Stability Analysis for Stochastic Differential Equations in Virology

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

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Abstract

In this paper, we propose a viral infection model governed by three stochastic differential equations. The global existence and positivity of solutions is investigated. Further, we give sufficient conditions for the stability in probability of the endemic equilibrium by using the direct Lyapunov method. Moreover, an application and numerical simulations are given to illustrate our theoretical results.

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1   Introduction

The mathematical modeling of the viral infections has played an important role in the better understanding of the dynamic of the viruses that invade almost any type of body tissue, from the brain to the skin [1], such as the human immunodeficiency virus (HIV), the hepatitis B virus (HBV), the hepatitis C virus (HCV) and the Influenza which are the major diseases in the world. In the last decade, ordinary differential equations have been used by many authors in epidemiology as well as virology [2–10]. The basic and the important research subjects of this systems are existence of the threshold value which distinguishes whether the local and global stability of steady states, existence of periodic solutions, persistence and extinction of disease.

Recently, Hattaf et al. [11] studied the dynamical behavior of a virus dynamics model with general incidence rate and cure rate described by the following viral infection model

$$
\begin{cases}
\dfrac{dx(t)}{dt} = \lambda - \delta x(t) - f\big(x(t), y(t), v(t)\big)v(t) + \rho y(t), \\
\dfrac{dy(t)}{dt} = f\big(x(t), y(t), v(t)\big)v(t) - (a + \rho)y(t), \\
\dfrac{dv(t)}{dt} = ky(t) - \mu v(t),
\end{cases}
\tag{1}
$$

where $x(t)$, $y(t)$ and $v(t)$ denote the concentration of uninfected cells, infected cells and virus particles produced by infected cell at time t, respectively. The λ and k are the recruitment rate of uninfected cells and the production rate of the free virus by an infected cell. The ρ is the cure rate of the infected cells to uninfected cells. The δ, a and μ are, respectively, the death rates of uninfected cells, infected cells and free virus with $\mu > a$. Biologically speaking, the natural death rate of free virus is always bigger then the natural death rate of infected cells. The term $f(x, y, v)v$ describes the incidence of virus infection of healthy x cells. The incidence function $f(x, y, v)$ is assumed to be continuously differentiable in the interior of $\mathbb{R}^3_+$ and satisfies the following hypotheses:

$$
f(0, y, v) = 0, \ for \ all \ y \geq 0 \ and \ v \geq 0,
\tag{H_1}
$$

$$
\frac{\partial f}{\partial x}(x, y, v) > 0, \ for \ all \ x > 0, y \geq 0 \ and \ v \geq 0,
\tag{H_2}
$$

$$
\frac{\partial f}{\partial y}(x, y, v) \leq 0 \ and \ \frac{\partial f}{\partial v}(x, y, v) \leq 0, \ for \ all \ x \geq 0, y \geq 0 \ and \ v \geq 0.
\tag{H_3}
$$

As in [11], the basic reproduction number is given by

$$
R_0 = \frac{kf(\frac{\lambda}{\delta}, 0, 0)}{(\rho + a)\mu},
$$

which biologically represents the average number of secondary infections produced by one infected cell during the period of infection when all cells are uninfected. Moreover, Hattaf et al. [11] has proved that if $R_0 \leq 1$, the system (1) has unique infection-free equilibrium corresponding to the extinction of virus, and it is globally asymptotically stable. If $R_0 > 1$, E_f becomes unstable and the system (1) has an endemic equilibrium of the form $E^*(x^*, y^*, v^*)$ and it is globally asymptotically stable.

On the other hand, the model (1) don't incorporate the effect of the environmental noise. While, it is essential to reveal how the environmental noise affects the viral infection models. Using stochastic models can attain more real benefits and can predict the future dynamics of the system accurately. For better understanding the dynamics of the viral infection models, we introduce stochastic perturbations into the deterministic model (1). Motivated by [12, 13], the corresponding to system (1), the stochastic viral infection model takes the following form

$$\begin{cases} dx(t) &= \Big[\lambda - \delta x(t) - f\big(x(t), y(t), v(t)\big)v(t) + \rho y(t)\Big]dt + \sigma_1\big[x - x^*\big]dB_1(t), \\ dy(t) &= \Big[f\big(x(t), y(t), v(t)\big)v(t) - (a + \rho)y(t)\Big]dt + \sigma_2\big[y - y^*\big]dB_2(t), \\ dv(t) &= \Big[ky(t) - \mu v(t)\Big]dt + \sigma_3\big[v - v^*\big]dB_3(t), \end{cases} \quad (2)$$

where the stochastic perturbations are of white noise type and that they are directly proportional to the deviation of a current state (x, y, v) from the endemic equilibrium $E^*(x^*, y^*, v^*)$ for the corresponding deterministic model (1). $B_i(t)$ $(i = 1, 2, 3)$ are independent standard Brownian motion defined on a complete probability space $(\Omega, \mathcal{F}, \mathbb{P})$ with a filtration $\{\mathcal{F}_t\}_{t \geq 0}$ satisfying the usual conditions, i.e., it is increasing and right continuous while $\mathcal{F}_0$ contains all P-null sets, and σ_i represent the intensities of $B_i(t)$ for $(i = 1, 2, 3)$, respectively.

The rest of paper is organized as follows. In the next section, we prove that system (2) is biologically well-posed by showing the global existence and positivity of solutions. The stochastic stability analysis is investigated in sections 3. In Section 4, we give an application to HIV infection and their numerical simulations to illustrate our main results. The paper ends with a brief discussion and conclusion.

2 Well-posedness

The aim of this section is to prove that the solution of system (2) is global and positive for any initial value. For this, we denote the set $\mathbb{R}^3_+$ by

$$\mathbb{R}^3_+ = \left\{(x_1, x_2, x_3) \in \mathbb{R}^3 \mid x_i > 0, i = 1, 2, 3\right\}.$$

Let $\phi(x)$ be a function defined on $(0, +\infty)$ as $\phi(x) = x - 1 - \ln(x)$.

First, we need the following lemma:

Lemma 2.1. *[14] For all $x > 0$, we have*

$$x \leq 2\phi(x) + 2\ln(2), \forall x > 0. \quad (3)$$

Theorem 2.2. *For any initial value $X(0) \in \mathbb{R}^3_+$, there exists a unique solution $X(t)$ of system (2) defined on $[0, +\infty)$ and this solution remains in $\mathbb{R}^3_+$ with probability 1, namely $X(t) \in \mathbb{R}^3_+$ for all $t \geq 0$ almost surely (briefly a.s.).*

Proof. From [15], we deduce that system (1) has a unique local solution $X(t)$ on $t \in [0, \tau_e)$, where τ_e is the explosion time. To prove that this solution is global, we need to prove that $\tau_e = \infty$ a.s. Let p_0 be sufficiently large so that every component of $X(0)$ lies within the interval $[\frac{1}{p_0}, p_0]$. For each integer $p \geq p_0$, define the stopping time

$$\tau_p = \inf\left\{t \in [0, \tau_e): \ x(t) \notin (\frac{1}{p}, p) \text{ or } y(t) \notin (\frac{1}{p}, p) \text{ or } v(t) \notin (\frac{1}{p}, p)\right\},$$

with the traditional setting $\inf \emptyset = \infty$, where $\emptyset$ denotes the empty set. It is clear that $\tau_p \leq \tau_e$ a.s. Now, we need to prove that $\tau_p = \infty$ a.s. Assume that this statement is false, then there is a pair of constants $\theta \geq 0$ and $\epsilon \in (0, 1)$ such that

$$P\big\{\tau_\infty \leq \theta\big\} > \epsilon.$$

Hence there is an integer $p_1 \geq p_0$ such that

$$P\{\tau_p \leq \theta\} \geq \epsilon \text{ for all } p \geq p_1. \tag{4}$$

We define a C^2-function $V : \mathbb{R}^3_+ \to \mathbb{R}_+$ as follows

$$V(X) = \phi(\frac{x}{x_0}) + \phi(y) + \frac{a}{k}\phi(v),$$

where $x_0 = \dfrac{\lambda}{\delta}$. Using It's formula, we obtain

$$
\begin{aligned}
dV(X(t)) &= \Big[\big(1 - \frac{x_0}{x}\big)\big(\lambda - \delta x - f(x,v)v\big) + \big(1 - \frac{1}{y}\big)\big(f(x,v)v - ay\big) \\
&\quad + \frac{a}{k}\big(1 - \frac{1}{v}\big)\big(ky - \mu v\big) + \frac{x_0}{2}\sigma_1^2\big(1 - \frac{x*}{x}\big)^2 + \frac{1}{2}\sigma_2^2\big(1 - \frac{y*}{y}\big)^2 \\
&\quad + \frac{a}{2k}\sigma_3^2\big(1 - \frac{v*}{v}\big)^2\Big]dt + \sigma_1\big(1 - \frac{x_0}{x}\big)(x - x^*)dB_1(t) \\
&\quad + \sigma_2\big(1 - \frac{1}{y}\big)(y - y^*)dB_2(t) + \frac{a}{k}\sigma_3\big(1 - \frac{1}{v}\big)(v - v^*)dB_3(t) \\
&= \Big[-\frac{\delta}{x}(x - x_0)^2 - \frac{f(x,v)v}{y} + f(x,v)v - \frac{a\mu}{k}v - a\frac{y}{v} + a + \frac{a\mu}{k} \\
&\quad + \frac{x_0}{2}\sigma_1^2\big(1 - \frac{x*}{x}\big)^2 + \frac{1}{2}\sigma_2^2\big(1 - \frac{y*}{y}\big)^2 + \frac{a}{2k}\sigma_3^2\big(1 - \frac{v*}{v}\big)^2\Big]dt \\
&\quad + \sigma_1\big(1 - \frac{x_0}{x}\big)(x - x^*)dB_1(t) + \sigma_2\big(1 - \frac{1}{y}\big)(y - y^*)dB_2(t) \\
&\quad + \frac{a}{k}\sigma_3\big(1 - \frac{1}{v}\big)(v - v^*)dB_3(t) \\
&\leq \Big[f(x,v)v + a + \frac{a\mu}{k} + \frac{x_0}{2}\sigma_1^2\big(1 - \frac{x*}{x}\big)^2 + \frac{1}{2}\sigma_2^2\big(1 - \frac{y*}{y}\big)^2 \\
&\quad + \frac{a}{2k}\sigma_3^2\big(1 - \frac{v*}{v}\big)^2\Big]dt + \sigma_1\big(1 - \frac{x_0}{x}\big)(x - x^*)dB_1(t) \\
&\quad + \sigma_2\big(1 - \frac{1}{y}\big)(y - y^*)dB_2(t) + \frac{a}{k}\sigma_3\big(1 - \frac{1}{v}\big)(v - v^*)dB_3(t).
\end{aligned}
$$

According to Lemma 2.1, we have

$$f(x_0, 0)v \leq 2f(x_0, 0)\ln(2) + 2f(x_0, 0)V(X(t)).$$

Hence,

$$
\begin{aligned}
dV(X(t)) &\leq \Big(M_1 + M_2 V(X(t))\Big)dt + \sigma_1\big(1 - \frac{x_0}{x}\big)(x - x^*)dB_1(t) \\
&\quad + \sigma_2\big(1 - \frac{1}{y}\big)(y - y^*)dB_2(s) + \frac{a}{k}\sigma_3\big(1 - \frac{1}{v}\big)(v - v^*)dB_3(t),
\end{aligned}
$$

where M_1 and M_2 are a positive constants.

Integrating both sides of the above inequality from 0 to $\tau_p \wedge \theta$, we get

$$
\begin{aligned}
\int_0^{\tau_p \wedge \theta} dV(X(t)) &\leq \int_0^{\tau_p \wedge \theta} M_3\big[1 + V(X(s))\big]ds + \int_0^{\tau_p \wedge \theta} \sigma_1\big(1 - \frac{x_0}{x}\big)(x - x^*)dB_1(s) \\
&\quad + \int_0^{\tau_p \wedge \theta} \sigma_2\big(1 - \frac{1}{y}\big)(y - y^*)dB_2(s) \\
&\quad + \int_0^{\tau_p \wedge \theta} \frac{a}{k}\sigma_3\big(1 - \frac{1}{v}\big)(v - v^*)dB_3(s),
\end{aligned}
$$

where $\tau_p \wedge \theta = \min\{\tau_p, \theta\}$ and $M_3 = \max\{M_1, M_2\}$. Then taking the expectations leads to

$$
\begin{aligned}
EV\big(X(\tau_p \wedge \theta)\big) &\leq V(X(0)) + E\int_0^{\tau_p \wedge \theta} M_3\big[1 + V\big(X(s)\big)\big]ds \\
&\leq V(X(0)) + M_3\theta + M_3\int_0^{\theta} EV\big(X(\tau_p \wedge \theta)\big)ds.
\end{aligned}
$$

According to Gronwall inequality we reduce that

$$
EV\big(X(\tau_p \wedge \theta)\big) \leq M_4, \tag{5}
$$

where $M_4 = \big(V(X(0)) + M_3\theta\big)e^{M_3\theta}$.
Set $\Omega_p = \{\tau_p \leq \theta\}$ for $p \geq p_1$ and by (4), $P(\Omega_p) \geq \epsilon$. Not that for every $\omega \in \Omega_p$, there is some component of $X(\tau_p, \omega)$ equal either p or $\frac{1}{p}$. Hence $V\big(X(\tau_p, \omega)\big)$ is not less than the smallest of

$$
p - 1 - \log(p) \text{ and } \frac{1}{p} - 1 - \log(\frac{1}{p}) = \frac{1}{p} - 1 + \log(p).
$$

Consequently,

$$
V\big(X(\tau_p, \omega)\big) \geq \big[p - 1 - \log(p)\big] \wedge \big[\frac{1}{p} - 1 + \log(p)\big].
$$

It then follows from (4) and (5) that

$$
M_4 \geq E\big[\mathbf{1}_{\Omega_p} V\big(X(\tau_p, \omega)\big)\big] \geq \epsilon\big(\big[p - 1 - \log(p)\big] \wedge \big[\frac{1}{p} - 1 + \log(p)\big]\big),
$$

where $\mathbf{1}_{\Omega_p}$ is the indicator function of Ω_p. Letting $p \to \infty$ leads to the contradiction $\infty > M_4 = \infty$. So we must therefore have $\tau_\infty = \infty$ a.s . ∎

3 Stability Analysis

Clearly, the system (2) has the same equilibria as the system (1). Throughout this section, we assume that $R_0 > 1$, and we discuss the stability of the endemic equilibrium E^* of system (2).
The stochastic system (2) can be centered at its interior endemic equilibrium E^* by the changes of the variables as follows

$$
u_1 = x - x^*, u_2 = y - y^* \text{ and } u_3 = v - v^*. \tag{6}
$$

Hence, the linearized version corresponding to system (2) around E^* is given by

$$
du(t) = F\big(u(t)\big)dt + G\big(u(t)\big)dB(t), \tag{7}
$$

where

$$
u(t) = \big(u_1(t), u_2(t), u_3(t)\big)^T,
$$

$F(u) =$

$$
\begin{pmatrix}
-\delta - v^*\dfrac{\partial f}{\partial x}(x^*, y^*, v^*) & -v^*\dfrac{\partial f}{\partial y}(x^*, y^*, v^*) + \rho & -v^*\dfrac{\partial f}{\partial v}(x^*, y^*, v^*) - f(x^*, y^*, v^*) \\
v^*\dfrac{\partial f}{\partial x}(x^*, y^*, v^*) & v^*\dfrac{\partial f}{\partial y}(x^*, y^*, v^*) - (a + \rho) & v^*\dfrac{\partial f}{\partial v}(x^*, y^*, v^*) + f(x^*, y^*, v^*) \\
0 & k & -\mu
\end{pmatrix} u,
$$

$$
G(u) = \begin{pmatrix} \sigma_1 u_1 & 0 & 0 \\ 0 & \sigma_2 u_2 & 0 \\ 0 & 0 & \sigma_3 u_3 \end{pmatrix},
$$

$$B(t) = \big(B_1(t), B_2(t), B_3(t)\big)^T,$$

and the superscript "T" represents transposition.

It is easy to see that the stability of the endemic equilibrium E^* of model (2) is equivalent to the stability of the trivial solution $u(t) = 0$ in (7).

Denote by $C^{1,2}([0, +\infty) \times \mathbb{R}^3; \mathbb{R})$ the family of non-negative functions $W(t, u)$ defined on $[0, +\infty) \times \mathbb{R}^3$ such that they are continuously differentiable with respect to t and twice with respect to u. From [16], we define the differential operator L for a function $W(t, u) \in C^{1,2}([0, +\infty) \times \mathbb{R}^3; \mathbb{R})$ by

$$LW(t, u) = \frac{\partial W(t, u)}{\partial t} + F^T(u)\frac{\partial W(t, u)}{\partial u} + \frac{1}{2}Tr\left[G^T(u)\frac{\partial^2 W(t, u)}{\partial u^2}G(u)\right], \tag{8}$$

where

$$\frac{\partial W(t, u)}{\partial u} = \left(\frac{\partial W(t, u)}{\partial u_1}, \frac{\partial W(t, u)}{\partial u_2}, \frac{\partial W(t, u)}{\partial u_3}\right)^T,$$

and

$$\frac{\partial^2 W(t, u)}{\partial u^2} = \left(\frac{\partial^2 W(t, u)}{\partial u_i \partial u_j}\right)_{i,j}.$$

In order to obtain stability conditions, we will use the following theorem (for the proofs of these theorem we refer the reader to [16]).

Theorem 3.1. *Suppose that there exists a function $W(t, u) \in C^{1,2}([0, +\infty) \times \mathbb{R}^3; \mathbb{R})$ satisfying the following inequalities:*

$$\eta_1|x|^p \leq W(t, u) \leq \eta_2|x|^p, \tag{9}$$

$$LW(t, u) \leq -\eta_3|x|^p, \tag{10}$$

where $\eta_i, (i = 1, 2, 3)$, and p are positive constants. Then the trivial solution of (7) is exponentially p-stable for $t \geq 0$. Moreover, if $p = 2$, then the trivial solution is also called asymptotically mean square stable and it is globally asymptotically stable in probability.

From theorem 3.1, we get the sufficient conditions for stochastic asymptotic stability of trivial solution of (7) which are given by the following theorem.

Theorem 3.2. *Assume that $R_0 > 1$. If the following conditions are satisfied:*

$$\sigma_1^2 < 2\delta, \ \sigma_2^2 < a \ and \ \sigma_3^2 < 2\mu - a, \tag{11}$$

then the trivial solution in (7) is asymptotically mean square stable and it is globally asymptotically stable in probability.

Proof. We define the Lyapunov function $W(t, u)$ as follows

$$W(t, u) = \frac{2k}{a}\left[u_1 + u_2\right]^2 + \frac{a}{k}u_3^2, \tag{12}$$

It is easy to verify that inequality (9) holds true with $p = 2$.

By applying the operator L on $W(t, u)$, we get

$$
\begin{aligned}
LW(t, u) \quad &= \frac{2k}{a}(u_1 + u_2)\Big[\big(-\delta - v^*\frac{\partial f}{\partial x}(x^*, y^*, v^*)\big)u_1 + \big(-v^*\frac{\partial f}{\partial y}(x^*, y^*, v^*) + \rho\big)u_2 \\
&\quad + \big(-v^*\frac{\partial f}{\partial v}(x^*, y^*, v^*) - f(x^*, y^*, v^*)\big)u_3 + v^*\frac{\partial f}{\partial x}(x^*, y^*, v^*)u_1 \\
&\quad + \big(v^*\frac{\partial f}{\partial y}(x^*, y^*, v^*) - a - \rho\big)u_2 + \big(v^*\frac{\partial f}{\partial x}(x^*, y^*, v^*) + f(x^*, y^*, v^*)\big)u_3\Big] \\
&\quad + \frac{2a}{k}(ku_2 - \mu u_3)u_3 + \frac{k\sigma_1^2}{a}u_1^2 + \frac{k\sigma_2^2}{a}u_2^2 + \frac{a\sigma_3^2}{k}u_3^2 \\
&= -\frac{2k}{a}\big(\delta - \frac{1}{2}\sigma_1^2\big)u_1^2 - \frac{2k}{a}\big(a - \frac{1}{2}\sigma_2^2\big)u_2^2 - \frac{a}{k}\big(2\mu - \sigma_3^2\big)u_3^2 - \frac{2k}{a}\big(a + \mu\big)u_1u_2 \\
&\quad + 2au_2u_3 \\
&\leq -\frac{2k}{a}\big(\delta - \frac{1}{2}\sigma_1^2\big)u_1^2 - \frac{2k}{a}\big(a - \frac{1}{2}\sigma_2^2\big)u_2^2 - \frac{a}{k}\big(2\mu - \sigma_3^2\big)u_3^2 + ku_2^2 + \frac{a^2}{k}u_3^2 \\
&= -\frac{2k}{a}\big(\delta - \frac{1}{2}\sigma_1^2\big)u_1^2 - \frac{k}{a}\big(a - \sigma_2^2\big)u_2^2 - \frac{a}{k}\big(2\mu - a - \sigma_3^2\big)u_3^2.
\end{aligned}
$$

Hence,

$$
LW(t, u) \leq -\big(Au_1^2 + Bu_2^2 + Cu_3^2\big), \tag{13}
$$

with

$$
A = \frac{2k}{a}\big(\delta - \frac{1}{2}\sigma_1^2\big), B = \frac{k}{a}\big(a - \sigma_2^2\big) \text{ and } C = \frac{a}{k}\big(2\mu - a - \sigma_3^2\big).
$$

From the assumptions of theorem 3.2, we deduce that A, B and C are positive constants since $\mu > a$. Let $0 < \eta = \min\{A, B, C\}$. From (13), one sees that

$$
LW(t, u) \leq -\eta|u|^2. \tag{14}
$$

According to theorem 3.1, we conclude that the trivial solution of system (7) is asymptotically mean square stable. So we have the assertion. ∎

Because the order of nonlinearity of system (2) is higher than one, we give the following corollary without any proof, since the proof is similar to that of [17].

Corollary 3.3. *Assume that the conditions of theorem 3.2 are satisfied, then the trivial solution or the endemic equilibrium E^* of system (2) is stable in probability.*

Remark 3.4. *Note that if all conditions (11) do not hold then $LW > 0$ and the trivial solution of the system (7) can not be asymptotically mean square stable.*

4 Application and Numerical Simulations

The main purpose of this section is to apply our theoretical results to the following stochastic HIV infection model with Hattaf-Yousfi incidence rate (see Section 4, [18])

$$
\begin{cases}
dx(t) &= \Big[\lambda - \delta x - \dfrac{\beta xv}{\alpha_0 + \alpha_1 x + \alpha_2 v + \alpha_3 xv} + \rho y\Big]dt + \sigma_1\big[x - x^*\big]dB_1(t), \\[3mm]
dy(t) &= \Big[\dfrac{\beta xv}{\alpha_0 + \alpha_1 x + \alpha_2 v + \alpha_3 xv} - (a + \rho)y\Big]dt + \sigma_2\big[y - y^*\big]dB_2(t), \\[3mm]
dv(t) &= \Big[ky - \mu v\Big]dt + \sigma_3\big[v - v^*\big]dB_3(t),
\end{cases} \tag{15}
$$

where $x(t)$, $y(t)$ and $v(t)$ denote the densities of uninfected represented by cytotoxic T lymphocytes cells (CD4$^+$T cells), infected cells and free virus particles at time t, respectively. The parameter β is

the infection rate and $\alpha_0, \alpha_1, \alpha_2, \alpha_3$ are non-negative constants. It is very important to note that this incidence rate includes many special cases existing in the literature such as the mass action called also the bilinear incidence function when $\alpha_0 = 1$ and $\alpha_1 = \alpha_2 = \alpha_3 = 0$; the saturation incidence rate when $\alpha_0 = 1$ and $\alpha_1 = \alpha_3 = 0$; the Beddington-DeAngelis functional response [19, 20] when $\alpha_0 = 1$ and $\alpha_3 = 0$; the Crowley-Martin functional response introduced in [10] and used by Zhou et al. [9] when $\alpha_0 = 1$ and $\alpha_3 = \alpha_1\alpha_2$; the more generalized response proposed by Hattaf et al. (see Section 5, [21]) and used in [13, 22–24] when $\alpha_0 = 1$.

In fact, system (15) is a special case of the model (2) with $f(x, y, v) = \dfrac{\beta x}{\alpha_0 + \alpha_1 x + \alpha_2 v + \alpha_3 xv}$. In this case, it is easy to see that the hypotheses (H_1)-(H_3) are checked. Further, the basic reproduction number of the corresponding deterministic of our model (15) is given by $R_0 = \dfrac{\lambda\beta k}{\mu(\rho + a)(\alpha_0\delta + \alpha_1\lambda)}$. In addition, if $R_0 > 1$, the system (15) has a unique endemic equilibrium of the form $E^*\big(x^*, \frac{\mu}{k}v^*, \frac{k}{a\mu}(\lambda - \delta x^*)\big)$ where

$$x^* = \frac{\sqrt{\Delta^2 + 4\alpha_3\delta k(a + \rho)\big(\alpha_0 a\mu(a + \rho) + \alpha_2\lambda k(\rho + a)\big)} - \Delta}{2\alpha_3\delta k(a + \rho)},$$

with

$$\Delta = \big[ka\beta - \alpha_1 a\mu(a + \rho) - \alpha_2\delta k(\rho - a) - \alpha_3\lambda k(\rho + a)\big].$$

Now, we numerically simulate the solution of the stochastic system (15) and the solution of his corresponding deterministic system, $\big(\sigma_i = 0, \ i = 1, 2, 3\big)$. Using Milstein's Higher Order Method mentioned in [25], we get the discretization equation, which is

$$\begin{cases} x_{i+1} & = x_i + \left[\lambda - \delta x_i - \dfrac{\beta x_i v_i}{\alpha_0 + \alpha_1 x_i + \alpha_2 v_i + \alpha_3 x_i v_i} + \rho y_i\right]\Delta t + \sigma_1\big[x_i - x^*\big]\sqrt{\Delta t}\xi_{1i} \\ & \quad + \dfrac{\sigma_1^2}{2}\big[x_i - x^*\big]\big[\Delta t\xi_{1i}^2 - \Delta t\big], \\ y_{i+1} & = y_i + \left[\dfrac{\beta x_i v_i}{\alpha_0 + \alpha_1 x_i + \alpha_2 v_i + \alpha_3 x_i v_i} - (a + \rho)y_i\right]\Delta t + \sigma_2\big[y_i - y^*\big]\sqrt{\Delta t}\xi_{2i} \\ & \quad + \dfrac{\sigma_2^2}{2}\big[y_i - y^*\big]\big[\Delta t\xi_{2i}^2 - \Delta t\big], \\ v_{i+1} & = v_i + \big[ky_i - \mu v_i\big]\Delta t + \sigma_3\big[v_i - v^*\big]\sqrt{\Delta t}\xi_{3i} + \dfrac{\sigma_3^2}{2}\big[v_i - v^*\big]\big[\Delta t\xi_{3i}^2 - \Delta t\big], \end{cases}$$

where ξ_{ji}, $j = 1, 2, 3$ and $i = 1, 2, ..., n$, are the independent Gaussian random variables $N(0, 1)$ and Δt is the time step. By using Matlab, we get the figures with initial conditions: $x(0) = 700$ cells mm^{-3}, $y(0) = 10$ cells mm^{-3}, $v(0) = 3.10^{-2}$ virions mm^{-3}. The all biological parameter values are taken from [24].

In Fig. 1, we choose the following parameter values: $\lambda = 10$ cells μl^{-1} day^{-1}, $\delta = 0.0139$ day^{-1}, $\beta = 0.0012$ μl virion^{-1} day^{-1}, $\rho = 0.01$ day^{-1}, $a = 0.27$ day^{-1}, $k = 600$ virion cell^{-1} day^{-1}, $\mu = 3$ day^{-1}, $\alpha_0 = 0.5$, $\alpha_1 = 0.1$, $\alpha_2 = 0.01$, $\alpha_3 = 0.00001$, $\sigma_1 = 0.02$, $\sigma_2 = 0.004$ and $\sigma_3 = 0.004$. It is obvious that $R_0 = 8.5123 > 1$, $\sigma_1^2 = 0.0004 < 2\delta = 0.0278$, $\sigma_2^2 = 1.6\ 10^{-5} < a = 0.27$ and $\sigma_3^2 = 1.6\ 10^{-5} < 2\mu - a = 5.73$ which satisfy theorem 3.2. Then the endemic equilibrium E^* is globally asymptotically stable. Fig. 1 demonstrates the above analysis.

In Fig. 2, we choose $\sigma_1 = 0.01$, $\sigma_2 = 0.001$, $\sigma_3 = 0.001$ and do not change the other parameter values. We show that the endemic equilibrium E^* is globally asymptotically stable, and the fluctuation is getting smaller with the decrease of the white noise (compare the Fig. 1 with the Fig. 2).
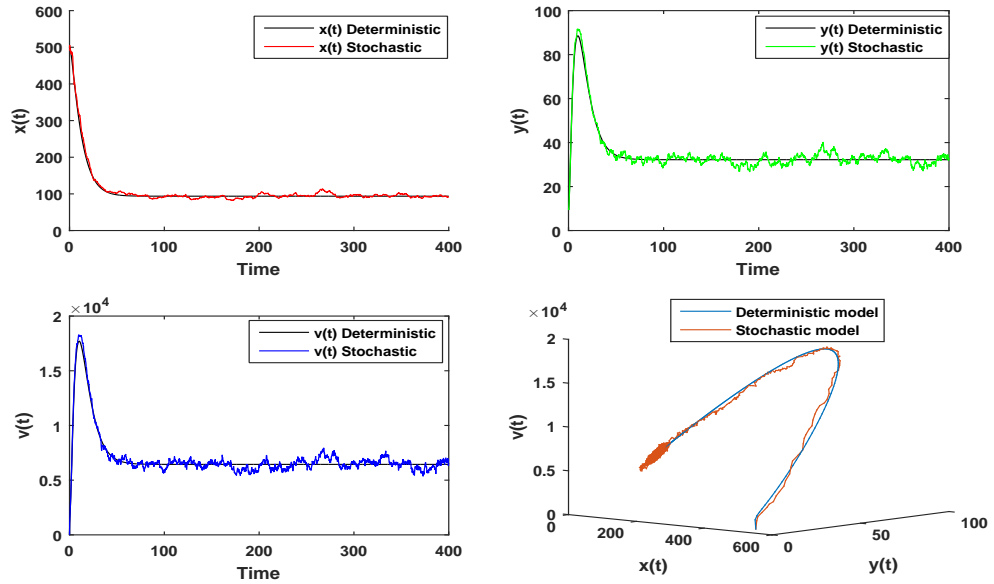
Fig. 1. Deterministic and stochastic trajectories of model (15) with $\sigma_1 = 0.02$, $\sigma_2 = 0.004$ and $\sigma_3 = 0.004$, when $R_0 > 1$
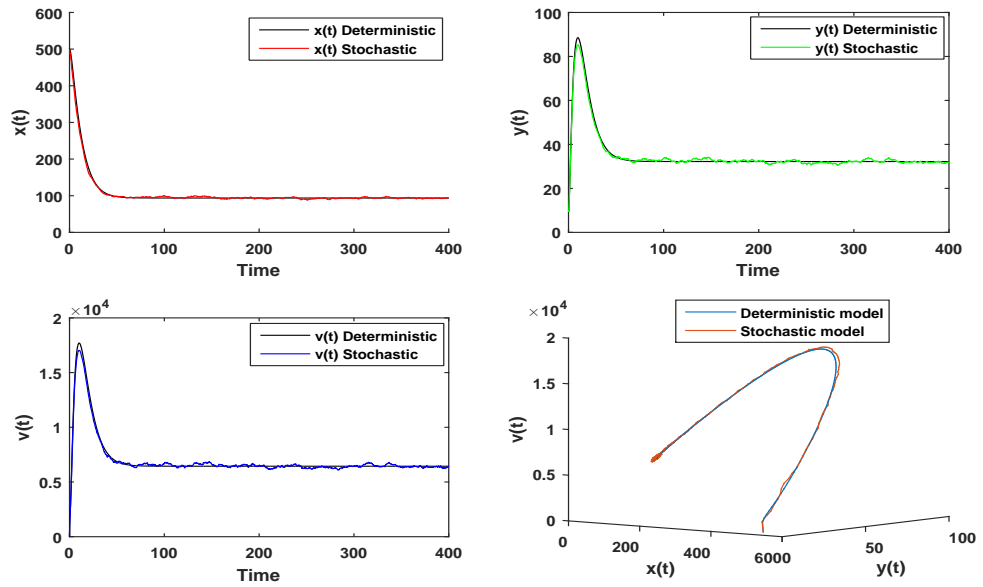

Fig. 2. Deterministic and stochastic trajectories of model (15) with $\sigma_1 = 0.01$, $\sigma_2 = 0.001$ and $\sigma_3 = 0.001$, when $R_0 > 1$

In Fig. 3, we keep parameters as Fig. 1. We see that the solutions of both deterministic and stochastic models converge to the endemic equilibrium E^* with different initial condition values. Then by theorem 3.2, E^* is globally asymptotically stable.
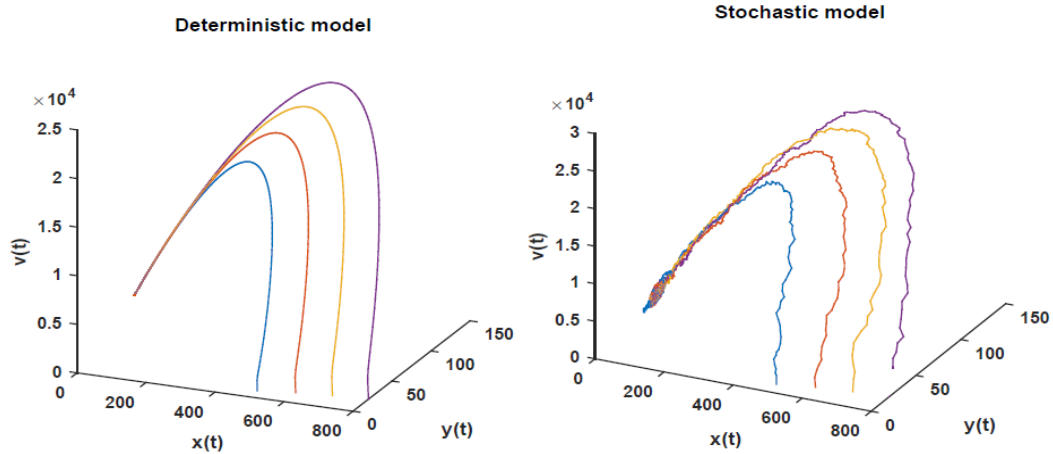
Fig. 3. Deterministic and stochastic trajectories of model (15) with different initial conditions, when $R_0 > 1$

In Fig. 4, we choose $\sigma_1^2 = 0.4 > 2\delta = 0.0278$, $\sigma_2^2 = 16 > a = 0.27$ and $\sigma_3^2 = 16 > 2\mu - a = 5.73$ which not satisfy the conditions (11) of theorem 3.2. Then the endemic equilibrium E^* is not asymptotically mean square stable.
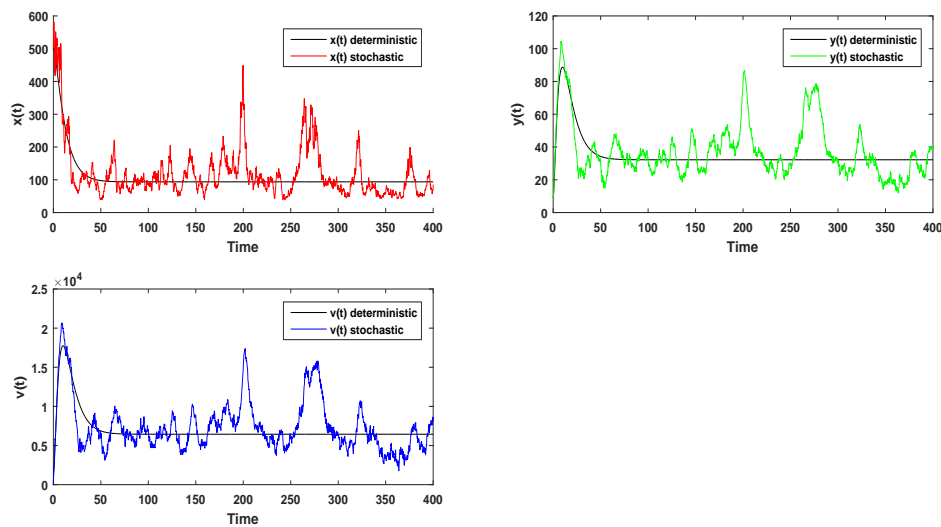

Fig. 4. Deterministic and stochastic trajectories of model (15) with $\sigma_1 = 0.2$, $\sigma_2 = 4$ and $\sigma_3 = 4$, when $R_0 > 1$

5 Discussion and Conclusion

The purpose of this work is to study the effects of the environmental fluctuations on the dynamical behavior of a viral infection model with general incidence rate by considering the white noise perturbation around the endemic equilibrium. We have proved the global existence and positivity of solution of system (2) to ensure the well-posedness of the problem. Further, we have shown that if $R_0 > 1$ and the intensities of white noise are less than certain threshold of parameters, then the trivial solution of linearized system (7) is asymptotically mean square stable which gives the stability in probability of the trivial solution of the original system (2). However, if there is no environmental stochastic perturbation which means that $\sigma_i = 0$ for $(i = 1, 2, 3)$, then the conditions of theorem (3.2) are reduced to $R_0 > 1$, which gives a nonlinear stability condition for the deterministic model (1).

From the theoretical and numerical results, we see that when the noise density is not large, the stochastic model (2) can preserves the property of the stability of the deterministic model (1). To a great extent, we can ignore the noise and use the deterministic model (1) to describe the viral dynamics. However, when the noise is sufficiently large it can force state variables to become largely fluctuating. In this case, we can not use deterministic model (1) but instead stochastic model (2) to describe the viral dynamics. Needless to say, both deterministic and stochastic epidemic models have their important roles in the study of epidemics's spreading.

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Competing Interests

Authors have declared that no competing interests exist.

References

[1] Freeman S. Biological science 3. Benjamin Cummings; 2007.

[2] Nowak MA, Bonhoeffer S, Hill AM, Boehme R, Thomas HC, Mcdade H. Viral dynamics in hepatitis B virus infection. Proc. Natl. Acad. Sci USA. 1996;93(9):4398-4402.

[3] Nowak MA, May RM. Viral dynamics. Oxford University Press, Oxford; 2000.

[4] Perelson A, Nelson P. Mathematical models of HIV dynamics in vivo. SIAM Rev. 1999;41:344.

[5] Min L, Su Y, Kuang Y. Mathematical analysis of a basic model of virus infection with application to HBV infection. Rocky Mountain J. Math. 2008;38(5):1573-1585.

[6] Hattaf K, Yousfi N. Hepatitis B virus infection model with logistic hepatocyte growth and cure rate. Appl. Math. Sci. 2011;5(47):2327-2335.

[7] Hews S, Eikenberry S, Nagy JD, Kuang Y. Rich dynamics of a Hepatitis B viral infection model with logistic hepatocyte growth. J. Math. Biol. 2010;60:573-590.

[8] Wang K, Fan A, Torres A. Global properties of an improved hepatitis B virus model. Nonlinear Anal. RWA. 2010;11:3131-3138.

[9] Zhou X, Cui J. Global stability of the viral dynamics with CrowleyMartin functional response. Bull Korean Math Soc. 2011;48(3):555-574.

[10] Crowley PH, Martin EK. Functional responses and interference within and between year classes of a dragonfly population. J. North. Am. Benth. Soc. 1989;8:211-221.

[11] Hattaf K, Yousfi N, Tridane A. Mathematical analysis of a virus dynamics model with general incidence rate and cure rate. Nonlinear Anal. RWA. 2012;13:1866-1872.

[12] Shaikhet L, Korobeinikov A. Stability of a stochastic model for HIV-1 dynamics within a host. Applicable Analysis. 2015:1-11.

[13] Adnani J, Hattaf K, Yousfi N. Stability analysis of a stochastic SIR epidemic model with specific Nnonlinear incidence rate. International Journal of Stochastic Analysis. 2013; ID 431257.

[14] Mahrouf M, Lotfi EM, Maziane M, Hattaf K, Yousfi N. A stochastic viral infection model with general functional response. Nonlinear Analysis and Differential Equations. 2016;4(9):435-445.

[15] Mao X. Stochastic Differential Equations and Applications. Horwood, Chichester; 1997.

[16] Afanasev VN, Kolmanowskii VB, Nosov VR. Mathematical theory of control systems design. Kluwer Academic, Dordrecht, Netherlands; 1996.

[17] Shaikhet L. Lyapunov functionals and stability of stochastic functional differential equations. Springer Science and Business Media; 2013.

[18] Hattaf K, Yousfi N. A class of delayed viral infection models with general incidence rate and adaptive immune response. International Journal of Dynamics and Control; 2015.
DOI: 10.1007/s40435-015-0158-1

[19] Beddington JR. Mutual interference between parasites or predators and its effect on searching efficiency. J. Animal Ecol. 1975;44:331-340.

[20] DeAngelis DL, Goldstein RA, O'Neill RV. A model for trophic interaction. Ecology. 1975;56:881-892.

[21] Hattaf K, Yousfi N, Tridane A. A Delay virus dynamics model with general incidence rate. Differ. Equ. Dyn. Syst. 2014;22(2):181-190.

[22] Adnani J, Hattaf K, Yousfi N. Analysis of a stochastic SIRS epidemic model with specific functional response. Applied Mathematical Sciences. 2016;301-314.

[23] Lotfi EM, Maziane M, Hattaf K, Yousfi N. Partial differential equations of an epidemic model with spatial diffusion. International Journal of Partial Differential Equations. 2014;2014. ID 186437.

[24] Maziane M, Lotfi EM, Hattaf K, Yousfi N. Dynamics of a class of HIV infection models with cure of infected cells in eclipse stage. Acta Biotheoretica. 2015;63(4):363-380.

[25] Higham DJ. An algorithmic introduction to numerical simulation of stochastic differential equations. SIAM Review. 20014;3(3):525-546.