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A STOCHASTICALLY PERTURBED HIV-1 AND HIV-2 EPIDEMIC MODEL WITH DRUG RESISTANCE

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Abstract. In this paper, a stochastic HIV-1 and HIV-2 epidemic model with drug resistance is presented to study the effect of white noise intensities. We firstly prove the existence and uniqueness of the global positive solution for the proposed stochastic model. The extinction of our studied disease is derived with sufficient conditions. In addition, the persistence in the mean of the infection is also established. Finally, numerical simulations for different noises disturbance are performed to illustrate the performance of our theoretical study.

Keywords: HIV-1; HIV-2; stochastic epidemic model; Itô's formula; extinction; permanence in mean.

2020 AMS Subject Classification: 92D30.

1. INTRODUCTION

Mathematical modeling of infectious diseases is a field of research that uses mathematical tools to study the spread and control of infectious diseases within a population. By using this approach, we can better understand diseases and their transmission mechanisms, assess the effectiveness of prevention and control measures, and make more informed decisions about public health [1, 2].

A multi-strain epidemic model is used to study and simulate the spread of an epidemic involving

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several strains of a pathogen such as VIH [3], influenza [4], Tuberculosis [5], Other researchers are exploring the modeling of diseases with multiple strains [6, 7, 8, 9].

In addition to deterministic models, mathematical models need to account for environmental white noise, which provides an additional level of realism relative to deterministic models [10, 11, 12, 13, 14, 15, 16, 17].

The aim of this study is to improve the deterministic HIV-1 and HIV-2 epidemic model recently proposed in [3]. The authors are studied a deterministically a HIV-1 and HIV-2 epidemic model with drug resistance.

$$(1.1) \quad \left\{ \begin{array}{l} \frac{dS(t)}{dt} = \Lambda - \beta_1 S(t)I_1(t) - \beta_2 S(t)I_2(t) - \mu S(t), \\ \frac{dI_1(t)}{dt} = \beta_1 S(t)I_1(t) - (\theta_1 + \omega_1 + \mu)I_1(t), \\ \frac{dI_2(t)}{dt} = \beta_2 S(t)I_2(t) - (\theta_2 + \omega_2 + \mu)I_2(t), \\ \frac{dD_R(t)}{dt} = \omega_1 I_1(t) + \omega_2 I_2(t) - (1 - \rho)\eta D_R(t) - (\eta\rho + \mu)D_R(t), \\ \frac{dA(t)}{dt} = (1 - \rho)\eta D_R(t) + \theta_1 I_1(t) + \theta_2 I_2(t) - (d + \mu)A(t), \\ \frac{dR(t)}{dt} = \eta\rho D_R(t) - \mu R(t). \end{array} \right.$$

Here S is the susceptibles, I_1 is HIV-1 infective individuals, I_2 HIV-2 infective individuals, D_R drug resistance individuals, A are AIDS individuals and R is the removed ones. The parameters in the model (1.1) are positive constants, where: Λ is recruitment rate, $\frac{1}{\mu}$ is natural mortality rate, β_1 is the infection rate of the HIV-1 strain, β_2 is the infection rate of the HIV-2 strain, θ_1 rate at which HIV-1 infected people progress to AIDS stage, θ_2 rate at which HIV-2 infected people progress to AIDS stage, ω_1 progression rate from HIV-1 to drug resistance compartment, ω_2 progression rate from HIV-2 to drug resistance compartment, ρ therapy efficacy, η removed rate of drug resistance, d AIDS induced death rate.

The diseases are both transmitted by contact between the individuals in the susceptible compartment and those in I_1 and I_2 compartments with two bilinear incidence rates. We assume that the populations who live in an environment with random accidents are mainly affected by the contact rate, in the environment will manifest themselves mainly as fluctuations in the bilinear response

rate, so that β_1 turn into $\beta_1 + \sigma_1 \dot{B}(t)$ and β_2 turn into $\beta_2 + \sigma_2 \dot{B}(t)$ where $B(t) = (B_1(t), B_2(t))$ is a standard Brownian motion with intensities $\sigma_1 > 0$ and $\sigma_2 > 0$. Hence, we reach a stochastic version of model (1.1) as follows

$$(1.2) \quad \left\{ \begin{array}{l} dS(t) = \left(\Lambda - \beta_1 S(t) I_1(t) - \beta_2 S(t) I_2(t) - \mu S(t) \right) dt \\ \quad - \sigma_1 S(t) I_1(t) dB_1(t) - \sigma_2 S(t) I_2(t) dB_2(t), \\ dI_1(t) = \left(\beta_1 S(t) I_1(t) - (\theta_1 + \omega_1 + \mu) I_1(t) \right) dt + \sigma_1 S(t) I_1(t) dB_1(t), \\ dI_2(t) = \left(\beta_2 S(t) I_2(t) - (\theta_2 + \omega_2 + \mu) I_2(t) \right) dt + \sigma_2 S(t) I_2(t) dB_2(t), \\ dD_R(t) = \left(\omega_1 I_1(t) + \omega_2 I_2(t) - (1 - \rho) \eta D_R(t) - (\eta \rho + \mu) D_R(t) \right) dt, \\ dA(t) = \left((1 - \rho) \eta D_R(t) + \theta_1 I_1(t) + \theta_2 I_2(t) - (d + \mu) A(t) \right) dt, \\ dR(t) = \left(\eta \rho D_R(t) - \mu R(t) \right) dt \end{array} \right.$$

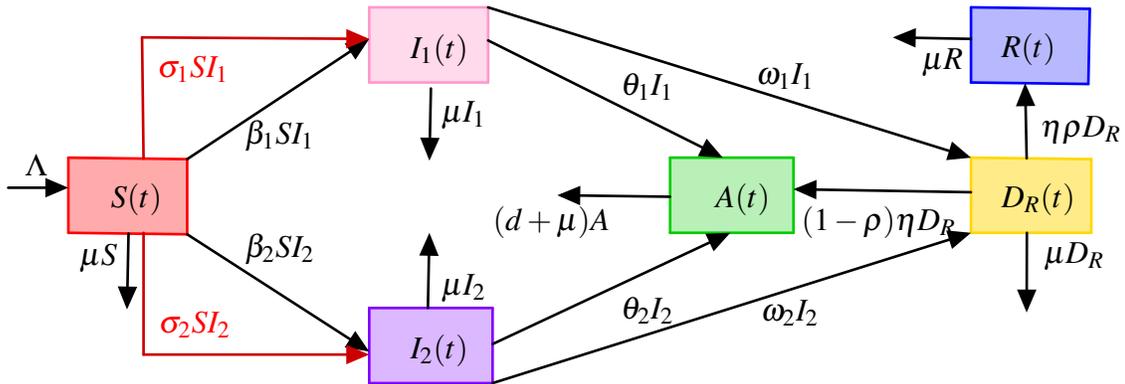


FIGURE 1. The diagram of the stochastic HIV-1 and HIV-2 model (1.2).

The rest of the paper is organized as follows. In the next section, we establish the existence and uniqueness of the solution for the stochastic system (1.2). In section , we analyze the conditions for disease extinction. In Section 4, the persistence in mean is established. Section 5 presents numerical examples that illustrate the theoretical results. Finally, Section 6 concludes the paper.

2. EXISTENCE AND UNIQUENESS OF THE GLOBAL POSITIVE SOLUTION

In this section, we present the notations, definitions, and lemmas that were employed to analyze our main findings.

Consider a filtration $\{\mathcal{F}_t\}_{t \geq 0}$ with a complete probability space $(\Omega, \mathcal{F}, \{\mathcal{F}_t\}_{t \geq 0}, \mathbb{P})$ that fulfills the usual conditions with increasing and right continuous while \mathcal{F}_0 is the set of \mathbb{P} -null sets.

For arbitrary integrable function h on $[0, +\infty)$, define $\langle h(t) \rangle = \frac{\int_0^t h(\theta) d\theta}{t}$.

Definition 1. (1) The diseases I_1 and I_2 are said to go extinction if $\lim_{t \rightarrow +\infty} I_1(t) = 0$ and

$$\lim_{t \rightarrow +\infty} I_2(t) = 0.$$

(2) The diseases I_1 and I_2 will be persist in mean if $\exists c_1 > 0$ and $c_2 > 0$ such that $\liminf_{t \rightarrow +\infty} \langle I_1(t) \rangle \geq c_1$ and $\liminf_{t \rightarrow +\infty} \langle I_2(t) \rangle \geq c_2$.

Remark 2. Let the set

$$\Gamma = \{(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t)) \in \mathbb{R}_+^6 : S(t) + I_1(t) + I_2(t) + D_R(t) + A(t) + R(t) \leq \frac{\Lambda}{\mu}\}$$

The total population $N(t) = S(t) + I_1(t) + I_2(t) + D_R(t) + A(t) + R(t)$ in systems (1.1) and (1.2) verifies, the equation

$$\frac{dN(t)}{dt} \leq \Lambda - \mu N(t),$$

which gives by integration

$$N(t) \leq e^{-\mu t} \left(N(0) - \frac{\Lambda}{\mu} \right) + \frac{\Lambda}{\mu} \leq \max\left(N(0), \frac{\Lambda}{\mu}\right),$$

If $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$, then $N(t) \leq \frac{\Lambda}{\mu}$ almost surely. Thus, the set Γ is almost surely positively invariant by the systems (1.1) and (1.2) respectively, throughout the rest, we assume that $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$.

Theorem 3. *For any initial value $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$, there exists a unique solution $(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t))$ of system (1.2) on $t \geq 0$ and the solution will remain in Γ with probability one for all $t \geq 0$ almost surely.*

Proof. Since the coefficients of system (1.2) satisfy the local Lipschitz condition, then for any given initial value $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$, there exists a unique local solution $(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t)) \in \Gamma$ on $t \in [0, \tau_e)$, where τ_e is the explosion time. To prove that this solution is global, we need only to show that $\tau_e = \infty$ almost surely.

To this end, let $p_0 \geq 1$ be sufficiently large such that $S(0), I_1(0), I_2(0), D_R(0), A(0)$ and $R(0)$ all lie within the interval $\left[\frac{1}{p_0}, p_0\right]$, for each integer $p \geq p_0$, define the stopping time

$$(2.1) \quad \tau_p = \inf \left\{ t \in [0, \tau_e) : S(t) \notin \left(\frac{1}{p}, p\right), \text{ or } I_1(t) \notin \left(\frac{1}{p}, p\right), \text{ or } I_2(t) \notin \left(\frac{1}{p}, p\right), \text{ or } D_R(t) \notin \left(\frac{1}{p}, p\right), \right. \\ \left. \text{ or } A(t) \notin \left(\frac{1}{p}, p\right), \text{ or } R(t) \notin \left(\frac{1}{p}, p\right) \right\},$$

Where throughout this paper, we set $\inf \emptyset = \infty$ (\emptyset denotes the emptyset). Clearly, τ_p is increasing as $p \rightarrow \infty$.

Set $\tau_\infty = \lim_{p \rightarrow +\infty} \tau_p$, whence $\tau_\infty \leq \tau_e$ almost surely. If $\tau_\infty = \infty$ almost surely is true, then $\tau_e = \infty$ almost surely and $(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t)) \in \mathbb{R}_+^6$ almost surely for all $t \geq 0$. In other words, to show that $\tau_\infty = \infty$ almost surely. If this statement is not true, then there exists a pair of constants $\mathcal{T} > 0$ and $\varepsilon \in (0, 1)$ such that

$$(2.2) \quad \mathbb{P}\{\tau_\infty \leq \mathcal{T}\} > \varepsilon$$

Hence, there exist an integer $p_1 \geq p_0$ such that

$$(2.3) \quad \mathbb{P}\{\tau_p \leq \mathcal{T}\} \geq \varepsilon \text{ for all } p \geq p_1$$

Let a \mathcal{C}^2 -function $\mathcal{V} : \mathbb{R}_+^6 \rightarrow \mathbb{R}_+^6$ by

$$(2.4) \quad \mathcal{V}(S, I_1, I_2, D_R, A, R) = (S - 1 - \log S) + (I_1 - 1 - \log I_1) + (I_2 - 1 - \log I_2) + (D_R - 1 - \log D_R) \\ + (A - 1 - \log A) + (R - 1 - \log R)$$

Clearly, \mathcal{V} is positive definite. Applying Itô's formula to \mathcal{V} , we get

$$(2.5) \quad d\mathcal{V}(S, I_1, I_2, D_R, A, R) = \mathcal{L}\mathcal{V}(S, I_1, I_2, D_R, A, R)dt + \sigma_1(I_1 - S)dB_1(t) + \sigma_2(I_2 - S)dB_2(t)$$

where $\mathcal{L}\mathcal{V} : \mathbb{R}_+^6 \rightarrow \mathbb{R}^6$ is defined by

$$\begin{aligned} \mathcal{L}\mathcal{V} &= \left(1 - \frac{1}{S}\right) (\Lambda - \beta_1 S(t)I_1(t) - \beta_2 S(t)I_2(t) - \mu S(t)) \\ &+ \left(1 - \frac{1}{I_1}\right) (\beta_1 S(t)I_1(t) - (\theta_1 + \omega_1 + \mu)I_1(t)) \\ &+ \left(1 - \frac{1}{I_2}\right) (\beta_2 S(t)I_2(t) - (\theta_2 + \omega_2 + \mu)I_2(t)) \\ &+ \left(1 - \frac{1}{D_R}\right) (\omega_1 I_1(t) + \omega_2 I_2(t) - (1 - \rho)\eta D_R(t) - (\eta\rho + \mu)D_R(t)) \\ &+ \left(1 - \frac{1}{A}\right) ((1 - \rho)\eta D_R(t) + \theta_1 I_1(t) + \theta_2 I_2(t) - (d + \mu)A(t)) \\ &+ \left(1 - \frac{1}{R}\right) (\eta\rho D_R(t) - \mu R(t)) \\ &\leq \Lambda + 6\mu + \theta_1 + \omega_1 + \theta_2 + \omega_2 + \eta + d + \beta_1 I_1 + \beta_2 I_2 + \frac{\sigma_1^2 I_1^2}{2} + \frac{\sigma_2^2 I_2^2}{2} + \frac{\sigma_1^2 S^2}{2} + \frac{\sigma_2^2 S^2}{2} \\ &\leq: = C \end{aligned}$$

where C is a positive constant. Therefore, we have

$$(2.6) \quad d\mathcal{V}(S, I_1, I_2, D_R, A, R) \leq Cdt + \sigma_1(I_1 - S)dB_1(t) + \sigma_2(I_2 - S)dB_2(t)$$

Integrating both sides of (2.6) from 0 to $\tau_p \wedge \mathcal{T} = \min\{\tau_p, \mathcal{T}\}$ and taking the expectations on both sides, we have

$$\begin{aligned} \mathbb{E}\mathcal{V}\left(S(\tau_p \wedge \mathcal{T}), I_1(\tau_p \wedge \mathcal{T}), I_2(\tau_p \wedge \mathcal{T}), D_R(\tau_p \wedge \mathcal{T}), A(\tau_p \wedge \mathcal{T}), R(\tau_p \wedge \mathcal{T})\right) \\ \leq \mathcal{V}\left(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)\right) + C\mathcal{T} \end{aligned}$$

Let $\Omega_p = \{\omega \in \Omega : \tau_p = \tau_p(\omega) \leq \mathcal{T}\}$ for $p \geq p_1$ and in view of (2.3), we have $\mathbb{P}(\Omega_p) \geq \varepsilon$. Note that for every $\omega \in \Omega_p$, there exists $S(\tau_p, \omega)$ or $I_1(\tau_p, \omega)$ or $I_2(\tau_p, \omega)$ or $D_R(\tau_p, \omega)$ or $A(\tau_p, \omega)$ or $R(\tau_p, \omega)$ equals either p or $\frac{1}{p}$. Then, $\mathcal{V}\left(S(\tau_p \wedge \mathcal{T}), I_1(\tau_p \wedge \mathcal{T}), I_2(\tau_p \wedge \mathcal{T}), D_R(\tau_p \wedge \mathcal{T}), A(\tau_p \wedge \mathcal{T}), R(\tau_p \wedge \mathcal{T})\right)$

$\mathcal{I}), R(\tau_p \wedge \mathcal{I})$) is not less than either $p - 1 - \log p$ or $\frac{1}{p} - 1 + \log p$. Therefore,

$$\begin{aligned} & \mathcal{V} \left(S(\tau_p \wedge \mathcal{I}), I_1(\tau_p \wedge \mathcal{I}), I_2(\tau_p \wedge \mathcal{I}), D_R(\tau_p \wedge \mathcal{I}), A(\tau_p \wedge \mathcal{I}), R(\tau_p \wedge \mathcal{I}) \right) \\ & \geq \left(p - 1 - \log p \right) \wedge \left(\frac{1}{p} - 1 + \log p \right) \end{aligned}$$

Then we attain

$$\begin{aligned} & \mathcal{V} \left(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0) \right) + C\mathcal{I} \\ (2.7) \quad & \geq \mathbb{E} \left(1_{\Omega_p} \mathcal{V} \left(S(\tau_p, \omega), I_1(\tau_p, \omega), I_2(\tau_p, \omega), D_R(\tau_p, \omega), A(\tau_p, \omega), R(\tau_p, \omega) \right) \right) \\ & \geq \varepsilon \left(p - 1 - \log p \right) \wedge \left(\frac{1}{p} - 1 + \log p \right) \end{aligned}$$

where $1_{\Omega_p(\omega)}$ is the indicator function of Ω_p . Letting $p \rightarrow \infty$, we get

$$(2.8) \quad \infty > \mathcal{V} \left(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0) \right) + C\mathcal{I} = \infty,$$

is a contradiction. Hence, we must have $\tau_\infty = \infty$. This completes the proof. \square

Lemma 4. ([18], *Strong Law of Large Numbers*) Let $M = \{M_t\}_{t \geq 0}$ be a real-valued continuous local martingale vanishing at $t = 0$. Then

$$\limsup_{t \rightarrow \infty} \frac{\langle M, M \rangle_t}{t} < \infty \quad a.s. \implies \lim_{t \rightarrow \infty} \frac{M_t}{t} = 0 \quad a.s.$$

3. EXTINCTION

We already have proved from the previous section that our model has a unique global positive bounded solution. Our main goal in this section is the investigation of the conditions under which disease will die out or persist in our stochastic model (1.2).

Proposition 5. If $\sigma_1 > \frac{\beta_1}{\sqrt{2(\theta_1 + \omega_1 + \mu)}}$, then the HIV-1 infection disease of system (1.2) go to extinction almost surely.

Proof. Let $(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t))$ be a solution of system (1.2) with initial value $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$.

Applying Itô's formula to system (1.2), we obtain

$$(3.1) \quad \begin{aligned} d \ln I_1(t) &= \left(\beta_1 S(t) - (\theta_1 + \omega_1 + \mu) - \frac{\sigma_1^2 S^2(t)}{2} \right) dt + \sigma_1 S(t) dB_1(t) \\ &\leq \left(-\frac{\sigma_1^2}{2} \left(S(t) - \frac{\beta_1}{\sigma_1^2} \right)^2 + \frac{\beta_1^2}{2\sigma_1^2} - (\theta_1 + \omega_1 + \mu) \right) dt + \sigma_1 S(t) dB_1(t), \end{aligned}$$

Integrating both sides of (3.1) from 0 to t and dividing by t , we get

$$(3.2) \quad \ln I_1(t) \leq - \left((\theta_1 + \omega_1 + \mu) - \frac{\beta_1^2}{2\sigma_1^2} \right) + \frac{M_1(t)}{t} + \frac{\ln I_1(0)}{t}$$

where $M_1(t) = \int_0^t \sigma_1 S(x) dB_1(x)$ is the local continuous martingale satisfying $M_1(0) = 0$, and by lemma 4, we get $\lim_{t \rightarrow +\infty} \frac{M_1(t)}{t} = 0$.

Since $\sigma_1 > \frac{\beta_1}{\sqrt{2(\theta_1 + \omega_1 + \mu)}}$, taking the limit superior of both sides of (3.2) leads to

$$\limsup_{t \rightarrow +\infty} \frac{\ln I_1(t)}{t} \leq - \left(\theta_1 + \omega_1 + \mu - \frac{\beta_1^2}{2\sigma_1^2} \right) < 0,$$

which implies $\lim_{t \rightarrow +\infty} I_1(t) = 0$. a.s. This completes the proof of Proposition. \square

Proposition 6. *If $\sigma_2 > \frac{\beta_2}{\sqrt{2(\theta_2 + \omega_2 + \mu)}}$, then the HIV-2 infection disease of system (1.2) go to extinction almost surely.*

Proof. Let $(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t))$ be a solution of system (1.2) with initial value $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$.

Applying Itô's formula to system (1.2), we obtain

$$(3.3) \quad \begin{aligned} d \ln I_2(t) &= \left(\beta_2 S(t) - (\theta_2 + \omega_2 + \mu) - \frac{\sigma_2^2 S^2(t)}{2} \right) dt + \sigma_2 S(t) dB_2(t) \\ &\leq \left(-\frac{\sigma_2^2}{2} \left(S(t) - \frac{\beta_2}{\sigma_2^2} \right)^2 + \frac{\beta_2^2}{2\sigma_2^2} - (\theta_2 + \omega_2 + \mu) \right) dt + \sigma_2 S(t) dB_2(t), \end{aligned}$$

Integrating both sides of (3.3) from 0 to t and dividing by t , we get

$$(3.4) \quad \ln I_2(t) \leq - \left((\theta_2 + \omega_2 + \mu) - \frac{\beta_2^2}{2\sigma_2^2} \right) + \frac{M_2(t)}{t} + \frac{\ln I_2(0)}{t}$$

where $M_2(t) = \int_0^t \sigma_2 S(x) dB_2(x)$ is the local continuous martingale satisfying $M_2(0) = 0$, and by lemma 4, we get $\lim_{t \rightarrow +\infty} \frac{M_2(t)}{t} = 0$.

Since $\sigma_2 > \frac{\beta_2}{\sqrt{2(\theta_2 + \omega_2 + \mu)}}$, taking the limit superior of both sides of (3.4) leads to

$$\limsup_{t \rightarrow +\infty} \frac{\ln I_2(t)}{t} \leq - \left(\theta_2 + \omega_2 + \mu - \frac{\beta_2^2}{2\sigma_2^2} \right) < 0,$$

which implies $\lim_{t \rightarrow +\infty} I_2(t) = 0$. a.s. This completes the proof of Proposition. \square

Remark 7. Proposition 5 and Proposition 6 shows that when $\sigma_1 > \frac{\beta_1}{\sqrt{2(\theta_1 + \omega_1 + \mu)}}$ and $\sigma_2 > \frac{\beta_2}{\sqrt{2(\theta_2 + \omega_2 + \mu)}}$, the HIV-1 and HIV-2 infectious diseases of system (1.2) die out almost surely. In other words, large white noise stochastic disturbance yields the HIV-1 and HIV-2 extinct. Therefore, we presume that the white noise stochastic disturbance is not too large in the rest of this manuscript.

Let

$$\mathcal{R}_1^* = \frac{\beta_1 \Lambda}{\mu (\theta_1 + \omega_1 + \mu)} - \frac{\sigma_1^2 \Lambda^2}{2\mu^2 (\theta_1 + \omega_1 + \mu)}$$

$$\mathcal{R}_2^* = \frac{\beta_2 \Lambda}{\mu (\theta_2 + \omega_2 + \mu)} - \frac{\sigma_2^2 \Lambda^2}{2\mu^2 (\theta_2 + \omega_2 + \mu)},$$

Theorem 8. Let $(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t))$ be a solution of system (1.2) with initial value $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$. Then

(1) If $\mathcal{R}_1^* < 1$ and $\sigma_1 \leq \sqrt{\frac{2\mu\beta_1}{\Lambda}}$, the HIV-1 disease of system (1.2) go to extinction almost surely, i.e.

$$\lim_{t \rightarrow +\infty} I_1(t) = 0.$$

(2) If $\mathcal{R}_2^* < 1$ and $\sigma_2 \leq \sqrt{\frac{2\mu\beta_2}{\Lambda}}$, the HIV-2 disease of system (1.2) go to extinction almost surely, i.e.

$$\lim_{t \rightarrow +\infty} I_2(t) = 0.$$

Meanwhile,

$$\lim_{t \rightarrow +\infty} S(t) = \frac{\Lambda}{\mu}, \quad \lim_{t \rightarrow +\infty} D_R(t) = 0, \quad \lim_{t \rightarrow +\infty} A(t) = 0 \text{ and } \lim_{t \rightarrow +\infty} R(t) = 0.$$

Proof. Firstly, for both sides of (3.1), integrating from 0 to t first and then dividing by t yields

$$\begin{aligned}
(3.5) \quad \frac{\ln I_1(t)}{t} &= \frac{1}{t} \int_0^t \left(\beta_1 S(x) - (\theta_1 + \omega_1 + \mu) - \frac{\sigma_1^2 S^2(x)}{2} \right) dx + \frac{M_1(t)}{t} + \frac{\ln I_1(0)}{t} \\
&\leq \left(\frac{\beta_1 \Lambda}{\mu} - (\theta_1 + \omega_1 + \mu) - \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right) + \frac{M_1(t)}{t} + \frac{\ln I_1(0)}{t} \\
&= (\theta_1 + \omega_1 + \mu) \left(\frac{\beta_1 \Lambda}{\mu(\theta_1 + \omega_1 + \mu)} - \frac{\sigma_1^2 \Lambda^2}{2\mu^2(\theta_1 + \omega_1 + \mu)} - 1 \right) + \frac{M_1(t)}{t} + \frac{\ln I_1(0)}{t}
\end{aligned}$$

where $M_1(t) = \int_0^t \sigma_1 S(x) dB_1(x)$ is the local continuous martingale satisfying $M_1(0) = 0$, and by lemma 4, we get $\lim_{t \rightarrow +\infty} \frac{M_1(t)}{t} = 0$.

Taking the superior limit of both sides of (3.5) yields

$$\limsup_{t \rightarrow +\infty} \frac{\ln I_1(t)}{t} \leq (\theta_1 + \omega_1 + \mu) (\mathcal{R}_1^* - 1) < 0$$

which implies $\lim_{t \rightarrow +\infty} I_1(t) = 0$.

Secondly, for both sides of (3.3), integrating from 0 to t first and then dividing by t yields

$$\begin{aligned}
(3.6) \quad \frac{\ln I_2(t)}{t} &= \frac{1}{t} \int_0^t \left(\beta_2 S(x) - (\theta_2 + \omega_2 + \mu) - \frac{\sigma_2^2 S^2(x)}{2} \right) dx + \frac{M_2(t)}{t} + \frac{\ln I_2(0)}{t} \\
&\leq \left(\frac{\beta_2 \Lambda}{\mu} - (\theta_2 + \omega_2 + \mu) - \frac{\sigma_2^2 \Lambda^2}{2\mu^2} \right) + \frac{M_2(t)}{t} + \frac{\ln I_2(0)}{t} \\
&= (\theta_2 + \omega_2 + \mu) \left(\frac{\beta_2 \Lambda}{\mu(\theta_2 + \omega_2 + \mu)} - \frac{\sigma_2^2 \Lambda^2}{2\mu^2(\theta_2 + \omega_2 + \mu)} - 1 \right) + \frac{M_2(t)}{t} + \frac{\ln I_2(0)}{t}
\end{aligned}$$

where $M_2(t) = \int_0^t \sigma_2 S(x) dB_2(x)$ is the local continuous martingale satisfying $M_2(0) = 0$, and by lemma 4, we get $\lim_{t \rightarrow +\infty} \frac{M_2(t)}{t} = 0$.

Taking the superior limit of both sides of (3.6) yields

$$\limsup_{t \rightarrow +\infty} \frac{\ln I_2(t)}{t} \leq (\theta_2 + \omega_2 + \mu) (\mathcal{R}_2^* - 1) < 0$$

which implies $\lim_{t \rightarrow +\infty} I_2(t) = 0$.

Lastly, without loss of generality, we may assume that $0 < I_1(t) < \varepsilon_1$ and $0 < I_2(t) < \varepsilon_2$ for all $t \geq 0$, by the first equation of system (1.2), we have

$$(3.7) \quad \frac{dS(t)}{dt} \geq \Lambda - (\mu + \beta_1 \varepsilon_1 + \beta_2 \varepsilon_2 + \sigma_1 \varepsilon_1 |\dot{B}_1(t)| + \sigma_2 \varepsilon_2 |\dot{B}_2(t)|) S(t)$$

As $\varepsilon_1 \rightarrow 0$ and $\varepsilon_2 \rightarrow 0$, taking the inferior limit of both sides of (3.7) yields

$$\liminf_{t \rightarrow +\infty} S(t) \geq \frac{\Lambda}{\mu}$$

and

$$\limsup_{t \rightarrow +\infty} S(t) \leq \frac{\Lambda}{\mu}$$

Then,

$$\lim_{t \rightarrow +\infty} S(t) = \frac{\Lambda}{\mu}.$$

Since $\lim_{t \rightarrow +\infty} I_1(t) = 0$ and $\lim_{t \rightarrow +\infty} I_2(t) = 0$, then, $\lim_{t \rightarrow +\infty} D_R(t) = 0$. a.s, $\lim_{t \rightarrow +\infty} A(t) = 0$ and $\lim_{t \rightarrow +\infty} R(t) = 0$. a.s. This finishes the proof of Theorem (8). \square

Remark 9. *From Theorem 8, we show that the HIV-1 and HIV-2 diseases will die out if the white noise stochastic disturbance are large than certain values or $\mathcal{R}_1^* < 1$ and $\mathcal{R}_2^* < 1$, and the white noise stochastic disturbance are not large.*

4. PERSISTENCE IN MEAN

This section is devoted to determine sufficient conditions for the persistence of the infectious disease.

Theorem 10. *Let $(S(t), I_1(t), I_2(t), D_R(t), A(t), R(t))$ be a solution of system (1.2) with initial value $(S(0), I_1(0), I_2(0), D_R(0), A(0), R(0)) \in \Gamma$*

(i) *If $\mathcal{R}_1^* > 1, \mathcal{R}_2^* < 1$ and $\sigma_2 \leq \sqrt{\frac{2\mu\beta_2}{\Lambda}}$, then the disease HIV-2 will go extinct and the disease HIV-1 will persist, furthermore, I_1 satisfies*

$$\liminf_{t \rightarrow +\infty} \langle I_1(t) \rangle \geq (\theta_1 + \omega_1 + \mu) (\mathcal{R}_1^* - 1).$$

(ii) *If $\mathcal{R}_2^* > 1, \mathcal{R}_1^* < 1$ and $\sigma_1 \leq \sqrt{\frac{2\mu\beta_1}{\Lambda}}$, then the disease HIV-1 will go extinct and the disease HIV-2 will persist, furthermore, I_2 satisfies*

$$\liminf_{t \rightarrow +\infty} \langle I_2(t) \rangle \geq (\theta_2 + \omega_2 + \mu) (\mathcal{R}_2^* - 1).$$

(iii) If $\mathcal{R}_1^* > 1$ and $\mathcal{R}_2^* > 1$, then the HIV-1 and HIV-2 infectious diseases I_1 and I_2 are permanent in mean, furthermore, I_1 and I_2 satisfy

$$\liminf_{t \rightarrow +\infty} \langle I_1(t) + I_2(t) \rangle \geq \frac{1}{\mathcal{W}_{\max}} [(\theta_1 + \omega_1 + \mu)(\mathcal{R}_1^* - 1) + (\theta_2 + \omega_2 + \mu)(\mathcal{R}_2^* - 1)],$$

where

$$\mathcal{W}_{\max} = \max \left\{ (\theta_1 + \omega_1 + \mu) \frac{\beta_1 + \beta_2}{\mu}; \frac{\beta_1 + \beta_2}{\mu} (\theta_2 + \omega_2 + \mu) \right\}.$$

Proof. Case (i). By Theorem 8, since $\mathcal{R}_2^* < 1$ and $\sigma_2 \leq \sqrt{\frac{2\beta_2\mu}{\Lambda}}$, then we have $\lim_{t \rightarrow +\infty} I_2(t) = 0$. Since $\mathcal{R}_1^* > 1$, for ε small enough, such that $0 < I_2(t) < \varepsilon$ for all t large enough and

$$\frac{\beta_1(\Lambda - (\theta_2 + \omega_2 + \mu)\varepsilon)}{\mu(\theta_2 + \omega_2 + \mu)} - \frac{\sigma_1^2\Lambda^2}{2\mu^2(\theta_1 + \omega_1 + \mu)} > 1$$

Integrating from 0 to t and dividing by t on both sides of system (1.2) yields

$$\begin{aligned} X(t) &\triangleq \frac{S(t) - S(0)}{t} + \frac{I_1(t) - I_1(0)}{t} + \frac{I_2(t) - I_2(0)}{t} \\ &= \Lambda - \mu \langle S(t) \rangle - (\theta_1 + \omega_1 + \mu) \langle I_1(t) \rangle - (\theta_2 + \omega_2 + \mu) \langle I_2(t) \rangle \\ &\geq \Lambda - \mu \langle S(t) \rangle - (\theta_1 + \omega_1 + \mu) \langle I_1(t) \rangle - (\theta_2 + \omega_2 + \mu) \varepsilon \end{aligned}$$

then we get

$$\langle S(t) \rangle \geq \frac{\Lambda - (\theta_2 + \omega_2 + \mu)\varepsilon}{\mu} - \frac{(\theta_1 + \omega_1 + \mu)}{\mu} \langle I_1(t) \rangle - \frac{X(t)}{\mu}$$

Applying Itô's formula gives

$$\begin{aligned} (4.1) \quad d(\ln I_1(t)) &= \left[\beta_1 S(t) - (\theta_1 + \omega_1 + \mu) - \frac{\sigma_1^2 S^2(t)}{2} \right] dt + \sigma_1 S(t) dB_1(t) \\ &\geq \left[\beta_1 S(t) - (\theta_1 + \omega_1 + \mu) - \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right] dt + \sigma_1 S(t) dB_1(t) \end{aligned}$$

Integrating from 0 to t and dividing by t on both sides of (4.1), gives

$$\begin{aligned} (4.2) \quad \frac{(\ln I_1(t) - \ln I_1(0))}{t} &\geq \beta_1 \langle S(t) \rangle - \left(\theta_1 + \omega_1 + \mu + \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right) + \frac{M_1(t)}{t} \\ &\geq \beta_1 \left(\frac{\Lambda - (\theta_2 + \omega_2 + \mu)\varepsilon}{\mu} - (\theta_1 + \omega_1 + \mu) \langle I_1(t) \rangle - \frac{X(t)}{\mu} \right) \\ &\quad + \frac{M_1(t)}{t} - \left(\theta_1 + \omega_1 + \mu + \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right) \end{aligned}$$

$$(4.3) \quad = (\theta_1 + \omega_1 + \mu) \left[\frac{\beta_1 (\Lambda - (\theta_2 + \omega_2 + \mu) \varepsilon)}{\mu (\theta_1 + \omega_1 + \mu)} - \frac{\sigma_1^2 \Lambda^2}{2\mu^2 (\theta_1 + \omega_1 + \mu)} - 1 \right] \\ - \frac{\beta_1 (\theta_1 + \omega_1 + \mu)}{\mu} \langle I_1(t) \rangle - \frac{\beta_1 X(t)}{\mu} + \frac{M_1(t)}{t},$$

So, we get,

$$(4.4) \quad \frac{\ln I_1(t)}{t} \geq (\theta_1 + \omega_1 + \mu) \left[\frac{\beta_1 (\Lambda - (\theta_2 + \omega_2 + \mu) \varepsilon)}{\mu (\theta_1 + \omega_1 + \mu)} - \frac{\sigma_1^2 \Lambda^2}{2\mu^2 (\theta_1 + \omega_1 + \mu)} - 1 \right] \\ - \frac{\beta_1 (\theta_1 + \omega_1 + \mu)}{\mu} \langle I_1(t) \rangle - \frac{\beta_1 X(t)}{\mu} + \frac{M_1(t)}{t} + \frac{\ln I_1(0)}{t},$$

where $M_1(t) = \int_0^t \sigma_1 S(x) dB_1(x)$ is the local continuous martingale satisfying $M_1(0) = 0$, and by lemma 4, we get $\lim_{t \rightarrow +\infty} \frac{M_1(t)}{t} = 0$ and $\lim_{t \rightarrow +\infty} X(t) = 0$.

Taking the inferior limit of both sides of (4.4) yields

$$\liminf_{t \rightarrow +\infty} \langle I_1(t) \rangle \geq (\theta_1 + \omega_1 + \mu) \left[\frac{\beta_1 (\Lambda - (\theta_2 + \omega_2 + \mu) \varepsilon)}{\mu (\theta_1 + \omega_1 + \mu)} - \frac{\sigma_1^2 \Lambda^2}{2\mu^2 (\theta_1 + \omega_1 + \mu)} - 1 \right]$$

Letting $\varepsilon \rightarrow 0$ yields

$$\liminf_{t \rightarrow +\infty} \langle I_1(t) \rangle \geq (\theta_1 + \omega_1 + \mu) (\mathcal{R}_1^* - 1).$$

By the similar arguments as in Case (i), one can prove the second case.

Case (iii). Notice that

$$\langle S(t) \rangle = \frac{\Lambda}{\mu} - \frac{(\theta_1 + \omega_1 + \mu)}{\mu} \langle I_1(t) \rangle - \frac{(\theta_2 + \omega_2 + \mu)}{\mu} \langle I_2(t) \rangle - \frac{X(t)}{\mu}.$$

Let define,

$$\mathcal{V}(t) = \ln(I_1(t)I_2(t)),$$

By Ito's formula, we have

$$(4.5) \quad d\mathcal{V}(t) = \left[(\beta_1 + \beta_2) S(t) - \left(\theta_1 + \omega_1 + \mu + \frac{\sigma_1^2 S^2}{2} \right) - \left(\theta_2 + \omega_2 + \mu + \frac{\sigma_2^2 S^2}{2} \right) \right] dt \\ + \sigma_1 S(t) dB_1(t) + \sigma_2 S(t) dB_2(t) \\ \geq \left[(\beta_1 + \beta_2) S(t) - \left(\theta_1 + \omega_1 + \mu + \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right) - \left(\theta_2 + \omega_2 + \mu + \frac{\sigma_2^2 \Lambda^2}{2\mu^2} \right) \right] dt \\ + \sigma_1 S(t) dB_1(t) + \sigma_2 S(t) dB_2(t)$$

Integrating both sides of (4.5) from 0 to t and dividing by t yields

$$(4.6) \quad \frac{\mathcal{V}(t)}{t} - \frac{\mathcal{V}(0)}{t} \geq (\beta_1 + \beta_2) \langle S(t) \rangle - \left(\theta_1 + \omega_1 + \mu + \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right) - \left(\theta_2 + \omega_2 + \mu + \frac{\sigma_2^2 \Lambda^2}{2\mu^2} \right) + \frac{M(t)}{t},$$

The inequality (4.6) can be rewritten as

$$(4.7) \quad \begin{aligned} \frac{\mathcal{V}(t)}{t} - \frac{\mathcal{V}(0)}{t} &\geq (\beta_1 + \beta_2) \frac{\Lambda}{\mu} - \left(\theta_1 + \omega_1 + \mu + \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right) - \left(\theta_2 + \omega_2 + \mu + \frac{\sigma_2^2 \Lambda^2}{2\mu^2} \right) + \frac{M(t)}{t} \\ &\quad - (\beta_1 + \beta_2) \frac{(\theta_1 + \omega_1 + \mu)}{\mu} \langle I_1(t) \rangle - (\beta_1 + \beta_2) \frac{(\theta_2 + \omega_2 + \mu)}{\mu} \langle I_2(t) \rangle - (\beta_1 + \beta_2) X(t) \end{aligned}$$

Hence

$$(4.8) \quad \begin{aligned} \langle I_1(t) \rangle + \langle I_2(t) \rangle &\geq \frac{1}{\mathcal{W}_{\max}} \left[(\beta_1 + \beta_2) \frac{\Lambda}{\mu} - \left(\theta_1 + \omega_1 + \mu + \frac{\sigma_1^2 \Lambda^2}{2\mu^2} \right) - \left(\theta_2 + \omega_2 + \mu + \frac{\sigma_2^2 \Lambda^2}{2\mu^2} \right) + \frac{M(t)}{t} \right. \\ &\quad \left. - \frac{\beta_1 + \beta_2}{\mu} X(t) - \frac{\mathcal{V}(t)}{t} + \frac{\mathcal{V}(0)}{t} \right], \end{aligned}$$

where $M(t) = \int_0^t \sigma_1 S(x) dB_1(x) + \int_0^t \sigma_2 S(x) dB_2(x)$ is the local continuous martingale satisfying $M(0) = 0$, and by lemma 4, we get $\lim_{t \rightarrow +\infty} \frac{M(t)}{t} = 0$, $\lim_{t \rightarrow +\infty} X(t) = 0$ and $\lim_{t \rightarrow +\infty} \frac{\mathcal{V}(t)}{t} = 0$.

Taking the inferior limit of both sides of (4.8) yields

$$\liminf_{t \rightarrow +\infty} \langle I_1(t) + I_2(t) \rangle \geq \frac{1}{\mathcal{W}_{\max}} [(\theta_1 + \omega_1 + \mu) (\mathcal{R}_1^* - 1) + (\theta_2 + \omega_2 + \mu) (\mathcal{R}_2^* - 1)],$$

where

$$\mathcal{W}_{\max} = \max \left\{ (\theta_1 + \omega_1 + \mu) \frac{\beta_1 + \beta_2}{\mu}; \frac{\beta_1 + \beta_2}{\mu} (\theta_2 + \omega_2 + \mu) \right\}.$$

This completes the proof. \square

5. NUMERICAL SIMULATIONS

This section will illustrate the mathematical results obtained in the previous section. To do this, we give the following system, which is a discretization transformation of system (1.2), using the Euler-Maruyama method for stochastic differential equations, as given in [19].

$$(5.1) \quad \left\{ \begin{array}{l} S^n = \left(\Lambda - \beta_1 S^n I_1^n - \beta_2 S^n I_2^n - \mu S^n \right) \Delta t - \sigma_1 S^n I_1^n \zeta_{1,n} \sqrt{\Delta t} - \sigma_2 S^n I_2^n \zeta_{2,n} \sqrt{\Delta t}, \\ I_1^n = \left(\beta_1 S^n I_1^n - (\theta_1 + \omega_1 + \mu) I_1^n \right) \Delta t + \sigma_1 S^n I_1^n \zeta_{1,n} \sqrt{\Delta t}, \\ I_2^n = \left(\beta_2 S^n I_2^n - (\theta_2 + \omega_2 + \mu) I_2^n \right) \Delta t + \sigma_2 S^n I_2^n \zeta_{2,n} \sqrt{\Delta t}, \\ D_R^n = \left(\omega_1 I_1^n + \omega_2 I_2^n - (1 - \rho) \eta D_R^n - (\eta \rho + \mu) D_R^n \right) \Delta t, \\ A^n = \left((1 - \rho) \eta D_R^n + \theta_1 I_1^n + \theta_2 I_2^n - (d + \mu) A^n \right) \Delta t, \\ R^{n+1} = \left(\eta \rho D_R^n - \mu R^n \right) \Delta t, \end{array} \right.$$

where $\zeta_{1,n}, \zeta_{2,n}$ are mutually independent $N(0, 1)$ random variables, with Δt is the step size. In the following, we give some numerical simulations of the stochastic model (1.2) and its corresponding deterministic model (1.1).

First, we set the following parameters values: $\Lambda = 4, \beta_1 = 0.08, \beta_2 = 0.012, \theta_1 = 0.27, \theta_2 = 0.25, \omega_1 = 0.2, \omega_2 = 0.15, \rho = 0.48, \eta = 0.05, d = 0.3, \mu = 0.2$ and $(\sigma_1, \sigma_2) = (0.01, 0.009)$. Within this parameters $\mathcal{R}_1^* = 1.1533 > 1, \mathcal{R}_2^* = 0.3197 < 1, \sigma_1 < \sqrt{\frac{2\mu\beta_1}{\Lambda}} = 0.0632$ and $\sigma_2 < \sqrt{\frac{2\mu\beta_2}{\Lambda}} = 0.0245$. Thus, conditions of Theorem 10 are fulfilled for the stochastic model (1.2) and the disease HIV-1 persists while the disease HIV-2 will die out. Clearly, Fig.2 supports the Theorem 10.

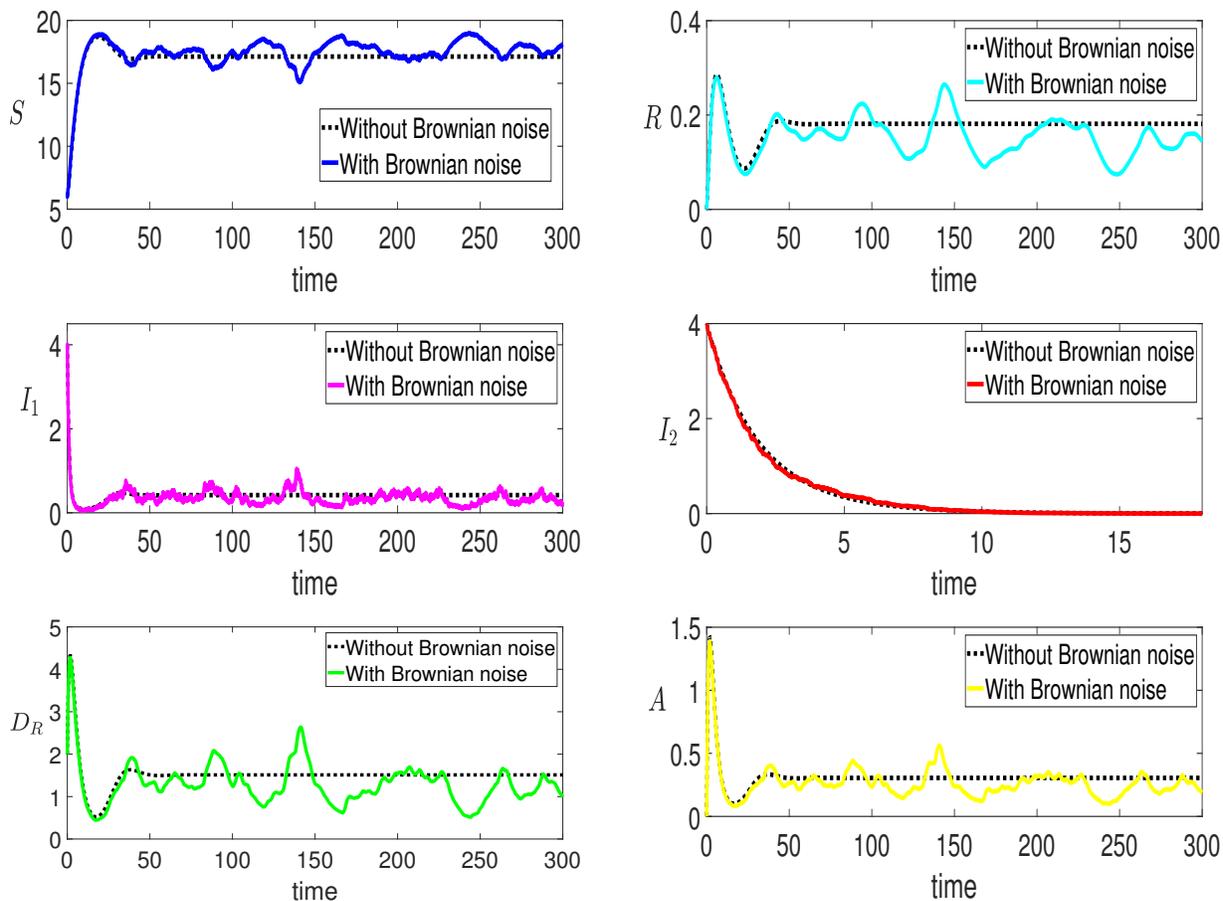


FIGURE 2. Dynamic of the deterministic and the stochastic models (1.1)-(1.2) describing the persistence of $I_1(t)$ and the extinction of $I_2(t)$.

In Fig.3, we take the parameters values: $\Lambda = 4$, $\beta_1 = 0.051$, $\beta_2 = 0.06$, $\theta_1 = 0.7$, $\theta_2 = 0.25$, $\omega_1 = 0.2$, $\omega_2 = 0.15$, $\rho = 0.48$, $\eta = 0.05$, $d = 0.3$, $\mu = 0.2$ and $(\sigma_1, \sigma_2) = (0.049, 0.01)$. Based on the above parameters, we have $\mathcal{R}_1^* = 0.4152 < 1$, $\mathcal{R}_2^* = 1.9667 > 1$, $\sqrt{\frac{2\mu\beta_1}{\Lambda}} = 0.0505$ and $\sqrt{\frac{2\mu\beta_2}{\Lambda}} = 0.0548$. Obviously, we obtain from Fig.3 that the disease HIV-1 will die out while the disease HIV-2 persists. This result is consistent with the theoretical result given in Theorem 10.

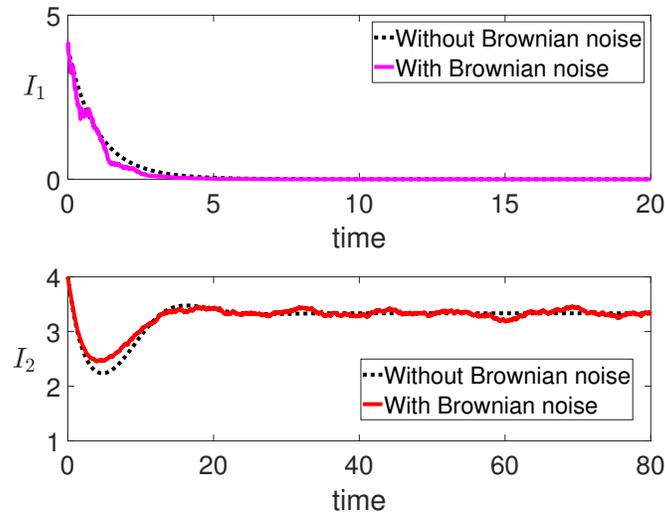


FIGURE 3. Dynamic of the deterministic and the stochastic models (1.1)-(1.2) describing the extinction of $I_1(t)$ and the persistence of $I_2(t)$.

Finally, using the parameters values $\Lambda = 4$, $\beta_1 = 0.095$, $\beta_2 = 0.09$, $\theta_1 = 0.27$, $\theta_2 = 0.25$, $\omega_1 = 0.2$, $\omega_2 = 0.15$, $\rho = 0.48$, $\eta = 0.05$, $d = 0.3$, $\mu = 0.2$ and $(\sigma_1, \sigma_2) = (0.013, 0.012)$. With these parameters we have, $\mathcal{R}_1^* = 2.7854 > 1$, and $\mathcal{R}_2^* = 2.9520 > 1$. Fig. 4 shows that the stochastic model (1.2) solution fluctuate for a large time around the endemic equilibrium of model (1.1). Hence, the diseases HIV-1 and HIV-2 persist.

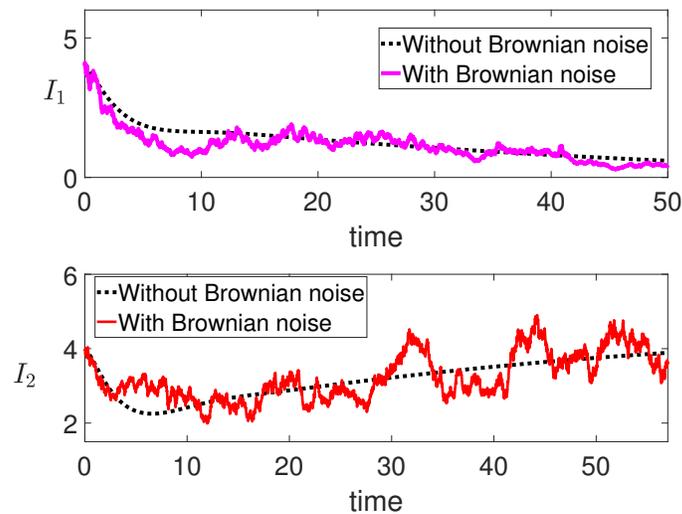


FIGURE 4. Dynamic of the deterministic and the stochastic models (1.1)-(1.2) describing the persistence of $I_1(t)$ and $I_2(t)$.

6. CONCLUSION AND DISCUSSION

In this research, we have delved into a comprehensive study of a stochastic epidemic model, which incorporates both HIV-1 and HIV-2, taking into account a critical aspect often encountered in real-world scenarios: drug resistance. Our analysis has yielded several important findings and contributions to our understanding of the dynamics of these infections in a stochastic environment.

First and foremost, we have rigorously established that the solutions of the stochastic system are not only positive but also bounded. This is a fundamental result, ensuring the biological relevance of our model's predictions. It confirms that our mathematical framework accurately captures the dynamics of HIV-1 and HIV-2 infections within populations affected by drug resistance.

Furthermore, we have identified and documented precise conditions governing the extinction and persistence of these diseases. These conditions are invaluable for healthcare practitioners and policymakers, as they provide insights into when and how interventions should be implemented to control and manage the spread of HIV-1 and HIV-2, particularly in cases involving drug-resistant strains. By recognizing the factors that drive these diseases toward extinction or persistence, we empower public health efforts to be more effective and targeted.

To strengthen the validity and applicability of our theoretical findings, we have conducted numerical simulations. These simulations serve as practical demonstrations of the outcomes predicted by our model under various scenarios. Through these simulations, we have not only validated our theoretical results but also provided a visual representation of how different factors, such as drug resistance, can influence the course of the HIV-1 and HIV-2 epidemics. This combination of theory and simulation contributes to a more holistic understanding of the complex dynamics at play in these infectious diseases.

In summary, this study has not only enhanced our comprehension of stochastic HIV-1 and HIV-2 epidemic models but has also provided valuable insights for disease control strategies. Our findings offer a solid foundation for future research in this field, and we hope they will be of practical use to those working tirelessly to combat the spread of these infections, particularly in the face of drug resistance challenges.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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