Threshold dynamics of a viral infection model with impulsive CTL immune response

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Keywords: Medical epidemiology; Reaction-diffusion equations; Viral infection model; Impulsive CTL immune response; Threshold dynamics

AMS Subject Classification (2010): 92C60; 35K57; 35R12

1 Introduction

In the past decades, pulse vaccination has been remarkably successful in controlling polio and measles throughout Central and South America. Prior theoretical results have noted that pulse vaccination strategies can be separated from classical strategies in causing disease eradication at low values of vaccination. Another considerably significant application is the vaccines that stimulate the cytotoxic T-lymphocyte (CTL) response, which stands for the best hope for controlling Human Immunodeficiency Virus (HIV) [2], since the rising HIV specific CTL response observed during prime infection is strongly associated with acute viral load decline. CTLs are host cells with the ability to recognize and kill viral infected cells in the body, and can be activated by specific recognition of viral fragments (called epitopes).

The nature of the CTL response is the proliferation of CTL under the stimulation of viral antigen, and the extending CTL population confronts with the viral population by killing the infected cells. Numerous literatures have considered the viral model with CTL immune response [8, 15], in which infected cells are lysed by CTLs at a constant rate that is bilinear to both the infected cells and the CTLs. In [12], Smith and Schwartz investigated such a model with the CTLs vaccinated at fixed time moments, by assuming that the production of infected $CD4^+$ T cells occurs at a constant rate. Nevertheless, this assumption loses some of its validity in the earliest or latest stages of infection. Bartholdy et al. [1] and Wodarz et al. [13] discovered that free virus populations turn over at greatly faster rates than the population of infected and uninfected cells, which enabled them to make a quasi-steady-state assumption. Therefore, the amount of the free virus is proportional to that of infected cells.

In particular, Yang and Xiao [16] recently still studied the threshold dynamics for compartmental epidemic models with periodic pulses as the import incentives of the CTLs. Motivated directly by such investigations, we try to consider the

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stronger growth mechanism that is not caused by impulse, but reaction term. Hence, we present the following model:

$$\begin{cases} \left.\begin{aligned} &\frac{\partial u}{\partial t} = d_c u_{xx} + \theta - \alpha u - \beta uv, \\ &\frac{\partial v}{\partial t} = d_c v_{xx} + \beta uv - \sigma v - \kappa vw, \\ &\frac{\partial w}{\partial t} = d_w w_{xx} + \mu vw + w(\gamma - w), \end{aligned}\right\} t \neq nT, x \in (0,l), n = 0,1,\cdots, \\ \left.\begin{aligned} &u((nT)^+, x) = u(nT, x), \\ &v((nT)^+, x) = v(nT, x), \\ &w((nT)^+, x) = g(w(nT, x)), \end{aligned}\right\} t = nT, x \in (0,l), \quad n = 0,1,\cdots \end{cases} \tag{1.1}$$

with Neumann boundary conditions

$$u_x(t,x) = v_x(t,x) = w_x(t,x) = 0, \quad t > 0, x = 0, l, \tag{1.2}$$

and initial conditions

$$u(0,x) = u_0(x), v(0,x) = v_0(x), w(0,x) = w_0(x), \geq, \not\equiv 0, \quad x \in (0,l), \tag{1.3}$$

where u, v and w denote the concentration of uninfected cells, infected cells, and CTLs, respectively. θ is called the generation rate of uninfected cells, α and σ are the death rate of uninfected and infected cells, respectively. β represents the infection rate. Under antigen stimulation, the proliferation rate of CTL is μ, and we assume that its growth obeys the well-known logistic equation. The parameter μ is also known as the CTL responsiveness. CTLs kill infected cells at a rate κ. In particular, we suppose that the CTLs are pulsed by the vaccine at fixed times nT, and the effect of the vaccine is transient, whereby solutions are continuous for $t \neq nT$ and go through a transient change in the case where $t = nT$. All parameters are positive.

Throughout this paper, we make the following assumptions about the impulsive function g:

($\mathbf{A}_1$) $g(w)$ is the first order continuously differentiable for $w \geq 0$, $g(0) = 0$, $g'(0) > 0$, and for $w > 0$, $g(w) > 0$, $g(w)/w$ is nonincreasing with respect to w and $0 < g(w)/w < 1$.

($\mathbf{A}_2$) $g(w)$ is nondecreasing with respect to $w \geq 0$.

($\mathbf{A}_3$) There are positive constants $D, \iota > 1$ and small ι_0 such that $g(w) \geq g'(0)w - Dw^\iota$ for $0 \leq w \leq \iota_0$.

In what follows, we first give some basic properties for problem (1.1)-(1.3).

Let $\mathbb{X} := \mathbb{C}(\mathbb{R}^3, [0,l])$ be the Banach space equipped with the supremum norm $\|\cdot\|_{\mathbb{X}}$. Define $\mathbb{X}_+ := \mathbb{C}(\mathbb{R}^3_+, [0,l])$, then $(\mathbb{X}, \mathbb{X}_+)$ is a strongly ordered space. For any given $\chi := (\chi_1, \chi_2, \chi_3) \in \mathbb{X}$, assume that $(\mathbb{T}_1(t), \mathbb{T}_2(t), \mathbb{T}_3(t)) : \mathbb{X} \to \mathbb{X}$, $t \geq 0$, are the strongly continuous semigroups associated with $d_c\partial^2_{xx} - \alpha$, $d_c\partial^2_{xx} - \sigma$ and $d_w\partial^2_{xx} - \rho$ subject to the Neumann boundary condition with some $\rho > 0$, respectively. According to [10, Section 7.1 and Corollary 7.2.3], we deduce that $\mathbb{T}_i(t)$ $(i = 1,2,3)$ is compact and strongly positive for all $t > 0$. Evidently, for any $\chi \in \mathbb{X}$, $t \geq 0$, we still have

$$\mathbb{T}_1(t)\chi(x) = e^{-\alpha t}\int_0^l \Gamma(d_c t, x, y)\chi(y)\mathrm{d}y, \;\; \mathbb{T}_2(t)\chi(x) = e^{-\sigma t}\int_0^l \Gamma(d_c t, x, y)\chi(y)\mathrm{d}y$$

and

$$\mathbb{T}_3(t)\chi(x) = e^{-\rho t}\int_0^l \Gamma(d_w t, x, y)\chi(y)\mathrm{d}y,$$

where functions $\Gamma(d_c t, x, y)$ and $\Gamma(d_w t, x, y)$ are the fundamental solutions corresponding to $d_c\partial^2_{xx}$ and $d_w\partial^2_{xx}$ subject to the Neumann boundary condition, respectively.

Define $\mathbb{F} = (\mathbb{F}_1, \mathbb{F}_2, \mathbb{F}_3) : \mathbb{X}_+ \to \mathbb{X}$ by

$$\mathbb{F}_1(\chi)(x) = \theta - \beta\chi_1\chi_2, \;\; \mathbb{F}_2(\chi)(x) = \beta\chi_1\chi_2 - \kappa\chi_2\chi_3, \;\; \mathbb{F}_3(\chi)(x) = \mu\chi_2\chi_3 + \chi_3(\gamma - \chi_3) + \rho\chi_3.$$

As a result, problem (1.1)-(1.3) can be written as the following integral form

$$\begin{cases} u(t) = \mathbb{T}_1(t)\chi_1 + \displaystyle\int_0^t \mathbb{T}_1(t-s)\mathbb{F}_1(u(s), v(s), w(s))\mathrm{d}s, \\ v(t) = \mathbb{T}_2(t)\chi_2 + \displaystyle\int_0^t \mathbb{T}_2(t-s)\mathbb{F}_2(u(s), v(s), w(s))\mathrm{d}s, \\ w(t) = \mathbb{T}_3(t-nT)g(w(nT)) + \displaystyle\int_{nT}^t \mathbb{T}_3(t-s)\mathbb{F}_3(u(s), v(s), w(s))\mathrm{d}s, \;\; t \in (nT, (n+1)T], \;\; n = 0,1,\cdots. \end{cases}$$

Hence, for any given initial functions $\chi := (\chi_1, \chi_2, \chi_3) \in \mathbb{X}_+$, we can straightforward obtain from [7, Corollary 4] that problem (1.1)-(1.3) admits a unique mild solution $U(t, x; \chi) := (u, v, w)(t, x; \chi)$ on $[0, \tau_0)$ with $U(0, \cdot; \chi) = \chi$, and $U(t, \cdot; \chi) \in \mathbb{X}_+$ for $t \in [0, \tau_0)$, where $\tau_0 \leq \infty$. Moreover, utilizing the completely similar comparison views such as employed in [6] and [14], the following boundedness result is valid, which means that the mild solution is global, i.e., $\tau_0 = \infty$.

Proposition 1.1 *The solutions of problem* (1.1)-(1.3) *are ultimately bounded and uniformly bounded in* $\mathbb{X}_+$. *Specifically, there exist* $\overline{M} > 0$ *and* $t^* > 0$ *such that* $(u, v, w)(t, x) \in \mathbb{E}_0 := \{(u, v, w) \mid 0 < u, v, w \leq \overline{M}\}$ *for all* $t \geq t^*$ *and* $x \in [0, l]$.

Next, we claim that the mild solution $U(t, x)$ of (1.1)-(1.3) obtained as above is still the classical one, that is, $U(t, x)$ is the first order continuously differentiable in time, and twice continuously differentiable in space. Actually, the initial value $\chi(\cdot) \in \mathbb{C}^1([0, l])$ and the fact that g is the first order continuously differentiable show that $U(0^+, \cdot) \in \mathbb{C}^1([0, l])$. By employing the standard theory for parabolic equations, we have $U(\cdot, \cdot) \in \mathbb{C}^{1,2}((0, T] \times (0, l))$. Thus, $w(T^+, x) = g(w(T, x)) \in \mathbb{C}^1([0, l])$ and $(u, v)(T^+, x) = (u, v)(T, x) \in \mathbb{C}^1([0, l])$ still hold. Once again, let $U(T^+, \cdot)$ be the new initial value for $t \in (T^+, 2T]$, then $U(t, x) \in \mathbb{C}^{1,2}((T, 2T] \times (0, l))$. Lastly, we can always deduce inductively the case for solution $U(\cdot, \cdot)$ of (1.1)-(1.3) for all $(t, x) \in [0, +\infty) \times (0, l)$ by the similar processes. Defining

$$\mathbb{PC}([0, +\infty) \times [0, l]) = \{U(t, \cdot) \mid U(t, \cdot) \in \mathbb{C}((nT, (n+1)T] \times [0, l]),\ n = 0, 1, \cdots\},$$

and

$$\mathbb{PC}^{1,2}((0, +\infty) \times (0, l)) = \{U(t, \cdot) \mid U(t, \cdot) \in \mathbb{C}^{1,2}((nT, (n+1)T] \times (0, l)),\ n = 0, 1, \cdots\},$$

we thus have the following statement.

Theorem 1.2 *For any given initial function* $U_0 := (u_0, v_0, w_0) \in \mathbb{X}_+$, *problem* (1.1)-(1.3) *admits a unique global positive solution* $U(t, x; \chi) \in \mathbb{PC}^{1,2}((0, +\infty) \times (0, l))$ *on* $(0, \infty)$ *with* $U(0, \cdot; U_0) = U_0(\cdot)$.

The remains of this paper are organized as follows. In Section 2, we discuss the infection-free steady state, and define the CTL-activated viral infection reproduction number R_0. In Section 3, we illustrate that R_0 is a critical threshold parameter to investigate the extinction and uniform persistence of virus. Finally, by utilizing the Lyapunov function, we still explore the special global attractivity of the positive periodic steady state to problem (1.1)-(1.3).

2 Preliminaries: infection-free steady state and CTL-activated viral infection reproduction number

As a baseline, we begin with some analyses about the existence of the infection-free steady state to problem (1.1)-(1.3), in which all infected cells are permanently absent from the population, i.e., $v = 0$.

In fact, we first consider the following scalar reaction-diffusion equation

$$\begin{cases} \dfrac{\partial u}{\partial t} = d_c u_{xx} + \theta - \alpha u, & t \neq nT, x \in (0, l), n = 0, 1, \cdots, \\ u_x(t, 0) = u_x(t, l) = 0, & t > 0, \\ u(0, x) = u_0(x), & x \in (0, l). \end{cases} \tag{2.1}$$

For problem (2.1), inspired by the global attractivity result of [17, Theorem 2.2.1], we have the following assertion.

Lemma 2.1 *There exists a unique positive steady state* $u^* = \theta/\alpha$ *to problem* (2.1), *which is globally attractive in* $\mathbb{C}(\mathbb{R}, [0, l])$.

Next, the equation only for w in problem (1.1)-(1.3) can be written as

$$\begin{cases} \dfrac{\partial w}{\partial t} = d_w w_{xx} + w(\gamma - w), & t \neq nT, x \in (0, l), n = 0, 1, \cdots, \\ w_x(t, 0) = w_x(t, l) = 0, & t > 0, \\ w(0, x) = w_0(x), & x \in (0, l), \\ w((nT)^+, x) = g(w(nT, x)), & t = nT, x \in (0, l), n = 0, 1, \cdots, \end{cases} \tag{2.2}$$

and its relevant steady periodic problem is thus

$$\begin{cases} \dfrac{\partial w}{\partial t} = d_w w_{xx} + w(\gamma - w), & t \neq nT, x \in (0, l), n = 0, 1, \cdots, \\ w_x(t, 0) = w_x(t, l) = 0, & t > 0, \\ w(0, x) = w(T, x), & x \in (0, l), \\ w((nT)^+, x) = g(w(nT, x)), & t = nT, x \in (0, l), n = 0, 1, \cdots. \end{cases} \tag{2.3}$$

The definition of upper and lower solutions to problem (2.2) with pulses are presented as follows

Definition 2.2 *We give that* $\widetilde{w}(t,x), \widehat{w}(t,x) \in \mathbb{PC}^{1,2}((0,+\infty)\times(0,l))\bigcap \mathbb{PC}([0,+\infty)\times[0,l])$ *satisfying* $0 \le \widehat{w}(t,x) \le \widetilde{w}(t,x)$ *are upper and lower solutions of problem* (2.2)*, respectively, if* $\widetilde{w}(t,x)$ *and* $\widehat{w}(t,x)$ *make the following problem hold:*

$$\begin{cases} \dfrac{\partial \widetilde{w}}{\partial t} \ge d_w \widetilde{w}_{xx} + \widetilde{w}(\gamma - \widetilde{w}), & t \ne nT, x \in (0,l), n = 0,1,\cdots, \\ \dfrac{\partial \widehat{w}}{\partial t} \le d_w \widehat{w}_{xx} + \widehat{w}(\gamma - \widehat{w}), & t \ne nT, x \in (0,l), n = 0,1,\cdots, \\ \widehat{w}_x(t,0) = 0 \le \widetilde{w}_x(t,0), \widehat{w}_x(t,l) = 0 \le \widetilde{w}_x(t,l), & t > 0, \\ \widehat{w}(0,x) \le \widehat{w}(T,x), \widetilde{w}(0,x) \ge \widetilde{w}(T,x), & x \in [0,l], \\ \widetilde{w}((nT)^+,x) \ge g(\widetilde{w}(nT,x)), & t = nT, x \in (0,l), n = 0,1,\cdots, \\ \widehat{w}((nT)^+,x) \le g(\widehat{w}(nT,x)), & t = nT, x \in (0,l), n = 0,1,\cdots, \\ 0 \le \widehat{w}(0,x) \le w_0(x) \le \widetilde{w}(0,x), & x \in [0,l]. \end{cases} \tag{2.4}$$

Furthermore, we still have the following fundamental lemma.

Lemma 2.3 *(*Comparison principle*) Assume that* $\widetilde{w}(t,x)$ *and* $\widehat{w}(t,x)$ *are the upper and lower solutions to problem* (2.2) *with initial value* $\widehat{w}(0,x) \le w(0,x) \le \widetilde{w}(0,x)$, $\forall\ x \in [0,l]$*, then any solution* $w(t,x)$ *of problem* (2.2) *satisfies*

$$\widehat{w}(t,x) \le w(t,x) \le \widetilde{w}(t,x), \quad t \in [0,\infty), x \in [0,l].$$

Let $f(w,t) = w(\gamma - w)$ and choose $k^* = \gamma$ such that $F(w,t) = k^* w + f(w,t)$ is monotonically nondecreasing with respect to w. If there are upper and lower solutions $\widetilde{w}$ and $\widehat{w}$ of problem (2.3), taking $\overline{w}^{(0)} = \widetilde{w}$ and $\underline{w}^{(0)} = \widehat{w}$ as initial iteration, we can construct the iteration sequences $\{\overline{w}^{(m)}\}$ and $\{\underline{w}^{(m)}\}$ by the following process

$$\begin{cases} \dfrac{\partial \overline{w}^{(m)}}{\partial t} - d_w \overline{w}^{(m)}_{xx} + k^* \overline{w}^{(m)} = k^* \overline{w}^{(m-1)} + \overline{w}^{(m-1)}(\gamma - \overline{w}^{(m-1)}), & t \ne nT, x \in (0,l), n = 0,1,\cdots, \\ \dfrac{\partial \underline{w}^{(m)}}{\partial t} - d_w \underline{w}^{(m)}_{xx} + k^* \underline{w}^{(m)} = k^* \underline{w}^{(m-1)} + \underline{w}^{(m-1)}(\gamma - \underline{w}^{(m-1)}), & t \ne nT, x \in (0,l), n = 0,1,\cdots, \\ \overline{w}^{(m)}_x(t,0) = \overline{w}^{(m)}_x(t,l) = \underline{w}^{(m)}_x(t,0) = \underline{w}^{(m)}_x(t,l) = 0, & t > 0, \\ \overline{w}^{(m)}(0,x) = \overline{w}^{(m-1)}(T,x), \underline{w}^{(m)}(0,x) = \underline{w}^{(m-1)}(T,x), & x \in (0,l), \\ \overline{w}^{(m)}((nT)^+,x) = g(\overline{w}^{(m-1)}((n+1)T,x)), & t = nT, x \in (0,l), n = 0,1,\cdots, \\ \underline{w}^{(m)}((nT)^+,x) = g(\underline{w}^{(m-1)}((n+1)T,x)), & t = nT, x \in (0,l), n = 0,1,\cdots. \end{cases} \tag{2.5}$$

Now, we study the existence, uniqueness and attractivity of a positive periodic steady state to the problem (2.2), i.e., the positive solution to the problem (2.3). Linearizing problem (2.2) at $w = 0$, we have the following eigenvalue problem

$$\begin{cases} \dfrac{\partial \psi}{\partial t} = d_w \psi_{xx} + \gamma\psi - \lambda\psi, & t \in ((nT)^+, (n+1)T], x \in (0,l), n = 0,1,\cdots, \\ \psi_x(t,0) = \psi_x(t,l) = 0, & t > 0, \\ \psi(0,x) = \psi(T,x), & x \in [0,l], \\ \psi((nT)^+,x) = g'(0)\psi(nT,x), & x \in (0,l), n = 0,1,\cdots. \end{cases} \tag{2.6}$$

The existence of the principal eigenvalue, denoted by λ_w henceforth, and it's eigenfunctions associated are explored thoroughly in [6], and we refer to it and discussions there for more details. In fact, by some direct calculations, we still have

$$\lambda_w = \gamma + \frac{1}{T}\ln g'(0) - d_w\lambda_0 = \gamma + \frac{1}{T}\ln g'(0),$$

where $\lambda_0 = 0$ is just the principal eigenvalue of the following problem

$$\begin{cases} -\varphi_{xx} = \lambda\varphi, & x \in (0,l), \\ \varphi_x(0) = \varphi_x(l) = 0. \end{cases} \tag{2.7}$$

The following analogous result has already been obtained in [6], but we present the proofs with some crucial modifications for completeness.

Theorem 2.4 *If the principal eigenvalue* $\lambda_w > 0$*, then the problem* (2.2) *admits a unique positive periodic steady state* $w^*(t,x)$*, which is globally attractive, i.e.,* $\lim_{m\to\infty} w(t + mT, x) \to w^*(t,x)$.

Proof. We divide the proof into three steps.

Step 1 The existence of the positive periodic steady states to problem (2.2).

We first construct the upper solution of problem (2.3). Let $\widetilde{w}$=$MW(t)(M>1)$ with $W(t)$ satisfying

$$\begin{cases} W_t(t)=\gamma W(t)-W^2(t), & t\neq nT, n=0,1,\cdots, \\ W(t)=W(t+T), & t\geq 0, \\ W((nT)^+)=g'(0)W(nT)\geq g(W(nT)), & t=nT, n=0,1,\cdots. \end{cases} \tag{2.8}$$

It is nature to verify that $\widetilde{w}$=$MW(t)(M>1)$ is an upper solution to problem (2.3). Actually, integrating from $(nT)^+$ to t $(t\in((nT)^+,(n+1)T])$, we can obtain that

$$W(t)=\frac{e^{\gamma t}W(nT^+)}{W(nT^+)\int_{nT^+}^{t}e^{\gamma\tau}\mathrm{d}\tau+e^{\gamma nT}},\quad t\in((nT)^+,(n+1)T],$$

then

$$\begin{aligned} W((n+1)T)&=\frac{e^{\gamma(n+1)T}W(nT^+)}{W(nT^+)\int_{nT^+}^{(n+1)T}e^{\gamma\tau}\mathrm{d}\tau+e^{\gamma nT}}=\frac{e^{\gamma(n+1)T}g'(0)W(nT)}{g'(0)W(nT)\int_0^T e^{\gamma\tau}\mathrm{d}\tau+e^{\gamma nT}} \\ &=\frac{e^{\gamma T}g'(0)W(nT)}{g'(0)W(nT)\int_0^T e^{\gamma\tau}\mathrm{d}\tau+1}. \end{aligned}$$

Owing to $\lambda_w>0$, we have $\gamma T>-\ln g'(0)$, i.e., $e^{\gamma T}g'(0)>1$. From the periodicity, we deduce that $W(nT)=\frac{e^{\gamma T}g'(0)-1}{g'(0)\int_0^T e^{\gamma\tau}\mathrm{d}\tau}>0$ and

$$W(t)=\frac{e^{\gamma t}(e^{\gamma T}g'(0)-1)}{(e^{\gamma T}g'(0)-1)\int_{nT^+}^{t}e^{\gamma\tau}\mathrm{d}\tau+e^{\gamma nT}\int_0^T e^{\gamma\tau}\mathrm{d}\tau},\quad t\in((nT)^+,(n+1)T].$$

Hence, we get the upper solution $\widetilde{w}$ to problem (2.3).

Next, we aim to consider the lower solution and define

$$\widehat{w}(t,x)=\begin{cases} \delta\psi(nT,x), & t=nT, n=0,1,\cdots, \\ \delta\frac{\rho_1}{g'(0)}\psi((nT)^+,x), & t=(nT)^+, n=0,1,\cdots, \\ \delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\psi(t,x), & t\in((nT)^+,(n+1)T], n=0,1,\cdots, \end{cases} \tag{2.9}$$

where the positive eigenfunction $\psi(t,x)$ is defined in (2.6) associated with the principal eigenvalue $\lambda_w>0$, and δ is a small enough positive constant to be chosen later. We select the positive constants $\epsilon=\frac{\lambda_w}{2}$ and $\rho_1=e^{-\frac{\lambda_w}{2}T}g'(0)$ such that $\widehat{w}$ is well-defined and $\widehat{w}(nT,x)=\widehat{w}((n+1)T,x)$ uniformly holds.

For $t\in((nT)^+,(n+1)T]$ and $x\in(0,l)$, if $\delta<\delta_1:=\epsilon$, we can obtain that

$$\begin{aligned} &\frac{\partial\widehat{w}}{\partial t}-\left[d_w\widehat{w}_{xx}+\gamma\widehat{w}-\widehat{w}^2\right] \\ =&\left[\lambda_w-\epsilon\right]\delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\psi+\delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\left[d_w\psi_{xx}+\gamma\psi-\lambda_w\psi\right] \\ &-\left[d_w\delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\psi_{xx}+\gamma\delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\psi-(\delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\psi)^2\right] \\ =&\left[-\epsilon+\delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\psi\right]\delta\frac{\rho_1}{g'(0)}e^{[\lambda_w-\epsilon](t-nT)}\psi \\ <&0. \end{aligned}$$

Besides, if $\delta<\delta_2:=\left(\frac{g'(0)-\rho_1}{D}\right)^{\frac{1}{\iota-1}}$, from the assumption $\mathbf{A}_3$, we have

$$\begin{aligned} g(\widehat{w}(nT,x))-\widehat{w}((nT)^+,x)&=g(\widehat{w}(nT,x))-\delta\frac{\rho_1}{g'(0)}\psi((nT)^+,x)=g(\widehat{w}(nT,x))-\rho_1\widehat{w}(nT,x) \\ &\geq(g'(0)-\rho_1)\widehat{w}(nT,x)-D(\delta\psi(nT,x))^\iota \\ &=[(g'(0)-\rho_1)-D(\delta\psi(nT,x))^{\iota-1}]\delta\psi(nT,x)\geq 0. \end{aligned}$$

Henceforth, we obtain that $\widehat{w}(t,x)$ is a lower solution to problem (2.3).

Further, we select the $\overline{w}^{(0)}=\widetilde{w}$ and $\underline{w}^{(0)}=\widehat{w}$ as initial iteration, the sequences $\{\overline{w}^{(m)}\}$ and $\{\underline{w}^{(m)}\}$ are defined by (2.5). It follows from problems (2.4) and (2.5) that we have

$$\widehat{w}\leq\underline{w}^{(m)}\leq\underline{w}^{(m+1)}\leq\overline{w}^{(m+1)}\leq\overline{w}^{(m)}\leq\widetilde{w}.$$

Due to the monotone convergence theorem, we obtain that the limits of the sequences $\{\overline{w}^{(m)}\}$ and $\{\underline{w}^{(m)}\}$ exist and $\lim_{m\to\infty}\overline{w}^{(m)}=\overline{w}$, $\lim_{m\to\infty}\underline{w}^{(m)}=\underline{w}$, where $\overline{w}$ and $\underline{w}$ are T-periodic solutions of problem (2.3). Moreover,

$$\widehat{w}\le\underline{w}^{(m)}\le\underline{w}^{(m+1)}\le\underline{w}\le\overline{w}\le\overline{w}^{(m+1)}\le\overline{w}^{(m)}\le\widetilde{w}.$$

Now, we claim that $\overline{w}$ and $\underline{w}$ are the maximal and minimal positive T-periodic solutions of problem (2.3). In fact, for any positive periodic solution $w(t,x)$ of problem (2.3) satisfies $\widehat{w}\le w\le\widetilde{w}$. Employing the same iteration as problem (2.5), we choose $\widetilde{w}$ and w as the initial iteration with $\overline{w}^{(0)}=\widetilde{w}$ and $\underline{w}^{(0)}=w$, it follows that $w(t,x)\le\overline{w}(t,x)$, $t\ge0, x\in(0,l)$, thus, $\overline{w}$ is the maximal positive T-periodic solution of problem (2.3). Similarly, $\underline{w}$ is the minimal positive T-periodic solution of problem (2.3).

Step 2 The uniqueness of a positive periodic steady state to problem (2.2).

Without loss of generality, suppose that w_1 and w_2 are the two solutions, and set

$$S=\left\{\varsigma\in[0,1],\varsigma w_1\le w_2, t=0, t=0^+, t\in(0^+,T], x\in[0,l]\right\},$$

which can be seen that S contains a neighbourhood of 0. We claim that $1\in\eta$. Suppose not, then we have $\varsigma_0=\sup S<1$. We note that $F(w,t)=f(w,t)+k^*w$ is nondecreasing and $\frac{f(w,t)}{w}$ is decreasing in w on $[0,\max\limits_{[0,T]\times[0,l]}w_2(t,x)]$, which yields that

$$\begin{aligned}&(w_2-\varsigma_0w_1)_t-d_w(w_2-\varsigma_0w_1)_{xx}+k^*(w_2-\varsigma_0w_1)\\&=f(w_2,t)+k^*w_2-\varsigma_0(f(w_1,t)+k^*w_1)\\&\ge f(\varsigma_0w_1,t)+k^*\varsigma_0w_1-\varsigma_0(f(w_1,t)+k^*w_1)\ge0\end{aligned}$$

for $t\in(0^+,T]$ and $x\in(0,l)$. By assumptions $\mathbf{A}_1$ and $\mathbf{A}_2$, we deduce that

$$\begin{aligned}w_2(0^+,x)-\varsigma_0w_1(0^+,x)&=g(w_2(0,x))-\varsigma_0g(w_1(0,x))\\&\ge g(\varsigma_0w_1(0,x))-\varsigma_0g(w_1(0,x))\ge0\end{aligned}$$

for $x\in(0,l)$. However, for $t>0$,

$$w_{2x}(t,0)-\varsigma_0w_{1x}(t,0)=w_{2x}(t,l)-\varsigma_0w_{1x}(t,l)=0.$$

Due to the strong maximum principle [9], we have the significant statements as follows:

(a) $w_2-\varsigma_0w_1>0$ holds for $t=0^+, t\in(0^+,T]$ and $x\in(0,l)$. Since w_1 and w_2 are T-periodic solutions, that is, $w_1(0,x)=w_1(T,x)$ and $w_2(0,x)=w_2(T,x)$ for $x\in(0,l)$, then $w_2-\varsigma_0w_1>0$ for $(t,x)\in(0,T]\times(0,l)$. Based on the Hopf's boundary lemma, we deduce that $\frac{\partial}{\partial\mathbf{n}}\mid_{x=0}(w_2-\varsigma_0w_1)>0$ and $\frac{\partial}{\partial\mathbf{n}}\mid_{x=l}(w_2-\varsigma_0w_1)<0$, where $\mathbf{n}$ is the outward unit normal vector. Then there is a constant $\epsilon_0>0$ such that $w_2-\varsigma_0w_1\ge\epsilon_0w_1$, we have $\varsigma_0+\epsilon_0\in S$. This contradicts the maximality of ς_0.

(b) $w_2-\varsigma_0w_1\equiv0$ holds for $t=0^+, t\in(0^+,T]$ and $x\in(0,l)$, we thus have $f(w_2,t)=\varsigma_0f(w_1,t)$. However, recalling $\varsigma_0<1$, $f(w_2,t)=f(\varsigma_0w_1,t)>\varsigma_0f(w_1,t)$, thus it is also impossible.

In conclusion, problem (2.3) admits a unique positive T-periodic solution $w^*(t,x)$.

Step 3 The attractivity of a positive periodic steady state to problem (2.2).

The Hopf's boundary lemma implies $\psi_x(0,0)>0$ and $\psi_x(0,l)<0$, and we select a small enough δ to make sure $\delta\psi(0,x)\le w(0,x)$. Meanwhile, there exists a large enough M such that $w(0,x)\le MW(0)$. For any given δ and M, the function $\widetilde{w}$=$MW(t)$ with $W(t)$ defined in (2.8) and $\widehat{w}$ defined in (2.9), satisfies

$$\widehat{w}(0,x)\le w(0,x)\le\widetilde{w}(0,x),\quad x\in[0,l].$$

It follows from ($\mathbf{A}_2$) that g is nondecreasing for w, we obtain that

$$\widehat{w}(0^+,x)\le g(\widehat{w}(0,x))\le g(w(0,x))=w(0^+,x)\le g(\widetilde{w}(0,x))=\widetilde{w}(0^+,x).$$

The classical comparison principal yields $\widehat{w}(t,x)\le w(t,x)\le\widetilde{w}(t,x)$, $t\in(0^+,T]$, $x\in[0,l]$. Induction reveals that $\widehat{w}(t,x)\le w(t,x)\le\widetilde{w}(t,x)$, $t=nT,(nT)^+,t\in((nT)^+,(n+1)T]$, $x\in[0,l]$. Besides, we have that $\widehat{w}(t,x)\le w(t,x)\le\widetilde{w}(t,x)$, $t>0, x\in[0,l_0]$. Therefore,

$$\underline{w}^{(0)}(t,x)\le w(t,x)\le\overline{w}^{(0)}(t,x),\quad t=nT,(nT)^+,t\in((nT)^+,(n+1)T],x\in[0,l],n=0,1,\cdots.$$

Moreover,

$$\underline{w}^{(0)}(T,x)\le w(T,x)\le\overline{w}^{(0)}(T,x),\quad x\in[0,l],\tag{2.10}$$

together with $\underline{w}^{(1)}(0,x)=\underline{w}^{(0)}(T,x)$ and $\overline{w}^{(1)}(0,x)=\overline{w}^{(0)}(T,x)$ yields

$$\underline{w}^{(1)}(0,x)\le w(T,x)\le \overline{w}^{(1)}(0,x),\quad x\in[0,l].$$

From the assumption $(\mathbf{A}_2)$ and (2.10), we obtain that

$$g(\underline{w}^{(0)}(T,x))\le g(w(T,x))\le g(\overline{w}^{(0)}(T,x)),\quad x\in[0,l].$$

Recalling the last two equations in (2.5) and the last equation in (1.1), one deduce that

$$\begin{aligned}\underline{w}^{(1)}(0^+,x)&=g(\underline{w}^{(0)}(T,x))\le g(w(T,x))\\&=w(T^+,x)\le g(\overline{w}^{(0)}(T,x))=\overline{w}^{(1)}(0^+,x),\quad x\in[0,l],\end{aligned}$$

that is,

$$\underline{w}^{(1)}(0^+,x)\le w(T^+,x)\le \overline{w}^{(1)}(0^+,x),\quad x\in[0,l].$$

The comparison principle implies that $\underline{w}^{(1)}(t,x)\le w(t+T,x)\le \overline{w}^{(1)}(t,x)$ holds for $(t,x)\in(0^+,T]\times[0,l]$. Utilizing induction again we have

$$\underline{w}^{(1)}(t,x)\le w(t+T,x)\le \overline{w}^{(1)}(t,x),\quad t=nT,(nT)^+,t\in((nT)^+,(n+1)T],x\in[0,l],n=0,1,\cdots,$$

together with the last two equations in problem (2.5) shows that

$$\underline{w}^{(m)}(t,x)\le w(t+mT,x)\le \overline{w}^{(m)}(t,x),\quad t\ge 0,x\in[0,l],$$

since the above inequality holds for $m=0$ and $m=1$. Recalling the uniqueness of the periodic solution of problem (2.3) provided with $\lim\limits_{m\to\infty}\underline{w}^{(m)}(t,x)=\lim\limits_{m\to\infty}\overline{w}^{(m)}(t,x)=w^*(t,x)$, we have

$$\lim_{m\to\infty}w(t+mT,x)\to w^*(t,x),\quad t\ge 0,x\in[0,l].$$

□

Since due to the comparison principle Lemma 2.3, the stronger the pulse vaccination is, the larger the steady state solution w^* is, we still note that has a positive effect on the CTL response, i.e., w^* increases as g increases.

To sum up, we obtain that problem (1.1)-(1.3) possesses an infection-free steady state solution $(u^*,0,w^*)$, where $u^*=\frac{\theta}{\alpha}$. Linearizing problem (1.1)-(1.3) at $(u^*,0,w^*)$, we obtain the following linearized system

$$\begin{cases}\dfrac{\partial V}{\partial t}=d_cV_{xx}+(\beta u^*-\sigma-\kappa w^*)V, & t\ne nT,x\in(0,l),n=0,1,\cdots,\\ V_x(t,0)=V_x(t,l)=0, & t>0,\\ V((nT)^+,x)=V(nT,x), & t=nT,x\in[0,l],n=0,1,\cdots.\end{cases}\tag{2.11}$$

Let C_T be the Banach space consisting of all T-periodic and continuous functions from $\mathbb{R}$ to $\mathbb{C}([0,l])$, which is equipped with the maximum norm $\|\cdot\|$ and the positive cone $C_T^+:=\{\zeta\in C_T\mid \zeta(t,x)\ge 0,\forall\ t\in\mathbb{R},x\in[0,l]\}$. It is clear that C_T is an ordered Banach space, and we henceforth take the nation $\zeta(t,x):=[\zeta(t)](x)$ for any given $\zeta\in C_T$.

Besides, assume that $E(t,s)(t\ge s)$ is the evolution operator of problem

$$\begin{cases}\dfrac{\partial V}{\partial t}=d_cV_{xx}-(\sigma+\kappa w^*)V, & t\ne nT,x\in(0,l),n=0,1,\cdots,\\ V_x(t,0)=V_x(t,l)=0, & t>0,\\ V((nT)^+,x)=V(nT,x), & t=nT,x\in(0,l),n=0,1,\cdots.\end{cases}$$

The standard semigroup theory implies that, there exist positive constants $K\ge 1$ and ω such that

$$\|E(t,s)\|\le Ke^{\omega(t-s)},\quad \forall t\ge s,t,s\in\mathbb{R}.$$

Now, suppose that $\zeta\in C_T$, and let $\zeta(s,x)=[\zeta(s)](x)$ be the density distribution of infected individuals at time s and spatial location $x\in[0,l]$. Then the term $\beta u^*(s,x)\zeta(s,x)$ is the distribution of newly infected individuals generated by the infectious individuals who were introduced at time s. Then, for any given $t\ge s$, $E(t,s)\beta u^*(s,x)\zeta(s,x)$ is the distribution at location x of those infected individuals who were newly infected at time s and remain in the infected compartments at time t. Considering all of such individuals together, the following expression

$$\int_{-\infty}^{t} E(t,s)\left[\beta u^*(\cdot,s)\zeta(\cdot,s)\right]\mathrm{d}s = \int_{0}^{\infty} E(t,t-s)\left[\beta u^*(\cdot,t-s)\zeta(\cdot,t-s)\right]\mathrm{d}s$$

thus represents the accumulative density distribution of the newly infected individuals at time t and spatial location $x \in [0,l]$, which are produced by all those individuals $\zeta(s,x)$ introduced at all the time before t.

According to the statement in [5], we define the operator $\mathfrak{L} : C_T \to C_T$:

$$[\mathfrak{L}\zeta](t) = \int_{-\infty}^{t} E(t,s)\left[\beta u^*(\cdot,s)\zeta(\cdot,s)\right]\mathrm{d}s = \int_{0}^{\infty} E(t,t-s)\left[\beta u^*(\cdot,t-s,)\zeta(\cdot,t-s,)\right]\mathrm{d}s,$$

which is called as the next generation operator. It is obvious that $\mathfrak{L}$ is continuous, strongly positive and compact on C_T. Hence, we define the spectral radius of $\mathfrak{L}$ as the CTL-activated viral infection reproduction number of problem (2.11), that is,

$$R_0 = r(\mathfrak{L}).$$

The following results are well known, and we refer to [5,6] for more details.

Lemma 2.5 *(i)* $R_0 = \mu_0$, *where* μ_0 *is the principal eigenvalue of the following periodic parabolic eigenvalue problem*

$$\begin{cases} \dfrac{\partial \phi}{\partial t} = d_c\phi_{xx} + \dfrac{\beta u^*}{\mu_0}\phi - (\sigma + \kappa w^*)\phi, & t \neq nT, x \in (0,l), n = 0,1,\cdots, \\ \phi_x(t,0) = \phi_x(t,l) = 0, & t > 0, \\ \phi(0,x) = \phi(T,x), & x \in [0,l], \\ \phi((nT)^+,x) = \phi(nT,x), & t = nT, x \in (0,l), n = 0,1,\cdots. \end{cases} \tag{2.12}$$

(ii) *sign*$(R_0 - 1) =$ *sign*(λ_c), *where* λ_c *is the principal eigenvalue of the following periodic parabolic eigenvalue problem*

$$\begin{cases} \dfrac{\partial \phi}{\partial t} = d_c\phi_{xx} + (\beta u^* - \sigma - \kappa w^*)\phi - \lambda_c\phi, & t \neq nT, x \in (0,l), n = 0,1,\cdots, \\ \phi_x(t,0) = \phi_x(t,l) = 0, & t > 0, \\ \phi(0,x) = \phi(T,x), & x \in [0,l], \\ \phi((nT)^+,x) = \phi(nT,x), & t = nT, x \in (0,l), n = 0,1,\cdots. \end{cases} \tag{2.13}$$

In fact, the CTL-activated viral infection reproduction number of problem (1.1)-(1.3) can be explicitly expressed by

$$R_0 = \frac{\beta u^*}{d_c\lambda_0 + \sigma + \frac{1}{T}\int_0^T \kappa w^* \mathrm{d}t} = \frac{\beta u^*}{\sigma + \frac{1}{T}\int_0^T \kappa w^* \mathrm{d}t},$$

while, similarly, the explicit expression of the principal eigenvalue $\lambda_c := \lambda_c(u^*, w^*)$ is given by

$$\lambda_c = \beta u^* - \sigma - d_c\lambda_0 - \frac{1}{T}\int_0^T \kappa w^* \mathrm{d}t = \beta u^* - \sigma - \frac{1}{T}\int_0^T \kappa w^* \mathrm{d}t,$$

where $u^* = \theta/\alpha$ is the unique positive steady state to problem (2.1), and $\lambda_0 = 0$ is the principal eigenvalue of problem (2.7).

Here, we could still note that in a sense, R_0 is thus monotone decreasing in w^*, and this fact further reveals that R_0 decreases as g increases, which implies that the pulse vaccination has a negative effect on the CTL-activated viral infection reproduction number.

3 Dynamical behaviors of the entire system: uniform persistence and global attractivity

In this section, we will explore the dynamical behaviors of entire system, including the extinction-persistence of virus, and global attractivity of the positive steady state. Particularly, for the general uniform persistence, it will be solved by adopting the comparison principal and eigenvalue theory, while employing the Lyapunov function and some necessary analyses to prove the special global attractivity.

3.1 The uniform persistence of the entire system

Theorem 3.1 *Assume that $U(t,x;\chi)$ is the solution to problem* (1.1)-(1.3) *with $U(0,\cdot;\chi)=\chi\in\mathbb{X}_+$. Then we have*

- *(i) If $R_0<1$, then the infection-free steady state solution $(u^*,0,w^*)$ of problem* (1.1)-(1.3) *is globally attractive in $\mathbb{X}_+$;*
- *(ii) If $R_0>1$, then problem* (1.1)-(1.3) *is uniformly persistent, that is, for any $\chi\in\mathbb{X}_+$ with $\chi_2(\cdot)\not\equiv 0$, there is a positive constant $\eta>0$ such that any positive solution of* (1.1)-(1.3) *satisfies $\liminf_{t\to\infty} v(t,x;\chi)\ge\eta$ uniformly for all $x\in[0,l]$.*

Proof. (i) From the first equation of (1.1), we obtain that

$$\frac{\partial u}{\partial t}\le d_c u_{xx}+\theta-\alpha u.$$

By Lemma 2.1 and the comparison principal, it follows that for $\forall\ \varepsilon_0>0$, there exist positive constants t_0 such that

$$u(t,x;\chi)\le u^*+\varepsilon_0,\forall\ t\ge t_0,x\in[0,l].$$

Moreover, for the equation of w in (1.1), we have

$$\begin{cases}\dfrac{\partial w}{\partial t}\ge d_w w_{xx}+w(\gamma-w), & t\ne nT,x\in(0,l),n=0,1,\cdots,\\ w((nT)^+,x)=g(w(nT,x)), & t=nT,x\in(0,l),n=0,1,\cdots.\end{cases}$$

Recalling Theorem 2.4 and the comparison principal, one can find that for $\forall\ \varepsilon_1>0$, there also exist $t_1\ge t_0$ such that

$$w(t,x;\chi)\ge w^*(t,x)-\varepsilon_1,\forall\ t\ge t_1,x\in[0,l].$$

Furthermore, for the second equation of (1.1), we can obtain that

$$\frac{\partial v}{\partial t}\le d_c v_{xx}+\beta(u^*+\varepsilon_0)v-\sigma v-\kappa(w^*-\varepsilon_1)v,\forall\ t\ge t_1,x\in(0,l).$$

Due to $R_0<1$, by Lemma 2.5 and [3, Lemma 4.5], there is a strongly positive eigenfunction $\hat{\phi}$ corresponding to $\lambda_c(u^*+\varepsilon_0,w^*-\varepsilon_1)$ and $\lambda_c(u^*+\varepsilon_0,w^*-\varepsilon_1)<0$. Note that the following linear problem

$$\begin{cases}\dfrac{\partial v}{\partial t}=d_c v_{xx}+\beta(u^*+\varepsilon_0)v-\sigma v-\kappa(w^*-\varepsilon_1)v, & t\ge t_1,x\in(0,l),\\ v_x(t,x)=0, & t>0,x=0,l,\\ v(0,x)=v_0(x)\ge,\not\equiv 0, & x\in(0,l)\end{cases}$$

admits a solution $\alpha_0 e^{\lambda_c(u^*+\varepsilon_0,w^*-\varepsilon_1)(t-t_1)}\widehat{\phi}$ for some $\alpha_0>0$. For $\forall\ t\ge t_1$, the comparison principal shows that $v(t,x;\chi)\le\alpha_0 e^{\lambda_c(u^*+\varepsilon_0,w^*-\varepsilon_1)(t-t_1)}\widehat{\phi}$, then we obtain $\lim_{t\to\infty}v(t,x;\chi)=0$ uniformly for all $x\in[0,l]$.

Accordingly, for any small $\varepsilon_2\in(0,1)$, there is $t_2\ge t_1$ such that $v(t,x;\chi)<\varepsilon^*$ for all $t>t_2$, $x\in[0,l]$. Plugging into the equations of u and w in (1.1) yields

$$\begin{cases}\dfrac{\partial u}{\partial t}\ge d_c u_{xx}+\theta-\alpha u-\beta u\varepsilon_2, & t\ne nT,t\ge t_2,x\in(0,l),n=0,1,\cdots,\\ \dfrac{\partial w}{\partial t}\le d_w w_{xx}+\mu\varepsilon_2 w+w(\gamma-w), & t\ne nT,t\ge t_2,x\in(0,l),n=0,1,\cdots.\end{cases}\tag{3.1}$$

By the comparison principal, there is $t_3\ge t_2$ such that $u(t,x;\chi)\ge\frac{\theta}{\alpha+\beta\varepsilon_2}$, $\forall\ t>t_3$, $x\in[0,l]$. Similar to Theorem 2.4, since $\lambda_w^{\varepsilon_2}=\gamma+\mu\varepsilon_2+\frac{1}{T}\ln g'(0)-d_w\lambda_0=\gamma+\mu\varepsilon_2+\frac{1}{T}\ln g'(0)>0$ for any sufficiently small ε_2, we also find that for arbitrary $\varepsilon_3>0$, there exist $t_4\ge t_3$ such that $w(t,x;\chi)\le w^{**}+\varepsilon_3$, $\forall\ t>t_4$, $x\in[0,l]$, where w^{**} is the positive steady state satisfying the following problem

$$\begin{cases}\dfrac{\partial w}{\partial t}=d_w w_{xx}+\mu\varepsilon_2 w+w(\gamma-w), & t\ne nT,x\in(0,l),n=0,1,\cdots,\\ w_x(t,0)=w_x(t,l), & t>0,\\ w(0,x)=w(T,x), & x\in(0,l),\\ w((nT)^+,x)=g(w(nT,x)), & t=nT,x\in(0,l),n=0,1,\cdots.\end{cases}$$

Due to the arbitrariness of $\varepsilon_0,\varepsilon_1,\varepsilon_2$ and ε_3, we immediately deduce that $\lim\limits_{t\to\infty}(u(t,x)-u^*)=0$ and $\lim\limits_{t\to\infty}(w(t,x)-w^*(t,x))=0$ uniformly for all $x\in[0,l]$. Thus, the infection-free steady state solution $(u^*,0,w^*)$ of (1.1)-(1.3) is globally attractive.

(ii) If $R_0 > 1$, we first prove that the inequality

$$\limsup_{t\to\infty} v(t,x;\chi) \geq \xi, \tag{3.2}$$

uniformly for all $x \in [0,l]$. Assume that (3.2) is false, then there is a $t_4 > 0$ such that $v(t,x;\chi) < \xi$, $\forall\ t \geq t_4$, $x \in [0,l]$. Recalling the analysis of (3.1) and the comparison principal, then there exists a $t_5 \geq t_4$ such that $u(t,x;\chi) \geq \frac{\theta}{\alpha+\beta\xi}$ for any $t \geq t_5$, $x \in [0,l]$. Due to $\lim\limits_{\xi\to 0} \frac{\theta}{\alpha+\beta\xi} = \frac{\theta}{\alpha}$, there is a ξ_1 small enough and a positive constant η_1 such that $\frac{\theta}{\alpha+\beta\xi} \geq \frac{\theta}{\alpha} - \eta_1$, $\xi < \xi_1$. Hence, we have $u(t,x;\chi) \geq \frac{\theta}{\alpha} - \eta_1$, $\forall\ t \geq t_4$, $\xi < \xi_1$, $x \in [0,l]$.

When $v(t,x;\chi) < \xi$ for $\forall\ t \geq t_4$, we now suppose $kT \geq t_4$ for any integer k. Then, the third equation of (1.1) implies $\frac{\partial w}{\partial t} \leq d_w w_{xx} + \mu\xi w + w(\gamma - w)$, $t \geq kT, x \in (0,l)$. Considering the auxiliary problem

$$\begin{cases} \dfrac{\partial z}{\partial t} = d_w z_{xx} + \mu\xi z + z(\gamma - z), & t \neq nT, n \geq k, x \in (0,l), n = 0,1,\cdots, \\ z((nT)^+, x) = g(z(nT,x)), & t = nT, n \geq k, x \in (0,l), n = 0,1,\cdots, \end{cases} \tag{3.3}$$

together with the aforementioned method and Theorem 2.4, we know that the periodic solution z^* of problem (3.3) is globally attractive when $\lambda_w^\xi > 0$, and z^* is continuous for small ξ associated with $\lim\limits_{\xi\to 0} z^*(t,x) = w^*(t,x)$. Next, we choose $\xi_2 < \xi_1$ small enough and a positive constant η_2 such that $z^* \leq w^* + \eta_2$, $\xi \leq \xi_2$. Then, combining with the comparison principal and the global stability of z^*, for a sufficiently small constant $\eta_3 > 0$, we obtain $w(t,x) \leq z(t,x) \leq z^* + \eta_3 \leq w^* + \eta_2 + \eta_3 := w^* + \eta_4$, $\xi \leq \xi_1$, $t \geq kT$, $x \in [0,l]$.

From the equation of v to (1.1), one can find

$$\frac{\partial v}{\partial t} \geq d_c v_{xx} + \beta(u^* - \eta_1)v - \sigma v - \kappa(w^* + \eta_4)v, \quad \forall\ t \geq kT, x \in (0,l).$$

Similar to the discussion in (i), we can still obtain $\lim\limits_{t\to\infty} v(t,x;\chi) = \infty$ uniformly for all $x \in [0,l]$, which contradicts the boundedness of v. Thus, we prove inequality (3.2). Next, we discuss the following two cases.

(*a*) $v(t,x) \geq \xi$ uniformly for all large t and $x \in (0,l)$;

(*b*) $v(t,x)$ oscillates around ξ for all large t and $x \in (0,l)$.

If (*a*) holds, let $\eta = \xi$, then our proof is completed. In the following, we only consider (*b*). Suppose that $\underline{t}$ and $\bar{t}$ are large enough such that $v(\underline{t},x) = v(\bar{t},x) = \xi$, $v(t,x) < \xi$, $t \in (\underline{t},\bar{t})$ uniformly for all $x \in [0,l]$. Together with the continuous, bounded and without impulses properties of $v(t,x)$ for all $t \in [\underline{t},\bar{t}]$, $x \in [0,l]$, we can conclude that it is uniformly continuous. Hence, there exists a constant $\tau > 0$ (τ is independent of the choice of $\underline{t}$) such that $v(t,x) \geq \frac{\xi}{2}$ for all $t \in [\underline{t},\underline{t}+\tau]$, $x \in [0,l]$.

If $\bar{t} - \underline{t} \leq \tau$, then $v(t,x) \geq \frac{\xi}{2}$ for all $t \in (\underline{t},\bar{t})$, $x \in [0,l]$. We can take $\eta = \frac{\xi}{2}$, then our proof is completed.

If $\bar{t} - \underline{t} > \tau$, then $v(t,x) \geq \frac{\xi}{2}$ for all $t \in [\underline{t},\underline{t}+\tau]$, $x \in [0,l]$.

Next, we aim to prove that $v(t,x) \geq \frac{\xi}{2}$ for all $t \in [\underline{t}+\tau,\bar{t}]$, $x \in [0,l]$. Assume, by contradiction, there exist a positive constant ω and $k_1 \in \mathbb{N}$ such that $\underline{t} + \tau + \omega = k_1 T$, and

$$\begin{aligned} &v(t,x) \geq \frac{\xi}{2}, && \text{for } \forall\ t \in [\underline{t}, k_1 T], x \in (0,l), \\ &v(k_1 T, x) = \frac{\xi}{2}, \quad v(t,x) \leq \frac{\xi}{2}, && \text{for } \forall\ t \in [\underline{t}+\tau+\omega, \bar{t}], x \in (0,l). \end{aligned}$$

Suppose that there exists $k_2 \in \mathbb{N}$ ($k_2 > k_1$), such that $k_2 T < \bar{t}$. For $t \in (k_1 T, k_2 T]$, repeating above procedure and method, we have $v(k_2 T) > \frac{\xi}{2}$. This contradicts our hypothesis. Henceforth, $v(t,x) \geq \frac{\xi}{2} := \eta$, for $\forall\ t \in [\underline{t},\bar{t}]$, $x \in [0,l]$. Since the interval $[\underline{t},\bar{t}]$ is arbitrary, we obtain $\lim_{t\to\infty} v(t,x;\chi) \geq \eta$ uniformly for all $x \in [0,l]$. □

From the above statements, we note that high vaccination rates are a effective condition to eradicate the virus. To be specific, high vaccination rates can enhance the CTL response resulting in producing a large w^*, which fact together with the negative feedback of R_0 on w^*, we can obtain that virus will eventually be forced to vanish.

3.2 The global attractivity investigation

Despite the weaker uniform persistence results for the entire system as stated above, we still are inclined to establish some stronger results about the global dynamics of the entire system. In fact, since the system is non-cooperative, we will utilize the theory of Lyapunov function and some necessary analyses to lift the threshold type results for problem (1.1)-(1.3).

As the starting point, we first present the compactness of the solution semiflow. Let $U = (u, v, w) \in L_p(0, l) \times L_p(0, l) \times L_p(0, l)$, $p > 1$, problem (1.1)-(1.3) can be written as

$$\begin{cases} \dfrac{\partial U}{\partial t} = BU + F(t, U), & t \neq nT, x \in (0, l), n = 0, 1, \cdots, \\ U_x(t, 0) = U_x(t, l) = 0, & t > 0, \\ U(0, x) = U_0(x) \geq, \not\equiv 0, & x \in (0, l), \end{cases} \tag{3.4}$$

and impulsive condition

$$u((nT)^+, x) = u(nT, x),\ v((nT)^+, x) = v(nT, x),\ w((nT)^+, x) = g(w(nT, x)), \quad x \in (0, l), n = 0, 1, \cdots, \tag{3.5}$$

where

$$B := \begin{bmatrix} d_c\partial_{xx}^2 - \varrho & 0 & 0 \\ 0 & d_c\partial_{xx}^2 - \varrho & 0 \\ 0 & 0 & d_w\partial_{xx}^2 - \varrho \end{bmatrix}, \varrho > 0, \quad F(t, U) := \begin{bmatrix} \theta - \alpha u - \beta uv + \varrho u \\ \beta uv - \sigma v - \kappa vw + \varrho v \\ \mu vw + w(\gamma - w) + \varrho w \end{bmatrix}.$$

The operator B has the domain of definition $\overline{\Lambda}(B) = \{\Psi : \Psi \in \Omega^{2,p}(0, l), \Psi_x(t, 0) = \Psi_x(t, l) = 0\}$, where $\Omega^{2,p}(0, l)$ is the Sobolev space of functions from $L_p(0, l)$ that possesses two generalized derivatives. Motivated by [11], we know that B is sectorial and $\Re\Upsilon(B) < -\varrho$, where $\Upsilon(B)$ is the spectrum of B. For $\forall\ \vartheta > 0$, the functional power $B^{-\vartheta}$ of B is defined by $B^{-\vartheta} = \frac{1}{\Gamma(\vartheta)} \int_0^{+\infty} e^{-tB} t^{\vartheta-1} \mathrm{d}t$, where Γ is the gamma function. Naturally, the operator $B^{-\vartheta}$ is bounded and bijective. Since $B^{\vartheta} = (B^{-\vartheta})^{-1}$ and $\overline{\Lambda}(B^{\vartheta}) = H(B^{-\vartheta})$, where H stands for the range of $B^{-\vartheta}$ and B^0 is the identity in $Y = L_p \times L_p \times L_p$ together with norm $\|\cdot\|$. Then, for $\vartheta \in [0, 1]$, we introduce a new space $Y^{\vartheta} = \Lambda(B^{\vartheta})$ such that $\|y\|_{\vartheta} = \|B^{\vartheta} y\|_{\vartheta}$. Hence, we have the following lemma ([4][Lemma 2.2]) about the compactness of the solution semiflow.

Lemma 3.2 *Assume that the function g is continuously differentiable and there exists a positive function $q(M)$ such that $\sup_{\|w\|_{\vartheta} \leq M} \|g(w)\| \leq q(M), \vartheta \in \left(\frac{1}{2} + \frac{n}{2p}, 1\right)$. Let $U(t, U_0) = (u(t, x, u_0, v_0, w_0), v(t, x, u_0, v_0, w_0), w(t, x, u_0, v_0, w_0))$ and $U_0 = (u_0, v_0, w_0) \in Y^{\vartheta}$ be a bounded solution of problem (3.4)-(3.5). Then the set $\{U(t, U_0) : t > 0\}$ is relatively compact in $\mathbb{C}^{1+\varpi}(\mathbb{R}_+^3, [0, l])$ for $0 < \varpi < 2\vartheta - 1 - \frac{n}{p}$.*

Now, according to the result of uniform persistence as stated above, we can strength the boundedness of solutions from $\mathbb{E}_0$ to $\mathbb{E} := \{(u, v, w) \mid \underline{M} \leq (u, v, w) \leq \overline{M}\}$ for sufficiently large t. In particular, we have the following investigation about the global attractivity of the entire system (1.1)-(1.3).

Theorem 3.3 *Suppose that $R_0 > 1$. If $\ln N + \lambda_A T < 0$, where $N = \max\left\{\max_{\underline{M} \leq s \leq \overline{M}} (g'(s))^2, 1\right\}$, and λ_A is the maximal eigenvalue of the matrix*

$$A = \begin{bmatrix} 2\big(-\alpha - \beta\underline{M}\big) & -\beta\underline{M} + \beta\overline{M} & 0 \\ -\beta\underline{M} + \beta\overline{M} & 2\big(\beta\overline{M} - \sigma - \kappa\underline{M}\big) & -\kappa\underline{M} + \mu\overline{M} \\ 0 & -\kappa\underline{M} + \mu\overline{M} & 2\big(-2\underline{M} + \mu\overline{M} + \gamma\big) \end{bmatrix}, \tag{3.6}$$

then problem (1.1)-(1.3) admits a unique positive steady state, which is T-periodic, piecewise continuous and globally attractive.

Proof. To begin with, we present the existence of the positive steady state.

Define the operator

$$\Theta : \mathbb{X}_+ \to \mathbb{X}_+, \Theta(u(0^+), v(0^+), w(0^+)) = (u((nT)^+), v((nT)^+), w((nT)^+)), n = 1, 2, \cdots.$$

Due to the system being persistent, the continuous operator Θ maps the closed, bounded, connected, and convex set $\mathbb{E}$ into itself. According to Brouwer's fixed point theorem, the operator Θ admits at least a fixed point $(u^{**}, v^{**}, w^{**}) \in \mathbb{E}$, which is a periodic solution of problem (1.1)-(1.3). Hence, problem (1.1)-(1.3) admits at least a strictly positive piecewise continuous T-periodic solution. The existence of the positive stable state is proved.

In the following, the global attractivity of the positive steady state will be given.

Let (u, v, w) be a periodic solution of problem (1.1)-(1.3) and let $(\breve{u}, \breve{v}, \breve{w})$ be an other solution of (1.1)-(1.3) in the set $\mathbb{E}$. Consider an auxiliary function

$$I(t) = \int_0^l [(u(t, x) - \breve{u}(t, x))^2 + (v(t, x) - \breve{v}(t, x))^2 + (w(t, x) - \breve{w}(t, x))^2] \mathrm{d}x.$$

Then

$$
\begin{aligned}
\frac{\mathrm{d}I(t)}{\mathrm{d}t} =& 2\int_0^l \left[(u-\breve{u})\left(\frac{\partial u}{\partial t}-\frac{\partial \breve{u}}{\partial t}\right)+(v-\breve{v})\left(\frac{\partial v}{\partial t}-\frac{\partial \breve{v}}{\partial t}\right)+(w-\breve{w})\left(\frac{\partial w}{\partial t}-\frac{\partial \breve{w}}{\partial t}\right)\right]\mathrm{d}x\\
=&2\int_0^l [d_c(u-\breve{u})(u_{xx}-\breve{u}_{xx})+d_c(v-\breve{v})(v_{xx}-\breve{v}_{xx})+d_w(w-\breve{w})(w_{xx}-\breve{w}_{xx})]\,\mathrm{d}x\\
&+2\int_0^l (u-\breve{u})\left[(\theta-\alpha u-\beta uv)-(\theta-\alpha\breve{u}-\beta\breve{u}\breve{v})\right]\mathrm{d}x+2\int_0^l (v-\breve{v})\left[(\beta uv-\sigma v-\kappa vw)-(\beta\breve{u}\breve{v}-\sigma\breve{v}-\kappa\breve{v}\breve{w})\right]\mathrm{d}x\\
&+2\int_0^l (w-\breve{w})\left[(\mu vw+w(\gamma-w))-(\mu\breve{v}\breve{w}+\breve{w}(\gamma-\breve{w}))\right]\mathrm{d}x\\
\le& -2d_c\int_0^l \mid u_x-\breve{u}_x\mid^2\mathrm{d}x-2d_c\int_0^l \mid v_x-\breve{v}_x\mid^2\mathrm{d}x-2d_w\int_0^l \mid w_x-\breve{w}_x\mid^2\mathrm{d}x\\
&+2\int_0^l (u-\breve{u})^2(-\alpha-\beta\breve{v})\mathrm{d}x+2\int_0^l (v-\breve{v})^2(\beta\breve{u}-\sigma-\kappa\breve{w})\mathrm{d}x+2\int_0^l (w-\breve{w})^2(-w+\mu\breve{v}+\gamma-\breve{w})\mathrm{d}x\\
&+2\int_0^l (u-\breve{u})(v-\breve{v})(-\beta u+\beta v)\mathrm{d}x+2\int_0^l (v-\breve{v})(w-\breve{w})(-\kappa v+\mu w)\mathrm{d}x\\
\le&2\int_0^l (u-\breve{u})^2(-\alpha-\beta\breve{v})\mathrm{d}x+2\int_0^l (v-\breve{v})^2(\beta\breve{u}-\sigma-\kappa\breve{w})\mathrm{d}x+2\int_0^l (w-\breve{w})^2(-w+\mu\breve{v}+\gamma-\breve{w})\mathrm{d}x\\
&+2\int_0^l (u-\breve{u})(v-\breve{v})(-\beta u+\beta v)\mathrm{d}x+2\int_0^l (v-\breve{v})(w-\breve{w})(-\kappa v+\mu w)\mathrm{d}x\\
\le&2\int_0^l (u-\breve{u})^2(-\alpha-\beta\underline{M})\mathrm{d}x+2\int_0^l (v-\breve{v})^2(\beta\overline{M}-\sigma-\kappa\underline{M})\mathrm{d}x+2\int_0^l (w-\breve{w})^2(\mu\overline{M}+\gamma-2\underline{M})\mathrm{d}x\\
&+2\int_0^l (u-\breve{u})(v-\breve{v})(-\beta\underline{M}+\beta\overline{M})\mathrm{d}x+2\int_0^l (v-\breve{v})(w-\breve{w})(-\kappa\underline{M}+\mu\overline{M})\mathrm{d}x\\
\le&\lambda_A\int_0^l \left[(u-\breve{u})^2+(v-\breve{v})^2+(w-\breve{w})^2\right]\mathrm{d}x,
\end{aligned}
$$

that is, $\frac{\mathrm{d}I(t)}{\mathrm{d}t}\le\lambda_A I(t)$. Straightforward calculation implies that $I((n+1)T)\le I((nT)^+)e^{\lambda_A T}$, and we have

$$
\begin{aligned}
I(((n+1)T)^+)=&\int_0^l [(u((n+1)T,x)-\breve{u}((n+1)T,x))^2+(v((n+1)T,x)-\breve{v}((n+1)T,x))^2\\
&+(g(w((n+1)T),x)-g(\breve{w}((n+1)T,x)))^2]\mathrm{d}x\\
\le&NI((n+1)T)\le NI((nT)^+)e^{\lambda_A T}.
\end{aligned}
$$

Now, we take the change of the function over the period T into consideration. Naturally, we have

$$
I(t+T)\le N_*I(t)=Ne^{\lambda_A T}I(t).
$$

Due to $\ln N+\lambda_A T<0$, we obtain that $N_*<1$. Consequently, we deduce that $I(\tilde{t}+mT)\le N_*^m I(\tilde{t})$ and $N_*^m I(\tilde{t})\to 0$ as $m\to\infty$, which implies that

$$
\lim_{t\to\infty}\|u(t,x)-\breve{u}(t,x)\|_{L_2}=\lim_{t\to\infty}\|v(t,x)-\breve{v}(t,x)\|_{L_2}=\lim_{t\to\infty}\|w(t,x)-\breve{w}(t,x)\|_{L_2}=0.
$$

From the solutions of problem (1.1)-(1.3) are bounded, we can obtain that

$$
\limsup_{t\to\infty x\in(0,l)}\mid u(t,x)-\breve{u}(t,x)\mid=\limsup_{t\to\infty x\in(0,l)}\mid v(t,x)-\breve{v}(t,x)\mid=\limsup_{t\to\infty x\in(0,l)}\mid w(t,x)-\breve{w}(t,x)\mid=0.
$$

Identically, the solutions of problem (1.1)-(1.3) are globally attractive.

Lastly, consider the sequence $(u(nT,x,u_0,v_0,w_0),v(nT,x,u_0,v_0,w_0),w(nT,x,u_0,v_0,w_0))=U(nT,U_0)$. Recalling the orbit compactness conclusion Lemma 3.2, we still have the compactness in space $C([0,l])\times C([0,l])\times C([0,l])$. Let U^* be a limit point of this sequence satisfying $U^*=\lim_{i\to\infty}U(n_iT,U_0)$, then $U(T,U^*)=U^*$. Due to $U(T,U(n_iT,U_0))=U(n_iT,U(T,U_0))$ and $\lim_{n_i\to\infty}U(n_iT,U(T,U_0))-U(n_iT,U_0)=0$, then as $i\to\infty$, we have

$$
\begin{aligned}
\|U(T,U^*)-U^*\|\le&\|U(T,U^*)-U(T,U(n_iT,U_0))\|+\|U(T,U(n_iT,U_0)-U(n_iT,U_0)\|\\
&+\|U(n_iT,U_0)-U^*\|\to 0.
\end{aligned}
\tag{3.7}
$$

Thus, the sequence $\{U(nT, U_0)\}$ admits a unique limit point. Without loss of generality, we assume that the sequence has two different limit points $U^* = \lim_{i\to\infty} U(n_iT, U_0)$ and $U_* = \lim_{i\to\infty} U(n_iT, U_0)$. According to (3.7) and $U_* = U(n_iT, U_*)$, then we have

$$\|U^* - U_*\| \leq \|U^* - U(n_iT, U_0)\| + \|U(n_iT, U_0) - U_*\| \to 0, \text{ as } i \to \infty, .$$

Thus, $U^* = U_*$. The solution $(u(t, x, u, v, w), v(t, x, u, v, w), w(t, x, u, v, w)) := U^*$ is the unique positive steady state of problem (1.1)-(1.3). The proof is completed. □

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