(\frac{d_1^2}{4}+c_1+\frac{\sigma_2^2}{2}\right)\Phi_1.$$

Taking the expected yield after integrating each side of Eq (3.5) from 0 to t

$$\mathbb{E}V_7(t)-\mathbb{E}V_7(0)\le -\frac{c_1}{2N^2}\mathbb{E}\int_0^t v^2(s)\mathrm{d}s+\gamma_1 t. \tag{3.6}$$

Taking the upper limit yield after dividing both sides of (3.6) by t

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t v^2(s)\mathrm{d}s\le\frac{2N^2\gamma_1}{c_1},\quad a.s.$$

Define

$$V_8=\left(U-U_0-U_0\ln\frac{U}{U_0}\right)+e^{d_2\omega}I+e^{d_2\omega}\frac{1}{N}v+\frac{U_0}{kD_0}\left(D-D_0-\int_{D_0}^{D}\frac{f(D_0)}{f(\xi)}\mathrm{d}\xi\right)+\int_{t-\omega}^{t}\beta f(D(s))v(s)U(s)\mathrm{d}s,$$

where

$$U_0=\frac{\lambda}{d_1},D_0=\frac{\lambda_1}{c_2},$$

then,

$$\begin{aligned}
LV_8=&\left(1-\frac{U_0}{U}\right)(\lambda-\beta f(D)vU-d_1U)+e^{d_2\omega}\left[e^{-d_2\tau}\beta v(t-\omega)f(D(t-\omega))U(t-\omega)-d_2I\right]\\
&+e^{d_2\omega}\frac{1}{N}(d_2NI-c_1v)+\frac{U_0}{kD_0}\left(1-\frac{f(D_0)}{f(D)}\right)(\lambda_1-k\beta f(D)vD-c_2D)+\beta f(D)vU\\
&-\beta v(t-\omega)f(D(t-\omega))U(t-\omega)+\frac{1}{2}U_0\sigma_1^2\\
=&\lambda\left(2-\frac{U_0}{U}-\frac{U}{U_0}\right)+\frac{c_1}{N}e^{d_2\omega}\left(\frac{e^{-d_2\omega}NU_0\beta f(D_0)}{c_1}-1\right)v+U_0\beta v\left[f(D)-f(D_0)\right]\\
&+\frac{U_0\beta f(D)vD}{D_0}\left[\frac{f(D_0)}{f(D)}-1\right]+\frac{U_0\lambda_1}{kD_0}\left[1-\frac{f(D_0)}{f(D)}\right]+\frac{U_0c_2D}{kD_0}\left[\frac{f(D_0)}{f(D)}-1\right]+\frac{1}{2}U_0\sigma_1^2\\
=&\lambda\left(2-\frac{U_0}{U}-\frac{U}{U_0}\right)+\frac{c_1}{N}e^{d_2\omega}(R_0-1)v+\left(\frac{U_0c_2}{kD_0}+\frac{\beta U_0f(D)v}{D_0}\right)(D-D_0)\left[\frac{f(D_0)}{f(D)}-1\right]+\frac{1}{2}U_0\sigma_1^2\\
\le&-\frac{U_0c_2}{kD_0}(D-D_0)\frac{f(D)-f(D_0)}{f(D)}+\frac{1}{2}U_0\sigma_1^2\\
=&-\frac{U_0c_2f'(\xi)}{kD_0f(D)}(D-D_0)^2+\frac{1}{2}U_0\sigma_1^2\\
\le&-\frac{U_0c_2}{kD_0}f'(\xi)(D-D_0)^2+\frac{1}{2}U_0\sigma_1^2,
\end{aligned}$$

where

$$f(D)-f(D_0)=f'(\xi)(D-D_0),$$

ξ is between D and D_0, and $f'(\xi) > 0$, so

$$LV_8 \leq -\frac{\lambda c_2^2}{k\lambda_1 d_1} f'(\xi)\left(D - \frac{\lambda_1}{c_2}\right)^2 + \frac{\lambda \sigma_1^2}{2d_1}. \tag{3.7}$$

Taking the expected yield after integrating each side of Eq (3.7) from 0 to t

$$\mathbb{E}V_8(t) - \mathbb{E}V_8(0) \leq -\frac{\lambda c_2^2}{k\lambda_1 d_1}\mathbb{E}\int_0^t f'(\xi)\left(D(s) - \frac{\lambda_1}{c_2}\right)^2 \mathrm{d}s + \frac{\lambda \sigma_1^2}{2d_1} t. \tag{3.8}$$

Taking the upper limit yield after dividing both sides of (3.8) by t

$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t f'(\xi)\left(D(s) - \frac{\lambda_1}{c_2}\right)^2 \mathrm{d}s \leq \frac{k\lambda_1 \sigma_1^2}{2c_2^2}, \quad a.s.$$

□

Remark 3.1. *When $\sigma_i = 0$ $(i = 1, 2)$, it is evident from Theorem 3.1 that*

$$\begin{cases} LV_3 \leq -e^{-d_2\omega} d_1 \left(U - \dfrac{\lambda}{d_1}\right)^2 \leq 0, \\ LV_5 \leq -\dfrac{1}{2} d_2 I^2 \leq 0, \\ LV_7 \leq -\dfrac{c_1}{2N^2} v^2 \leq 0, \\ LV_8 \leq -\dfrac{\lambda c_2^2}{k\lambda_1 d_1} f'(\xi)\left(D - \dfrac{\lambda_1}{c_2}\right)^2 \leq 0, \end{cases}$$

this means that the disease-free equilibrium point E_0 of system (1.1) is globally asymptotically stable, from which the nature of the deterministic system can be introduced.

3.2. Asymptotic properties near the E^*

System (1.1) has a globally asymptotically stable equilibrium point

$$E^* = (U^*, I^*, v^*, D^*)$$

when $R_0 > 1$. The asymptotic characteristics of the system (1.2) solution in the vicinity of E^* are investigated in this subsection.

Theorem 3.2. *Suppose $(U(t), I(t), v(t), D(t))$ is the solution of system (1.2) with the initial conditions (1.3). If $R_0 > 1$ and $\sigma_1^2 < d_1, 2\sigma_2^2 < d_2$ are valid, then*

$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t (U(s) - U^*)^2\, ds \leq \frac{\psi_2}{d_1 - \sigma_1^2}, \quad a.s.,$$
$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t (I(s) - I^*)^2\, ds \leq \Phi_2, \quad a.s.,$$

$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t (v(s)-v^*)^2\,ds \le \frac{2N^2\gamma_2}{c_1}, \quad a.s.,$$
$$\limsup_{t\to\infty} \frac{1}{t}\mathbb{E}\int_0^t f'(\xi)\,(D(s)-D^*)^2\,ds \le \frac{kD^*\varphi_2}{e^{-d_2\omega}c_2U^*}, \quad a.s.,$$

where

$$\begin{aligned}
\psi_2 &= \frac{2d_1+\beta v^* f(D^*)}{2d_1}(U^*)^2\sigma_1^2 + \frac{(d_1+\beta v^* f(D^*))\,U^*}{2d_1}e^{d_2\omega}I^*\sigma_2^2,\\
\Phi_2 &= \frac{2}{d_2-2\sigma_2^2}\left[\frac{e^{-2d_2\omega}}{d_1-\sigma_1^2}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)\psi_2 + e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2\right],\\
\gamma_2 &= e^{-2d_2\omega}\left(1+d_1+c_1+\frac{d_1^2}{c_1}+\sigma_1^2\right)\psi_2 + \left(\frac{d_1^2}{4}+c_1+\sigma_2^2\right)\Phi_2 + e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2,\\
\varphi_2 &= \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2.
\end{aligned}$$

Proof. Observing that the positive equilibrium of the system (1.1) is (U^*, I^*, v^*, D^*), we have

$$\begin{cases}
\lambda - \beta v^* f(D^*)U^* - d_1U^* = 0,\\
e^{-d_2\omega}\beta v^* f(D^*)U^* - d_2I^* = 0,\\
d_2NI^* - c_1v^* = 0,\\
\lambda_1 - k\beta v^* f(D^*)D^* - c_2D^* = 0.
\end{cases}$$

Define

$$V_1 = U - U^* - U^*\ln\frac{U}{U^*}.$$

Applying Itô's formula, we can show that

$$\mathrm{d}V_1 = LV_1\mathrm{d}t + \sigma_1(U-U^*)\mathrm{d}B_1(t),$$

where

$$\begin{aligned}
LV_1 &= \left(1-\frac{U^*}{U}\right)[\lambda - \beta v f(D)U - d_1U] + \frac{1}{2}U^*\sigma_1^2\\
&= \lambda - \beta v f(D)U - d_1U - \frac{\lambda U^*}{U} + \beta v f(D)U^* + d_1U^* + \frac{1}{2}U^*\sigma_1^2\\
&= [\beta v^* f(D^*)U^* + d_1U^*]\left(2-\frac{U^*}{U}-\frac{U}{U^*}\right) + \beta v^* f(D^*)(U-U^*) - \beta v f(D)(U-U^*) + \frac{1}{2}U^*\sigma_1^2\\
&= -[\beta v^* f(D^*) + d_1]\frac{(U-U^*)^2}{U} - [\beta v f(D) - \beta v^* f(D^*)](U-U^*) + \frac{1}{2}U^*\sigma_1^2.
\end{aligned}$$

Define

$$V_2 = I - I^* - I^*\ln\frac{I}{I^*}.$$

Utilizing Itô's formula results in

$$\mathrm{d}V_2 = LV_2\mathrm{d}t + \sigma_2(I - I^*)\mathrm{d}B_2(t),$$

where

$$\begin{aligned}
LV_2 =&\left(1 - \frac{I^*}{I}\right)\left[e^{-d_2\omega}\beta v(t-\omega)f(D(t-\omega))U(t-\omega) - d_2 I\right] + \frac{1}{2}I^*\sigma_2^2\\
=&e^{-d_2\omega}\beta v(t-\omega)f(D(t-\omega))U(t-\omega) - d_2 I - e^{-d_2\omega}\beta v(t-\omega)f(D(t-\omega))U(t-\omega)\frac{I^*}{I} + d_2 I^* + \frac{1}{2}I^*\sigma_2^2\\
=&e^{-d_2\omega}\beta v(t-\omega)f(D(t-\omega))U(t-\omega) - d_2 I - e^{-d_2\omega}\beta v(t-\omega)f(D(t-\omega))U(t-\omega)\frac{I^*}{I}\\
&+ e^{-d_2\omega}\beta v^* f(D^*)U^* + \frac{1}{2}I^*\sigma_2^2\\
=&e^{-d_2\omega}\beta v^* f(D^*)U^*\left[\frac{v(t-\omega)f(D(t-\omega))U(t-\omega)}{v^* f(D^*)U^*} + 1 - \frac{I^* v(t-\omega)f(D(t-\omega))U(t-\omega)}{I v^* f(D^*)U^*} - \frac{I}{I^*}\right] + \frac{1}{2}I^*\sigma_2^2\\
\leq&e^{-d_2\omega}\beta v^* f(D^*)U^*\left[\frac{v(t-\omega)f(D(t-\omega))U(t-\omega)}{v^* f(D^*)U^*} - \ln\frac{I^* v(t-\omega)f(D(t-\omega))U(t-\omega)}{I v^* f(D^*)U^*} - \frac{I}{I^*}\right] + \frac{1}{2}I^*\sigma_2^2.
\end{aligned}$$

Define

$$V_3 = e^{-d_2\omega}\beta v^* f(D^*)U^*\int_{t-\omega}^{t}\left[\frac{v(s)f(D(s))U(s)}{v^* f(D^*)U^*} - \ln\frac{v(s)f(D(s))U(s)}{v^* f(D^*)U^*} - 1\right]\mathrm{d}s,$$

then,

$$\begin{aligned}
LV_3 =&e^{-d_2\omega}\beta v^* f(D^*)U^*\left[\frac{vf(D)U}{v^* f(D^*)U^*} - \ln\frac{vf(D)U}{v^* f(D^*)U^*} - \frac{v(t-\omega)f(D(t-\omega))U(t-\omega)}{v^* f(D^*)U^*}\right.\\
&\left.+ \ln\frac{v(t-\omega)f(D(t-\omega))U(t-\omega)}{v^* f(D^*)U^*}\right].
\end{aligned}$$

Define

$$V_4 = \frac{1}{d_2 N I^*}\left(v - v^* - v^*\ln\frac{v}{v^*}\right).$$

Applying Itô's formula, we can show that

$$\begin{aligned}
LV_4 &= \frac{1}{d_2 N I^*}\left(1 - \frac{v^*}{v}\right)(d_2 N I - c_1 v)\\
&= \frac{I}{I^*} - \frac{c_1 v}{d_2 N I^*} - \frac{v^* I}{v I^*} + \frac{c_1 v^*}{d_2 N I^*}\\
&= \frac{I}{I^*} - \frac{v}{v^*} - \frac{v^* I}{v I^*} + 1\\
&\leq \frac{I}{I^*} - \frac{v}{v^*} - \ln\frac{v^* I}{v I^*}\\
&= \frac{I}{I^*} - \frac{v}{v^*} - \ln\frac{I}{I^*} + \ln\frac{v}{v^*}.
\end{aligned}$$

Define

$$V_5 = V_2 + V_3 + e^{-d_2\omega}\beta v^* f(D^*)U^* V_4.$$

Then, we can easy to get that

$$\begin{aligned}
LV_5 \leq & e^{-d_2\omega}\beta v^* f(D^*)U^* \left[\frac{vf(D)U}{v^*f(D^*)U^*} - \ln\frac{vf(D)U}{v^*f(D^*)U^*} - \frac{I}{I^*} + \ln\frac{I}{I^*}\right] + \frac{1}{2}I^*\sigma_2^2 \\
& + e^{-d_2\omega}\beta v^* f(D^*)U^* \left(\frac{I}{I^*} - \ln\frac{I}{I^*} - \frac{v}{v^*} + \ln\frac{v}{v^*}\right) \\
= & e^{-d_2\omega}\beta v^* f(D^*)U^* \left[\frac{vf(D)U}{v^*f(D^*)U^*} - \ln\frac{vf(D)U}{v^*f(D^*)U^*} - \frac{v}{v^*} + \ln\frac{v}{v^*}\right] + \frac{1}{2}I^*\sigma_2^2 \\
= & e^{-d_2\omega}\beta v^* f(D^*)U^* \left[\frac{vf(D)U}{v^*f(D^*)U^*} - \ln\frac{f(D)U}{f(D^*)U^*} - \frac{v}{v^*}\right] + \frac{1}{2}I^*\sigma_2^2 \\
= & e^{-d_2\omega}\beta v^* f(D^*)U^* \left(\frac{U}{U^*} - \ln\frac{U}{U^*} - 1\right) + e^{-d_2\omega}\beta v^* f(D^*)U^* \Big[\frac{vf(D)U}{v^*f(D^*)U^*} \\
& - \ln\frac{f(D)}{f(D^*)} - \frac{v}{v^*} - \frac{U}{U^*} + 1\Big] + \frac{1}{2}I^*\sigma_2^2 \\
\leq & e^{-d_2\omega}\beta v^* f(D^*)U^* \left(\frac{U}{U^*} + \frac{U^*}{U} - 2\right) \\
& + e^{-d_2\omega}\beta v^* f(D^*)U^* \left[\frac{vf(D)U}{v^*f(D^*)U^*} - \frac{vf(D)}{v^*f(D^*)} - \frac{U}{U^*} + 1\right] + \frac{1}{2}I^*\sigma_2^2 \\
= & e^{-d_2\omega}\beta v^* f(D^*)\frac{(U-U^*)^2}{U} + e^{-d_2\omega}\left[\beta vf(D) - \beta v^* f(D^*)\right](U-U^*) + \frac{1}{2}I^*\sigma_2^2.
\end{aligned}$$

Define

$$V_6 = \frac{1}{2}(U-U^*)^2.$$

Then,

$$\mathrm{d}V_6 = LV_6\mathrm{d}t + \sigma_1 U(U-U^*)\mathrm{d}B_1(t),$$

where

$$\begin{aligned}
LV_6 = & (U-U^*)\left[\lambda - \beta vf(D)U - d_1U\right] + \frac{1}{2}\sigma_1^2U^2 \\
= & (U-U^*)\left[\beta v^* f(D^*)U^* + d_1U^* - d_1U - \beta vf(D)U\right] + \frac{1}{2}\sigma_1^2U^2 \\
\leq & -d_1(U-U^*)^2 + [\beta v^* f(D^*)U^* - \beta vf(D)U](U-U^*) + \sigma_1^2(U-U^*)^2 + \sigma_1^2(U^*)^2 \\
= & -(d_1-\sigma_1^2)(U-U^*)^2 - \beta vf(D)(U-U^*)^2 - \beta U^*\left[vf(D) - v^*f(D^*)\right](U-U^*) + \sigma_1^2(U^*)^2 \\
\leq & -(d_1-\sigma_1^2)(U-U^*)^2 - \beta U^*\left[vf(D) - v^*f(D^*)\right](U-U^*) + \sigma_1^2(U^*)^2.
\end{aligned}$$

Define

$$V_7 = \frac{\beta v^* f(D^*)U^*}{d_1}V_1 + e^{d_2\omega}\frac{(d_1+\beta v^* f(D^*))U^*}{d_1}V_5 + V_6,$$

then, we can derive that

$$
\begin{aligned}
LV_7 \leq & \frac{\beta v^* f(D^*) U^*}{d_1}\left[-(\beta v^* f(D^*)+d_1)\frac{(U-U^*)^2}{U}-(\beta v f(D)-\beta v^* f(D^*))(U-U^*)+\frac{1}{2}U^*\sigma_1^2\right] \\
&+e^{d_2\omega}\frac{(d_1+\beta v^* f(D^*))U^*}{d_1}\Big[e^{-d_2\omega}\beta v^* f(D^*)\frac{(U-U^*)^2}{U}+e^{-d_2\omega}(\beta v f(D)-\beta v^* f(D^*))(U-U^*) \\
&+\frac{1}{2}I^*\sigma_2^2\Big]-(d_1-\sigma_1^2)(U-U^*)^2-\beta U^*\left[v f(D)-v^* f(D^*)\right](U-U^*)+\sigma_1^2(U^*)^2 \\
=&-(d_1-\sigma_1^2)(U-U^*)^2+\frac{2d_1+\beta v^* f(D^*)}{2d_1}(U^*)^2\sigma_1^2+\frac{(d_1+\beta v^* f(D^*))U^*}{2d_1}e^{d_2\omega}I^*\sigma_2^2 \\
=&-(d_1-\sigma_1^2)(U-U^*)^2+\psi_2,
\end{aligned}
\tag{3.9}
$$

where

$$
\psi_2=\frac{2d_1+\beta v^* f(D^*)}{2d_1}(U^*)^2\sigma_1^2+\frac{(d_1+\beta v^* f(D^*))U^*}{2d_1}e^{d_2\omega}I^*\sigma_2^2.
$$

Taking the expected yield after integrating each side of Eq (3.9) from 0 to t

$$
\mathbb{E}V_7(t)-\mathbb{E}V_7(0)\leq-(d_1-\sigma_1^2)\mathbb{E}\int_0^t (U(s)-U^*)^2\,\mathrm{d}s+\psi_2 t. \tag{3.10}
$$

Dividing each side of (3.10) by t and then taking the upper limit yield

$$
\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t (U(s)-U^*)^2\,\mathrm{d}s\leq\frac{\psi_2}{(d_1-\sigma_1^2)},\quad a.s.
$$

Define

$$
V_8=\frac{1}{2}\left[e^{-d_2\omega}(U-U^*)+(I(t+\tau)-I^*)\right]^2.
$$

Then,

$$
\begin{aligned}
LV_8=&\left[e^{-d_2\omega}(U-U^*)+(I(t+\omega)-I^*)\right]\left[e^{-d_2\omega}(\lambda-\beta v f(D)U-d_1U)+e^{-d_2\omega}\beta v f(D)U-d_2I(t+\omega)\right] \\
&+\frac{1}{2}e^{-2d_2\omega}\sigma_1^2+\frac{1}{2}\sigma_2^2I^2(t+\omega) \\
=&\left[e^{-d_2\omega}(U-U^*)+(I(t+\omega)-I^*)\right]\left[e^{-d_2\omega}(\beta v^* f(D^*)U^*+d_1U^*-d_1U)+e^{-d_2\omega}\beta v f(D)U\right. \\
&\left.-d_2I(t+\omega)\right]+\frac{1}{2}e^{-2d_2\omega}\sigma_1^2+\frac{1}{2}\sigma_2^2I^2(t+\omega) \\
=&\left[e^{-d_2\omega}(U-U^*)+(I(t+\omega)-I^*)\right][-d_1(U-U^*)-d_2(I(t+\omega)-I^*)]+\frac{1}{2}e^{-2d_2\omega}\sigma_1^2+\frac{1}{2}\sigma_2^2I^2(t+\omega) \\
=&-e^{-2d_2\omega}d_1(U-U^*)^2-e^{-d_2\omega}d_1(U-U^*)(I(t+\omega)-I^*)-d_2(I(t+\omega)-I^*)^2 \\
&-e^{-d_2\omega}d_2(U-U^*)(I(t+\omega)-I^*)+\frac{1}{2}e^{-2d_2\omega}\sigma_1^2+\frac{1}{2}\sigma_2^2I^2(t+\omega) \\
\leq&-e^{-2d_2\omega}d_1(U-U^*)^2-d_2(I(t+\omega)-I^*)^2-e^{-d_2\omega}(d_1+d_2)(U-U^*)(I(t+\omega)-I^*) \\
&+e^{-2d_2\omega}\sigma_1^2(U-U^*)^2+e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I(t+\omega)-I^*)^2+\sigma_2^2(I^*)^2 \\
\leq&-e^{-2d_2\omega}(d_1-\sigma_1^2)(U-U^*)^2-(d_2-\sigma_2^2)(I(t+\omega)-I^*)^2+e^{-2d_2\omega}\frac{(d_1+d_2)^2}{2d_2}(U-U^*)^2 \\
&+\frac{d_2}{2}(I(t+\omega)-I^*)^2+e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2 \\
=&e^{-2d_2\omega}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)(U-U^*)^2-\frac{1}{2}(d_2-2\sigma_2^2)(I(t+\omega)-I^*)^2+e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2,
\end{aligned}
$$

in the above inequality, we apply the Young inequality

$$-e^{-d_2\omega}(d_1+d_2)(U-U^*)(I(t+\omega)-I^*) \le e^{-2d_2\omega}\frac{(d_1+d_2)^2}{2d_2}(U-U^*)^2 + \frac{d_2}{2}(I(t+\omega)-I^*)^2.$$

Define

$$V_9 = \frac{e^{-2d_2\omega}}{d_1-\sigma_1^2}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)V_7 + V_8 + \frac{1}{2}(d_2-2\sigma_2^2)\int_t^{t+\omega}(I(s)-I^*)^2\mathrm{d}s.$$

Then,

$$\begin{aligned}
LV_9 \le& \frac{e^{-2d_2\omega}}{d_1-\sigma_1^2}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)\left[-(d_1-\sigma_1^2)(U-U^*)^2+\psi_2\right] \\
&+ e^{-2d_2\omega}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)(U-U^*)^2 - \frac{1}{2}(d_2-2\sigma_2^2)(I(t+\omega)-I^*)^2 + e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2 \\
&+ \frac{1}{2}(d_2-2\sigma_2^2)(I(t+\omega)-I^*)^2 - \frac{1}{2}(d_2-2\sigma_2^2)(I-I^*)^2 \\
=& -\frac{1}{2}(d_2-2\sigma_2^2)(I-I^*)^2 + \frac{e^{-2d_2\tau}}{d_1-\sigma_1^2}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)\psi_2 + e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2.
\end{aligned} \tag{3.11}$$

Taking the expected yield after integrating each side of Eq (3.11) from 0 to t

$$\begin{aligned}
\mathbb{E}V_9(t)-\mathbb{E}V_9(0) \le& -\frac{1}{2}(d_2-2\sigma_2^2)\mathbb{E}\int_0^t (I(s)-I^*)^2\,\mathrm{d}s \\
&+ \left[\frac{e^{-2d_2\omega}}{d_1-\sigma_1^2}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)\psi_2 + e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2\right]t.
\end{aligned} \tag{3.12}$$

Taking the upper limit yield after dividing both sides of (3.12) by t

$$\begin{aligned}
\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t (I(s)-I^*)^2\,\mathrm{d}s \le& \frac{2}{d_2-2\sigma_2^2}\left[\frac{e^{-2d_2\omega}}{d_1-\sigma_1^2}\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_1^2\right)\psi_2 + e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2\right] \\
=& \Phi_2, \quad a.s.
\end{aligned}$$

Define

$$V_{10} = \frac{1}{2}\left[e^{-d_2\omega}(U-U^*)+(I(t+\omega)-I^*)+\frac{1}{N}(v(t+\omega)-v^*)\right]^2.$$

Then,

$$
\begin{aligned}
LV_{10} =&\left[e^{-d_2\omega}(U-U^*)+(I(t+\omega)-I^*)+\frac{1}{N}(v(t+\omega)-v^*)\right]\left[e^{-d_2\omega}(\lambda-d_1U)-\frac{c_1}{N}v(t+\omega)\right]\\
&+\frac{1}{2}e^{-2d_2\omega}\sigma_1^2U^2+\frac{1}{2}\sigma_2^2I^2(t+\omega)\\
=&\left[e^{-d_2\omega}(U-U^*)+(I(t+\omega)-I^*)+\frac{1}{N}(v(t+\omega)-v^*)\right]\left[-e^{-d_2\omega}d_1(U-U^*)-\frac{c_1}{N}(v(t+\omega)-v^*)\right]\\
&+\frac{1}{2}e^{-2d_2\omega}\sigma_1^2U^2+\frac{1}{2}\sigma_2^2I^2(t+\omega)\\
=&-e^{-2d_2\omega}d_1(U-U^*)^2-\frac{c_1}{N^2}(v(t+\omega)-v^*)^2-e^{-d_2\omega}d_1(U-U^*)(I(t+\omega)-I^*)\\
&-e^{-d_2\omega}\frac{(d_1+c_1)}{N}(U-U^*)(v(t+\omega)-v^*)-\frac{c_1}{N}(I(t+\omega)-I^*)(v(t+\omega)-v^*)+\frac{1}{2}e^{-2d_2\omega}\sigma_1^2U^2\\
&+\frac{1}{2}\sigma_2^2I^2(t+\omega)\\
\le&-e^{-2d_2\omega}d_1(U-U^*)^2-\frac{c_1}{N^2}(v(t+\omega)-v^*)^2+e^{-2d_2\omega}(U-U^*)^2+\frac{d_1^2}{4}(I(t+\omega)-I^*)^2\\
&+e^{-2d_2\omega}\frac{(d_1+c_1)^2}{c_1}(U-U^*)^2+\frac{c_1}{4N^2}(v(t+\omega)-v^*)^2+c_1(I(t+\omega)-I^*)^2+\frac{c_1}{4N^2}(v(t+\omega)-v^*)^2\\
&+e^{-2d_2\omega}\sigma_1^2(U-U^*)^2+\sigma_2^2(I(t+\omega)-I^*)^2+e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2\\
=&e^{-2d_2\omega}\left(1+d_1+c_1+\frac{d_1^2}{c_1}+\sigma_1^2\right)(U-U^*)^2+\left(\frac{d_1^2}{4}+c_1+\sigma_2^2\right)(I(t+\omega)-I^*)^2\\
&-\frac{c_1}{2N^2}(v(t+\omega)-v^*)^2+e^{-2d_2\omega}\sigma_1^2(U^*)^2+\sigma_2^2(I^*)^2,
\end{aligned}
$$

where, we use the Young inequality to simplify the above inequalities

$$
\begin{cases}
-e^{-d_2\omega}d_1(U-U^*)(I(t+\omega)-I^*)\le e^{-2d_2\omega}(U-U^*)^2+\dfrac{d_1^2}{4}(I(t+\omega)-I^*)^2,\\
-e^{-d_2\omega}\dfrac{(d_1+c_1)}{N}(U-U^*)(v(t+\omega)-v^*)\le e^{-2d_2\omega}\dfrac{(d_1+c_1)^2}{c_1}(U-U^*)^2+\dfrac{c_1}{4N^2}(v(t+\omega)-v^*)^2,\\
-\dfrac{c_1}{N}(I(t+\omega)-I^*)(v(t+\omega)-v^*)\le c_1(I(t+\omega)-I^*)^2+\dfrac{c_1}{4N^2}(v(t+\omega)-v^*)^2.
\end{cases}
$$

Define

$$
V_{11}=e^{-2d_2\omega}p_2V_7+h_2V_8+V_{10}+\frac{c_1}{2N^2}\int_t^{t+\omega}(v(s)-v^*)^2\mathrm{d}s,
$$

where

$$
\begin{aligned}
p_2&=\frac{1}{d_1-\sigma_1^2}\left[\left(1+d_1+c_1+\frac{d_1^2}{c_1}+\sigma_1^2\right)+h_2\left(\frac{d_1^2+d_2^2}{2d_2}+\sigma_2^2\right)\right],\\
h_2&=\frac{2}{d_2-2\sigma_2^2}\left(\frac{d_1^2}{4}+c_1+\sigma_2^2\right).
\end{aligned}
$$

Therefore,

$$\begin{aligned}LV_{11} \leq & -\frac{c_1}{2N^2}(v-v^*)^2 + e^{-2d_2\omega}\left(1+d_1+c_1+\frac{d_1^2}{c_1}+\sigma_1^2\right)\psi_2 + \left(\frac{d_1^2}{4}+c_1+\sigma_2^2\right)\Phi_2 \\ & + e^{-2d_2\omega}\sigma_1^2(U^*)^2 + \sigma_2^2(I^*)^2 \\ = & -\frac{c_1}{2N^2}(v-v^*)^2 + \gamma_2,\end{aligned} \tag{3.13}$$

where

$$\gamma_2 = e^{-2d_2\omega}\left(1+d_1+c_1+\frac{d_1^2}{c_1}+\sigma_1^2\right)\psi_2 + \left(\frac{d_1^2}{4}+c_1+\sigma_2^2\right)\Phi_2 + e^{-2d_2\omega}\sigma_1^2(U^*)^2 + \sigma_2^2(I^*)^2.$$

Taking the expected yield after integrating each side of Eq (3.13) from 0 to t

$$\mathbb{E}V_{11}(t) - \mathbb{E}V_{11}(0) \leq -\frac{c_1}{2N^2}\mathbb{E}\int_0^t (v(s)-v^*)^2\,\mathrm{d}s + \gamma_2 t. \tag{3.14}$$

Taking the upper limit yield after dividing both sides of (3.14) by t

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t (v(s)-v^*)^2\,\mathrm{d}s \leq \frac{2N^2\gamma_2}{c_1}, \quad a.s.$$

Define

$$\begin{aligned}V_{12} =& e^{-d_2\omega}\left(U-U^*-U^*\ln\frac{U}{U^*}\right) + \left(I-I^*-I^*\ln\frac{I}{I^*}\right) + \frac{1}{N}\left(v-v^*-v^*\ln\frac{v}{v^*}\right) \\ & + \frac{e^{-d_2\omega}U^*}{kD^*}\left(D-D^*-\int_{D^*}^{D}\frac{f(D^*)}{f(s)}\mathrm{d}s\right) + d_2I^*\int_{t-\omega}^{t} g\left(\frac{v(s)f(D(s))U(s)}{v^*f(D^*)U^*}\right)\mathrm{d}s.\end{aligned}$$

Then,

$$\begin{aligned}LV_{12} =& e^{-d_2\omega}\left(1-\frac{U^*}{U}\right)[\beta v^*f(D^*)U^* - \beta v f(D)U + d_1(U^*-U)] \\ & + \left(1-\frac{I^*}{I}\right)\left[e^{-d_2\omega}\beta v(t-\omega)f(D(t-\omega))U(t-\omega) - d_2I\right] + \frac{1}{N}\left(1-\frac{v^*}{v}\right)(d_2NI - c_1v) \\ & + \frac{e^{-d_2\omega}U^*}{kD^*}\left(1-\frac{f(D^*)}{f(D)}\right)[k\beta v^*f(D^*)D^* - k\beta v f(D)D + c_2D^* - c_2D] + d_2I^*g\left(\frac{vf(D)U}{v^*f(D^*)U^*}\right) \\ & - d_2I^*g\left(\frac{v(t-\omega)f(D(t-\omega))U(t-\omega)}{v^*f(D^*)U^*}\right) + \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2 \\ =& e^{-d_2\omega}\left(1-\frac{U^*}{U}\right)[\beta v^*f(D^*)U^* - \beta v f(D)U + d_1(U^*-U)] \\ & + \left(1-\frac{I^*}{I}\right)\left[e^{-d_2\omega}\beta v(t-\omega)f(D(t-\omega))U(t-\omega) - d_2I\right] + \frac{1}{N}(1-\frac{v^*}{v})(d_2NI - c_1v) \\ & + \frac{e^{-d_2\omega}U^*}{kD^*}\left(1-\frac{f(D^*)}{f(D)}\right)[k\beta v^*f(D^*)D^* - k\beta v f(D)D + c_2D^* - c_2D] + d_2I^*\frac{vf(D)U}{v^*f(D^*)U^*} \\ & - d_2I^*\frac{v(t-\omega)f(D(t-\omega))U(t-\omega)}{v^*f(D^*)U^*} + d_2I^*\ln\frac{v(t-\omega)f(D(t-\omega))U(t-\omega)}{vf(D)U} + \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2.\end{aligned}$$

We have

$$\beta v^* f(D^*)U^* = e^{d_2\omega} d_2 I, c_1 v^* = d_2 N I^*$$

and use the equality

$$\ln \frac{v(t-\omega) f(D(t-\omega))U(t-\omega)}{v f(D)U} = \ln \frac{v(t-\omega) f(D(t-\omega))U(t-\omega)I^*}{v^* f(D^*)U^* I} + \ln \frac{f(D^*)}{f(D)} + \ln \frac{v^* I}{v I^*} + \ln \frac{U^*}{U}.$$

So,

$$\begin{aligned}
LV_{12} =& -\frac{d_1 e^{-d_2\omega}}{U}(U-U^*)^2 - \left(\frac{e^{-d_2\omega}\beta v U^*}{D^*} + \frac{e^{-d_2\omega}c_2 U^*}{f(D)kD^*}\right)(D-D^*)[f(D)-f(D^*)] - d_2 I^* \left[g\left(\frac{U^*}{U}\right)\right. \\
&\left. + g\left(\frac{v^* I}{v I^*}\right) + g\left(\frac{f(D^*)}{f(D)}\right) + g\left(\frac{v(t-\omega) f(D(t-\omega))U(t-\omega)I^*}{v^* f(D^*)U^* I}\right)\right] + \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2 \\
\le& -\frac{e^{-d_2\omega}c_2 U^*}{f(D)kD^*}(D-D^*)[f(D)-f(D^*)] + \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2 \\
=& -\frac{e^{-d_2\omega}c_2 U^* f'(\xi)}{f(D)kD^*}(D-D^*)^2 + \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2 \\
\le& -\frac{e^{-d_2\omega}c_2 U^* f'(\xi)}{kD^*}(D-D^*)^2 + \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2 \\
=& -\frac{e^{-d_2\omega}c_2 U^*}{kD^*} f'(\xi)(D-D^*)^2 + \varphi_2,
\end{aligned} \tag{3.15}$$

where

$$f(D) - f(D_0) = f'(\xi)(D - D_0),$$

ξ is between D and D_0, $f'(\xi) > 0$, and

$$\varphi_2 = \frac{1}{2}e^{-d_2\omega}U^*\sigma_1^2 + \frac{1}{2}I^*\sigma_2^2.$$

Taking the expected yield after integrating each side of Eq (3.15) from 0 to t

$$\mathbb{E}V_{14}(t) - \mathbb{E}V_{14}(0) \le -\frac{e^{-d_2\omega}c_2 U^*}{kD^*}\mathbb{E}\int_0^t f'(\xi)\,(D(s)-D^*)^2\,\mathrm{d}s + \varphi_2 t. \tag{3.16}$$

Taking the upper limit yield after dividing both sides of (3.16) by t

$$\limsup_{t\to\infty}\frac{1}{t}\mathbb{E}\int_0^t f'(\xi)\,(D(s)-D^*)^2\,\mathrm{d}s \le \frac{kD^*\varphi_2}{e^{-d_2\omega}c_2 U^*}, \quad a.s.$$

□

Remark 3.2. *When $\sigma_i = 0$ $(i = 1, 2)$, it is evident from Theorem 3.2 that*

$$\begin{cases}
LV_7 \le -d_1(U-U^*)^2 \le 0, \\
LV_9 \le -\frac{1}{2}d_2(I-I^*)^2 \le 0, \\
LV_{11} \le -\frac{c_1}{2N^2}(v-v^*)^2 \le 0, \\
LV_{14} \le -\frac{e^{-d_2\omega}c_2 U^*}{kD^*} f'(\xi)(D-D^*)^2 \le 0,
\end{cases}$$

this means that the disease-free equilibrium point E^* of system (1.1) is globally asymptotically stable, from which the nature of the deterministic system can be introduced.

4. Numerical simulations

In this subsection, we provide some numerical simulations to confirm the validity of the above theorem and validate the conclusions in the paper. We set the initial value to

$$(U(0), I(0), v(0), D(0)) = (6, 3, 4, 4)$$

before the numerical simulation.

Case 1. Let $\lambda = 2$, $\lambda_1 = 1.2$, $d_1 = 0.4$, $d_2 = 0.4$, $c_1 = 0.3$, $c_2 = 0.4$, $\beta = 0.05$, $\omega = 2$, $N = 2$, $k = 0.5$, $D_1 = 0.2$. Then calculate that the basic reproduction number $R_0 = 0.7470 < 1$. Let $\sigma_i = 0.1$ $(i = 1, 2)$ in Figure 1a. Let $\sigma_i = 0.2$ $(i = 1, 2)$ in Figure 1b. As seen in Figure 1, the solution of system (1.2) swings asymptotically about E_0, confirming the Theorem 3.1.

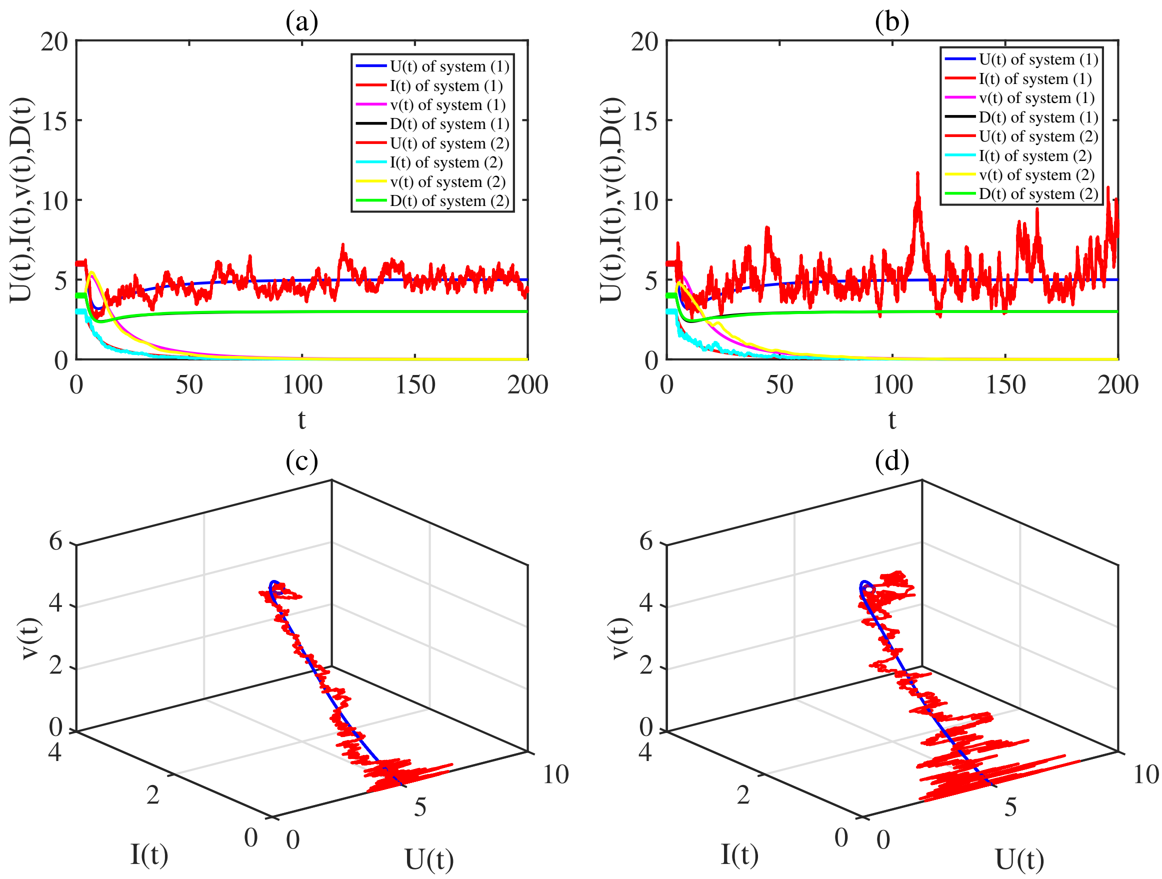

Figure 1. (a) and (b) are the time sequence diagrams at $\sigma_i = 0.1$ and $\sigma_i = 0.2$ $(i = 1.2)$, respectively, and (c) and (d) are the corresponding spatial phases.

Case 2. Let $\lambda = 6$, $\lambda_1 = 2$, $d_1 = 0.4$, $d_2 = 0.4$, $c_1 = 0.8$, $c_2 = 0.2$, $\beta = 0.05$, $\omega = 2$, $N = 3$, $k = 0.5$, $D_1 = 0.2$. Then calculate that the basic reproduction number $R_0 = 1.2606 > 1$. Let $\sigma_i = 0.1$ $(i = 1, 2)$ in Figure 2a. Let $\sigma_i = 0.2$ $(i = 1, 2)$ in Figure 2b. As seen in Figure 2, the solution of system (1.2) swings asymptotically about E^*, confirming the Theorem 3.2.

Case 3. Let $\lambda = 3$, $\lambda_1 = 2$, $d_1 = 0.4$, $d_2 = 0.4$, $c_1 = 0.4$, $c_2 = 0.2$, $\beta = 0.05$, $\omega = 2$, $N = 3$, $k =$

0.5, $D_1 = 0.2$, $\sigma_1 = 0.1$, $\sigma_2 = 0.1$. We can observe that the viruses and the infected target cells are going to persist from Figure 3c,d.

Case 4. Let $\lambda = 3$, $\lambda_1 = 2$, $d_1 = 0.4$, $d_2 = 0.4$, $c_1 = 0.4$, $c_2 = 0.2$, $\beta = 0.05$, $\omega = 2$, $N = 3$, $k = 0.5$, $D_1 = 0.2$, $\sigma_1 = 0.1$, $\sigma_2 = 1$. We can see that the viruses and the infected target cells will become extinct from Figure 4c,d.

Case 5. Let $\lambda = 6$, $\lambda_1 = 2$, $d_1 = 0.4$, $d_2 = 0.4$, $c_1 = 0.8$, $c_2 = 0.2$, $\beta = 0.05$, $\omega = 2$, $N = 3$, $k = 0.5$, $D_1 = 0.2$. In Figure 5a, let $\sigma_i = 0.1$ $(i = 1, 2)$. In Figure 5b, let $\sigma_i = 0.8$ $(i = 1, 2)$. Figure 5 shows that under strong noise interference conditions, infected target cells and viruses go extinct.

Case 6. Let $\lambda = 6$, $\lambda_1 = 2$, $d_1 = 0.4$, $d_2 = 0.4$, $c_1 = 0.8$, $c_2 = 0.2$, $\beta = 0.05$, $N = 3$, $k = 0.5$, $D_1 = 0.2$, $\sigma_1 = \sigma_2 = 0.1$. In Figure 6, let $\omega = 1.8, \omega = 2.2, \omega = 4$, respectively. According to Figure 6, infected target cells and viruses will go extinct as the time delay gets longer.

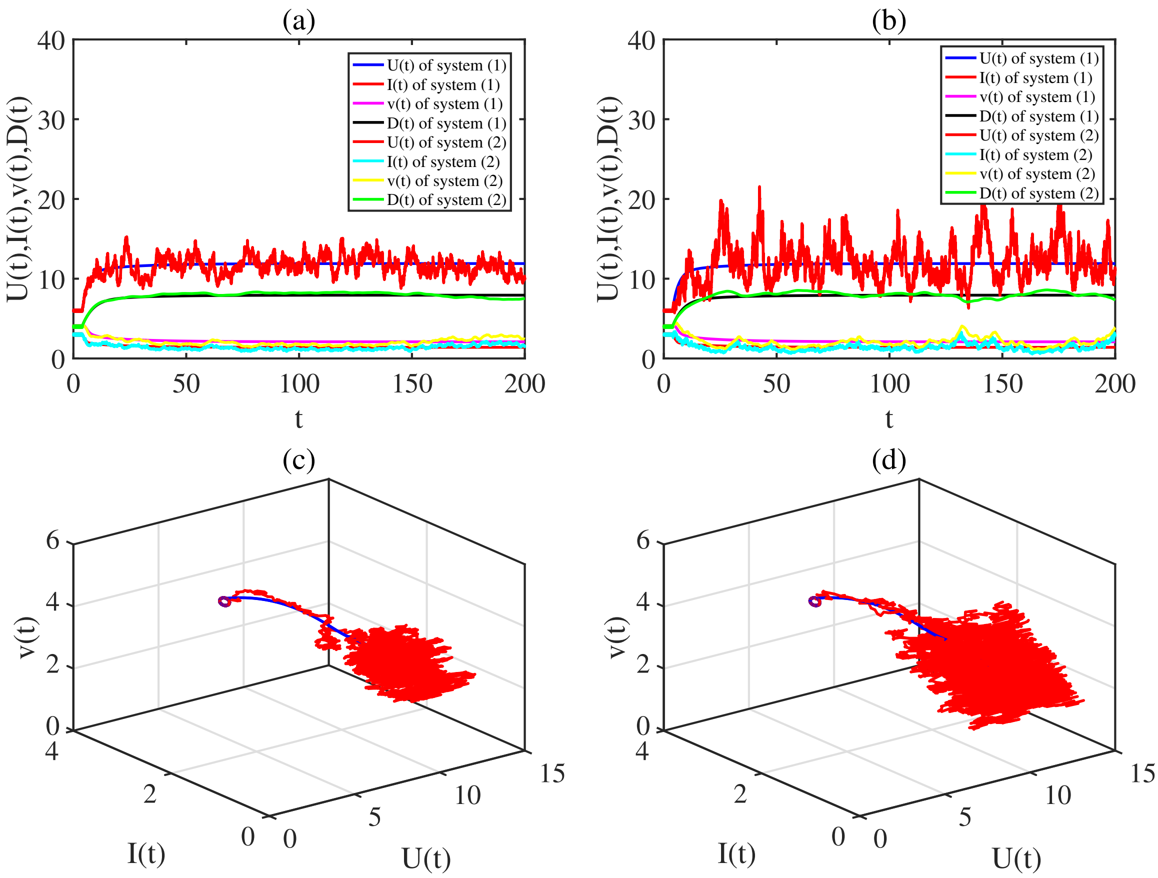

Figure 2. (a) and (b) are the time sequence diagrams at $\sigma_i = 0.1$ and $\sigma_i = 0.2$ $(i = 1.2)$, respectively, and (c) and (d) are the corresponding spatial phases.

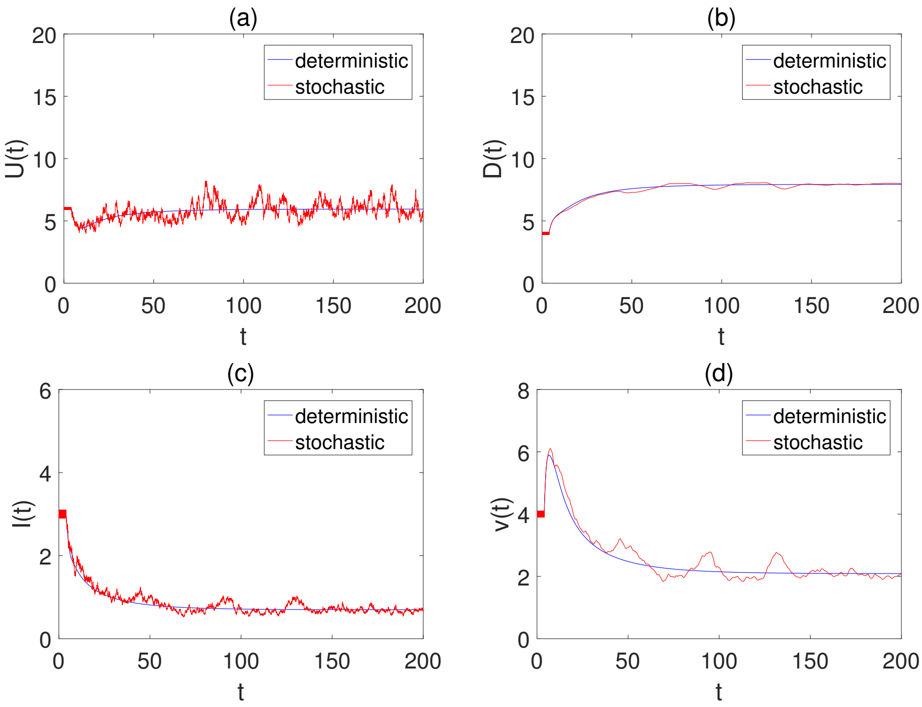

Figure 3. The time sequence diagrams for $U(t)$, $D(t)$, $I(t)$, and $v(t)$ are represented by the symbols for (a), (b), (c), and (d). $\sigma_1 = 0.1, \sigma_2 = 0.1$.

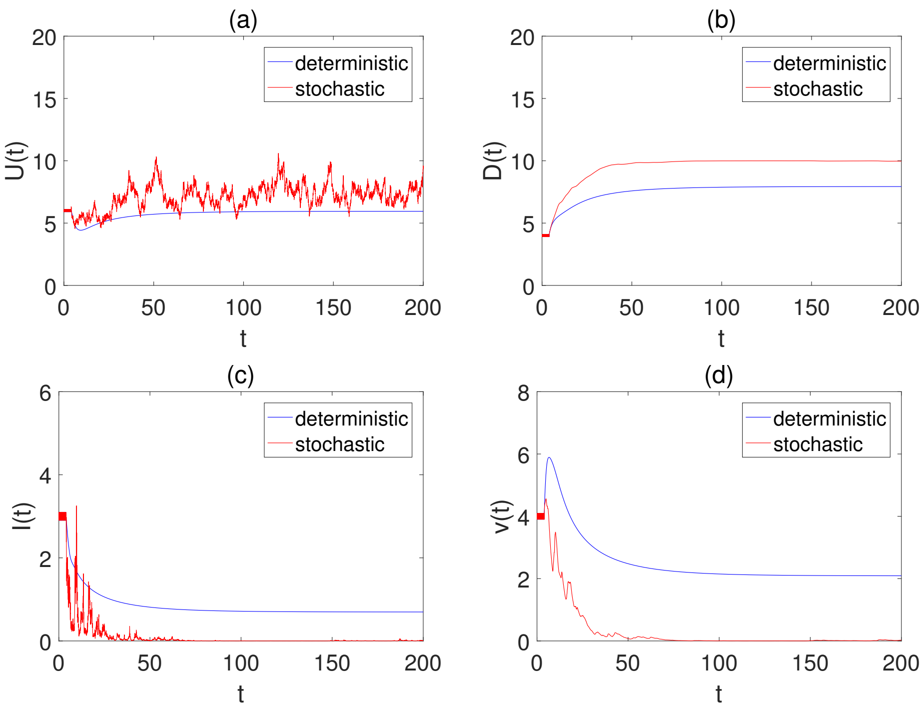

Figure 4. The time sequence diagrams for $U(t)$, $D(t)$, $I(t)$, and $v(t)$ are represented by the symbols for (a), (b), (c), and (d). $\sigma_1 = 0.1, \sigma_2 = 1$.

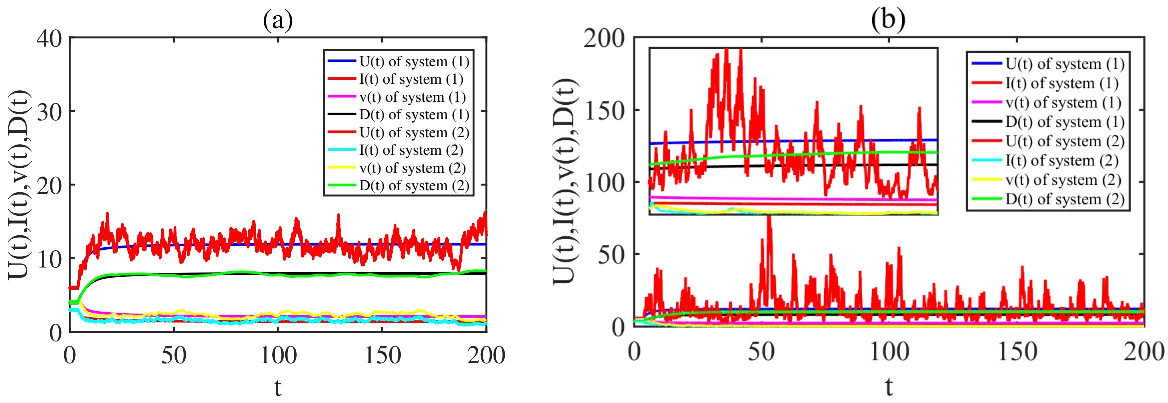

Figure 5. (a) and (b) are time sequence diagrams at $\sigma_i = 0.1$ and $\sigma_i = 0.8$ $(i = 1, 2)$, respectively.

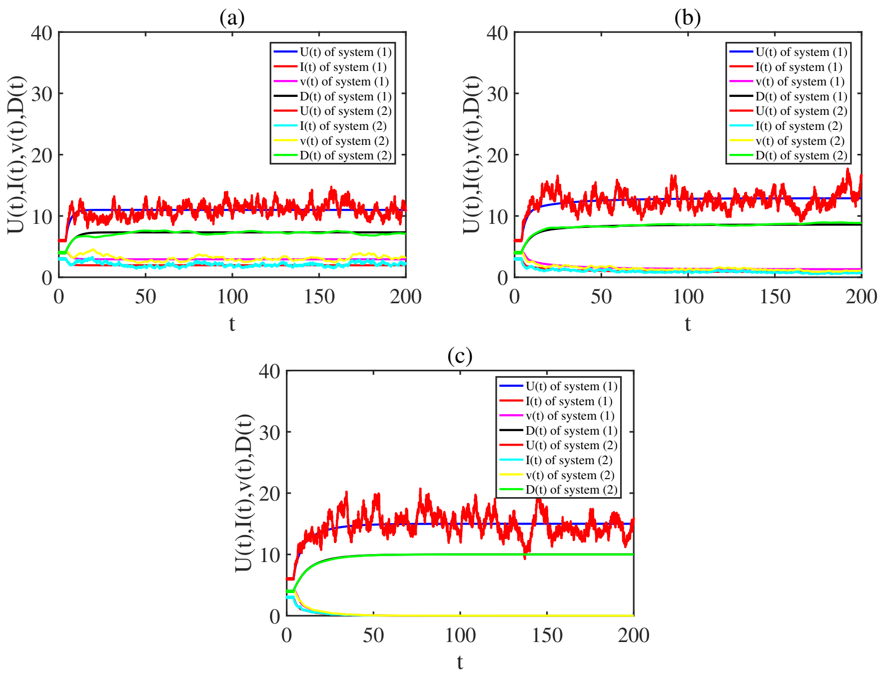

Figure 6. The time series plots (a), (b) and (c) are at $\omega = 1.8$, $\omega = 2.2$ and $\omega = 4$, respectively.

5. Conclusions

We investigate the dynamic impact of stochastic fluctuations in the environment, mediated by the ACE2 receptor protein, on the SARS-CoV-2 virus infection system with time delay. The long-term asymptotic properties of the stochastic time-delay system are obtained by building the suitable Lyapunov functions and applying the differential inequality techniques. The results indicate that the solution of the stochastic system (1.2) swings in the vicinity of the no-disease equilibrium point E_0

when $R_0 < 1$. When $R_0 > 1$, the solution of the stochastic system (1.2) swings in the vicinity of the endemic equilibrium point E^*.

The major results are as follows:

(1) The system (1.2) is stochastically ultimately bounded.

(2) When $R_0 < 1$ and $\sigma_i^2 < d_i$ $(i = 1, 2)$, the solution of the system (1.2) will oscillate in the vicinity of the disease-free equilibrium E_0 of its deterministic system (1.1), which means the viruses and the infected target cells will go extinct.

(3) When $R_0 > 1$ and $\sigma_1^2 < d_1, 2\sigma_2^2 < d_2$, the solution of the system (1.2) will oscillate in the vicinity of the endemic equilibrium E^* of its deterministic system (1.1), which means the viruses and the infected target cells will persist.

The following conclusions are obtained via theoretical analysis and numerical simulations:

(i) The solution of the stochastic system (1.2) oscillates in the neighborhood of the equilibrium of the deterministic system (1.1), the amplitude of the oscillation increases with the intensity of the environmental disturbances, and when the intensity of noise grows large enough, both virus and infected target cells go extinct, which suggests that fluctuations in the environment have an impact on the dynamics of the SARS-CoV-2 virus infection system (1.2).

(ii) Time delay also affects the dynamic properties of the SARS-CoV-2 virus infection system (1.2), and a long time delay leads to the extinction of the virus and infected target cells of system (1.2).

As a consequence, the spread of the SARS-CoV-2 virus can be controlled by increasing the intensity of random disturbances in the environment or by prolonging the time it takes for the virus to invade uninfected target cells or for infected cells to generate new viruses.

Use of AI tools declaration

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

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Conflict of interest

The authors declare that they have no competing interests.

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