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Effects of randomness on viral infection model with application

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ABSTRACT

Virus population disease dynamics in various species of ecosystem keep the research interests alive for many centuries. In this research article, an attempt has been made to understand the qualitative behavior of a virus infection model with Lytic and Non-Lytic Immune Responses by perturbing with randomness (white noise) via Lyapunov technique. The conditions for the extinction and permanence of the viral infection in the interacting populations has been found, analyzed and supported with numerical simulations. An application to HIV infection model has also been presented for drawing a comparative study of the model under various modeling methods. The research findings of this paper reveal that a study that includes random fluctuations of the environment prove to be the ideal way to bring out the qualitative analysis of a mathematical model that will depict the real world scenario.

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1. Introduction

Viral infections continue to haunt the population dynamics ever since its discovery. The combat between the scientists and infectious diseases never seems to take a break and continue even in this contemporary world despite many advancements in the science and technology. Mathematical modeling techniques appeared as boon to the biological scientists as they provided them an artificial environment to experiment without affecting the population directly and cost effective, so they continue to attract millions of scientists even today. Modeling the viral infections in vivo has caught the attention of scientists in recent years with the discoveries of many new members in the family of viral diseases like SARS (Severe Acute Respiratory Syndrome) despite the presence of senior citizens (AIDS – Acquired Immune Deficiency Syndrome, conjunctivitis etc.). The different approaches adopted by mathematical biologists like Huang et al. in Huang, Yokoi, Takeuchi, Kajiwara, and Sasaki (2011), Herz et al in Herz, Bonhoeffer, Anderson, May, and nowak (1996) tried their hand with Delay Differential Equations and Fractional Differential Equations in Zhang, Huang, Liu, and Fan (2015) with regard to intracellular delay in viral dynamics and HIV infection Models with Non-linear incidence rates respectively while M. Pitchaimani et al. in Pitchaimani and Monica (2015) focussed on HIV-1 infection model with three time delays. Also, Pitchaimani and Rajaji contributed works in Stochastic Nowak – May Model analysis as in Pitchaimani and Rajaji (2016). Also the works of R. Almeida in Almeida (2018), Wang et al. in Wang and Mulone (2004) is noted for its contribution to the theory in the row. In those papers, many discussions have been attempted with simulation results trying to present a clear insight in the viral dynamics. Natural query, now, in the heads are why viral dynamics deserves due attention and capitulates the interests beyond centuries. So, before getting into the model briefing, let us take a short tour on the biological aspects behind the motivation to research the viral dynamics for centuries. In general, any biologically identified organism possess immune system to safeguard itself from the enemies those attack them both anatomically and physiologically, in particular, the genus Homo sapiens being the largely dominating population in terms of evolution as in Bonhoeffer, May, Shaw, and Nowak (1997), Nowak and Bangham (1996) and Wodarz (2003). The immune system of the H. sapiens are said to showcase two types of immune responses viz., innate and antigen mediated immunity which are further being put into broader categories of Lytic and Non-Lytic Immune responses when it comes to Antiviral immune effector mechanisms to fight against viral infections which we are about to analyze mathematically through modeling with random effects shortly. The study of viral dynamics continue to be an area of greater research interest as they give an opportunity to unearth the mysterious behavior of the physiological mechanisms of the human body. These studies help us in deciding the factors like the type of immune response to be effected in the host system to combat the viral infection and the level of treatment such that the hosts are not being exposed to lethal complications. Also, mathematical models provide deeper insights into the various drug therapy strategies used.

Let us now shift our focus on the biological aspects of viral infections and immune responses for a short while to gain an core
idea on the immunological effects on the host. As we discussed in
the beginning of introduction, the Lytic and Non-Lytic immune re-
sponses play a vital role as the virus not only tend to cause infection
in the susceptible cells i.e., its target victims but also tend to spend
its life within the poor victims i.e., in the infected cell by replicating
its viral DNA thereby adding more victims and spreading infections
on a larger scale within the host system. The Lytic components kill
infected cells while the Non-Lytic inhibit viral replication through
soluble mediators. In the innate type of immunity response, natural
killer cells can lyse infected cells and cytokines (for example, inter-
feron α (IFN-α1) and IFN-β1) secreted by various cell types, can
inhibit viral replication in a Non-Lytic fashion. In antigen mediated
immune response, cytotoxic T Lymphocytes (CTLs) kill infected
cells, whereas antibodies neutralize free virus particles. Also, in
addition, CD4+ and CD8+ T cells can secrete cytokines that inhibit
viral replication (e.g., IFN-γ1 and tumor necrosis factor α1 (TNF-
α1)). The antiviral immune effector mechanisms enter into action
field, thereby discovering chances of eliminating the infectious
guests (virus particles) under the capicity of immune responses
(Lytic & Non-Lytic immune responses). The relative roles of
the immune responses are decided by the cytopathicity of the virus
relative to its replication because if the viral cytopathicity is low
in comparison with its rate of replication then a treatment that
together induce both the type of immune responses are needed
for action while on the contrary situation both types are given
space for independent actions to get the situation (infection) under
control. A study on mortality deceleration rate has been carried out
by Pitchaimani and T. Eakin in Pitchaimani and Eakin (2008).}

Having had a small briefing on the viral infections and their
 dynamical behaviours, we now get into the mathematical analysis
without any further due. However, necessary biological interpre-
tations will be given then and there. To bring out an understanding
on the significant role of mathematical modeling in viral dynamical
studies, we begin with a simple mathematical model in vivo as
given below

\[
\begin{align*}
dx &= \dot{x} = \lambda - \mu x - \beta xz \\
dy &= \dot{y} = \beta xz - ay \\
dz &= \dot{z} = p_1 y - c_1 z \\
\end{align*}
\]

Here, \(x, y\) and \(z\) represent the populations of the uninfected target
cells, infected target cells, and free virus particles, respectively. The
uninfected cells are generated from sources within the body at rate
\(\lambda\), and become infected at rate \(\beta xz\), where \(\beta\) is the infection
rate constant. The uninfected and infected cells die with rate constants
\(\mu\) and \(a\), respectively. The virus particles are produced by the
infected cells with rate constant \(p_1\), and are removed from the
system with rate constant \(c_1\).

It is clear from the above representation that unlike other epi-
demic compartment models, virus models focus on the disease
dynamics within an infected individual.

Let us begin our main course of action by analyzing the lit-
erature survey on the modeling of viral dynamics that suggested
an effective and detailed study in this regard which has been
by Bartholdy et al. (Bartholdy, Christensen, Wodarz, & Thomsen,
2000) and Wodarz et al. (Wodarz, Christensen, & Thomsen, 2002)
describing the basic dynamics of the interaction between suscep-
tible host cells, a virus population, and immune responses that
investigated the role of direct Lytic and Non-Lytic inhibition of
viral replication by immune cells in viral infections, with non-
linear incidence rate \(\frac{Pzx}{1 + qk}\) and is given by the following ordinary
differential equations,

\[
\begin{align*}
\frac{dx}{dt} &= \dot{x} = \gamma - \mu x - \frac{\beta \alpha x \lambda}{1 + qk} \\
\frac{dy}{dt} &= \dot{y} = \beta xz - ay \\
\frac{dz}{dt} &= \dot{z} = p_1 y - c_1 z \\
\end{align*}
\]

Figure 1. Viral Infection Model.

### Table 1

| Parameters | Meaning |
|------------|---------|
| \(\alpha\)  | Susceptible cells |
| \(\lambda\) | Infected Cells |
| \(\kappa\)  | Immune Response |
| \(\gamma\)  | Production rate of Susceptible Cells |
| \(\mu\alpha\) | Natural death rate of Susceptible Cells |
| \(\beta\alpha\lambda\) | Infection rate in absence of Immune response |
| \(1 + qk\) | Inhibition rate of Viral replication (Non-Lytic activity) |
| \(\alpha\lambda\) | Natural death rate of Infected Cells |
| \(p\alpha\lambda\) | Death rate due to Immune Response |
| \(c\lambda\)   | Production rate of Immune Cells proportional to \(\lambda\) |
| \(\beta\)     | Efficacy of the Lytic component |
| \(\kappa\)    | Efficacy of the Non-Lytic component |

The parameters used in the system modeling with their mean-
ing is listed in the Table 1 below.

We assume that the immune responses get stronger at a rate
proportional to the number of infected cells, \(c\lambda\), and also decay
to a rate proportional to its current strength, \(\kappa\), here the vari-
able \(\kappa\) represents the total immunity that can be generated in
response to viral infection. The parameter \(p\) expresses the strength
of the Lytic component, while the efficacy of the Non-Lytic com-
ponent is being expressed by the parameter \(q\). The dynamics of the
free virus has not been included explicitly in the model (1) be-
cause (Bartholdy et al., 2000; Wodarz et al., 2002) assume that
the free virus turnover is much faster than that of infected cells,
which allows to make a quasi steady-state assumption, where the
amount of free virus is proportional to the number of infected cells.
Hence, the number of infected cells \(\lambda\) can also be considered as
a measure of virus load. In the model by Bartholdy et al. (2000)
and Wodarz et al. (2002), the non-linear incidence rate needs a
mention with its effects in biological sense because viral infection
models with other incidence rates like saturated incidence rate,
linear incidence rates do exist and been analyzed by many biol-
ologists, so naturally there arises a doubt in the minds how they
differ from one another and their effective contribution in the
analyzation process. The non-linear incidence rates brings to light
that the spread of infection may be through physical movement
or any other means of dispersion that an infected individual will

\[
\begin{align*}
\frac{d\lambda}{dt} &= \lambda = \frac{\beta \alpha \lambda}{1 + qk} - \alpha \lambda - p\lambda k \\
\frac{dk}{dt} &= \kappa = c\lambda - bk, \\
\end{align*}
\]
have contact with a given number of susceptible individuals in the population. The potential to effectively disperse the disease (virus) could be thought of as being proportional to that number of susceptibles with whom the infected individual makes contact: indeed, more the contact, the infected individual has with susceptibles, the more likely the host is to effectively transmit the disease. It then follows that the magnitude of the realized disease spread could be measured, for example, in terms of the contagious spreading ability of the infected individual. Accordingly, every infected individual will be expected to realize a certain virus (or micro-parasite) spread potential. It can be noted here, that often, a non-linear function could be a better choice to account for factors such as crowding of infected individuals, multiple pathways to infection, stage of infection and its severity or protective measures taken by susceptible individuals.

Now, let us move into the discussion of our model of interest (i.e., a model with random effects).

2. Modeling viral dynamics

In the real world, all infections are subject to randomness in terms of natural transmission. The random fluctuations exhibited by the birth and death rates, transmission coefficients and the other parameters in the system to a greater or lesser extent due to environmental fluctuations was revealed by May in May (2001) while the presence of even a small amount of white noise can suppress a potential population was studied by Mao et al. (Mao, Marion, & Renshaw, 2002). This implies the significance of investigating the effect of random fluctuations in the environment on population dynamics. Many authors (Lahrouz & Omari, 2013; Lahrouz, Omari, Klouach, & Belmaâti, 2011a; Schurz, 2001a, b; Yang & Mao, 2014) have studied the effect of environmental noise on the transmission dynamics of disease by proposing SDE models with stochastic disturbances through the perturbation technique which is a standard technique adopted by majority of the researchers in the recent years. A detailed study on the stability analysis for various mathematical models and its applicability in stochastic modeling can be grasped via (Arrowsmith & Place, 1990; Gard, 1998; Khasminskii, 1980; Lahrouz, Omari, & Klouch, 2011b; LaSalle, 1976; Ruan & Wang, 2003; Schurz, 2007; Schurz & Tousan, 2014; Zhao, Yuan, & Ma, 2015). In our proposed study, we felt that it is wise to include the randomness by perturbing the infection rate \( \frac{\beta \alpha t}{1 + qk} \) with white noise because the effective treatment to curb the infection spread and a detailed analysis on the dynamics of the virus in the host system can be explored thereby adding little more knowledge to the literature and the pathologists. With this measure of random effects within the host cell, studies reveal the type of immune cells to be activated in the immune system, for instance antibodies like cytotoxic lymphocytes or CD4+ cells in evoking a specific type of immune response in the host at the present stage of infection so that the spread may be put under the control of therapeutic mechanisms. Also, one cannot deny the fact that some evidences (Hethcote & Vanden Driessche, 1991; Korobeinikov, 2004, 2009a,b; Liu, Hethcote, & Levin, 1987; Xiao & Ruan, 2007) do exist showing that bilinear incidence rate is not much effective as non-linear incidence rate, in case, if the uninfected cells are at large. The random effect included in the infection rate can come out with additional information for curtailing the infectious period (i.e., the chances of reducing the guest stay) duration in the host will reduce the treatment period consequently. In short, the chemotherapy or any other means by which the host can be treated for infection will be shortened once if the dynamical behavior spread can be clearly analyzed and treated earlier. This view cogwheels us the introduction of randomness in the infection rate \( \frac{\beta \alpha t}{1 + qk} \) with Gaussian White noise that takes the new form \( \frac{(\beta + F(\alpha, \lambda, \kappa))\alpha \lambda}{1 + qk} \), where \( F(\alpha, \lambda, \kappa) \) is a locally Lipschitz-continuous function on \( \Omega \) and \( W \) is i.i.d. via perturbation techniques. In this form, let us not forget the fact that the unboundness of contact rate have also been prevented.

In this paper, we, hereby, present the stochastic version of the deterministic system (1) by defining Wiener processes on a filtered complete probability space, unless otherwise specified, \((\Omega, F, \{F_t\}_{t \geq 0}, \mathbb{P})\), where the filtration \( \{F_t\} \) satisfies the usual conditions of right continuity, increasing while \( F_0 \) contains all the \( \mathbb{P} \)-null sets together with the domain

\[
\mathbb{D} = \{ (\alpha, \lambda, \kappa) \in \mathbb{R}_+^3, \ t \geq t_0 : \alpha > 0, \lambda > 0, \kappa > 0, \\
\alpha + \lambda \leq \gamma, \lambda - \mu \leq \gamma, \kappa \leq \mu \}
\]

in which we analyze the stability of the equilibrium solutions of our stochastic model presented to you in the form below

\[
\begin{align*}
\frac{d\alpha}{dt} &= \dot{\alpha} = \gamma - \mu \alpha - \frac{\beta \alpha \lambda}{1 + qk} - \frac{F(\alpha, \lambda, \kappa)\alpha \lambda}{1 + qk} dW \\
\frac{d\lambda}{dt} &= \dot{\lambda} = \frac{\beta \alpha \lambda}{1 + qk} - \alpha \lambda - p \lambda \kappa + \frac{F(\alpha, \lambda, \kappa)\alpha \lambda}{1 + qk} dW \\
\frac{d\kappa}{dt} &= \dot{\kappa} = \kappa - b \kappa 
\end{align*}
\]

with the initial conditions \( \alpha(0) = \alpha_0 > 0, \lambda(0) = \lambda_0 > 0, \kappa(0) = \kappa_0 > 0 \).

The organizational structure of our paper follows the following pattern: The dynamics of the viral infection have been analyzed in this paper with the commencement of few introductory remarks on viral diseases and a bite of literature survey in this regard in introduction followed by the modeling process which displays a clear view on the care taken in modeling the viral infection without affecting the real world scenario in the maximum possible way. With this, the focus shift landed towards the methods of mathematical analysis in a step by step process followed by observations on the conditions that would effect the disease free dynamics together with the chances of existence for chronic infection in the model. Then comes the question about the behavior on the endemic equilibrium solutions (permanency) of the infection model in the longer run and is been answered therein (i.e.), despite the treatment given to the host the chances of permanency is established via mathematical terminologies. Although, the theoretical results assure the authenticity on the dynamics, we tried to prove that these observational results hold on for a larger scale population through the theory of stationary distribution and positive recurrence exhibited by the model. Our primary objective in this paper (i.e.), observational study with empirical data is met by showcasing the simulation results in the form of graphs. An application of this observational study has been tested with a HIV infection model with Non-linear incidence rate in the follow up before concluding the paper with discussions. Some of the mathematical preliminaries that helped to bring out the observational study in this topic viz definitions, results are included in the appendix as they should not form an obstacle in the flow of our objective to analyze the effects of randomness.

Considering the biological aspects, it is crucial to have a check note on the stochastically perturbed parameter that may bloom with the possibilities of showing effective change in the host system infected with virus. In other words, the compatibility of model (2) after perturbation has to be examined (i.e.), we have to look for some effective changes in the behavior of host system (2) post the introduction of natural disturbances in the form randomness which would either induce or inhibit the infection.
2.1. Model analysis

The initial step towards the existence of unique solution begins with the construction of suitable domain which meaningful in view of both aspects viz mathematical and biological. Considering the domain $\mathbb{D}$ where it is found that the coefficients of the system (2) are locally Lipschitz continuous satisfying linear growth condition for any initial value $(\alpha_0, \lambda_0, \kappa_0) \in \mathbb{D}$. Thus, it is trivial that there exists unique local solution for any $t \in [t_0, \tau(\mathbb{D}))$, where $\tau(\mathbb{D})$ is the random time of first exit of stochastic process (the first exit time refers to the time at which the solution moves out of the domain for the very first time once the process has begun). $(\alpha(t), \lambda(t), \kappa(t))$ from the domain $\mathbb{D}$, started with $(\alpha(\tau), \lambda(\tau), \kappa(\tau)) = (\alpha_0, \lambda_0, \kappa_0) \in \mathbb{D}$ at the initial time $s \in [t_0, \infty)$. To make the solution valid on the entire domain $\mathbb{D}$, we have to prove $P(\tau(\mathbb{D}) = \infty) = 1$ a.s.

For this we make another construction

$$\mathbb{D}_n := \left\{ (\alpha, \lambda, \kappa) : e^{-n} < \alpha < \frac{\gamma}{\mu} - e^{-n}, e^{-n} < \lambda < \frac{\gamma}{\mu} - e^{-n}, \
\quad e^{-n} < \kappa < \frac{\gamma}{\mu} - e^{-n}, \alpha + \lambda + \kappa \leq \frac{\gamma}{\mu}, \kappa \leq \frac{\gamma}{\mu} - e^{-n}, \right\},$$

for $n \in \mathbb{N}$. Clearly, the system (2), has a unique solution up to stopping time $\tau(\mathbb{D}_n)$. As our aim is clear in proving $P(\tau(\mathbb{D}) = \infty) = 1$ a.s., it is enough if we could establish $P(\tau(\mathbb{D}) < t) = P(\tau(\mathbb{D}_n) < t) = 0$, for $(\alpha_0, \lambda_0, \kappa_0) \in \mathbb{D}$ and $t \geq t_0$. A detailed proof has been given following the ideas of Schurz and Tosun (2014) and the theorem on invariance of $\mathbb{D}$ due to Khasminskii in 1980 as appears in the book of Gard (1998) page:132. Now, we can establish that the following theorem that will sum up the expected result for existence.

**Theorem 1.** Let $(\alpha(t_0), \lambda(t_0), \kappa(t_0)) = (\alpha_0, \lambda_0, \kappa_0) \in \mathbb{D}$, where

$$\mathbb{D} = \left\{ (\alpha, \lambda, \kappa) : (\alpha, \lambda, \kappa) \in \mathbb{R}^3_+, t \geq t_0 : \alpha > 0, \lambda > 0, \kappa > 0, \alpha + \lambda \leq \frac{\gamma}{\mu}, \kappa \leq \frac{\gamma}{\mu} - e^{-n}, \right\},$$

and $(\alpha_0, \lambda_0, \kappa_0)$ is independent of $W(t)$. Then the stochastic model (2) admits a unique continuous, Markovian global solution $(\alpha(t), \gamma(t), \kappa(t))$ on $t \geq t_0$ and this solution is invariant (a.s) with respect to $\mathbb{D}$.

**Proof.** Let us begin the proof with the Lyapunov function as follows

$$V(\alpha, \lambda, \kappa) = -\ln \lambda + \alpha - \ln \alpha + \left( \frac{\gamma}{\mu} - \alpha \right)$$

$$- \ln \left( \frac{\gamma}{\mu} - \alpha \right) + \left( \frac{\gamma}{\mu} - \kappa \right) - \ln \left( \frac{\gamma}{\mu} - \kappa \right), \quad (4)$$

defined on $\mathbb{D}$ and assume that $E[V(\alpha, \lambda, \kappa)] < \infty$.

Also, we get to know $V(\alpha, \lambda, \kappa) \geq 4$, for $(\alpha, \lambda, \kappa) \in \mathbb{D}$.

Let $W(\alpha, \lambda, \kappa, \tau) = e^{-\int_{t_0}^{\tau} V(\alpha, \lambda, \kappa)}$, be defined on $\mathbb{D} \times [s, \infty)$, where

$$h = \frac{1}{4} \left( 2\mu + 6\beta \lambda (1 + \alpha) + \frac{c\lambda}{\gamma - \mu} + a + \kappa (p + b) \right)$$

$$+ \sup_{(\alpha, \lambda, \kappa) \in \mathbb{D}} \frac{1}{4} \left( \frac{3\gamma^2}{2\mu^2} F^2(\alpha, \lambda, \kappa) \right), \quad (5)$$

From Itô’s Formula, upon applying the infinitesimal operator $\mathcal{L}$ on (4), we get

$$\mathcal{L}V(\alpha, \lambda, \kappa) = \left( \gamma - \mu \alpha - \beta \alpha \gamma + \frac{1}{1 + qk} \left( \frac{1}{\mu - \alpha} - \frac{1}{\alpha} \right) \right)$$

$$+ \left( \frac{\beta \alpha \lambda}{1 + qk} - a \lambda - p \lambda k \right) \left( 1 - \frac{1}{\lambda} \right)$$

$$+ (c\lambda - b\kappa) \left( \frac{1}{\mu - k} \right) - 1$$

$$+ \frac{1}{2} F^2(\alpha, \lambda, \kappa) \alpha^2 \lambda^2 \left( \frac{1}{\gamma - \mu} + \frac{1}{\alpha^2} + \frac{1}{\lambda^2} \right),$$

$$\leq 2\mu + \beta \lambda (1 + \alpha) + \frac{c\lambda}{\gamma - \mu} + a + \kappa (p + b)$$

$$+ \sup_{(\alpha, \lambda, \kappa) \in \mathbb{D}} \frac{3\gamma^2}{2\mu^2} F^2(\alpha, \lambda, \kappa) \right),$$

$$= 4h.$$

where

$$h = \frac{1}{4} \left( 2\mu + 6\beta \lambda (1 + \alpha) + \frac{c\lambda}{\gamma - \mu} + a + \kappa (p + b) \right)$$

$$+ \sup_{(\alpha, \lambda, \kappa) \in \mathbb{D}} \frac{1}{4} \left( \frac{3\gamma^2}{2\mu^2} F^2(\alpha, \lambda, \kappa) \right).$$

So, $\mathcal{L}V(\alpha, \lambda, \kappa) \leq h V(\alpha, \lambda, \kappa)$, since $V(\alpha, \lambda, \kappa) \geq 4$, for $(\alpha, \lambda, \kappa) \in \mathbb{D}$.

Hence, we get $\mathcal{L}V(\alpha, \lambda, \kappa, \tau) = e^{-\int_{t_0}^{\tau} (-4V(\alpha, \lambda, \kappa) + \mathcal{L}V(\alpha, \lambda, \kappa, \tau))} \leq 0$.

Also, here, $\inf_{(\alpha, \lambda, \kappa) \in \mathbb{D}_n} V(\alpha, \lambda, \kappa) > n + 2$, for $n \in \mathbb{N}$.

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

$$E[W(\alpha(t_n), \lambda(t_n), \kappa(t_n))]$$

$$= E[W(\alpha(s), \lambda(s), \kappa(s))]$$

$$+ E \left[ \int_s^{t_n} \mathcal{L}W(\alpha(u), \lambda(u), \kappa(u), s) du \right]$$

$$\leq E[W(\alpha(s), \lambda(s), \kappa(s), s)]$$

$$= E[V(\alpha(s), \lambda(s), \kappa(s))]$$

$$= E[V(\alpha_0, \lambda_0, \kappa_0)]$$

Next, to show that $P(\tau(\mathbb{D}_n) < t) = 0$, we take the expected value of $e^{h(t_n-t)} V(\alpha(t_n), \lambda(t_n), \kappa(t_n), t_n)$, i.e.,

$$E[e^{h(t_n-t)} V(\alpha(t_n), \lambda(t_n), \kappa(t_n), t_n)]$$

$$= E[e^{h(t_n-t)} e^{-\int_{t}^{t_n} \mathcal{L}V(\alpha(t_n), \lambda(t_n), \kappa(t_n), t_n)}]$$

$$= E[e^{h(t_n-t)} W(\alpha(t_n), \lambda(t_n), \kappa(t_n), t_n)]$$

$$\leq e^{h(t_n-t)} E[V(\alpha_0, \lambda_0, \kappa_0)].$$
and obtain
\[0 \leq \mathbb{P}(\tau(D) < t) \leq \mathbb{P}(\tau(D_n) < t), \quad \text{since} \quad D_n \subseteq D\]
\[= \mathbb{P}(\tau_n < t) = \mathbb{E}(1_{\tau_n < t}), \quad \text{where} \quad 1 \text{ is the indicator function}\]
\[\leq \mathbb{E} \left( e^{h(t-s)} \mathbb{V}(\alpha(t(D_n)), \lambda(t(D_n)), \kappa(t(D_n))) \right) \]
\[\leq e^{D(t-s)} \mathbb{V}(\alpha(0), \lambda(0), \kappa(0)) \int_{(a_0, \lambda_0, \kappa_0)} \mathbb{D}_n \frac{\mathbb{V}(\alpha, \lambda, \kappa)}{n + 2}\]

Since \(e^{D(t-s)} \mathbb{V}(\alpha(0), \lambda(0), \kappa(0)) \rightarrow 0\) as \(n \rightarrow \infty\) for all \((a_0, \lambda_0, \kappa_0) \in D_n\) (for large \(n\)), and for all fixed \(t \in [s, \infty)\).

Thus, \(\mathbb{P}(\tau(D) < t) = \mathbb{P}(\tau(D_n) < t) = 0\), for \((a_0, \lambda_0, \kappa_0) \in D\) and \(t \geq t_0\), that is, \(\mathbb{P}(\tau(D) = \infty) = 1\).

Thus, this proves the invariance property and the global existence of the solution \((\alpha(t), \lambda(t), \kappa(t))\) on \(D\) whereas the continuity and uniqueness of the solution is given by the theorem in Appendix. \(\square\)

Thus, the above theorem assures that the system does not show up any adverse effects on the host even after including randomness in the infective rate of the virus and guarantee positive immune response.

Also, we can conclude that our model \((2)\) has shown good compatibility in finding unique global solution which would enhance the study of global dynamics of the viral infection with respect to Lytic and Non-Lytic immune responses in an effective way.

Once the existence is confirmed, the next move is to analyze the nature and number of solutions that the system \((2)\) would admit in the dynamics of viral infection will be of more concern. It is clear that the stochastic model in our consideration admits atmost two equilibrium solutions, namely, infection-free equilibrium and endemic equilibrium.

We are familiar with certain viral infections which have signs of curing the disease to a little extent when the immune responses from the innate and adaptive immunity are strong enough to eradicate the entire infection in the host system. In such cases, the mathematical models admit infection-free equilibrium which will be undertaken into analytic study in the following section. We are pretty aware of the fact that the Lytic immune responses have the ability to kill the infected cells henceforth bringing down the population of infected cells to a larger extent and also preventing the replication of virus inside the host to a minimal level which can be accelerated high with Non-Lytic immune response. In order to make a decision on the type of immune response to be effected in the infected individual to become infection-free it is pivotal to analyze the stability of our proposed model \((2)\) with respect to this condition of equilibrium to initiate Lytic immune response based on the nature of infection caused.

2.2. Stability around disease free dynamics

We begin our discussion on the stochastic asymptotic stability of infection-free equilibrium solution of system \((2)\) with reference to the existing mathematical theories via Lyapunov technique.

The infection-free equilibrium solution \((\alpha_1, \lambda_1, \kappa_1)\) is obtained when
\[\alpha_1 = \frac{\gamma}{\mu}, \quad \lambda_1 = 0, \quad \kappa_1 = 0\]  \hspace{1cm} (6)

We first identify the conditions that has to be met by the system \((2)\) to exhibit asymptotic stability of infection-free equilibrium solution via the following theorem. (i.e.), we know that not all viral infections are chronic in the sense that there are certain viral infections namely the swine flu, chikungunya, chicken pox, smallpox etc which can be cured by proper treatment. As the model we have constructed is a generalized one for all type of viral infections, it is important to analyze the criteria in which the model \((2)\) admits disease free dynamics. The mathematical theory that aids help, is the concept of Basic Reproduction Number \(R_0\), a quantity that tells about the secondary infection that can be caused by an single infected host during his entire infection period. To make use of this, we first construct a Lyapunov function as follows:

\[V_1(\alpha, \lambda, \kappa) = \frac{1}{2} (\alpha + \lambda - \frac{\gamma}{\mu})^2 + K_1\lambda + K_2\kappa^2\]  \hspace{1cm} (7)

where \(K_1 = \frac{\gamma}{\mu} + \frac{\gamma}{\mu} + \frac{\gamma}{\mu}\) and \(K_2 = \frac{\mu}{2\alpha\gamma}\).

The fact that if upon acting the infinitesimal generator on this Lyapunov functional, the resultant is negative definite on \(D\), then the system admits disease free dynamics is well known. In other words, the infection-free equilibrium solution \((\alpha_1, \lambda_1, \kappa_1)\) of \((8)\) is stochastically asymptotically stable if \(R_0 \leq 1\), where \(R_0 = \frac{\gamma}{\mu}\) is the basic reproduction number of virus. It is evident from the following steps:

\[\mathcal{L}V_1 = \left( \gamma - \mu\alpha - \beta\alpha\lambda + \frac{\beta\alpha\lambda}{1 + qK} \right) \left( \alpha + \lambda - \frac{\gamma}{\mu} \right) + \left( \frac{\beta\alpha\lambda}{1 + qK} - a\lambda - p\lambda\kappa \right) \left( \left( \alpha + \lambda - \frac{\gamma}{\mu} \right) + K_1 \right) + \left( \gamma - \mu\alpha - \beta\alpha\lambda - \gamma\lambda \kappa \right) \left( \alpha + \lambda - \frac{\gamma}{\mu} \right) + 2K_2k(\lambda - b\kappa), \]

\[\leq -\mu\left( \alpha - \frac{\gamma}{\mu} \right)^2 - a\lambda^2 - \gamma\lambda\kappa \]

Thus, we sum up our examined results on disease free dynamics with the theorem below

**Theorem 2.** The infection-free equilibrium solution \((\alpha_1, \lambda_1, \kappa_1)\) of \((2)\) is stochastically asymptotically stable on \(D\) as \((8)\) becomes negative definite on \(D\) if \(R_0 \leq 1\), where \(R_0 = \frac{\gamma}{\mu}\) is the basic reproduction number of virus.

Thus, the stochastic system \((2)\) with perturbation in the infective rate \(\frac{\beta\alpha\lambda}{1 + qK}\) stabilizes on \(D\). Thus, we have found sufficient condition based on which the system \((2)\) stabilizes on \(D\). It is clear from Eq. \((8)\), the spread of infection in the host system is dependent on the basic reproduction number as any other deterministic system.

Thus, in general, if the infection rate can be controlled by stimulating the activities of CytoToxic Lymphocytes (CTL) and cytokines in the host immune system through chemotherapy for some viral infectious diseases as they kill infected cells whereas antibodies neutralize the free virus particles, our system \((2)\) admits the chances of disease free equilibrium even though persistence of the model \((2)\) has been discussed in later sections. Hereby, we can also arrive at the conclusion that together with Non-Lytic immune response (i.e.), increase in the activities of CD4+ and CD8+ cells in...
the host immune system, the success rate is increased with higher probability.

**Remarks 1.** The empirical evidence that strengthens the above arguments in Theorem 2 have been presented in Fig. 2 based on the simulation results obtained from the parameter values in Table 2.

In addition, we also find the disease free equilibrium at the initial values \((a_0, b_0, \kappa_0) = (100, 15, 45)\) together with the parameter values \(\gamma = 300, \beta = 0.002, a = 0.9, \mu = 0.8, p = 0.4, q = 0.5, b = 0.31, c = 0.95\) giving \(R_0 = 0.8333 < 1\) at \((a_1, \lambda_1, \kappa_1) = (375, 0, 0)\) adding strength to the stability of infection free equilibrium empirically.

Now, we are interested in the inquiry about the endemic equilibrium solution’s stability on \(\mathbb{D}\) of the model (2) as our main aim is to try to control the viral infection although the host continue to survive with the chronic infection till the end of life with the intention to increase the life expectancy of the host. In other words, to prolong the life period of the host infected with chronic infection. So, it would be logical to study the stability behavior of the system (2) when the host lives with persistent viral infection. So, without further due we proceed towards the investigation to substantiate the conditions for permanency of infection.

### 2.3. Stochastic stability of endemic equilibrium

Many viral infections are chronic in nature, so it is very crucial to make an analytical study on their permanence in the host. For instance, consider HIV infection which shows no symptoms at initial stage but kills the host in matter of no time as it grows very fast without any indication of its presence in the system. In such cases, it is important to sketch out a check note that any such stage the disease has to be controlled with medications. So here, the discussion is all about the mathematical theory on stochastic stability of the endemic equilibrium solution \((a_2, \lambda_2, \kappa_2)\) of the system (2) given by

\[
\begin{align*}
\alpha_2 &= \frac{(a + px_2)(1 + qx_2)}{\beta}, \\
\lambda_2 &= \frac{b}{c}, \\
\kappa_2 &= \frac{-(pc\mu + ab\beta + ac\mu q)}{2(b\beta + c\mu q)} + \frac{\sqrt{(pc\mu + ab\beta + ac\mu q)^2 - 4p(b\beta + c\mu q)(ac\mu - c\gamma\beta)}}{2(b\beta + c\mu q)}.
\end{align*}
\]

As we have seen in the previous lines, the model (2) manifests disease free equilibrium if \(R_0 < 1\), so the natural life would be unique endemic equilibrium solution if \(R_0 > 1\) and \(F(a_2, \lambda_2, \kappa_2) = 0\) and the stability is established by tracing the following steps that leads to theorem which would cumulate our scrutiny. With the Lyapunov functional, \(V_2 = \frac{1}{2}((a - \alpha_2)^2 + n(\lambda - \lambda_2 - \lambda_2 \ln \frac{\lambda}{\lambda_2}) + b(\kappa - \kappa_2)^2)\) (9)

the infinitesimal generator acting on the Lyapunov function \(V_2\) can be written as:

\[
\mathcal{L}V_2 = \frac{\gamma - \mu a \alpha - \beta a \lambda}{1 + \kappa} (a - \alpha_2) + n\frac{\beta a \alpha - a \lambda - p \kappa}{1 + \kappa} (1 - \frac{\lambda_2}{\lambda}) + K_1(\lambda - b \kappa)(\kappa - \kappa_2) + \frac{1}{2} F^2(\alpha, \lambda, \kappa) + \frac{1}{2} F^2(\alpha, \lambda, \kappa) + \frac{1}{2} F^2(\alpha, \lambda, \kappa).
\]

**Table 2** Parameters and Values — Disease free dynamics.

| Parameter | Value | Parameter | Value |
|-----------|-------|-----------|-------|
| \(\gamma\) | 180   | \(p\)     | 0.04  |
| \(\mu\)   | 0.5   | \(q\)     | 0.005 |
| \(\beta\) | 0.001 | \(b\)     | 0.31  |
| \(a\)     | 0.8   | \(c\)     | 0.025 |

**Table 3** Parameters and Values — Endemic infection dynamics.

| Parameter | Value | Parameter | Value |
|-----------|-------|-----------|-------|
| \(\gamma\) | 180   | \(p\)     | 0.25  |
| \(\mu\)   | 0.5   | \(q\)     | 0.68  |
| \(\beta\) | 0.7   | \(b\)     | 0.15  |
| \(a\)     | 0.25  | \(c\)     | 0.5   |

\[
\begin{align*}
\mathcal{L}V_2 &= \left(\frac{\gamma - \mu a \alpha - \beta a \lambda}{1 + \kappa}\right)(a - \alpha_2) + \left[\frac{\beta a \alpha - a \lambda - p \kappa}{1 + \kappa}\right] (1 - \frac{\lambda_2}{\lambda}) + K_1(\lambda - b \kappa)(\kappa - \kappa_2) + \frac{1}{2} F^2(\alpha, \lambda, \kappa) + \frac{1}{2} F^2(\alpha, \lambda, \kappa).
\end{align*}
\]

Let \(E_1 = \sqrt{\frac{q^2\beta a^2}{8c(1 + q)(1 + qk_2)}((\kappa - \kappa_2)^2) + \frac{2c^2q^2\beta a^2}{(1 + qk_2)^2}}\) and \(E_2 = \sqrt{\frac{2c^2q^2\beta a^2}{(1 + qk_2)^2}}\) (10). It should be noted that \(\mathcal{L}V_2(\alpha, \lambda, \kappa) = 0\) only at \((a_2, \lambda_2, \kappa_2)\).

By choosing suitable functions \(F(a, \lambda, \kappa)\), we can obtain \(\mathcal{L}V(\alpha, \lambda, \kappa) < 0\) on \(\mathbb{D}\) for some suitable \(F(a, \lambda, \kappa)\). The existence of such type of functions is apparent when we look at the system (20) in the later section, with which we carried out our empirical study.

Biologically, irrespective of the adaptive and innate immune responses by the Lytic and Non-Lytic components the disease continues to exist in the host but stabilizes globally on \(\mathbb{D}\). As we said in the beginning, the summary leads to the following theorem:

**Theorem 3.** The endemic equilibrium solution \((a_2, \lambda_2, \kappa_2)\) of the system (2) is stochastically asymptotically stable on \(\mathbb{D}\) if \(R_0 > 1\); \(F(a_2, \lambda_2, \kappa_2) = 0\) and also satisfies \(\eta(\alpha, \lambda, \kappa) \leq 0\), where

\[
\eta(\alpha, \lambda, \kappa) = -\left(\frac{4c^2q^2\beta a^2}{bn^2}\right)(a - \alpha_2)^2 - \frac{bn^2}{c}(\kappa - \kappa_2)^2 + \frac{1}{2} F^2(\alpha, \lambda, \kappa) + \frac{1}{2} F^2(\alpha, \lambda, \kappa).
\]

for \(n = a_2\) and \(b = \frac{p\alpha_2}{c} + \frac{q^2\beta a_2}{c(1 + qk_2)(1 + qk)}\).
Fig. 2. By taking the parameters values as in Table 2, for the initial values \((α₀, λ₀, κ₀) = (125, 25, 75)\), and upon simulating the model given by Eq. (20), we get the infection-free equilibrium \((α₁, λ₁, κ₁) = (360, 0, 0)\) and \(R₀ = 0.4500 < 1\), clearly, the model admits stochastically asymptotically stable solution around the disease-free equilibrium for the above parameters from which we can conclude that the disease free equilibrium agrees with Theorem 2 under the assumed conditions.

Fig. 3. By taking the parameters values as in Table 3, for the initial values \((α₀, λ₀, κ₀) = (125, 25, 75)\), and upon simulating the model given by Eq. (20), we get the endemic equilibrium \((α₂, λ₂, κ₂) = (226.6796, 8.7951, 29.3170)\) and \(R₀ = 1.0080e + 03 > 1\). Clearly, the model admits stochastically asymptotically stable solution around the endemic equilibrium for the above parameters from Table 3, with which we can draw a conclusion that the endemic equilibrium agrees with Theorem 3 under the assumed conditions.

This condition though assures the existence of disease in the host system in the long-run yet promises of the stabilizing chances of the infection in host so that the virulence of viral strains can be reduced which in turn increases the chances of survival of the host despite chronic viral infection. In such cases, our aim takes a small diversion to decide on the type of immune responses to be effected on the host through treatment and the admissible level of treatment to be given such that the host is less prone to the side effects of the treatment while enhancing the longevity.

The study in this article provides a general notion for the survival of the host with permanent infection in the long run. It may also exhibit two fates (normal or apoptosis). Since, this study is a mathematical analysis of the model, a general condition that would fit both would be more appropriate thereby strongly assuring the possibilities of survival of the host in long term so that whatever
be the fate the host may experience, the physician may choose appropriate treatment accordingly.

**Remarks 2.** The conditions in the above Theorem 3 are lived up with the support of empirical data that has been put into simulation with values in Table 3 and has been showcased by Fig. 3. We emphasise that the values are mere samples and similar kind of choice for parameters that would result in $R_0 > 1$ will always lead to endemicity. For instance, consider the parameter values $\gamma = 300$, $\beta = 0.002$, $a = 0.8$, $\mu = 0.5$, $p = 0.04$, $q = 0.005$, $b = 0.31$, $c = 0.025$ resulted in endemic (permanent) infection at $(\alpha_2, \lambda_2, \kappa_2) = (496.4030, 53.2950, 4.2980)$ with $R_0 = 1.500 > 1$ for the initial values $(\alpha_0, \lambda_0, \kappa_0) = (100, 15, 45)$.

The choice of parameters above has been chosen carefully after a detailed study in the literature so that they will give a realistic empirical support to the results as the authors could not afford a biological experiment. Even then the parameters are meticulously chosen that at any point they will not breach the underlying biological phenomena.

To achieve global stability, it is important to analyze the dynamics of disease for any initial conditions and is achieved by using persistence property which implies that the disease continues to exist for any initial conditions over a larger period. Next, we move on to the persistence theory of stochastically perturbed model (2) as it is a logical leap with the establishment of the conditions for the stability of endemic equilibrium solution.

### 2.4. Persistence — infection in long run

Let us begin this analysis by looking at the persistence theory with the hope for some useful results. The infection over a larger period of time has been given after a detailed study on a theorem given by Liu, Wang, and Wu (2011) in his paper. Following similar ideas of proof for our system (2) we came out with the following theorem which validates our statement for the persistence.

**Theorem 4.** If $s_1 = \mu$ and $\Psi\left(\frac{\gamma}{\mu}\right) > 0$, then for any initial value $(\alpha(0), \lambda(0), \kappa(0)) \in \mathbb{R}$, the solution $(\alpha(t), \lambda(t), \kappa(t))$ of system (2) has the property that

1. $\lim_{t \to \infty} \inf \int_0^t \alpha(u) \, du > 0$.
2. $\lim_{t \to \infty} \inf \int_0^t \lambda(u) \, du > 0$.
3. $\lim_{t \to \infty} \inf \int_0^t \kappa(u) \, du > 0$.

**Proof.** Let $(\alpha(t), \lambda(t), \kappa(t))$ be a solution of system (2) with any initial value $(\alpha(0), \lambda(0), \kappa(0)) \in \mathbb{R}$.

By Theorem 1, it is evident that $\lambda(t) \leq \frac{\gamma}{s_1}$ for all $\omega \in \Omega$.

From Eq. (1) of system (2),

$$d\alpha(t) \geq \left(\gamma - \mu \alpha \frac{\beta \alpha \lambda}{1 + q \sigma} \right) \, dt - F(\alpha, \lambda, \kappa) \, dW_t,$$

$$= \left(\gamma - \left(\mu + \frac{\beta \alpha \lambda}{1 + q \sigma} \right) \right) \, dt - F(\alpha, \lambda, \kappa) \, dW_t,$$

$$= \left(\gamma - \left(\mu + \frac{\beta}{s_1} \right) \right) \, dt - F(\alpha, \lambda, \kappa) \, dW_t,$$

$$= \left(\gamma - \left(\mu + \frac{\beta}{s_1} \right) \right) \, dt - F(\alpha, \lambda, \kappa) \, dW_t.$$

Upon integration and dividing on both sides by $t$, we get

$$\int_0^t \alpha(u) \, du \geq \gamma - \frac{\alpha(t) - \alpha(0)}{t} - F(\alpha, \lambda, \kappa) \int_0^t \alpha(u) \lambda(u) \, dW(u).$$

By Strong Law of Large Numbers for local martingales, We have

$$\lim_{t \to \infty} \left(\frac{\alpha(t) - \alpha(0)}{t} - F(\alpha, \lambda, \kappa) \int_0^t \alpha(u) \lambda(u) \, dW(u)\right) = 0 \quad \text{a.s.}$$

From Eqs. (11) & (12), We obtain

$$\lim_{t \to \infty} \int_0^t \alpha(u) \, du \geq \frac{\gamma \left(s_1 + q \gamma \mu \right)}{s_1 + q \gamma \mu + \beta \gamma b} \quad \text{a.s.}$$

Thus we proved the assertion (1).

To prove (2), we perform the following steps,

By the Ito’s formula, the Eq. (2) of the system (2) takes the form as follows,

$$d \log(\lambda(t)) = \left(\frac{\beta \alpha}{1 + q \sigma} - a - p \frac{\gamma \mu c}{\mu b} - \frac{1}{2} \left(\frac{F^2(\alpha, \lambda, \kappa)}{\mu b} \right) \right) \, dt$$

$$+ \left(\frac{F(\alpha, \lambda, \kappa)}{1 + q \sigma} \right) \, dW(t).$$

Also, we know $k \leq \frac{\gamma \mu c}{\mu b}$, then

$$d \log(\lambda(t)) \geq \left(\frac{\beta \alpha}{1 + q \sigma} - a - p \frac{\gamma \mu c}{\mu b} - \frac{1}{2} \left(\frac{F^2(\alpha, \lambda, \kappa)}{\mu b} \right) \right) \, dt$$

$$+ \left(\frac{F(\alpha, \lambda, \kappa)}{1 + q \sigma} \right) \, dW(t).$$

$$d \log(\lambda(t)) \geq \left(\frac{\beta \alpha}{1 + q \sigma} - a - p \frac{\gamma \mu c}{\mu b} - \frac{1}{2} \left(\frac{F^2(\alpha, \lambda, \kappa)}{\mu b} \right) \right) \, dt$$

$$= \frac{\beta \mu b}{\mu b + \beta \gamma c} \, dW(t) \quad \text{a.s.}$$
\[
\Psi(\alpha) = \left(\frac{\beta \mu b}{\mu b + q \gamma c} - a + \frac{p \gamma c}{\mu b} \right) - \frac{1}{2} \left(1 + q \gamma c \right)^2 - \alpha^2 > 0.
\]

Integrating on both sides, we get
\[
\log(\lambda(t)) \geq \log(\lambda(0)) + \int_0^t \Psi(\alpha(u)) du + \int_0^t \frac{F(\alpha, \lambda, \kappa) \mu b}{\mu b + q \gamma c} \alpha(u) dW(u).
\]

From Eq. (1) of the system (2),
\[
d\alpha \geq \left(\gamma - \mu \alpha - \beta \frac{\gamma}{\mu} \lambda \right) dt - \frac{F(\alpha, \lambda, \kappa) \alpha \lambda}{1 + q \gamma} dW(t),
\]

Take \(\frac{\mu b}{\mu b + q \gamma c} = A_1\), Eq. (14) becomes,
\[
\log(\lambda(t)) \geq \log(\lambda(0)) + \int_0^t \Psi(\alpha(u)) du + A_1 \int_0^t F(\alpha, \lambda, \kappa) \alpha(u) dW(u).
\]

Next, we proceed in computing
\[
\Psi(\alpha) - \Psi \left(\frac{\gamma}{s_1}\right) = \beta A_1 \alpha - \left(a + \frac{p \gamma c}{\mu b} \right) - \frac{1}{2} A_1^2 F(\alpha, \lambda, \kappa)^2 \alpha^2 - \beta A_1 \frac{\gamma}{s_1} \left(1 - \frac{s_1}{\gamma} \right),
\]

Substituting the above inequality in Eq. (16), we arrive at
\[
\log(\lambda(t)) \geq \log(\lambda(0)) + \Psi \left(\frac{\gamma}{s_1}\right) t - \left(\beta A_1 - \frac{A_1^2 F(\alpha, \lambda, \kappa)^2}{2 \mu} \right) \left(1 - \frac{s_1}{\gamma} \right) \int_0^t \alpha(u) du + A_1 \int_0^t F(\alpha, \lambda, \kappa) \alpha(u) dW(u).
\]

By our assumption \(s_1 = \mu\). Therefore
\[
\log(\lambda(t)) \geq \log(\lambda(0)) + \Psi \left(\frac{\gamma}{\mu}\right) t - \left(\beta A_1 - \frac{A_1^2 F(\alpha, \lambda, \kappa)^2}{2 \mu} \right) \left(1 - \frac{s_1}{\gamma} \right) \int_0^t \alpha(u) du + A_1 \int_0^t F(\alpha, \lambda, \kappa) \alpha(u) dW(u).
\]

From Eq. (3) of system (2),
\[
d\alpha \geq \left(c \left(\frac{\gamma}{s_1}\right) - bx\right) dt.
\]

By Strong Law of large numbers for martingales,
\[
\lim_{t \to \infty} A(t) = 0 \quad \text{a.s.}
\]

Thus,
\[
\lim \inf_{t \to \infty} \frac{1}{t} \int_0^t \alpha(u) du \geq \frac{\Psi \left(\frac{\gamma}{\mu}\right) t}{A_1^2 F(\alpha, \lambda, \kappa)^2} \frac{1}{2 \mu} \left(1 - \frac{s_1}{\gamma} \right) \int_0^t A_1 \int_0^t F(\alpha, \lambda, \kappa) \alpha(u) dW(u).
\]
Upon integration on both sides and dividing by \(t\),
\[
\frac{b}{t} \int_0^t \kappa(u) \, du \geq c \left( \frac{\kappa(t) - \kappa(0)}{t} \right)
\]
As \(t \to \infty\), we have
\[
\lim_{t \to \infty} \left( \frac{\kappa(t) - \kappa(0)}{t} \right) = 0.
\]
Finally,
\[
\liminf_{t \to \infty} \int_0^t \kappa(u) \, du \geq \frac{\gamma c}{\mu b} \text{ a.s.}
\]
which proves our assertion (3).

This completes the proof of Theorem 4. \(\square\)

In most dynamical systems, our aim in the analysis of mathematical models is to determine the asymptotic behavior of its solutions. To be precise, in the language of dynamical systems, to determine the nature of global attractor. Biologically speaking, the nature of treatment that would evoke appropriate immune response in the host such that the severity of the infection is stabilized.

**Remarks 3.** The Local Lipschitz condition of the function \(F(\alpha, \lambda, \kappa)\) is sufficient because it is evident from Theorem 1 that the solution to the system exists globally in the domain \(\mathbb{D}\) for infinite time and the above theorem also speaks about the infection dynamics in the host system even for the permanent type under any initial value of \(\alpha, \lambda, \kappa\).

The above Theorem 4 ensures the survival of the members of the interacting population ensuring their existence despite infrequent large perturbations which is often experienced by biological systems in nature over a longer period of time whatever be the state of the system. Our aim is to control the infection at any stage even though it is permanent.

It is also important to analyze that the results achieved should represent a larger population irrespective of time which is next in row.

### 2.5. Time invariance-stationary distribution and positive recurrence

Before moving to empirical analysis, let us discuss the stationary distribution and positive recurrence of the persistence of system (2) whose implications are given above and are established by the following theorem.

**Theorem 5.** The solution \((\alpha(t), \lambda(t), \kappa(t))\) of system (2) with any positive initial value \((\alpha(0), \lambda(0), 0)\) \(\in \mathbb{D}\), where \(F(\alpha, \lambda, \kappa) = f(\alpha - \alpha_2) \neq 0\) is positive recurrent and admits a unique ergodic stationary distribution in \(\mathbb{D}\) if \(R_0 > 1\) and
\[
\eta_1 = \left( \mu - \frac{4q \beta \alpha_2 \kappa_2}{bn^2} \right)(\alpha - \alpha_2)^2
+ \frac{1}{2} \left( \frac{\gamma}{\mu} + \frac{q \beta \alpha^2}{c(1 + q \kappa^2)} \right) \left( \frac{\gamma}{\mu} \right)^4
\]
is positive on \(\mathbb{H}\) for \(n = \alpha_2\) and \(b = \frac{\mu \alpha_2}{c} + \frac{q \beta \alpha^2}{c(1 + q \kappa^2)}\).

**Proof.** The ideas in the proof have been rented from the Lemma in appendix by Zhu (Zhu & Yin, 2007) in his paper that begins with defining a bounded open subset \(H\) of \(\mathbb{R}^3\) as
\[
H = \left\{ (\alpha, \lambda, \kappa) \in \mathbb{D} \mid \alpha < \frac{\gamma}{\mu}, N < \alpha < \frac{\gamma}{\mu} - M, P < \kappa < \frac{\gamma}{\mu} - P \right\}
\]
where \(N, M\) and \(P\) are positive constants to be chosen as \(\alpha_2 \notin \hat{H}\), and \(\lambda_2, \kappa_2 \in H\) followed by the diffusion matrix associated with the system
\[
dX(t) = b(X) \, dt + \sum_{r=1}^{k} \sigma_r(X) \, dW_r(t),
\]
given by
\[
A(\alpha, \lambda, \kappa) = \begin{pmatrix} a_1^2 \lambda^2 F^2(\alpha, \lambda, \kappa) & -a_1^2 \lambda^2 F^2(\alpha, \lambda, \kappa) & 0 \\ -a_1^2 \lambda^2 F^2(\alpha, \lambda, \kappa) & a_1^2 \lambda^2 F^2(\alpha, \lambda, \kappa) & 0 \\ 0 & 0 & 0 \end{pmatrix}
\]
We know that \(\hat{H} \subset \mathbb{R}_1^3\),
\[
a_{11}(\alpha, \lambda, \kappa) = a_1^2 \lambda^2 F^2(\alpha, \lambda, \kappa) \geq \min_{(\alpha, \lambda, \kappa) \in \hat{H}} a_1^2 \lambda^2 F^2(\alpha, \lambda, \kappa) \geq k_1,
\]
where \(k_1\) is a positive constant. Thus, the condition (i) in the Lemma is satisfied. It remains to prove (ii) of Lemma for which we adapt the following steps.

Define a non-negative function
\[
V_2 = \frac{1}{2}(\alpha - \alpha_2)^2 + \left( \lambda - \lambda_2 - \kappa_2 \log \frac{\lambda}{\theta} \right) + \frac{b}{2}(\kappa - \kappa_2)^2.
\]
for \(n = \alpha_2\) and \(b = \frac{\mu \alpha_2}{c} + \frac{q \beta \alpha^2}{c(1 + q \kappa^2)}\).

Applying \(L\) on \(V_2(\alpha, \lambda, \kappa)\), we have
\[
\mathcal{L}V_2 \leq -\left( \mu - \frac{4q \beta \alpha_2 \kappa_2}{bn^2} \right)(\alpha - \alpha_2)^2 - \frac{b \alpha_2^2}{c} (\kappa - \kappa_2)^2
+ \frac{1}{2} F^2(\alpha, \lambda, \kappa) \alpha^2 \kappa_2^2
\]
Since \(\alpha + \lambda \leq \frac{\gamma}{\mu}\) and \(\kappa \leq \frac{\gamma}{\mu} - \mu\), we get,
\[
\mathcal{L}V_2 \leq -\left( \eta_1(\alpha, \lambda, \kappa) + \frac{b}{2}(\kappa - \kappa_2)^2 \right).
\]
Also, since \(\eta_1(\alpha, \lambda, \kappa) > 0\) on \(\mathbb{H}\), we have
\[
\eta_1(\alpha, \lambda, \kappa) + \frac{b}{2}(\kappa - \kappa_2)^2 \geq \inf_{(\alpha, \lambda, \kappa) \in \mathbb{H}} \frac{b}{2}(\kappa - \kappa_2)^2 = \theta > 0.
\]
From this, we get
\[
\mathcal{L}V_2(\alpha, \lambda, \kappa) \geq -\theta \quad \text{for all} \quad (\alpha, \lambda, \kappa) \in \mathbb{H}.
\]
Hence, the assertion (ii) of the Lemma is proved. \(\square\)

Thus, we have established the existence of a unique ergodic stationary distribution to our model.

Before moving on to the task of numerical simulations (i.e.), the empirical support which we spoke often in the previous sections, let us halt here for a moment to introspect ourselves why we need to simulate the mathematical model. The simple reason that comes first in our mind is that the construction is made under certain assumptions that differs from the real world problem to a little extent to make the models mathematically analyzable. So, it is necessary that our model lives up to our expectations i.e., copes up with the real world situation. Next, we have to ensure the robustness of the model under any situations not breaching the assumptions we made earlier during construction. All those questions get answered when we put the model into an artificial environment similar to the real world and simulate to show the results we achieved theoretically in the previous sections.
3. Empirical support via simulations

In this section, let us consider some examples to visualize our findings by simulating the stochastic system (2) using an algorithm similar to Monte-Carlo simulation. In Monte-Carlo simulation, we generate a set of suitable multidimensional sample paths on \([0, T]\). We generate a large finite set of paths, large enough so that, for example, any statistical information for the solution that we want to extract is sufficiently robust. For each sample path, we generate a sample path solution to the stochastic differential equation on \([0, T]\). Consider an example as follows:

\[
dx = \left( \gamma - \mu a - \frac{\beta a \lambda}{1 + qk} \right) dt - \left( \mu \frac{\alpha}{\gamma} \alpha \lambda (\alpha - \alpha_2) \right) dW(t)
\]

\[
d\lambda = \left( \frac{\beta a \lambda}{1 + qk} - a - p \lambda \right) dt + \left( \frac{\mu}{\gamma} \alpha \lambda (\alpha - \alpha_2) \right) dW(t)
\]

\[
dc = (c\lambda - bk) dt
\]

where \(\alpha, \lambda, \kappa, \gamma, p, q, a, b, c\) are positive constants.

One can compare the above example with our stochastically perturbed model (2). Here, \(\alpha_2 = \frac{c\gamma (1 + qk)}{c^2 \mu + (b \kappa + c \mu) k^2}\) with \(R_0 = \frac{\gamma \beta}{\alpha \mu}\).

All the simulations are carried out with step size \(10^{-2}\). The expectations and variances are taken for about 10,000 trajectories with time scaled over days.

The following figures in the succeeding pages will give a crystal clear idea on the dynamical behavior of random effects in the viral infection model and their drastic influence in the course of infection and treatment. All the figures from 1–5 appear to be smooth because they are mean approximations of 10,000 sample paths simulated under random perturbation. It does not represent the smoothness of the system. However, the effect of environmental fluctuation of the system (2) is presented through Figs. 6 and 7 which will give a clear picture of the importance of including randomness in the mathematical model.

Table 2 represents parameter values for which the system (2) evinces disease free dynamics around equilibrium solutions.

It is observed that with the above parameter values, the system (2) explores the chances the desired population may be free from disease. Also, hereby we may arrive at the conclusion that the system under our analysis admits global stable solutions at both the equilibrium points with the following results depicted in the form of graphs.

The following parameter values in Table 3 ratify permanent infection in the system (2).

Next, we simulated the example (20) with different initial values \((\alpha_0, \lambda_0, k_0) = (100, 15, 45)\) and that resulted in Figs. 2 and 3 again, respectively. We inferred that there is no change in the stability of disease free equilibrium and endemic equilibrium systems and is globally asymptotically stable on \(D\) irrespective of any initial value. i.e., biologically speaking whenever (at any stage of infection) we started our inspection in the host system, our model is compatible enough to analyze the stability in the host disease dynamics irrespective of the time which proves the Theorem 5 which gives theoretical strength for the long term behavior analysis of our model.

Though the model showed disease-free equilibrium for small changes in \(b\) with proportional increase in the treatment rate, it ends up in the case of endemic equilibrium that upon decrease in treatment rate i.e., if the same infection rate is simulated but for different values of \(a = 0.8, \mu = 0.5, p = 0.04, q = 0.005, b = 0.31, c = 0.025\) resulted in Fig. 5.

Since, the Figs. 1–5 above show the mean approximations of the sample paths under numerical simulations conditions, it will be more realistic if we could a comparative study in the analysis of the stability between Model (1) and (2) which was an idea followed in the paper (Lahrouz et al., 2011b).

Similarly for the endemic equilibrium solutions the comparative study in the analysis of the stability between Model (1) and (2) gives the following Fig. 7.

3.1. Observations and discussions

Let us make a momentary stay here before moving to the applications. We thought some discussions would be more fruitful based on our observations in empirical simulation.

1. Based on the simulated results in Fig. 2, it is evident that the infected cells and the immune responses evoked are both stable and tend to zero under the conditions deduced in Theorem 2 with the parameter values from Table 2 with \(R_0 = 0.45 < 1\) (i.e.), both the infective population and the immune response tend to zero implying that the viral dynamics is free from infection which has been assured in Theorem 2 as the system (2) will remain disease free as long as \(R_0 < 1\).

2. However, Fig. 3, displays clearly, the dynamics of virus in the course of research towards permanence of infection in the system (2) (i.e.), the behavior of the solution around endemic equilibrium with values from Table 3 under the specified conditions of Theorem 3 which imposes the conditions for the system (2) to revolve around the chronic infection, it has to exhibit the behavior that leads to \(R_0 > 1\).

3. An interesting fact is inspected when simulating the model (2) with parameter values giving \(R_0 = 1\). Even though there have been different attitudinal behavior with the values of \(R_0 < 1\) or \(R_0 > 1\), the system (2) behaved in the similar way of revolving around disease free equilibrium solution when the value of \(R_0\) is exactly 1.

4. Upon paying due attention, the results further proved that the model under our study displayed invariance towards the initial conditions, i.e., the system showed no changes when they are simulated with different initial values, for they are the dependents on the values of \(R_0\) only, thus supporting the results of Theorem 1.

5. Since, the parameter values used in the simulations are not from literature, we further extended our study in the direction of individual behavior of the members of the system (2) so that they guarantee validity as any other models in the similar Literature. Here comes the Fig. 5 to extend its support in this regard showcasing that with the increase in infection rates and lack/failure of appropriate treatment at the right time, the host population may end up in the outbreak of epidemics or at cellular level, uncontrolled spread may lead to immediate death.

6. The Figs. 6 and 7 shows the effects of random noise and the importance of introducing randomness in the model (1). It is clear that the disease-free and endemic equilibrium solutions of the model (2) are not smooth and environmental fluctuations have great influence in the dynamical behavior of the disease.

7. The major difference one can see while comparing the deterministic and stochastic models is that in deterministic system the parameters are assumed to be constant which is not true biologically in day to day life. So, to make our analysis more realistic there arises a need for better theory which is provided by including the environmental variations while modeling the real world scenario mathematically. It is the place where Stochastic Perturbation theory comes
into the play and gives valuable informations even in the absence of any biological experiments which prove to be cost effective and time consuming.

Next, we present an application to our system (2) with a HIV Infection Model.

4. Applications to HIV Model

Even though, the above simulation results give clear picture of the robustness of the model (2) which gives the results for generalized viral infection types, it would be more appropriate to discuss with infection disease models of special and global threat types thereby imparting knowledge about the advantages and disadvantages of adopting different approaches. So, next, we chose the universally spread viral infection viz., HIV with Non-linear incidence. This proposed model has already been analyzed for fractional order by Gang Huang et al. in Zhang et al. (2015). Let us recall here that we have justified the advantages of using nonlinear incidence rate and look forward to some interesting results when we simulate with Stochastic Differential Equations by adding the environmental noise. The model under our consideration take up the following form with small perturbation in the infection rate

\[
\frac{\beta_{xy}}{1 + qx} \text{ as } \frac{\beta + F(x, y, z)xy}{1 + qx} \text{ SDE}
\]

\[
\frac{dx}{dt} = \dot{x} = \lambda - \frac{\beta_{xy}}{1 + qx} - \frac{F(x, y, z)xy}{1 + qx} \text{ dW}
\]
\[
\begin{align*}
\frac{dy}{dt} &= \dot{y} = \frac{\beta xy}{1+qx} - ay - pyz + \frac{F(x, y, z)xy}{1+qx} dW \\
\frac{dz}{dt} &= \dot{z} = cyz - bz,
\end{align*}
\]

where \( x \) denotes the uninfected population, \( y \) represents the infected population and \( z \), immune response evoked corresponding to the system (21). Here, the immune response gets stronger at the rate \( cyz \) as assumed, is proportional to the number of infected cells and their concentration at present time. Also, we note that the immune response decays exponentially at a rate \( bz \) proportional to its present time concentration whereas the parameter \( q \) corresponds to the efficacy rate of Non-Lytic component with \( d \) and \( q \) referring the natural death rates of uninfected and infected population respectively. This model admits three equilibrium solutions namely disease-free equilibrium and endemic equilibrium in the presence of immune response and endemic equilibrium solution in the absence of immune response to the HIV infection in the host with the basic reproduction number i.e., the possibility of causing secondary infection by a single infected host in the entire infection period.

Before proceeding further we would like to give clear definitions of Immune presence equilibrium and Immune absence equilibrium states of the system.

**Definition (Immune Absence and Immune Presence Equilibrium).** The immune absence equilibrium is the state of Latent infection stage in which the virus is entered into the host but is yet to produce infection so there is no role for the immunity to play.

Immune presence equilibrium comes into the scene when the host shows signs of infection by the virus and the immune system starts its work to evade the infection from the host system.

The basic reproduction numbers are given by \( R_1 = \frac{(\beta -aq)}{c(d +q\lambda)} \) and \( R_0 = \frac{b(\beta -aq)}{c(d + q\lambda)} \) respectively. Here \( x_1 = \frac{a}{\beta -aq} \), \( y_1 = \frac{d + q\lambda}{\beta -aq} (R_0 - 1); \)

\( z_1 = 0 \) indicates the endemic equilibrium point representing the immune absence equilibrium solutions whereas

\[
x_2 = \frac{-(b\beta + cd - cq\lambda) + \sqrt{(b\beta + cd - cq\lambda)^2 + 4c^2dq\lambda}}{2cdq},
\]

\[
y_2 = \frac{b}{c}; \quad z_2 = \frac{c}{bp} (\lambda - dx_2) - \frac{a}{p}
\]

represents the immune presence endemic equilibrium solutions.

We simulated the above system (21) in the following form and reviewed the results

\[
\begin{align*}
dx &= \left(\lambda - dx - \frac{\beta xy}{1+qz}\right) dt - \left(\frac{d}{\lambda}\right)^5 xy(x - x_2) dW(t) \\
dy &= \left(\frac{\beta xy}{1+qz} - ay - pyz\right) dt + \left(\frac{d}{\lambda}\right)^5 xy(x - x_2) dW(t) \\
dz &= (cyz - bz) dt
\end{align*}
\]

where \( x, y, z, \lambda, p, q, a, b \) and \( c \) are positive constants. The simulation is examined using an algorithm similar to Monte-Carlo Simulations.

1. The disease free equilibrium is achieved at the point \((33, 333, 0, 0)\) for the parameter values in Table 4 as shown in the Fig. 6(A–F).

Parameter values for infection free dynamics is presented in Table 4.

2. The immune present endemic equilibrium solutions are obtained for the values of parameters in the system (22) given by Table 5 with initial values \( x_0 = 70, y_0 = 15, z_0 = 25 \) in Fig. 7.

Parameter values that express chronic infection are presented in Table 5.

One may get puzzled why simulations for endemic equilibrium solutions are being carried out for the immune present case only. This is because our model (2) has been modeled in such a way.
Fig. 7. This graph presents a clear picture of the effects of random noise in the endemic equilibrium solution of the system (2) for the initial values \((a_0, \lambda_0, \kappa_0) = (125, 25, 75)\) and \(\gamma = 500, \quad \beta = 0.005, \quad p = 0.04, \quad a = 0.8, \quad \mu = 0.5, \quad q = 0.005, \quad b = 0.31, \quad c = 0.025\) with \(R_0 = 6.25 > 1\) and \((a_1, \lambda_1, \kappa_1) = (329.8183, 221.3320, 17.8494)\).

Fig. 8. This graph represents the disease-free equilibrium solution for the initial values \(x_0 = 50, \quad y_0 = 5, \quad z_0 = 15\) with parameter values in Table 4 when \(R_1 = 0.9753 < 1\). Also, not forget that the \(R_0 = 0.8547 < 1\).

Table 4
| Parameter | Value | Parameter | Value |
|-----------|-------|-----------|-------|
| \(\lambda\) | 10 | \(p\) | 0.6 |
| \(d\) | 0.3 | \(q\) | 0.009 |
| \(\beta\) | 0.01 | \(b\) | 0.3 |
| \(a\) | 0.3 | \(c\) | 0.332 |

Table 5
| Parameter | Value | Parameter | Value |
|-----------|-------|-----------|-------|
| \(\lambda\) | 10 | \(p\) | 0.1 |
| \(d\) | 0.3 | \(q\) | 0.01 |
| \(\beta\) | 0.2 | \(b\) | 0.9 |
| \(a\) | 0.9 | \(c\) | 0.2 |
that the infection rate is being approximated in proportion to the immune response evoked due to the infection of uninfected cells. The above simulated example gave illustrous support to our theorems in practical view. Next, we conclude our works in this paper with some discussions based on the results observed. In the mean time, a spark flashed to draw an comparative study between the results observed by Huang et al. in Zhang et al. (2015) when we surveyed through the simulation results. We found that even though both methods (Fractional Differential Equations (FDE’s) and Stochastic Differential Equations (SDE’s)) could discover conditions for stability at equilibrium solutions the method by SDE’s seems to emphasis early detection of infection outbreak in the host than FDE’s. This conclusion was drawn based on the simulation results in the paper by Huang et al.

The parameter values are taken from the paper cited in Zhang et al. (2015) to draw a comparative analysis of the model under different kinds of simulation (see Figs. 8 and 9). So, modeling the infectious diseases using SDE’s will give better approximations and represents a closer scenario to nature in the concept of best fit model.

5. Conclusion

In Mathematical Modeling, the kind of differential equations that appeared in the play are Ordinary Differential Equations (ODE’s) and Partial Differential Equations (PDE’s). However, Ordinary Differential Equations are the widely used models when modeling real-life situations as they require only shorter simulation time and can be plotted easily with the available data. Stochastic Differential Equations (SDE’s) are derived from ODE’s when the reaction rates between the components of system take up probabilistic values. Computationally, they are slight complex than ODE’s and are difficult to parametrize comparing ODE’s. Thus, they promise more closer approximation to reality than ODE models.

In this paper, we present a mathematical analysis on global dynamics of the viral infection model constructed by Bartholdy et al. in Bartholdy et al. (2000) and Wodarz et al. in Wodarz et al. (2002) and include the immune responses (the efficacy of Non-Lytic and Lytic components) directly which is very difficult to obtain in the viral infection models. We studied the existence of strong unique solution of nonlinear SDE’s and provided a rigorous proof. This task is non-trivial as we deal with non-linear SDE’s. Further, our investigation revealed a biologically relevant domain on which random dynamics of Susceptible, Virus Population and Immune Responses with non-globally Lipschitz-continuous coefficients takes place. In the presence of erratic unbounded martingale-type noises this fact is non-trivial. Also, stochastic asymptotic stability of disease free and endemic equilibria has been discussed with the help of invariance principle and Lyapunov’s second method.

Generally, stochastic asymptotic stability of equilibria is connected to the basic reproduction number \( R_0 \). There may some possibilities in the real stochastic viral dynamics, that the infection can extinct even if the basic reproduction number is \( R_0 > 1 \) and can develop if \( R_0 < 1 \) but not in all cases. There is no such effect observed in the proposed model. The only possibility what the authors show is that for \( \frac{R_0}{1} \) the infection does extinct as it is in the deterministic model. In the proposed viral infection model no such effects are observed at both theoretical and simulated experimental levels. Sufficient conditions for stochastic asymptotic stability can found in terms of parameters and functional dependence on the variable contact and recovery rates. A remarkable fact of the criteria is that a sufficient condition for stability can be found for general local Lipschitz continuous \( F_i \)’s. The applicability of mathematical approach is demonstrated by some graphical illustrations and the simulations show parametric dependence of asymptotic stability of related equilibria in view of expectations and variances. In this paper, equal importance has been given for both disease-free equilibrium and endemic equilibrium solutions as we look at the current research scenario. In recent years, we felt that many actively researches are being carried on those cases in which the disease or infections that continue to exist in the system for instance, HIV infections, AIDS etc and those infections like conjunctivitis are receiving less attention which one cannot deny. So, we thought of carrying out simulations with criteria that would provide a clear idea of the entire dynamics of the disease which may explore the possibilities of extinction as well as survival of the host, in cases of endemicity. Based on our observations, we would also like to add a comment on the type of immune response to be effected in the host because reducing the replicative rate of the virus population by Non-Lytic effector mechanisms is always beneficial whereas increasing the death rate of infected cells can

Fig. 9. This graph represents the immune present endemic equilibrium solution at the point \((x_2, y_2, z_2) = (8.8760, 4.5000, 7.3049)\) when \( R_1 = 1.3851 > 1 \). Also, we found \( R_0 = 5.5556 > 1 \).
be both detrimental and beneficial, in short, we are prone to side effects on larger scale. We also observed when we simulated the system (22) it seems much effective in comparison with simulation results carried out with Fractional Order as it gives stability conditions in stronger sense. This statement is validated with the simulation results gained in Huang et al. in Zhang et al. (2015) showed that the with the parameter values $\lambda = 23.3$, $\beta = 0.5$, $a = 0.02$, $p = 10$, $q = 0.79$, $d = 0.09$, $b = 0.15$, $c = 0.0031$ even with higher efficacy rates of the Lytic and Non-Lytic Immune responses the basic reproduction numbers for both immune absence equilibrium $R_0 = 31.4916 > 1$ and immune presence equilibrium $R_1 = 30.2250 > 1$. The graphs in the paper (Zhang et al., 2015) with the above values evidently shows that the endemic equilibrium stabilizes only after 150 days for smaller order of fractions $\alpha = 0.56$, $\alpha = 0.65$. If we look at the empirical study carried out in our paper, it is evident even a smaller rate of efficacies of Lytic and Non-Lytic components, the stabilization is at a much faster rate as our parameter values are nearly closer to those values in Zhang et al. (2015). Also, based on our observations we conclude that our model seems to be sensitive to infective rates even though any explicit sensitivity analysis has not been carried out in this paper. The future scope of this article lies in introducing the idea of multi group models with random perturbation in the papers (Ji. Jiang, & Shi, 2011; Tan, Pan, Qiao, Zou, & Pan, 2012; Yu, Jiang, & Shi, 2009) by Ji. et al., J. Yu et al. and J. Tan et al. respectively, which will form a new frame work in the literature to analyze the mathematical models with more precision and accuracy.

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Appendix

In this section, we would like to introduce some preliminaries such as notations, definitions and theorems that would help in investigating the global dynamics of the stochastic model (2) theoretically. For detailed content refer (Arnold, 1974; Gard, 1998; Khasminskii, 1980).

A.1.

Consider the $d$-dimensional stochastic differential equation (SDE) of the form

$$dX(t) = f(X(t), t)dt + g(X(t), t)dW(t)$$

(23)

with an initial value $X(t_0) = x_0$, $t_0 \leq t \leq T < \infty$ 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, $W = [W(t)]_{t \geq 0}$ is an $\mathbb{R}^m$-valued random variable.

The infinitesimal generator $\mathcal{L}$ associated with the SDE (23) is given by

$$\mathcal{L} = \frac{\partial}{\partial t} + \sum_{i=1}^d f_i(x, t) \frac{\partial}{\partial x_i} + \frac{1}{2} \sum_{i,j=1}^m (g_i(x, t)g_i^T(x, t)) \frac{\partial^2}{\partial x_i \partial x_j}$$

(24)

**Theorem.** ($\mathcal{D}$-invariance). Khasminskii (1980) as appears in Gard (1998, page: 132).

Let $\mathcal{D}$ and $\mathcal{D}_n$ be open sets in $\mathbb{R}^d$ with $\mathcal{D}_n \subseteq \mathcal{D}_{n+1}$, $\overline{\mathcal{D}_n} \subseteq \mathcal{D}$, $\mathcal{D} = \bigcup_n \mathcal{D}_n$ and suppose $f$ and $g$, satisfy the existence and uniqueness conditions for solutions of (23), on each set $(t, x) : t > t_0, x \in \mathcal{D}_n$. Suppose there is a non-negative continuous function $V$ on $\mathcal{D} \times [t_0, T]$ with continuous partial derivatives and satisfying $\mathcal{L}V \leq cV$ for some positive constant $c$ and $t > t_0, x \in \mathcal{D}$. If also,

$$\inf_{t \to t_0, x \in \mathcal{D} \times \mathcal{D}_n} V(x, t) \to \infty \text{ as } n \to \infty$$

then, for any $X_0 = x_0$ independent of $W(t)$ such that $P(X_0 \in \mathcal{D}) = 1$, there is a unique Markovian, continuous time solution $X(t)$ of (23) with $X(0) = x_0$, and $X(t) \in \mathcal{D}$ for all $t > 0$ (a.s.).

A.2.

Consider the $d$-dimensional SDE

$$dX(t) = f(X(t), t)dt + g(X(t), t)dW(t), \quad t > t_0, \quad X(t_0) = x_0.$$  

(25)

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 us assume that $x_0$ be a non-random constant with probability 1.

**Definition (Stable in Probability).** The equilibrium solution $x^*$ of the SDE (25) is stochastically stable (stable in probability) if for every $\epsilon > 0$ and $s \geq t_0$

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

(26)

where $X_{x_0}(t)$ denotes the solution of (25), satisfying $X(s) = x_0$, at time $t \geq s$.

**Definition (Asymptotically Stable in Probability).** The equilibrium solution $x^*$ of the SDE (25) is said to be stochastically asymptotically stable if it is stochastically stable and

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

(27)

**Theorem** (Arnold, 1974, page: 183). 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

$$V \in C^2([U_0 \times [t_0, \infty)) = \{ f : (U_0 \times [t_0, \infty)) \to \mathbb{R} : f \text{ is continuous} \}$$

where $U_0 = \{ x \in \mathbb{R}^d : \|x - x^*\| < h \}$, for $h > 0$, such that for all $t \geq t_0$, $x \in U_0 : LV(x, t) \leq 0$. Then, the equilibrium solution $x^*$ of (25) is stochastically stable.

(ii) If, in addition, $V$ is decreasent (there exists a positive definite function $V_1$ such that $V(x, t) \leq V_1(x)$ for all $x \in U_0$ and $LV(x, t)$ is negative definite, then the equilibrium solution $x^*$ is stochastically asymptotically stable.

A.3.

**Definition (Persistence in Mean).** The Stochastic Model (2) is said to be persistent in mean (Chen & Chen, 1993), if

$$\lim_{t \to \infty} \frac{1}{t} \int_0^t \alpha(u)du > 0, \quad \lim_{t \to \infty} \frac{1}{t} \int_0^t \lambda(u)du > 0,$$

$$\lim_{t \to \infty} \frac{1}{t} \int_0^t \kappa(u)du > 0,$$

where $(\alpha(t), \lambda(t), \kappa(t))$ is any positive solution of the system (2).
Lemma (Liu et al., 2011). Suppose $A \in C(\mathbb{R}_+ \times \mathbb{R}_+ \times \mathbb{R})$ and $\Lambda \in C(\mathbb{R}_+ \times \mathbb{R}_+ \times \mathbb{R}).$

If there exist positive constants $v_0$ and $v$ such that for all $t \geq 0$,

\[
\log A(t) \geq v_0 t - v \int_0^t A(u) du + A(t) \quad \text{and} \quad \lim_{t \to \infty} \frac{A(t)}{t} = 0 \quad \text{a.s.} \quad \text{then}
\]

\[
\lim_{t \to \infty} \inf \int_0^t \frac{A(u) du}{v} \geq v_0 \quad \text{a.s.}
\]

A.4

Consider a $d$-dimensional stochastic differential equation

\[
dX(t) = b(X) dt + \sum_{i=1}^k \sigma_i(X) dW_i(t),
\]

and the diffusion matrix is defined as follows

\[
A(x) = (a_{ij}(x)), \quad a_{ij}(x) = \sum_{k=1}^d \sigma_i^k(x) \sigma_j^k(x).
\]

Lemma (Zhu (Zhu & Yin, 2007)). The system (29) is positive recurrent if there is a bounded open subset $H$ of $\mathbb{R}^d$ with regular (i.e., smooth) boundary, and

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

\[
a_i(x) \geq k \quad \text{for any} \quad x \in H,
\]

(ii) there exists a non-negative function $V: H^c \to \mathbb{R}$ such that $V$ is twice continuously differentiable and that for some $\theta > 0$, $LV(x) \leq -\theta$, for any $x \in H^c$.

Moreover, the positive recurrence process $X(t)$ has a unique stationary distribution $\mu(.)$ of density $\mathbb{E}[B]$ 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 $\mu$.

Next, we include references that are helpful to bring out this study on viral infections.

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