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STABILITY ANALYSIS OF A STOCHASTIC VIRAL INFECTION MODEL WITH IMMUNE IMPAIRMENT AND VARIABLE DIFFUSION RATE

M. Pitchaimani[1] and R. Rajaji[2]

[1]Ramanujan Institute for Advanced Study in Mathematics
University of Madras, Chennai -600 005, India
e-mail: mpitchaimani@yahoo.com

[2]Ramanujan Institute for Advanced Study in Mathematics
University of Madras, Chennai -600 005, India
e-mail: rajajiranga@gmail.com

Abstract. In this paper, we consider the stochastic viral infection model with immune impairment and variable diffusion rate. We prove the global existence of unique strong solution. Using the Lyapunov method, we find sufficient conditions for the stochastic asymptotic stability of equilibrium solutions of this model. Finally, establish the existence of a unique ergodic stationary distribution and illustrate our results.

1. Introduction

Mathematical modeling has been an important approach in analyzing the spread and control of infectious diseases. A simple model may play a significant role in the development of a better understanding of the disease and the various drug therapy strategies used against it.

During the process of viral infection, a host is induced which is initially rapid and nonspecific (natural killer cells, macrophage cells, etc.) and then delayed and specific (cytotoxic T lymphocyte cells, antibody cell). But in most virus infections, cytotoxic T lymphocyte (CTL) cells which attack infected cells, and antibody cells which attack viruses, play a critical part in antiviral defense. In

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order to investigate the role of the population dynamics of viral infection with CTL response, Regoes [12] and Wang [14] construct a mathematical model describing the basic dynamics of the interaction between activated $CD4^+$ T cells, $x(t)$, infected $CD4^+$ T cells, $y(t)$, and immune cells, $z(t)$. The model is given by

$$\begin{aligned} \frac{dx}{dt} &= s - \mu x - \beta xy, \\ \frac{dy}{dt} &= \beta xy - ay - pyz, \\ \frac{dz}{dt} &= cy - bz - myz. \end{aligned} \tag{1.1}$$

where activated $CD4^+$ T cells are produced at a rate of s cells day^{-1}, decay at a rate μ day^{-1}, and can become infected at a rate that is proportional to the number of infected $CD4^+$ T cells $y(t)$ with a transmission rate constant β day^{-1} cell^{-1}. The infected $CD4^+$ T cells are assumed to decay at the rate of a day^{-1}. The CTL responses eliminate at a rate that is proportional to the number of CTLs with a killing rate constant p day^{-1} cell^{-1}, proliferate at the rate of c day^{-1} and decay at a rate of b day^{-1} and the immune impairment rate m day^{-1} cell^{-1}. Let us assume that $\mu \leq \min\left\{\frac{a}{2}, b\right\}$.

The model (1.1) can have at most two equilibrium solutions, namely uninfected equilibrium solution $E_1 = (x_1, y_1, z_1)$, where

$$x_1 = \frac{s}{\mu}, \qquad y_1 = 0, \qquad z_1 = 0$$

and infected equilibrium solution $E_2 = (x_2, y_2, z_2)$, where

$$\begin{aligned} x_2 &= \frac{1}{\beta}\left(a + \frac{cpy_2}{b + my_2}\right), \\ y_2 &= \frac{1}{2A}\left\{-B + \sqrt{B^2 + 4Ab(s\beta - a\mu)}\right\}, \\ z_2 &= \frac{cy_2}{b + my_2}, \end{aligned}$$

where $A = \beta(am + cp)$ and $B = ab\beta + c\mu p - m(s\beta - a\mu)$. The infected equilibrium solution exists if the condition

$$\mathcal{R}_0 = \frac{s\beta}{a\mu} > 1,$$

where R_0 is the basic reproduction number, holds.

Wang [14] have investigated the global stability of uninfected equilibrium and infected equilibrium solutions of the model (1.1).

However, any system is inevitably affected by the environmental noise, it is an important component in an ecosystem. May [9] has revealed that due to environmental fluctuation, the birth rate, death rate, transmission coefficient and other parameters involved with the system exhibit random fluctuations to a greater or lesser extent. Mao *et al.* [8] found the presence of even a small amount of white noise can suppress a potential population explosion. Therefore, it is important to investigate the effect of random fluctuations in the environment on population dynamics.

There are many types of approaches for applying modeling techniques of stochastic differential equation (SDE) to introduce environmental noises into biological systems. One of the technique is parameter perturbation, which is the most commonly used procedure in constructing SDE models [3, 7, 10, 11, 13, 16]. In recent years, several authors have studied the effect of environmental noise on the transmission dynamics of diseases by proposing epidemic SDE model with stochastic disturbances via the above technique [5, 6, 11, 13, 15, 16].

Using the above technique, we perturbed the deterministic system (1.1), by a white noise and obtained a stochastic counterpart by replacing the rates β by $\beta + F(x, y, z)\dfrac{dW}{dt}$ where F is locally Lipschitz-continuous functions on $\mathbb{D}$ and W is Wiener processes defined on a filtered complete probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t\geq 0}, \mathbb{P})$.

The stochastic model takes a form as,

$$\begin{aligned} dx &= (s - \mu x - \beta xy)\,dt - xyF(x, y, z)dW, \\ dy &= (\beta xy - ay - pyz)\,dt + xyF(x, y, z)dW, \\ dz &= (cy - bz - myz)\,dt, \end{aligned} \tag{1.2}$$

where the functions F is locally Lipschitz-continuous on $\mathbb{D}$ and

$$\mathbb{D} = \left\{(x, y, z) \in \mathbb{R}^3 : x > 0,\ y > 0,\ z > 0,\ x + y + \frac{a}{2c}z \leq \frac{s}{\mu}\right\}.$$

The rest of this paper is organized as follows. In section 2, we discuss existence of a unique global solution for the stochastic model (1.2). In section 3, we discuss the stochastic asymptotic stability of uninfected equilibrium and the infected equilibrium with the help of Lyapunov functions. In section 4, we show the existence of a unique ergodic stationary distribution. In section 5, we visualize our results.

2. Existence of a unique global solution

In this section, we discuss existence of a unique global solution of the model (1.2).

Consider the d-dimensional stochastic differential equation of the form

$$dX(t) = f(X(t), t)dt + g(X(t), t)dW(t) \tag{2.1}$$

with an initial value $X(t_0) = X_0$, $t_0 \le t \le T < \infty$, where $f : \mathbb{R}^d \times [t_0, T] \to \mathbb{R}^d$ and $g : \mathbb{R}^d \times [t_0, T] \to \mathbb{R}^{d\times m}$ are Borel measurable, $W = \{W(t)\}_{t\ge t_0}$ is an $\mathbb{R}^m$-valued Wiener process, and X_0 is an $\mathbb{R}^d$-valued random variable.

The infinitesimal generator $\mathcal{L}$ associated with the SDE (2.1) is given by

$$\mathcal{L} = \frac{\partial}{\partial t} + \sum_{i=1}^{d} f_i(x,t)\frac{\partial}{\partial x_i} + \frac{1}{2}\sum_{i,j=1}^{m} \left(g(x,t)g^T(x,t)\right)_{ij} \frac{\partial^2}{\partial x_i \partial x_j}. \tag{2.2}$$

Theorem 2.1. ($\mathbb{D}$-invariance. Khasminskii [4] as appears in [2]) *Let $\mathbb{D}$ and $\mathbb{D}_n$ be open sets in $\mathbb{R}^d$ with*

$$\mathbb{D}_n \subseteq \mathbb{D}_{n+1}, \qquad \overline{\mathbb{D}}_n \subseteq \mathbb{D} \qquad \text{and} \qquad \mathbb{D} = \bigcup_n \mathbb{D}_n$$

and suppose f and g satisfy the existence and uniqueness conditions for solutions of (2.1) on each set $\{(t,x) : t > t_0, x \in \mathbb{D}_n\}$. Suppose there is a non-negative continuous function $V : \mathbb{D}\times[t_0,T] \to \mathbb{R}_+$ with continuous partial derivatives and satisfying $\mathcal{L}V \le cV$ for some positive constant c and $t > t_0$, $x \in \mathbb{D}$. If also,

$$\inf_{t>t_0,\ x\in\mathbb{D}\setminus\mathbb{D}_n} V(x,t) \to \infty \quad \text{as} \quad n \to \infty,$$

then for any X_0 independent of $W(t)$ such that $\mathbb{P}(X_0 \in \mathbb{D}) = 1$, there is a unique Markovian, continuous time solution $X(t)$ of (2.1) with $X(0) = X_0$, and $X(t) \in \mathbb{D}$ for all $t > 0$ (a.s.).

Now, we prove existence of a unique global solution of (1.2).

Theorem 2.2. *Let $(x(t_0), y(t_0), z(t_0)) = (x_0, y_0, z_0) \in \mathbb{D}$, and (x_0, y_0, z_0) is independent of $W(t)$. Then the stochastic model (1.2), admits a unique continuous time, Markovian global solution $(x(t), y(t), z(t))$ on $t \ge t_0$ and this solution is invariant (a.s.) with respect to $\mathbb{D}$.*

Proof. We use Theorem 2.1 and follow ideas of [13]. Since the coefficients of the system (1.2), are locally Lipschitz-continuous and satisfy linear growth condition on $\mathbb{D}$, for any initial value $(x_0, y_0, z_0) \in \mathbb{D}$, there is a unique local solution on $t \in [t_0, \tau(\mathbb{D}))$, where $\tau(\mathbb{D})$ is the random time of first exit of stochastic process $(x(t), y(t), z(t))$ from the domain $\mathbb{D}$, started in $(x(s), y(s), z(s)) =$

$(x_0, y_0, z_0) \in \mathbb{D}$ at the initial time $s \in [t_0, \infty)$. To make this solution global, we need to prove that

$$\mathbb{P}(\tau(\mathbb{D}) = \infty) = 1 \quad \text{a.s.}$$

Let

$$\begin{aligned}\mathbb{D}_n := \Bigg\{ (x, y, z) : e^{-n} < x < \frac{s}{\mu} - e^{-n},\ \ e^{-n} < y < \frac{s}{\mu} - e^{-n}, \\ e^{-n} < \frac{a}{2c} z < \frac{s}{\mu} - e^{-n},\ \ x + y + \frac{a}{2c} z \leq \frac{s}{\mu} \Bigg\}\end{aligned}$$

for $n \in \mathbb{N}$. The system (1.2), has a unique solution up to stopping time $\tau(\mathbb{D}_n)$. Let

$$\begin{aligned} V(x, y, z) = x - \ln x + \left(\frac{s}{\mu} - x\right) - \ln\left(\frac{s}{\mu} - x\right) + y - \ln y \\ + \left(\frac{s}{\mu} - \frac{a}{2c} z\right) - \ln\left(\frac{s}{\mu} - \frac{a}{2c} z\right), \end{aligned} \tag{2.3}$$

defined on $\mathbb{D}$ and assume that $\mathbb{E}\left(V(x, y, z)\right) < \infty$. Note that $V(x, y, z) \geq 4$ for $(x, y, z) \in \mathbb{D}$. Let $W(x, y, z, t) = e^{-c(t-s)} V(x, y, z)$, defined on $\mathbb{D} \times [s, \infty)$, where

$$\begin{aligned} c = \frac{1}{4}\left(2\mu + \frac{3}{2} a + \left(\beta + \frac{2cp}{a} + b\right)\frac{s}{\mu} + (\beta + m)\left(\frac{s}{\mu}\right)^2\right) \\ + \frac{3}{8}\left(\frac{s}{\mu}\right)^2 \sup_{(x,y,z)\in\mathbb{D}} F^2(x, y, z). \end{aligned}$$

Apply the infinitesimal operator $\mathcal{L}$ on equation (2.3), we obtain

$$\begin{aligned} \mathcal{L}V(x, y, z) = (s - \mu x - \beta x y)\left(\frac{1}{\left(\frac{s}{\mu} - x\right)} - \frac{1}{x}\right) + (\beta x y - a y - p y z)\left(1 - \frac{1}{y}\right) \\ + (c y - b z - m y z)\frac{a}{2c}\left(\frac{1}{\left(\frac{s}{\mu} - \frac{a}{2c} z\right)} - 1\right) \\ + \frac{1}{2} x^2 y^2 F^2(x, y, z)\left(\frac{1}{\left(\frac{s}{\mu} - x\right)^2} + \frac{1}{x^2} + \frac{1}{y^2}\right). \end{aligned}$$

After a little algebra, we have

$$\begin{aligned}
\mathcal{L}V(x,y,z) = \mu - &\frac{\beta xy}{\left(\frac{s}{\mu}-x\right)} - \frac{s}{x} + \mu + \beta y + \beta xy - ay - pyz - \beta x + a \\
&+ pz + \frac{a}{2}\frac{y}{\left(\frac{s}{\mu}-\frac{a}{2c}z\right)} - \frac{ab}{2c}\frac{z}{\left(\frac{s}{\mu}-\frac{a}{2c}z\right)} - \frac{am}{2c}\frac{yz}{\left(\frac{s}{\mu}-\frac{a}{2c}z\right)} \\
&- \frac{a}{2}y + \frac{ab}{2c}z + \frac{am}{2c}yz + \frac{1}{2}\frac{x^2y^2}{\left(\frac{s}{\mu}-x\right)^2}F^2(x,y,z) \\
&+ \frac{1}{2}y^2F^2(x,y,z) + \frac{1}{2}x^2F^2(x,y,z).
\end{aligned}$$

Since $x+y+\frac{a}{2c}z \leq \dfrac{s}{\mu}$, we have

$$\begin{aligned}
\mathcal{L}V(x,y,z) &\leq 2\mu + \frac{3}{2}a + \beta y + \beta xy + (p+\frac{ab}{2c})z + \frac{am}{2c}yz \\
&\quad + x^2F^2(x,y,z) + \frac{1}{2}y^2F^2(x,y,z), \\
\mathcal{L}V(x,y,z) &\leq 2\mu + \frac{3}{2}a + \left(\beta + \frac{2cp}{a} + b\right)\frac{s}{\mu} + (\beta+m)\left(\frac{s}{\mu}\right)^2 \\
&\quad + \frac{3}{2}\left(\frac{s}{\mu}\right)^2 \sup_{(x,y,z)\in\mathbb{D}} F^2(x,y,z) = 4c.
\end{aligned}$$

Since $V(x,y,z) \geq 4$ for $(x,y,z)\in\mathbb{D}$, so $\mathcal{L}V(x,y,z) \leq cV(x,y,z)$, Hence

$$\mathcal{L}W(x,y,z,t) = e^{-c(t-s)}\left(-cV(x,y,z) + \mathcal{L}V(x,y,z)\right) \leq 0.$$

Note that

$$\inf_{(x,y,z)\in\mathbb{D}\setminus\mathbb{D}_n} V(x,y,z) > n+1 \quad \text{for } \; n\in\mathbb{N}.$$

Now define $\tau_n := \min\{t, \tau(\mathbb{D}_n)\}$ and apply Dynkin's formula to get

$$\begin{aligned}
\mathbb{E}\left[W(x(\tau_n), y(\tau_n), z(\tau_n), \tau_n)\right] &= \mathbb{E}\left[W(x(s), y(s), z(s), s)\right] \\
&\quad + \mathbb{E}\left[\int_s^{\tau_n} \mathcal{L}W(x(u), y(u), z(u), u)du\right] \\
&\leq \mathbb{E}\left[W(x(s), y(s), z(s), s)\right] \\
&= \mathbb{E}\left[V(x(s), y(s), z(s))\right] = \mathbb{E}\left[V(x_0, y_0, z_0)\right].
\end{aligned}$$

Next, to show that $\mathbb{P}(\tau(\mathbb{D}_n) < t) = 0$, we take the expected value of $e^{c(t-\tau_n)}V(x(\tau_n), y(\tau_n), z(\tau_n))$.

$$\begin{aligned}
\mathbb{E}\left[e^{c(t-\tau_n)}V(x(\tau_n), y(\tau_n), z(\tau_n))\right] &= \mathbb{E}\left[e^{c(t-s)}e^{-c(\tau_n-s)}V(x(\tau_n), y(\tau_n), z(\tau_n))\right] \\
&= \mathbb{E}\left[e^{c(t-s)}W(x(\tau_n), y(\tau_n), z(\tau_n), \tau_n)\right] \\
&\leq e^{c(t-s)}\mathbb{E}\left[V(x_0, y_0, z_0)\right],
\end{aligned}$$

and obtain

$$\begin{aligned}
0 &\leq \mathbb{P}(\tau(\mathbb{D}) < t) \leq \mathbb{P}(\tau(\mathbb{D}_n) < t), \qquad \text{since} \quad \mathbb{D}_n \subseteq \mathbb{D} \\
&= \mathbb{P}(\tau_n < t) \\
&= \mathbb{E}(\mathbf{1}_{\tau_n < t}), \qquad \text{where } \mathbf{1} \text{ is the indicator function} \\
&\leq \mathbb{E}\left(e^{c(t-\tau_n)}\frac{V(x(\tau(\mathbb{D}_n)), y(\tau(\mathbb{D}_n)), z(\tau(\mathbb{D}_n)))}{\inf\limits_{(x,y,z)\in\mathbb{D}\setminus\mathbb{D}_n} V(x,y,z)}\mathbf{1}_{\tau_n<t}\right) \\
&\leq e^{c(t-s)}\frac{\mathbb{E}\left(V(x_0, y_0, z_0)\right)}{\inf\limits_{(x,y,z)\in\mathbb{D}\setminus\mathbb{D}_n} V(x,y,z)} \\
&\leq e^{c(t-s)}\frac{\mathbb{E}\left(V(x_0, y_0, z_0)\right)}{n+1}.
\end{aligned}$$

Since $e^{c(t-s)}\dfrac{\mathbb{E}\left(V(x_0, y_0, z_0)\right)}{n+1} \to 0$ as $n \to \infty$ for all $(x_0, y_0, z_0) \in \mathbb{D}_n$ (for large n) and for all fixed $t \in [s, \infty)$, thus $\mathbb{P}(\tau(\mathbb{D}) < t) = \mathbb{P}(\tau(\mathbb{D}_n) < t) = 0$, for $(x_0, y_0, z_0) \in \mathbb{D}$ and $t \geq t_0$, that is, $\mathbb{P}(\tau(\mathbb{D}) = \infty) = 1$.

This proves the invariance property and the global existence of the solution $(x(t), y(t), z(t))$ on $\mathbb{D}$. Uniqueness and continuity of the solution is obtained by Theorem 2.1. □

3. Stochastic asymptotic stability of uninfected and infected equilibrium solutions

In this section, we discus stochastic asymptotic stability of equilibrium solutions of (1.2).

Before giving the main results, we present definitions and theorem. Theorem 3.4 is a useful criterion for stochastic asymptotic stability of equilibrium solutions in terms of Lyapunov function [1].

Consider the d-dimensional SDE

$$dX(t) = f(X(t), t)dt + g(X(t), t)dW(t), \ t \geq t_0, \ X(t_0) = x_0. \tag{3.1}$$

Assume that f and g satisfy, in addition to the existence and uniqueness assumptions, $f(x^*, t) = 0$ and $g(x^*, t) = 0$, for equilibrium solution x^*, for $t \geq t_0$. Furthermore, let's assume that x_0 be a non-random constant with probability 1.

Definition 3.1. The equilibrium solution x^* of the SDE (3.1) is stochastically stable (stable in probability) if for every $\epsilon > 0$ and $s \geq t_0$

$$\lim_{x_0 \to x^*} \mathbb{P}\left(\sup_{s \leq t} \|X_{s,x_0}(t) - x^*\| \geq \epsilon \right) = 0, \tag{3.2}$$

where $X_{s,x_0}(t)$ denotes the solution of (3.1), satisfying $X(s) = x_0$, at time $t \geq s$.

Definition 3.2. The equilibrium solution x^* of the SDE (3.1) is said to be stochastically asymptotically stable if it is stochastically stable and

$$\lim_{x_0 \to x^*} \mathbb{P}\left(\lim_{t \to \infty} X_{s,x_0}(t) = x^* \right) = 1. \tag{3.3}$$

Definition 3.3. The equilibrium solution x^* of the SDE (3.1) is said to be globally stochastically asymptotically stable if it is stochastically stable and for every x_0 and every s

$$\mathbb{P}\left(\lim_{t \to \infty} X_{s,x_0}(t) = x^* \right) = 1. \tag{3.4}$$

Theorem 3.4. ([1]) *Assume that f and g satisfy the existence and uniqueness assumptions and they have continuous coefficients with respect to t.*

(i) *Suppose that there exist a positive definite function*

$$V \in C^{2,1}\left(U_h \times [t_0, \infty)\right),$$

where $U_h = \{x \in \mathbb{R}^d : \|x - x^*\| < h\}$ for $h > 0$ such that

$$\mathcal{L}V(x,t) \leq 0, \quad \forall\, t \geq t_0, \quad x \in U_h, \tag{3.5}$$

then the equilibrium solution x^* of (3.1) is stochastically stable.

(ii) *If, in addition, V is decrescent (there exists a positive definite function V_1 such that $V(x,t) \leq V_1(x)$ for all $x \in U_h$) and $\mathcal{L}V(x,t)$ is negative definite, then the equilibrium solution x^* is stochastically asymptotically stable.*

(iii) *If the assumptions of part ii) hold for a radially unbounded function $V \in C^{2,1}\left(\mathbb{R}^d \times [t_0, \infty)\right)$ defined everywhere, then the equilibrium solution x^* is globally stochastically asymptotically stable.*

Now, we discuss equilibrium solutions of the stochastic model (1.2). The stochastic model (1.2) can have at most two equilibrium solutions, namely uninfected equilibrium solution $E_1 = (x_1, y_1, z_1)$ and infected equilibrium solution $E_2 = (x_2, y_2, z_2)$. The infected equilibrium solution exists if the condition

$$\mathcal{R}_0 = \frac{s\beta}{ae} > 1 \quad \text{and} \quad F(x_2, y_2, z_2) = 0.$$

holds.

Theorem 3.5. *The uninfected equilibrium solution $E_1 = (x_1, y_1, z_1)$ of (1.2) is globally stochastically asymptotically stable on $\mathbb{D}$, if $\mathcal{R}_0 \leq 1$.*

Proof. We use Theorem 3.4 and define a Lyapunov function

$$V_1(x, y, z) = \frac{1}{2}(x - x_1 + y)^2 + 2x_1 y + \frac{px_1}{2c} z^2. \tag{3.6}$$

The infinitesimal generator $\mathcal{L}$ acting on the Lyapunov function V_1 can be written as:

$$\begin{aligned}
&\mathcal{L}V_1(x, y, z) \\
&= (s - \mu x - \beta xy)(x - x_1 + y) + (\beta xy - ay - pyz)\big(x - x_1 + y + 2x_1\big) \\
&\quad + (cy - bz - myz)\left(\frac{px_1}{c} z\right) + x^2 y^2 F^2(x, y, z)(1 - 1), \\
&\mathcal{L}V_1(x, y, z) \\
&= (x - x_1 + y)(s - \mu x - \beta xy + \beta xy - ay - pyz) \\
&\quad + 2x_1(\beta xy - ay - pyz) + \frac{px_1}{c} z(cy - bz - myz).
\end{aligned}$$

Since E_1 is equilibrium and $\mu \leq a$, we have

$$\begin{aligned}
\mathcal{L}V_1(x, y, z) &\leq (x - x_1 + y)(-\mu(x - x_1 + y) - pyz) \\
&\quad + 2x_1(\beta xy - ay - pyz) + \frac{px_1}{c} z(cy - bz - myz), \\
\mathcal{L}V_1(x, y, z) &\leq -\mu(x - x_1 + y)^2 - pxyz + px_1 yz - py^2 z + 2\beta x_1 xy \\
&\quad - 2ax_1 y - 2px_1 yz + px_1 yz - \frac{pbx_1}{c} z^2 - \frac{pmx_1}{c} yz^2, \\
\mathcal{L}V_1(x, y, z) &\leq -\mu(x - x_1 + y)^2 - pxyz - py^2 z - 2x_1\left(a - \frac{\beta s}{\mu}\right) y \\
&\quad - \frac{pbx_1}{c} z^2 - \frac{pmx_1}{c} yz^2, \\
\mathcal{L}V_1(x, y, z) &\leq -\mu(x - x_1 + y)^2 - pxyz - py^2 z - 2ax_1(1 - \mathcal{R}_0) y \\
&\quad - \frac{pbx_1}{c} z^2 - \frac{pmx_1}{c} yz^2.
\end{aligned}$$

If $\mathcal{R}_0 \leq 1$, then $\mathcal{L}V_1(x,y,z)$ becomes negative definite on $\mathbb{D}$. By Theorem 2.1, the uninfected equilibrium solution E_1 of the stochastic model (1.2) is globally stochastically asymptotically stable on $\mathbb{D}$. □

Theorem 3.6. *The infected equilibrium solution, $E_2 = (x_2, y_2, z_2)$ of the system (1.2) is stochastically asymptotically stable on $\mathbb{D}$ if $\mathcal{R}_0 > 1$ and satisfies $\eta(x,y,z) \leq 0$, where*

$$\eta(x,y,z) = -\mu(x-x_2)^2 - bk(z-z_2)^2 + \frac{1}{2}x^2\left(y^2 + x_2y_2\right)F^2(x,y,z) \tag{3.7}$$

for $k = \dfrac{px_2}{(c-mz_2)}$.

Proof. Note that the condition $\mathcal{R}_0 > 1$ and $F(S_2, I_2, R_2) = 0$ are needed for the existence of the infected equilibrium solution. Define a Lyapunaov function

$$V_2(x,y,z) = \frac{1}{2}(x-x_2)^2 + x_2\left(y - y_2 - y_2\ln\left(\frac{y}{y_2}\right)\right) + \frac{k}{2}(z-z_2)^2, \tag{3.8}$$

where k is positive and chosen later.

The infinitesimal generator $\mathcal{L}$ acting on the Lyapunov function V_2 can be written as:

$$\begin{aligned}\mathcal{L}V_2(x,y,z) &= (s-\mu x-\beta xy)(x-x_2) + (\beta xy - ay - pyz)\,x_2\left(1-\frac{y_2}{y}\right)\\ &\quad + (cy - bz - myz)\,k\,(z-z_2) + \frac{1}{2}x^2y^2F^2(x,y,z)\\ &\quad + \frac{1}{2}\frac{x_2y_2x^2y^2}{y^2}F^2(x,y,z).\end{aligned}$$

After a little algebra, we have

$$\begin{aligned}&\mathcal{L}V_2(x,y,z)\\ &= (s-\mu x-\beta xy)(x-x_2) + (\beta x - a - pz)\,x_2\,(y-y_2)\\ &\quad + (cy-bz-myz)\,k\,(z-z_2) + \frac{1}{2}x^2\left(y^2+x_2y_2\right)F^2(x,y,z).\end{aligned} \tag{3.9}$$

The following identities help to simplify $\mathcal{L}V_2(x,y,z)$

(i) $s-\mu x-\beta xy = -\mu(x-x_2) - \beta(x-x_2)y - \beta x_2(y-y_2)$,
(ii) $\beta x - a - pz = \beta(x-x_2) - p(z-z_2)$,
(iii) $cy - bz - myz = c(y-y_2) - b(z-z_2) - m(y-y_2)z_2 - my(z-z_2)$.

Substituting the above identities into (3.9), we get

$$\begin{aligned}
\mathcal{L}V_2(x,y,z) &= \left(-\mu(x-x_2)-\beta(x-x_2)y-\beta x_2(y-y_2)\right)(x-x_2)\\
&\quad+\left(\beta(x-x_2)-p(z-z_2)\right)x_2\,(y-y_2)\\
&\quad+\left(c(y-y_2)-b(z-z_2)-m(y-y_2)z_2-my(z-z_2)\right)k\,(z-z_2)\\
&\quad+\frac{1}{2}x^2\left(y^2+x_2y_2\right)F^2(x,y,z),\\
\mathcal{L}V_2(x,y,z) &= -\mu(x-x_2)^2-\beta(x-x_2)^2y-\beta x_2(x-x_2)(y-y_2)\\
&\quad+\beta x_2(x-x_2)(y-y_2)-px_2(y-y_2)(z-z_2)\\
&\quad+ck(y-y_2)(z-z_2)-bk(z-z_2)^2-mk(y-y_2)(z-z_2)z_2\\
&\quad-mky(z-z_2)^2+\frac{1}{2}x^2\left(y^2+x_2y_2\right)F^2(x,y,z).
\end{aligned}$$

Choose $k=\dfrac{px_2}{(c-mz_2)}$, we have

$$\begin{aligned}
\mathcal{L}V_2(x,y,z) &= -\mu(x-x_2)^2-\beta(x-x_2)^2y-bk(z-z_2)^2\\
&\quad-mky(z-z_2)^2+\frac{1}{2}x^2\left(y^2+x_2y_2\right)F^2(x,y,z).
\end{aligned}$$

Hence $\mathcal{L}V_2(x,y,z)=0$ only at (x_2,y_2,z_2) and by the choice of suitable functions $F(x,y,z)$, one can obtain $\mathcal{L}V_2(x,y,z)<0$ on $\mathbb{D}\setminus(x_2,y_2,z_2)$. Hence $\mathcal{L}V_2(x,y,z)$ is negative definite on $\mathbb{D}$ for some suitable $F(x,y,z)$. Therefore, by Theorem 3.4, the infected equilibrium is stochastically asymptotically stable on $\mathbb{D}$ if $\mathcal{R}_0>1$ and for some suitable $F(x,y,z)$ such that $F(x_2,y_2,z_2)=0$ and satisfies the condition (3.7). $\square$

4. Stationary distribution and positive recurrence

We first present a lemma, which is a useful criterion for positive recurrence in terms of Lyapunov function ([17]).

Consider the d-dimensional stochastic differential equation

$$dX(t)=b(X)dt+\sum_{r=1}^{k}\sigma_r(X)dW_r(t) \tag{4.1}$$

and the diffusion matrix is defined as follows

$$A(x)=(a_{ij}(x)),\qquad a_{ij}(x)=\sum_{r=1}^{k}\sigma_r^i(x)\sigma_r^j(x).$$

Lemma 4.1. ([17]) *The system* (4.1) *is positive recurrent if there is a bounded open subset H of $\mathbb{R}^d$ with a regular* (*i.e., smooth*) *boundary and*

(i) *there exist some* $i = 1, 2, \cdots, d$ *and a positive constant* k *such that*

$$a_{ii}(x) \geq k \quad \text{for any} \quad x \in H,$$

(ii) *there exists a nonnegative function* $V : H^c \to \mathbb{R}$ *such that* V *is twice continuously differentiable and that for some* $\theta > 0$,

$$\mathcal{L}V(x) \leq -\theta \quad \text{for any} \quad x \in H^c.$$

Moreover, the positive recurrent process $X(t)$ *has a unique stationary distribution* $\mu(.)$ *with density in* $\mathbb{R}^d$ *such that for any Borel set* $B \subset \mathbb{R}^d$

$$\lim_{t\to\infty} \mathbb{P}(t, x, B) = \mu(B)$$

and

$$\mathbb{P}\left\{\lim_{T\to\infty} \frac{1}{T}\int_0^T f(X(t))dt = \int_{\mathbb{R}^d} f(x)\mu(dx)\right\} = 1$$

for all $x \in \mathbb{R}^d$ *and* $f : \mathbb{R}^d \to \mathbb{R}$ *be a function integrable with respect to the measure* μ.

Theorem 4.2. *The solution* $(x(t), y(t), z(t))$ *of system* (1.2) *with any positive initial value* $(x(0), y(0), z(0)) \in \mathbb{D}$, *where* $F(x, y, z) = f(x - x_2, y - y_2)$ *is positive recurrent and admits a unique ergodic stationary distribution in* $\mathbb{D}$ *if* $\mathcal{R}_0 > 1$ *and*

$$\eta_1(x, y, z) = \mu(x-x_2)^2 + bk(z-z_2)^2 - \frac{1}{2}\left(\frac{s}{\mu}\right)^2\left(\left(\frac{s}{\mu}\right)^2 + x_2 y_2\right) F^2(x, y, z).$$

is positive definite on H^c *for* $k = \dfrac{px_2}{(c - mz_2)}$.

Proof. Define the following bounded open subset H of $\mathbb{R}^3$

$$H = \left\{(x, y, z) \in \mathbb{D} \;\middle|\; \frac{1}{N} < x < \frac{s}{\mu} - \frac{1}{N},\ \frac{1}{M} < y < \frac{s}{\mu} - \frac{1}{M},\ \frac{1}{P} < \frac{a}{2c}z < \frac{s}{\mu} - \frac{1}{P}\right\},$$

where N, M and P are sufficiently large positive constants to be chosen in the following, x_2 and $y_2 \notin \overline{H}$ and $z_2 \in H$. The diffusion matrix associated with the system (1.2) is given by

$$A(x, y, z) = \begin{pmatrix} x^2y^2F^2(x, y, z) & -x^2y^2F^2(x, y, z) & 0 \\ -x^2y^2F^2(x, y, z) & x^2y^2F^2(x, y, z) & 0 \\ 0 & 0 & 0 \end{pmatrix}.$$

Since $\overline{H} \subset \mathbb{R}^3_+$, then

$$\begin{aligned} a_{11}(x,y,z) &= x^2y^2F^2(x,y,z) \\ &\geq \inf_{(x,y,z)\in\overline{H}} x^2y^2F^2(x,y,z) \\ &\geq k_1, \end{aligned}$$

where k_1 is positive constant. This implies the condition (i) in Lemma 4.1 is satisfied. It remains for us to verify the condition (ii) in Lemma 4.1. Define the following nonnegative function

$$V(x,y,z) = \frac{1}{2}(x-x_2)^2 + x_2\left(y - y_2 - y_2\ln\left(\frac{y}{y_2}\right)\right) + \frac{k}{2}(z-z_2)^2$$

for $k = \dfrac{px_2}{(c-mz_2)}$. Apply $\mathcal{L}$ on $V(x,y,z)$, we have

$$\begin{aligned} \mathcal{L}V(x,y,z) &= -\mu(x-x_2)^2 - \beta(x-x_2)^2y - bk(z-z_2)^2 \\ &\quad - mky(z-z_2)^2 + \frac{1}{2}x^2\left(y^2 + x_2y_2\right)F^2(x,y,z), \\ \mathcal{L}V(x,y,z) &\leq -\eta_1(x,y,z). \end{aligned}$$

Since $\eta_1(x,y,z) > 0$ on H^c,

$$\eta_1(x,y,z) \geq \inf_{(x,y,z)\in H^c} \eta_1(x,y,z) = \theta > 0.$$

From this, we have

$$\mathcal{L}V(x,y,z) \leq -\theta \quad \text{for all} \quad (x,y,z) \in H^c.$$

So the condition (ii) of Lemma 4.1 is met. This completes the proof. □

We proved analytically sufficient condition for stochastic asymptotic stability of equilibrium solutions of the model (1.2) and connected to the basic reproduction number $\mathcal{R}_0$. We now illustrate our analytical results.

5. Illustrative example

In this section, we visualize our results. Consider the stochastic viral infection model with immune impairment.

$$\begin{aligned} dx &= (s - \mu x - \beta xy)\,dt - \left(\frac{\mu}{s}\right)^3 xy(x-x_2)dW, \\ dy &= (\beta xy - ay - pyz)\,dt + \left(\frac{\mu}{s}\right)^3 xy(x-x_2)dW, \\ dz &= (cy - bz - myz)\,dt, \end{aligned} \tag{5.1}$$

where s, μ, β, a, p, c, b and m are positive constants and

$$\begin{aligned} x_2 &= \frac{1}{\beta}\left(a + \frac{cpy_2}{b+my_2}\right), \\ y_2 &= \frac{1}{2A}\left\{-B + \sqrt{B^2 + 4Ab(s\beta - a\mu)}\right\}, \\ z_2 &= \frac{cy_2}{b+my_2}, \end{aligned}$$

where $A = \beta(am + cp)$ and $B = ab\beta + c\mu p - m(s\beta - a\mu)$ and $\mathcal{R}_0 = \dfrac{s\beta}{a\mu}$.

Global existence of a unique solution of the system (5.1) in

$$\mathbb{D} = \left\{(x, y, z) \in \mathbb{R}^3 : x > 0,\ y > 0,\ z > 0,\ x + y + \frac{a}{2c}z \leq \frac{s}{\mu}\right\}$$

is proven by Theorem 2.2.

In Figure 1(A), 1(B), 1(C) and 2(A), 2(B), 2(C), dynamics of expected values of x, y and z versus time are plotted. They show that CD4$^+$T cell, Infected CD4$^+$T cell and Immune cell populations, in average, settle around the equilibrium. In Figure 1(D), 1(E), 1(F) and 2(D), 2(E), 2(F) display the evaluation of the variances of x, y and z versus time. As it seen, variances rapidly go to zero. Hence the equilibrium solutions are approached.

Figure 1 verifies Theorem 3.5 which states, if $\mathcal{R}_0 = 0.8333 \leq 1$, then the uninfected equilibrium solution $E_1 = (666.6667, 0, 0)$ of the system (5.1) is globally stochastically asymptotically stable on $\mathbb{D}$.

Figure 2 agrees to Theorem 3.6 which proves stochastic asymptotic stability of the infected equilibrium solution $E_2 = (893.3824, 282.2222, 2.3346)$ to the system (5.1) on $\mathbb{D}$ under the assumption $\mathcal{R}_0 = 16.8750 > 1$ and η is negative definite, which requires non-negative of the constant

$$\phi = \mu - \frac{1}{2}\left(\frac{\mu}{s}\right)^4\left(\left(\frac{s}{\mu}\right)^2 + x_2y_2\right) = 0.0200,$$

where

$$\eta(x, y, z) \leq -\phi(x - x_2)^2 - bk(z - z_2)^2 \quad \text{for} \quad k = \frac{px_2}{(c - mz_2)}.$$

If we choose the parameter $s = 270$, $\mu = 0.02$, $\beta = 0.001$, $a = 0.80$, $p = 0.04$, $c = 0.025$, $b = 0.2$ and $m = 0.01$, then the conditions of Theorem 4.2 are holds. Hence the system 5.1 is positive recurrent, moreover, the positive recurrent has unique stationary distribution in $\mathbb{D}$.

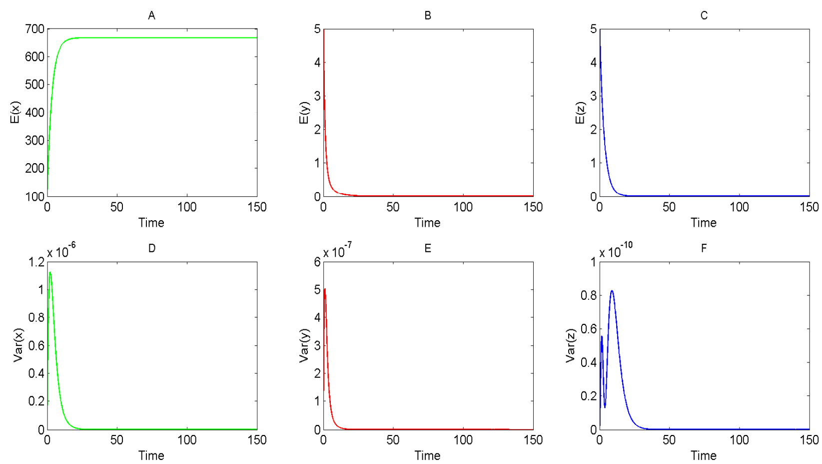

FIGURE 1. The uninfected equilibrium $E_1 = (x_1, y_1, z_1) = (666.6667, 0, 0)$ is globally asymptotically stochastically stable for the parameters: $s = 200$, $\mu = 0.3$, $\beta = 0.001$, $a = 0.80$, $p = 0.04$, $c = 0.025$, $b = 0.31$, $m = 0.01$ ($\mathcal{R}_0 = 0.8333 < 1$).

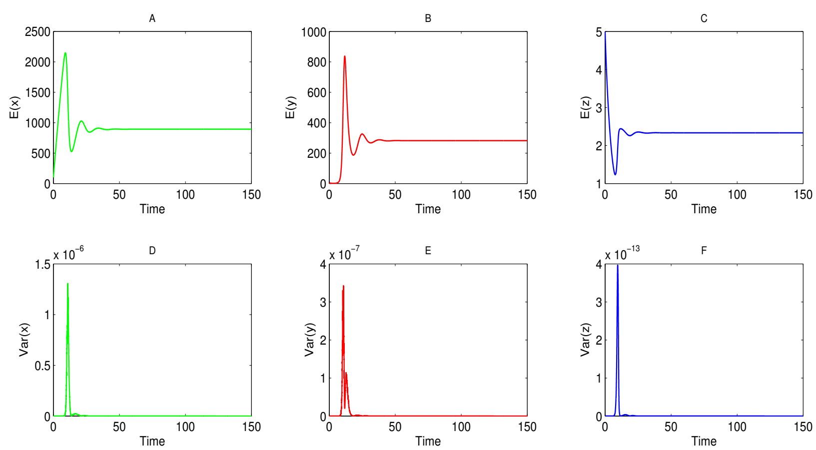

FIGURE 2. The infected equilibrium $E_2 = (x_2, y_2, z_2) = (893.3824, 282.2222, 2.3346)$ is globally asymptotically stochastically stable for the parameters: $s = 270$, $\mu = 0.02$, $\beta = 0.001$, $a = 0.80$, $p = 0.04$, $c = 0.025$, $b = 0.2$, $m = 0.01$, ($\mathcal{R}_0 = 16.8750 > 1$).

6. CONCLUSION

In our model (1.2), we consider general diffusion term. Hence, we have a family of stochastic model. We established in this paper, the model (1.2) possesses a non-negative unique solution as this is essential in any population dynamics models. We discussed stochastic asymptotic stability of uninfected and infected equilibria by the help of invariance principle and Lyapunov's second method. As common, stochastic asymptotic stability of equilibria is connected to the basic reproduction number $\mathcal{R}_0$. A sufficient condition for stochastic asymptotic stability is found in terms of parameters and functional dependence on the variable. A remarkable fact of the criteria (3.7) is that a sufficient condition for stability can be found even for general local Lipschitz continuous F. Our results reveal that a certain type of stochastic perturbation may help stabilize the system and also the solution of the system (1.2) is positive recurrent and admits a unique ergodic stationary distribution in $\mathbb{D}$. Furthermore, we visualized our results.

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References

[1] L. Arnold, *Stochastic Differential Equations: Theory and Applications*, Wiley, New York (1974).

[2] T.C. Gard, *Introduction to Stochastic Differential Equations*, Marcel Dekker, New York and Basel (1998).

[3] C. Ji, D. Jiang and N. Shi, *Multigroup SIR epidemic model with stochastic perturbation*, Phys A, **390** (2011), 1747–1762.

[4] R. Khasminskii, *Stochastic Stability of Differential Equations*, Sijthoff & Noordhoff, Alpen (1980).

[5] A. Lahrouz and L. Omari, *Extinction and stationary distribution of a stochastic SIRS epidemic model with non-linear incidence*, Statist. Probab. Lett., **83** (2013), 960–968.

[6] A. Lahrouz, L. Omari, D. Kiouach and A. Belmaâti, *Deterministic and stochastic stability of a mathematical model of smoking*, Statist. Probab. Lett., **81** (2011), 1276–1284.

[7] M. Liu, K. Wang and Q. Wu, *Survival analysis of stochastic competitive models in a polluted environment and stochastic competitive exclusion principle*, Bull. Math. Biol., **73** (2011), 1969–2012.

[8] X. Mao, G. Marion and E. Renshaw, *Environmental Brownian noise suppresses explossins in population dynamics*, Stoch. Process. Appl., **97** (2002), 95–110.

[9] R.M. May, *Stability and Complexity in Model Ecosystems*, Princeton University Press, NJ (2001).

[10] B. Mukhopadhyay and R. Bhattacharyya, *Effects of deterministic and random refuge in a prey-predator model with parasite infection*, Math. Biosci., **239** (2012), 124–130.

[11] M. Pitchaimani and R. Rajaji, *Stochastic asymptotic stability of Nowak-May model with variable diffusion rates*, Methodol. Comput. Appl. Probab., 2016, DOI 10.1007/s11009-016-9494-7.

[12] R.R. Regoes, D. Wodarz and M.A. Nowak, *Virus dynamics: the effect of target cell limitation and immune responses on virus evolution*, J. Theor. Biol., **191** (1998), 451–462.

[13] H. Schurz and K. Tosun, *Stochastic asymptotic stability of SIR model with variable diffusion rates*, J. Dyn. Diff. Equat., **27** (2014), 69–82.

[14] S. Wang, X. Song and Z. Ge, *Dynamics analysis of a delayed viral infection model with immune impairment*, Appl. Math. Model, **35** (2011), 4877–4885.

[15] Q. Yang and X. Mao, *Stochastic dynamics of SIRS epidemic models with random perturbation*, Math. Biosci. Eng., **11**(4) (2014), 1003–1025.

[16] Y. Zhao, S. Yuan and J. Ma, *Survival and stationary distribution analysis of a stochastic competitive model of three species in a polluted environment*, Bull. Math. Biol., **77**(7) (2015), 1285–1326.

[17] C. Zhu and G. Yin, *Asymptotic properties of hybrid diffusion systems*, SIAM J. Control Optim., **46** (2007), 1155–1179.