Journal of Applied Analysis and Computation
Volume 13, Number 6, December 2023, 3606–3631
Website:http://www.jaac-online.com
DOI:10.11948/20230207

THE SEIR MODEL WITH PULSE AND DIFFUSION OF VIRUS IN THE ENVIRONMENT*

Yue Tang[1], Inkyung Ahn[2] and Zhigui Lin[1,†]

Abstract This paper addresses a reaction-diffusion problem featuring impulsive effects under Neumann boundary conditions. The model simulates the periodic eradication of viruses in an environment. Initially, we establish the well-posedness of the reaction-diffusion model. We define the basic reproduction number R_0 for the problem in the absence of pulsing and compute the principal eigenvalue of the corresponding elliptic eigenvalue problem. Utilizing Lyapunov functionals and Green's first identity, we derive the global threshold dynamics of the system. Specifically, when $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable; conversely, if $R_0 > 1$, the system exhibits uniform persistence, and the endemic equilibrium is globally asymptotically stable. Additionally, we consider the generalized principal eigenvalues for the problem with pulsing and provide sufficient conditions for the stability of both the disease-free equilibrium and the positive periodic solution. Finally, we corroborate our theoretical findings through numerical simulations, particularly discussing the impacts of periodic environmental cleaning.

Keywords Infectious disease model, pulse, spatial heterogeneity, basic reproduction number, threshold dynamics.

MSC(2010) 35K55, 35K57, 35R35, 92D30.

1. Introduction

It is widely recognized that certain viruses, including the human immunodeficiency virus (HIV) and hepatitis B and C viruses (HBV, HCV), possess the ability to survive and propagate for extended periods in the absence of hosts [4, 5, 8, 9, 29]. This capability amplifies their potential for causing further infections, complicating efforts to prevent and control viral spread, and posing significant risks to public health. Given these challenges, there is considerable importance in investigating the influence of environmental transmission of free-living viruses on the effectiveness of

[†]The corresponding author.
[1]School of Mathematical Science, Yangzhou University, Yangzhou 225002, China
[2]Department of Mathematics, Korea University, 2511 Sejong-ro, Sejong 339-700, South Korea
[*]The second and third authors are supported by the National Natural Science Foundation of China (No. 12271470), and the second author is also supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (NRF-2022R1F1A1063068).
Email: 1084913416@qq.com(Y. Tang), ahnik@korea.ac.kr(I. Ahn), zglin68@hotmail.com (Z. Lin)

viral control measures.

It has been posited that the likelihood of viral infection is often related to spatial location [10, 28]. The diffusive process essentially represents the random spatial movement of the virus, which exhibits no preferential direction as indicated in [31]. As a result, reaction-diffusion models serve as reliable mathematical frameworks for exploring the influence of diffusion and spatial heterogeneity on disease transmission. For further details and discussions, please refer to [17, 18, 24, 26, 32–34] and the references cited therein.

Numerous theoretical studies have been conducted on epidemic models incorporating diffusion. For example, Allen et al. introduced a classical SIS reaction-diffusion system with spatial heterogeneity in 2008 [2]. This work was later extended in 2014, where a HIV viral infection model that accounted for both virus diffusion and spatial heterogeneity was considered [23]. More recently, Pang and Xiao examined a SIS-W model aimed at controlling hospital infections and explored the effects of direct transmission via free-living viruses (W) on disease progression [15].

Considering individuals in the "exposed"(E) category-who do not exhibit symptoms immediately after coming into contact with the virus-research has been conducted on SEIR models both without diffusion [12, 35] and with diffusion [1, 7]. Moreover, transient perturbations in virus levels can be triggered by various factors, such as climatic changes or human interventions like periodic environmental disinfection, which result in a rapid decline in environmental viral concentrations over short periods. The primary objective of this article is to investigate and elucidate the dynamics of virus transmission at the population level, specifically in the context of hospital-acquired infections. In this study, we assume that only the virus undergoes diffusion, while the populations themselves do not. This leads to a set of hybrid differential equations: the first three equations are ordinary differential equations representing the dynamics of the susceptible, exposed, and infected populations, while the final equation is a partial differential equation modeling virus diffusion. Consequently, we propose the following SEIW epidemic model, which incorporates pulse effects as well as diffusion of the virus within the environment.

$$
\begin{cases}
\dfrac{\partial S}{\partial t} = \alpha(x) - \mu_1(x)SW - \mu_2(x)SI & \\
\qquad - \gamma_1(x)S, & x \in \Omega,\ t \in \left((nT)^+, (n+1)T\right], \\
\dfrac{\partial E}{\partial t} = \delta\mu_1(x)SW + \delta\mu_2(x)SI - a(x)E & \\
\qquad - \gamma_2(x)E, & x \in \Omega,\ t \in \left((nT)^+, (n+1)T\right], \\
\dfrac{\partial I}{\partial t} = (1-\delta)\mu_1(x)SW + (1-\delta)\mu_2(x)SI & \\
\qquad + a(x)E - \gamma_3(x)I, & x \in \Omega,\ t \in \left((nT)^+, (n+1)T\right], \\
\dfrac{\partial W}{\partial t} = d\Delta W + b(x)I - \gamma_4(x)W, & x \in \Omega,\ t \in \left((nT)^+, (n+1)T\right], \\
W(x,(nT)^+) = cW(x,nT), & x \in \Omega, n = 0,1,2,..., \\
V(x,(nT)^+) = V(x,nT), & x \in \Omega, V = S, E, I, \\
\dfrac{\partial W}{\partial \eta} = 0, & x \in \partial\Omega, t > 0, \\
\quad (S(x,0), E(x,0), I(x,0), W(x,0)) & \\
= (S_0(x), E_0(x), I_0(x), W_0(x)) \geq 0, & x \in \overline{\Omega},
\end{cases}
\tag{1.1}
$$

where $t \in ((nT)^+, (n+1)T]$ means the equations hold for $t \in (nT, (n+1)T]$, while the initial value of the unknown takes its right-hand limit at $t = nT$. $S(x,t)$, $E(x,t)$, $I(x,t)$ and $W(x,t)$ represent the density of susceptible patients, exposed patients, infected patients, free viruses in the environment, respectively. $\alpha(x)$ is the location-dependent growth rate of the susceptible patients, $\mu_1(x)$ means the transmission rate between the susceptible and the environmental virus. $\mu_2(x)$ expresses the transmission rate between the susceptible and the infectious individuals, $\gamma_1(x)$ is the death rate of the susceptible patients. δ represents the proportion of individuals who progress from susceptible to exposed, and $a(x)$ is the rate of exposed turn into infectious individuals. $\gamma_2(x)$ and $\gamma_3(x)$ are the death rate of the exposed patients and the infected patients, respectively. d expresses the diffusion coefficient of the virus, $b(x)$ is the rate of virus production and $1/\gamma_4(x)$ is the average survival time of free viruses without hosts. Owing to regular cleaning at each time $t = nT$, some of free viruses remain in the environment, we assume that its ratio is $c(0 < c \leq 1)$, while all patients do not change significantly in a short time. Apparently, $c = 1$ means no cleaning and $c = 0$ implies that there is no virus existing in the environment after thorough cleaning. We assume all location-dependent parameters are continuous and strictly positive.

This paper is arranged as follows. Section 2 deals with the well-posedness of the problem. In Section 3, we first establish the basic reproduction number and the threshold dynamics for a corresponding linearized system when $c = 1$, and then the generalized eigenvalue is defined to obtain the sufficient conditions for the stability of the disease-free equilibrium and the positive periodic solution when $0 < c < 1$. Numerical simulations in Section 4 are devoted to discussing the impacts of spatial heterogeneity and diffusion rate d on the basic reproduction number, and the role of the cleaning ratio c on the control of virus. A brief discussion is finally presented in Section 5.

2. Analysis of the model

Some basic properties of the solution to problem (1.1) is firstly analysed in this section.

Let $\mathbf{X} = C(\bar{\Omega}, \mathbf{R}^4)$ be a Banach space with the supremum norm $||\cdot||_X$. Define $\mathbf{X}^+ = C(\bar{\Omega}, \mathbf{R}^4_+)$ is a positive cone of $\mathbf{X}$, then $(\mathbf{X}, \mathbf{X}^+)$ is an ordered Banach Space.

For any initial function $\phi = (S_0(x), E_0(x), I_0(x), W_0(x))^T \in \mathbf{X}^+$, we next define

$$\begin{aligned}
(T_1(t)S_0)(x) &= e^{-\gamma_1(x)t} S_0(x), \\
(T_2(t)E_0)(x) &= e^{-(a(x)+\gamma_2(x))t} E_0(x), \\
(T_3(t)I_0)(x) &= e^{-\gamma_3(x)t} I_0(x).
\end{aligned}$$

Let $T_4(t) : C(\bar{\Omega}, \mathbf{R}) \to C(\bar{\Omega}, \mathbf{R})$ be a C_0-semigroup corresponding to $d\Delta - \gamma_4(x)$, which satisfies the Neumann boundary condition, that is,

$$(T_4(t)W_0)(x) = \int_\Omega G(x,y,t) W_0(y) dy, \quad t \geq 0,$$

where G is a Green function related to $d\Delta - \gamma_4(x)$ subject to the Neumann boundary condition. It follows from Corollary 7.2.3 in [21] that $T_4(t) : C(\bar{\Omega}, \mathbf{R}) \to C(\bar{\Omega}, \mathbf{R})$ is compact and strongly positive for any $t > 0$.

In the following, we define a linear operator A

$$A(u) = \begin{pmatrix} -\gamma_1(x)S \\ -(a(x)+\gamma_2(x))E \\ -\gamma_3(x)I \\ d\Delta W - \gamma_4(x)W \end{pmatrix}$$

and a nonlinear operator F

$$F(u) = \begin{pmatrix} \alpha(x) - \mu_1(x)SW - \mu_2(x)SI \\ \delta\left(\mu_1(x)SW + \mu_2(x)SI\right) \\ (1-\delta)(\mu_1(x)SW + \mu_2(x)SI) + a(x)E \\ b(x)I \end{pmatrix}$$

of problem (1.1), respectively. Then equation in problem (1.1) can be rewritten as an integral equation

$$u(t) = T(t)\phi + \int_0^t T(t-s)F(u(s))ds,$$

where $u(t) = (S(x,t), E(x,t), I(x,t), W(x,t))^T$, $T(t) = \mathrm{diag}(T_1(t), T_2(t), T_3(t), T_4(t))$ and $\phi = (S_0(x), E_0(x), I_0(x), W_0(x))^T \in \mathbf{X}^+$.

Lemma 2.1. *Problem* (1.1) *admits a unique positive solution* $u(\cdot, 0) \in \bar{\Omega} \times [0, \tau_\phi)$ *for any initial function* $\phi \in \mathbf{X}^+$ *with* $0 < \tau_\phi \leq +\infty$*. Especially, if* $\tau_\phi < +\infty$*, then* $||u(t)||_{\mathbf{X}} \to +\infty$ *for* $t \to \tau_\phi^-$*.*

Proof. For any $\phi \in \mathbf{X}^+$, let

$$\phi_0(x) = u(x, 0^+) = (S(x,0), E(x,0), I(x,0), cW(x,0))^T$$

be the new initial value. Hence, it is clear that

$$\begin{aligned} &\phi_0(x) + hF(\phi_0)(x) \\ &= \begin{pmatrix} S_0(x) + h\left(\alpha(x) - c\mu_1(x)S_0(x)W_0(x) - \mu_2(x)S_0(x)I_0(x)\right) \\ E_0(x) + h\left[\delta\left(c\mu_1(x)S_0(x)W_0(x) + \mu_2(x)S_0(x)I_0(x)\right)\right] \\ I_0(x) + h\left[(1-\delta)\left(c\mu_1(x)S_0(x)W_0(x) + \mu_2(x)S_0(x)I_0(x)\right) + a(x)E_0(x)\right] \\ cW_0(x) + hb(x)I_0(x) \end{pmatrix} \\ &\geqslant \begin{pmatrix} S_0(x)\left(1 - hc\bar{\mu}_1 W_0(x) - h\bar{\mu}_2 I_0(x)\right) \\ E_0(x) \\ I_0(x) \\ cW_0(x) \end{pmatrix} \end{aligned}$$

for $t \in (0, T]$, where
$$\bar{\mu}_1 = \max_{x\in\bar{\Omega}} \mu_1(x),\ \bar{\mu}_2 = \max_{x\in\bar{\Omega}} \mu_2(x).$$

A sufficiently small constant $h > 0$ can be taken such that $\phi_0 + hF(\phi_0) \in \mathbf{X}^+$, and then
$$\lim_{h\to 0^+} \frac{1}{h} \mathrm{dist}(\phi_0 + hF(\phi_0), \mathbf{X}^+) = 0, \quad \forall \phi_0 \in \mathbf{X}^+.$$

Considering the pulse, we first study the solution in $[0, T]$. It then follows from Theorem 7.3.1 in [21] that problem (1.1) admits a unique positive solution $u(\cdot, t)$ in $\bar{\Omega} \times [0, \tau_\phi)$. If $\tau_\phi \le T$, then $||u(t)||_{\mathbf{X}} \to +\infty$ for $t \to \tau_\phi^-$. Otherwise, we have the solution for $t \in [0, T]$.

When $t \in (T, 2T]$, let $\phi_1(x)$ be a new initial value in $t \in (T^+, 2T]$, where
$$\phi_1(x) = u(x, T^+) = (S(x, T), E(x, T), I(x, T), cW(x, T))^T,$$
and subsequently we have the solution $u(\cdot, t) \in \bar{\Omega} \times [T, \tau_{\phi_1}]$. If $\tau_{\phi_1} \le 2T$, then $||u(t)||_{\mathbf{X}} \to +\infty$ for $t \to \tau_{\phi_1}^-$. Otherwise, we have the solution for $t \in [T, 2T]$. By uniqueness of the solution, $u(\cdot, t) \in \bar{\Omega} \times [0, 2T]$.

Step by step, the solution to problem (1.1) satisfies $u(\cdot, t) \in \bar{\Omega} \times [0, \tau_\phi)$ with $0 < \tau_\phi \le +\infty$. In addition, if $\tau_\phi < +\infty$, then $\lim_{t\to\tau_\phi^-} ||u(t)||_{\mathbb{X}} = +\infty$. □

Lemma 2.2. *For any initial value $\phi \in \mathbf{X}^+$, problem* (1.1) *admits a unique positive solution $u(\cdot, t)$ in $[0, +\infty)$, which is bounded in $\mathbf{X}^+$.*

Proof. Let $P(x, t) = S(x, t) + E(x, t) + I(x, t)$. Adding the first three equations of problem (1.1) yields
$$\frac{\partial P(x,t)}{\partial t} \le \bar{\alpha} - \gamma_0 P(x, t), \quad x \in \Omega, t \in [0, \tau_\phi), \tag{2.1}$$
where $\bar{\alpha} = \max_{x\in\bar{\Omega}} \alpha(x)$ and $\gamma_0 = \min\{\min_{x\in\bar{\Omega}}\{\gamma_1(x)\}, \min_{x\in\bar{\Omega}}\{\gamma_2(x)\}, \min_{x\in\bar{\Omega}}\{\gamma_3(x)\}\}$.

It can be derived from (2.1) that
$$P(x, t) \le \frac{\bar{\alpha}}{\gamma_0} + (S_0(x) + E_0(x) + I_0(x))e^{-\gamma_0 t}, \quad x \in \Omega, t \in [0, \tau_\phi). \tag{2.2}$$

Therefore, there exists a positive constant M, which is dependent of initial value ϕ, such that
$$||P(x, t)|| \le M,$$
where $||u|| = ||u||_\infty = ess\sup_{x\in\bar{\Omega}}|u|$.

Using the forth equation in problem (1.1), which together with $c \le 1$ and the definition of $T_4(t)$, yields
$$W(x, t) = T_4(t)W_0(x) + \int_0^t T_4(t - s)b(x)I(x, s)ds.$$

Recall that $\gamma_4(x) > 0$, let $c_0(> 0)$ be the principal eigenvalue of $-d\Delta + \gamma_4(x)$ that subject to the Neumann boundary condition, so
$$||W(x, t)|| \le ||T_4(t)W_0(x)|| + \left|\left|\int_0^t T_4(t - s)b(x)I(x, s)ds\right|\right|$$

$$\leq e^{-c_0 t}||W_0(x)|| + \bar{b}\int_0^t e^{-c_0(t-s)}||I(x,s)||ds$$

$$\leq ||W_0(x)|| + \frac{\bar{b}M}{c_0},$$

where $\bar{b} = \max_{x\in\bar{\Omega}} b(x)$. It follows from Lemma 2.1 that $\tau_\phi = +\infty$. Thus, problem (1.1) has a unique nonnegative global solution $u(\cdot, t)$ in $[0, +\infty)$. $\square$

Lemma 2.3. *The solution to problem* (1.1) *is ultimately bounded for any initial value* $\phi \in \mathbf{X}^+$.

Proof. It can be deduced form (2.2) that

$$\limsup_{t\to\infty}(S(x,t) + E(x,t) + I(x,t)) \leq \frac{\bar{\alpha}}{\gamma_0}, \quad \forall x \in \bar{\Omega}.$$

Hence, for any $0 < \varepsilon_0 \leq 1$, there is $t_0 > 0$ such that

$$S(x,t) + E(x,t) + I(x,t) = P(x,t) \leq (1+\varepsilon_0)\frac{\bar{\alpha}}{\gamma_0},\ x \in \overline{\Omega},\ t \geq t_0, \tag{2.3}$$

which means $S(x,t), E(x,t)$ and $I(x,t)$ are ultimately bounded.

Equation (2.3) and the forth equation in (1.1) assert

$$\begin{cases} \dfrac{\partial W(x,t)}{\partial t} \leq d\Delta W(x,t) + \dfrac{\bar{b}\bar{\alpha}}{\gamma_0}(1+\varepsilon_0) - \underline{\gamma_4} W(x,t), & x \in \Omega,\ t \geq t_0, \\ \dfrac{\partial W(x,t)}{\partial \eta} = 0, & x \in \partial\Omega,\ t \geq t_0, \end{cases}$$

where $\underline{\gamma}_4 = \min_{x\in\bar{\Omega}} \gamma_4(x)$.

It then follows from the comparison principal and Lemma 1 in [13] that there exists a $t_1 > t_0 > 0$ such that

$$W(x,t) \leq (1+2\varepsilon_0)\frac{\bar{b}\bar{\alpha}}{\underline{\gamma}_4\gamma_0}, \quad \forall t \geq t_1. \tag{2.4}$$

Therefore, $W(x,t)$ is ultimately bounded. $\square$

3. Threshold dynamics

It is easy to see that problem (1.1) admits a disease-free equilibrium $E_0(S^*(x)$,0,0,0), where $S^*(x) = \frac{\alpha(x)}{\gamma_1(x)}$. We first linearize problem (1.1) in E_0 and consider the following problem

$$\begin{cases} \dfrac{\partial W}{\partial t} = d\Delta W + b(x)I - \gamma_4(x)W, & x \in \Omega, t \in \left((nT)^+, (n+1)T\right], \\ \dfrac{\partial I}{\partial t} = (1-\delta)\mu_1(x)S^*(x)W + a(x)E & \\ \qquad + ((1-\delta)\mu_2(x)S^*(x) - \gamma_3(x))I, & x \in \Omega, t \in \left((nT)^+, (n+1)T\right], \\ \dfrac{\partial E}{\partial t} = \delta\mu_1(x)S^*(x)W + \delta\mu_2(x)S^*(x)I & \\ \qquad - (a(x) + \gamma_2(x))E, & x \in \Omega, t \in \left((nT)^+, (n+1)T\right], \\ \dfrac{\partial W}{\partial \eta} = 0, & x \in \partial\Omega, \\ W(x, (nT)^+) = cW(x, nT), & x \in \Omega, n = 0, 1, 2..., \\ V(x, (nT)^+) = V(x, nT), & x \in \Omega, V = S, E, I. \end{cases} \tag{3.1}$$

If $c = 1$, then there is no impulse in problem (3.1). Let $E(x,t) = e^{\lambda t}\varphi_2(x), I(x,t) = e^{\lambda t}\varphi_3(x)$ and $W(x,t) = e^{\lambda t}\varphi_4(x)$, we obtain the following eigenvalue problem

$$\begin{cases} d\Delta\varphi_4(x) + b(x)\varphi_3(x) - \gamma_4(x)\varphi_4(x) = \lambda\varphi_4(x), & x \in \Omega, \\ \quad (1-\delta)\mu_1(x)S^*(x)\varphi_4(x) + ((1-\delta)\mu_2(x)S^*(x) - \gamma_3(x))\varphi_3(x) & \\ = -a(x)\varphi_2(x) + \lambda\varphi_3(x), & x \in \Omega, \\ \quad \delta\mu_1(x)S^*(x)\varphi_4(x) + \delta\mu_2(x)S^*(x)\varphi_3(x) & \\ = (a(x) + \gamma_2(x))\varphi_2(x) + \lambda\varphi_2(x), & x \in \Omega, \\ \dfrac{\partial \varphi_4}{\partial \eta} = 0, & x \in \partial\Omega. \end{cases} \tag{3.2}$$

Let $R(t)$ be the solution semiflows on $C(\bar{\Omega}, \mathbf{R}^2)$ corresponding to linear system (3.1). Then $R(t)$ is a positive C_0-semigroup with generator A

$$A = \begin{pmatrix} d\Delta - \gamma_4(x) & b(x) & 0 \\ (1-\delta)\mu_1(x)S^*(x) & (1-\delta)\mu_2(x)S^*(x) - \gamma_3(x) & a(x) \\ \delta\mu_1(x)S^*(x) & \delta\mu_2(x)S^*(x) & -(a(x) + \gamma_2(x)) \end{pmatrix}.$$

It follows from Theorem 3.12 in [11] that A is a closed and resolvent positive operator and $A = F + V$, where

$$F = \begin{pmatrix} 0 & 0 & 0 \\ (1-\delta)\mu_1(x)S^*(x) & (1-\delta)\mu_2(x)S^*(x) & 0 \\ \delta\mu_1(x)S^*(x) & \delta\mu_2(x)S^*(x) & 0 \end{pmatrix},$$

and

$$V = \begin{pmatrix} d\Delta - \gamma_4(x) & b(x) & 0 \\ 0 & -\gamma_3(x) & a(x) \\ 0 & 0 & -(a(x) + \gamma_2(x)) \end{pmatrix}.$$

Let $\tilde{R}(t)$ be the solution semigroup generated by the operator V. We describe the distribution of initial infections by $\tilde{\varphi}(x) = (\tilde{\varphi}_2(x), \tilde{\varphi}_3(x), \tilde{\varphi}_4(x))$. Thus, $\tilde{R}(t)\tilde{\varphi}$ is the distribution of infected individuals that affected by mobility, mortality, recovery or transform. The distribution of new infections at time t becomes $F(x)\tilde{R}(t)\tilde{\varphi}(x)$. The total distribution of new infections can be described by L as the following

$$L(\tilde{\varphi})(x) = \int_0^\infty F(x)\tilde{R}(t)\tilde{\varphi}(x)dt = F(x)\int_0^\infty \tilde{R}(t)\tilde{\varphi}(x)dt, \quad \tilde{\varphi} \in C(\bar{\Omega}, \mathbf{R}^3), \ x \in \bar{\Omega}.$$

The basic reproduction number R_0 can be defined by the spectral radius of L as

$$R_0 := r(L) = r(-FV^{-1}).$$

Let η_0 be the principal eigenvalue of the following eigenvalue problem

$$\begin{pmatrix} d\Delta - \gamma_4(x) & b(x) & 0 \\ \eta(1-\delta)\mu_1(x)S^* & \eta(1-\delta)\mu_2(x)S^* - \gamma_3(x) & a(x) \\ \eta\delta\mu_1(x)S^* & \eta\delta\mu_2(x)S^* & -(a(x)+\gamma_2(x)) \end{pmatrix} \begin{pmatrix} \hat{\Psi}_4 \\ \hat{\Psi}_3 \\ \hat{\Psi}_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}, \tag{3.3}$$

we have $R_0 = \frac{1}{\eta_0}$. It is easy to see that the expression of R_0 is difficult to give, so we here take the following auxiliary eigenvalue problem (3.4) into account. Let τ_0 be the principal eigenvalue of eigenvalue problem (3.4)

$$\begin{pmatrix} d\Delta - \gamma_4(x) & b(x) & 0 \\ \tau(1-\delta)\mu_1(x)S^* & (1-\delta)\mu_2(x)S^* - \gamma_3(x) & a(x) \\ \tau\delta\mu_1(x)S^* & \delta\mu_2(x)S^* & -(a(x)+\gamma_2(x)) \end{pmatrix} \begin{pmatrix} \tilde{\Psi}_4 \\ \tilde{\Psi}_3 \\ \tilde{\Psi}_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}. \tag{3.4}$$

We will prove that $R_0 - 1$ and $\frac{1}{\tau_0} - 1$ have the same sign. Since the principal eigenvalue of A and A^T are same, so τ_0 is also the principal eigenvalue of problem (3.5)

$$\begin{pmatrix} d\Delta - \gamma_4(x) & \tau(1-\delta)\mu_1(x)S^* & \tau\delta\mu_1(x)S^* \\ b(x) & (1-\delta)\mu_2(x)S^* - \gamma_3(x) & \delta\mu_2(x)S^* \\ 0 & a(x) & -(a(x)+\gamma_2(x)) \end{pmatrix} \begin{pmatrix} \Psi_4 \\ \Psi_3 \\ \Psi_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix}, \tag{3.5}$$

which can be written by

$$\begin{cases} d\Delta\Psi_4(x) - \gamma_4(x)\Psi_4(x) + \tau(1-\delta)\mu_1(x)S^*\Psi_3(x) + \tau\delta\mu_1(x)S^*\Psi_2(x) = 0, \\ b(x)\Psi_4(x) + ((1-\delta)\mu_2(x)S^* - \gamma_3(x))\Psi_3(x) + \delta\mu_2(x)S^*\Psi_2(x) = 0, \\ a(x)\Psi_3(x) - (a(x)+\gamma_2(x))\Psi_2(x) = 0. \end{cases} \tag{3.6}$$

It is clear that

$$\Psi_2(x) = \frac{a(x)}{a(x)+\gamma_2(x)}\Psi_3(x) \tag{3.7}$$

and

$$\Psi_3(x) = \frac{b(x)(a(x)+\gamma_2(x))}{\gamma_3(x)(a(x)+\gamma_2(x)) - \mu_2(x)S^*(x)(a(x)+(1-\delta)\gamma_2(x))}\Psi_4(x) \tag{3.8}$$

hold. Substituting (3.7) and (3.8) into the first equation of (3.6) yields

$$\begin{cases} -d\Delta\Psi_4(x)+\gamma_4(x)\Psi_4(x)=\tau G(x)\Psi_4(x), & x\in\Omega,\\ \dfrac{\partial\Psi_4(x)}{\partial\eta}=0, & x\in\partial\Omega, \end{cases} \tag{3.9}$$

where

$$G(x)=\frac{\mu_1(x)S^*(x)b(x)(a(x)+(1-\delta)\gamma_2(x))}{\gamma_3(x)(a(x)+\gamma_2(x))-\mu_2(x)S^*(x)(a(x)+(1-\delta)\gamma_2(x))}. \tag{3.10}$$

It follows form Theorem 2.4 in [6] that elliptic eigenvalue problem (3.9) admits a unique principal eigenvalue τ_0 and its corresponding positive eigenfunction is $\Psi_4^*(x)$. If $\gamma_3(x)(a(x)+\gamma_2(x))-\mu_2(x)S^*(x)(a(x)+(1-\delta)\gamma_2(x))>0$, the positivity of $\Psi_3^*(x)$ and $\Psi_2^*(x)$ can be obtained by equations (3.7) and (3.8), respectively.

The following results can be obtained by Theorem 3.2 in [26].

Theorem 3.1. *The eigenvalue problem* (3.5) *admits a unique positive principal eigenvalue τ_0, and its corresponding positive eigenfunction is $(\Psi_4^*,\Psi_3^*,\Psi_2^*)$. In addition,*

$$\frac{1}{\tau_0}=\sup_{\Psi\in H^1(\Omega),\Psi\neq 0}\left\{\frac{\int_\Omega G(x)\Psi^2(x)dx}{\int_\Omega[d|\nabla\Psi(x)|^2+\gamma_4(x)\Psi^2(x)]dx}\right\}. \tag{3.11}$$

Remark 3.1. It is easy to see from the expression of $\frac{1}{\tau_0}$ that τ_0 is an nondecreasing function with respect to d.

Remark 3.2. Considering the impact of the virus reproduction rate in the heterogeneous environment, we take $b(x):=b_0\left(1+k\sin\left(\frac{9\pi x}{10}\right)\right)$ in Example 4.2 in Section 4. It can be seen from simulations of $\frac{1}{\tau_0}$ that if b_0 is fixed, $\frac{1}{\tau_0}$ is a nondecreasing function with respect to k.

Lemma 3.1. *Assume that λ_0 be the principal eigenvalue of the following eigenvalue problem*

$$\begin{cases} d\Delta\psi(x)-\gamma_4(x)\psi(x)+G(x)\psi(x)=\lambda\psi(x), & x\in\Omega,\\ \dfrac{\partial\psi(x)}{\partial\eta}=0, & x\in\partial\Omega, \end{cases} \tag{3.12}$$

where $G(x)$ is defined in (3.10)*. Then $\frac{1}{\tau_0}-1$ and λ_0 have the same sign.*

Proof. In view of Krein-Rutman Theorem in [21] and references therein, the eigenvalue problem (3.12) admits a principal eigenvalue λ_0 and a positive eigenfunction $\psi^*(x)$, satisfying

$$\begin{cases} d\Delta\psi^*(x)-\gamma_4(x)\psi^*(x)+G(x)\psi^*(x)=\lambda_0\psi^*(x), & x\in\Omega,\\ \dfrac{\partial\psi^*(x)}{\partial\eta}=0, & x\in\partial\Omega. \end{cases} \tag{3.13}$$

It follows from (3.9) and Theorem 3.1 that

$$\begin{cases} d\Delta\Psi_4^*(x)-\gamma_4(x)\Psi_4^*(x)+\tau_0G(x)\Psi_4^*(x)=0, & x\in\Omega,\\ \dfrac{\partial\Psi_4^*(x)}{\partial\eta}=0, & x\in\partial\Omega. \end{cases} \tag{3.14}$$

Multiplying the first equation in (3.13) by $\Psi_4^*(x)$ and the first equation in (3.14) by $\psi^*(x)$, then abstracting and integrating for $x \in \Omega$, yield

$$(1-\tau_0)\int_\Omega G(x)\Psi_4^*(x)\psi^*(x)dx = \lambda_0 \int_\Omega \Psi_4^*(x)\psi^*(x)dx.$$

Since $\int_\Omega G(x)\Psi_4^*(x)\psi^*(x)dx$ and $\int_\Omega \Psi_4^*(x)\psi^*(x)dx$ are positive, then $\tau_0 > 0$ owing to the expression of τ_0. Therefore, $\frac{1}{\tau_0} - 1$ and λ_0 have the same sign. $\square$

The following lemma can be obtained by Theorem 3.1 in [26].

Lemma 3.2. *The eigenvalue problem* (3.2) *admits a unique principal eigenvalue* λ_0. *Additionally,* $R_0 - 1$ *and* λ_0 *have the same sign.*

It follows from Lemma 3.1 and 3.2 that $R_0 - 1$ and $\frac{1}{\tau_0} - 1$ have the same sign.

When $0 < c < 1$ in problem (3.1), it means harvesting pulse occurs in this system and $1 - c$ is the harvesting rate. Let $E(x,t) = e^{-\lambda t}\phi_2(x,t), I(x,t) = e^{-\lambda t}\phi_3(x,t)$ and $W(x,t) = e^{-\lambda t}\phi_4(x,t)$ in problem (3.1), we obtain the corresponding eigenvalue problem

$$\begin{cases} (\varphi_2)_t = \delta\mu_1(x)S^*\varphi_4 + \delta\mu_2(x)S^*\varphi_3(x) \\ \qquad\quad - a(x)\varphi_2 + \gamma_2(x)\varphi_2 + \lambda\varphi_2, & x \in \Omega, t \in (0^+, T], \\ (\varphi_2)_t = (1-\delta)\mu_1 S^*\varphi_4(x) + ((1-\delta)\mu_2(x)S^* \\ \qquad\quad - \gamma_3(x))\varphi_3 + a(x)\varphi_2 + \lambda\varphi_3, & x \in \Omega, t \in (0^+, T], \\ (\varphi_4)_t - d\Delta\varphi_4 = -\gamma_4\varphi_4 + b(x)\varphi_3 + \lambda\varphi_4, & x \in \Omega, t \in (0^+, T], \\ \varphi_4(x, 0^+) = c\varphi_4(x, 0), & x \in \Omega, \\ \varphi_i(x, 0) = \varphi_i(x, T), & x \in \Omega, i = 2, 3, 4, \\ \dfrac{\partial\varphi_4}{\partial\eta} = 0, & x \in \partial\Omega. \end{cases} \tag{3.15}$$

Problem (3.15) is the periodic and degenerate eigenvalue problem with pulse, as we know, there is no results for the existence of the principal eigenvalue for this kind of problem, so now we consider the generalized principal eigenvalues.

Similarly as in [19], the generalized principal eigenvalues of problem (3.15) are defined as

$$\begin{aligned} \lambda_* = \sup\{\lambda \in \mathbf{R} : &\ \lambda \text{ satisfies } (3.15), \text{ where the equal signs} \\ &\text{of the first three equations are replaced by } \geq\}, \\ \lambda^* = \inf\{\lambda \in \mathbf{R} : &\ \lambda \text{ satisfies } (3.15), \text{ where the equal signs} \\ &\text{of the first three equations are replaced by } \leq\}. \end{aligned}$$

In the following, we will present the estimates of the generalized principal eigenvalues. Substituting $\varphi_2(x,t) = f_1(t)\psi_2(x), \varphi_3(x,t) = f_1(t)\psi_3(x)$ and $\varphi_4(x,t) = f_2(t)\psi_4(x)$ into (3.15), where $\psi_4(x)$ is the eigenfunction corresponding to the principal eigenvalue λ_1 for the eigenvalue problem

$$\begin{cases} -\psi_{xx} = \lambda\psi, & x \in \Omega, \\ \dfrac{\partial\psi}{\partial\eta} = 0, & x \in \partial\Omega. \end{cases} \tag{3.16}$$

Then problem (3.15) is converted into

$$\begin{cases} (f_1)_t\psi_2 = \delta\mu_1(x)S^* f_2\psi_4 + \delta\mu_2(x)S^* f_1\psi_3 - a(x)f_1\psi_2 & \\ \qquad + \gamma_2(x)f_1\psi_2 + \lambda f_1\psi_2, & x\in\Omega, t\in(0^+,T], \\ (f_1)_t\psi_3 = (1-\delta)\mu_1(x)S^* f_2\psi_4 + (1-\delta)\mu_2(x)S^* f_1\psi_3 & \\ \qquad - \gamma_3(x)f_1\psi_3 + a(x)f_1\psi_2 + \lambda f_1\psi_3, & x\in\Omega, t\in(0^+,T], \\ (f_2)_t\psi_4 + d\lambda_1 f_2\psi_4 = b(x)f_1\psi_3 - \gamma_4(x)f_2\psi_4 + \lambda f_2\psi_4, & x\in\Omega, t\in(0^+,T], \\ f_2(0^+) = cf_2(0), & \\ f_i(0) = f_i(T), & i=1,2. \end{cases} \tag{3.17}$$

Letting $\psi_4(x) = \psi_3(x) = \hat{\psi}(x), \psi_2(x) = m\hat{\psi}(x)$ for further simplification yields

$$\begin{cases} (f_1)_t = \frac{1}{m}\delta\mu_1(x)S^* f_2 + \frac{1}{m}\delta\mu_2(x)S^* f_1 - a(x)f_1 & \\ \qquad + \gamma_2(x)f_1 + \lambda f_1, & x\in\Omega, t\in(0^+,T], \\ (f_1)_t = (1-\delta)\mu_1(x)S^* f_2 + ((1-\delta)\mu_2(x)S^* - \gamma_3(x))f_1 & \\ \qquad + ma(x)f_1 + \lambda f_1, & x\in\Omega, t\in(0^+,T], \\ (f_2)_t + d\lambda_1 f_2 = b(x)f_1 - \gamma_4(x)f_2 + \lambda f_2, & x\in\Omega, t\in(0^+,T], \\ f_2(0^+) = cf_2(0), & \\ f_i(0) = f_i(T), & i=1,2. \end{cases} \tag{3.18}$$

To estimate the generalized principal eigenvalues λ_* and λ^*, the corresponding inequality problems

$$\begin{cases} (g_1)_t \geq \frac{1}{m}\delta\bar{\mu}_1\bar{S}^* g_2 + \frac{1}{m}\delta\bar{\mu}_2\bar{S}^* g_1 - (\underline{a} + \underline{\gamma}_2)g_1 + \lambda g_1, & t\in(0^+,T], \\ (g_1)_t \geq (1-\delta)\bar{\mu}_1\bar{S}^* g_2 + ((1-\delta)\bar{\mu}_2\bar{S}^* - \underline{\gamma}_3)g_1 + m\bar{a}g_1 + \lambda g_1, & t\in(0^+,T], \\ (g_2)_t \geq -d\lambda_1 g_2 + \bar{b}g_1 - \underline{\gamma}_4 g_2 + \lambda g_2, & t\in(0^+,T], \\ g_2(0^+) = cg_2(0), & \\ g_i(0) = g_i(T), & i=1,2 \end{cases} \tag{3.19}$$

and

$$\begin{cases} (h_1)_t \leq \frac{1}{m}\delta\underline{\mu}_1\underline{S}^* h_2 + \frac{1}{m}\delta\underline{\mu}_2\underline{S}^* h_1 - (\bar{a} + \bar{\gamma}_2)h_1 + \lambda h_1, & t\in(0^+,T], \\ (h_1)_t \leq (1-\delta)\underline{\mu}_1\underline{S}^* h_2 + ((1-\delta)\underline{\mu}_2\underline{S}^* - \bar{\gamma}_3)h_1 + m\underline{a}h_1 + \lambda h_1, & t\in(0^+,T], \\ (h_2)_t \leq -d\lambda_1 h_2 + \underline{b}h_1 - \bar{\gamma}_4 h_2 + \lambda h_2, & t\in(0^+,T], \\ h_2(0^+) = ch_2(0), & \\ h_i(0) = h_i(T), & i=1,2 \end{cases} \tag{3.20}$$

are considered, where $\overline{v} = \max_{x\in\overline{\Omega}} v(x)$ and $\underline{v} = \min_{x\in\overline{\Omega}} v(x)$ for $v(x) = \mu_1(x)$, $\mu_2(x)$, $S^*(x), a(x), b(x), \gamma_2(x), \gamma_3(x), \gamma_4(x)$. For simplicity, we choose $g_2 \le g_1$ and $h_2 \le h_1$, then (3.19) holds as long as

$$\begin{cases} (g_1)_t \ge \frac{1}{m}\delta\bar{\mu}_1\bar{S}^* g_1 + \frac{1}{m}\delta\bar{\mu}_2\bar{S}^* g_1 - (\underline{a} + \underline{\gamma}_2)g_1 + \lambda g_1, & t \in (0^+, T], \\ (g_1)_t \ge (1-\delta)\bar{\mu}_1\bar{S}^* g_1 + ((1-\delta)\bar{\mu}_2\bar{S}^* - \underline{\gamma}_3)g_1 + m\bar{a}g_1 + \lambda g_1, & t \in (0^+, T], \\ (g_2)_t \ge -d\lambda_1 g_2 + \bar{b}g_1 - \underline{\gamma}_4 g_2 + \lambda g_2, & t \in (0^+, T], \\ g_2(0^+) = cg_2(0), \\ g_i(0) = g_i(T), & i = 1, 2 \end{cases} \tag{3.21}$$

holds, and (3.20) holds as long as

$$\begin{cases} (h_1)_t \le \frac{1}{m}\delta\underline{\mu}_1\underline{S}^* h_2 + \frac{1}{m}\delta\underline{\mu}_2\underline{S}^* h_1 - (\bar{a} + \bar{\gamma}_2)h_1 + \lambda h_1, & t \in (0^+, T], \\ (h_1)_t \le (1-\delta)\underline{\mu}_1\underline{S}^* h_2 + ((1-\delta)\underline{\mu}_2\underline{S}^* - \bar{\gamma}_3)h_1 + m\underline{a}h_1 + \lambda h_1, & t \in (0^+, T], \\ (h_2)_t \le -d\lambda_1 h_2 + \underline{b}h_2 - \bar{\gamma}_4 h_2 + \lambda h_2, & t \in (0^+, T], \\ h_2(0^+) = ch_2(0), \\ h_i(0) = h_i(T), & i = 1, 2 \end{cases} \tag{3.22}$$

holds. Denote

$$c_1 = \frac{1}{m}\delta\bar{\mu}_1\bar{S}^* + \frac{1}{m}\delta\bar{\mu}_2\bar{S}^* - (\underline{a} + \underline{\gamma}_2),\ c_2 = (1-\delta)\bar{\mu}_1\bar{S}^* + ((1-\delta)\bar{\mu}_2\bar{S}^* - \underline{\gamma}_3) + m\bar{a},$$
$$c_3 = \bar{b},\ c_4 = -d\lambda_1 - \underline{\gamma}_4,\ k_1 = \frac{1}{m}\delta\underline{\mu}_2\underline{S}^* - (\bar{a} + \bar{\gamma}_2),\ k_2 = \frac{1}{m}\delta\underline{\mu}_1\underline{S}^*,$$
$$k_3 = ((1-\delta)\underline{\mu}_2\underline{S}^* - \bar{\gamma}_3) + m\underline{a},\ k_4 = (1-\delta)\underline{\mu}_1\underline{S}^*,\ k_5 = -d\lambda_1 + \underline{b} - \bar{\gamma}_4.$$

By careful calculation, problem (3.21) reduces to

$$\begin{cases} (g_1)_t \ge c_1 g_1 + \lambda g_1, & t \in (0^+, T], \\ (g_1)_t \ge c_2 g_1 + \lambda g_1, & t \in (0^+, T], \\ (g_2)_t \ge c_3 g_1 + c_4 g_2 + \lambda g_2, & t \in (0^+, T], \\ g_2(0^+) = cg_2(0), \\ g_i(0) = g_i(T), & i = 1, 2, \end{cases} \tag{3.23}$$

and problem (3.22) reduces to

$$\begin{cases} (h_1)_t \le k_1 h_1 + k_2 h_2 + \lambda h_1, & t \in (0^+, T], \\ (h_1)_t \le k_3 h_1 + k_4 h_2 + \lambda h_1, & t \in (0^+, T], \\ (h_2)_t \le k_5 h_2 + \lambda h_2, & t \in (0^+, T], \\ h_2(0^+) = ch_2(0), \\ h_i(0) = h_i(T), & i = 1, 2. \end{cases} \tag{3.24}$$

The first inequality in problem (3.23) can be written as

$$\frac{(g_1)_t}{g_1} \ge c_1 + \lambda. \tag{3.25}$$

Integrating both sides of inequality in (3.25) over $(0^+, T)$, which together with the last two equations of problem (3.23), yields that $\lambda \le -c_1$. It then follows from problems (3.23) and (3.25) that $g_1(t) \geq e^{(c_1+\lambda)t}$. Similarly, $\lambda \leq -c_2$ and $g_1(t) \geq e^{(c_2+\lambda)t}$ can be deduced by the second inequality of problem (3.23).

In what follows, we construct

$$g_1(t) = \frac{1}{c},\ g_2(t) = \begin{cases} e^{-\frac{\ln c}{T}t}, & t \in (0^+, T], \\ \frac{1}{c}, & t = 0, \end{cases}$$

which is substituted into the third inequality in problem (3.23) to derive that $\lambda \leq -c_4 - \frac{1}{T}\ln c - \frac{c_3}{c}e^{\frac{\ln c}{T}t}$. Then we have $\lambda \leq -c_4 - \frac{1}{T}\ln c - \frac{c_3}{c}$, and

$$\lambda_* \geq \min\left\{-c_1, -c_2, -c_4 - \frac{1}{T}\ln c - \frac{c_3}{c}\right\} \tag{3.26}$$

by the definition of the generalized eigenvalue λ_*.

Similarly, the third inequality in problem (3.24) can be written as

$$\frac{(h_2)_t}{h_2} \leq k_5 + \lambda, \tag{3.27}$$

and then integrating both sides of inequality aforementioned over $(0^+, T)$ to get $\lambda \geq -k_5 - \frac{1}{T}\ln c$. It can be derived through problems (3.24) and (3.27) that $h_2(t) \leq e^{-\frac{\ln c}{T}t}, t \in (0^+, T]$ and $h_2(0) \leq \frac{1}{c}$.

We still construct

$$h_1(t) = \frac{1}{c},\ h_2(t) = \begin{cases} e^{-\frac{\ln c}{T}t}, & t \in (0^+, T], \\ \frac{1}{c}, & t = 0, \end{cases}$$

which is substituted into the first two inequalities in (3.24), assert $\lambda \geq -k_1 - ck_2$ and $\lambda \geq -k_3 - ck_4$. Therefore, we obtain

$$\lambda^* \leq \max\left\{-k_1 - ck_2, -k_3 - ck_4, -k_5 - \frac{1}{T}\ln c\right\} \tag{3.28}$$

by the definition of the generalized eigenvalue λ^*.

To sum up, we have the following estimates of the generalized principal eigenvalues.

Theorem 3.2. *The generalized principal eigenvalues of problem* (3.15) *satisfy*

$$\begin{aligned} \lambda_* &\geq \min\left\{-c_1, -c_2, -c_4 - \frac{1}{T}\ln c - \frac{c_3}{c}\right\}, \\ \lambda^* &\leq \max\left\{-k_1 - ck_2, -k_3 - ck_4, -k_5 - \frac{1}{T}\ln c\right\}. \end{aligned}$$

Remark 3.3. Let $\delta = \mu_1(x) = \mu_2(x) = a(x) = \gamma_2(x) = b(x) = 0, \gamma_3(x) = \gamma_3, \gamma_4(x) = \gamma_4$ and $\gamma_3 = d\lambda_1 + \gamma_4 - \frac{\ln c}{T}$ in problem (3.15). A simple calculation yields $\lambda^* = \lambda_* = \gamma_3$, which means that the principal eigenvalue of problem (3.15) exists and $\lambda = \gamma_3$.

Similar as Lemma 2.3 in [15], we have the following positivity of the solution by using the strong maximum principle and the Hopf boundary lemma.

Lemma 3.3. *Assume that $u(x,t)$ is the solution to problem* (1.1)*with nontrivial initial value $\phi \in \mathbf{X}^+$. Then $S(x,t) > 0, E(x,t) > 0, I(x,t) > 0$ and $W(x,t) > 0$ for any $x \in \bar{\Omega}, t > 0$.*

Next, we give the long time behavior of the solution according to the principal eigenvalue (for $c = 1$) or the generalized principal eigenvalues (for $0 < c < 1$).

Theorem 3.3. *When $c = 1$, i.e. there is no pulse in problem* (1.1)*, if $R_0 < 1$, then the disease-free equilibrium $E_0(S^*(x), 0, 0, 0)$ of problem* (1.1) *is globally asymptotically stable.*

Proof. We first define a Lyapunov function through positive eigenfunction pair $(\Psi_4^*(x), \Psi_3^*(x), \Psi_2^*(x))$ defined in (3.6),

$$\begin{aligned} W = \int_\Omega \Big[& \frac{[a(x) + (1-\delta)\gamma_2(x)]\Psi_2^*(x)}{a(x)} S^*(x) g\left(\frac{S}{S^*(x)}\right) + \Psi_2^*(x)E \\ & + \Psi_3^*(x)I + \Psi_4^*(x)W \Big]\, dx, \end{aligned}$$

where $g(x) = x - 1 - \ln x$.

Recall problem (3.5), we get

$$\begin{aligned} &\Psi_2^*(x) = \frac{a(x)}{a(x) + \gamma_2(x)} \Psi_3^*(x), \\ &\Psi_3^*(x) = \frac{b(x)(a(x) + \gamma_2(x))}{\gamma_3(x)(a(x) + \gamma_2(x)) - \mu_2(x)S^*(x)(a(x) + (1-\delta)\gamma_2(x))} \Psi_4^*(x), \\ &\gamma_4(x)\Psi_4^*(x) = d\Delta\Psi_4^*(x) + \tau_0 \left[(1-\delta)\mu_1(x)S^*(x)\Psi_3^*(x) + \delta\mu_1(x)S^*(x)\Psi_2^*(x)\right] \Psi_4^*(x). \end{aligned}$$

Direct calculation to the derivative of W yields

$$\begin{aligned} \frac{dW}{dt} = & \int_\Omega \frac{[a(x) + (1-\delta)\gamma_2(x)]\Psi_2^*(x)}{a(x)} \left(1 - \frac{S^*(x)}{S}\right) [\gamma_1(x)S^*(x) - \mu_1(x)SW \\ & - \mu_2(x)SI - \gamma_1(x)S] + \Psi_2^*(x) \left[\delta\mu_1(x)SW + \delta\mu_2(x)SI - a(x)E - \gamma_2(x)E\right] \\ & + \Psi_3^*(x) \left[(1-\delta)\mu_1(x)SW + (1-\delta)\mu_2(x)SI + a(x)E - \gamma_3(x)I\right] \\ & + \Psi_4^*(x) \left[d\Delta W + b(x)I - \gamma_4(x)W\right] dx \\ = & \int_\Omega \frac{[a(x) + (1-\delta)\gamma_2(x)]\Psi_2^*(x)}{a(x)} \Bigg[\gamma_1(x)S^*(x) \left(2 - \frac{S^*(x)}{S} - \frac{S}{S^*(x)}\right) \\ & + \mu_1(x)S^*(x)W\Bigg]dx - \int_\Omega \Psi_3^*(x)\gamma_3(x)I dx + \int_\Omega \Psi_4^*(x) \left[d\Delta W + b(x)I - \gamma_4(x)W\right] dx \\ = & \int_\Omega \frac{[a(x) + (1-\delta)\gamma_2(x)]\Psi_2^*(x)}{a(x)} \Bigg[\gamma_1(x)S^*(x) \left(2 - \frac{S^*(x)}{S} - \frac{S}{S^*(x)}\right) \\ & + (\mu_1(x)S^*(x)W - \tau_0\mu_1(x)S^*(x)W)\Bigg]dx + \int_\Omega d\left(\Psi_4^*(x)\Delta W - W\Delta\Psi_4^*(x)\right) dx. \end{aligned}$$

It follows from the Green's first formula and Neumann boundary condition that

$$\int_\Omega d\left(\Psi_4^*(x)\Delta W(x,t) - W(x,t)\Delta\Psi_4^*(x)\right) dx = 0.$$

Therefore, we obtain

$$\begin{aligned} \frac{dW}{dt} = \int_\Omega & \frac{[a(x) + (1-\delta)\gamma_2(x)]\Psi_2^*(x)}{a(x)} \Bigg[\gamma_1(x)S^*(x) \left(2 - \frac{S^*(x)}{S} - \frac{S}{S^*(x)}\right) \\ & + \mu_1(x)S^*(x)W\left(1 - \tau_0\right)\Bigg]dx. \end{aligned}$$

Recalling that R_0-1 and $\frac{1}{\tau_0}-1$ have the same sign, $R_0<1$ means that $1-\tau_0<0$, we then have $\frac{dW}{dt}\leq 0$, and $E_0(S^*(x),0,0,0)$ is globally asymptotically stable by the similar argument as in [16]. □

Theorem 3.4. *When $0<c<1$, i.e. harvesting pulse takes place in problem* (1.1), *if $\lambda_*>0$, then the disease-free equilibrium $E_0(S^*(x),0,0,0)$ of problem* (1.1) *is globally asymptotically stable.*

Proof. First, it follows from (1.1) and the comparison principle that $S(x,t)\leq\tilde{S}(x,t)$, where $\tilde{S}$ satisfies

$$\begin{cases}\dfrac{\partial\tilde{S}}{\partial t}=\alpha(x)-\gamma_1(x)\tilde{S}, & x\in\Omega, t>0,\\ \tilde{S}(x,0)=S_0(x), & x\in\overline{\Omega}.\end{cases}\tag{3.29}$$

It is easy to check that $\lim\limits_{t\to\infty}\tilde{S}(x,t)=S^*(x)$ uniformly for $x\in\overline{\Omega}$, therefore, for any small $\varepsilon_0>0$, there exists $T_0>0$ such that $S(x,t)<S^*(x)+\varepsilon_0$ for $t>T_0$ and $x\in\overline{\Omega}$.

Since $\lambda_*>0$, there exists $\lambda>0$ and positive function pair $(\varphi_2^*(x,t),\varphi_3^*(x,t),\varphi_4^*(x,t))$, satisfying

$$\begin{cases}(\varphi_2^*)_t\geq\delta\mu_1(x)S^*\varphi_4^*+\delta\mu_2(x)S^*\varphi_3^*-(a(x)+\gamma_2(x))\varphi_2^* & \\ \qquad\quad+\lambda\varphi_2^*, & x\in\Omega, t\in(0^+,T],\\ (\varphi_3^*)_t\geq(1-\delta)\mu_1(x)S^*\varphi_4^*+((1-\delta)\mu_2(x)S^*-\gamma_3(x))\varphi_3^* & \\ \qquad\quad+a(x)\varphi_2^*+\lambda\varphi_3^*, & x\in\Omega, t\in(0^+,T],\\ (\varphi_4^*)_t\geq d\Delta\varphi_4^*-\gamma_4\varphi_4^*+b(x)\varphi_3^*+\lambda\varphi_4^*, & x\in\Omega, t\in(0^+,T],\\ \varphi_4^*(x,0^+)=c\varphi_4^*(x,0), & x\in\Omega,\\ \varphi_i^*(x,0)=\varphi_i^*(x,T), & x\in\Omega, i=2,3,4,\\ \dfrac{\partial\varphi_4^*}{\partial\eta}=0, & x\in\partial\Omega.\end{cases}$$

Let $(\tilde{E},\tilde{I},\tilde{W})=(Me^{kt}\varphi_2^*,Me^{kt}\varphi_3^*,Me^{kt}\varphi_4^*)$ with $-\lambda<k<0$. We show that $(\tilde{E},\tilde{I},\tilde{W})\geq(E,I,W)$, where (S,E,I,W) is the solution of (1.1). In fact,

$$\begin{aligned}&\tilde{E}_t-\delta\mu_1(x)\tilde{S}\tilde{W}-\delta\mu_2(x)\tilde{S}\tilde{I}+a(x)\tilde{E}+\gamma_2(x)\tilde{E}\\ &=\tilde{E}_t-\delta\mu_1(x)(S^*(x)+\varepsilon_0)\tilde{W}-\delta\mu_2(x)(S^*(x)+\varepsilon_0)\tilde{I}+a(x)\tilde{E}+\gamma_2(x)\tilde{E}\\ &=kMe^{kt}\varphi_2^*+Me^{kt}(\varphi_2^*)_t-\delta\mu_1(x)(S^*(x)+\varepsilon_0)Me^{kt}\varphi_4^*+a(x)Me^{kt}\varphi_2^*\\ &\quad-\delta\mu_2(x)(S^*(x)+\varepsilon_0)Me^{kt}\varphi_3^*+\gamma_2(x)Me^{kt}\varphi_2^*\\ &\geq kMe^{kt}\varphi_2^*+\delta\mu_1(x)S^*(x)Me^{kt}\varphi_4^*+\delta\mu_2(x)S^*(x)Me^{kt}\varphi_3^*+\lambda Me^{kt}\varphi_2^*\\ &\quad-(a(x)+\gamma_2(x))Me^{kt}\varphi_2^*-\delta\mu_1(x)(S^*(x)+\varepsilon_0)Me^{kt}\varphi_4^*+a(x)Me^{kt}\varphi_2^*\\ &\quad-\delta\mu_2(x)(S^*(x)+\varepsilon_0)Me^{kt}\varphi_3^*+\gamma_2(x)Me^{kt}\varphi_2^*\\ &=(k+\lambda)\tilde{E}-\varepsilon_0\delta\mu_1(x)\tilde{W}-\varepsilon_0\delta\mu_2(x)\tilde{I}.\end{aligned}$$

In consideration of $\lambda+k>0$, we can take a sufficiently small ε_0 such that

$$\tilde{E}_t-\delta\mu_1(x)\tilde{S}\tilde{W}-\delta\mu_2(x)\tilde{S}\tilde{I}+a(x)\tilde{E}+\gamma_2(x)\tilde{E}\geq 0.$$

Similarly, it can be deduced that

$$\tilde{I}_t - (1-\delta)\mu_1(x)\tilde{S}\tilde{W} - (1-\delta)\mu_2(x)\tilde{S}\tilde{I} - a(x)\tilde{E} + \gamma_3(x)\tilde{I} \geq 0,$$
$$\tilde{W}_t - d\Delta\tilde{W} - b(x)\tilde{I} + \gamma_4(x)\tilde{W} \geq 0$$

as long as ε_0 is sufficiently small. Hence, if we choose a sufficiently big M, then $(\tilde{E}, \tilde{I}, \tilde{W})$ is an upper solution of the following problem

$$\begin{cases} \dfrac{\partial E}{\partial t} = \delta\mu_1(x)SW + \delta\mu_2(x)SI - a(x)E - \gamma_2(x)E, & x \in \Omega,\ t \in \left((nT)^+, (n+1)T\right], \\ \dfrac{\partial I}{\partial t} = (1-\delta)\mu_1(x)SW + (1-\delta)\mu_2(x)SI & \\ \qquad + a(x)E - \gamma_3(x)I, & x \in \Omega,\ t \in \left((nT)^+, (n+1)T\right], \\ \dfrac{\partial W}{\partial t} = d\Delta W + b(x)I - \gamma_4(x)W, & x \in \Omega,\ t \in \left((nT)^+, (n+1)T\right], \\ W(x, (nT)^+) = cW(x, nT), & x \in \Omega, n = 0, 1, 2, ..., \\ V(x, (nT)^+) = V(x, nT), & x \in \Omega, V = E, I, \\ \dfrac{\partial W}{\partial \eta} = 0, & x \in \partial\Omega, t > 0, \\ \quad (E(x,0), I(x,0), W(x,0)) & \\ = (E_0(x), I_0(x), W_0(x)) \geq 0, & x \in \overline{\Omega}, \end{cases}$$

which means that $(\tilde{E}, \tilde{I}, \tilde{W}) \geq (E, I, W)$.

On the other hand, since $\lim\limits_{t\to\infty}(\tilde{E}(x,t), \tilde{I}(x,t), \tilde{W}(x,t)) = (0,0,0)$, then we have

$$\lim_{t\to\infty}(E(x,t), I(x,t), W(x,t)) = (0,0,0) \text{ for } x \in \overline{\Omega},$$

which implies that for any $\varepsilon > 0$, there exists $T_1 > 0$ such that $0 \leq I(x,t) \leq \varepsilon$ and $0 \leq W(x,t) \leq \varepsilon$ for $x \in \overline{\Omega}$ and $t \geq T_1$. By the first equation in problem (1.1), we have

$$\alpha(x) - \varepsilon\mu_1(x)S - \varepsilon\mu_2(x)S - \gamma_1(x)S \leq S_t \leq \alpha(x) - \gamma_1(x)S,$$

for $x \in \overline{\Omega}$ and $t \geq T_1$.

The arbitrariness of ε yields $\lim\limits_{t\to\infty} S(x,t) = S^*(x)$, and the disease-free equilibrium $E_0(S^*(x), 0, 0, 0)$ of problem (1.1) with harvesting pulse is globally asymptotically stable. □

According to Lemma 2.8 in [15] and Theorem 4.2 in [30], we have the following results.

Lemma 3.4. *Suppose $c = 1$, i.e. there is no pulse in problem* (1.1)*. If $R_0 > 1$, then steady state solution E_0 is a uniform weak repeller, that is,*

$$\limsup_{t\to+\infty} ||(S, E, I, W) - (S^*, 0, 0, 0)|| \geq \varepsilon_0$$

for some $\varepsilon_0 > 0$.

Lemma 3.5. *Suppose $c = 1$, i.e. there is no pulse in problem* (1.1)*. If $R_0 > 1$, then there exists a constant $\varepsilon > 0$, such that the positive solution (S, E, I, W) to problem* (1.1) *satisfies*

$$\liminf_{t\to+\infty} S(x,t) \geq \varepsilon,\ \liminf_{t\to+\infty} E(x,t) \geq \varepsilon,\ \liminf_{t\to+\infty} I(x,t) \geq \varepsilon,\ \liminf_{t\to+\infty} W(x,t) \geq \varepsilon \tag{3.30}$$

for $x \in \overline{\Omega}$. Furthermore, problem (1.1) *admits a unique positive steady state* $E_1(\overline{S}(x), \overline{E}(x), \overline{I}(x), \overline{W}(x))$ *when* $\gamma_1(x)\gamma_3(x)(a(x)+\gamma_2(x)) - \alpha(x)\mu_2(x)[a(x)+(1-\delta)\gamma_2(x)] > 0$, *where* $\overline{S}(x), \overline{E}(x), \overline{I}(x), \overline{W}(x)$ *satisfying*

$$\begin{cases} \alpha(x) - \mu_1(x)\overline{SW} - \mu_2(x)\overline{SI} - \gamma_1(x)\overline{S} = 0, & x \in \Omega, \\ \delta\mu_1(x)\overline{SW} + \delta\mu_2(x)\overline{SI} - (a(x)+\gamma_2(x))\overline{E} = 0, & x \in \Omega, \\ (1-\delta)\mu_1(x)\overline{SW} + (1-\delta)\mu_2(x)\overline{SI} + a(x)\overline{E} - \gamma_3(x)\overline{I} = 0, & x \in \Omega, \\ d\Delta\overline{W} + b(x)\overline{I} - \gamma_4(x)\overline{W} = 0, & x \in \Omega, \\ \dfrac{\partial \overline{W}}{\partial \eta} = 0, & x \in \partial\Omega. \end{cases} \tag{3.31}$$

Proof. The result (3.30) is followed from the positivity of the solution, Lemma 3.4 and Theorem 3 in [22], and the existence of positive steady state solution to problem (1.1) is similar as Lemma 2.9(ii) in [15] and Theorem 4.2 in [30], we omit the proofs here with obvious modifications. In the following, we will prove the uniqueness.

The first three equations of problem (3.31) indicates that $\overline{I}(x)$ satisfies

$$\begin{aligned} &\gamma_3(x)\mu_2(x)(a(x)+\gamma_2(x))\overline{I}^2 + \gamma_3(x)[\gamma_1(x)+\mu_1(x)\overline{W}](a(x)+\gamma_2(x))\overline{I} \\ &- \alpha(x)\mu_2(x)[a(x)+(1-\delta)\gamma_2(x)]\overline{I} - \alpha(x)\mu_1(x)\overline{W}[a(x)+(1-\delta)\gamma_2(x)] = 0. \end{aligned} \tag{3.32}$$

In view of $\overline{I}(x) > 0$, we get

$$\overline{I}(x) = \frac{\alpha(x)\mu_2(x)[a(x)+(1-\delta)\gamma_2(x)] - \gamma_3(x)[\gamma_1(x)+\mu_1(x)\overline{W}](a(x)+\gamma_2(x)) + \sqrt{\Delta}}{2\gamma_3(x)\mu_2(x)(a(x)+\gamma_2(x))},$$

where

$$\begin{aligned} \Delta = &\left\{\gamma_3(x)[\gamma_1(x)+\mu_1(x)\overline{W}](a(x)+\gamma_2(x)) - \alpha(x)\mu_2(x)[a(x)+(1-\delta)\gamma_2(x)]\right\}^2 \\ &+ 4(a(x)+\gamma_2(x))\gamma_3(x)\mu_1(x)\mu_2(x)\alpha(x)[a(x)+(1-\delta)\gamma_2(x)]\overline{W}. \end{aligned}$$

If $\gamma_1(x)\gamma_3(x)(a(x)+\gamma_2(x)) - \alpha(x)\mu_2(x)[a(x)+(1-\delta)\gamma_2(x)] > 0$, then the equation (3.32) can be rewritten as

$$A\overline{I}^2(x) + (B\overline{W}(x)+C)\overline{I}(x) - D\overline{W}(x) = 0,$$

where $A = \gamma_3(x)\mu_2(x)(a(x)+\gamma_2(x)) > 0$, $B = \gamma_3(x)\mu_1(x)(a(x)+\gamma_2(x)) > 0$, $C = \gamma_1(x)\gamma_3(x)(a(x)+\gamma_2(x)) - \alpha(x)\mu_2(x)[a(x)+(1-\delta)\gamma_2(x)] > 0$ and $D = \alpha(x)\mu_1(x)[a(x) + (1-\delta)\gamma_2(x)] > 0$.

Let $f\left(\overline{W}\right) = -\gamma_4(x)\overline{W} + b(x)\overline{I}$, we can see from $-d\Delta\overline{W}(x) = -\gamma_4(x)\overline{W}(x) + b(x)\overline{I}(x)$ that the monotonicity of $\frac{f(\overline{W})}{\overline{W}}$ and $\frac{\overline{I}(x)}{\overline{W}(x)}$ is consistent.

Denote $g(\overline{W}(x)) = \frac{\overline{I}(x)}{\overline{W}(x)} = \frac{-(B+\frac{C}{\overline{W}})+\sqrt{(B+\frac{C}{\overline{W}})^2+\frac{4AD}{\overline{W}}}}{2A}$. After careful calculation, we derive that the derivative of $\frac{\overline{I}(x)}{\overline{W}(x)}$ with respect to $\overline{W}$ is less than zero when $\gamma_1(x)\gamma_3(x)(a(x)+\gamma_2(x)) - \alpha(x)\mu_2(x)[a(x)+(1-\delta)\gamma_2(x)] > 0$, which implies $\frac{f(\overline{W})}{\overline{W}}$ is nonincreasing with respect to $\overline{W}$. The uniqueness is now completed. □

Next we consider global asymptotic property of the endemic equilibrium of the system (1.1) with no pulse.

Theorem 3.5. *Assume that $c = 1$, which means no pulse occurs. If $R_0 > 1$, then the endemic equilibrium $E_1(\overline{S}(x), \overline{E}(x), \overline{I}(x), \overline{W}(x))$ of problem (1.1) is globally asymptotically stable.*

Proof. Define

$$H(t) = \int_\Omega \frac{b(x)\overline{I}(x)}{\mu_1(x)\overline{S}(x)} \left[\overline{S}(x) g\left(\frac{S}{\overline{S}(x)}\right) + \overline{E}(x) g\left(\frac{E}{\overline{E}(x)}\right) + \overline{I}(x) g\left(\frac{I}{\overline{I}(x)}\right) \right.$$
$$\left. + \frac{\mu_1(x)\overline{S}(x)\overline{W}(x)}{b(x)\overline{I}(x)} \overline{W}(x) g\left(\frac{W}{\overline{W}(x)}\right)\right] dx,$$

where $g(x) = x - 1 - \ln x$.

By calculating the derivative of H along the positive solution of system (1.1), we have

$$\begin{aligned} \frac{dH}{dt} =& \int_\Omega \frac{b(x)\overline{I}(x)}{\mu_1(x)\overline{S}(x)} \left[\left(1 - \frac{\overline{S}(x)}{S}\right)(\alpha(x) - \mu_1(x)SW - \mu_2(x)SI - \gamma_1(x)S) \right. \\ &+ \left(1 - \frac{\overline{E}(x)}{E}\right)(\delta\mu_1(x)SW + \delta\mu_2(x)SI - a(x)E - \gamma_2(x)E) \\ &+ \left(1 - \frac{\overline{I}(x)}{I}\right)((1-\delta)\mu_1(x)SW + (1-\delta)\mu_2(x)SI + a(x)E - \gamma_3(x)I) \\ &\left. + \frac{\mu_1(x)\overline{S}(x)\overline{W}(x)}{b(x)\overline{I}(x)}\left(1 - \frac{\overline{W}(x)}{W}\right)(d\Delta W + b(x)I - \gamma_4(x)W)\right] dx. \end{aligned} \tag{3.33}$$

Since E_1 is the steady state solution to problem (1.1), substituting (3.31) into (3.33) yields

$$\begin{aligned} \frac{dH}{dt} =& \int_\Omega \overline{W}(x)\left[\left(1 - \frac{\overline{W}(x)}{W}\right) d\Delta W + \left(1 - \frac{W}{\overline{W}(x)}\right) d\Delta\overline{W}(x)\right] dx \\ &+ \int_\Omega \frac{b(x)\overline{I}(x)}{\mu_1(x)\overline{S}(x)} \left[\gamma_1(x)\overline{S}(x)\left(2 - \frac{S}{\overline{S}(x)} - \frac{\overline{S}(x)}{S}\right)\right. \\ &+ (1-\delta)\mu_1(x)\overline{S}(x)\overline{W}(x)\left(3 - \frac{SW\overline{I}(x)}{\overline{S}(x)\overline{W}(x)I} - \frac{\overline{S}(x)}{S} - \frac{\overline{W}(x)I}{W\overline{I}(x)}\right) \\ &+ \delta\mu_1(x)\overline{S}(x)\overline{W}(x)\left(4 - \frac{\overline{S}(x)}{S} - \frac{SW\overline{E}(x)}{\overline{S}(x)\overline{W}(x)E} - \frac{E\overline{I}(x)}{\overline{E}(x)I} - \frac{\overline{W}(x)I}{W\overline{I}(x)}\right) \\ &+ (1-\delta)\mu_2(x)\overline{S}(x)\overline{I}(x)\left(2 - \frac{\overline{S}(x)}{S} - \frac{S}{\overline{S}(x)}\right) \\ &+ \delta\mu_2(x)\overline{S}(x)\overline{I}(x)\left(3 - \frac{\overline{S}(x)}{S} - \frac{SI\overline{E}(x)}{\overline{S}(x)\overline{I}(x)E} - \frac{E\overline{I}(x)}{\overline{E}(x)I}\right) \end{aligned} \tag{3.34}$$

$$-\gamma_2(x)\overline{E}(x)\left(1+\frac{E}{\overline{E}(x)}-\frac{I}{\overline{I}(x)}-\frac{E\overline{I}(x)}{\overline{E}(x)I}\right)\Bigg]dx.$$

It then follows from Green's first formula and Neumann boundary condition that

$$\begin{aligned}
&\int_\Omega \overline{W}(x)\left[\left(1-\frac{\overline{W}(x)}{W}\right)d\Delta W+\left(1-\frac{W}{\overline{W}(x)}\right)d\Delta\overline{W}(x)\right]dx\\
=&d\left[\int_{\partial\Omega}\overline{W}(x)\left(1-\frac{\overline{W}(x)}{W}\right)\nabla W\cdot\eta dS-\int_\Omega\nabla\overline{W}(x)\left(1-\frac{\overline{W}(x)}{W}\right)\nabla W dx\right.\\
&\left.+\int_{\partial\Omega}\overline{W}(x)\left(1-\frac{W}{\overline{W}(x)}\right)\nabla\overline{W}(x)\cdot\eta dS-\int_\Omega\nabla\overline{W}(x)\left(1-\frac{W}{\overline{W}(x)}\right)\nabla\overline{W}(x)dx\right]\\
=&-d\int_\Omega\sum_{j=1}^n\left(\frac{\overline{W}(x)}{W}\frac{\partial W}{\partial x_j}-\frac{\partial\overline{W}(x)}{\partial x_j}\right)^2dx.
\end{aligned}$$

Hence, $\frac{dH}{dt}\le 0$, and the equality sign holds if and only if

$$(S(x,t),E(x,t),I(x,t),W(x,t))=\left(\overline{S}(x),\overline{E}(x),\overline{I}(x),\overline{W}(x)\right).$$

We finally obtain that E_1 is globally asymptotically stable. □

It is quite difficult to analyze the stability of the endemic equilibrium of problem (1.1) with harvesting pulse (i.e. $0<c<1$), however, the following numerical approximations (see Fig. 6) show that if $\lambda^*<0$, the solution to problem (1.1) tends to a positive periodic solution.

4. Numerical simulations

In this section, numerical approximations are carried out to verify the correctness of the theoretical results and explore the impact of virus reproduction rate and diffusion coefficient on the basic reproduction number.

We choose function $b(x)=b_0\left(1+k\sin\left(\frac{9\pi x}{10}\right)\right)$, and fix other parameters ([3, 14, 20, 25, 27])

$$\begin{aligned}
&\alpha=0.86\times10^5,\ \gamma_1=0.01,\ \mu_1=0.105\times10^{-5},\ \mu_2=0.4\times10^{-8},\\
&\delta=0.001,\ a=0.1,\ \gamma_2=0.004,\ \gamma_3=7,\ \Omega=[0,10],\\
&(S_0(x),E_0(x),I_0(x),W_0(x))=(10^6,0,0,0.001\times e^{-(x-5)^2}).
\end{aligned}\tag{4.1}$$

Example 4.1. The virus reproduction rate $b(x)=b_0\left(1+0.5\sin\left(\frac{9\pi x}{10}\right)\right)$.

We first fix $d=0.01, c=1, b_0=0.05$, then $\frac{1}{\tau_0}\approx 0.8141<1$ and the basic reproduction number $R_0<1$. Problem (3.1) admits a disease-free equilibrium $E_0(5\times10^6,0,0,0)$, and if $R_0<1$, E_0 is globally asymptotically stable. It is shown in Fig. 1 that $I(x,t)$ and $W(x,t)$ decay to 0 with time evolution.

We secondly fix $d=0.01, c=1, b_0=0.12$, then $\frac{1}{\tau_0}\approx 1.9537>1$ and $R_0>1$. Problem (3.1) admits an endemic equilibrium E_1, and if $R_0>1$, E_1 is globally asymptotically stable. Fig. 2 indicates that $I(x,t)$ and $W(x,t)$ ultimately stabilize to a positive steady state.

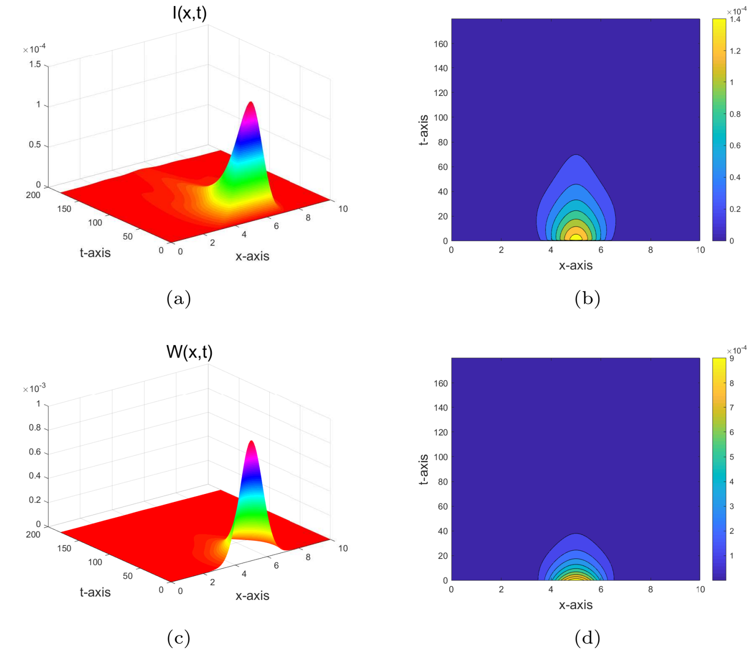


Figure 1. Choose $b_0 = 0.05$ and other parameters fixed in (4.1)($R_0 < 1$). $I(x,t)$ and $W(x,t)$ decay to zero.

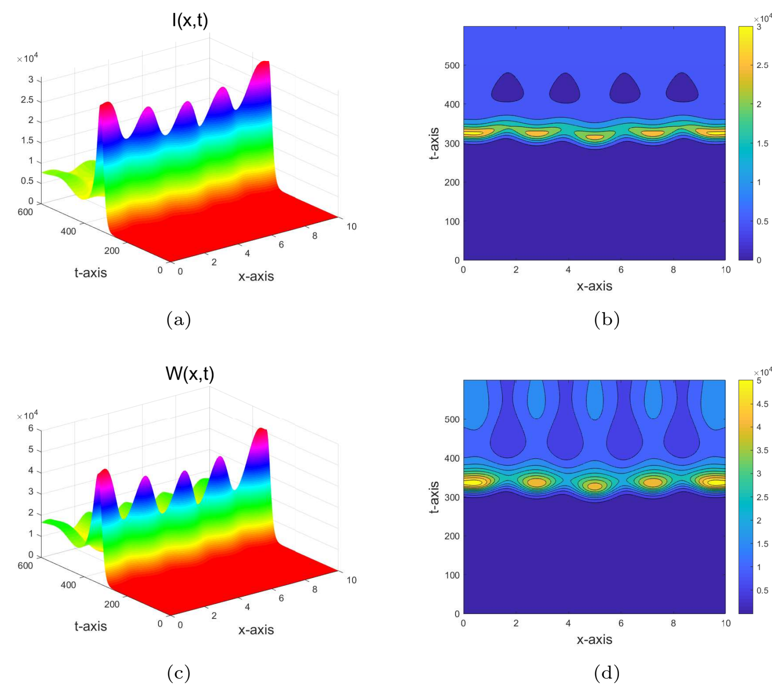
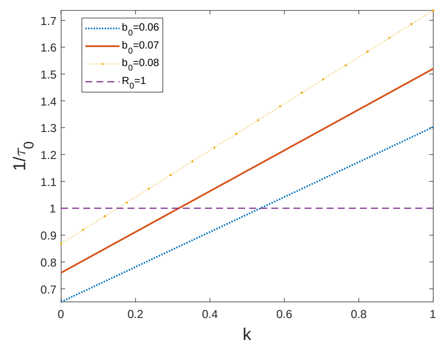


Figure 2. Choose $b_0 = 0.12$ and other parameters fixed in (4.1) ($R_0 > 1$). $I(x,t)$ and $W(x,t)$ tend to a positive steady state.

Example 4.2. The virus reproduction rate $b(x) = b_0\left(1 + k\sin\left(\frac{9\pi x}{10}\right)\right)$ with $0 \leq k < 1$.

We still fix $d = 0.01, c = 1$, and then choose $b_0 = 0.06,\ 0.07,\ 0.08$, respectively. It is worth noting in Fig. 3 that $\frac{1}{\tau_0}$ is a nondecreasing function with respect to k. Owing to the same sign of $R_0 - 1$ and $\frac{1}{\tau_0} - 1$, we can see that the increase of the virus reproduction rate in heterogeneous environment will lead to an increase in R_0, which increases the risk of disease infection and bring about more infections.



(a)

Figure 3. Choose $b_0 = 0.06, 0.07, 0.08$ and other parameters fixed in (4.1). The impact of k on $\frac{1}{\tau_0}$.

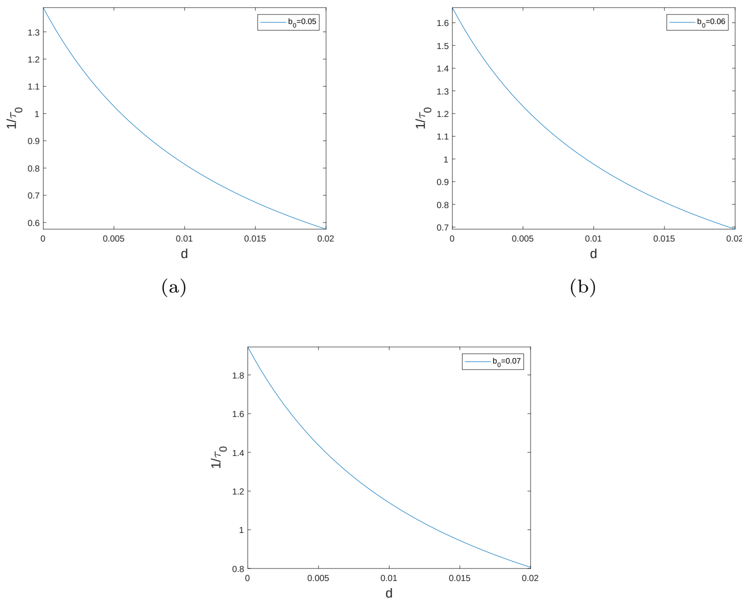
Example 4.3. The impact of virus diffusion coefficient d on basic reproduction number R_0 in heterogeneous environment.

In order to investigate the effect of virus diffusion coefficient on R_0, we first let the diffusion coefficient d changes over $[0, 0.02]$. Then fix $c = 1$, $b(x) = b_0\left(1 + 0.5\sin\left(\frac{9\pi x}{10}\right)\right)$, and select $b_0 = 0.05,\ 0.06,\ 0.07$. It is clear in Fig. 4 that $\frac{1}{\tau_0}$ is nonincreasing with respect to d. Since $R_0 - 1$ and $\frac{1}{\tau_0} - 1$ have the same sign, an increase of virus diffusion rate in the environment can effectively lead to a decline in the number of newly infected individuals.

Example 4.4. The environment with impulse.

In the following, the stability of the solution is illustrated by numerical simulation. Firstly, fix parameters $b(x) = 0.6\left(1 + 0.5\sin(\frac{9\pi x}{10})\right), d = 0.137, c = 0.8$, and choose $\gamma_4 = 0.5$, then $\lambda_* \geq 0.1029 > 0$. From Fig. 5 we can see that the density of viruses in the environment eventually goes to zero. Secondly, Choose $\gamma_4 = 0.1$, then $\lambda^* \leq -0.2495 < 0$. Numerical approximation in Fig. 6 indicates the virus in the environment stabilizes to a positive periodic steady state.

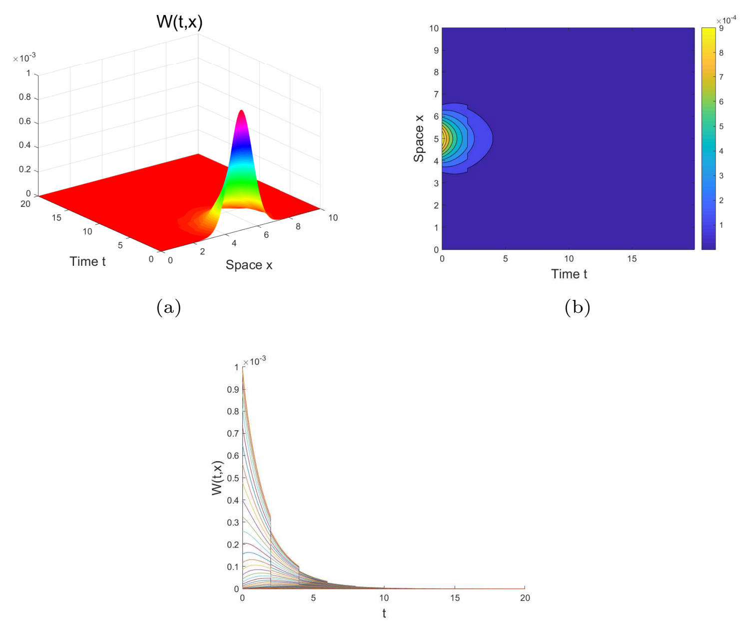
This indicates that the smaller $\gamma_4(x)$ is, the longer the average survival time of free viruses without hosts has, the more likely viruses are to persist in the environment. Therefore, it can be seen that, the average survival time of free viruses without hosts which is $1/\gamma_4(x)$ plays an important role in the persistence or extinction of viruses in the environment. We also note that a short average survival time of free viruses is beneficial for the extinction of the viruses when the pulse takes place.



(a) (b)

(c)

Figure 4. Fix parameters in (4.1). The relation between d and $\frac{1}{\tau_0}$. (a) $b_0 = 0.05$; (b) $b_0 = 0.06$; (c) $b_0 = 0.07$.



(a) (b)

(c)

Figure 5. $\lambda_* > 0$ and the density of viruses in the environment eventually goes to zero.

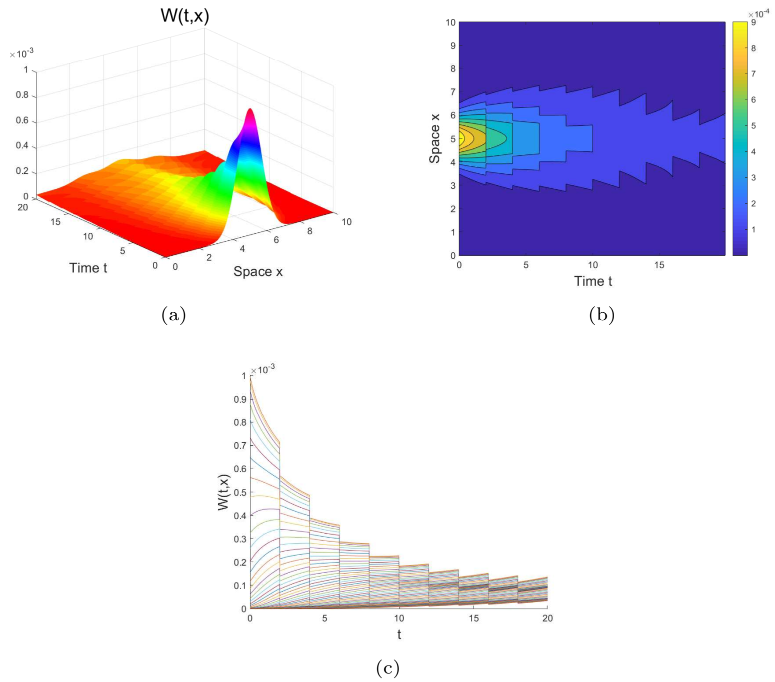


Figure 6. $\lambda^* < 0$ and viruses in the environment eventually tend to a positive steady state.

5. Discussion

This paper focuses on a reaction-diffusion problem featuring impulsive effects under Neumann boundary conditions. Initially, we formulate an infectious disease model that incorporates both pulsing and environmental virus diffusion, and prove the well-posedness of problem (1.1). Subsequently, we utilize the principal eigenvalue τ_0 of the corresponding elliptic eigenvalue problem to establish a symbolic relationship with R_0 in problem (1.1) when $c = 1$ (no pulse). We also estimate the generalized eigenvalues in problem (1.1) for $0 < c < 1$ (harvesting pulse). In the case where $c = 1$, we examine the global stability of both the disease-free and endemic equilibria in heterogeneous environments by constructing a Lyapunov functional. Specifically, we find that if $R_0 < 1$, the disease-free equilibrium is globally asymptotically stable. Conversely, if $R_0 > 1$, problem (1.1) exhibits uniform persistence and admits a unique, globally asymptotically stable, positive steady-state solution. Furthermore, in the case where $0 < c < 1$, we establish that if $\lambda^* > 0$, the disease-free equilibrium is globally asymptotically stable. However, if $\lambda^* < 0$, the solution to problem (1.1) converges to a positive periodic solution.

Our numerical simulations demonstrate that an elevated rate of viral reproduction contributes to an increase in new infections in spatially heterogeneous environments. In the other hand, extensive viral diffusion coupled with regular environmental cleaning results in a decrease in new infections. These results suggest strategy for infection control. Specifically, frequent ventilation can facilitate the diffusion of the virus, thereby reducing the number of new infections. Additionally, regular environmental disinfection is effective in eliminating viruses originating from the environment.

References

[1] N. Ahmed, S. S. Tahira, M. Rafiq, et al., *Positivity preserving operator splitting nonstandard finite difference methods for SEIR reaction diffusion model*, Open Math., 2019, 17, 313–330.

[2] L. J. Allen, B. M. Bolker, Y. Lou, et al., *Asymptotic profiles of the steady states for an SIS epidemic reaction-diffusion model*, Discrete Contin. Dyn. Syst., 2008, 21(1), 1–20.

[3] R. J. Boer and A. S. Perelson, *Quantifying T lymphocyte turnover*, J. Theo. Biol., 2013, 327, 45–87.

[4] J. M. Boyce, *Environmental contamination makes an important contribution to hospital infection*, J. Hosp. Infect., 2007, 65, 50–54.

[5] J. M. Boyce, G. Potter-Bynoe, C. Chenevert, et al., *Environmental contamination due to methicillin-resistant Staphylococcus aureus: possible infection control implications*, Infect. Control Hosp. Epidemiol., 1997, 18(9), 622–627.

[6] R. S. Cantrell and C. Cosner, *Spatial Ecology Via Reaction-Diffusion Equations*, John Wiley Sons, New York, 2004.

[7] F. Capone, V. De Cataldis and R. De Luca, *On the Stability of a SEIR Reaction Diffusion Model for Infections Under Neumann Boundary Conditions*, Acta Appl. Math., 2014, 132(1), 165–176.

[8] S. J. Dancer, *Importance of the environment in meticillin-resistant Staphylococcus aureus acquisition: the case for hospital cleaning*, Lancet Infect. Dis., 2008, 8(2), 101–113.

[9] S. J. Dancer, *The role of environmental cleaning in the control of hospital acquired infection*, J. Hosp. Infect., 2009, 73(4), 378–385.

[10] A. Haase, K. Henry, M. Zupancic, et al., *Quantitative image analysis of HIV-1 infection in lymphoid tissue*, Science, 1996, 274(5289), 985–989.

[11] J. K. Hale, *Asymptotic Behavior of Dissipative Systems*, American Mathematical Society Providence, Providence, Rhode Island, 1988.

[12] X. Z. Li, G. Gupur and G. T. Zhu, *Threshold and stability results for an age-structured SEIR epidemic model*, Comput. Math. Appl., 2001, 42(6–7), 883–907.

[13] Y. J. Lou and X. Q. Zhao, *A reaction-diffusion malaria model with incubation period in the vector population*, J. Math. Biol., 2011, 62(4), 543–568.

[14] S. Nakaoka, S. Iwami and K. Sato, *Dynamics of HIV infection in lymphoid tissue network*, J. Math. Biol., 2016, 72(4), 909–938.

[15] D. F. Pang and Y. N. Xiao, *The SIS model with diffusion of virus in the environment*, Math. Biosci. Eng., 2019, 16(4), 2852–2874.

[16] M. Pedersen and Z. G. Lin, *The profile near blowup time for solutions of diffusion systems coupled with localized nonlinear reactions*, Nonlinear Anal., 2002, 50(7), 1013–1024.

[17] R. Peng, *Asymptotic profiles of the positive steady state for an SIS epidemic reaction-diffusion model. Part I*, J. Diff. Equ., 2009, 247(4), 1096–1119.

[18] R. Peng and X. Q. Zhao, *A reaction-diffusion SIS epidemic model in a time-periodic environment*, Nonlinearity, 2009, 25(5), 1451–1471.

[19] L. Q. Pu, Z. G. Lin and Y. Lou, *A West Nile virus nonlocal model with free boundaries and seasonal succession*, J. Math. Biol., 2023, 86(2), 1–52.

[20] L. B. Rong and A. S. Perelson, *Asymmetric division of activated latently infected cells may explain the decay kinetics of the HIV-1 latent reservoir and intermittent viral blips*, Math. Biosci., 2009, 217(1), 77–87.

[21] H. L. Smith, *Monotone Dynamical Systems: An Introduction to the Theory of Competitive and Cooperative Systems*, American Mathematical Society Providence, Providence, Rhode Island, 1995.

[22] H. L. Smith and X. Q. Zhao, *Robust persistence for semidynamical systems*, Nonlinear Anal., 2001, 47(9), 6169–6179.

[23] F. B. Wang, Y. Huang and X. F. Zou, *Global dynamics of a PDE in-host viral model*, Appl. Anal., 2014, 93(11), 2312–2329.

[24] J. L. Wang and J. Yang, T. Kuniya, *Dynamics of a PDE viral infection model incorporating cell-to-cell transmission*, J. Math. Anal. Appl., 2016, 444(2), 1542–1564.

[25] S. L. Wang, X. Y. Song and Z. H. Ge, *Dynamics analysis of a delayed viral infection model with immune impairment*, Appl. Math. Model., 2011, 35(10), 4877–4885.

[26] W. D. Wang and X. Q. Zhao, *Basic reproduction numbers for reaction-diffusion epidemic models*, SIAM J. Appl. Dyn. Syst., 2012, 11(4), 1652–1673.

[27] X. Wang, Y. N. Xiao, J. R. Wang, et al., *A mathematical model of effects of environmental contamination and presence of volunteers on hospital infections in China*, J. Theo. Biol., 2012, 293, 161–173.

[28] X. Y. Wang, J. Y. Yang and X. F. Luo, *Asymptotical profiles of a viral infection model with multi-target cells and spatial diffusion*, Comput. Math. Appl., 2019, 77(2), 389–406.

[29] D. J. Weber and W. A. Rutala, *Role of environmental contamination in the transmission of vancomycin-resistant enterococci*, Infect. Control Hosp. Epidemiol., 1997, 18(5), 306–309.

[30] R. Xu and C. W. Song, *Dynamics of an HIV infection model with virus diffusion and latently infected cell activation*, Nonlinear Anal., 2022, 67, 103618.

[31] C. Y. Yang and J. Wang, *Basic reproduction numbers for a class of reaction-diffusion epidemic models*, Bull. Math. Biol., 2020, 82(8), 1–25.

[32] L. Zhang, Z. C. Wang and X. Q. Zhao, *Threshold dynamics of a time periodic reaction-diffusion epidemic model with latent period*, J. Diff. Equ., 2015, 258(9), 3011–3036.

[33] M. Y. Zhang, J. GE and Z. G. Lin, *Logistic diffusion problem and its analysis on three types of domains*, Journal of Guangxi Normal University(Natural Science Edition), 2023, 41(01), 17–23.

[34] X. Q. Zhao, *Dynamical Systems in Population Biology*, Springer, New York, 2017.

[35] X. Q. Zhao, *Basic Reproduction Ratios for Periodic Compartmental Models with Time Delay*, J. Dyn. Diff. Equ., 2017, 29(1), 67–82.