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The stochastic Differential Equations Model for the Spread of Viral Hepatitis and Immune Response

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Abstract

The investigate of the dynamic behavior of viral hepatitis to stop the illness from spreading have been studied in this paper. A novel stochastic mathematical model was created in order to conduct the study. We prove this proposed model has a positive unique solution. By looking up the basic reproduction number, we also demonstrated the requirements that must be fulfilled for the injured person to heal. If $R_0^s < 1$ it means that the liver will get rid of the virus and heal the infected person. While if $R_0^s > 1$, the infection grows and the disease can invade all liver cells. Computer simulations have also been used to illustrate these findings.

Keywords: Basic reproduction number, Immune responses, Stochastic epidemic model, Ito's formula, Numerical simulation

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نموذج المعادلات التفاضلية التصادفية لانتشار التهاب الكبد الفيروسي والاستجابة المناعية

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الخلاصة

تمت دراسة السلوك الديناميكي لالتهاب الكبد الفيروسي لوقف انتشار المرض في هذا البحث . تم إنشاء نموذج رياضي عشوائي جديد لإجراء الدراسة. اثبتنا ان لهذا النموذج المقترح له حل فريد موجب. ومن خلال أنشاء رقم التكاثر الأساسي، أظهرنا أيضًا المتطلبات التي يجب استيفاؤها حتى يشفى الشخص المصاب. اذا كان رقم التكاثر الاساسي اقل من واحد, فهذا يعني أن الكبد سيتخلص من الفيروس ويشفى الشخص المصاب, وبالعكس اذا كان رقم التكاثر الاساسي اكبر من واحد في هذه الحالة تنمو العدوى ويمكن للمرض ان يغزو جميع خلايا الكبد. كما تم استخدام المحاكاة الحاسوبية لتوضيح هذه النتائج.

1- Introduction

The liver is irritated by hepatitis. This illness may be brought on by active drug and alcohol use, autoimmune conditions, germs, viruses, or other foreign bodies. The hepatitis virus comes in five primary strains, which are called types A, B, C, D, and E. Though they all result in liver disease, they range significantly in terms of the illness's severity, and geographic prevalence. Specifically, types B and C together cause the majority of liver cirrhosis, liver cancer, and fatalities from viral hepatitis. They also cause chronic illness in hundreds of millions of people.

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Hepatitis B or C is thought to affect 354 million people globally, and for the majority, testing and treatment are still unattainable, [1].

Vaccination can help prevent some cases of hepatitis. A World Health Organization study revealed that immunization, diagnostic procedures, medications, and awareness campaigns could potentially avert 4.5 million preventable deaths in low- and middle-income nations by 2030 [1]. To interpret experimental results and comprehend the underlying biological mechanism causing the epidemic's development, mathematical models of the dynamics of viral hepatitis were devised [2-4]. Ordinary differential equations (ODEs) have been the main tool used in the enormous quantity of scientific studies on simulating the interaction between viruses that cause viral hepatitis and human liver cells [5–8]. Stochastic differential equations have received attention recently and have been used to represent several viral diseases, including viral hepatitis, AIDS, and coronavirus disease [9-15]. In this work, we will employ a stochastic differential equations model to study how viruses that cause liver disorders interact with liver cells when immunity is present. We employ stochastic differential equation models rather than deterministic ordinary differential equation models for a variety of reasons. Particularly when simulating viral hepatitis outbreak phenomena like hepatitis C virus dynamics or B virus dynamics, real life is stochastic rather than deterministic. This is because virus particles that interact with target liver cells are in the same environmental conditions but produce different products. The impact of adding randomness to a deterministic ordinary differential equation model is discussed in this study. The utilization of the random differential equations model multiple times might lead to the expected distribution of the findings, which makes the novel mathematical modeling approach more transparent than the deterministic ordinary differential equation models. For instance, the deterministic differential equations model will provide us with one anticipated value for the total number of HCV or HBV-infected cells at time t. The structure of this article is as follows: in Section 2, we developed a novel mathematical model that illustrates how, in the presence of immunity, viral hepatitis illness spreads inside liver cells. In Section 3 we discuss the existence and uniqueness of the solution for the proposed stochastic differential equation model. Section 4 describes the stochastic basic reproduction number and equilibriums for the new stochastic differential equation model. We define the circumstances under which the equilibrium points will be stable or unstable in Section 5. While Section 6 presents the key findings. Finally, the conclusion and a few suggestions are covered in Section 7.

2. Formulation of the model

To comprehend how viral hepatitis spreads within the human liver, how it engages with hepatic cells, and to make clear how immunity and therapy affect the processes of dissemination and recuperation, as well as the effect of the patient's psychological state and its representation by introducing environmental stochasticity, where the better the patient's psychological state is the higher environmental randomness gives me and this randomness contributes to the stability of the system and the recovery of the liver from viruses. Several mathematical models have been developed to study the spread of viruses within the liver, the most important of which is the model developed by [6]. The behavior of the virus was studied in the presence of the treatment, since it was presumed in this model that the hepatocytes were infected and uninfected $x_1(t)$ cells multiply, and we concur with this hypothesis since the human liver's population homeostasis system allows the liver to regenerate (see, for instance, [16]). Therefore, the multiplication of already-existing hepatocytes can make up for any loss of hepatocytes and the mathematical model offered by [6] as follows:

$$\begin{cases} \dfrac{d\mathrm{x}_1(\mathrm{t})}{dt} = G + n\mathrm{x}_1(\mathrm{t})\left(1 - \dfrac{\mathrm{x}_1(\mathrm{t}) + \mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - b\mathrm{x}_1(\mathrm{t}) - (1-u)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}), \\ \dfrac{d\mathrm{x}_2(\mathrm{t})}{dt} = (1-u)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}) + n\mathrm{x}_2(\mathrm{t})\left(1 - \dfrac{\mathrm{x}_1(\mathrm{t}) + \mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - s\mathrm{x}_2(\mathrm{t}), \\ \dfrac{d\mathrm{x}_3(\mathrm{t})}{dt} = (1-\mu)q\mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}). \end{cases} \quad (1)$$

We observe that the immune system responses which are the primary factor in activating therapeutic cells are disregarded by the mathematical model (1). While researchers in the reference [7] proposed a mathematical model that deals with the interaction between viruses that cause liver disease and the host's immune responses, which is as follows:

$$\begin{aligned} &\frac{d\mathrm{x}_1(\mathrm{t})}{dt} = G - b\mathrm{x}_1(\mathrm{t}) - w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}), \\ &\frac{d\mathrm{x}_2(\mathrm{t})}{dt} = w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}) - s\mathrm{x}_2(\mathrm{t}) - \beta\mathrm{x}_2(\mathrm{t})\mathrm{x}_4(\mathrm{t}), \\ &\frac{d\mathrm{x}_3(\mathrm{t})}{dt} = q\mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - k\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t}), \\ &\frac{d\mathrm{x}_4(\mathrm{t})}{dt} = m\mathrm{x}_2(\mathrm{t})\mathrm{x}_4(\mathrm{t}) - d\mathrm{x}_4(\mathrm{t}), \\ &\frac{d\mathrm{x}_5(\mathrm{t})}{dt} = \tau\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t}) - h\mathrm{x}_5(\mathrm{t}). \end{aligned} \quad (2)$$

In this paper, we integrate mathematical model (1) with mathematical model (2) to provide a new mathematical model that represents the interaction of viruses with hepatocytes. Several intricate biological elements influence the mechanism by which the virus multiplies inside the human body by entering liver cells. These factors also affect treatment efficacy, which differs from patient to patient, as well as the psychological state of the patient. For all these reasons, we were inspired to introduce random parameters in the new proposed model, which is as follows:

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$$\begin{cases} d\mathrm{x}_1(\mathrm{t}) = \left(G + n\mathrm{x}_1(\mathrm{t})\left(1 - \frac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - b\mathrm{x}_1(\mathrm{t}) - (1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t})\right)dt + \sigma_1 u_1 w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t})dB_1(t), \\ d\mathrm{x}_2(\mathrm{t}) = \left((1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}) + n\mathrm{x}_2(\mathrm{t})\left(1 - \frac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - s\mathrm{x}_2(\mathrm{t}) - \beta\mathrm{x}_2(\mathrm{t})\mathrm{x}_4(\mathrm{t})\right)dt - \sigma_1 u_1 w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t})dB_1(t), \\ d\mathrm{x}_3(\mathrm{t}) = \left((1-u_2)q\mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - k\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t})\right)dt - \sigma_2 u_2 q\mathrm{x}_2(\mathrm{t})dB_2(t), \\ d\mathrm{x}_4(\mathrm{t}) = \left(m\mathrm{x}_2(\mathrm{t})\mathrm{x}_4(\mathrm{t}) - d\mathrm{x}_4(\mathrm{t})\right)dt, \\ d\mathrm{x}_5(\mathrm{t}) = \left(\tau\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t}) - h\mathrm{x}_5(\mathrm{t})\right)dt, \end{cases} \quad (3)$$

with initial conditions

$x_1(0) \geq 0, x_2(0) \geq 0, x_3(0) \geq 0, x_4(0) \geq 0, \& \; x_5(0) \geq 0.$

Table 1 lists and illustrates every parameter utilized in the mathematical models (1) and (2) as well as the new mathematical model (3).

Table 1: Model States and Model parameters

Parameter	Description
x_{max}	The liver's maximum growing size.
$x_1(t)$	Symbolizes cells that are prone to infection.
$x_2(t)$	Symbolizes the infected cells.
$x_3(t)$	Symbolize the particles of viruses.
$x_4(t)$	CTLs response.
$x_5(t)$	Symbolize antibody response.
G	It shows the number of uninfected cells produced in a certain amount of time.
n	The fastest rate of both infected and uninfected cell growth.
b	It shows how many healthy cells are removed in a certain amount of time.
w	It shows the rate at which viral particles enter liver cells.
s	Symbolizes the rate of elimination of infected cells.
β	Show the rate at which infected cells are eliminated by CTLs.
q	It is the highest quantity of contagious virus particles generated from afflicted cells in the case of a feeble or ineffectual vaccination.
α	Symbolizes the rate at which virus particles are eliminated in a certain amount of time.
k	Symbolize rate at which antibody $x_5(t)$ neutralized the virus particles $x_3(t)$.
m	Increase the rate of CTLs $x_4(t)$ in reaction to an antigen of a virus.
d	The rate of removal of CTLs ($x_4(t)$) when there are no antigenic.
τ	The rate at which antibodies grow ($x_5(t)$) in response to virus particles $x_3(t)$
h	The rate at which antibodies disappear naturally $x_5(t)$.
$(1-u_1)$	It stands for a treatment that prevents infectious viral particles from interacting with healthy target cells. $x_1(t)$.
$(1-u_2)$	It is a form of treatment that stops virus particles from congregating in the right way, weakening the virus and making it incapable of replicating.
σ_1 & σ_2	Represents stochastic parameters.
$B_1(t)$ &$B_2(t)$	It symbolizes independent standard Brownian motions.

3. Existence and uniqueness

In this section, we discuss the existence and uniqueness of the solution of the proposed stochastic differential equation for the spread of viral hepatitis

Theorem 3.1: The solution $(x_1(t), x_2(t), x_3(t), x_4(t), x_5(t))$ of the proposed stochastic viral hepatitis epidemic model (3) is unique on $t \geq 0$ for any initial value $(x_1(0), x_2(0), x_3(0), x_4(0), x_5(0)) \in R_+^5$ and the solution will stay in R_+^5 with probability one, i.e. $(x_1(t), x_2(t), x_3(t), x_4(t), x_5(t)) \in R_+^5$ for all $t \geq 0$ a.s.(almost surely).

proof: The equations of the coefficient are locally Lipchitz continuous for every given initial size of population $(x_1(0), x_2(0), x_3(0), x_4(0), x_5(0)) \in R_+^5$. There is a single local solution $(x_1(t), x_2(t), x_3(t), x_4(t), x_5(t))$ on $t \in [0, \tau_e)$, where τ_e is the moment of explosion. To demonstrate that this solution is universal, we prove that $\tau_e = \infty$ a.s. let $k_0 \geq 0$ be big enough, so that $x_1(0), x_2(0), x_3(0), x_4(0)$ and $x_5(0)$ all lie within the interval $\left[\frac{1}{k_0}, k_0\right]$ for every integer $k \geq k_0$ .Define the stopping time as

$$\tau_k = \Big\{ t \in [0, \tau_e) : \min\{x_1(t), x_2(t), x_3(t), x_4(t), x_5(t)\} \leq \frac{1}{k} \text{ or } max\{x_1(t), x_2(t), x_3(t), x_4(t), x_5(t)\} \geq k \Big\}. \quad (4)$$

Where throughout this manuscript we consider $\inf\emptyset = \infty$ as usual $\emptyset$ denotes the empty set. Where τ_k is increasing as $k \to \infty$.

set $\tau_\infty = \lim_{k\to\infty} \tau_k$, whence $\tau_\infty \le \tau_e$ a.s. If we are able to demonstrate that $\tau_\infty = \infty$ a.s. then $\tau_e = \infty$ and $x_i(t) \in R_+^5$ where $1 \le i \le 5$, a.s for all $t \ge 0$. Put otherwise, all we have to demonstrate to finish the proof is that $\tau_\infty = \infty$ a.s. for if this assertion is untrue, after which there are two constants $T > 0$ and $\varepsilon \in (0,1)$ such that

$$P\{\tau_\infty \le T\} > \epsilon. \tag{5}$$

Thus, an integer exists $k_1 \ge k_0$ such that

$$P\{\tau_k \le T\} \ge \epsilon \text{ for everyone } k \ge k_1 . \tag{6}$$

Define a C^2 – function $v: R_+^5 \to R_+$ by $v(x) = \sum_{i=1}^5 [x_i + 1 - \log(x_i)]$.

This function's non-negativity is evident from $u + 1 - \log(u) \ge 0, \forall u > 0$. Applying Ito's formula [11], we obtain

$$\begin{aligned}
dv(x(t) =& \\
&\{(1-\frac{1}{x_1(t)})\left[G + n\mathrm{x}_1(\mathrm{t})\left(1-\frac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - b\mathrm{x}_1(\mathrm{t}) - (1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t})\right] \\
+ &\left(1-\tfrac{1}{x_2(t)}\right)\left[(1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}) + n\mathrm{x}_2(\mathrm{t})\left(1-\tfrac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - s\mathrm{x}_2(\mathrm{t}) - \beta\mathrm{x}_2(\mathrm{t})\mathrm{x}_4(\mathrm{t})\right] \\
+&\left(1-\tfrac{1}{x_3(t)}\right) \\
&\left[\left((1-u_2)q\mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - k\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t})\right) + \frac{1}{2}\sigma_1^2u_1^2w^2x_3^2 + \frac{1}{2}x_2^{-2}\sigma_1^2u_1^2w^2x_3^2x_1^2\right. \\
&\left. + \frac{1}{2}x_3^2\sigma_2^2u_2^2q^2x_2^2\right]dt + \left(\frac{\sigma_1u_1wx_3x_1}{x_2} - \sigma_1u_1wx_3\right)dB_1(t) \\
&+ \left(\frac{\sigma_2u_2qx_2}{x_3} - \sigma_2u_2qx_2\right)dB_2(t) \\
= \quad &[G + n\mathrm{x}_1(\mathrm{t})\left(1-\tfrac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - b\mathrm{x}_1(\mathrm{t}) - (1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}) + (1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t}) + \\
&n\mathrm{x}_2(\mathrm{t})\left(1-\tfrac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - s\mathrm{x}_2(\mathrm{t}) - \beta\mathrm{x}_2(\mathrm{t})\mathrm{x}_4(\mathrm{t}) + \left((1-u_2)q\mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - \right. \\
&\left. k\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t})\right) - \tfrac{G}{\mathrm{x}_1(\mathrm{t})} - \\
&n\left(1-\tfrac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) + b + (1-u_1)w\mathrm{x}_3(\mathrm{t}) - \tfrac{(1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t})}{\mathrm{x}_2(\mathrm{t})} - n\left(1-\tfrac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) + s + \\
&\beta\mathrm{x}_4(\mathrm{t}) - \tfrac{(1-u_2)q\mathrm{x}_2(\mathrm{t})}{\mathrm{x}_3(\mathrm{t})} + \propto + k\mathrm{x}_5(\mathrm{t}) + \tfrac{1}{2}\sigma_1^2u_1^2w^2x_3^2 + \tfrac{1}{2}x_2^{-2}\sigma_1^2u_1^2w^2x_3^2x_1^2 + \\
&\tfrac{1}{2}x_3^2\sigma_2^2u_2^2q^2x_2^2]dt + \left(\tfrac{\sigma_1u_1wx_3x_1}{x_2} - \sigma_1u_1wx_3\right)dB_1(t) + \left(\tfrac{\sigma_2u_2qx_2}{x_3} - \sigma_2u_2qx_2\right)dB_2(t).
\end{aligned}$$

Hence,

$$\begin{aligned}
&dv(x(t) \le [G + b + s + \\
&\propto + n\left(1-\frac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right)\mathrm{x}_1(\mathrm{t}) + ((1-u_2)q + n\left(1-\frac{x_1(t)+x_2(t)}{x_{max}}\right))x_2(t) \\
&+ (1-u_1)w\mathrm{x}_3(\mathrm{t}) + \beta\mathrm{x}_4(\mathrm{t}) + k\mathrm{x}_5(\mathrm{t}) + \left(\frac{\sigma_1u_1wx_3x_1}{x_2} - \sigma_1u_1wx_3\right)dB_1(t) \\
&+ \left(\frac{\sigma_2u_2qx_2}{x_3} - \sigma_2u_2qx_2\right)dB_2(t) \\
&= Q .
\end{aligned} \tag{7}$$

Consequently,

$$E[v(\mathrm{x}_1(\mathrm{t})(\tau_k \wedge T), \mathrm{x}_2(\mathrm{t})(\tau_k \wedge T), \mathrm{x}_3(\mathrm{t})(\tau_k \wedge T), \mathrm{x}_4(\mathrm{t})(\tau_k \wedge T), \mathrm{x}_5(\mathrm{t})(\tau_k \wedge T)]$$
$$\leq v\big(x_1(0), x_2(0), x_3(0), x_4(0), x_5(0)\big) + E\left[\int_0^{\tau_k \wedge T} Q dt\right]$$
$$\leq v\big(x_1(0), x_2(0), x_3(0), x_4(0), x_5(0)\big) + QT. \quad (8)$$

Let $\Omega_k = \tau_k \leq T$ for $k \geq k_1$ and via equation (6) $P(\Omega_k) \geq \epsilon$. Note that for each $\omega \in \Omega_k$,there is at least one $\mathrm{x}_1(\mathrm{t})(\tau_k, \omega), \mathrm{x}_2(\mathrm{t})(\tau_k, \omega), \mathrm{x}_3(\mathrm{t})(\tau_k, \omega), \mathrm{x}_4(\mathrm{t})(\tau_k, \omega), \mathrm{x}_5(\mathrm{t})(\tau_k, \omega)$ that is equivalent k or $\frac{1}{k}$,and so $v\big((\mathrm{x}_1(\mathrm{t})(\tau_k), \mathrm{x}_2(\mathrm{t})(\tau_k), \mathrm{x}_3(\mathrm{t})(\tau_k), \mathrm{x}_4(\mathrm{t})(\tau_k), \mathrm{x}_5(\mathrm{t})(\tau_k)\big)$ is no less then $k - 1 - \log k$ or $\left(\frac{1}{k}\right) - 1 + \log k$. As a result

$$v\big((\mathrm{x}_1(\mathrm{t})(\tau_k), \mathrm{x}_2(\mathrm{t})(\tau_k), \mathrm{x}_3(\mathrm{t})(\tau_k), \mathrm{x}_4(\mathrm{t})(\tau_k), \mathrm{x}_5(\mathrm{t})(\tau_k)\big)$$
$$\geq E(k - 1 - \log k) \wedge \left(\left(\frac{1}{k}\right) - 1 + \log k\right). \quad (9)$$

Consequently, Equations (6) and (8) imply that

$$v\big(x_1(0), x_2(0), x_3(0), x_4(0), x_5(0)\big) + QT$$
$$\geq E\left[1_{\Omega_{(\omega)}} v\big((\mathrm{x}_1(\mathrm{t})(\tau_k), \mathrm{x}_2(\mathrm{t})(\tau_k), \mathrm{x}_3(\mathrm{t})(\tau_k), \mathrm{x}_4(\mathrm{t})(\tau_k), \mathrm{x}_5(\mathrm{t})(\tau_k)\big)\right]$$
$$\geq \epsilon\left[(k - 1 - \log k) \wedge \left(\left(\frac{1}{k}\right) - 1 + \log k\right)\right]. \quad (10)$$

Where $1_{\Omega_{(\omega)}}$ is the indicator function of Ω. Letting $k \to \infty$ leads to the contradiction $\infty > v\big(x_1(0), x_2(0), x_3(0), x_4(0), x_5(0)\big) + QT = \infty$ This means $\tau_\infty = \infty \; a.s$, ■

4. The stochastic basic reproduction number (R_0^S) and equilibriums

To comprehend the dynamic viral movement that results in viral hepatitis, in addition to understanding whether the liver can mend and get rid of infections. We will use the stochastic basic reproduction number, which is expressed by the symbol R_0^S .This represents the number of secondary infections generated by a single infected cell in a hepatocyte population. If $R_0^S < 1$, this means that the liver will get rid of the virus and heal the infected person, because any cell carrying the virus will transmit the viruses to less than one cell. Unlike that if $R_0^S > 1$ so, each infected cell produces on average more than one new infected cell and in this case, the infection grows and the disease can invade all liver cells. We can derive the stochastic basic reproduction number (R_0^S) for the new mathematical model (3) as follows:

The disease classes for model (3) are:

$$d\mathrm{x}_2(\mathrm{t}) = \left((1 - u_1) w \mathrm{x}_3(\mathrm{t}) \mathrm{x}_1(\mathrm{t}) + n \mathrm{x}_2(\mathrm{t}) \left(1 - \frac{\mathrm{x}_1(\mathrm{t}) + \mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - s \mathrm{x}_2(\mathrm{t}) - \beta \mathrm{x}_2(\mathrm{t}) \mathrm{x}_4(\mathrm{t})\right) dt$$
$$- \sigma_1 u_1 w \mathrm{x}_3(\mathrm{t}) \mathrm{x}_1(\mathrm{t}) dB_1(t),$$
$$d\mathrm{x}_3(\mathrm{t}) = \big((1 - u_2) q \mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - k \mathrm{x}_3(\mathrm{t}) \mathrm{x}_5(\mathrm{t})\big) dt - \sigma_2 u_2 q \mathrm{x}_2(\mathrm{t}) dB_2(t),$$
$$F = \begin{pmatrix} (1 - u_1) w \mathrm{x}_3(\mathrm{t}) \mathrm{x}_1(\mathrm{t}) + n \mathrm{x}_2(\mathrm{t}) \left(1 - \frac{\mathrm{x}_1(\mathrm{t}) + \mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - \sigma_1 u_1 w \mathrm{x}_3(\mathrm{t}) \mathrm{x}_1(\mathrm{t}) \\ 0 \end{pmatrix}$$
$$V = \begin{pmatrix} s \mathrm{x}_2(\mathrm{t}) - \beta \mathrm{x}_2(\mathrm{t}) \mathrm{x}_4(\mathrm{t}) \\ (1 - u_2) q \mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - k \mathrm{x}_3(\mathrm{t}) \mathrm{x}_5(\mathrm{t}) - \sigma_2 u_2 q \mathrm{x}_2(\mathrm{t}) \end{pmatrix}.$$

The dependent variables are $\mathrm{x}_2(\mathrm{t})$ and $\mathrm{x}_3(\mathrm{t})$

From F, let $f(x_2(t), x_3(t)) = (1 - u_1) w \mathrm{x}_3(\mathrm{t}) \mathrm{x}_1(\mathrm{t}) + n \mathrm{x}_2(\mathrm{t}) \left(1 - \frac{\mathrm{x}_1(\mathrm{t}) + \mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - \sigma_1 u_1 w \mathrm{x}_3(\mathrm{t}) \mathrm{x}_1(\mathrm{t})$ & $g(x_2(t), x_3(t)) = 0$.

Let find the Jacobin matrix for F, which is

$$\mathrm{F} = \begin{pmatrix} \frac{\partial f}{\partial \mathrm{x}_2(\mathrm{t})} & \frac{\partial f}{\partial \mathrm{x}_3(\mathrm{t})} \\ \frac{\partial g}{\partial \mathrm{x}_2(\mathrm{t})} & \frac{\partial g}{\partial \mathrm{x}_3(\mathrm{t})} \end{pmatrix} = \begin{pmatrix} n - \frac{n\mathrm{x}_1(\mathrm{t}) + 2n\mathrm{x}_2(\mathrm{t})}{x_{max}} & (1-u_1)w\mathrm{x}_1(\mathrm{t}) - \sigma_1 u_1 w\mathrm{x}_1(\mathrm{t}) \\ 0 & 0 \end{pmatrix}.$$

Evaluating F at disease- free equilibrium

$$\mathrm{F} = \begin{pmatrix} n - \frac{nx_1^*(t)}{x_{max}} & (1-u_1)wx_1^*(t) - \sigma_1 u_1 wx_1^*(t) \\ 0 & 0 \end{pmatrix}$$

from V, let $f\big(x_2(t), x_3(t)\big) = s\mathrm{x}_2(\mathrm{t}) - \beta \mathrm{x}_2(\mathrm{t})\mathrm{x}_4(\mathrm{t})$ & $g(x_2(t), x_3(t)) = (1-u_2)q\mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - k\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t}) - \sigma_2 u_2 q\mathrm{x}_2(\mathrm{t})$.

Let find the Jacobin matrix for V, which is

$$\mathrm{V} = \begin{pmatrix} \frac{\partial f}{\partial \mathrm{x}_2(\mathrm{t})} & \frac{\partial f}{\partial \mathrm{x}_3(\mathrm{t})} \\ \frac{\partial g}{\partial \mathrm{x}_2(\mathrm{t})} & \frac{\partial g}{\partial \mathrm{x}_3(\mathrm{t})} \end{pmatrix} = \begin{pmatrix} s - \beta \mathrm{x}_4(\mathrm{t}) & 0 \\ (1-u_2)q - \sigma_2 u_2 q & -\propto -kx_5 \end{pmatrix}.$$

Evaluating V at disease- free equilibrium

$$\mathrm{V} = \begin{pmatrix} s & 0 \\ (1-u_2)q - \sigma_2 u_2 q & -\propto \end{pmatrix}$$

find $V^{-1} = \frac{1}{-\propto s}\begin{pmatrix} -\propto & 0 \\ -[(1-u_2)q - \sigma_2 u_2 q] & s \end{pmatrix}$

find $FV^{-1} =$

$$\begin{pmatrix} n - \frac{nx_1^*(t)}{x_{max}} & (1-u_1)wx_1^*(t) - \sigma_1 u_1 wx_1^*(t) \\ 0 & 0 \end{pmatrix} \frac{1}{-\propto s}\begin{pmatrix} -\propto & 0 \\ -[(1-u_2)q - \sigma_2 u_2 q] & s \end{pmatrix}$$

$$= \begin{pmatrix} \frac{1}{s}\left(n - \frac{nx_1^*(t)}{x_{max}}\right) + \frac{[(1-u_1)wx_1^*(t) - \sigma_1 u_1 wx_1^*(t)][(1-u_2)q - \sigma_2 u_2 q]}{\propto s} & \frac{(1-u_1)wx_1^*(t) - \sigma_1 u_1 wx_1^*(t)}{-\propto} \\ 0 & 0 \end{pmatrix}$$

finding the Eigenvalues for FV^{-1} which are as

$$\lambda_1 = \frac{1}{s}\left(n\left(1 - \frac{\mathrm{x}_1(\mathrm{t})^*}{x_{max}}\right) + \frac{(1-u_1-\sigma_1 u_1)(1-u_2-\sigma_2 u_2)w\mathrm{x}_1(\mathrm{t})^* q}{\propto}\right) \quad and\ \lambda_2 = 0.$$

Hence, $\frac{1}{s}\left(n\left(1 - \frac{\mathrm{x}_1(\mathrm{t})^*}{x_{max}}\right) + \frac{(1-u_1-\sigma_1 u_1)(1-u_2-\sigma_2 u_2)w\mathrm{x}_1(\mathrm{t})^* q}{\propto}\right)$ is the dominant eigenvalue and that yields R_0^s .

$$R_0^s = \frac{1}{s}\left(n\left(1 - \frac{\mathrm{x}_1(\mathrm{t})^*}{x_{max}}\right) + \frac{(1-u_1-\sigma_1 u_1)(1-u_2-\sigma_2 u_2)w\mathrm{x}_1(\mathrm{t})^* q}{\propto}\right). \quad (11)$$

To determine the stability of the new model (3), we evaluate the steady states or the equilibrium points of this model. The new model has an equilibrium point known as the "disease-free equilibrium," just as models (1) and (2). This symbolizes the absence of a virus as well as the absence of infected cells (i.e.,$\mathrm{x}_3(\mathrm{t})^* = 0 \& \mathrm{x}_2(\mathrm{t})^* = 0$). So when solving the equations in model (3), we obtain disease- free equilibrium which is as follows:

$$(\mathrm{x}_1(\mathrm{t})^*, \mathrm{x}_2(\mathrm{t})^*, \mathrm{x}_3(\mathrm{t})^*, \mathrm{x}_4(\mathrm{t})^*, \mathrm{x}_5(\mathrm{t})^*) = \left(\frac{x_{max}}{2n}\left[n - b \pm \sqrt{(n-b)^2 + \frac{4nG}{x_{max}}}\right], 0,0,0,0\right). \quad (12)$$

5. Stability of equilibriums

The circumstances under which the equilibrium points will be stable or unstable are defined in this section. For this aim first, we will study the stability analysis of the disease-free equilibrium. For the new model (3), the Jacobin matrix looks like this:

$J(x_1(t), x_2(t), x_3(t), x_4(t), x_5(t))=$

$$\begin{bmatrix} n\left(1-\frac{2x_1(t)+x_2(t)}{x_{max}}\right)-b-(1-u_1)wx_3(t)+\sigma_1u_1wx_3(t) & \frac{-nx_1(t)}{x_{max}} & -(1-u_1)wx_1(t)+\sigma_1u_1wx_1(t) & 0 & 0 \\ (1-u_1)wx_3(t)-\frac{nx_2(t)}{x_{max}}-\sigma_1u_1wx_3(t) & n\left(1-\frac{x_1(t)+2x_2(t)}{x_{max}}\right)-s-\beta x_4(t) & (1-u_1)wx_1(t)-\sigma_1u_1wx_1(t) & -\beta x_2(t) & 0 \\ 0 & (1-u_2)q-\sigma_2u_2q & -\propto -kx_5(t) & 0 & -Kx_3(t) \\ 0 & mx_4(t) & 0 & mx_2(t)-d & 0 \\ 0 & 0 & \tau x_5(t) & 0 & \tau x_3(t)-h \end{bmatrix}.$$

In the uninfected steady state, the Jacobin matrix will look like this:

$J_0(x_1(t)^*, 0,0,0,0) =$

$$\begin{bmatrix} n\left(1-\frac{2x_1(t)^*}{x_{max}}\right)-b & \frac{-nx_1(t)^*}{x_{max}} & -(1-u_1)wx_1(t)^*+\sigma_1u_1wx_1(t)^* & 0 & 0 \\ 0 & n\left(1-\frac{x_1(t)^*}{x_{max}}\right)-s & (1-u_1)wx_1(t)^*-\sigma_1u_1wx_1(t)^* & 0 & 0 \\ 0 & (1-u_2)q-\sigma_2u_2q & -\propto & 0 & 0 \\ 0 & 0 & 0 & -d & 0 \\ 0 & 0 & 0 & 0 & -h \end{bmatrix}.$$

The characteristic equation about $J_0(x_1(t)^*, 0,0,0,0)$ is $|J_0(x_1(t)^*, 0,0,0,0) - \lambda I| = 0$

$$\begin{vmatrix} n\left(1-\frac{2x_1(t)^*}{x_{max}}\right)-b-\lambda & \frac{-nx_1(t)^*}{x_{max}} & -(1-u_1)wx_1(t)^*+\sigma_1u_1wx_1(t)^* & 0 & 0 \\ 0 & n\left(1-\frac{x_1(t)^*}{x_{max}}\right)-s-\lambda & (1-u_1)wx_1(t)^*-\sigma_1u_1wx_1(t)^* & 0 & 0 \\ 0 & (1-u_2)q-\sigma_2u_2q & -\propto -\lambda & 0 & 0 \\ 0 & 0 & 0 & -d-\lambda & 0 \\ 0, & 0 & 0 & 0 & -h-\lambda \end{vmatrix} = 0.$$

Clearly, the roots of the characteristic equation or the eigenvalue are $\lambda_1 = -d$, $\lambda_2 = -h$, $\lambda_3 = -b + n[1 - \frac{2x_1[t]^*}{x_{amx}}]]$, and the other two eigenvalues are determined by the following quadratic equation.

$\lambda^2 + a_1\lambda + a_2 = 0.$ (13)

Where $a_1 = -\left(n - \frac{nx_1(t)^*}{x_{max}} - s - \propto\right)$,

and $a_2 = -\propto \left(n - \frac{nx_1(t)^*}{x_{max}} - s\right) - (1 - u_1 - \sigma_1u_1)(1 - u_2 - \sigma_2u_2)wT_0q.$

Obviously, $a_1 > 0$ and $a_2 > 0$ if and only if $R_0^s < 1$. Hence, all the eigenvalue have negative real parts if and only if $R_0^s < 1$. So, $J_0(x_1(t)^*, 0,0,0,0)$ is locally asymptotically stable for $R_0^s < 1$and unstable for $R_0^s > 1$.

6. Main results

In this section, we carried out several numerical simulations to support the theoretical results by employing computer simulations. We found from the theoretical results $x_2(t)$ and $x_3(t)$ are exponentially stable, and $\lim_{t\to\infty} x_2(t) = 0$, and $\lim_{t\to\infty} x_3(t) = 0$, if $R_0^s < 1$. While

$x_2(t)$ and $x_3(t)$ are unstable if $R_0^s > 1$. We will use two examples to show how immune responses, active therapy, and stochastic factors all contribute to system stabilization.

Example 6.1: If we take the parameter values as in the table below:

Parameter	The value
x_{max}	$1.0 * 10^7\ cells\ ml^{-1}$
G	$1.0 * 10^5 cells\ ml^{-1} day^{-1}$
n	$0.1\ day^{-1}$
b	$1.0 * 10^{-2}\ day^{-1}$
w	$4 * 10^{-7}\ ml day^{-1} virions^{-1}$
s	$0.1\ day^{-1}$
β	$6.4 * 10^{-2} day^{-1}$
q	$4.0 * 10^0\ virions\ cells^{-1} day^{-1}$
α	$5.0 * 10^0\ day^{-1}$
k	$2.0 * 1 day^{-1}$
m	$4.4 * 10^{-7} day^{-1}$
d	$1.0 * 10^{-2} day^{-1}$
τ	$1.0 * 10^{-5} day^{-1}$
h	$0.01 day^{-1}$
(u_1)	$0.9\ unit\ less$
(u_2)	$0.9\ unit\ less$
σ_1	0.01
σ_2	0.01

To calculate the stochastic basic reproduction number first, we find $x_1(t)^*$ by equation (12) which is equal to $x_1(t)^* = 10^7$. We substitute this value with the rest of the values given in equation (11) to find (R_0^s) as follows

$$R_0^s = \frac{1}{s}\left(n\left(1 - \frac{x_1(t)^*}{x_{max}}\right) + \frac{(1-u_1-\sigma_1 u_1)(1-u_2-\sigma_2 u_2) w x_1(t)^* q}{\propto}\right)$$

$$R_0^s = 10\left(0.1\left(1 - \frac{10^7}{10^7}\right) + \frac{(0.091)(0.091) * 4 * 10^{-7} 10^7 * 4}{5}\right).$$

So, $R_0^s = 0.264992 < 1$. Because the value of (R_0^s) is less than one, this indicates that the liver will mend and get rid of the infections. To confirm, we will take the equation of the infected cells.

$$dx_2(t) = \left((1-u_1) w x_3(t) x_1(t) + n x_2(t)\left(1 - \frac{x_1(t) + x_2(t)}{x_{max}}\right) - s x_2(t) - \beta x_2(t) x_4(t)\right) dt$$
$$- \sigma_1 u_1 w x_3(t) x_1(t) dB_1(t)).$$

Thus, by applying Ito's formula [11] and substitution the parameter values ,we have the solution of the infected cells as $x_2(t) = 10^3 e^{-(62.799608)t}$. Thus, in 50 days, the infected cells $x_2(t)$ go to zero exponentially. These results were verified using the MATLAB program, as shown in Figure (1).

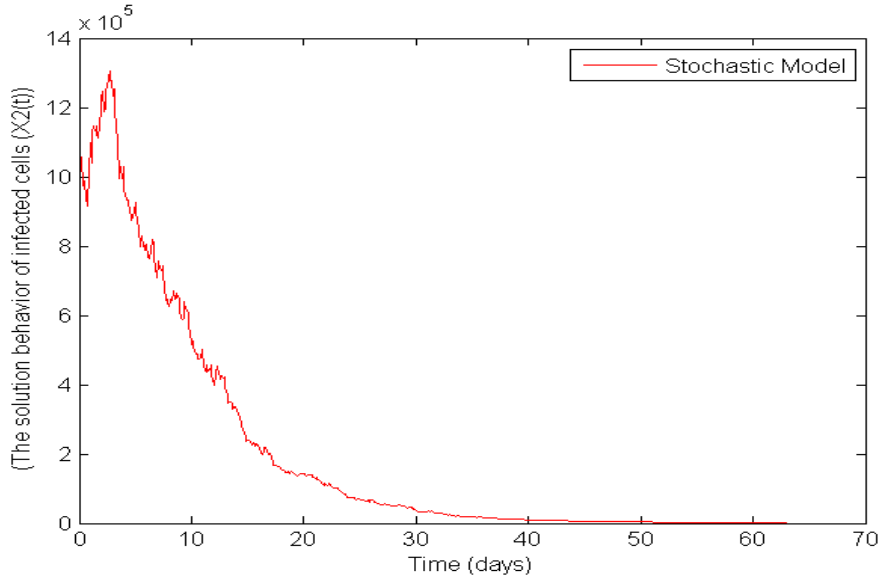

Figure 1. According to computer simulations, when $R_0^s < 1$, the number of infected cells exponentially decreases and goes to zero in 50 days.

If we take the virus particle equation

$d\mathrm{x}_3(\mathrm{t}) = \big((1-u_2)q\mathrm{x}_2(\mathrm{t}) - \propto \mathrm{x}_3(\mathrm{t}) - k\mathrm{x}_3(\mathrm{t})\mathrm{x}_5(\mathrm{t})\big)dt - \sigma_2 u_2 q\mathrm{x}_2(\mathrm{t})dB_2(t).$

Also, by substituting the parameter values in the virus particle equation and using Ito's formula [11], we obtain the following solution: $\mathrm{x}_3(\mathrm{t}) = 10^3 e^{-(1587)t}$. Thus, in 30 days, the virus particles $\mathrm{x}_3(\mathrm{t})$ tend to zero exponentially. These results were verified using the MATLAB program, as shown in Figure (2).

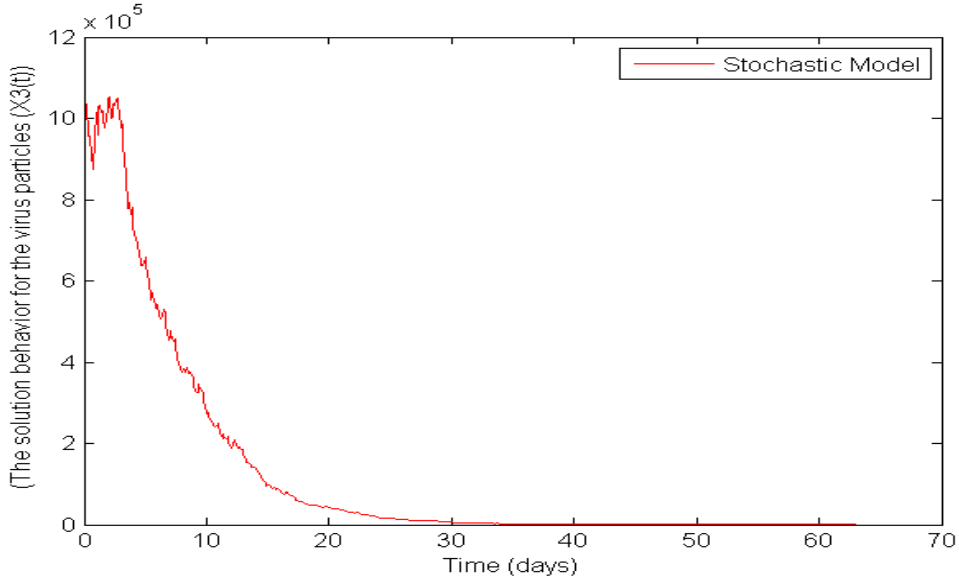

Figure 2: The computer simulation programs the virus particles goes to zero exponentially in 30 days when $R_0^s < 1$,

While if we take equation of cells susceptible to infection

$$d\mathrm{x}_1(\mathrm{t}) = \left(G + n\mathrm{x}_1(\mathrm{t})\left(1 - \frac{\mathrm{x}_1(\mathrm{t})+\mathrm{x}_2(\mathrm{t})}{x_{max}}\right) - b\mathrm{x}_1(\mathrm{t}) - (1-u_1)w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t})\right)dt +$$

$\sigma_1 u_1 w\mathrm{x}_3(\mathrm{t})\mathrm{x}_1(\mathrm{t})dB_1(t).$

Thus, after substituting the parameters in the preceding equation, and solve it we find the solution equal to $x_1(t) = 10^3 e^{100000.089t}$. We note from this result that healthy cells $x_1(t)$did not go to zero exponentially when $t \to \infty$. This result was shown using the MATLAB program, as shown in Figure (3).

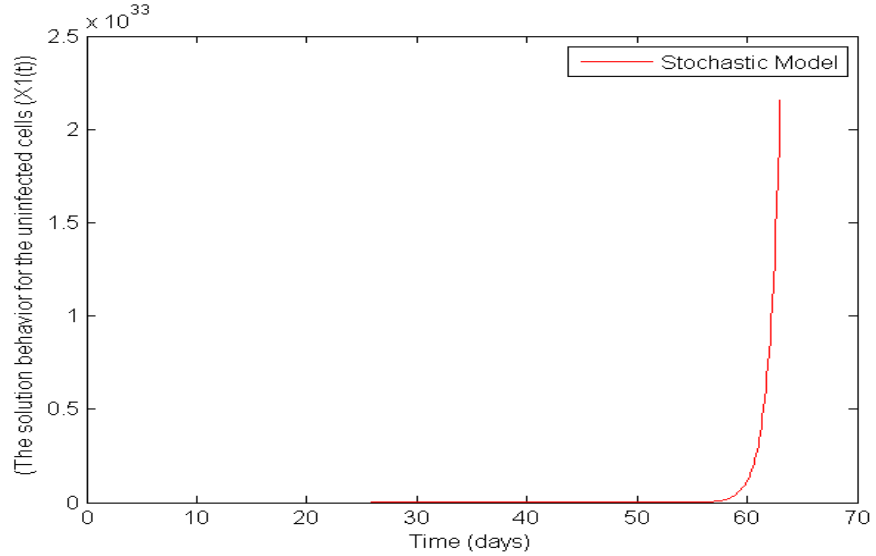

Figure 3: The computer simulation programs the uninfected cells did not go to zero exponentially when $R_0^s < 1$,

Example 6.2: In contrast to the previous example, we assume that the immunity represented by lymphocytes (CTLs) is weak, the treatment is weakly effective, and also the random variation (σ_1) and (σ_2) is not large enough. Therefore, the parameters will be as in table 3:

Parameter	The value
x_{max}	$1.0 * 10^7\ cells\ ml^{-1}$
G	$1.0 * 10^5 cells\, ml^{-1} day^{-1}$
n	$0.2\ day^{-1}$
b	$1.0 * 10^{-2}\ day^{-1}$
w	$5 * 10^{-8}\ ml day^{-1} virions^{-1}$
s	$0.1\ day^{-1}$
β	$6.4 * 10^{-2} day^{-1}$
q	$5.0 * 10^0\ virions\ cells^{-1} day^{-1}$
α	$4.0 * 10^0\ day^{-1}$
k	$2.0 * 1 day^{-1}$
m	$4.4 * 10^{-7} day^{-1}$
d	$1.0 * 10^{-2} day^{-1}$
τ	$1.0 * 10^{-5} day^{-1}$
h	$0.01 day^{-1}$
(u_1)	$0.1\ unit\ less$
(u_2)	$0.2\ unit\ less$
σ_1	0.001
σ_2	0.001

When finding the basic reproduction number by substituting the values of the parameters in equation (11), we find that $R_0^s = 4.498875125 > 1$. This outcome indicates that the illness will become chronic. To understand this outcome, we use the equation for infected cells.

$$dx_2(t) = \left((1-u_1)wx_3(t)x_1(t) + nx_2(t)\left(1 - \frac{x_1(t)+x_2(t)}{x_{max}}\right) - sx_2(t) - \beta x_2(t)x_4(t) \right)dt - \sigma_1 u_1 w x_3(t)x_1(t)dB_1(t))$$

Thus, by substituting the parameter values in the infected cells equation and applying Ito's formula, we obtain the following solution: $x_2(t) = 10^3 e^{(0.08098)t}$. So, the infected cells $x_2(t)$ do not tend to zero exponentially when $t \to \infty$. Will use computer simulation, as shown in Figure 4, to bolster these findings.

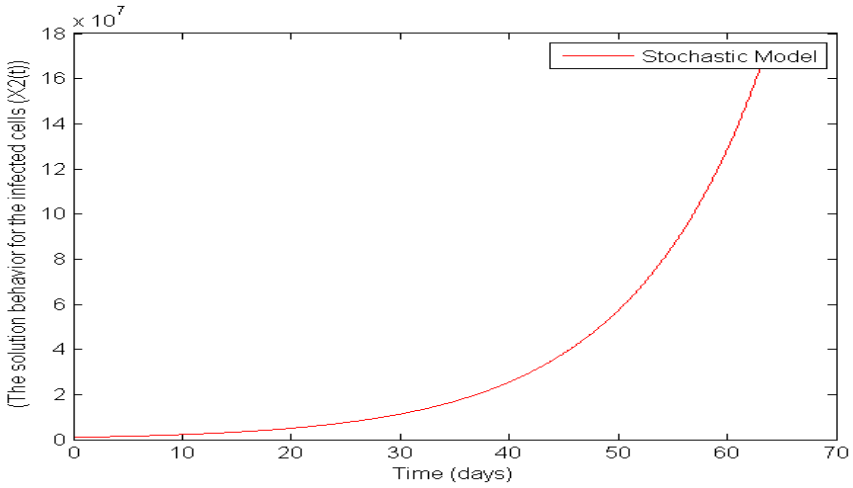

Figure 4: The computer simulation programs the infected cells not tend to zero exponentially in 70 days when $R_0^s > 1$,

When we substitute the parameter values into the virus particle equation, we find the solution $x_3(t) = 10^3 e^{1995.5t}$. So, the virus particles $x_3(t)$ do not tend to zero exponentially as $t \to \infty$. This result was proven using computer simulations, as shown in Figure (5).

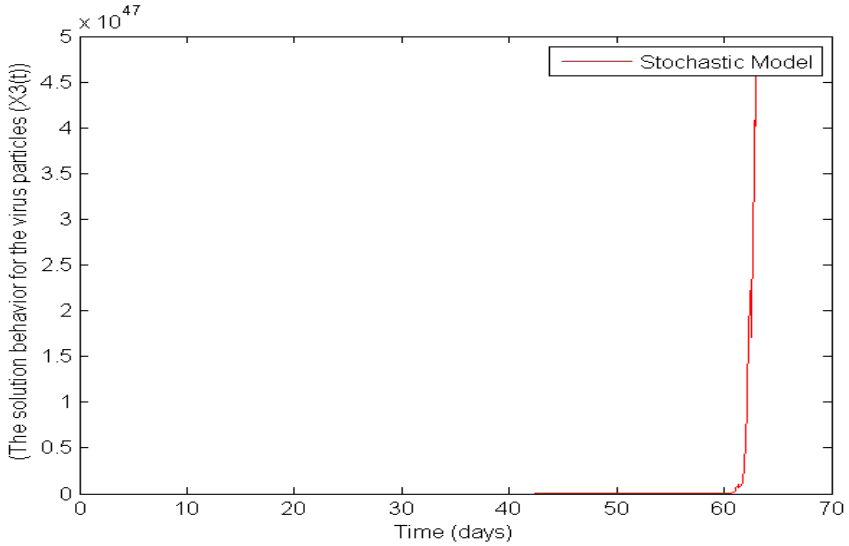

Figure 5: Computer simulation programs virus particles not tend to zero exponentially in 70 days when $R_0^s > 1$,

7. Conclusions

The following summarizes our article's novelty: By combining two deterministic systems and adding environmental stochasticity to them, the behavior of viral hepatitis is examined. We have proven using this new mathematical model that if the body has high immunity and takes appropriate treatment, and the stochastic variance σ_1 and σ_2 are large enough. This gives $R_0^s <$

1 When R_0^s is less than one, this means that each sick cell will transmit the disease to less than one cell, and this means that the liver will get rid of the virus and heal the infected person, as in Figures 1, 2, and 3. Conversely, in cases of insufficient immunity, therapy is unsuccessful and the random variation σ_1 and σ_2 is negligible, resulting in $R_0^s > 1$, therefore in this instance, every unhealthy cell spreads the infection to multiple healthy cells, This means that the virus will invade all liver cells and the infected person will not recover, as shown in Figures 4 and 5. Because immunity is crucial for protecting the liver from viruses. Therefore, it is necessary to maintain immunity by abstaining from drugs, alcohol, and high-sugar foods and beverages.

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