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Existence of order-1 periodic solutions for a viral infection model with state-dependent impulsive control

Huilan Wang[1], Binxiang Dai[2*] and Qizhen Xiao[1]

*Correspondence:
bxdai@csu.edu.cn
[2]School of Mathematics and Statistics, Central South University, Changsha, P.R. China
Full list of author information is available at the end of the article

Abstract

It is well known that the drug treatment is always combined with the injection of immune factors. In this paper, a virus infection model with state-dependent impulsive control is considered. Firstly, by deriving three categories of Bendixson domain and using the methods of geometry and successor function, we establish some criteria for the existence of positive order-1 periodic solution for a general model, which extends the existing results in the literature. Further, the criteria are used to obtain the existence of positive order-1 periodic solutions in the two cases that the positive equilibrium point is on the left or right side of the pulse line, respectively. Finally, an example is presented to illustrate our results.

MSC: 37N25; 34A37; 34C25

Keywords: State-dependent; Impulse; Periodic solution; Successor function; Bendixson domain

1 Introduction

With respect to the mathematical analysis of virus copies in vivo, differential equations are important tools modeling the evolution mechanism of normal cells and virus [1–4]. Without the treatment of drugs, the turnover of free virus is much faster than that of infected cells, which allows them to make a quasi-steady-state assumption, whereby the amount of free virus is proportional to and hence incorporated into the number of infected cells [5, 6]. Practically, the amount of uninfected cells and the virus load is the main criterion in the control of disease. Therefore, we simplify the virus infection model as follows:

$$\begin{cases} \frac{dx}{dt} = f(x) - vg(x), \\ \frac{dv}{dt} = v[g(x) - a], \end{cases} \tag{1.1}$$

where $x(t)$ and $v(t)$ are the densities of uninfected cells and virus particles, respectively. The positive constant a is the natural death rate of free virus. $f(x)$ is the growth rate at which new target cells are generated, which incorporating the natural death rate of the cells; $g(x)$ represents the rate at which an uninfected cell infected by virus. In fact, system (1.1) can also be characterized as a predator–prey model when one regards $x(t)$ as the density of prey and $v(t)$ as that of predator. As is well known, the different functional response between predator and prey is depicted by the function $g(x)$, such as Holling type I or Holling type II. In vivo dynamics, the normal cell is produced by the specific organ often at a constant rate, while the death rate is constrained by the density of itself, which causes the growth function $f(x)$ to decrease. Hence, we assume that

(A_1) $f \in C^1(R,R), f(0) = \lambda > 0, f'(x) < 0$ and there exists a positive number n such that $f(n) = 0$;

(A_2) $g \in C^1(R,R)$, $g(0) = 0$, $g'(x) > 0$, and there exists a number $m \in (0,n)$ such that $g(m) = a$.

Define

$$\varphi(x) = \frac{f(x)}{g(x)}.$$

As is well known, system (1.1) possesses two possible equilibria,

$$E_0 = (n,0), \qquad E_1 = (x^*, v^*) = \left(m, \frac{f(m)}{g(m)}\right) = (m, \varphi(m)). \tag{1.2}$$

Since $f(m) > 0$, the equilibrium E_1 is asymptotically stable, which will be verified in the following section. Therefore, the virus cannot be eradicated without control under the assumptions (A_1)–(A_2).

The principle of controlling the virus infection is either eradicating the virus or keeping the virus concentration at a low level while the 'good' cells at a high level. Since some classes of virus replicate so rapidly and irregularly that it is hardly possible to eradicate, the strategy of controlling the virus infection is to find a certain dynamical balance which does not lead to a disaster.

In fact, people often take measures to control the infected system before it reaches the worst case. For example, some scientists suggest that an HIV-1 infected person should receive a corresponding treatment when the amount of $CD4^+T$ decreases to 350 or 500 mm^{-3}. So the value 350 or 500 is regarded as one of the 'therapy thresholds'. Theoretically, if the density of normal cells is always higher than the 'therapy threshold', we need not take the corresponding treatment measure. Otherwise, we must find an effective therapy to suppress the decline of 'good' cells. It is well known that a regular therapy for HIV infection is a continuous ART (antiretroviral therapy). However, in view of the viral reservoir it cannot be sufficiently targeted, the latent virus will be productive after a discontinuation of ART, which will lead to a burst of virus. Therefore, an integrate therapy is required. For example, in the treatment of HIV/SIV infection, the combination of Ad26/MVA vaccination and TLR7 stimulation results in decreased levels of viral DNA in lymph nodes and peripheral blood as well as in delays viral rebound for eight weeks following ART discontinuation [7].

Compared with the process of the disease, the impact of taking drugs or immune factors is short enough for it to be assumed that the therapy leads to an impulsive effect. On one hand, the drugs and immune injectors suppress the reproduction of the virus particles as well as the target cells at a certain rate; on the other hand, the immune injectors will stimulate the increasing of target cells.

Thus, we introduce a state-dependent impulsive model as follows:

$$\begin{cases} \left.\begin{array}{l} \frac{dx}{dt} = f(x) - vg(x), \\ \frac{dv}{dt} = v[g(x) - a], \end{array}\right\} \quad x > h, \\ \left.\begin{array}{l} \Delta x(t) = \tau - px(t), \\ \Delta v(t) = -qv(t), \end{array}\right\} \quad x = h, \\ x(0^+) = x_0^+ > h, \qquad y(0^+) = v_0^+ > 0, \end{cases} \tag{1.3}$$

where $0 < p < 1$, $0 < q < 1$ are the impulsive rate at which the target cells and virus decrease due to the cytotoxicity of drugs, respectively. The constant τ represents the average increasing amount of activated target cells after each time immunization. h is the therapy threshold which is associated with a critical state. $\triangle x(t) = x(t^+) - x(t)$.

The existence and the stability of positive periodic solutions are key issues on the study of mathematical biology models, so do for state-dependent impulsive differential equations (see [8–21] and the references therein). In [13] and [14], the first integral of a system exists and therefore the Lambert W function is used to establish the existence of periodic solutions. However, if the first integral or the explicit solution of a system cannot be solved, then it is difficult to use the Lambert W function. For a start, Zeng, Chen and Sun [14] established a Poincaré–Bendixson ring-domain principle which is associated with a compression mapping. Some researchers considered such models by the geometric methods or successor function [15, 16, 18], and obtained some existence results of order-1 periodic solution. The difficulty lies in the fact that the non-tangent property is necessary to consider when we utilize the continuity of a successor function.

Motivated by the previous work, we are aiming to establish some criteria for different Bendixson domains, and hence to obtain an impulsive control strategy for system (1.3). We try to find the sufficient conditions that ensure the existence of order-1 periodic solution which is superior to the 'critical state', or consider whether the control is required.

The structure of this paper is as follows. In Sect. 2, we begin with the qualitative analysis for system (1.1) without impulse, then introduce some notation and lemmas which will be used in the next sections. In particular, we derive three categories of Bendixson domain to deal with the tangent segment and to extend the existing Poincaré–Bendixson ring-domain principle in [14]. In Sect. 3, we obtain main results under two cases $x^* < h$ and $x^* > h$ ($x^* = m$). For the former, we consider the existence of positive order-1 periodic solution by constructing an appropriate Bendixson domain. Under the case $x^* > h$, we discuss how to determine an impulsive control based on the parameter q and the initial value. Finally, a conclusion and some examples are put forward in Sect. 4.

Throughout this paper, we assume:

(A_3) $\tau > ph$ (the stimulation of immune injectors on target cells is stronger than the suppression on them);

(A_4) $m < h + (\tau - ph) < n$ (once the cells are infected, the stimulation of immune injectors is limited).

2 Preliminaries

First, we start from system (1.1). Set a Cartesian coordinate system xOv, and let x axis be the horizontal axis. Denote any solution $(x(t), v(t))$ of system (1.1) by (x, v).

Lemma 2.1 *Any solution of system* (1.1) *is positive for positive initial value and the region*

$$\Omega = \left\{ (x,v) \middle| x > 0, v > 0, x + v \le \frac{f(0)}{a} + n \right\}$$

is positively invariant.

Proof From the second equation of (1.1), it follows that

$$v(t) = v(0) \exp\left\{ -at + \int_0^t g\bigl(x(s)\bigr)\, ds \right\}.$$

If $v(0) > 0$, then $v(t) > 0$. Moreover, when $x(0) = 0$,

$$\dot{x}(0) = f(0) = \lambda > 0,$$

which implies that any solution of system (1.1) is positive with positive initial values.

Denote $l_1 : x = n$ and $l_2 : L(x,v) = 0$, where $L(x,v) = x + v - (\frac{f(0)}{a} + n)$.

Calculating the time derivative of l_1 and l_2 along the trajectories of system (1.1), respectively, gives

$$\frac{dl_1}{dt} = \frac{dx}{dt}\bigg|_{x=n} = f(n) - vg(n) = -vg(n) < 0$$

and

$$\frac{dl_2}{dt} = \left(\frac{dx}{dt} + \frac{dv}{dt} \right)\bigg|_{L(x,v)=0} = f(x) - f(0) - a(n-x) < 0 \quad \text{for } 0 < x < n.$$

Consequently, the region Ω is positively invariant. □

Lemma 2.2 *Under the assumptions* (A_1) *and* (A_2), *the positive equilibrium* E_1 *of system* (1.1) *is asymptotically stable and* E_0 *is unstable.*

Proof The Jacobian matrix along system (1.1) is

$$J = \begin{bmatrix} f'(x) - vg'(x) & -g(x) \\ g'(x)v & g(x) - a \end{bmatrix}.$$

The Jacobian matrix J at the equilibrium $E_0(n,0)$ takes the form

$$J_0 = \begin{bmatrix} f'(n) & -g(n) \\ 0 & g(n) - a \end{bmatrix}.$$

By a direct calculation, we have the eigenvalues such that $\lambda_1 = f'(n) < 0$ and $\lambda_2 = g(n) - a > 0$. Therefore, E_0 is unstable.

At the equilibrium $E_1(m,\varphi(m))$, the Jacobian matrix is given by

$$J_1 = \begin{bmatrix} f'(m) - \varphi(m)g'(m) & -g(m) \\ g'(m)\varphi(m) & 0 \end{bmatrix},$$

and the characteristic equation is

$$\lambda^2 - \left[f'(m) - \varphi(m)g'(m)\right]\lambda + g'(m)f(m) = 0.$$

Since the eigenvalues λ_1 and λ_2 satisfy $\lambda_1 + \lambda_2 = f'(m) - \varphi(m)g'(m) < 0$ and $\lambda_1 + \lambda_2 = g'(m)f(m) > 0$, E_1 is asymptotically stable. □

From Lemma 2.1, it follows that the solutions of (1.3) are positive with positive initial values since $\Delta x(t) = \tau - px(t)$, $\Delta v(t) = -qv(t)$ and $0 < p < 1$, $0 < q < 1$.

The signs of the derivatives $\dot{x}$ and $\dot{v}$ on t are shown in Fig. 1. The expression of the uninfected cells' isoline $\dot{x} = 0$ is $v = \varphi(x)$.

Denote

$$\bar{h} = h + (\tau - ph), \qquad v_0 = \varphi(\bar{h}), \qquad \omega_0 = \varphi(h),$$
$$t_h = \frac{f(0)}{a} + n - h, \qquad t_{\bar{h}} = \frac{f(0)}{a} + n - \bar{h}.$$

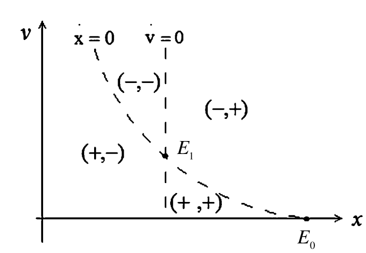
Then we have four characteristic points named

$$P_0(\bar{h}, v_0), \qquad W_0(h, \omega_0), \qquad T_h(h, t_h), \qquad T_{\bar{h}}(\bar{h}, t_{\bar{h}}).$$

Obviously, the trajectory of system (1.1) is tangent to line $x = h$, $x = \bar{h}$ at P_0 and W_0, respectively. Also, the line l_2: $x + v = \frac{f(0)}{a} + n$ intersects with line $x = \bar{h}$, $x = h$ at T_h and $T_{\bar{h}}$, respectively.

The general location of characteristic points and domains, see Fig. 2.

Figure 1 The sign of derivative $\dot{x}$ and $\dot{v}$ on t



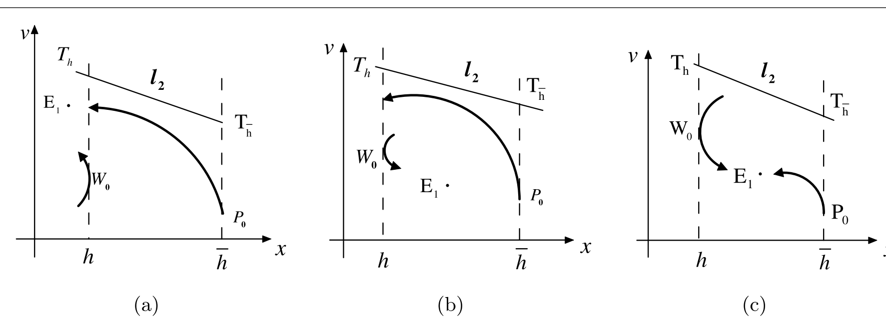


Figure 2 The general location of the characteristic points. (**a**) $x^* < h$; (**b**) $h < x^* < \bar{h}$, the trajectory from P_0 can hit the line $x = h$; (**c**) $h < x^* < \bar{h}$, the trajectory from P_0 cannot hit the line $x = h$

Lemma 2.3 *Under the assumptions* (A_1)–(A_4), *we have*

$$v_0 < t_{\bar{h}}; \tag{2.1}$$

$$v_0 < \omega_0. \tag{2.2}$$

Proof It follows from (A_1)–(A_2) that $\varphi(x)$ is decreasing on x, and (A_3)–(A_4) gives

$$v_0 = \varphi(\bar{h}) < \varphi(m) < \varphi(m) + n - \bar{h} < \frac{f(0)}{a} + n - \bar{h} = t_{\bar{h}}.$$

Similarly, $h < \bar{h}$ implies $v_0 = \varphi(\bar{h}) < \varphi(h) = \omega_0$. □

Let two subsets M and N be

$$M = \{(x,v)|v > 0, x = h\}, \qquad N = \{(x,v)|v > 0, x = \bar{h}\}$$

and the impulsive function be I. Then $I(M) \subseteq N$.

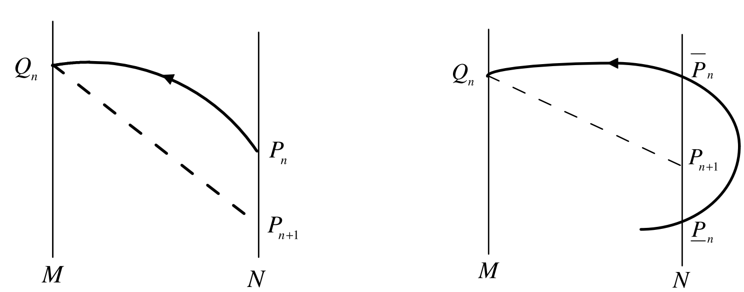
We define the positive orbit (or solution) starting from $P(x(t),v(t)) \in \mathbb{R}_+^2$ by $O^+(P)$ and the negative orbit arriving at it by $O^-(P)$. Obviously, the positive trajectories initiated from N will intersect with the impulse segment M or cannot approach it. Similarly, the negative trajectory initiated from M will be reachable or unreachable to the segment N. If $O^+(P_n)(\bar{h}, v_n)$ intersects firstly with M at point $Q_n \triangleq (h, \tilde{v}_n)$, we denote $O_M^+(P_n) = Q_n$.

If $O^-(Q_n)$ intersects with the phase line N at unique point $P_n(\bar{h}, v_n)$, we denote $O_N^-(Q_n) = P_n$; If $O^-(Q_n)$ intersects with N at two points $\bar{P}_n$ and $\underline{P}_n$ in recent time series, which lie above P_0 and below P_0, respectively, we denote $O_N^-(\bar{P}_n) = \underline{P}_n$, $O_N^+(\underline{P}_n) = \bar{P}_n$ and $O_M^+(\underline{P}_n) = O_M^+(\overline{P}_n) = Q_n$. And hence, O_M^+, O_N^-, and O_N^+ can be regarded as maps from N to M or inverse direction (see Fig. 3, O_N^- may be a multi-valued map).

For any $A, B \in N$, if A lies above B, we denote $A > B$. Moreover, we define $AB = B - A = v_B - v_A$, where v_A, v_B is the ordinates of A and B, respectively.

If $O_M^+(P_n) \neq \emptyset$ for any $P_n(\bar{h}, v_n) \in N$, we define a Poincaré map $\mathfrak{F}$ and a successor function F as follows:

$$\mathfrak{F}(P_n) = IO_M^+(P_n) = P_{n+1}, \qquad F(P_n) = IO_M^+(P_n) - P_n = v_{n+1} - v_n. \tag{2.3}$$



(a) $O_M^+(P_n) = Q_n, O_N^-(Q_n) = P_n$

(b) $O_M^+(\bar{P}_n) = O_M^+(\underline{P}_n) = Q_n$, $O_N^-(\bar{P}_n) = \underline{P}_n$, and $O_N^+(\underline{P}_n) = \bar{P}_n$

Figure 3 The illustration for O_M^+, O_N^-, O_N^+ and I, where $I(Q_n) = P_{n+1}$

Thus $\mathfrak{F}(P_n)$ and $F(P_n)$ are continuous on P_n due to the continuity of I and continuous dependence on the initial value of the solutions to system (1.1).

Lemma 2.4 [12] *The successor function is continuous if it is well defined.*

Based on the definition of order-k periodic solution for an impulsive dynamics system in [12], we give the definition of order-1 periodic solution.

Definition 2.1 ([12]) A trajectory $O^+(P_n)$ of system (1.3) together with the impulsive line $\overline{Q_nP_n}$ is called an order-1 cycle if $v_{n+1} = v_n$.

From (2.3), $F(P_n) = 0$ implies the existence of order-1 periodic solution.

To ensure that the successor function is well defined, we consider three categories of Bendixson domain for system (1.3).

Definition 2.2 For system (1.3), suppose a Bendixson domain D is composed of M, N, L_1 and L_2, and such that

(i) there is no singularity in it;

(ii) trajectory L_1 intersects with N, M at A_0 and B_0 in order; trajectory L_2 intersects with N, M at A_1 and B_1 in order, respectively;

(iii) segments $\overline{A_0A_1}$ and $\overline{B_0B_1}$ cannot be tangent to trajectories of system (1.3) except at the end point.

If L_1 is tangent to N at A_0, and $A_0 < A_1$ gives $B_0 < B_1$, then we call the region D a *parallel trajectory rectangle* (see Fig. 4(a));

If L_1 is tangent to N at A_0, and $A_0 > A_1$ gives $B_0 < B_1$, then we call the region D a *sub-parallel trajectory rectangle* (see Fig. 4(b));

If L_1 is tangent with M at B_0 and intersects with N at A_0 and $\bar{A}_0$ in order, L_2 intersects with N at A_1 and $\bar{A}_1$ in order, and $A_0 > A_1$, then we call the region D a *semi-ring domain* (see Fig. 4(c)).

Lemma 2.5 *Suppose a parallel or sub-parallel domain D is composed of $\widetilde{A_0B_0}$, $\overline{A_0A_1}$, $\widetilde{A_1B_1}$ and $\overline{B_0B_1}$ and with $F(A_0)F(A_1) < 0$. Then there exists an order-1 periodic solution in D.*

Proof Since D is parallel or sub-parallel as defined above, we have $O^+_M(A_n) \neq \emptyset$ for any $A_n \in \overline{A_0A_1}$. As the successor function $F(A_n)$ is continuous on $A_n \in \overline{A_0A_1}$, it follows from

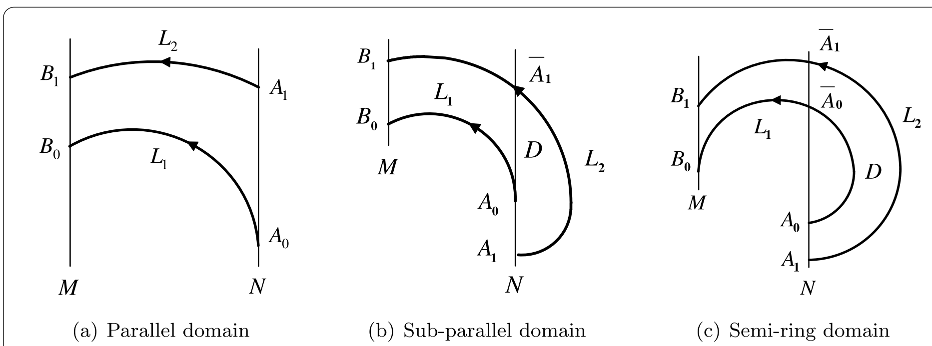


Figure 4 The illustration for three categories of Bendixson domain. A_0 is a tangent point in (**a**) and (**b**), while B_0 is a tangent point in (**c**)

$F(A_0)F(A_1) < 0$ that there must exist an $A_N \in \overline{A_0A_1}$ such that $F(A_N) = 0$, which implies the existence of an order-1 periodic solution in D. □

Lemma 2.6 *Suppose a semi-ring domain D of system (1.3) is composed of $\widetilde{A_0B_0}$, $\overline{A_0A_1}$, $\widetilde{A_1B_1}$ and $\overline{B_0B_1}$. Then we have the following principle*:

(i) *if $\mathfrak{F}(\overline{A_0A_1}) \subseteq \overline{A_0A_1}$ or $\mathfrak{F}(\overline{A_0A_1}) \subseteq \overline{\bar{A}_0\bar{A}_1}$, then there exists an order-1 periodic solution which is initiated from $\overline{A_0A_1}$ or $\overline{\bar{A}_0\bar{A}_1}$, respectively*;

(ii) *if $\mathfrak{F}(\overline{A_0A_1}) \subseteq \overline{\bar{A}_0A_0}$, then there is no order-1 periodic solution in D.*

Proof (i) Obviously, if $\mathfrak{F}(\overline{A_0A_1}) \subseteq \overline{A_0A_1}$, then the continuous map $\mathfrak{F} = IO_M^+$ is a compression mapping. Thus there exists a fixed point $A_n \in \overline{A_0A_1}$ such that $\mathfrak{F}(A_n) = A_n$, which implies the existence of order-1 periodic solution initiated from $\overline{A_0A_1}$. If $\mathfrak{F}(\overline{A_0A_1}) \subseteq \overline{\bar{A}_0\bar{A}_1}$, then $F(\bar{A}_0)F(\bar{A}_1) < 0$, which implies the existence of order-1 periodic solution initiated from $\overline{\bar{A}_0\bar{A}_1}$.

(ii) If $\mathfrak{F}(\overline{A_0A_1}) \subseteq \overline{A_0\bar{A}_0}$, then all the trajectories initiated from $\overline{A_0A_1}$ will be mapped onto $\overline{A_0\bar{A}_0}$, from which the trajectories will not approach M since L_2 is tangent to M at B_0. Therefore, there is no order-1 periodic solution in D. □

3 Main results

Suppose $O_M^+(P_0) = Q_0 \triangleq (h, \tilde{v}_0)$ and denote the trajectories $\widetilde{P_0Q_0}$, $\widetilde{P_1Q_1}$ by functions $v_0(x)$ and $v_1(x)$, respectively. Then we have the following lemmas.

Lemma 3.1 *Under the assumption (A_1)–(A_4), if $O_M^+(P_0) \neq \emptyset$, then $v_0(x) > \varphi(x)$ for $x \in (h, \bar{h})$.*

Proof Provided that there exists an $x_0 \in (h, \bar{h})$ such that $v_0(x_0) = \varphi(x_0)$, then the trajectory $\widetilde{P_0Q_0}$ will intersect with the trajectory initiated from $(x_0, \varphi(x_0))$ which is tangent to the line $x = x_0$. It will contradict the uniqueness of the solution to system (1.1). □

Lemma 3.2 *Suppose $O_M^+(P_0) \neq \emptyset$. If $F(P_0) > 0$, then there exists a point $P \in N$ which lies above P_0 such that $F(P) \leq 0$.*

Proof Let $O_M^+(P_0) = Q_0$. Then all the trajectories initiated from N will approach M. $F(P_0) > 0$ implies $IO_M^+(P_0) = P_1 > P_0$. We consider two cases:

Case 1: $x^* = m < h$.

We claim $F(P_k) < F(P_{k-1})$ $(k = 1, 2, \ldots)$.

Firstly, we prove that $\overline{Q_0Q_1} < (1 - q)\overline{P_0P_1}$.

Since $x^* < h < \bar{h} < n$, there does not exist any equilibrium which lies between M and N. Therefore $v_0(x)$ and $v_1(x)$ are continuous on $[h, \bar{h}]$ and derivative on the open interval $(h, \bar{h})$. Based on the Cauchy mean theorem, there exists a $\xi \in (h, \bar{h})$ such that

$$\frac{v_1(h) - v_1(\bar{h})}{v_0(h) - v_0(\bar{h})} = \frac{v_1'(\xi)}{v_0'(\xi)} = \frac{\frac{v_1(\xi)[g(\xi)-a]}{f(\xi)-v_1(\xi)g(\xi)}}{\frac{v_0(\xi)[g(\xi)-a]}{f(\xi)-v_0(\xi)g(\xi)}} = \frac{v_1(\xi)[f(\xi) - v_0(\xi)g(\xi)]}{v_0(\xi)[f(\xi) - v_1(\xi)g(\xi)]} = \frac{\frac{\varphi(\xi)}{v_0(\xi)} - 1}{\frac{\varphi(\xi)}{v_1(\xi)} - 1}. \tag{3.1}$$

Since $P_1 > P_0$, we have $v_1(\xi) > v_0(\xi)$ for $\xi \in (h, \bar{h})$. Furthermore, Lemma 3.1 implies that $v_0(\xi) > \varphi(\xi)$. Therefore $\frac{\varphi(\xi)}{v_1(\xi)} - 1 < \frac{\varphi(\xi)}{v_0(\xi)} - 1 < 0$ $(i = 0, 1)$. Thus (3.1) gives

$$\frac{v_1(h) - v_1(\bar{h})}{v_0(h) - v_0(\bar{h})} < 1. \tag{3.2}$$

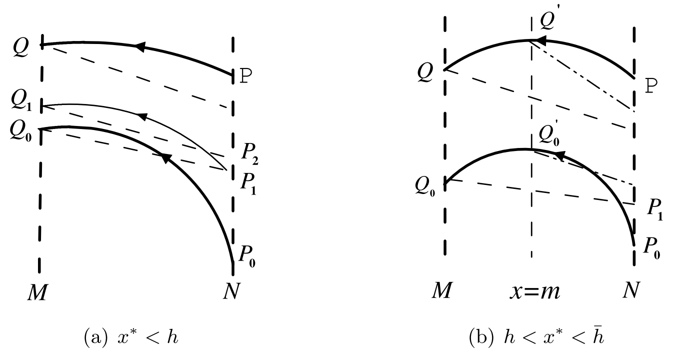


Figure 5 There exists a $P \in N$ such that $F(P) \leq 0$ when $F(P_0) > 0$

In view of $v_0'(x) < 0$ for $x \in (h, \bar{h})$ (which can also be illustrated by Fig. 1), we have $v_0(h) > v_0(\bar{h})$. Hence, (3.2) implies $v_1(h) - v_1(\bar{h}) < v_0(h) - v_0(\bar{h})$, that is, $v_1(h) - v_0(h) < v_1(\bar{h}) - v_0(\bar{h})$ or $\overline{Q_0Q_1} < \overline{P_0P_1}$.

Next, we get

$$P_2 - P_1 = I(Q_1) - I(Q_0) = (1-q)(Q_1 - Q_0) < (1-q)(P_1 - P_0), \tag{3.3}$$

which implies $F(P_1) < (1-q)F(P_0)$.

Similarly, by induction, we can prove that $F(P_{k+1}) < (1-q)F(P_k)$ $(k = 1, 2, \dots)$, which implies $F(P_k) < (1-q)^k F(P_0)$ $(k = 1, 2, \dots)$. Since $(1-q)^k F(P_0) \to 0$ as $k \to +\infty$, there exists a point $P \in N$ which lies above P_0 such that $F(P) \leq 0$ (see Fig. 5(a)).

Case 2: $h < x^* = m < \bar{h}$.

In this case, the trajectories reach the highest point at $x = m$. Suppose $O^+(P_0) \cap \{x = m\} = Q_0'$. Since $(1-q)Q_0 > P_0$ and $v_{Q_0'} > v_{Q_0}$, we have $(1-q)Q_0' > (1-q)Q_0 > P_0$. Obviously, $v_0(x)$ and $v_1(x)$ are continuous on $[m, \bar{h}]$ and derivative on the open interval $(m, \bar{h})$. We apply the Cauchy mean theorem on interval $[m, \bar{h}]$. It follows from the proof of (i) that there exists a point $P \in N$ which lies above P_0 such that $(1-q)Q' \leq P$, where $Q' = O^+(P) \cap \{x = m\}$. Similarly, we have $v_{Q'} > v_Q$, which gives $(1-q)Q < (1-q)Q' < P$, that is, $F(P) \leq 0$ (see Fig. 5(b)). □

In the following, we discuss the existence of periodic solutions in the cases of $x^* < h$ and $h < x^* < \bar{h}$.

3.1 $x^* < h$

If $x^* = m < h$, then all the trajectories initiated from N intersect with M and cross it since the equilibrium E_1 is asymptotically stable.

Theorem 3.1 *Suppose $x^* < h$ holds. Then there must exist an order-*1 *periodic solution for* (1.3) *under the assumptions* (A_1)–(A_4).

Proof We consider two possible cases according to $F(P_0)$.

Case 1. Suppose $F(P_0) > 0$ holds. By Lemma 3.2, there exists a $P \in N$ which lies above P_0 such that $F(P) \leq 0$. Therefore, the domain composed of $\widetilde{P_0Q_0}$, $\overline{P_0P}$, $\widetilde{PQ}$ and $\overline{Q_0Q}$ is parallel,

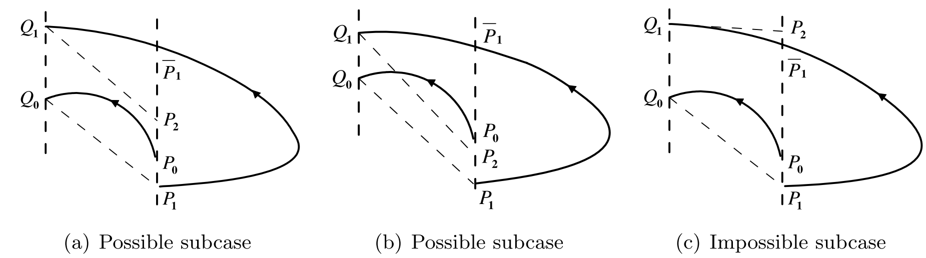


Figure 6 Case 2 $F(P_0) < 0$

and thus $F(P_0)F(P) < 0$. By Lemma 2.5, there exists an order-1 periodic solution initiated from $\overline{P_0P}$.

Case 2. Suppose $F(P_0) < 0$ holds (see Fig. 6).

Since P_0 is the tangent point and $P_1 < P_0$, the region D composed of $\widetilde{P_0Q_0}$, $\overline{P_0P_1}$, $\widetilde{P_1Q_1}$ and $\overline{Q_1Q_0}$ is sub-parallel. Obviously, $F(P_1) > 0$. Otherwise, it contradicts the fact that I is increasing. Hence, $F(P_0)F(P_1) < 0$, by Lemma 2.5, there exists an order-1 periodic solution in D.

Claim *The periodic solution is initiated from* $\overline{P_0P_1}$ *when* $F(P_0) < 0$. *We need only to prove that* $P_2 < \bar{P}_1$. *Provided* $P_2 > \bar{P}_1$, *then* $\overline{P_1P_2} > \overline{P_0\bar{P}_1}$ *as* $P_1 < P_0$. *However, by Lemma* 3.2, *we have* $\overline{Q_0Q_1} < \overline{P_0\bar{P}_1}$, *which gives* $\overline{P_1P_2} = (1-q)\overline{Q_0Q_1} < \overline{P_0\bar{P}_1} < \overline{P_1P_2}$. *It comes to a contradiction* (*see Fig.* 6(c)). □

Corollary 3.1 *Suppose that* $x^* < h$ *holds. Under the assumptions* (A_1)–(A_4), *if*

$$1-q \leq \frac{t_{\bar{h}}}{t_h}, \tag{3.4}$$

then there must exist an order-1 *periodic solution under the line* $x + v = \frac{f(0)}{a} + n$ *for system* (1.3).

Proof By Lemma 2.1, $O_M^+(T_{\bar{h}}) \triangleq S_h(h, s_h) < T_h$. It follows from $1-q \leq \frac{t_{\bar{h}}}{t_h}$ that $I(S_h) < I(T_h) = (1-q)t_h < t_{\bar{h}}$, which gives $F(T_{\bar{h}}) < 0$.

If $F(P_0) > 0$, then $T_{\bar{h}}$ can be regarded as P in Theorem 3.1. Since $v_0 < t_{\bar{h}}$, the order-1 periodic solution, which initiated from $\overline{P_0T_{\bar{h}}}$, lies below the line $x + v = \frac{f(0)}{a} + n$.

If $F(P_0) < 0$, by Theorem 3.1 there must exist an order-1 periodic solution initiated from $\overline{P_0P_1}$, which lies below the line $x + v = \frac{f(0)}{a} + n$. □

Remark 3.1 In fact, according to Lemma 2.5, if $1-q \leq \frac{t_{\bar{h}}}{s_h}$, then there must exist an order-1 periodic solution under the line $x + v = \frac{f(0)}{a} + n$ for system (1.3). Obviously, the condition $1-q \leq \frac{t_{\bar{h}}}{t_h}$ is stronger than $1-q \leq \frac{t_{\bar{h}}}{s_h}$ in the sense that $s_h < t_h$. In view of the computation of t_h being more visible than s_h, we prefer the former. On the other hand, if it does not hold, there maybe exists an order-1 periodic solution above the line $x + v = \frac{f(0)}{a} + n$. However, the state is not optimal because of the higher load of v.

3.2 $h < x^* < \bar{h}$

In this case, the trajectory $O^+(P_0)$ does not necessarily approach the line $x = h$.

Lemma 3.3 *Suppose $h < x* < \bar{h}$ holds. We have:*

(i) $O_N^-(W_0) = \emptyset \Longleftrightarrow O_M^+(P_0) \neq \emptyset$;

(ii) *if $\omega_0 > t_h$, then $O^-(W_0)$ will intersect with $x = \bar{h}$ at unique point $W_0^- \triangleq (\bar{h}, \omega_0^-)$, and such that $\omega_0^- > t_{\bar{h}}$.*

Proof (i) If $O_N^-(W_0) = \emptyset$, then the trajectory $O^-(W_0)$ intersects with the isoline $v = \varphi(x)$ at the point which lies on the left to P_0 (see Fig. 1 and Fig. 2(b)). It is obvious that $O^+(P_0)$ will intersect with M, otherwise, $O^+(P_0)$ will pass through $O^-(W_0)$ and approach E_1, which contradicts the uniqueness of solution to system (1.1).

Suppose that $O_M^+(P_0) = Q_0(h, \tilde{v}_0) \neq \emptyset$. By Lemma 3.1, we have $\tilde{v}_0 = v_0(h) > \varphi(h) = \omega_0$. Therefore, the trajectory $O^-(W_0)$ will intersect with the isoline $v = \varphi(x)$ at the point that lies on the left to P_0, which means $O_N^-(W_0) = \emptyset$. The proof for (i) is completed.

(ii) We divided the proof into three steps.

Firstly, we prove that $O_N^-(W_0) \neq \emptyset$. Assume that $O_N^-(W_0) = \emptyset$. According to the result of (i), we have $O_M^+(P_0) = Q_0(h, \tilde{v}_0) \neq \emptyset$ and $\tilde{v}_0 = v_0(h) > \varphi(h) = \omega_0$, which implies the trajectory $O^+(P_0)$ will go out from Ω. Thus $O_N^-(W_0) \neq \emptyset$.

Next, we prove that $O_N^-(W_0) > T_{\bar{h}}$. Otherwise, $O_N^-(W_0) < T_{\bar{h}}$ will lead to a similar contradiction that the trajectory passing through W_0 goes out from Ω.

Finally, we prove that $O^-(W_0)$ intersects with $x = \bar{h}$ at unique point. Assume that $O^-(W_0)$ intersects with N at two points above $T_{\bar{h}}$. The tangent point P_0 will lie between the two intersected points, which means $v_0 > t_{\bar{h}}$, it is a contradiction to the fact that $v_0 < t_{\bar{h}}$.

Thus $O^-(W_0)$ will intersect with $x = \bar{h}$ at a unique point and $\omega_0^- > t_{\bar{h}}$ (see Fig. 7). □

Theorem 3.2 *If $\omega_0 \geq t_h$, then there is no periodic solution below the line $x + v = \frac{f(0)}{a} + n$ for system (1.3).*

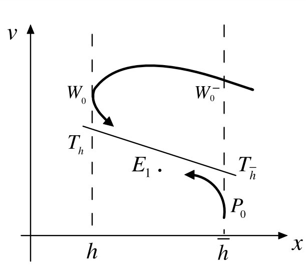
Proof If $\omega_0 > t_h$, according to Lemma 3.3, $O^-(W_0)$ will intersect with $x = \bar{h}$ at unique point W_0^-, which implies that all the trajectories, initiated from the points under W_0^- in N, will not hit the line $x = h$. Further $\omega_0^- > t_{\bar{h}}$, therefore, there is no order-1 periodic solution that lies in the domain Ω for system (1.3). □

Remark 3.2 Theorem 3.2 implies that we may take no measure to control the system (1.1) if $\omega_0 \geq t_h$ and the initial point (x_0^+, v_0^+) lies in the domain $\Omega \cap \{(x, v) | x > h\}$.

Theorem 3.3 *Suppose $\omega_0 < t_h$. We have:*

(i) *If $O_N^-(W_0) = \emptyset$, then there must exist an order-1 periodic solution; particularly, if $1 - q < \frac{t_{\bar{h}}}{t_h}$, then the order-1 periodic solution is below the line $x + v = \frac{f(0)}{a} + n$ for (1.3).*

Figure 7 The case $\omega_0 \geq t_h$



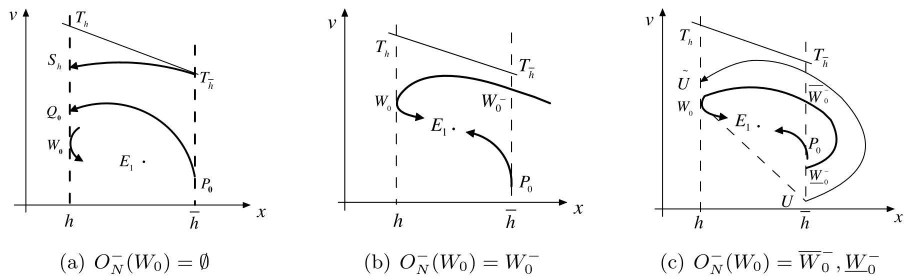


Figure 8 The case $\omega_0 < t_h$

(ii) *If $O^-(W_0)$ intersects with N at an unique intersected point $W_0^-(\bar h, \omega_0^-)$ and $1 - q < \frac{v_0}{t_h}$, then there is no order-1 periodic solution below the line $x + v = \frac{f(0)}{a} + n$ for system (1.3).*

(iii) *If $O^-(W_0)$ intersects with N at two points $\overline{W}_0^-(\bar h, \overline{\omega}_0^-)$ and $\underline{W}_0^-(\bar h, \underline{\omega}_0^-)$, provided $\frac{\overline{\omega}_0^-}{\omega_0} < 1 - q < \frac{t_{\bar h}}{t_h}$ or $1 - q < \frac{\omega_0^-}{t_h}$, then there exists an order-1 periodic solution initiated from $\overline{W}_0^- T_{\bar h}$ or from the line segment between $\underline{W}_0^-$ and $I(W_0)$, respectively.*

Proof (i) If $O^-_N(W_0) = \emptyset$, then $O^+(P_0)$ hits $x = h$ and the equilibrium E_1 is under the trajectory (Fig. 8(a)). The proof is similar to that in the case $x^* < h$.

(ii) From $\omega_0 < t_h$, it gives $W_0 < T_h$. Since $O^-(W_0)$ intersects with N at an unique intersected point W_0^-, we have $O^+(P_0) = \emptyset$. Obviously, $W_0^- > P_0$, that is, $\omega_0^- > v_0$. It follows from $1 - q < \frac{v_0}{t_h}$ that $1 - q < \frac{\omega_0^-}{t_h}$, which implies that all the points in $\overline{W_0 T_h}$ will be mapped onto the segment below W_0^- by impulsive map I, and the trajectories initiated from segment under W_0^- will not hit M any more. Therefore, there is no order-1 periodic solution under the line $x + v = \frac{f(0)}{a} + n$ (see Fig. 8(b)).

(iii) Since $O^-(W_0)$ intersects with N at two points $\overline{W}_0^- \triangleq (h_0, \bar\omega_0^-)$ and $\underline{W}_0^- \triangleq (h_0, \underline{\omega}_0^-)$, $\frac{\bar\omega_0^-}{\omega_0} < 1 - q < \frac{t_{\bar h}}{t_h}$ implies $F(T_{\bar h})F(\overline{W}_0^-) < 0$ and the domain composed of $\widetilde{\bar W_0^- W_0}$, $\overline{W_0 S_h}$, $\widetilde{T_{\bar h} S_h}$ and $\overline{T_h \bar W_0^-}$ is parallel. By Lemma 2.5, there exists an order-1 periodic solution which is initiated from $\overline{W}_0^- T_{\bar h}$. Similarly, it follows from $1 - q < \frac{\omega_0^-}{t_h}$ that $1 - q < \frac{\omega_0^-}{\omega_0}$, that is, $I(W_0) \triangleq U < \underline{W}_0^-$. Denote $O^+_M(U) = \tilde U$. Then the domain composed of $\widetilde{\underline{W}_0^- W_0}$, $\overline{W_0 \tilde U}$, $\widetilde{U \tilde U}$ and $\overline{U \underline{W}_0^-}$ is semi-ring. It is obvious that $I(W_0 \tilde U) \subseteq U \underline{W}_0^-$. By Lemma 2.6, there is an order-1 periodic solution which is initiated from $U \underline{W}_0^-$ (see Fig. 8(c)). □

Now, we will consider the stability of the order-1 periodic solution for system (1.3).

Lemma 3.4 (Analog of Poincaré criterion [10, 11, 15]) *The T-periodic solution $x = \xi(t)$, $y = \eta(t)$ of the system*

$$\begin{cases} \frac{dx}{dt} = P(x,y), & \frac{dy}{dt} = Q(x,y), \quad \text{if } \phi(x,y) \neq 0, \\ \Delta x = I_1(x,y), & \Delta y = I_2(x,y), \quad \text{if } \phi(x,y) = 0, \end{cases} \tag{3.5}$$

is orbitally asymptotically stable, where P, Q are continuous differentiable functions and ϕ is a sufficiently smooth function with $\nabla\phi \neq 0$, if the Floquet multiplier μ such that $|\mu| < 1$, *where*

$$\mu = \prod_{j=1}^{n} \kappa_j \exp\left\{ \int_0^T \left[\frac{\partial P(\xi(t),\eta(t))}{\partial x} + \frac{\partial Q(\xi(t),\eta(t))}{\partial y} \right] dt \right\} \tag{3.6}$$

with

$$\kappa_j = \frac{(\frac{\partial I_2}{\partial y}\frac{\partial \phi}{\partial x} - \frac{\partial I_2}{\partial x}\frac{\partial \phi}{\partial y} + \frac{\partial \phi}{\partial x})P_+ + (\frac{\partial I_1}{\partial x}\frac{\partial \phi}{\partial y} - \frac{\partial I_1}{\partial y}\frac{\partial \phi}{\partial x} + \frac{\partial \phi}{\partial y})Q_+}{\frac{\partial \phi}{\partial x}P + \frac{\partial \phi}{\partial y}Q} \tag{3.7}$$

and P, Q, $\frac{\partial I_1}{\partial x}$, $\frac{\partial I_1}{\partial y}$, $\frac{\partial I_2}{\partial x}$, $\frac{\partial I_2}{\partial y}$, $\frac{\partial \phi}{\partial x}$, $\frac{\partial \phi}{\partial y}$ *are calculated at the point* $(\xi(\tau_j),\eta(\tau_j))$, $P_+ = P(\xi(\tau_j^+), \eta(\tau_j^+))$, $Q_+ = Q(\xi(\tau_j^+),\eta(\tau_j^+))$, *and* τ_j *is the time of the jth jump.*

Theorem 3.4 *Let* $(X(t),V(t))$ *be the order-*1 *periodic solution of system* (1.3) *with period* T. *If* $g'(x) \geq \frac{g(x)}{x}$ *for* $x > 0$, *and*

$$\left| \frac{v_0 - (1-q)V(T)}{\omega_0 - V(T)} \right| \frac{g(\bar{h})h}{g(h)\bar{h}} < 1, \tag{3.8}$$

then $(X(t),V(t))$ *is orbitally asymptotically stable, where* $V(T)$ *is the load of virus when* $X(T) = h$.

Proof Suppose that (X,V) intersects the sections M and N at points $O(h,V(T))$ and $O^+(\bar{h},(1-q)V(T))$, respectively.

Rewriting the system (1.3) as the form of (3.5) gives

$$P(x,v) = f(x) - vg(x), \qquad Q(x,v) = v\big[g(x) - a\big],$$
$$I_1(x,v) = \tau - px, \qquad I_2(x,v) = -qv, \qquad \phi(x,v) = x - h$$

and

$$\frac{\partial P}{\partial x} = f'(x) - vg'(x), \qquad \frac{\partial Q}{\partial v} = g(x) - a, \qquad \frac{\partial I_1}{\partial x} = -p,$$
$$\frac{\partial I_2}{\partial v} = -q, \qquad \frac{\partial \phi}{\partial x} = 1, \qquad \frac{\partial I_1}{\partial v} = \frac{\partial I_2}{\partial x} = \frac{\partial \phi}{\partial v} = 0.$$

Then it follows from (3.7) that

$$\begin{aligned} \kappa_1 &= \frac{(\frac{\partial I_2}{\partial v}\frac{\partial \phi}{\partial x} - \frac{\partial I_2}{\partial x}\frac{\partial \phi}{\partial v} + \frac{\partial \phi}{\partial x})P_+ + (\frac{\partial I_1}{\partial x}\frac{\partial \phi}{\partial v} - \frac{\partial I_1}{\partial v}\frac{\partial \phi}{\partial x} + \frac{\partial \phi}{\partial v})Q_+}{\frac{\partial \phi}{\partial x}P + \frac{\partial \phi}{\partial v}Q} \\ &= \frac{(1-q)[f(\bar{h}) - g(\bar{h})(1-q)V(T)]}{f(h) - g(h)V(T)}. \end{aligned} \tag{3.9}$$

Since $f'(x) < 0$ and $g'(x) \geq \frac{g(x)}{x}$ for $x > 0$, we have

$$\begin{aligned}
&\int_0^T \frac{\partial P(X,V)}{\partial X}\,dt \\
&\quad= \int_0^T \bigl[f'\bigl(X(t)\bigr) - V(t)g'\bigl(X(t)\bigr)\bigr]\,dt \\
&\quad< \int_0^T \frac{f(X(t)) - V(t)g(X(t))}{X(t)}\,dt = \int_{\bar{h}}^{h} \frac{dx}{x} = \ln\frac{h}{\bar{h}}.
\end{aligned} \tag{3.10}$$

Moreover,

$$\int_0^T \frac{\partial Q(X,V)}{\partial V}\,dt = \int_0^T \bigl(g\bigl(X(t)\bigr) - a\bigr)\,dt = \int_{(1-q)V(T)}^{V(T)} \frac{dv}{v} = \ln\frac{1}{1-q}. \tag{3.11}$$

Hence,

$$\begin{aligned}
&\exp\left\{\int_0^T \left[\frac{\partial P(X,V)}{\partial X} + \frac{\partial Q(X,V)}{\partial V}\right] dt\right\} \\
&\quad< \exp\left\{\ln\frac{h}{\bar{h}} + \ln\frac{1}{1-q}\right\} = \frac{h}{(1-q)\bar{h}}.
\end{aligned} \tag{3.12}$$

Therefore, from (3.8), (3.9) and (3.12), we have

$$|\mu| < \left|\frac{(1-q)[f(\bar{h}) - g(\bar{h})(1-q)V(T)]}{f(h) - g(h)V(T)}\right| \frac{h}{(1-q)\bar{h}} = \left|\frac{v_0 - (1-q)V(T)}{\omega_0 - V(T)}\right| \frac{g(\bar{h})h}{g(h)\bar{h}} < 1,$$

which implies the order-1 periodic solution $(X(t), V(t))$ is orbitally asymptotically stable. □

4 Example

Choosing $f(x) = \lambda - dx$ and $g(x) = \beta x$, we obtain the following model:

$$\begin{cases}
\left.\begin{array}{l} \frac{dx}{dt} = \lambda - dx - \beta xv, \\ \frac{dv}{dt} = \beta xv - av, \end{array}\right\} & x > h, \\
\left.\begin{array}{l} \Delta x(t) = \tau - px(t), \\ \Delta v(t) = -qv(t), \end{array}\right\} & x = h,
\end{cases} \tag{4.1}$$

where d is the natural death rate of uninfected cells; β represents the rate at which an uninfected cell contacted by virus. It is not difficult to compute that $n = \frac{\lambda}{d}$, $m = \frac{a}{\beta}$. If $\lambda\beta > ad$, then $m < n$ and the system possesses one positive equilibrium $E_1 = (x^*, v^*) = (\frac{a}{\beta}, \frac{\lambda\beta - ad}{a\beta})$, which is asymptotically stable. The region

$$\Omega = \left\{(x,v) \middle| x > 0, v > 0, x + v \leq \frac{\lambda}{a} + \frac{\lambda}{d}\right\}$$

is positive invariant. Further, the characteristic points are

$$P_0(\bar{h}, v_0), \qquad W_0(h, \omega_0), \qquad T_h(h, t_h), \qquad T_{\bar{h}}(\bar{h}, t_{\bar{h}})$$

with

$$\nu_0 = \frac{\lambda - d\bar{h}}{\beta\bar{h}}, \qquad \omega_0 = \frac{\lambda - dh}{\beta h}, \qquad t_h = \frac{\lambda}{a} + \frac{\lambda}{d} - h, \qquad t_{\bar{h}} = \frac{\lambda}{a} + \frac{\lambda}{d} - \bar{h}.$$

Assume that $\lambda\beta > ad$. According to Theorems 3.1–3.3 and Corollary 3.1, we have the following results.

Proposition 4.1 *If $\frac{a}{\beta} < h$, then there must exist an order-1 periodic solution for (4.1). Additionally, if $1 - q < \frac{t_{\bar{h}}}{t_h}$, then the order-1 periodic solution lies below the line $x + \nu \leq \frac{\lambda}{a} + \frac{\lambda}{d}$.*

Proposition 4.2 *Suppose $h < \frac{a}{\beta} < \bar{h}$ holds. We have*

(i) *if $\frac{\lambda - dh}{\beta h} > \frac{\lambda}{a} + \frac{\lambda}{d} - h$, then there is no order-1 periodic solution lies below the line $x + \nu \leq \frac{\lambda}{a} + \frac{\lambda}{d}$;*

(ii) *if $O_N^+(P_0) \neq \emptyset$ and $1 - q < \frac{\frac{\lambda}{a} + \frac{\lambda}{d} - \bar{h}}{\frac{\lambda}{a} + \frac{\lambda}{d} - h}$, then there must exist an order-1 periodic solution below the line $x + \nu \leq \frac{\lambda}{a} + \frac{\lambda}{d}$ for (4.1).*

Moreover, $g(x) = \beta x$ shows that $g'(x) \geq \frac{g(x)}{x}$. Suppose $(X(t), V(t))$ is an order-1 periodic solution of system (4.1). According to Theorem 3.4, we have the following.

Proposition 4.3 *If*

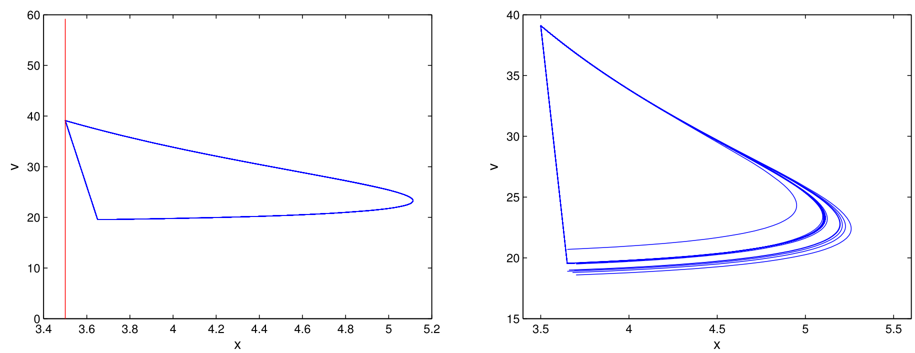
$$\left| \frac{\lambda - d\bar{h} - (1 - q)V(T)]}{\lambda - dh - V(T)} \right| < 1, \tag{4.2}$$

then the order-1 periodic solution of system (4.1) is orbitally asymptotically stable, where $V(T)$ is the load of virus when $X(T) = h$.

To verify the conditions of Propositions 4.1–4.3, we choose global parameters $p = 0.1$, $\tau = 0.5$ and $h = 3.5$, which implies $\bar{h} = 3.65$.

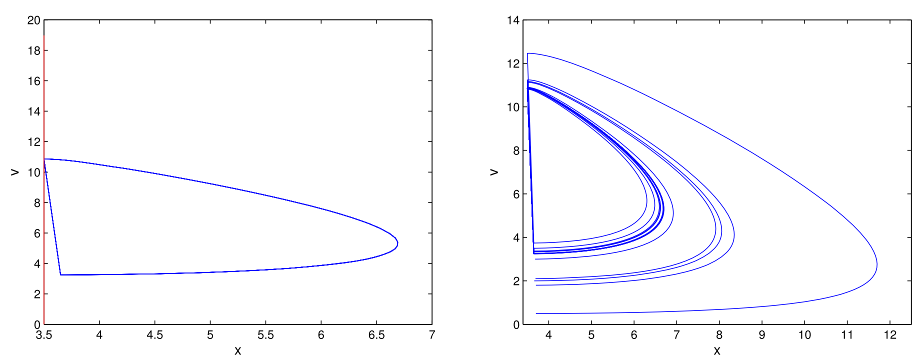
When $\lambda = 8$, $a = 0.1$, $d = 0.4$, $\beta = 0.05$, $q = 0.5$, we have $x^* = 2 < 3.5 = h$. It is easy to computer the characteristic value $\nu_0 = 35.8356$, $\omega_0 = 37.7143$, $t_h = 56.5$ and $t_{\bar{h}} = 56.35$. Obviously, $1 - q = 0.5 < \frac{t_{\bar{h}}}{t_h} = 0.9973$. Numerical simulation gives $\tilde{\nu}_0 = 38.9002$ and the periodic solution initiated from $(3.65, 19.5478)$ such that $V(T) = 39.0939$. Substituting $V(T) = 39.0939$ into (4.2), it is verified that $|\mu| = 0.4003 < 1$. Thus the conditions of Proposition 4.1 and Proposition 4.3 hold. Figures 9(a) and 9(b) illustrate the existence and stability of order-1 periodic solution for (4.1), respectively.

Let $\lambda = 0.6$, $a = 0.053$, $d = 0.01$, $\beta = 0.015$, $q = 0.7$. Then $x^* = 3.533 > 3.5$, $\nu_0 = 10.2922$, $\omega_0 = 10.7619$, $t_h = 67.8208$, $t_{\bar{h}} = 67.6708$. Obviously $1 - q = 0.3 < \frac{t_{\bar{h}}}{t_h} = 0.9978$. Numerical simulation shows that $O_N^+(P_0) \neq \emptyset$ and there is an order-1 periodic solution which initiates from $(3.65, 3.2535)$ and $V(T) = 10.8476$. Similarly, substituting $V(T) = 10.8476$ into (4.2), it is verified that $|\mu| = 0.0085 < 1$. Thus the second condition in Proposition 4.2 and the conditions in Proposition 4.3 hold. The numerical simulations are presented by Figs. 10(a) and 10(b).



(a) The existence of order-1 periodic solution (b) The stability of order-1 periodic solution

Figure 9 $\lambda = 8$, $d = 0.4$, $\beta = 0.05$, $a = 0.1$, $q = 0.5$ and $x^* < h$



(a) The existence of order-1 periodic solution (b) The stability of order-1 periodic solution

Figure 10 $\lambda = 0.6$, $d = 0.01$, $\beta = 0.015$, $a = 0.053$, $q = 0.7$ and $h < x^* < \bar{h}$

5 Conclusion and discussion

Theoretically, we are aiming to establish some criteria for the existence of order-1 periodic solution based on the Bendixson domain types. Lemmas 2.5 and 2.6 can be extended to other models.

From the biological point of view, we are aiming to control the system when E_1 is asymptotically stable since the natural state may lead to a disaster. We hope that the impulsive treatment can improve the natural state.

In the case $x^* < h$, by Theorem 3.1, the impulsive treatment can prevent the deterioration since there always exists an order-1 periodic solution between M and N. Further, when $1 - q < \frac{v_0}{\bar{v}_0}$, the periodic solution lies in a sub-parallel domain. The periodic solution lies in a parallel domain while $1 - q > \frac{v_0}{\bar{v}_0}$. Obviously, the former is superior to the latter because of the lower load of v and higher load of x. As is shown in Corollary 3.1, if $1 - q < \frac{t_{\bar{h}}}{t_h}$, the periodic solution will lie under the line $x + v = \frac{f(0)}{a} + n$. Therefore, we hold that $1 - q$ is the smaller the better.

In the case $h < x^* < \bar{h}$, if $\omega_0 > t_h$ and the initiate value of v is small enough, then there is no need to control the system in the sense that any trajectory cannot cross the line $x = h$ or the natural state is superior to the critical state; if $\omega_0 < t_h$ and $O_M^+(P_0) \neq \emptyset$, then it is necessary to take the measure and let $1 - q < \frac{t_{\bar{h}}}{t_h}$, so that there exist an order-1 periodic solution that lies in Ω; if $\omega_0 < t_h$ and $O_M^+(P_0) = \emptyset$, as long as the impulsive point in N is close enough to P_0, the impulsive control can prevent the trajectories from crossing the line $x = h$. This also contributes to the fulfillment of the condition (3.8).

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Competing interests
The authors declare that they have no competing interests.

Authors' contributions
All authors contributed equally to the writing of this article. All authors read and approved the final manuscript.

Author details
[1]School of Mathematics and Physics, University of South China, Hengyang, P.R. China. [2]School of Mathematics and Statistics, Central South University, Changsha, P.R. China.

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