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A NUMERICAL METHOD FOR A DIFFUSIVE HBV INFECTION MODEL WITH MULTI-DELAYS AND TWO MODES OF TRANSMISSION

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Abstract. In this study, we propose a numerical method for four partial differential equations that describe the dynamics of hepatitis B virus (HBV) with capsids, three discrete delays and two modes of transmission which are the classical virus-to-cell infection and the direct cell-to-cell transmission. Firstly, we show that the proposed numerical method maintains the positivity and boundedness of solutions in order to ensure the well-posedness of the problem. By constructing Lyapunov functionals, we prove that the numerical method preserves the global dynamical behaviors of the corresponding continuous system for any spacial and temporal step sizes. The delayed discrete model obtained by the proposed numerical method includes various special cases available in the literature. To depict the theoretical results graphically, we present some numerical illustrations at the end of the study.

Keywords: HBV infection; partial difference equations; diffusion; global stability.

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1. INTRODUCTION

Hepatitis B is a potentially life-threatening liver infection caused by the hepatitis B virus (HBV). It is a major global health problem. It can cause chronic infection and puts people at

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high risk of death from cirrhosis and cancer of the liver [1]. In addition, this virus can spread by two fundamental modes, firstly, by cell-to-cell transfer involving direct cell-to-cell contact and secondly, by virus-to-cell infection through the extracellular space [2, 3, 4]. Nowadays, HBV has an important place in terms of public health. According to World Health Organization (WHO), an estimated 296 million individuals are living with chronic hepatitis B infection and 820 000 individuals have died from HBV complications [1].

In recent years, several authors were interested to study the dynamics of HBV infection by proposing the mathematical models with delays and different sorts of incidence rate. Yousfi et al. [5] modeled the adaptive immune response in HBV infection and discussed a possible explanation of the immune response failure to the infection. Hattaf and Yousfi [6] designed and investigated an generalized HBV infection model comprising a system of three partial differential equations (PDEs) for uninfected cells, infected cells and free virus. Manna and Chakrabarty [7] modeled the HBV infection giving consideration both uninfected and infected hepatocytes along with the intracellular HBV DNA-containing capsids and the virions. Yang et al. [8] proposed and analyzed a diffusive within-host virus dynamics model with both virus-to-cell and cell-to-cell transmissions. In 2017, Manna [9] extended the system gived in [7] by including both delay and diffusion for the HBV model. Xu et al. [10] improved and generalized the model presented in [8] by considering the global dynamics of an HBV infection model with nonlinear incidence function. In 2020, Hattaf and Yousfi [11] generalized all the models cited above by considering an HBV model of nonlinear partial differential equations (or reaction-diffusion equations) with two transmission modes and three distributed delays by taking into consideration the spatial mobility of capsids and virions. This model is described by the following system of PDEs,

$$
(1)\quad \begin{cases} \dfrac{\partial H}{\partial t} &= s-\mu H(x,t)-f\big(H(x,t),I(x,t),V(x,t)\big)V(x,t)-g\big(H(x,t),I(x,t)\big)I(x,t),\\ \dfrac{\partial I}{\partial t} &= e^{-\alpha_1\tau_1}\Big[f\big(H(x,t-\tau_1),I(x,t-\tau_1),V(x,t-\tau_1)\big)V(x,t-\tau_1)\\ &\quad +g\big(H(x,t-\tau_1),I(x,t-\tau_1)\big)I(x,t-\tau_1)\Big]-\delta I(x,t),\\ \dfrac{\partial D}{\partial t} &= d_D\triangle D+ae^{-\alpha_2\tau_2}I(x,t-\tau_2)-(\beta+\delta)D(x,t),\\ \dfrac{\partial V}{\partial t} &= d_V\triangle V+\beta e^{-\alpha_3\tau_3}D(x,t-\tau_3)-cV(x,t), \end{cases}
$$

where $H(x,t)$, $I(x,t)$, $D(x,t)$ and $V(x,t)$ are the densities of the uninfected hepatocytes, infected hepatocytes, HBV DNA-containing capsids, and the virions at position x and time t, respectively. Uninfected hepatocytes are produced at rate s, die at rate μH and become infected by contact with virions at rate $f(H,I,V)V$ and by contact with infected hepatocytes at rate $g(H,I)I$. The parameter δ is the death rate of infected hepatocytes and capsids. The parameters a, β and c are, respectively, the production rate of capsids from infected hepatocytes, the rate at which the capsids are transmitted to blood which gets converted to virions, and the clearance rate of virions. In addition, we assume that the virion or hepatocyte cell contacts a susceptible hepatocyte at time $t-\tau_1$ and the cell becomes infected at time t. The factor $e^{-\alpha_1\tau_1}$ accounts for the probability of surviving from time $t-\tau_1$ to time t, where α_1 is the death rate for infected but not yet virus-producing cells. The probability of survival of immature capsids is given by $e^{-\alpha_2\tau_2}$ and the average life time of an immature capsid is given by $\frac{1}{\alpha_2}$. The factor $e^{-\alpha_3\tau_3}$ accounts for the probability of surviving from time $t-\tau_3$ to time t, where $\frac{1}{\alpha_3}$ is the average life time of an immature virion. Finally, d_D and d_V are the diffusion coefficients of capsids and virions, respectively with $\triangle$ being the Laplacian operator.

As in [12, 13, 14], the incidence functions $f(H,I,V)$ and $g(H,I)$ for both modes of infection are continuously differentiable and satisfy the following hypotheses:

- **(H_0):** $g(0,I)=0$, for all $I\geq 0$; $\dfrac{\partial g}{\partial H}(H,I)\geq 0$ $\big($or $g(H,I)$ is a strictly monotone increasing function with respect to H when $f\equiv 0\big)$ and $\dfrac{\partial g}{\partial I}(H,I)\leq 0$, for all $H\geq 0$ and $I\geq 0$.
- **(H_1):** $f(0,I,V)=0$, for all $I\geq 0$ and $V\geq 0$,
- **(H_2):** $f(H,I,V)$ is a strictly monotone increasing function with respect to H $\big($or $\dfrac{\partial f}{\partial H}(H,I,V)\geq 0$ when $g(H,I)$ is a strictly monotone increasing function with respect to $H\big)$, for any fixed $I\geq 0$ and $V\geq 0$,
- **(H_3):** $f(H,I,V)$ is a monotone decreasing function with respect to I and V.

Biologically, the four hypotheses are reasonable and consistent with the reality. For more details on the biological significance of these four hypotheses, we refer the reader to the works [12, 14, 15, 16].

On the other hand, the exact solution of system (1) is difficult to be solved analytically. Furthermore, statistical and clinical data on HBV infection are collected and analyzed at discrete

times. For these both reasons, we'll discretize system (1) by using mixed Euler method that is a mix of both forward and backward Euler methods. The selection of the discretization scheme is motivated by the work of Hattaf et al. [17].

In this paper, we will prove that the delayed discrete model obtained by the mixed Euler method retains essential dynamical properties, such as positivity, boundedness and global behaviors of the solutions without restrictions on the spatial and temporal step sizes. So, the remainder of the paper is outlined as follows: In Section 2, we introduce the numerical method to discretize system (1). In Section 3, we investigate the global dynamics of the delayed discrete model obtained by the mixed Euler method. Numerical simulations are carried out in Section 4 to validate the analytical results. A brief conclusion finishes the paper.

2. Numerical Method and Special Cases

In the following, we consider the model (1) in the spatial domain $\Omega = [x_{min}, x_{max}]$ where $x_{min}, x_{max} \in \mathbb{R}$. Let Δt be the time step size and $\Delta x = (x_{max} - x_{min})/N$ be the space step size with N is a positive integer. Assume that there exist three integers $(m_1, m_2, m_3) \in \mathbb{N}^3$ with $\tau_1 = m_1 \Delta t$, $\tau_2 = m_2 \Delta t$ and $\tau_3 = m_3 \Delta t$. The space and time grid points are $x_n = x_{min} + n\Delta x$ for $n \in \{0, 1, ..., N\}$ and $t_m = m\Delta t$ for $m \in \mathbb{N}$. The solution of system (1) at the discretized spatio-temporal point (x_n, t_m) is $\big(H(x_n,t_m),\ I(x_n,t_m), D(x_n,t_m), V(x_n,t_m)\big)$. Hence, we denote the approximations of $H(x_n,t_m)$, $I(x_n,t_m)$, $D(x_n,t_m)$ and $V(x_n,t_m)$ by H_n^m, I_n^m, D_n^m and V_n^m, respectively. For the sake of convenience, we set all the approximation solutions at the time t_m by the $(N+1)-$dimensional vector $U^m = (U_0^m, U_1^m, ..., U_N^m)^T$, where $U \in \{H, I, D, V\}$ and the notation $(.)^T$ denotes the transposition of a vector. If all components of a vector U are nonnegative, we denote it by $U \geq 0$. By applying the mixed Euler method and using the above approximations, we obtain the following system of partial deference equations:

$$
(2) \qquad \begin{cases} \frac{H_n^{m+1} - H_n^m}{\Delta t} &= s - \mu H_n^{m+1} - f\big(H_n^{m+1}, I_n^m, V_n^m\big) V_n^m - g\big(H_n^{m+1}, I_n^m\big) I_n^m, \\ \frac{I_n^{m+1} - I_n^m}{\Delta t} &= e^{-\alpha_1 \tau_1} \big[f\big(H_n^{m-m_1+1}, I_n^{m-m_1}, V_n^{m-m_1}\big) V_n^{m-m_1} \\ & \quad + g\big(H_n^{m-m_1+1}, I_n^{m-m_1}\big) I_n^{m-m_1} \big] - \delta I_n^{m+1}, \\ \frac{D_n^{m+1} - D_n^m}{\Delta t} &= d_D \frac{D_{n+1}^{m+1} - 2D_n^{m+1} + D_{n-1}^{m+1}}{(\Delta x)^2} + a e^{-\alpha_2 \tau_2} I_n^{m-m_2+1} - (\beta + \delta) D_n^{m+1}, \\ \frac{V_n^{m+1} - V_n^m}{\Delta t} &= d_V \frac{V_{n+1}^{m+1} - 2V_n^{m+1} + V_{n-1}^{m+1}}{(\Delta x)^2} + \beta e^{-\alpha_3 \tau_3} D_n^{m-m_3+1} - c V_n^{m+1}. \end{cases}
$$

It is important to note that the discrete model formulated by system (2) includes several cases existing in the literature. For instance:

- Model of Hattaf and Yousfi [18], when we ignore the role of capsids and when the classical virus-to-cell mode is only considered.
- Model of Manna and Chakrabarty [19], when $f(H,I,V) = kH$, $g(H,I) = 0$, and $\alpha_i = \tau_i = 0$ for $i = 1,2,3$.
- Model of Yang et al. [8], when the role of capsids is negliged and $f(H,I,V) = k_1 H$, $g(H,I) = k_2 H$, and $\alpha_i = \tau_i = 0$ for $i = 1,2,3$.
- Model of Geng et al. [20], when $g(H,I) = 0$, $\alpha_1 = \alpha_2 = \alpha_3 = \tau_3 = 0$ and

$$f(H,I,V) = \begin{cases} \dfrac{kH\varphi(V)}{V}, & V \neq 0 \\ kH\varphi'(V), & V = 0 \end{cases}$$

where $\varphi(V)$ satisfies: $\varphi(0) = 0$, $\varphi'(V) > 0$ and $\varphi''(V) \leq 0$.

In this study, we associate the discrete model (2) with the following initial conditions:

$$H_n^s = \phi_1(x_n, t_s), \quad I_n^s = \phi_2(x_n, t_s), \tag{3}$$

$$D_n^s = \phi_3(x_n, t_s), \quad V_n^s = \phi_4(x_n, t_s),$$

for $n \in \{0,1,...,N\}$ and $s \in \{-p, -p+1, ..., 0\}$, where $p = \max\{m_1, m_2, m_3\}$. Also, the discrete boundary conditions are given by

$$V_{-1}^m = V_0^m, \ V_{N+1}^m = V_N^m, \ D_{-1}^m = D_0^m \text{ and } D_{N+1}^m = D_N^m \text{ for } m \in \mathbb{N}. \tag{4}$$

By taking consideration the study done by Hattaf and Yousfi in [11], the delayed discrete model (2) has the same equilibria as system (1), namely, the infection-free equilibrium $E_f\big(\frac{s}{\mu}, 0, 0, 0\big)$. Further, the basic reproduction number is given as follows

$$\mathscr{R}_0 = \frac{e^{-\alpha_1\tau_1 - \alpha_2\tau_2 - \alpha_3\tau_3} a\beta f\big(\frac{s}{\mu}, 0, 0\big)}{\delta c(\beta + \delta)} + \frac{e^{-\alpha_1\tau_1}}{\delta} g\big(\frac{s}{\mu}, 0\big).$$

When $\mathscr{R}_0 > 1$, there exists another equilibrium called the chronic infection equilibrium of the form $E^*(H^*, I^*, D^*, V^*)$, with $H^* \in \big(0, \frac{s}{\mu}\big)$, $I^* > 0$, $D^* > 0$ and $V^* > 0$.

Theorem 1. *For any $\Delta t > 0$ and $\Delta x > 0$, the solutions of the delayed discrete model (2) remain nonnegative and bounded for all $m \in \mathbb{N}$.*

Proof. The delayed discrete model (2) can be written as follows

$$(5)\qquad \begin{cases} H_n^{m+1} &= \frac{H_n^m + s\Delta t - \Delta t\left(f\left(H_n^{m+1}, I_n^m, V_n^m\right)V_n^m + g\left(H_n^{m+1}, I_n^m\right)I_n^m\right)}{1+\mu\Delta t}, \\ I_n^{m+1} &= \frac{I_n^m + e^{-\alpha_1\tau_1\Delta t}\left(f\left(H_n^{m-m_1+1}, I_n^{m-m_1}, V_n^{m-m_1}\right)V_n^{m-m_1} + g\left(H_n^{m-m_1+1}, I_n^{m-m_1}\right)I_n^{m-m_1}\right)}{1+\delta\Delta t}, \\ AD^{m+1} &= D^m + a\Delta t I^{m-m_2+1}e^{-\alpha_2\tau_2}, \\ BV^{m+1} &= V^m + \beta\Delta t D^{m-m_3+1}e^{-\alpha_3\tau_3}, \end{cases}$$

where A and B are two square matrixs of dimensions $(N+1)\times(N+1)$ given by

$$A = \begin{pmatrix} a_1 & a_2 & 0 & \dots & 0 & 0 & 0 \\ a_2 & a_3 & a_2 & \dots & 0 & 0 & 0 \\ 0 & a_2 & a_3 & \dots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & a_3 & a_2 & 0 \\ 0 & 0 & 0 & \dots & a_2 & a_3 & a_2 \\ 0 & 0 & 0 & \dots & 0 & a_2 & a_1 \end{pmatrix} \text{ and } B = \begin{pmatrix} b_1 & b_2 & 0 & \dots & 0 & 0 & 0 \\ b_2 & b_3 & b_2 & \dots & 0 & 0 & 0 \\ 0 & b_2 & b_3 & \dots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & b_3 & b_2 & 0 \\ 0 & 0 & 0 & \dots & b_2 & b_3 & b_2 \\ 0 & 0 & 0 & \dots & 0 & b_2 & b_1 \end{pmatrix},$$

with

$$a_1 = 1 + d_D\frac{\Delta t}{(\Delta x)^2} + (\beta+\delta)\Delta t, \quad a_2 = -d_D\frac{\Delta t}{(\Delta x)^2}, \quad a_3 = 1 + 2d_D\frac{\Delta t}{(\Delta x)^2} + (\beta+\delta)\Delta t,$$

$$b_1 = 1 + d_V\frac{\Delta t}{(\Delta x)^2} + c\Delta t, \quad b_2 = -d_V\frac{\Delta t}{(\Delta x)^2} \text{ and } b_3 = 1 + 2d_V\frac{\Delta t}{(\Delta x)^2} + c\Delta t.$$

It is not difficult to verify that A is a strictly diagonally dominant matrix. Hence, A is non-singular. From the third and last equation of the system (2), we have

$$D^{m+1} = A^{-1}(D^m + a\Delta t I^{m-m_2+1}e^{-\alpha_2\tau_2}),\ V^{m+1} = B^{-1}(V^m + \beta\Delta t D^{m-m_3+1}e^{-\alpha_3\tau_3}).$$

Obviously, $H^m > 0$ for all $m \in \mathbb{N}$. In fact, assuming the contrary and letting $q_1 > 0$ be the first time such that $H^{q_1} \leq 0$ and $I^m \geq 0$, $D^m \geq 0$, $V^m \geq 0$ for $m < q_1$. From the first equation of (2),

we have

$$H_n^{q_1-1} = H_n^{q_1} - \Delta t\left(s - \mu H_n^{q_1} - f\left(H_n^{q_1}, I_n^{q_1-1}, V_n^{q_1-1}\right)V_n^{q_1-1} - g\left(H_n^{q_1}, I_n^{q_1-1}\right)I_n^{q_1-1}\right).$$

According to $(H_0)-(H_2)$ and $H_n^{q_1} \leq 0$, we get $H_n^{q_1-1} \leq 0$. This contradicts our assumption and so $H^m > 0$ for all $m \in \mathbb{N}$. Now, we prove the nonnegativity of the sequences I^m, D^m and V^m by using mathematical induction. When $m = 0$, we have

$$\begin{aligned} I_n^1 &= \frac{I_n^0 + e^{-\alpha_1\tau_1}\Delta t\left(f\left(H_n^{-m_1+1}, I_n^{-m_1}, V_n^{-m_1}\right)V_n^{-m_1} + g\left(H_n^{-m_1+1}, I_n^{-m_1}\right)I_n^{-m_1}\right)}{1+\delta\Delta t}, \\ D^1 &= A^{-1}\left(D^0 + a\Delta t I^{-m_2+1}e^{-\alpha_2\tau_2}\right), \\ V^1 &= B^{-1}\left(V^0 + \beta\Delta t D^{-m_3+1}e^{-\alpha_3\tau_3}\right). \end{aligned}$$

Then $I^1 \geqslant 0$. From the property of M-matrix (see, [21]), we deduce that $D^1 \geqslant 0$ and $V^1 \geqslant 0$. Thus, by using the induction, we get $I^m \geqslant 0$, $D^m \geqslant 0$ and $V^m \geqslant 0$ for all $m \in \mathbb{N}$. This proves the nonnegativity of solutions.

Next, we establish the boundedness of solutions. To proceed, we define a sequence $\{G^m\}$ as follows

$$G_n^m = H_n^m + e^{\alpha_1\tau_1}I_n^{m+m_1}.$$

Then we have

$$\begin{aligned} G_n^{m+1} - G_n^m &= H_n^{m+1} - H_n^m + e^{\alpha_1\tau_1}(I_n^{m+m_1+1} - I_n^{m+m_1}) \\ &= \Delta t\left[s - \mu H_n^{m+1} - f\left(H_n^{m+1}, I_n^m, V_n^m\right)V_n^m - g\left(H_n^{m+1}, I_n^m\right)I_n^m\right] \\ &\quad + \Delta t\left[f\left(H_n^{m+1}, I_n^m, V_n^m\right)V_n^m + g\left(H_n^{m+1}, I_n^m\right)I_n^m\right] - e^{\alpha_1\tau_1}\Delta t\,\delta I_n^{m+m_1+1} \\ &= \Delta t(s - \mu H_n^{m+1} - e^{\alpha_1\tau_1}\delta I_n^{m+m_1+1}) \\ &\leq \Delta t(s - \eta G_n^{m+1}), \end{aligned}$$

where $\eta = \min\{\mu, \delta\}$. Thus, we get

$$G_n^{m+1} \leq \frac{1}{1+\eta\Delta t}G_n^m + \frac{s\Delta t}{1+\eta\Delta t}.$$

By using the induction, we obtain

$$G_n^m \leq \left(\frac{1}{1+\eta\Delta t}\right)^m G_n^0 + \frac{s}{\eta}\left[1-\left(\frac{1}{1+\eta\Delta t}\right)^m\right].$$

Then we have

$$\limsup_{m\longrightarrow\infty} G_n^m \leq \frac{s}{\eta} \quad for\ all\ \ n \in \{0,1,...,N\}.$$

Then we claim that $\{G^m\}$ is bounded. Therefore, $\{H^m\}$ and $\{I^m\}$ are bounded. It follows from the third equation of model (5) that

$$\sum_{n=0}^{N} D_n^{m+1} = \frac{1}{1+\Delta t\,(\beta+\delta)}\left(\sum_{n=0}^{N} D_n^m + a\Delta t e^{-\alpha_2\tau_2}\sum_{n=0}^{N} I_n^{m-m_2+1}\right).$$

Since $\{I^m\}$ is bounded, there exists a M such that $I_n^m \leq M$, for all $m \in \{-m_2, -m_2+1, ..., 0, 1, ...\}$ and $n \in \{0,1,...,N\}$. Then we have

$$\sum_{n=0}^{N} D_n^{m+1} \leq \frac{1}{1+\Delta t\,(\beta+\delta)}\left(\sum_{n=0}^{N} D_n^m + a\Delta t e^{-\alpha_2\tau_2} M(N+1)\right).$$

By induction, we obtain that

$$\begin{aligned}\sum_{n=0}^{N} D_n^m &\leq \frac{1}{(1+\Delta t\,(\beta+\delta))^m}\sum_{n=0}^{N} D_n^0 \\ &\quad + \frac{ae^{-\alpha_2\tau_2}M(N+1)}{(\beta+\delta)}\left[1-\left(\frac{1}{1+\Delta t\,(\beta+\delta)}\right)^m\right]. \\ &\leq \sum_{n=0}^{N} D_n^0 + \frac{ae^{-\alpha_2\tau_2}M(N+1)}{(\beta+\delta)}.\end{aligned}$$

Which implies that $\{D^m\}$ is bounded. Similarly, the boundedness of $\{V^m\}$ can be obtained. This completes the proof.

3. Stability Analysis

In this section, we will investigate the global dynamics of system (2) by constructing appropriate discrete Lyapunov functionals. First, we have the following result.

Theorem 2. *If $\mathscr{R}_0 \leqslant 1$, then the infection-free equilibrium E_f is globally asymptotically stable for all $\triangle t > 0$ and $\triangle x > 0$.*

Proof. Based on the method introduced in [22], we construct a Lyapunov functional as follows

$$L^m = \frac{1}{\Delta t}\sum_{n=0}^{N} l_n^m,$$

where

$$\begin{aligned} l_n^m &= e^{\alpha_1\tau_1}\left(1+\delta\Delta t - \frac{a\beta f\big(H_0,0,0\big)e^{-\alpha_2\tau_2-\alpha_3\tau_3}}{c(\beta+\delta)}\right)I_n^m + \frac{\beta f\big(H_0,0,0\big)e^{-\alpha_3\tau_3}}{c(\beta+\delta)}D_n^m \\ &+\frac{f\big(H_0,0,0\big)}{c}\big(1+c\Delta t\big)V_n^m + \Delta t\sum_{j=m-m_1}^{m-1} f\big(H_n^{j+1},I_n^j,V_n^j\big)V_n^j \\ &+\Delta t\sum_{j=m-m_1}^{m-1} g\big(H_n^{j+1},I_n^j\big)I_n^j + \frac{a\beta f\big(H_0,0,0\big)e^{-\alpha_2\tau_2-\alpha_3\tau_3}}{c(\beta+\delta)}\Delta t\sum_{j=m-m_2}^{m-1} I_n^{j+1} \\ &+\frac{\beta f\big(H_0,0,0\big)e^{-\alpha_3\tau_3}}{c}\Delta t\sum_{j=m-m_3}^{m-1} D_n^{j+1}. \end{aligned}$$

We have

$$\begin{aligned} l_n^{m+1}-l_n^m &= e^{\alpha_1\tau_1}\left(1+\delta\Delta t - \frac{a\beta f\big(H_0,0,0\big)e^{-\alpha_2\tau_2-\alpha_3\tau_3}}{c(\beta+\delta)}\right)(I_n^{m+1}-I_n^m) \\ &+\frac{\beta f\big(H_0,0,0\big)e^{-\alpha_3\tau_3}}{c(\beta+\delta)}(D_n^{m+1}-D_n^m) \\ &+\frac{f\big(H_0,0,0\big)}{c}\big(1+c\Delta t\big)(V_n^{m+1}-V_n^m) \\ &+\Delta t\left(f\big(H_n^{m+1},I_n^m,V_n^m\big)V_n^m - f\big(H_n^{m-m_1+1},I_n^{m-m_1},V_n^{m-m_1}\big)V_n^{m-m_1}\right) \\ &+\Delta t\left(g\big(H_n^{m+1},I_n^m\big)I_n^m - g\big(H_n^{m-m_1+1},I_n^{m-m_1}\big)I_n^{m-m_1}\right) \\ &+\frac{a\beta f\big(H_0,0,0\big)e^{-\alpha_2\tau_2-\alpha_3\tau_3}}{c(\beta+\delta)}\Delta t\big(I_n^{m+1}-I_n^{m-m_2+1}\big) \\ &+\frac{\beta f\big(H_0,0,0\big)e^{-\alpha_3\tau_3}}{c}\Delta t\big(D_n^{m+1}-D_n^{m-m_3+1}\big). \end{aligned}$$

Hence,

$$\begin{aligned} l_n^{m+1}-l_n^m &= \Delta t e^{\alpha_1\tau_1}\delta(I_n^{m+1}-I_n^m) - \Delta t e^{\alpha_1\tau_1}\delta I_n^{m+1} + \frac{a\Delta t\beta f\big(H_0,0,0\big)e^{-\alpha_2\tau_2-\alpha_3\tau_3}}{c(\beta+\delta)}I_n^m \\ &+\Delta t\left(f\big(H_n^{m+1},I_n^m,V_n^m\big)V_n^m + g\big(H_n^{m+1},I_n^m\big)I_n^m\right) - \Delta t f\big(H_0,0,0\big)V_n^m \end{aligned}$$

$$+\frac{\Delta t\beta f\big(H_0,0,0\big)e^{-\alpha_3\tau_3}}{c(\beta+\delta)}\left(d_D\frac{D_{n+1}^{m+1}-2D_n^{m+1}+D_{n-1}^{m+1}}{(\Delta x)^2}\right)$$
$$+\frac{\Delta t f\big(H_0,0,0\big)}{c}\big(1+c\Delta t\big)\left(d_V\frac{V_{n+1}^{m+1}-2V_n^{m+1}+V_{n-1}^{m+1}}{(\Delta x)^2}\right).$$

According to the first equation of the discrete system (2), we obtain

$$H_n^{m+1}\leq\frac{1}{1+\mu\Delta t}H_n^m+\frac{s\Delta t}{1+\mu\Delta t}.$$

By using the induction, we easily get

$$H_n^m\leq\left(\frac{1}{1+\mu\Delta t}\right)^m H_n^0+\frac{s}{\mu}\left(1-\left(\frac{1}{1+\mu\Delta t}\right)^m\right).$$

Thus,

$$\limsup_{m\longrightarrow\infty}H_n^m\leq\frac{s}{\mu}=H_0\qquad\text{for all n}\in\{0,...,N\}.$$

This implies that the difference of L^m satisfies

$$\begin{aligned}L_n^{m+1}-L_n^m &\leq \sum_{n=0}^{N}\left[\left(f\big(H_n^{m+1},I_n^m,V_n^m\big)-f\big(H_0,0,0\big)\right)V_n^m\right.\\ &\quad\left.+\frac{\delta}{e^{-\alpha_1\tau_1}}\left(\mathscr{R}_0-1\right)I_n^m\right]\\ &\quad+\frac{d_D\beta f\big(H_0,0,0\big)e^{-\alpha_3\tau_3}}{c(\Delta x)^2(\beta+\delta)}\left(D_{N+1}^{m+1}-D_N^{m+1}+D_{-1}^{m+1}-D_0^{m+1}\right)\\ &\quad+\frac{d_V f\big(H_0,0,0\big)}{c(\Delta x)^2}\big(1+c\Delta t\big)\left(V_{N+1}^{m+1}-V_N^{m+1}+V_{-1}^{m+1}-V_0^{m+1}\right),\\ &\leq \frac{\delta}{e^{-\alpha_1\tau_1}}\left(\mathscr{R}_0-1\right)I_n^m.\end{aligned}$$

Thus, if $\mathscr{R}_0\leq 1$, then $L^{m+1}-L^m\leq 0$, for all $m\in\mathbb{N}$. This implies that the sequence $\{L^m\}$ is monotone decreasing sequence. Then there exists a constant $\tilde{L}$ such that $\lim_{m\to\infty}L^m=\tilde{L}$. Hence, $\lim_{m\to\infty}(L^{m+1}-L^m)=0$, from which we get $\lim_{m\to\infty}(\mathscr{R}_0-1)I_n^m=0$ for all $n\in\{0,1,...,N\}$. We discuss two cases:

(i) If $\mathscr{R}_0<1$, then $\lim_{m\to\infty}(L^{m+1}-L^m)=0$ implies that $\lim_{m\to\infty}H_n^m=H_0$, $\lim_{m\to\infty}I_n^m=0$, $\lim_{m\to\infty}D_n^m=0$, $\lim_{m\to\infty}V_n^m=0$, for all $n\in\{0,1,...,N\}$.

(ii) If $\mathscr{R}_0=1$, then $\lim_{m\to\infty}(L^{m+1}-L^m)=0$ implies that $\lim_{m\to\infty}H_n^m=H_0$ for all $n\in\{0,1,...,N\}$. It follows from the above discussion that E_f is globally asymptotically stable. This completes the proof.

Finally, we establish the global stability of the chronic infection equilibrium E^*. To do this, we assume that $\mathscr{R}_0 > 1$ and the incidence functions f and g satisfy the following further hypothesis

$$(H_4)\qquad \begin{cases} \left(1-\dfrac{f(H,I,V)}{f(H,I^*,V^*)}\right)\left(\dfrac{f(H,I^*,V^*)}{f(H,I,V)}-\dfrac{V}{V^*}\right)\leq 0, \\ \left(1-\dfrac{f(H^*,I^*,V^*)g(H,I)}{f(H,I^*,V^*)g(H^*,I^*)}\right)\left(\dfrac{f(H,I^*,V^*)g(H^*,I^*)}{f(H^*,I^*,V^*)g(H,I)}-\dfrac{I}{I^*}\right)\leq 0. \end{cases}$$

We based on the following Hattaf-Yousfi lemma [23]:

Lemma 1. *Let $\overline{T},\overline{I},\overline{V}$ and σ be four nonnegative real numbers and $\overline{E}(\overline{T},\overline{I},\overline{V})$ be an arbitrary point. The function $\psi_{(\overline{E},\sigma)}$ defined on interval $[0,+\infty)$ by*

$$\psi_{(\overline{E},\sigma)}(T) = T-\sigma-\int_{\sigma}^{T}\frac{f(\overline{T},\overline{I},\overline{V})}{f(X,\overline{I},\overline{V})}dX,$$

has the global minimum at $T=\overline{T}$ and satisfies

$$\left(1-\frac{f(\overline{T},\overline{I},\overline{V})}{f(\sigma,\overline{I},\overline{V})}\right)(T-\sigma)\leq \psi_{(\overline{E},\sigma)}(T)\leq \left(1-\frac{f(\overline{T},\overline{I},\overline{V})}{f(T,\overline{I},\overline{V})}\right)(T-\sigma)\quad \textit{for all } T>0.$$

Thus, we have the following result.

Theorem 3. *Assume that $\mathscr{R}_0 > 1$ and (H_4) holds. Then the chronic infection equilibrium E^* is globally asymptotically stable.*

Proof. Construct a Lyapunov functional as follows

$$W_n^m = \frac{1}{\Delta t}\sum_{n=0}^{N} w_n^m,$$

where

$$\begin{aligned} w_n^m &= \psi_{(E^*,H^*)}(H_n^m) + \left(e^{\alpha_1\tau_1} + g(H^*,I^*)\right) I^* \Phi\left(\frac{I_n^m}{I^*}\right) \\ &+ \frac{f(H^*,I^*,V^*)V^* e^{\alpha_2\tau_2}}{aI^*} D^* \Phi\left(\frac{D_n^m}{D^*}\right) \\ &+ f(H^*,I^*,V^*)\left(1 + \frac{(\beta+\delta)V^*}{a\beta e^{-\alpha_2\tau_2-\alpha_3\tau_3}I^*}\right) V^* \Phi\left(\frac{V_n^m}{V^*}\right) \\ &+ f(H^*,I^*,V^*)V^*\Delta t \sum_{j=m-m_1}^{m-1} \Phi\left(\frac{f\left(H_n^{j+1},I_n^j,V_n^j\right)V_n^j}{f(H^*,I^*,V^*)V^*}\right) \\ &+ g(H^*,I^*)I^*\Delta t \sum_{j=m-m_1}^{m-1} \Phi\left(\frac{g\left(H_n^{j+1},I_n^j\right)I_n^j}{g(H^*,I^*)I^*}\right) \\ &+ f(H^*,I^*,V^*)V^*\Delta t \sum_{j=m-m_2}^{m-1} \Phi\left(\frac{I_n^{j+1}}{I^*}\right) \\ &+ f(H^*,I^*,V^*)V^*\Delta t \sum_{j=m-m_3}^{m-1} \Phi\left(\frac{D_n^{j+1}}{D^*}\right), \end{aligned}$$

where $\Phi(u) = u - 1 - \ln(u) \quad (u > 0)$ with a global minimum at $u = 1$ and satisfies $\Phi(1) = 0$. It follows from Lemma 1 that $\psi_{(E^*,H^*)}(H_n^m) \geqslant 0$. By the inequality given in Lemma 1 and $\ln(u) \leq u - 1$, we obtain

$$\begin{aligned} w_n^{m+1} - w_n^m &\leq \left(H_n^{m+1} - H_n^m\right)\left(1 - \frac{f(H^*,I^*,V^*)}{f(H_n^{m+1},I^*,V^*)}\right) \\ &+ e^{\alpha_1\tau_1}\left(I_n^{m+1} - I_n^m\right)\left(1 - \frac{I^*}{I_n^{m+1}}\right) \\ &+ g(H^*,I^*)I^*\left(\frac{I_n^{m+1}}{I^*} - \frac{I_n^m}{I^*} + \ln\left(\frac{I_n^m}{I_n^{m+1}}\right)\right) \\ &+ \frac{f(H^*,I^*,V^*)V^* e^{\alpha_2\tau_2}}{aI^*}\left(D_n^{m+1} - D_n^m\right)\left(1 - \frac{D^*}{D_n^{m+1}}\right) \\ &+ \frac{(\beta+\delta)f(H^*,I^*,V^*)V^*}{a\beta e^{-\alpha_2\tau_2-\alpha_3\tau_3}I^*}\left(V_n^{m+1} - V_n^m\right)\left(1 - \frac{V^*}{V_n^{m+1}}\right) \\ &+ f(H^*,I^*,V^*)V^*\left(\frac{V_n^{m+1}}{V^*} - \frac{V_n^m}{V^*} + \ln\left(\frac{V_n^m}{V_n^{m+1}}\right)\right) \\ &+ f(H^*,I^*,V^*)V^*\Delta t\left[\sum_{j=m-m_1+1}^{m} \Phi\left(\frac{f\left(H_n^{j+1},I_n^j,V_n^j\right)V_n^j}{f(H^*,I^*,V^*)V^*}\right)\right. \end{aligned}$$

$$
\begin{aligned}
&- \sum_{j=m-m_1}^{m-1} \Phi\left(\frac{f\left(H_n^{j+1}, I_n^j, V_n^j\right) V_n^j}{f(H^*, I^*, V^*) V^*}\right)\Bigg] \\
&+ g(H^*, I^*) I^* \Delta t \Bigg[\sum_{j=m-m_1+1}^{m} \Phi\left(\frac{g\left(H_n^{j+1}, I_n^j\right) I_n^j}{g(H^*, I^*) I^*}\right) \\
&- \sum_{j=m-m_1}^{m-1} \Phi\left(\frac{g\left(H_n^{j+1}, I_n^j\right) I_n^j}{g(H^*, I^*) I^*}\right)\Bigg] \\
&+ f(H^*, I^*, V^*) V^* \Delta t \Bigg[\sum_{j=m-m_2+1}^{m} \Phi\left(\frac{I_n^{j+1}}{I^*}\right) - \sum_{j=m-m_2}^{m-1} \Phi\left(\frac{I_n^{j+1}}{I^*}\right)\Bigg] \\
&+ f(H^*, I^*, V^*) V^* \Delta t \Bigg[\sum_{j=m-m_3+1}^{m} \Phi\left(\frac{D_n^{j+1}}{D^*}\right) - \sum_{j=m-m_3}^{m-1} \Phi\left(\frac{D_n^{j+1}}{D^*}\right)\Bigg].
\end{aligned}
$$

By using the equilibrium conditions for E^* that are

$$
s - \mu H^* = f(H^*, I^*, V^*) V^* + g(H^*, I^*) I^* = \delta e^{\alpha_1 \tau_1} I^* = \frac{\delta e^{\alpha_1 \tau_1 + \alpha_2 \tau_2} (\beta + \delta)}{a} D^*,
$$

and

$$
\delta e^{\alpha_1 \tau_1} I^* = \frac{\delta c (\beta + \delta) e^{\alpha_1 \tau_1 + \alpha_2 \tau_2 + \alpha_3 \tau_3}}{a\beta} V^*.
$$

Then we have

$$
\begin{aligned}
w_n^{m+1} - w_n^m \;=\;& \Delta t \mu H^* \left(1 - \frac{H_n^{m+1}}{H^*}\right)\left(1 - \frac{f(H^*, I^*, V^*)}{f(H_n^{m+1}, I^*, V^*)}\right) \\
&+ f(H^*, I^*, V^*) V^* \Delta t \Bigg[1 - \frac{f(H^*, I^*, V^*)}{f(H_n^{m+1}, I^*, V^*)} \\
&+ \frac{f(H_n^{m+1}, I_n^m, V_n^m) V_n^m}{f(H_n^{m+1}, I^*, V^*) V^*} - \frac{f(H_n^{m-m_1+1}, I_n^{m-m_1}, V_n^{m-m_1}) V_n^{m-m_1} I^*}{f(H^*, I^*, V^*) V^* I_n^{m+1}} \\
&- \frac{D^* I_n^{m-m_2+1}}{D_n^{m+1} I^*} + \frac{e^{\alpha_2 \tau_2} D^* (\beta + \delta)}{a I^*} \\
&- \frac{c(\beta + \delta) V_n^{m+1}}{a\beta I^* e^{-\alpha_2 \tau_2 - \alpha_3 \tau_3}} - \frac{(\beta + \delta) D_n^{m-m_3+1} V^*}{a I^* e^{-\alpha_2 \tau_2} V_n^{m+1}} + \frac{c(\beta + \delta) V^*}{a\beta I^* e^{-\alpha_2 \tau_2 - \alpha_3 \tau_3}} \\
&+ \frac{V_n^{m+1}}{V^*} - \frac{V_n^m}{V^*} + \frac{I_n^{m+1}}{I^*} - \frac{I_n^{m+1}}{I^*}
\end{aligned}
$$

$$
\begin{aligned}
&+\ln\left(\frac{f(H_n^{m-m_1+1},I_n^{m-m_1},V_n^{m-m_1})V_n^{m-m_1}I_n^{m-m_2+1}D_n^{m-m_3+1}}{f(H_n^{m+1},I_n^m,V_n^m)V_n^{m+1}I_n^{m+1}D_n^{m+1}}\right)\Bigg]\\
&+\Delta t g(H^*,I^*)I^*\Bigg[2-\frac{f(H^*,I^*,V^*)}{f(H_n^{m+1},I^*,V^*)}\\
&+\frac{f(H^*,I^*,V^*)g(H_n^{m+1},I_n^m)I_n^m}{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)I^*}\\
&+\frac{I_n^{m+1}}{I^*}-\frac{I_n^m}{I^*}-\frac{I_n^{m+1}}{I^*}\\
&-\frac{g(H_n^{m-m_1+1},I_n^{m-m_1})I_n^{m-m_1}}{g(H^*,I^*)I_n^{m+1}}+\ln\left(\frac{g(H_n^{m-m_1+1},I_n^{m-m_1})I_n^{m-m_1}}{g(H_n^{m+1},I_n^m)I_n^{m+1}}\right)\Bigg]\\
&+\sum_{m=0}^{N}\frac{d_D\Delta t}{(\Delta x)^2}\frac{e^{\alpha_2\tau_2}f(H^*,I^*,V^*)V^*}{aI^*}\left(1-\frac{D^*}{D_n^{m+1}}\right)\left(D_{n+1}^{m+1}-2D_n^{m+1}\right.\\
&\left.+D_{n-1}^{m+1}\right)+\sum_{m=0}^{N}\frac{d_V\Delta t}{(\Delta x)^2}\frac{e^{\alpha_2\tau_2+\alpha_3\tau_3}}{f(H^*,I^*,V^*)V^*}a\beta I^*\left(1-\frac{V^*}{V_n^{m+1}}\right)\left(V_{n+1}^{m+1}\right.\\
&\left.-2V_n^{m+1}+V_{n-1}^{m+1}\right).
\end{aligned}
$$

Hence, the first difference of W^m satisfies

$$
\begin{aligned}
W_n^{m+1}-W_n^m \;\leq\;& \Delta t\mu H^*\left(1-\frac{H_n^{m+1}}{H^*}\right)\left(1-\frac{f(H^*,I^*,V^*)}{f(H_n^{m+1},I^*,V^*)}\right)\\
&+f(H^*,I^*,V^*)V^*\left(-1-\frac{V_n^m}{V^*}+\frac{f(H_n^{m+1},I^*,V^*)}{f(H_n^{m+1},I_n^m,V_n^m)}\right.\\
&\left.+\frac{f(H_n^{m+1},I_n^m,V_n^m)V_n^m}{f(H_n^{m+1},I^*,V^*)V^*}\right)+g(H^*,I^*)I^*\left(-1-\frac{I_n^m}{I^*}\right.\\
&+\frac{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)}{f(H^*,I^*,V^*)g(H_n^{m+1},I_n^m)}\\
&\left.+\frac{f(H^*,I^*,V^*)g(H_n^{m+1},I_n^m)I_n^m}{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)I^*}\right)\\
&-f(H^*,I^*,V^*)V^*\left[\Phi\left(\frac{f(H^*,I^*,V^*)}{f(H_n^{m+1},I^*,V^*)}\right)\right.\\
&+\Phi\left(\frac{f(H_n^{m-m_1+1},I_n^{m-m_1},V_n^{m-m_1})V_n^{m-m_1}I^*}{f(H^*,I^*,V^*)V^*I_n^{m+1}}\right)\\
&\left.+\Phi\left(\frac{f(H_n^{m+1},I^*,V^*)}{f(H_n^{m+1},I_n^m,V_n^m)}\right)\right]
\end{aligned}
$$

$$
\begin{aligned}
&-g(H^*,I^*)I^*\left[\Phi\left(\frac{f(H^*,I^*,V^*)}{f(H_n^{m+1},I^*,V^*)}\right)\right.\\
&+\Phi\left(\frac{g(H_n^{m-m_1+1},I_n^{m-m_1})I_n^{m-m_1}}{g(H^*,I^*)I_n^{m+1}}\right)\\
&\left.+\Phi\left(\frac{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)}{f(H^*,I^*,V^*)g(H_n^{m+1},I_n^m)}\right)\right]\\
&-f(H^*,I^*,V^*)V^*\Phi\left(\frac{D^*I_n^{m-m_2+1}}{D_n^{m+1}I^*}\right)\\
&-f(H^*,I^*,V^*)V^*\Phi\left(\frac{V^*D_n^{m-m_3+1}}{V_n^{m+1}D^*}\right)\\
&-\frac{d_D}{(\Delta x)^2}\frac{e^{\alpha_2\tau_2}f(H^*,I^*,V^*)V^*}{aI^*}\sum_{n=0}^{N-1}\frac{(D_{n+1}^{m+1}-D_n^{m+1})^2}{D_{n+1}^{m+1}D_n^{m+1}}\\
&-\frac{d_V}{(\Delta x)^2}\frac{e^{\alpha_2\tau_2+\alpha_3\tau_3}f(H^*,I^*,V^*)V^*}{a\beta I^*}\sum_{n=0}^{N-1}\frac{(V_{n+1}^{m+1}-V_n^{m+1})^2}{V_{n+1}^{m+1}V_n^{m+1}}.
\end{aligned}
$$

Since the function $f(H,I,V)$ is strictly monotonically increasing with respect to H, we have

$$
\left(1-\frac{H_n^{m+1}}{H^*}\right)\left(1-\frac{f(H^*,I^*,V^*)}{f(H_n^{m+1},I^*,V^*)}\right)\leq 0.
$$

Based on the hypothesis (H_4), we have

$$
\begin{aligned}
&-1-\tfrac{V_n^m}{V^*}+\tfrac{f(H^{m+1},I^*,V^*)}{f\left(H_n^{m+1},I_n^m,V_n^m\right)}+\tfrac{f\left(H_n^{m+1},I_n^m,V_n^m\right)V_n^m}{f(H_n^{m+1},I^*,V^*)V^*}=\\
&\left(1-\tfrac{f\left(H_n^{m+1},I_n^m,V_n^m\right)}{f(H_n^{m+1},I^*,V^*)}\right)\left(\tfrac{f(H_n^{m+1},I^*,V^*)}{f\left(H_n^{m+1},I_n^m,V_n^m\right)}-\tfrac{V_n^m}{V^*}\right)\leq 0.
\end{aligned}
$$

and

$$
\begin{aligned}
&-1-\tfrac{I_n^m}{I^*}+\tfrac{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)}{f(H^*,I^*,V^*)g\left(H_n^{m+1},I_n^m\right)}+\tfrac{f(H^*,I^*,V^*)g\left(H_n^{m+1},I_n^m\right)I_n^m}{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)I^*}=\\
&\left(1-\tfrac{f(H^*,I^*,V^*)g\left(H_n^{m+1},I_n^m\right)}{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)}\right)\left(\tfrac{f(H_n^{m+1},I^*,V^*)g(H^*,I^*)}{f(H^*,I^*,V^*)g\left(H_n^{m+1},I_n^m\right)}-\tfrac{I_n^m}{I^*}\right)\leq 0.
\end{aligned}
$$

Recall that $\Phi(u)\geq 0$ for all $u>0$, thus we get $W^{m+1}-W^m\leq 0$, for all $m\in\mathbb{N}$. Then there exists a constant $\tilde{W}$ such that $\lim\limits_{m\to\infty}W^m=\tilde{W}$, which implies that $\lim\limits_{m\to\infty}(W^{m+1}-W^m)=0$. Furthermore, from system (2), it can be shown that $\lim\limits_{m\to\infty}H_n^m=H^*$, $\lim\limits_{m\to\infty}I_n^m=I^*$, $\lim\limits_{m\to\infty}D_n^m=D^*$, $\lim\limits_{m\to\infty}V_n^m=V^*$, for all $n\in\{0,1,...,N\}$, which implies that E^* of system (2) is globally asymptotically stable. This completes the proof.

4. Application and Numerical Simulations

In this section, we apply our theoretical results obtained within the preceding sections to the subsequent model:

$$\begin{aligned}
\frac{H_n^{m+1}-H_n^m}{\Delta t} &= s-\mu H_n^{m+1}-\frac{k_1 H_n^{m+1}V_n^m}{1+b_1V_n^m}-\frac{k_2 H_n^{m+1}I_n^m}{1+b_2I_n^m},\\
\frac{I_n^{m+1}-I_n^m}{\Delta t} &= e^{-\alpha_1\tau_1}\left[\frac{k_1 H_n^{m-m_1+1}V_n^{m-m_1}}{1+b_1V_n^{m-m_1}}+\frac{k_2 H_n^{m-m_1+1}I_n^{m-m_1}}{1+b_2I_n^{m-m_1}}\right]-\delta I_n^{m+1},\\
\frac{D_n^{m+1}-D_n^m}{\Delta t} &= d_D\triangle D+ae^{-\alpha_2\tau_2}I_n^{m-m_2+1}-(\beta+\delta)D_n^{m+1}, \qquad (8)\\
\frac{V_n^{m+1}-V_n^m}{\Delta t} &= d_V\triangle V+\beta e^{-\alpha_3\tau_3}D_n^{m-m_3+1}-cV_n^{m+1},
\end{aligned}$$

where k_1 and k_2 denote the virus-to-cell infection and therefore the cell-to-cell transmission rates. The non-negative constants b_1 and b_2 measure the saturation effect. The other state variables and parameters have an equivalent biological meanings as in system (1). As before, we consider model (8) with initial conditions

$$\begin{aligned}
&H_n^s=\phi_1(x_n,t_s)\geq 0,\ \ I_n^s=\phi_2(x_n,t_s)\geq 0, \qquad (9)\\
&D_n^s=\phi_3(x_n,t_s)\geq 0,\ \ V_n^s=\phi_4(x_n,t_s)\geq 0,
\end{aligned}$$

for $n\in\{0,1,...,N\}$ and $s\in\{-p,-p+1,...,0\}$, where $p=\max\{m_1,m_2,m_3\}$. In addition, the discrete boundary conditions are given by

$$V_{-1}^m=V_0^m,\ \ V_{N+1}^m=V_N^m,\ \ D_{-1}^m=D_0^m \ \text{ and } \ D_{N+1}^m=D_N^m \ \text{ for } m\in\mathbb{N}. \qquad (10)$$

The problem $(8)-(10)$ is a particular case of system $(2)-(4)$ with $f(H,I,V)=\dfrac{k_1H}{1+b_1V}$ and $g(H,I)=\dfrac{k_2H}{1+b_2I}$.

On the other hand, the hypotheses $(H_0)-(H_4)$ are satisfied and the basic reproduction number of system (8) is given by

$$\mathscr{R}_0=\frac{a\beta k_1 s e^{-\alpha_1\tau_1-\alpha_2\tau_2-\alpha_3\tau_3}}{\delta\mu c(\beta+\delta)}+\frac{k_2 s e^{-\alpha_1\tau_1}}{\delta\mu}.$$

Therefore, by applying Theorems 2 and 3, we conclude the following result.

Corollary 1.

(i): *If $\mathscr{R}_0 \leq 1$, then the infection-free equilibrium E_f of system $(8)-(10)$ is globally asymptotically stable.*

(ii): *If $\mathscr{R}_0 > 1$, then the infection-free equilibrium E_f becomes unstable and the chronic infection equilibrium E^* of $(8)-(10)$ is globally asymptotically stable.*

For numerical simulations, we consider $\Omega = [0,50]$, $d_D = 0.005$, $d_V = 0.001$, $\Delta t = 0.1$ and $\Delta x = 0.5$. Also, we choose the following parameter values: $s = 100$, $\mu = 0.14$, $\delta = 0.5$, $b_1 = 0.00001$, $b_2 = 0.0001$, $\alpha_1 = 0.0139$, $\alpha_2 = 0.65$, $\alpha_3 = 0.001$, $a = 0.002$, $\beta = 2$, $c = 3$, $\tau_1 = 2.5$, $\tau_2 = 3.5$, $\tau_3 = 4.5$, $k_1 = 10^{-6}$, $k_2 = 3 \times 10^{-5}$. By a simple computation, we have $\mathscr{R}_0 = 0.0414 < 1$. Hence, system (8) features an infection-free equilibrium $E_f(701.1449,0,0,0)$. From Corollary 1, E_f is globally asymptotically stable, which suggests that the virus is cleared, the infection dies out and therefore the patient are going to be completely cured (see, Fig. 1).

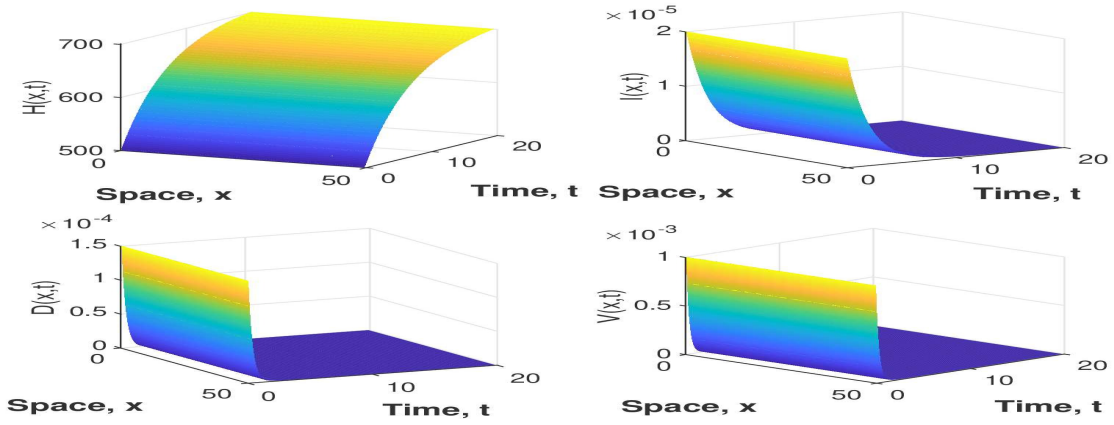

FIGURE 1. Stability of the infection-free equilibrium E_f.

Next, we choose $s = 1.3 \times 10^{2.8}$, $\mu = 0.023$, $\delta = 0.53$, $b_1 = 0.01$, $b_2 = 0.0001$, $a = 150$, $\beta = 0.87$, $c = 3.8$, $\tau_1 = 4.5$, $\tau_2 = 2.5$, $\tau_3 = 1.5$ and that we keep the opposite parameter values. During this case, $\mathscr{R}_0 = 1.8963 > 1$ and system (8) has a unique chronic infection equilibrium $E^*(2.0007 \times 10^4, 6.382 \times 10^2, 1.6059 \times 10^4, 3.21 \times 10^3)$. By Corollary 1, we deduce that E^* is globally asymptotically stable, which suggests that the virus persists within the host and therefore the infection becomes chronic (see, Fig. 2).

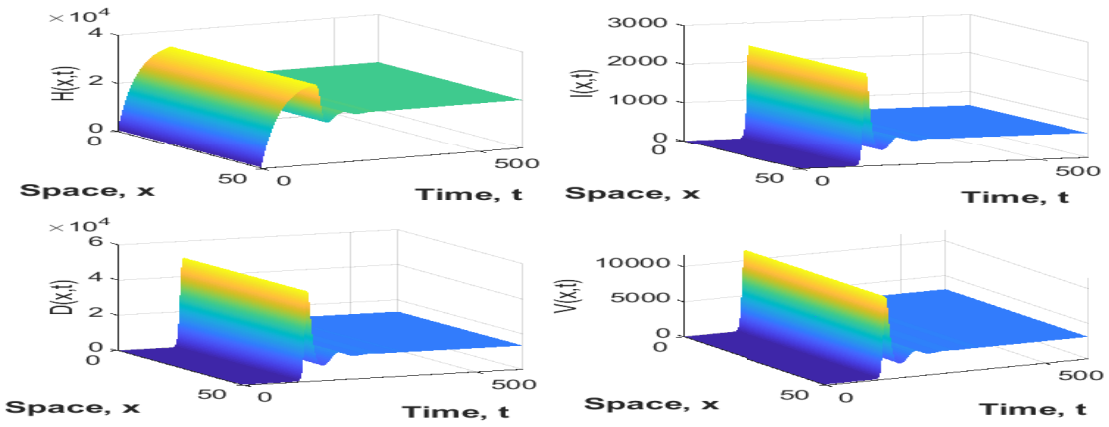

FIGURE 2. Stability of the chronic infection equilibrium E^*.

5. CONCLUSION

In this paper, we have proposed a numerical method to discretize a continuous model for HBV infection with multi-delays and two modes of transmission. We firstly proved that the proposed numerical method preserves the nonnegativity and boundedness of solutions. In addition, we have proved that the numerical method also preserves the global dynamics of the corresponding continuous system for any spacial and temporal step sizes.

Furthermore, the numerical method and results investigated in [8, 18, 19, 20] are improved and extended. On the other hand, the study of this article is based on a continuous model which neglects the memory effect and considers only the derivative of integer order. It will be interesting to study the memory effect on the dynamics of HBV infection by using the generalized Hattaf fractional derivative with non-singular kernel presented in [24] instead of the classical derivative used in (1). This will be done in our future work.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests.

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