

## ARTICLE TYPE

# Dynamics of an Intra-host Diffusive Pathogen Infection Model

Shohel Ahmed\* | Shah Abdullah Al Nahian

<sup>1</sup>Department of Mathematics, Bangladesh University of Engineering and Technology, Dhaka-1000, Bangladesh

**Correspondence**

\*Shohel Ahmed, Department of Mathematics, Bangladesh University of Engineering and Technology, Dhaka-1000, Bangladesh. Email: shohel2443@math.buet.ac.bd

**Summary**

In this paper, we first propose a diffusive pathogen infection model with general incidence rate which incorporates cell-to-cell transmission. By applying the theory of monotone dynamical systems, we prove that the model admits the global threshold dynamics in terms of the basic reproduction number ( $\mathcal{R}_0$ ), which is defined by the spectral radius of the next generation operator. Then, we derive a discrete counterpart of the continuous model by nonstandard finite difference scheme. The results show that the discrete model preserves the positivity and boundedness of solutions in order to ensure the well-posedness of the problem. Moreover, this method preserves all equilibria of the original continuous model. By constructing appropriate Lyapunov functionals for both models, we show that the global threshold dynamics is completely determined by the basic reproduction number. Further, with the help of sensitivity analysis we also have identified the most sensitive parameters which effectively contribute to change the disease dynamics. Finally, we conclude the paper by an example and numerical simulations to improve and generalize some known results.

**KEYWORDS:**

Mathematical Modelling, Stability Analysis, Nonstandard finite difference, General nonlinear incidence, Cell-to-cell transmission, Lyapunov function

## 1 | INTRODUCTION

Over the past few decades, there has been a great effort in the mathematical modelling of within-host pathogen infection models. These models have been used to describe the dynamics inside the host of various infectious diseases such as HIV, HCV, HBV and HTLV, etc. The classical model for within-host virus dynamics is a system of three ordinary differential equations<sup>1,2</sup>, where the key assumption is that cells and viruses are well mixed, and ignores the mobility of viruses. To study the influences of spatial structures of virus dynamics, Wang and Wang<sup>3</sup> proposed the following diffusive system by assuming the motion of virus follows the Fickian diffusion<sup>4</sup>

$$\begin{cases} \frac{\partial S(x,t)}{\partial t} = \Lambda - \beta_1 SV - d_S S, \\ \frac{\partial I(x,t)}{\partial t} = \beta_1 SV - d_I I, \\ \frac{\partial V(x,t)}{\partial t} = D_3 \Delta V + \alpha I - d_V V. \end{cases} \quad (1)$$

where  $S$ ,  $I$  and  $V$  are the concentrations of susceptible or uninfected cells, infected cells and free pathogens at the position  $x$  at time  $t$ , respectively. The susceptible cells are produced at a constant rate  $\Lambda$  and are infected by free virions at a rate  $\beta_1 SV$ .

Parameters  $d_S$ ,  $d_I$  and  $d_V$  represent the death rates of uninfected cells, infected cells and free virus, respectively. The free virions are produced from the infected cells at a rate  $\alpha I$ .  $D_3$  is the diffusion coefficient and  $\Delta$  is the Laplacian operator.

Notice that the above system (1) only focus on virus-to-cell spread in the bloodstream even though some literatures reveal that cell-to-cell (infected source cell and a susceptible target cell) transmission is vital to spread of virus in vivo<sup>5,6,7,8</sup>. An understanding of viral cell-to-cell spreading will enhance our ability to intervene in the efficient spreading of viral infections. For more information on dealing with target cell dynamics and cell-to-cell transmission one can refer<sup>9,10,11,12,13,14,15,16,17</sup> and references therein. On the other hand, the bilinear incidence rate is a simple description of the infection in system (1). As mentioned in<sup>14,18</sup>, a general incidence rate may help us to gain the unification theory by the omission of unessential details. Hence, inspired by the aforementioned work, in this article we propose the following pathogen infection model on domain  $Q = \mathbb{R}^+ \times \Omega$ ,

$$\begin{cases} \frac{\partial S(x,t)}{\partial t} = D_1 \Delta S + \Lambda - Sf(V) - Sg(I) - d_S S, & x \in \Omega, t > 0, \\ \frac{\partial I(x,t)}{\partial t} = D_2 \Delta I + Sf(V) + Sg(I) - (\gamma + d_I)I, & x \in \Omega, t > 0, \\ \frac{\partial V(x,t)}{\partial t} = D_3 \Delta V + \alpha I - d_V V, & x \in \Omega, t > 0. \end{cases} \quad (2)$$

Here  $D_1$  and  $D_2$  are the diffusion coefficients of susceptible and infected cells, respectively<sup>19</sup> with  $\gamma$  is the lysis rate of infected cells<sup>20</sup>. The incidences are assumed to be the nonlinear responses to the concentrations of virus particles and infected cells, taking the forms  $Sf(V)$  and  $Sg(I)$ , where  $f(V)$  and  $g(I)$  denote the force of infection by virus particles and infected cells and satisfy the following properties<sup>21</sup>:

(C1)  $f(0) = g(0) = 0$  and  $f(V), g(I) > 0$ , for  $V, I > 0$ ;

(C2)  $f'(V), g'(I) < 0$  and  $f''(V), g''(I) \leq 0$ , for  $V, I \geq 0$ .

Based on condition (C1) and (C2), it follows from the Mean Value Theorem that

$$f'(V)V \leq f(V) \leq f'(0)V, \quad g'(I)I \leq g(I) \leq g'(0)I, \quad \text{for } V, I \geq 0 \quad (3)$$

Biologically, condition (C1) and (C2) indicates that: (i) the disease cannot spread if there is no infection; (ii) the incidences  $Sf(V)$  and  $Sg(I)$  become faster as the densities of the virus particles and infected cells increase; (iii) the per capita infection rates by virus particles and infected cells will slow down due to certain inhibition effect since (3) implies that  $\left(\frac{f(V)}{V}\right)' \leq 0$

and  $\left(\frac{g(I)}{I}\right)' \leq 0$ . Obviously, the incidence rate with above conditions contains the bilinear and the saturation incidences such as  $f(V) = \beta_1 V$  or  $\frac{\beta_1 V}{1+V}$  and  $g(I) = \beta_2 I$  or  $\frac{\beta_2 I}{1+I}$ , where incidence rates  $\beta_1, \beta_2 > 0$ . In this paper, we consider the system (2) with initial conditions as follows

$$S(x, 0) = \varphi_1(x) \geq 0, \quad I(x, 0) = \varphi_2(x), \quad V(x, 0) = \varphi_3(x), \quad x \in \Omega, \quad (4)$$

where  $S_0(x), I_0(x), V_0(x) \in C^2(\Omega) \cap C^0(\overline{\Omega})$ , and homogeneous Neumann boundary conditions

$$\frac{\partial S}{\partial \nu} = \frac{\partial I}{\partial \nu} = \frac{\partial V}{\partial \nu} = 0, \quad x \in \partial\Omega, \quad t > 0, \quad (5)$$

where  $\Omega$  is an open bounded subset of  $\mathbb{R}^n$  with piecewise smooth boundary  $\partial\Omega$  and  $\nu$  being the unit outer normal to  $\partial\Omega$ .

Generally, the exact solution for a system like (2) is difficult or even impossible to be determined. It is a natural requirement of an adequate numerical method that it possess the discrete equivalents of the qualitative properties the continuous system satisfies. However, how to select the proper discrete scheme so that the global dynamics of solutions of the corresponding continuous models can be efficiently preserved is still an open problem<sup>22</sup>. Actually, Mickens has made an attempt in this regard, by proposing a robust non-standard finite difference (NSFD) scheme<sup>23</sup>, which has been widely employed in the study of different

models<sup>24,25,26,27,28,29</sup>. Motivated by the work of<sup>23</sup>, we apply the NSFD scheme to discretize system (2) and obtain

$$\begin{cases} \frac{S_n^{k+1} - S_n^k}{\Delta t} = D_1 \frac{S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}}{(\Delta x)^2} + \Lambda - S_n^{k+1} f(V_n^k) - S_n^{k+1} g(I_n^k) - d_S S_n^{k+1}, \\ \frac{I_n^{k+1} - I_n^k}{\Delta t} = D_2 \frac{I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1}}{(\Delta x)^2} + S_n^{k+1} f(V_n^k) + S_n^{k+1} g(I_n^k) - (\gamma + d_I) I_n^{k+1}, \\ \frac{V_n^{k+1} - V_n^k}{\Delta t} = D_3 \frac{V_{n+1}^{k+1} - 2V_n^{k+1} + V_{n-1}^{k+1}}{(\Delta x)^2} + \alpha I_n^{k+1} - d_V V_n^{k+1}. \end{cases} \quad (6)$$

Here, we set the spatial domain  $x \in \Omega = [a, b]$  where  $a, b \in \mathbb{R}$  and  $\Delta x = (b - a)/M$  be the space step-size generating  $M$  equal sub-interval over the domain and the length of uniform time intervals be  $\Delta t$ . We denote approximations of  $S(x_n, t_k)$ ,  $I(x_n, t_k)$  and  $V(x_n, t_k)$  by  $S_n^k$ ,  $I_n^k$  and  $V_n^k$ , respectively at each mesh point  $\{(x_n, t_k), n \in \{0, 1, \dots, M\}, k \in \mathbb{N}\}$  with  $x_n = a + n\Delta x$  and  $t_k = k\Delta t$ . The discrete initial and boundary conditions

$$S_n^0 = \varphi_1(x_n) > 0, \quad I_n^0 = \varphi_2(x_n) > 0 \quad \text{and} \quad V_n^0 = \varphi_3(x_n) > 0 \quad (7)$$

and

$$S_{-1}^k = S_0^k, \quad S_M^k = S_{M+1}^k, \quad I_{-1}^k = I_0^k, \quad I_M^k = I_{M+1}^k, \quad V_{-1}^k = V_0^k, \quad V_M^k = V_{M+1}^k, \quad (8)$$

respectively. Our aim is to show that the discretized system (6) which derived by using NSFD scheme can efficiently preserves the global asymptotic stability of the equilibria to the original system (2). The rest of this paper is organized as follows. In Section 2, we study the dynamical behavior of the continuous system (2), such as the existence of positive solutions and its uniqueness, the existence of equilibria, basic reproduction number, local stability and global stability. In Section 3, we investigate the global dynamics of discrete system (6). Numerical simulations are carried out to validate the theoretical results in section 4 and a brief conclusion finishes the paper.

## 2 | DYNAMICAL BEHAVIOR OF THE CONTINUOUS SYSTEM

### 2.1 | Existence, Uniqueness and Positivity

To discuss the dynamical behavior of system (2), first we give the definition of upper and lower solution.

**Definition 1.** Let  $(\hat{S}, \hat{I}, \hat{V})$  and  $(\check{S}, \check{I}, \check{V})$  in  $C(\bar{\Omega} \times [0, \infty)) \cap C^{1,2}(\Omega \times [0, \infty))$  are a pair of upper and lower solution to the problem (2), if  $\check{S} \leq \hat{S}$ ,  $\check{I} \leq \hat{I}$ ,  $\check{V} \leq \hat{V}$  in  $\bar{\Omega} \times [0, \infty)$  and the following differential inequalities hold:

$$\begin{aligned} \frac{\partial \hat{S}(x, t)}{\partial t} &\geq D_1 \Delta \hat{S} + \Lambda - \hat{S} f(\check{V}) - \hat{S} g(\check{I}) - d_S \hat{S}, \\ \frac{\partial \hat{I}(x, t)}{\partial t} &\geq D_2 \Delta \hat{I} + \hat{S} f(\hat{V}) + \hat{S} g(\hat{I}) - (\gamma + d_I) \hat{I}, \\ \frac{\partial \hat{V}(x, t)}{\partial t} &\geq D_3 \Delta \hat{V} + \alpha \hat{I} - d_V \hat{V}, \\ \frac{\partial \check{S}(x, t)}{\partial t} &\leq D_1 \Delta \check{S} + \Lambda - \check{S} f(\hat{V}) - \check{S} g(\hat{I}) - d_S \check{S}, \\ \frac{\partial \check{I}(x, t)}{\partial t} &\leq D_2 \Delta \check{I} + \check{S} f(\check{V}) + \check{S} g(\check{I}) - (\gamma + d_I) \check{I}, \\ \frac{\partial \check{V}(x, t)}{\partial t} &\leq D_3 \Delta \check{V} + \alpha \check{I} - d_V \check{V}, \end{aligned}$$

for  $(x, t) \in \Omega \times (0, \infty)$  and

$$\begin{aligned} \frac{\partial \check{S}}{\partial \nu} \leq 0 \leq \frac{\partial \hat{S}}{\partial \nu}, \quad \frac{\partial \check{I}}{\partial \nu} \leq 0 \leq \frac{\partial \hat{I}}{\partial \nu}, \quad \frac{\partial \check{V}}{\partial \nu} \leq 0 \leq \frac{\partial \hat{V}}{\partial \nu}, \quad (x, t) \in \partial\Omega \times (0, \infty), \\ \check{S}(x, t) \leq \varphi_1(x, t) \leq \hat{S}(x, t), \quad \check{I}(x, t) \leq \varphi_2(x, t) \leq \hat{I}(x, t), \\ \check{V}(x, t) \leq \varphi_3(x, t) \leq \hat{V}(x, t), \quad (x, t) \in \bar{\Omega} \times (0, \infty). \end{aligned}$$

It is easy to see that  $\mathbf{0} = (0, 0, 0)$  and  $\mathbf{K} = (K_1, K_2, K_3)$  are a pair of coupled lower-upper solutions to problem (2), where

$$\begin{aligned} M_1 &= \max \left\{ \frac{\Lambda}{d}, \|\varphi_1\|_{C(\bar{\Omega}, \mathbb{R})} \right\}, \\ M_2 &= \max \left\{ \frac{\Lambda}{d}, \|\varphi_2\|_{C(\bar{\Omega}, \mathbb{R})} \right\}, \\ M_3 &= \max \left\{ \frac{\alpha\Lambda}{d_V d}, \|\varphi_1\|_{C(\bar{\Omega}, \mathbb{R})} \right\} \end{aligned}$$

and  $d = \min\{d_S, d_I\}$ . Using the following lemma provided by Redinger<sup>30</sup>, we get the existence and uniqueness of the solution.

**Lemma 1.** Let  $\hat{U}$  and  $\check{U}$  be a pair of coupled upper and lower solutions for problem (2) and suppose that the initial functions  $\varphi_i, (i = 1, 2, 3)$  are Hölder continuous in  $\bar{\Omega}$ . Then problem (2) has exactly one regular solution  $U(x, t) = (S(x, t), I(x, t), V(x, t))$  satisfying  $\check{U} \leq U \leq \hat{U}$  in  $\bar{\Omega} \times [0, \infty)$ .

Hence,  $0 \leq S(x, t) \leq M_1, 0 \leq I(x, t) \leq M_2, 0 \leq V(x, t) \leq M_3$  for  $(x, t) \in \bar{\Omega} \times [0, \infty)$ . And also, by the maximum principle, if  $\varphi_i(x, 0) \neq 0, (i = 1, 2, 3)$ , we have  $S(x, t) > 0, I(x, t) > 0, V(x, t) > 0$  for all  $t > 0, x \in \bar{\Omega}$ .

## 2.2 | Equilibria and Basic reproduction number

It is easy to verify that system (2) always has a disease-free equilibrium  $E_0(S_0, 0, 0)$  with  $S_0 = \frac{\Lambda}{d_S}$ , and if exists the endemic equilibrium  $E^*(S^*, I^*, V^*)$  satisfies

$$\begin{cases} \Lambda - Sf(V) - Sg(I) - d_S S = 0, \\ Sf(V) + Sg(I) - (\gamma + d_I)I = 0, \\ \alpha I - d_V V = 0. \end{cases} \quad (9)$$

In order to find the basic reproduction number ( $\mathcal{R}_0$ ) for the system (2), we obtain the following linear system at  $E_0$  for the infected classes:

$$\begin{cases} \frac{\partial I(x, t)}{\partial t} = D_2 \Delta I + S_0 f'(0)V + S_0 g'(0)I - (\gamma + d_I)I, & x \in \Omega, t > 0, \\ \frac{\partial V(x, t)}{\partial t} = D_3 \Delta V + \alpha I - d_V V, & x \in \Omega, t > 0, \\ \frac{\partial I}{\partial \nu} = \frac{\partial V}{\partial \nu} = 0, & x \in \partial\Omega, t > 0. \end{cases} \quad (10)$$

Substituting  $I(x, t) = e^{\lambda t} \psi_2(x)$  and  $V(x, t) = e^{\lambda t} \psi_3(x)$  into (10), we obtain the following cooperative eigenvalue problem:

$$\begin{cases} \lambda \psi_2(x) = D_2 \Delta \psi_2(x) + S_0 f'(0) \psi_3(x) + S_0 g'(0) \psi_2(x) - (\gamma + d_I) \psi_2(x), & x \in \Omega, \\ \lambda \psi_3(x) = D_3 \Delta \psi_3(x) + \alpha \psi_2(x) - d_V \psi_3(x), & x \in \Omega, \\ \frac{\partial \psi_2(x)}{\partial \nu} = \frac{\partial \psi_3(x)}{\partial \nu} = 0, & x \in \partial\Omega. \end{cases} \quad (11)$$

By<sup>31</sup>(Theorem 7.6.1), we conclude that (11) has a principal eigenvalue  $\lambda(S_0, f'(0), g'(0))$  with a positive eigenfunction. Now we are in a position to apply the ideas and the theory in<sup>32</sup> to define  $\mathcal{R}_0$  for the model (2). Let  $\tilde{T} : C(\bar{\Omega}, \mathbb{R}^2) \rightarrow C(\bar{\Omega}, \mathbb{R}^2)$  be the solution semigroup of the following reaction-diffusion system:

$$\begin{cases} \frac{\partial I(x, t)}{\partial t} = D_2 \Delta I - (\gamma + d_I)I, & x \in \Omega, t > 0, \\ \frac{\partial V(x, t)}{\partial t} = D_3 \Delta V + \alpha I - d_V V, & x \in \Omega, t > 0, \\ I(x, 0) = \psi_2(x), V(x, 0) = \psi_3(x), & x \in \Omega, t > 0, \\ \frac{\partial I}{\partial \nu} = \frac{\partial V}{\partial \nu} = 0, & x \in \partial\Omega. \end{cases} \quad (12)$$

Thus, with initial infection  $\Psi(x) = (\psi_2(x), \psi_3(x))$ , the distribution of those infection members becomes  $\tilde{T}(t)\Psi(x)$  as time evolves. As in<sup>32</sup>, the matrices  $F$  and  $V$  defined as

$$F(x) = \begin{pmatrix} S_0 g'(0) & S_0 f'(0) \\ 0 & 0 \end{pmatrix}, \quad V(x) = \begin{pmatrix} \gamma + d_I & 0 \\ -\alpha & d_V \end{pmatrix}.$$

Therefore, the distribution of total new infections is

$$\int_0^{\infty} F(x)\tilde{T}(t)\Psi(x)dt,$$

Then, we define

$$L(\Psi)(x) := \int_0^{\infty} F(x)\tilde{T}(t)\Psi(x)dt = F(x) \int_0^{\infty} \tilde{T}(t)\Psi(x)dt.$$

It is clear that  $L$  is a positive and continuous operator which maps the initial infection distribution  $\Psi$  to the distribution of the total infective members produced during the infection period. Applying the idea of next generation operators<sup>32</sup>, we define the spectral radius of  $L$  as the basic reproduction number

$$\mathcal{R}_0 := \rho(L).$$

By some calculations, we obtain that

$$\mathcal{R}_0 = \frac{S_0 \alpha f'(0)}{d_V(\gamma + d_I)} + \frac{S_0 g'(0)}{(\gamma + d_I)} := \mathcal{R}_{01} + \mathcal{R}_{02},$$

where  $\mathcal{R}_{01}$  and  $\mathcal{R}_{02}$  are partial basic reproduction numbers induced by virus-to-cell transmission and cell-to-cell transmission, respectively. The following theorem now prove regarding the meaningful steady states.

**Theorem 1.** If  $\mathcal{R}_0 < 1$ , then the disease-free equilibrium  $E_0(S_0, 0, 0)$  is the only equilibrium of the system (2); when  $\mathcal{R}_0 > 1$ , it also has a unique endemic equilibrium  $E^*(S^*, I^*, V^*)$  where

$$S^* = \frac{\Lambda - (\gamma + d_I)I^*}{d_S} \quad \text{and} \quad V^* = \frac{\alpha I^*}{d_V}$$

*Proof.* It is easy to proof for the case  $\mathcal{R}_0 < 1$ . Consider  $\mathcal{R}_0 > 1$ , it follows from (9) that

$$S = \frac{\Lambda - (\gamma + d_I)I}{d_S} \quad \text{and} \quad V = \frac{\alpha I}{d_V}$$

Let

$$\mathcal{G}(I) = \frac{\Lambda - (\gamma + d_I)I}{d_S} \left( f\left(\frac{\alpha I}{d_V}\right) + g(I) \right) - (\gamma + d_I)I.$$

With  $\mathcal{G}(0) = 0$ ,  $\mathcal{G}'\left(\frac{\Lambda}{\gamma + d_I}\right) = -\Lambda < 0$  and

$$\mathcal{G}'(0) = \frac{\Lambda}{d_S} \left( \frac{\alpha}{d_V} f'(0) + g'(0) \right) - (\gamma + d_I) = (\gamma + d_I)(\mathcal{R}_0 - 1) > 0,$$

Hence, equation  $\mathcal{G}(I) = 0$  has at least one positive root  $I^* \in \left(0, \frac{\Lambda}{\gamma + d_I}\right)$ . That implies the existence of positive equilibrium of the system (2). In order to show that the positive equilibrium is unique, we use

$$\begin{aligned} S^* f(V^*) + S^* g(I^*) &= (\gamma + d_I)I^*, \\ \alpha I^* &= d_V V^*. \end{aligned}$$

Then

$$\begin{aligned} \mathcal{G}'(I^*) &= -\frac{\gamma + d_I}{d_S} \left( f\left(\frac{\alpha I^*}{d_V}\right) + g(I^*) \right) + S^* \left( \frac{\alpha}{d_V} f'\left(\frac{\alpha I^*}{d_V}\right) + g'(I^*) \right) - (\gamma + d_I) \\ &= -\frac{\gamma + d_I}{d_S} \left( f\left(\frac{\alpha I^*}{d_V}\right) + g(I^*) \right) + \frac{S^*}{I^*} \left( \frac{\alpha I^*}{d_V} f'\left(\frac{\alpha I^*}{d_V}\right) - f\left(\frac{\alpha I^*}{d_V}\right) + I^* g'(I^*) - g(I^*) \right). \end{aligned}$$

According to equation (3), we have

$$V f'(V) \leq f(V) \quad \text{and} \quad I g'(I) \leq g(I), \quad \text{for } V, I \geq 0 \quad (13)$$

which implies that  $\mathcal{G}'(I^*) < 0$ . If there exists the second positive equilibrium  $E^\circ(S^\circ, I^\circ, V^\circ)$ , then one has  $\mathcal{G}'(I^\circ) < 0$ . But which contradict the conditions (13). This completes the proof.  $\square$

## 2.3 | Local Stability

Let  $0 = \mu_0 < \mu_i < \mu_{i+1}, i = 1, 2, \dots$  be the eigenvalues of  $-\Delta$  on  $\Omega$  with homogeneous Neumann boundary condition,  $E(\mu_i)$  the space of eigenfunctions corresponding to  $\mu_i$  and  $\{\phi_{ij} : j = 1, 2, \dots, \dim E(\mu_i)\}$  an orthogonal basis of  $E(\mu_i)$ . Then  $\mathbb{X} = [C^1(\bar{\Omega})]^3$  can be decomposed as

$$\mathbb{X} = \bigoplus_{i=1}^{\infty} \mathbb{X}_i, \quad \mathbb{X}_i = \bigoplus_{j=1}^{\dim E(\mu_i)} \mathbb{X}_{ij}$$

where  $\mathbb{X}_{ij} = \{c\phi_{ij} : c \in \mathbb{R}^3\}$ . Then we can prove the local stability of equilibrium as in<sup>33,34</sup>.

**Theorem 2.** If  $\mathcal{R}_0 < 1$ , then the disease-free equilibrium  $E_0$  of system (2) is locally asymptotically stable.

*Proof.* The linearization of system (2) at  $E_0$  can be expressed by

$$\frac{\partial Z(x, t)}{\partial t} = D\Delta Z(x, t) + \mathcal{A}Z(x, t),$$

where  $Z = (S, I, V)$ ,  $D = \text{diag}(D_1, D_2, D_3)$  and

$$\mathcal{A} = \begin{pmatrix} -d_S & -S_0 g'(0) & -S_0 f'(0) \\ 0 & S_0 g'(0) - (\gamma + d_I) & S_0 f'(0) \\ 0 & \alpha & -d_V \end{pmatrix}.$$

Therefore, the characteristic equation at  $E_0$  is

$$(\lambda + d_S + \mu_i D_1)[(\lambda - S_0 g'(0) + \gamma + d_I + \mu_i D_2)(\lambda + d_V + \mu_i D_3) - \alpha S_0 f'(0)] = 0. \quad (14)$$

It is obvious that (14) has an eigenvalue  $\lambda_1 = -(d_S + \mu_i D_1)$ . The other two eigenvalues  $\lambda_2$  and  $\lambda_3$  are roots of

$$\lambda^2 - [S_0 g'(0) - (\gamma + d_I + \mu_i D_2) - (d_V + \mu_i D_3)]\lambda - (S_0 g'(0) - (\gamma + d_I + \mu_i D_2))(d_V + \mu_i D_3) - \alpha S_0 f'(0) = 0.$$

It is easy to see that

$$\begin{aligned} \lambda_2 + \lambda_3 &= S_0 g'(0) - (\gamma + d_I + \mu_i D_2) - (d_V + \mu_i D_3) \\ &= S_0 g'(0) - (\gamma + d_I + d_V) - \mu_i (D_2 + D_3) \\ &< S_0 g'(0) - (\gamma + d_I) - \mu_i (D_2 + D_3) \\ &= (\gamma + d_I)(\mathcal{R}_{02} - 1) - \mu_i (D_2 + D_3), \end{aligned}$$

and

$$\begin{aligned} \lambda_2 \lambda_3 &= d_V (\gamma + d_I) - d_V S_0 g'(0) - \alpha S_0 f'(0) + \mu_i D_2 (d_V + \mu_i D_3) + \mu_i D_3 (\gamma + d_I - S_0 g'(0)) \\ &= d_V (\gamma + d_I) (1 - \mathcal{R}_0) + \mu_i D_3 (\gamma + d_I) (1 - \mathcal{R}_{02}) + \mu_i D_2 (d_V + \mu_i D_3). \end{aligned}$$

Since  $\mathcal{R}_{02} < \mathcal{R}_0 < 1$ , we have  $\lambda_2 + \lambda_3 < 1$  and  $\lambda_2 \lambda_3 > 0$ . This gives that  $\text{Re}(\lambda_2) < 0$  and  $\text{Re}(\lambda_3) < 0$ . Thus, all eigenvalues of (14) have a negative real parts when  $\mathcal{R}_0 < 1$ . Hence,  $E_0$  is locally asymptotically stable. This completes the proof.  $\square$

Now we turn our attention to the endemic equilibrium  $E^*$ .

**Theorem 3.** If  $\mathcal{R}_0 > 1$ , then the endemic equilibrium  $E^*$  of system (2) is locally asymptotically stable.

*Proof.* Linearizing system (2) at  $E^*$  gives

$$\frac{\partial Z(x, t)}{\partial t} = D\Delta Z(x, t) + BZ(x, t),$$

where

$$B = \begin{pmatrix} -(f(V^*) + g(I^*) + d_S) & -S^* g'(I^*) & -S^* f'(V^*) \\ f(V^*) + g(I^*) & S^* g'(I^*) - (\gamma + d_I) & S^* f'(V^*) \\ 0 & \alpha & -d_V \end{pmatrix}.$$

Thus, the characteristic equation at  $E^*$  is

$$Q(\lambda) = \lambda^3 + Q_2 \lambda^2 + Q_1 \lambda + Q_0 = 0, \quad (15)$$

where

$$\begin{aligned} Q_2 &= f(V^*) + g(I^*) + d_S + \mu_i D_1 - S^* g'(I^*) + \gamma + d_I + \mu_i D_2 + d_V + \mu_i D_3, \\ Q_1 &= (f(V^*) + g(I^*) + d_S + \mu_i D_1)(\gamma + d_I + \mu_i D_2 + d_V + \mu_i D_3) - \alpha S^* f'(V^*) \\ &\quad + (\gamma + d_I + \mu_i D_2)(d_V + \mu_i D_3) - (d_S + \mu_i D_1 + d_V + \mu_i D_3) S^* g'(I^*), \\ Q_0 &= (f(V^*) + g(I^*) + d_S + \mu_i D_1)(\gamma + d_I + \mu_i D_2)(d_V + \mu_i D_3) \\ &\quad - (d_S + \mu_i D_1)[\alpha S^* f'(V^*) + (d_V + \mu_i D_3) S^* g'(I^*)]. \end{aligned}$$

From (9) and (13), we get

$$\begin{aligned} \alpha S^* f'(V^*) &\leq \alpha S^* \frac{f(V^*)}{V^*} = (\gamma + d_I) d_V \frac{f(V^*)}{f(V^*) + g(I^*)}, \\ S^* g'(I^*) &\leq S^* \frac{g(I^*)}{I^*} = (\gamma + d_I) \frac{g(I^*)}{f(V^*) + g(I^*)}. \end{aligned}$$

Hence,

$$\begin{aligned} Q_2 &\geq f(V^*) + g(I^*) + d_S + \mu_i D_1 - (\gamma + d_I) \frac{g(I^*)}{f(V^*) + g(I^*)} + \gamma + d_I + \mu_i D_2 + d_V + \mu_i D_3 \\ &= f(V^*) + g(I^*) + d_S + \mu_i D_1 + (\gamma + d_I) \frac{f(V^*)}{f(V^*) + g(I^*)} + \mu_i D_2 + d_V + \mu_i D_3, \\ Q_1 &\geq (f(V^*) + g(I^*) + d_S + \mu_i D_1)(\gamma + d_I + \mu_i D_2 + d_V + \mu_i D_3) - (\gamma + d_I) d_V \frac{f(V^*)}{f(V^*) + g(I^*)} \\ &\quad + (\gamma + d_I + \mu_i D_2)(d_V + \mu_i D_3) - (d_S + \mu_i D_1 + d_V + \mu_i D_3)(\gamma + d_I) \frac{g(I^*)}{f(V^*) + g(I^*)} \\ &= (f(V^*) + g(I^*))(\gamma + d_I + \mu_i D_2 + d_V + \mu_i D_3) + (d_S + \mu_i D_1)(\mu_i D_2 + d_V + \mu_i D_3) \\ &\quad + \mu_i D_2(d_V + \mu_i D_3) + (\gamma + d_I)(d_S + \mu_i D_1 + \mu_i D_3) \frac{f(V^*)}{f(V^*) + g(I^*)}, \end{aligned}$$

and

$$\begin{aligned} Q_0 &\geq (f(V^*) + g(I^*) + d_S + \mu_i D_1)(\gamma + d_I + \mu_i D_2)(d_V + \mu_i D_3) \\ &\quad - (d_S + \mu_i D_1) \left[ (\gamma + d_I) d_V \frac{f(V^*)}{f(V^*) + g(I^*)} + (d_V + \mu_i D_3)(\gamma + d_I) \frac{g(I^*)}{f(V^*) + g(I^*)} \right] \\ &= (f(V^*) + g(I^*))(\gamma + d_I + \mu_i D_2)(d_V + \mu_i D_3) \\ &\quad + (d_S + \mu_i D_1) \left[ \mu_i D_2(d_V + \mu_i D_3) + \mu_i D_3(\gamma + d_I) \frac{f(V^*)}{f(V^*) + g(I^*)} \right] > 0. \end{aligned}$$

Hence,  $Q_2 Q_1 - Q_0 > 0$ . Then, by using Routh-Hurwitz criterion we claim that all eigenvalues of (15) have negative real parts. Thus, the endemic equilibrium  $E^*$  of system (2) is locally asymptotically stable when  $\mathcal{R}_0 > 1$ . This completes the proof.  $\square$

## 2.4 | Global Stability

Now, we discuss the global stability of the equilibria for the system (2) by considering Lyapunov functional based on the Volterra function  $\Phi(x) = x - 1 - \ln x$ . Clearly,  $\Phi(x) \geq 0$  for all  $x > 0$  and the equality holds if and only if  $x = 1$ . In presence of diffusion, the aim is to show that every solution of the system (2) with a positive initial value that is different from the equilibrium point will converge to the equilibrium.

**Theorem 4.** If  $\mathcal{R}_0 \leq 1$ , then the disease-free equilibrium  $E_0$  of system (2) is globally asymptotically stable.

*Proof.* Define a Lyapunov function

$$\mathcal{L}(t) = \int_{\Omega} \mathcal{L}_1(x, t) dx,$$

Where

$$\mathcal{L}_1(x, t) = S_0 \Phi\left(\frac{S(x, t)}{S_0}\right) + I(x, t) + BV(x, t)$$

and  $B$  is a positive constant to be determined later. Then, along the solutions of the system (2), we have

$$\begin{aligned}\frac{\partial \mathcal{L}_1(x, t)}{\partial t} &= \left(1 - \frac{S_0}{S}\right) \frac{\partial S}{\partial t} + \frac{\partial I}{\partial t} + B \frac{\partial V}{\partial t} \\ &= \left(1 - \frac{S_0}{S}\right) (D_1 \Delta S + \Lambda - Sf(V) - Sg(I) - d_S S) \\ &\quad D_2 \Delta I + Sf(V) + Sg(I) - (\gamma + d_I)I + BD_3 \Delta V + B(\alpha I - d_V V).\end{aligned}$$

By equation (3) and choosing  $B = (\gamma + d_I - S_0 g'(0))/\alpha$ , we obtain

$$\begin{aligned}\frac{\partial \mathcal{L}_1(x, t)}{\partial t} &\leq -\frac{d_S}{S} (S_0 - S)^2 + \frac{d_V(\gamma + d_I)}{\alpha} (R_0 - 1)V \\ &\quad + \left(1 - \frac{S_0}{S}\right) D_1 \Delta S + D_2 \Delta I + BD_3 \Delta V.\end{aligned}$$

Using Green's formula and the Neumann boundary conditions in (5), we obtain

$$\int_{\Omega} \left(1 - \frac{S_0}{S}\right) D_1 \Delta S dx = -D_1 \int_{\Omega} \nabla \left(1 - \frac{S_0}{S}\right) \nabla S dx = -D_1 \int_{\Omega} \frac{S_0}{S^2} |\nabla S|^2 dx \leq 0,$$

and

$$\int_{\Omega} \Delta I dx = \int_{\Omega} \Delta V dx = 0.$$

Using above conditions, we obtain

$$\frac{d\mathcal{L}(t)}{dt} = \int_{\Omega} \frac{\partial \mathcal{L}_1(x, t)}{\partial t} dx \leq \int_{\Omega} \left( -\frac{d_S}{S} (S_0 - S)^2 + \frac{d_V(\gamma + d_I)}{\alpha} (R_0 - 1)V - \frac{D_1 S_0}{S^2} |\nabla S|^2 \right) dx$$

Therefore,  $\frac{d\mathcal{L}(t)}{dt} \leq 0$  whenever  $R_0 \leq 1$ . It follows that the largest invariant subset of  $\{\frac{d\mathcal{L}(t)}{dt} = 0\}$  is the singleton  $E_0$ . By LaSalle's Invariance Principle<sup>35</sup>, the infection-free equilibrium of the system (2) is globally asymptotically stable when  $R_0 \leq 1$ .  $\square$

Next, we turn our attention to show the global stability of the endemic equilibrium  $E^*$ .

**Theorem 5.** If  $R_0 > 1$ , then the endemic equilibrium  $E^*$  is globally asymptotically stable by considering a Lyapunov function as

$$\mathcal{H}(t) = \int_{\Omega} \mathcal{H}_1(x, t) dx,$$

with

$$\mathcal{H}_1(x, t) = S^* \Phi\left(\frac{S}{S^*}\right) + I^* \Phi\left(\frac{I}{I^*}\right) + \frac{S^* f(V^*)}{d_V} \Phi\left(\frac{V}{V^*}\right).$$

Note that,  $\mathcal{H}(t)$  is non-negative and is strictly minimized at the unique equilibrium  $(S^*, I^*, V^*)$ , i.e. it is a valid Lyapunov function.

*Proof.* According to (2), we

$$\begin{aligned}\frac{\partial \mathcal{H}_1(x, t)}{\partial t} &= \left(1 - \frac{S^*}{S}\right) \frac{\partial S}{\partial t} + \left(1 - \frac{I^*}{I}\right) \frac{\partial I}{\partial t} + \frac{S^* f(V^*)}{d_V V^*} \left(1 - \frac{V^*}{V}\right) \frac{\partial V}{\partial t} \\ &= \left(1 - \frac{S^*}{S}\right) (D_1 \Delta S + d_S S^* + S^* f(V^*) + S^* g(I^*) - Sf(V) - Sg(I) - d_S S) \\ &\quad + \left(1 - \frac{I^*}{I}\right) (D_2 \Delta I + Sf(V) + Sg(I) - (\gamma + d_I)I) \\ &\quad + \frac{S^* f(V^*)}{d_V V^*} \left(1 - \frac{V^*}{V}\right) (D_3 \Delta V + \alpha I - d_V V)\end{aligned}$$



$$\begin{aligned}
&= \left(1 - \frac{S^*}{S}\right) (d_S S^* - d_S S) + S^* g(I^*) \left(2 - \frac{S^*}{S} + \frac{g(I)}{g(I^*)} - \frac{Sg(I)I^*}{S^*g(I^*)I} - \frac{I}{I^*}\right) \\
&\quad + S^* f(V^*) \left(3 - \frac{S^*}{S} + \frac{f(V)}{f(V^*)} - \frac{Sf(V)I^*}{S^*f(V^*)I} - \frac{V^*I}{VI^*} - \frac{V}{V^*}\right) \\
&\quad + \left(1 - \frac{S^*}{S}\right) D_1 \Delta S + \left(1 - \frac{I^*}{I}\right) D_2 \Delta I + \frac{S^* f(V^*)}{d_V V^*} \left(1 - \frac{V^*}{V}\right) D_3 \Delta V \\
&= -\frac{d_S}{S} (S - S^*)^2 - S^* g(I^*) \left(\Phi\left(\frac{S^*}{S}\right) + \Phi\left(\frac{Sg(I)I^*}{S^*g(I^*)I}\right) + \Phi\left(\frac{I}{I^*}\right) - \Phi\left(\frac{g(I)}{g(I^*)}\right)\right) \\
&\quad - S^* f(V^*) \left(\Phi\left(\frac{S^*}{S}\right) + \Phi\left(\frac{Sf(V)I^*}{S^*f(V^*)I}\right) + \Phi\left(\frac{V^*I}{VI^*}\right) + \Phi\left(\frac{V}{V^*}\right) - \Phi\left(\frac{f(V)}{f(V^*)}\right)\right) \\
&\quad + \left(1 - \frac{S^*}{S}\right) D_1 \Delta S + \left(1 - \frac{I^*}{I}\right) D_2 \Delta I + \frac{S^* f(V^*)}{d_V V^*} \left(1 - \frac{V^*}{V}\right) D_3 \Delta V.
\end{aligned}$$

Using Green's formula and the Neumann boundary conditions in (5), we obtain

$$\int_{\Omega} \left(1 - \frac{S^*}{S}\right) D_1 \Delta S dx = -D_1 \int_{\Omega} \nabla \left(1 - \frac{S^*}{S}\right) \nabla S dx = -D_1 \int_{\Omega} \frac{S^*}{S^2} |\nabla S|^2 dx \leq 0,$$

similarly

$$\int_{\Omega} \left(1 - \frac{I^*}{I}\right) D_2 \Delta I dx = -D_2 \int_{\Omega} \nabla \left(1 - \frac{I^*}{I}\right) \nabla I dx = -D_2 \int_{\Omega} \frac{I^*}{I^2} |\nabla I|^2 dx \leq 0,$$

$$\frac{S^* f(V^*)}{d_V V^*} \int_{\Omega} \left(1 - \frac{V^*}{V}\right) D_3 \Delta V dx = -\frac{D_3 S^* f(V^*)}{d_V V^*} \int_{\Omega} \nabla \left(1 - \frac{V^*}{V}\right) \nabla V dx = -\frac{D_3 S^* f(V^*)}{d_V V^*} \int_{\Omega} \frac{1}{V^2} |\nabla V|^2 dx \leq 0,$$

By assumption (C2), we get

$$\begin{aligned}
\Phi\left(\frac{f(V)}{f(V^*)}\right) - \Phi\left(\frac{V}{V^*}\right) &= \frac{f(V)}{f(V^*)} - \frac{V}{V^*} + \ln\left(\frac{Vf(V^*)}{V^*f(V)}\right) \\
&\leq \frac{f(V)}{f(V^*)} - \frac{V}{V^*} + \frac{Vf(V^*)}{V^*f(V)} - 1 \\
&= \left(\frac{f(V)}{f(V^*)} - \frac{V}{V^*}\right) \left(1 - \frac{f(V^*)}{f(V)}\right) \\
&\leq 0.
\end{aligned}$$

Similarly, we have

$$\Phi\left(\frac{g(I)}{g(I^*)}\right) - \Phi\left(\frac{I}{I^*}\right) \leq \left(\frac{g(I)}{g(I^*)} - \frac{I}{I^*}\right) \left(1 - \frac{g(I^*)}{g(I)}\right) \leq 0.$$

Using above conditions, we conclude that

$$\begin{aligned}
\frac{d\mathcal{H}(t)}{dt} &= \int_{\Omega} \frac{\partial \mathcal{H}_1(x, t)}{\partial t} dx \\
&\leq \int_{\Omega} \left[ -\frac{d_S}{S} (S - S^*)^2 - S^* g(I^*) \left(\Phi\left(\frac{S^*}{S}\right) + \Phi\left(\frac{Sg(I)I^*}{S^*g(I^*)I}\right)\right) \right. \\
&\quad \left. - S^* f(V^*) \left(\Phi\left(\frac{S^*}{S}\right) + \Phi\left(\frac{Sf(V)I^*}{S^*f(V^*)I}\right) + \Phi\left(\frac{V^*I}{VI^*}\right)\right) \right. \\
&\quad \left. - \frac{D_1 S^*}{S^2} |\nabla S|^2 - \frac{D_2 I^*}{I^2} |\nabla I|^2 - \frac{D_3 S^* f(V^*)}{d_V V^2} |\nabla V|^2 \right] dx \\
&\leq 0.
\end{aligned}$$

Furthermore we have  $\frac{d\mathcal{H}(t)}{dt} = 0$  only at steady state  $E^* = (S^*, I^*, V^*)$ . Therefore, by Lyapunov's direct method, the steady state solution  $E^*$  is globally asymptotically stable.  $\square$

### 3 | DYNAMICAL BEHAVIOR OF THE DISCRETIZED MODEL

In preceding section, we have shown that the global asymptotic stability of the equilibria for the continuous system (2) is completely determined by the basic reproduction number ( $\mathcal{R}_0$ ) using appropriate Lyapunov functionals. This arises a natural question that whether the global asymptotic stability of the equilibria of the discrete system (6) can be preserved. In this section, we will discuss this problem. Clearly, the discretized system (6) has the same two steady states as the continuous system (2). In the following theorem, we show the system (6) is non-negative and bounded.

**Theorem 6.** For any  $\Delta t > 0$  and  $\Delta x > 0$ , the solution of system (6)-(8) is non-negative and bounded for all  $k \in \mathbb{N}$ .

*Proof.* The positivity of the solutions of the discretized system (6) can be proved using the M-matrix theory<sup>26</sup>. From the first equation of system (6), we get

$$\mathcal{A}^k S^{k+1} = S^k + \lambda \Delta t,$$

where

$$\mathcal{A}^k = \begin{pmatrix} a_0^k & a & 0 & \cdots & 0 & 0 & 0 \\ a & a_1^k & a & \cdots & 0 & 0 & 0 \\ 0 & a & a_2^k & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & a_{M-2}^k & a & 0 \\ 0 & 0 & 0 & \cdots & a & a_{M-1}^k & a \\ 0 & 0 & 0 & \cdots & 0 & a & a_M^k \end{pmatrix},$$

$\lambda = (\Lambda, \Lambda, \dots, \Lambda)^T$  and the coefficients  $a = -D_1 \Delta t / (\Delta x)^2$ ,  $a_0^k = 1 + D_1 \Delta t / (\Delta x)^2 + \Delta t(f(V_0^k) + g(I_0^k) + d_S)$ ,  $a_M^k = 1 + D_1 \Delta t / (\Delta x)^2 + \Delta t(f(V_M^k) + g(I_M^k) + d_S)$  and  $a_i^k = 1 + 2D_1 \Delta t / (\Delta x)^2 + \Delta t(f(V_i^k) + g(I_i^k) + d_S)$  with  $i = 1, 2, \dots, M-1$ . It is clear that  $\mathcal{A}^k$  is a strictly diagonally dominant matrix. Thus, the first equation of system (6) is equivalent to

$$S^{k+1} = (\mathcal{A}^k)^{-1}(S^k + \lambda \Delta t) > 0.$$

From the second equation of the system (6), we have

$$BI^{k+1} = I^k + \Delta t T^{k+1},$$

where  $T^{k+1} = (S_0^{k+1}(f(V_0^k) + g(I_0^k)), S_1^{k+1}(f(V_1^k) + g(I_1^k)), \dots, S_M^{k+1}(f(V_M^k) + g(I_M^k)))^T$  and

$$B = \begin{pmatrix} b_1 & b_2 & 0 & \cdots & 0 & 0 & 0 \\ b_2 & b_3 & b_2 & \cdots & 0 & 0 & 0 \\ 0 & b_2 & b_3 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & b_3 & b_2 & 0 \\ 0 & 0 & 0 & \cdots & b_2 & b_3 & b_2 \\ 0 & 0 & 0 & \cdots & 0 & b_2 & b_1 \end{pmatrix},$$

with  $b_1 = 1 + D_2 \Delta t / (\Delta x)^2 + \Delta t(\gamma + d_I)$ ,  $b_2 = -D_2 \Delta t / (\Delta x)^2$  and  $b_3 = 1 + 2D_2 \Delta t / (\Delta x)^2 + \Delta t(\gamma + d_I)$ . Since  $B$  is a M-matrix, we get

$$I^{k+1} = B^{-1}(I^k + \Delta t T^{k+1}).$$

Similarly, from the third equation of system (6), we have

$$CV^{k+1} = V^k + \alpha \Delta t I^{k+1},$$

where

$$C = \begin{pmatrix} c_1 & c_2 & 0 & \cdots & 0 & 0 & 0 \\ c_2 & c_3 & c_2 & \cdots & 0 & 0 & 0 \\ 0 & c_2 & c_3 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & \cdots & c_3 & c_2 & 0 \\ 0 & 0 & 0 & \cdots & c_2 & c_3 & c_2 \\ 0 & 0 & 0 & \cdots & 0 & c_2 & c_1 \end{pmatrix}$$

with  $c_1 = 1 + D_3\Delta t/(\Delta x)^2 + d_V\Delta t$ ,  $c_2 = -D_3\Delta t/(\Delta x)^2$  and  $c_3 = 1 + 2D_3\Delta t/(\Delta x)^2 + d_V\Delta t$ . Since  $C$  is a M-matrix, we obtain

$$V^{k+1} = C^{-1}(V^k + \alpha\Delta t I^{k+1}).$$

Since all parameters in the system (6) are positive, it is easy to see that the solution remains non-negative for all  $k \in \mathbb{N}$ .

Next, we prove the boundedness of the solution. Define a sequence  $\{G^k\}$  as follows:

$$Q^k = \sum_{n=0}^M (S_n^k + I_n^k).$$

It follows from the first two equations of system (6) that

$$\begin{aligned} Q^{k+1} - Q^k &= \Lambda(M+1)\Delta t - d_S\Delta t \sum_{n=0}^M S_n^{k+1} - (\gamma + d_I)\Delta t \sum_{n=0}^M I_n^{k+1} \\ &\leq \Lambda(M+1)\Delta t - d\Delta t Q^{k+1}. \end{aligned}$$

where  $d = \min\{d_S, d_I\}$ . Hence, we have

$$Q^{k+1} \leq \frac{\Lambda(M+1)\Delta t}{1 + d\Delta t} + \frac{Q^k}{1 + d\Delta t}.$$

By mathematical induction, we obtain

$$\limsup_{k \rightarrow +\infty} Q^k \leq N(M+1).$$

By the third equation of the system (6), we get

$$\sum_{n=0}^M V_n^{k+1} = \frac{\alpha\Delta t}{1 + d_V\Delta t} \sum_{n=0}^M I_n^{k+1} + \frac{1}{1 + d_V\Delta t} \sum_{n=0}^M V_n^k.$$

Since  $\{G^k\}$  is bounded, there exists a positive constant  $\xi$  such that  $\sum_{n=0}^M I_n^k \leq \xi$ . Thus, we have

$$\limsup_{k \rightarrow +\infty} \sum_{n=0}^M V_n^{k+1} \leq \frac{\alpha\xi}{d_V}.$$

This completes the proof. □

### 3.1 | Global Stability

In this section, we establish the global asymptotic stability of the steady states  $E_0$  and  $E^*$  of the discrete system (6), by constructing discrete Lyapunov functions.

**Theorem 7.** For any  $\Delta t > 0$  and  $\Delta x > 0$ , if  $\mathcal{R}_0 \leq 1$ , then the disease-free equilibrium  $E_0$  of system (6) is globally asymptotically stable.

*Proof.* Define a discrete Lyapunov function as follows

$$\mathcal{L}^k = \sum_{n=0}^M \frac{1}{\Delta t} \left[ S_0 \Phi \left( \frac{S_n^k}{S_0} \right) + (1 + \rho_0\Delta t) I_n^k + \rho_1(1 + \rho_2\Delta t) V_n^k \right],$$

where  $\rho_0$ ,  $\rho_1$  and  $\rho_2$  are positive constant to be determined later. Applying the inequality  $\ln x \leq x - 1$ , the difference of  $\mathcal{L}^k$  satisfies

$$\begin{aligned}\mathcal{L}^{k+1} - \mathcal{L}^k &= \sum_{n=0}^M \frac{1}{\Delta t} \left[ S_n^{k+1} - S_n^k + S_0 \ln \left( \frac{S_n^k}{S_n^{k+1}} \right) + (1 + \rho_0 \Delta t)(I_n^{k+1} - I_n^k) + \rho_1(1 + \rho_2 \Delta t)(V_n^{k+1} - V_n^k) \right] \\ &\leq \sum_{n=0}^M \frac{1}{\Delta t} \left[ \left( 1 - \frac{S_0}{S_n^{k+1}} \right) (S_n^{k+1} - S_n^k) + (1 + \rho_0 \Delta t)(I_n^{k+1} - I_n^k) + \rho_1(1 + \rho_2 \Delta t)(V_n^{k+1} - V_n^k) \right] \\ &= \sum_{n=0}^M \left[ \left( 1 - \frac{S_0}{S_n^{k+1}} \right) (\Lambda - S_n^{k+1} f(V_n^k) - S_n^{k+1} g(I_n^k) - d_S S_n^{k+1}) + S_n^{k+1} f(V_n^k) + S_n^{k+1} g(I_n^k) \right. \\ &\quad \left. - (\gamma + d_I) I_n^{k+1} + \rho_0(I_n^{k+1} - I_n^k) + \rho_1(\alpha I_n^{k+1} - d_V V_n^{k+1}) + \rho_1 \rho_2 (V_n^{k+1} - V_n^k) \right] + \mathcal{R}^k \\ &= \sum_{n=0}^M \left[ -\frac{d_S}{S_n^{k+1}} (S_n^{k+1} - S_0)^2 + S_0 f(V_n^k) + S_0 g(I_n^k) - (\gamma + d_I) I_n^{k+1} + \rho_0(I_n^{k+1} - I_n^k) \right. \\ &\quad \left. + \rho_1(\alpha I_n^{k+1} - d_V V_n^{k+1}) + \rho_1 \rho_2 (V_n^{k+1} - V_n^k) \right] + \mathcal{R}^k,\end{aligned}$$

where

$$\begin{aligned}\mathcal{R}^k &= \sum_{n=0}^M \frac{1}{(\Delta x)^2} \left[ D_1 \left( 1 - \frac{S_0}{S_n^{k+1}} \right) (S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}) + D_2 (I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1}) \right. \\ &\quad \left. + \rho_1 D_3 (V_{n+1}^{k+1} - 2V_n^{k+1} + V_{n-1}^{k+1}) \right] \\ &= \sum_{n=0}^M \frac{1}{(\Delta x)^2} \left[ D_1 (S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}) - S_0 D_1 \left( \frac{S_{n+1}^{k+1}}{S_n^{k+1}} - 2 + \frac{S_{n-1}^{k+1}}{S_n^{k+1}} \right) \right. \\ &\quad \left. + D_2 (I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1}) + \rho_1 D_3 (V_{n+1}^{k+1} - 2V_n^{k+1} + V_{n-1}^{k+1}) \right]\end{aligned}$$

Using the arithmetic-geometric inequality

$$2 - \frac{S_{n+1}^{k+1}}{S_n^{k+1}} - \frac{S_n^{k+1}}{S_{n+1}^{k+1}} \leq 0, \quad \text{for } n \in \{0, 1, \dots, M-1\}, \quad (16)$$

we get

$$\begin{aligned}\mathcal{R}^k &\leq \frac{1}{(\Delta x)^2} \left[ D_1 (S_{M+1}^{k+1} - S_M^{k+1} + S_{-1}^{k+1} - S_0^{k+1}) - S_0 D_1 \left( \frac{S_{-1}^{k+1}}{S_0^{k+1}} - 2 + \frac{S_{M+1}^{k+1}}{S_M^{k+1}} \right) \right. \\ &\quad \left. + D_2 (I_{M+1}^{k+1} - I_M^{k+1} + I_{-1}^{k+1} - I_0^{k+1}) + \rho_1 D_3 (V_{M+1}^{k+1} - V_M^{k+1} + V_{-1}^{k+1} - W_0^{k+1}) \right] \\ &= 0.\end{aligned}$$

By using equation (3), we obtain

$$\begin{aligned}\mathcal{L}^{k+1} - \mathcal{L}^k &\leq \sum_{n=0}^M \left[ -\frac{d_S}{S_n^{k+1}} (S_n^{k+1} - S_0)^2 + S_0 f'(0) V_n^k + S_0 g'(0) I_n^k - (\gamma + d_I) I_n^{k+1} + \rho_0(I_n^{k+1} - I_n^k) \right. \\ &\quad \left. + \rho_1(\alpha I_n^{k+1} - d_V V_n^{k+1}) + \rho_1 \rho_2 (V_n^{k+1} - V_n^k) \right].\end{aligned}$$

Letting  $\rho_0 = S_0 g'(0)$ ,  $\rho_1 = (\gamma + d_I - S_0 g'(0))/\alpha$  and  $\rho_2 = d_V$ , we get

$$\mathcal{L}^{k+1} - \mathcal{L}^k \leq \sum_{n=0}^M \left[ -\frac{d_S}{S_n^{k+1}} (S_n^{k+1} - S_0)^2 + \frac{d_V(\gamma + d_I)}{\alpha} (\mathcal{R}_0 - 1) V_n^k \right].$$

If  $\mathcal{R}_0 \leq 1$ , for all  $k \in \mathbb{N}$  we get

$$\mathcal{L}^{k+1} - \mathcal{L}^k \leq 0,$$

which gives that  $\{\mathcal{L}^k\}_{k \in \mathbb{N}}$  is a monotone decreasing sequence. That means there exists a constant  $\tilde{\mathcal{L}} \geq 0$  such that  $\lim_{k \rightarrow +\infty} \mathcal{L}^k = \tilde{\mathcal{L}}$  and we have  $\lim_{k \rightarrow +\infty} (\mathcal{L}^{k+1} - \mathcal{L}^k) = 0$ . Arguing on the lines of<sup>26</sup> to system (6), we obtain

$$\lim_{k \rightarrow +\infty} S_n^k = S_0, \quad \lim_{k \rightarrow +\infty} I_n^k = 0 \quad \text{and} \quad \lim_{k \rightarrow +\infty} V_n^k = 0,$$

for all  $n \in \{0, 1, \dots, M\}$  and when  $\mathcal{R}_0 \leq 1$ . This completes the proof.  $\square$

Next, we discuss the global stability of the endemic equilibrium  $E^*$  when  $\mathcal{R}_0 > 1$ .

**Theorem 8.** For any  $\Delta t > 0$  and  $\Delta x > 0$ , then the endemic equilibrium  $E^*$  of system (6) is globally asymptotically stable when  $\mathcal{R}_0 > 1$ .

*Proof.* We define the following discretized Lyapunov function

$$\mathcal{H}^k = \sum_{n=0}^M \frac{1}{\Delta t} \left[ S^* \Phi \left( \frac{S_n^k}{S^*} \right) + (I^* + S^* g(I^*) \Delta t) \Phi \left( \frac{I_n^k}{I^*} \right) + \frac{S^* f(V^*)}{d_V} (1 + d_V \Delta t) \Phi \left( \frac{V_n^k}{V^*} \right) \right].$$

Obviously,  $\mathcal{H}^k \geq 0$  for all  $k \in \mathbb{N}$  with the equality holds if and only if  $S_n^k = S^*$ ,  $I_n^k = I^*$  and  $V_n^k = V^*$  for all  $n \in \{0, 1, \dots, M\}$  and  $k \in \mathbb{N}$ . Using  $\ln x \leq x - 1$ , the difference of  $\mathcal{H}^k$  satisfies

$$\begin{aligned} \mathcal{H}^{k+1} - \mathcal{H}^k &= \sum_{n=0}^M \frac{1}{\Delta t} \left[ S_n^{k+1} - S_n^k + S^* \ln \left( \frac{S_n^k}{S_n^{k+1}} \right) + I_n^{k+1} - I_n^k - I^* \ln \left( \frac{I_n^k}{I_n^{k+1}} \right) \right. \\ &\quad + S^* g(I^*) \Delta t \left( \frac{I_n^{k+1}}{I^*} - \frac{I_n^k}{I^*} + \ln \left( \frac{I_n^k}{I_n^{k+1}} \right) \right) + \frac{S^* f(V^*)}{d_V} \left( \frac{V_n^{k+1}}{V^*} - \frac{V_n^k}{V^*} + \ln \left( \frac{V_n^k}{V_n^{k+1}} \right) \right) \\ &\quad \left. + S^* f(V^*) \Delta t \left( \frac{V_n^{k+1}}{V^*} - \frac{V_n^k}{V^*} + \ln \left( \frac{V_n^k}{V_n^{k+1}} \right) \right) \right] \\ &\leq \sum_{n=0}^M \frac{1}{\Delta t} \left[ \left( 1 - \frac{S^*}{S_n^{k+1}} \right) (S_n^{k+1} - S_n^k) + \left( 1 - \frac{I^*}{I_n^{k+1}} \right) (I_n^{k+1} - I_n^k) \right. \\ &\quad + S^* g(I^*) \Delta t \left( \frac{I_n^{k+1}}{I^*} - \frac{I_n^k}{I^*} + \ln \left( \frac{I_n^k}{I_n^{k+1}} \right) \right) + \frac{S^* f(V^*)}{d_V V^*} \left( 1 - \frac{V^*}{V_n^{k+1}} \right) (V_n^{k+1} - V_n^k) \\ &\quad \left. + S^* f(V^*) \Delta t \left( \frac{V_n^{k+1}}{V^*} - \frac{V_n^k}{V^*} + \ln \left( \frac{V_n^k}{V_n^{k+1}} \right) \right) \right] \\ &= \sum_{n=0}^M \left[ \left( 1 - \frac{S^*}{S_n^{k+1}} \right) (\Lambda - S_n^{k+1} f(V_n^k) - S_n^{k+1} g(I_n^k) - d_S S_n^{k+1}) \right. \\ &\quad + \left( 1 - \frac{I^*}{I_n^{k+1}} \right) (S_n^{k+1} f(V_n^k) + S_n^{k+1} g(I_n^k) - (\gamma + d_I) I_n^{k+1}) + \frac{S^* f(V^*)}{d_V V^*} \left( 1 - \frac{V^*}{V_n^{k+1}} \right) (\alpha I_n^{k+1} - d_V V_n^{k+1}) \\ &\quad \left. + S^* g(I^*) \left( \frac{I_n^{k+1}}{I^*} - \frac{I_n^k}{I^*} + \ln \left( \frac{I_n^k}{I_n^{k+1}} \right) \right) + S^* f(V^*) \left( \frac{V_n^{k+1}}{V^*} - \frac{V_n^k}{V^*} + \ln \left( \frac{V_n^k}{V_n^{k+1}} \right) \right) \right] + \mathcal{Z}^k \end{aligned}$$

where

$$\begin{aligned} \mathcal{Z}^k &= \sum_{n=0}^M \frac{1}{(\Delta x)^2} \left[ D_1 \left( 1 - \frac{S^*}{S_n^{k+1}} \right) (S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}) + D_2 \left( 1 - \frac{I^*}{I_n^{k+1}} \right) (I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1}) \right. \\ &\quad \left. + \frac{S^* f(V^*) D_3}{d_V V^*} \left( 1 - \frac{V^*}{V_n^{k+1}} \right) (V_{n+1}^{k+1} - 2V_n^{k+1} + V_{n-1}^{k+1}) \right] \\ &= \sum_{n=0}^M \frac{1}{(\Delta x)^2} \left[ D_1 (S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}) - S^* D_1 \left( \frac{S_{n+1}^{k+1}}{S_n^{k+1}} - 2 + \frac{S_{n-1}^{k+1}}{S_n^{k+1}} \right) \right. \\ &\quad \left. + D_2 (I_{n+1}^{k+1} - 2I_n^{k+1} + I_{n-1}^{k+1}) - I^* D_2 \left( \frac{I_{n+1}^{k+1}}{I_n^{k+1}} - 2 + \frac{I_{n-1}^{k+1}}{I_n^{k+1}} \right) \right] \end{aligned}$$

$$+ \frac{S^* f(V^*) D_3}{d_V V^*} (V_{n+1}^{k+1} - 2V_n^{k+1} + V_{n-1}^{k+1}) - \frac{S^* f(V^*) D_3}{d_V} \left( \frac{V_{n+1}^{k+1}}{V_n^{k+1}} - 2 + \frac{V_{n-1}^{k+1}}{V_n^{k+1}} \right) \Big].$$

Using the similar arithmetic-geometric inequality (16) for  $S$ ,  $I$  and  $V$ , we get

$$\begin{aligned} \mathcal{Z}^k &\leq \frac{1}{(\Delta x)^2} \left[ D_1 (S_{M+1}^{k+1} - S_M^{k+1} + S_{-1}^{k+1} - S_0^{k+1}) - S^* D_1 \left( \frac{S_{-1}^{k+1}}{S_0^{k+1}} - 2 + \frac{S_{M+1}^{k+1}}{S_M^{k+1}} \right) \right. \\ &\quad + D_2 (I_{M+1}^{k+1} - I_M^{k+1} + I_{-1}^{k+1} - I_0^{k+1}) - I^* D_2 \left( \frac{I_{-1}^{k+1}}{I_0^{k+1}} - 2 + \frac{I_{M+1}^{k+1}}{I_M^{k+1}} \right) \\ &\quad \left. + \frac{S^* f(V^*) D_3}{d_V V^*} (V_{M+1}^{k+1} - V_M^{k+1} + V_{-1}^{k+1} - V_0^{k+1}) - \frac{S^* f(V^*) D_3}{d_V} \left( \frac{V_{-1}^{k+1}}{V_0^{k+1}} - 2 + \frac{V_{M+1}^{k+1}}{V_M^{k+1}} \right) \right] \\ &= 0. \end{aligned}$$

By assumption (C2), we have the following inequality

$$\begin{aligned} \Phi \left( \frac{f(V_n^k)}{f(V^*)} \right) - \Phi \left( \frac{V_n^k}{V^*} \right) &= \frac{f(V_n^k)}{f(V^*)} - \frac{V_n^k}{V^*} + \ln \left( \frac{V_n^k f(V^*)}{V^* f(V_n^k)} \right) \\ &\leq \frac{f(V_n^k)}{f(V^*)} - \frac{V_n^k}{V^*} + \frac{V_n^k f(V^*)}{V^* f(V_n^k)} - 1 \\ &= \left( \frac{f(V_n^k)}{f(V^*)} - \frac{V_n^k}{V^*} \right) \left( 1 - \frac{f(V^*)}{f(V_n^k)} \right) \\ &\leq 0. \end{aligned}$$

Similarly, we get

$$\Phi \left( \frac{g(I_n^k)}{g(I^*)} \right) - \Phi \left( \frac{I_n^k}{I^*} \right) \leq \left( \frac{g(I_n^k)}{g(I^*)} - \frac{I_n^k}{I^*} \right) \left( 1 - \frac{g(I^*)}{g(I_n^k)} \right) \leq 0.$$

Hence, using above conditions, we conclude that

$$\begin{aligned} \mathcal{H}^{k+1} - \mathcal{H}^k &= \sum_{n=0}^M \left[ -\frac{d_S}{S_n^{k+1}} (S_n^{k+1} - S^*)^2 - S^* g(I^*) \left( \Phi \left( \frac{S^*}{S_n^{k+1}} \right) + \Phi \left( \frac{S_n^{k+1} g(I_n^k) I^*}{S^* g(I^*) I_n^{k+1}} \right) + \Phi \left( \frac{I_n^k}{I^*} \right) - \Phi \left( \frac{g(I_n^k)}{g(I^*)} \right) \right) \right. \\ &\quad \left. - S^* f(V^*) \left( \Phi \left( \frac{S^*}{S_n^{k+1}} \right) + \Phi \left( \frac{S_n^{k+1} f(V_n^k) I^*}{S^* f(V^*) I_n^{k+1}} \right) + \Phi \left( \frac{V_n^{k+1} I^*}{V_n^{k+1} I^*} \right) + \Phi \left( \frac{V_n^k}{V^*} \right) - \Phi \left( \frac{f(V_n^k)}{f(V^*)} \right) \right) \right] + \mathcal{Z}^k \\ &\leq \sum_{n=0}^M \left[ -\frac{d_S}{S_n^{k+1}} (S_n^{k+1} - S^*)^2 - S^* g(I^*) \left( \Phi \left( \frac{S^*}{S_n^{k+1}} \right) + \Phi \left( \frac{S_n^{k+1} g(I_n^k) I^*}{S^* g(I^*) I_n^{k+1}} \right) \right) \right. \\ &\quad \left. - S^* f(V^*) \left( \Phi \left( \frac{S^*}{S_n^{k+1}} \right) + \Phi \left( \frac{S_n^{k+1} f(V_n^k) I^*}{S^* f(V^*) I_n^{k+1}} \right) + \Phi \left( \frac{V_n^{k+1} I^*}{V_n^{k+1} I^*} \right) \right) \right] \\ &\leq 0. \end{aligned}$$

This implies that  $\mathcal{H}^k$  is a monotone decreasing sequence, then there exists a constant  $\tilde{\mathcal{H}}$  such that  $\lim_{k \rightarrow \infty} \mathcal{H}^k = \tilde{\mathcal{H}}$ , and we have  $\lim_{k \rightarrow \infty} (\mathcal{H}_{k+1} - \mathcal{H}^k) = 0$ . Which conclude that

$$\lim_{k \rightarrow \infty} S_n^k = S^*, \quad \lim_{k \rightarrow \infty} \frac{g(I_n^k) I^*}{g(I^*) I_n^{k+1}} = \lim_{k \rightarrow \infty} \frac{f(V_n^k) I^*}{f(V^*) I_n^{k+1}} = \lim_{k \rightarrow \infty} \frac{V_n^* I_n^{k+1}}{V_n^{k+1} I^*} = 1.$$

By the first equation of system (6), we obtain

$$\begin{aligned} \frac{S_n^{k+1} - S_n^k}{\Delta t} &= D_1 \frac{S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}}{(\Delta x)^2} + \Lambda - S_n^{k+1} f(V_n^k) - S_n^{k+1} g(I_n^k) - d_S S_n^{k+1} \\ &= D_1 \frac{S_{n+1}^{k+1} - 2S_n^{k+1} + S_{n-1}^{k+1}}{(\Delta x)^2} + \Lambda - d_S S_n^{k+1} - I_n^{k+1} \left( \frac{S_n^{k+1} f(V_n^k)}{I_n^{k+1}} + \frac{S_n^{k+1} g(I_n^k)}{I_n^{k+1}} \right). \end{aligned}$$

Taking  $k \rightarrow +\infty$  in the above equality, we have

$$0 = 0 + \Lambda - d_S S^* - \lim_{k \rightarrow +\infty} I_n^{k+1} \left( \frac{S^* f(V^*)}{I^*} + \frac{S^* g(I^*)}{I^*} \right)$$

Using  $\Lambda - d_S S^* = S^* f(V^*) + S^* g(I^*)$ , we have

$$\lim_{k \rightarrow +\infty} I_n^{k+1} = I^*.$$

Similarly, we get

$$\lim_{k \rightarrow +\infty} V_n^k = V^*.$$

This completes the proof.  $\square$

Thus, using the Theorems 7 and 8, we conclude that the discretized system (6) exhibits dynamic consistency with the continuous system (2) as well as the global asymptotic stability of both the uninfected and the infected steady states.

## 4 | NUMERICAL RESULTS

In this section, we present numerical example that illustrate and confirm the findings of this study for the linear incidence function such as  $f(V) = \beta_1 V$  and  $g(I) = \beta_2 I$ . Thus the system (2) becomes

$$\begin{cases} \frac{\partial S(x, t)}{\partial t} = D_1 \Delta S + \Lambda - \beta_1 S V - \beta_2 S I - d_S S, & x \in \Omega, t > 0, \\ \frac{\partial I(x, t)}{\partial t} = D_2 \Delta I + \beta_1 S V + \beta_2 S I - (\gamma + d_I) I, & x \in \Omega, t > 0, \\ \frac{\partial V(x, t)}{\partial t} = D_3 \Delta V + \alpha I - d_V V, & x \in \Omega, t > 0, \\ S(x, 0) = \varphi_1(x) \geq 0, \quad I(x, 0) = \varphi_2(x), \quad V(x, 0) = \varphi_3(x), & x \in \Omega, \\ \frac{\partial S}{\partial \nu} = \frac{\partial I}{\partial \nu} = \frac{\partial V}{\partial \nu} = 0, & x \in \partial\Omega, t > 0, \end{cases} \quad (17)$$

The basic reproduction number of the system (17) is

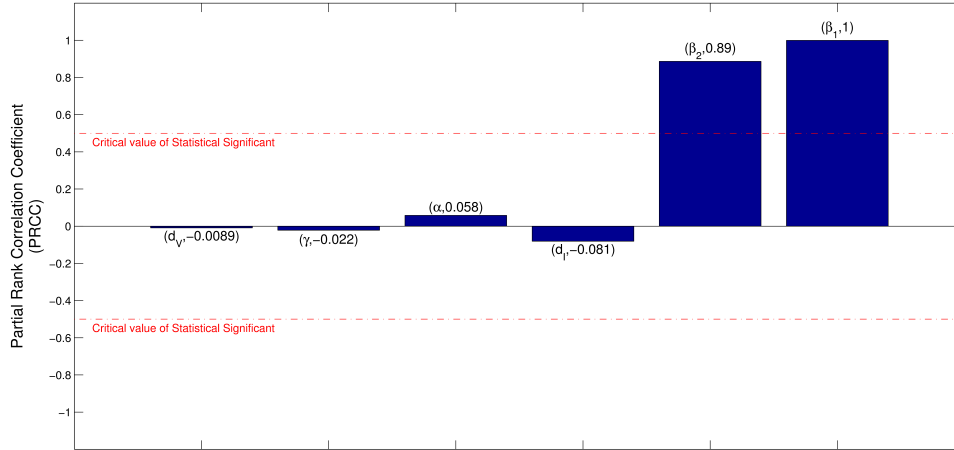
$$\mathcal{R}_0 = \frac{\Lambda \alpha \beta_1}{d_S d_V (\gamma + d_I)} + \frac{\Lambda \beta_2}{d_S (\gamma + d_I)}.$$

The system (17) possesses an uninfected steady state  $E_0 \left( \frac{\Lambda}{d_S}, 0, 0 \right)$  and also has an infected steady state

$$E^* \left( \frac{\Lambda}{d_S \mathcal{R}_0}, \frac{\Lambda \left( 1 - \frac{1}{\mathcal{R}_0} \right)}{\gamma + d_I}, \frac{\alpha \Lambda \left( 1 - \frac{1}{\mathcal{R}_0} \right)}{d_V (\mu + d_I)} \right) \text{ for } \mathcal{R}_0 > 1.$$

At first sensitivity analysis is used to determine the response of the model to variations in its parameter values. In the present case, focus is given to determining how changes in the model parameters impact the basic reproduction number. This is done through the Latin hypercube sampling (LHS) and the partial correlation coefficients (PRCC) to determine the relative importance of the parameters in  $\mathcal{R}_0$  for the disease transmission<sup>36</sup>. In such a scenario, it is more appropriate to treat each parameter as a random variable, distributed according to an appropriate probability distribution. We assume that our model parameters are normally distributed although it is quite possible that some parameters are constant towards a particular value such as recruitment rate ( $\Lambda$ ) and death rate ( $d_T$ ) of susceptible cells. PRCC reduces the non-linearity effects by rearranging the data in ascending order, replacing the values with their ranks and then providing the measure of monotonicity after the removal of the linear

effects of each model parameter keeping all other parameters constant<sup>37</sup>. The corresponding Tornado plots based on a random sample of 1000 points for the six parameters in  $\mathcal{R}_0$  are shown in Figure 1. The horizontal lines represent the significant range of correlation, i.e.,  $|\text{PRCC}| > 0.5$ . The sensitivity analysis suggests that the most significant parameters are  $\beta_1$  and  $\beta_2$ , an increase in these values will have an increase in the spread of the disease. Hence, these parameters should be estimated with precision to accurately capture the dynamics of the infection.



**FIGURE 1** Partial rank correlation coefficient (PRCC) results for significance of parameters involved in  $\mathcal{R}_0$

Now, we numerically illustrate the results for global stability for both the steady states. Accordingly, we use two sets of system parameters, one corresponding to  $\mathcal{R}_0 < 1$  (when  $E_0$  is globally asymptotically stable for both the continuous and discretized models) and the other for  $\mathcal{R}_0 > 1$  (when  $E^*$  is globally asymptotically stable for both the continuous and discretized models). The numerical simulation is carried out using the NSFD scheme described by the system (6) with initial condition taken as

$$S(x, 0) = 10^7, \quad I(x, 0) = 100e^x, \quad V(x, 0) = 100e^x.$$

For the purpose of illustration of both the scenarios, we choose the equal diffusion coefficients as  $D_1 = D_2 = 1 \text{ mm}^2 \text{d}^{-1}$  and  $D_3 = 1 \text{ mm}^2 \text{d}^{-1}$ <sup>38</sup>. The one-dimensional spatial domain is taken as  $\Omega = [0, 50]$  and the simulation carried out for a time window of 100 days. The grid sizes used in the spatial and temporal directions are  $\Delta x = 0.5$  and  $\Delta t = 1$ , respectively. The parameter set  $\Lambda = 10^7 \text{ cells d}^{-1}$ ,  $\beta_1 = \beta_2 = 5 \times 10^{-12} \text{ virion}^{-1} \text{ d}^{-1}$ ,  $d_S = 0.1 \text{ d}^{-1}$ ,  $\gamma = 0.01 \text{ d}^{-1}$ ,  $d_I = 0.04 \text{ d}^{-1}$ ,  $\alpha = 100 \text{ d}^{-1}$ ,  $d_V = 5 \text{ d}^{-1}$ <sup>26</sup>, results in  $\mathcal{R}_0 = 0.21 < 1$ . Thus, in this case, the uninfected steady state  $E^0$  is globally asymptotically stable. It can be observed from Figure 2 that this is indeed the case and the system eventually approaches the uninfected steady state  $E_0 = (10^8, 0, 0)$ .

For the other scenario, all the parameter values are identical with the exception of  $\beta_1 = \beta_2 = 3 \times 10^{-10} \text{ virion}^{-1} \text{ d}^{-1}$ <sup>26</sup> which renders  $\mathcal{R}_0 = 12.59 > 1$ . In this case, the infected steady state is stable as can be observed numerically in Figure 3, where the state variables approach the infected steady state  $E^* = (8 \times 10^6, 1.8 \times 10^8, 3.7 \times 10^9)$ . For both the sets of simulations it can be easily seen that the steady states do not depend on the initial spatial points.

We have also shown that the global asymptotically stable results are dependent only on the parameters of the non-diffusive system because of  $\mathcal{R}_0$  and independent of the choices of the diffusion coefficients. This is also illustrated by way of numerical simulations. For illustrative purpose we only show the case for  $\mathcal{R}_0 > 1$  using the corresponding parameter values used above. We extend our diffusion coefficient to  $D_1 = D_2 = D_3 = 100 \text{ mm}^2 \text{d}^{-1}$  and see from Figure 4, that the steady states of the model dynamics are very similar to each other in the long run. Similar results can be observed for different combinations of  $(D_1, D_2, D_3)$ . Another crucial advantage of using the NSFD scheme over standard finite difference (SFD) scheme is that the positivity of solutions for long time simulation which already been demonstrated in many works<sup>26,39</sup>.



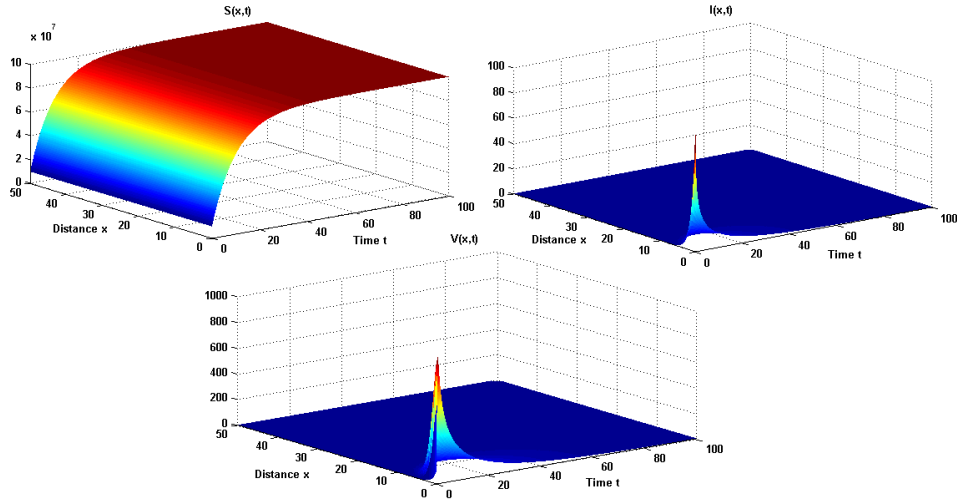


FIGURE 2 When  $\mathcal{R}_0 = 0.21 < 1$ , the disease-free equilibrium  $E_0$  of system (17) is globally asymptotically stable.

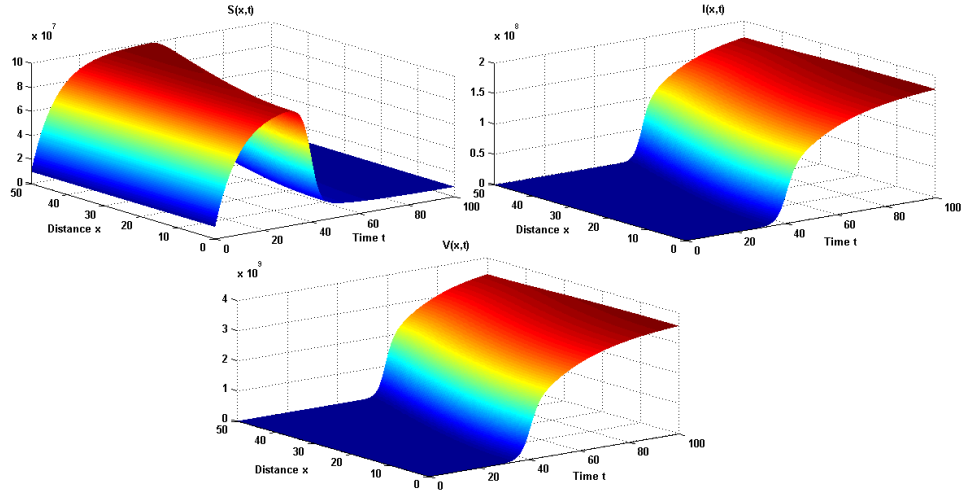
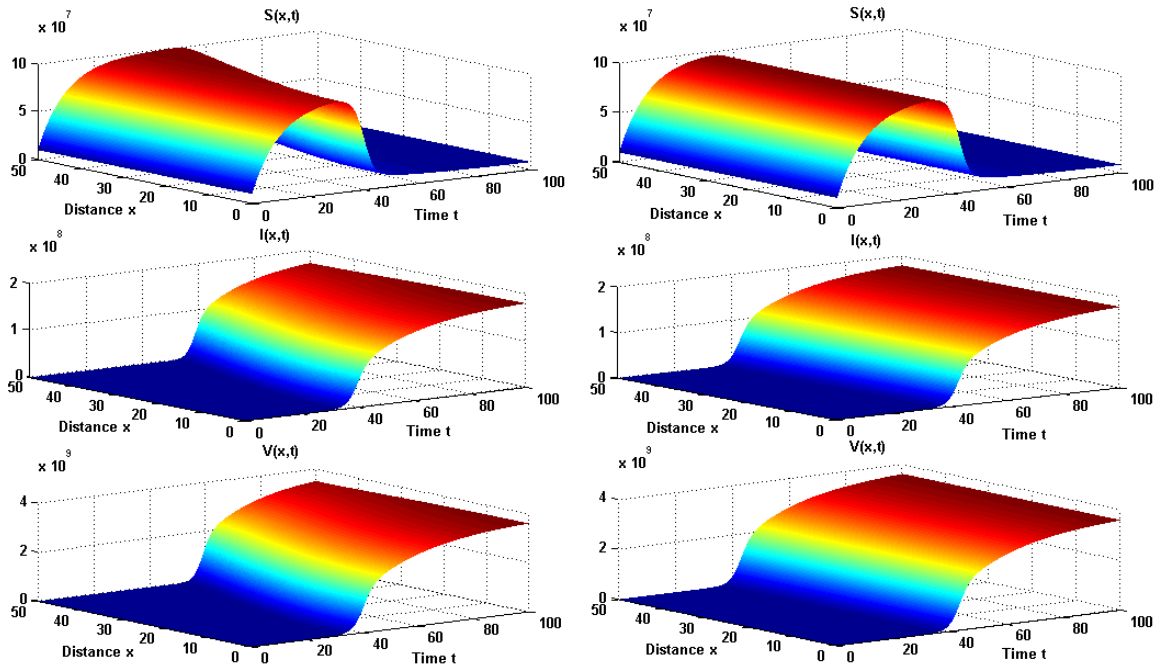


FIGURE 3 When  $\mathcal{R}_0 = 12.59 > 1$ , the disease-free equilibrium  $E^*$  of system (17) is globally asymptotically stable.

## 5 | CONCLUSION

In order to investigate the mechanism of virus infection and viral replication, we have carried out the mathematical analysis for a diffusive intra-host virus dynamics model with cell-to-cell transmission, while allowing for a general nonlinear incidence functions. The well posedness and linear stability of equilibria of this model is investigated. The basic reproduction number  $\mathcal{R}_0$  is a threshold index which predicts the extinction and persistence of the disease. It is shown that the global stability of the equilibria is completely determined by  $\mathcal{R}_0$ : if  $\mathcal{R}_0 \leq 1$ , then the disease-free equilibrium  $E_0$  is globally asymptotically stable, which means that the virus is eventually cleared and the infection dies out; if  $\mathcal{R}_0 > 1$ , then the endemic equilibrium  $E^*$  is globally asymptotically stable. From the expression of the basic reproduction number of virus, we can know that the basic reproduction number could be under-evaluated without considering either the virus-to-cell transmission or cell-to-cell transmission; it is not enough to eliminate the disease by decreasing the basic reproduction number of virus-to-cell transmission due to the existence of cell-to-cell transmission. Our results also imply that diffusion coefficients have no effect on the global behaviors of such virus dynamics model with homogeneous Neumann boundary conditions. Then, by using the NSFD scheme, we derived the discrete counterpart of the continuous model. Our results show that the discretization scheme can preserve the



**FIGURE 4** Dynamics of system (17) under diffusion coefficients  $D_1 = D_2 = D_3 = 1 \text{ mm}^2\text{d}^{-1}$  (left) and  $D_1 = D_2 = D_3 = 100 \text{ mm}^2\text{d}^{-1}$  (right).

global properties of solutions for original continuous model, including the positivity, ultimate boundedness and global stability of the equilibria with no restriction on the space and time step sizes.

In addition, the model proposed in this paper is an extension of some previous works<sup>40,41,42,43,44,45</sup> and the obtained results improve some known results. It is interesting to improve the model (2) by incorporating logistic growth term for uninfected target cells and a more general infection function. We leave these for future consideration.

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