Research Article

SVEIRS: A New Epidemic Disease Model with Time Delays and Impulsive Effects

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We first propose a new epidemic disease model governed by system of impulsive delay differential equations. Then, based on theories for impulsive delay differential equations, we skillfully solve the difficulty in analyzing the global dynamical behavior of the model with pulse vaccination and impulsive population input effects at two different periodic moments. We prove the existence and global attractivity of the "infection-free" periodic solution and also the permanence of the model. We then carry out numerical simulations to illustrate our theoretical results, showing us that time delay, pulse vaccination, and pulse population input can exert a significant influence on the dynamics of the system which confirms the availability of pulse vaccination strategy for the practical epidemic prevention. Moreover, it is worth pointing out that we obtained an epidemic control strategy for controlling the number of population input.

1. Introduction

In epidemic modeling, susceptible-infectious-recovered type of models is well known [1-18] although such models very often ignore the incubation period in the development of mathematical models for some diseases. However, recent research shows for certain diseases, such as smallpox, rabies, BSE, and some skin diseases, the incubation period has significant effect on the epidemic dynamics so that it is nonnegligible. The incubation period varies greatly from a couple of days (e.g., H1N1 outbreaking worldwide has generally an incubation period of one to seven days) to several years (e.g., AIDS virus sometimes can be several years). When taking the incubation period into account in the development of models, we reach SEIR model, which is short for susceptible, exposed, infectious, and recovered [19-30]. And some researchers used time delay to describe the incubation period; for example, Cooke [31], Beretta and Takeuchi [4], Takeuchi et al. [32], and Ma et al. [5] studied a SIR model with time delay and nonlinear incidence rate $\beta S(t)I(t - \tau)$. Liu et al. [33, 34] used a nonlinear incidence rate $\beta S^{p}(t)I^{q}(t)$, and Meng et al. [35] and Jiang et al. [30],

respectively, studied an impulsively vaccinating SIR model with nonlinear incidences $\beta S^q(t)I(t-\tau)$ and $\beta S^q(t-\tau)I(t-\tau)$, which are better to describe the spread process of diseases than linear one.

In order to prevent infectious diseases, [36, 37] suggested that vaccination to the susceptible population is an important strategy. The traditional vaccinations are applied to each individual, while impulsive ones are to periodically vaccinate people within certain age groups [7-10, 38]. Some diseases may have a vaccination period after being cured but may cause losing immunity gradually. In this case, people might be infected again. So it is of great significance to investigate epidemic models with time delay and impulsive effects due to the incubation period and vaccination period [26-29]. For some certain regional systems, the immigrations can be periodic impulsive population input because the immigratory population might be susceptible. Certainly two different impulsive effects for periodic vaccination and population input do not usually happen simultaneously. Therefore, motivated by Jiang et al. [30] and Song et al. [19], we built a new mathematical model: susceptible, vaccinated, exposed, infectious, recovered, and susceptible epidemic model with two time delays and two nonlinear incidences with pulse vaccination and a constant periodic population input at two different moments as follows:

$$\begin{aligned} \frac{dS(t)}{dt} &= -bS(t) - \beta S^{p}(t) I(t) + \gamma I(t-\omega) e^{-b\omega}, \\ \frac{dV(t)}{dt} &= -\delta \beta V^{q}(t) I(t) - \gamma_{1} V(t) - bV(t), \\ \frac{dE(t)}{dt} &= -bE + \beta S^{p}(t) I(t) + \delta \beta V^{q}(t) I(t) \\ &- \beta e^{-b\tau} S^{p}(t) I(t-\tau) - \delta \beta e^{-b\tau} V^{q}(t) I(t-\tau), \\ \frac{dI(t)}{dt} &= \beta e^{-b\tau} S^{p}(t) I(t-\tau) + \delta \beta e^{-b\tau} V^{q}(t) I(t-\tau) \\ &- (\gamma + b + \alpha) I(t), \\ \frac{dR(t)}{dt} &= \gamma_{1} V(t) + \gamma I(t) - bR(t) - \gamma I(t-\omega) e^{-b\omega}, \\ &t \neq (n+l-1) T, \quad t \neq nT, \\ \Delta S(t) &= -\theta S(t), \quad \Delta V(t) = \theta S(t), \quad \Delta E(t) = 0, \\ &\Delta I(t) = 0, \quad \Delta R(t) = 0, \\ &\Delta I(t) = 0, \quad \Delta R(t) = 0, \\ &\Delta I(t) = 0, \quad \Delta R(t) = 0, \\ &LI(t) = 0, \quad \Delta R(t) = 0, \\ &t = nT. \end{aligned}$$

Here all parameters of system (1) are nonnegative constants. For the significance of parameters in (1), please see literatures Jiang et al. [30] and Song et al. [19]. Terms $\beta S^P I$ and $V^q I$ are the nonlinear incidence rates, and in our paper we only discuss the case

$$1 \le q \le p. \tag{2}$$

2. Preliminaries

Let N(t) = S(t) + V(t) + E(t) + I(t) + R(t), and then it is easy to see that N(t) satisfies the following:

$$N'(t) \le b(1 - N(t)), \qquad \lim_{t \to \infty} \sup N(t) \le 1.$$
(3)

Hence, for time *t* which is large, we obtain $0 \le S(t) + V(t) + I(t) \le 1$. Let $\omega = \max\{\tau, \omega\}$ and $C^+ = \{\varphi = (\varphi_1(s), \dots, \varphi_5(s)) \in C : \varphi_i(0) > 0\}$; here $\varphi_i(s) > 0$ is bounded function on interval $[-\omega, 0]$. Since variable R(t) only appears in the fifth equation, system (1) can be further reduced as

$$\frac{dS(t)}{dt} = -bS(t) - \beta S^{p}(t) I(t) + \gamma I(t-\omega) e^{-b\omega},$$
$$\frac{dV(t)}{dt} = -\delta \beta V^{q}(t) I(t) - \gamma_{1} V(t) - bV(t),$$

$$\frac{dI(t)}{dt} = \beta e^{-b\tau} S^{p}(t) I(t-\tau) + \delta \beta e^{-b\tau} V^{q}(t) I(t-\tau)$$

$$- (\gamma + b + \alpha) I(t),$$

$$t \neq (n+l-1) T, \quad t \neq nT,$$

$$\Delta S(t) = -\theta S(t), \quad \Delta V(t) = \theta S(t), \quad \Delta I(t) = 0,$$

$$t = (n+l-1) T,$$

$$\Delta S(t) = \mu, \quad \Delta V(t) = 0, \quad \Delta I(t) = 0,$$

$$t = nT,$$
(4)

with the initial conditions

$$(\varphi_1(s), \varphi_2(s), \varphi_4(s)) \in C^+, \quad \varphi_i(0) > 0, \ i = 1, 2, 4.$$
 (5)

Lemma 1 (see [39, 40]). For the following impulse differential inequalities

$$s'(t) \leq (\geq) q(t) s(t) + r(t), \quad t \neq t_k,$$

$$s(t_k^+) \leq (\geq) b_k s(t_k) + p_k, \quad t = t_k, \ k \in N,$$
(6)

where q(t), $r(t) \in C(R_+, R)$, $b_k \ge 0$, and p_k are constants. Assume the following:

- (A₀) the sequence { t_k } satisfies $0 \le t_0 < t_1 < t_2 < \cdots$, with $\lim_{t \to \infty} t_k = \infty$;
- $(A_1) w \in PC'(R_+, R)$ and s(t) is left-continuous at $t_k, k \in N$.

Then

$$s(t) \leq (\geq) s(t_0) \prod_{t_0 < t_k < t} b_k \exp\left(\int_{t_0}^t q(u) \, du\right) + \sum_{t_0 < t_k < t} \left(\prod_{t_k < t_j < t} b_j \exp\left(\int_{t_k}^t q(u) \, du\right)\right) p_k$$
(7)
+
$$\int_{t_0}^t \prod_{u < t_k < t} b_k \exp\left(\int_{u}^t q(\theta) \, d\theta\right) r(u) \, du,$$
$$t > t_0.$$

Lemma 2 (see [41]). For the following delay differential equation

$$\frac{dz(t)}{dt} = az(t-\theta) - bz(t), \qquad (8)$$

where *a*, *b*, and θ are all positive constants and z(t) > 0 for $t \in [-\theta, 0]$, then we have

$$\lim_{t \to \infty} z(t) = \begin{cases} 0, & \text{if } a < b; \\ +\infty, & \text{if } a > b. \end{cases}$$
(9)

Lemma 3 (see [42]). The following system,

$$\frac{dx(t)}{dt} = -bx(t), \qquad \frac{dy(t)}{dt} = -(a+b)y(t),$$
$$t \neq nT, \quad t \neq (n+l-1)T,$$
$$\Delta x(t) = -\theta x(t), \quad \Delta y(t) = \theta x(t), \quad t = (n+l-1)T,$$
$$\Delta x(t) = \mu, \quad \Delta y(t) = 0, \quad t = nT,$$
(10)

has a unique positive *T*-periodic solution:

$$x^{*}(t) = \begin{cases} \frac{\mu \exp\left(-b\left(t-(n-1)T\right)\right)}{1-(1-\theta)\exp\left(-bT\right)}, \\ t \in ((n-1)T, (n+l-1)T], \\ \frac{\mu(1-\theta)\exp\left(-b\left(t-(n-1)T\right)\right)}{1-(1-\theta)\exp\left(-bT\right)}, \\ t \in ((n+l-1)T, \le nT], \end{cases}$$
$$y^{*}(t) = \frac{\mu\theta\exp\left(-blT\right)\exp\left(-(a+b)\left(t-(n+l-1)T\right)\right)}{\left(1-\exp\left(-(a+b)T\right)\right)\left(1-(1-\theta)\exp\left(-bT\right)\right)}, \\ t \in ((n+l-1)T, (n+l)T], \end{cases}$$
(11)

and we further have $x(t) \rightarrow x^*(t)$ and $y(t) \rightarrow y^*(t)$ as $t \rightarrow +\infty$.

3. The Existence and Global Attractivity of "Infection-Free" Periodic Solution

3.1. Existence. In this section, we are committed to investigate the existence of "infection-free" periodic solution. In this case, we have

$$I(t) = 0, \quad t \ge 0.$$
 (12)

From systems (4) and (12), we obtain

$$\frac{dS(t)}{dt} = -bS(t), \qquad \frac{dV(t)}{dt} = -(\gamma_1 + b)V(t),$$
$$t \neq (n+l-1)T, \quad t \neq nT, \quad n \in N,$$
$$\Delta S(t) = -\theta S(t), \qquad \Delta V(t) = \theta S(t),$$

$$t = (n+l-1)T, \quad n \in N,$$

$$\Delta S(t) = \mu, \quad \Delta V(t) = 0, \quad t = nT, \ n \in N.$$
(13)

By Lemma 3, system (13) has a unique positive *T*-periodic solution:

$$S^{*}(t) = \begin{cases} \frac{\mu \exp\left(-b\left(t-(n-1)T\right)\right)}{1-(1-\theta)\exp\left(-bT\right)}, \\ t \in ((n-1)T, (n+l-1)T], \\ \frac{\mu(1-\theta)\exp\left(-b\left(t-(n-1)T\right)\right)}{1-(1-\theta)\exp\left(-bT\right)}, \\ t \in ((n+l-1)T, \le nT], \end{cases}$$
$$V^{*}(t) = \frac{\mu\theta\exp\left(-blT\right)\exp\left(-(a+b)\left(t-(n+l-1)T\right)\right)}{(1-\exp\left(-(a+b)T\right)\left(1-(1-\theta)\exp\left(-bT\right)\right)}, \\ t \in ((n+l-1)T, (n+l)T]. \end{cases}$$
(14)

Furthermore, we can prove that it is the unique globally asymptotically stable positive periodic solution of system (4). We summarize this conclusion in the following lemma.

Lemma 4. The system (4) has an "infection-free" periodic solution $(S^*(t), V^*(t), 0)$, for $t \in ((n + l - 1)T, (n + l)T]$ and $n \in N$; for any solution (S(t), V(t), I(t)) of it, the following holds true:

$$S(t) \longrightarrow S^{*}(t), \qquad V(t) \longrightarrow V^{*}(t)$$
 (15)

as $t \to \infty$.

This lemma indicates that in between the vaccination the susceptible and vaccinated populations oscillate with period T in synchronization with the periodic pulse vaccination. Next we prove the global attractivity of such solution.

3.2. Global Attractivity. In this section, we will prove our main result on the global attractivity of the infection-free solution. It is stated in the following theorem.

Theorem 5. The system (4) has a unique infection-free periodic solution ($S^*(t), V^*(t), 0$), and when it exists, it is globally attractive if

$$\mathcal{R}_1 < 1,$$
 (16)

where

with

$$\mathscr{R}_{1} = \beta e^{-b\tau} \frac{\left(A_{1}^{p} + \delta A_{2}^{q}\right)}{\gamma + b + \alpha},\tag{17}$$

 $A_{1} = \frac{\gamma e^{-b\omega}}{b} + \frac{\mu e^{bT}}{e^{bT} - 1},$ $A_{2} = \frac{\theta e^{-blT}}{(1 - \theta) \left(1 - (1 - \theta) e^{-bT}\right) \left(1 - e^{-(\gamma_{1} + b)T}\right)}.$ (18)

Proof. Let (S(t), V(t), I(t)) be a solution of (4) satisfied initial condition (5). Since $\mathcal{R}_1 < 1$, one can choose an $\varepsilon > 0$ small enough such that

$$\beta e^{-b\tau} \left(\left(\Delta_1 \right)^p + \delta \left(\Delta_2 \right)^q \right) - \left(\gamma + b + \alpha \right) < 0, \tag{19}$$

where

$$\Delta_{1} = \frac{\gamma e^{-b\omega}}{b} + \frac{\mu e^{bT}}{e^{bT} - 1} + \varepsilon,$$

$$\Delta_{2} = \frac{\theta e^{-blT}}{(1 - \theta) \left(1 - (1 - \theta) e^{-bT}\right) \left(1 - e^{-(\gamma_{1} + b)T}\right)} + \varepsilon.$$
(20)

For $n > n_1$, we have

$$\frac{dS(t)}{dt} \le b - bS(t) + \gamma e^{-b\omega},$$

$$t \ne (n+l-1)T, \quad t \ne nT, \quad n \in N,$$

$$\Delta S(t) = -\theta S(t), \quad t = (n+l-1)T, \quad n \in N,$$

$$\Delta S(t) = \mu, \quad t = nT, \quad n \in N.$$
(21)

By impulsive differential inequality Lemma 1, we have

$$S(t) \leq S(n_{1}T^{+}) \prod_{n_{1}T^{+} < nT < t} \exp\left(\int_{n_{1}T}^{t} (-b) \, ds\right)$$

+
$$\sum_{n_{1}T < nT < t} \left(\prod_{nT < t_{j} < t} \exp\left(\int_{nT}^{t} (-b) \, ds\right)\right) \mu$$

+
$$\int_{n_{1}T}^{t} \prod_{s < nT < t} \exp\left(\int_{s}^{t} (-b) \, d\theta\right) \gamma e^{-b\omega} ds$$

=
$$S_{1} + S_{2} + S_{3},$$
 (22)

where

$$S_{1} = S(n_{1}T^{+}) \prod_{n_{1}T^{+} < nT < t} \exp\left(\int_{n_{1}}^{t/T} (-b) dT\xi\right)$$
$$= S(n_{1}T^{+}) e^{-b(t-n_{1}T)},$$
$$S_{2} = \sum_{n_{1}T < nT < t} \left(\prod_{nT < t_{j} < t} \exp\left(\int_{nT}^{t} (-b) ds\right)\right) \mu$$
$$= \sum_{n_{1}T < nT < t} \left(\mu e^{-b(t-nT)}\right)$$

$$= \mu \frac{e^{-b(t-n_1)T} - e^{-b(t-(n+n_1))T}}{1 - e^{bT}},$$

$$S_3 = \int_{n_1T}^t \prod_{s < nT < t} \exp\left(\int_s^t (-b) \, d\theta\right) \gamma e^{-b\omega} ds$$

$$= \gamma e^{-b\omega} \int_{n_1T}^t \prod_{s < nT < t} \exp\left(\int_s^t (-b) \, d\theta\right) ds$$

$$= \frac{\gamma e^{-b\omega} e^{-bt}}{b} \int_{n_1T}^t \prod_{s < nT < t} e^{bs} d \, (bs)$$

$$= \frac{\gamma e^{-b\omega} e^{-bt}}{b} \left(e^{bt} - e^{bn_1T}\right).$$
(23)

Thus

$$\begin{split} S(t) &\leq S_{1} + S_{2} + S_{3} \\ &= S\left(n_{1}T^{+}\right)e^{-b(t-n_{1}T)} \\ &+ \mu \frac{e^{-b(t-n_{1})T} - e^{-b(t-(n+n_{1}))T}}{1 - e^{bT}} \\ &+ \frac{\gamma e^{-b\omega}e^{-bt}}{b}\left(e^{bt} - e^{bn_{1}T}\right) \\ &\leq e^{-bt}S\left(n_{1}T^{+}\right)e^{n_{1}bT} + \frac{\mu e^{-b(t-n_{1}T)}}{1 - e^{bT}} \\ &+ \frac{\gamma e^{-b\omega}}{b}e^{-b(t-n_{1}T)} + \frac{\gamma e^{-b\omega}}{b} + \frac{\mu e^{bT}}{e^{bT} - 1}, \end{split}$$
(24)

and then we have

$$\lim_{t \to \infty} \sup S(t) < \frac{\gamma e^{-b\omega}}{b} + \frac{\mu e^{bT}}{e^{bT} - 1}.$$
(25)

Thus there exists a positive integer $n_2 > n_1$ and constant $\varepsilon > 0$ small enough such that, for all $t > n_2 T$,

$$S(t) \le \frac{\gamma e^{-b\omega}}{b} + \frac{\mu e^{bT}}{e^{bT} - 1} + \varepsilon = \Delta_1.$$
(26)

For $n > n_1$, system (4) yields

$$\frac{dV(t)}{dt} \le -(\gamma_1 + b)V(t), \quad t \ne (n+l-1)T, \ n \in N,$$

$$\Delta V(t) = \theta S(t), \quad t = (n+l-1)T, \ n \in N.$$
(27)

We obtain the following comparison impulsive differential system:

$$\frac{dx(t)}{dt} = -(\gamma_1 + b)x(t), \quad t \neq (n+l-1)T, \ n \in N,$$
$$\Delta x(t) = \theta S(t), \quad t = (n+l-1)T, \ n \in N.$$
(28)

By Lemma 3, the system has a periodic solution given by

$$x^{*}(t) = \frac{\theta e^{-blT} e^{-(\gamma_{1}+b)(t-(n+l-1)T)}}{(1-\theta)(1-(1-\theta)e^{-bT})(1-e^{-(\gamma_{1}+b)T})},$$
$$t \in ((n+l-1)T, (n+l)T], \quad (29)$$

$$x(0^{+}) = \frac{\theta e^{-\theta T}}{(1-\theta)(1-(1-\theta)e^{-bT})(1-e^{-(\gamma_{1}+b)T})},$$

which is globally asymptotically stable.

Now, assume that x(t) is the solution of system (28) with initial value $x(0^+) = V_0$. Then by Lemma 1, we know there exists a positive integer *n* such that

$$V(t) < x(t) < x^{*}(t) + \varepsilon, \quad t \in (nT, (n+1)T].$$
 (30)

Hence,

$$V(t) < x(t) < x^{*}(t) + \varepsilon$$

$$< \frac{\theta e^{-blT}}{(1-\theta) \left(1 - (1-\theta) e^{-bT}\right) \left(1 - e^{-(\gamma_{1}+b)T}\right)} + \varepsilon_{0} \quad (31)$$

$$= \Delta_{2}.$$

From (27), (31), and the third equation in (4), for $t > n_2T + \tau$ we have

$$\frac{dI(t)}{dt} \leq \beta e^{-b\tau} \left(\Delta_1^p + \delta \Delta_2^q \right) I(t-\tau) - \left(\gamma + b + \alpha \right) I(t) \,.$$
(32)

Consider the comparison equation:

$$\frac{dy(t)}{dt} \le \beta e^{-b\tau} \left(\Delta_1^p + \delta \Delta_2^q\right) y(t-\tau) - \left(\gamma + b + \alpha\right) y(t).$$
(33)

From (19), we have

$$\beta e^{-b\tau} \left(\Delta_1^p + \delta \Delta_2^q \right) - \left(\gamma + b + \alpha \right) < 0. \tag{34}$$

According to Lemma 2, we then obtain

$$\lim_{t \to \infty} y(t) = 0.$$
(35)

Notice the fact that $I(s) = y(s) = \phi_3(s) > 0$ for all $s \in [-\tau, 0]$ and $I(t) \ge 0$, and the comparison theorem implies $I(t) \to 0$ as $t \to \infty$. Without loss of generality, we may assume that $0 < I(t) < \varepsilon_1$ for all $t \ge 0$. By using the first and second equations in (4), we reach

$$\begin{split} \frac{dS\left(t\right)}{dt} &\geq -bS\left(t\right) - \beta\varepsilon_{1}S^{p}\left(t\right),\\ \frac{dV\left(t\right)}{dt} &\geq -\delta\beta\varepsilon_{1}V^{q}\left(t\right) - \gamma_{1}V\left(t\right) - bV\left(t\right),\\ t &\neq \left(n+l-1\right)T, \quad t \neq nT, \quad n \in N, \end{split}$$

$$\Delta S(t) = -\theta S(t), \qquad \Delta V(t) = \theta S(t),$$

$$t = (n+l-1)T, \quad n \in N,$$

$$\Delta S(t) = \mu, \quad \Delta V(t) = 0, \quad t = nT, \quad n \in N.$$
(36)

For 1 < q < p, we have

$$\frac{dS(t)}{dt} \ge -bS(t) - \beta\varepsilon_1 S(t),$$

$$\frac{dV(t)}{dt} \ge -\delta\beta\varepsilon_1 V(t) - \gamma_1 V(t) - bV(t),$$

$$t \ne (n+l-1)T, \quad t \ne nT, \quad n \in N,$$

$$\Delta S(t) = -\theta S(t), \quad \Delta V(t) = \theta S(t),$$

$$t = (n+l-1)T, \quad n \in N,$$

$$\Delta S(t) = \mu, \quad \Delta V(t) = 0, \quad t = nT, \quad n \in N$$

considering the following system:

$$\frac{df(t)(t)}{dt} = -bf(t) - \beta\varepsilon_1 f(t),$$

$$\frac{dg(t)}{dt} = -\delta\beta\varepsilon_1 g(t) - \gamma_1 g(t) - bg(t),$$

$$t \neq (n+l-1)T, \quad t \neq nT, \quad n \in N,$$

$$\Delta f(t) = -\theta f(t), \quad \Delta g(t) = \theta f(t),$$

$$t = (n+l-1)T, \quad n \in N,$$

$$\Delta f(t) = \mu, \quad \Delta g(t) = 0, \quad t = nT, \quad n \in N.$$
(38)

We obtain

$$\widetilde{f}(t) = \begin{cases} \frac{(b+\beta\varepsilon_1)\mu}{(b+\beta\varepsilon_1)(1-(1-\theta)e^{-(b+\beta\varepsilon_1)T})} \\ \times e^{-(b+\beta\varepsilon_1)(t-(n-1)T)}, \\ t \in ((n-1)T, (n+l-1)T], \\ \frac{(b+\beta\varepsilon_1)\mu(1-\theta)e^{-(b+\beta\varepsilon_1)lT}}{(b+\beta\varepsilon_1)(1-(1-\theta)e^{-(b+\beta\varepsilon_1)T})} \\ \times e^{-(b+\beta\varepsilon_1)(t-(n+l-1)T)}, \\ t \in ((n+l-1)T, nT], \end{cases}$$

$$\widetilde{g}(t) = \left(\left(\theta \left(b + \beta \varepsilon_1 \right) \mu e^{-(b+\beta \varepsilon_1)lT} - \beta \varepsilon_1 \theta \left(1 - e^{-(b+\beta \varepsilon_1)T} \right) \right) \\ \times e^{-(\gamma_1 + b + \delta \beta \varepsilon_1)(t - (n+l-1)T)} \right) \\ \times \left(\left(b + \beta \varepsilon_1 \right) \left(1 - (1-\theta) e^{-(b+\beta \varepsilon_1)T} \right) \\ \times \left(1 - e^{-(\gamma_1 + b)T} \right) \right)^{-1}, \\ t \in \left((n+l-1)T, (n+l)T \right].$$
(39)

Now by using comparison theorem of impulsive equations, for any $\varepsilon_2 > 0$ there exists a $T_1 > 0$ such that

$$S(t) > \tilde{f}(t) - \varepsilon_2,$$

$$V(t) > \tilde{g}(t) - \varepsilon_2,$$
(40)

for $t > T_1$. On the other side, from the first and second equations of (4), we have

$$\frac{dS(t)}{dt} \le -bS(t) + \gamma \varepsilon_1 e^{-b\omega},$$

$$\frac{dV(t)}{dt} \le -\gamma_1 V(t) - bV(t),$$

$$t \ne (n+l-1)T, \quad t \ne nT, \quad n \in N,$$

$$\Delta S(t) = -\theta S(t), \quad \Delta V(t) = \theta S(t),$$

$$t = (n+l-1)T, \quad n \in N,$$

$$\Delta S(t) = b, \quad \Delta V(t) = 0, \quad t = nT, \quad n \in N.$$

(41)

Then we have $S(t) \leq \tilde{h}(t)$, $V(t) \leq \tilde{g}(t)$ and $\tilde{h}(t) \rightarrow S^*(t)$, $\tilde{g}(t) \rightarrow V^*(t)$, as $\varepsilon_1 \rightarrow 0$, where $(\tilde{h}(t), \tilde{g}(t))$ is a unique positive periodic solution of

$$\frac{dh(t)}{dt} = -bh(t) + \gamma \varepsilon_1 e^{-b\omega},$$

$$\frac{dg(t)}{dt} = -\gamma_1 g(t) - bg(t),$$

$$t \neq (n+l-1)T, \quad t \neq nT, \quad n \in N,$$

$$\Delta h(t) = -\theta h(t), \quad \Delta g(t) = \theta h(t),$$

$$t = (n+l-1)T, \quad n \in N,$$

$$\Delta h(t) = \mu, \quad \Delta g(t) = 0, \quad t = nT, \quad n \in N,$$

(42)

from which we have that, for $nT < t \le (n+1)T$,

$$\widetilde{h}(t) = \begin{cases} \frac{\gamma \varepsilon_{1} e^{-b\omega} \theta e^{-b(1-l)T} + b\mu}{b(1 - (1 - \theta) e^{-bT})} \\ \times e^{-b(t - (n-1)T)} - \frac{\gamma \varepsilon_{1} e^{-b\omega}}{b}, \\ (n-1)T < t \le (n+l-1)T, \\ \frac{b\mu(1-\theta) e^{-blT} + \gamma \varepsilon_{1} e^{-b\omega} \theta}{b(1 - (1 - \theta) e^{-bT})} \\ \times e^{-b(t - (n+l-1)T)} - \frac{\gamma \varepsilon_{1} e^{-b\omega}}{b}, \\ (n+l-1)T < t \le nT, \end{cases}$$

$$\widetilde{g}(t) = \frac{\left(\theta b \mu e^{-blT} - \gamma \varepsilon_1 e^{-b\omega} \theta \left(1 - e^{-bT}\right)\right) e^{-(\gamma_1 + b)(t - (n+l-1)T)}}{b \left(1 - (1 - \theta) e^{-bT}\right) \left(1 - e^{-(\gamma_1 + b)T}\right)},$$

$$(n+l-1) T < t \le (n+l) T.$$
(43)

Applying the comparison theorem again, for any $\varepsilon_2>0,$ there exists a $T_2>0$ such that

$$S(t) < \tilde{h}(t) - \varepsilon_2,$$

$$V(t) < \tilde{g}(t) - \varepsilon_2,$$
(44)

for $t > T_2$. Let $\varepsilon_1 \rightarrow 0$, and then from (40) and (44) we have

$$S^{*}(t) - \varepsilon_{2} < S(t) < S^{*}(t) - \varepsilon_{2},$$

$$V^{*}(t) - \varepsilon_{2} < V(t) < V^{*}(t) - \varepsilon_{2},$$
(45)

for t large enough, which implies $S(t) \rightarrow S^*(t), V(t) \rightarrow V^*(t)$ as $t \rightarrow \infty$. This completes the proof.

Corollary 6. If $\tau > \tau^*$ or $\mu < \mu^*$, then the infection-free periodic solution ($S^*(t), V^*(t), 0$) is globally attractive, where the critical values are given below:

$$\tau^{*} = \frac{1}{b} \ln \frac{\beta \left(A_{1}^{p} + \delta A_{2}^{q}\right)}{\gamma + b + \alpha},$$

$$\mu^{*} = \left(1 - e^{-bT}\right)$$

$$\times \left(\sqrt[p]{\frac{\gamma + b + \alpha}{\beta}} e^{b\tau} - \delta A_{2}^{q} - \frac{\gamma e^{-b\omega}}{b} - \frac{\mu e^{bT}}{e^{bT} - 1}\right).$$
(46)

4. Permanence

In this section, we discuss the permanence of the infectious population. First, we introduce the following definition.

Definition 7. System (4) is said to be permanent if there exist positive constants m_i , M_i , i = 1, 2, 3 (independent of initial value), and a finite time T_0 , which may depend on the initial condition, such that every positive solution (S(t), V(t), I(t)) with initial condition (5) satisfies $m_1 \leq S(t) \leq M_1$, $m_2 \leq I(t) \leq M_2$, $m_3 \leq V(t) \leq M_3$ for all $t > T_0$.

Let

$$S^{*} = \sqrt[\gamma]{\frac{\gamma + b + \alpha}{\beta e^{-b\tau}}},$$

$$V^{*} = \sqrt[\eta]{\frac{\gamma_{1} + b}{\delta\beta e^{-b\tau}}},$$

$$m^{*} = \frac{(1/T) \ln \left(\left(\Re_{1} \left(e^{bT} - 1 + \theta \right) + 1 - \theta + e^{bT} \right) / 2 \right) - b}{\beta},$$

$$\Re_{1} = \sqrt[\gamma]{\frac{\beta e^{-b\tau}}{\gamma + b + \alpha}} \left(\frac{\mu (1 - \theta) e^{-bT}}{1 - (1 - \theta) e^{-bT}} \right),$$

$$\Re_{2} = \sqrt[\eta]{\frac{\beta e^{-b\tau}}{\gamma_{1} + b}} \frac{\mu \theta e^{-(\gamma_{1} + b + bl)T}}{(1 - e^{-(\gamma_{1} + b)T})(1 - (1 - \theta) e^{-bT})},$$

$$\Re_{2} = \min \{\Re_{1}, \Re_{2}\}.$$
(47)

$$\begin{split} &-\delta\beta e^{-b\tau} (V^{*})^{q} I(t-\tau) \\ &= \beta e^{-b\tau} \left(S^{p}(t) - (S^{*})^{p} \right) I(t-\tau) \\ &+ \beta e^{-b\tau} \left(V^{q}(t) - (V^{*})^{q} \right) I(t-\tau) \\ &+ \left(\beta e^{-b\tau} (S^{*})^{p} - (\gamma + b + \alpha) \right) I(t) \\ &+ \left(\delta\beta e^{-b\tau} (V^{*})^{q} - (\gamma_{1} + b) \right) I(t) \\ &= \beta e^{-b\tau} \left(S^{p}(t) - (S^{*})^{p} \right) I(t-\tau) \\ &+ \beta e^{-b\tau} \left(V^{q}(t) - (V^{*})^{q} \right) I(t-\tau) \\ &= \beta e^{-b\tau} \left(S^{p-1}(t) + S^{p-2}(t) S^{*} + \cdots \right. \\ &+ S(t) \left(S^{*} \right)^{p-2} + \left(S^{*} \right)^{p-1} \right) \\ &\times \left(S(t) - S^{*} \right) I(t-\tau) \\ &+ \delta\beta e^{-b\tau} \left(V^{q-1}(t) + V^{q-2}(t) V^{*} + \cdots \right. \\ &+ V(t) \left(V^{*} \right)^{q-2} + \left(V^{*} \right)^{q-1} \right) \\ &\times \left(V(t) - V^{*} \right) I(t-\tau) \end{split}$$

(50)

Then we have our main result of this section.

Theorem 8. Let $1 \le q \le p$, if $\Re_2 > 1$, and then there exists a positive constant η small enough such that

$$I(t) \ge \min\left\{\frac{\eta m^*}{2}, \eta m^* e^{-(\gamma+b+\alpha)\omega}\right\} = m_1 \qquad (48)$$

with t large enough.

Proof. As before, we suppose that X(t) = (S(t), V(t), I(t)) is a positive solution of system (4) with initial condition (5). Then for $t \ge 0$, we construct a function as follows:

$$U(t) = I(t) + V(t) + \beta e^{-b\tau} (S^*)^p$$

$$\times \int_{t-\tau}^t I(\varrho) \, d\varrho + \delta \beta e^{-b\tau} (V^*)^q \int_{t-\tau}^t V(\varrho) \, d\varrho.$$
(49)

And then differentiating U(t) along the trajectory of (4) yields

$$\dot{U}(t) = \dot{I}(t) + \dot{V}(t) + \beta e^{-b\tau} (S^*)^p I(t) - \beta e^{-b\tau} (S^*)^p I(t-\tau) + \delta \beta e^{-b\tau} (V^*)^q I(t)$$

for $t \ge 0$. Let

$$m^{*} = \frac{(1/T)\ln\left(\left(\Re_{1}\left(e^{bT}-1+\theta\right)+1-\theta+e^{bT}\right)/2\right)-b}{\beta},$$

$$S^{*} = \sqrt[p]{\frac{\gamma+b+\alpha}{\beta e^{-b\tau}}}.$$
(51)

Since $\Re_2 > 1$, we get $\Re_1 > 1$, $\Re_2 > 1$. Then we have $m^* > 0$. And from $\Re_1 > 1$, we can get

$$\sqrt[p]{\frac{\beta e^{-b\tau}}{\gamma+b+\alpha}} \left(\frac{\mu\left(1-\theta\right)e^{-bT}}{1-\left(1-\theta\right)e^{-bT}}\right) > 1.$$
(52)

Thus, we have

$$\frac{\mu(1-\theta)e^{-bT}}{1-(1-\theta)e^{-bT}} > \sqrt[p]{\frac{\gamma+b+\alpha}{\beta e^{-b\tau}}} = S^*.$$
 (53)

Form $\Re_2 > 1$, we have

$$\sqrt[q]{\frac{\beta e^{-b\tau}}{\gamma_1 + b}} \frac{\mu \theta e^{-(\gamma_1 + b + bl)T}}{\left(1 - e^{-(\gamma_1 + b)T}\right)\left(1 - (1 - \theta) e^{-bT}\right)} > 1;$$
(54)

that is,

$$\frac{\mu\theta e^{-(\gamma_1+b+bl)T}}{(1-e^{-(\gamma_1+b)T})(1-(1-\theta)e^{-bT})} > \sqrt[q]{\frac{\gamma_1+b}{\beta e^{-b\tau}}} = V^*.$$
 (55)

We can take η small enough such that

$$\frac{\mu (1-\theta) e^{-(\beta \eta m^*+b)T}}{1-(1-\theta) e^{-(\beta \eta m^*+b)T}} > S^*,$$
$$\frac{\mu \theta e^{-(\beta (\delta+l)\eta m^*+\gamma_1+b+bl)T}}{(1-e^{-(\delta \beta \eta m^*+\gamma_1+b)T}) (1-(1-\theta) e^{-(\beta \eta m^*+b)T})} > V^*.$$
(56)

Thus we can choose $\varepsilon_1, \varepsilon_2 > 0$ to be small enough such that

$$S^{*} < \frac{\mu (1-\theta) e^{-(\beta \eta m^{*}+b)T}}{1-(1-\theta) e^{-(\beta \eta m^{*}+b)T}} - \varepsilon_{1} \equiv S_{\Delta},$$

$$V^{*} < \frac{\mu \theta e^{-(\beta (\delta+l)\eta m^{*}+\gamma_{1}+b+l)T}}{(1-e^{-(\delta \beta \eta m^{*}+\gamma_{1}+b)T}) (1-(1-\theta) e^{-(\beta \eta m^{*}+b)T})} - \varepsilon_{2} \equiv V_{\Delta}.$$
(57)

Then we claim that there exists an $m_2 > 0$ such that $I(t) > m_2$ for *t* is large enough. We next prove this claim in two steps.

Step I. For any positive constant t_0 , that $I(t) \le \eta m^*$ for all $t \ge t_0$ is not true.

Otherwise, there is a positive constant t_0 , such that $I(t) \le \eta m^*$ for all $t \ge t_0$. First, if $I(t) < \eta m^*$ for all $t \ge t_0$, it follows from the first, fourth, and fifth equations of (4) that, for $t \ge t_0$,

$$\frac{dS(t)}{dt} \ge -\left(\beta\eta m^* + b\right)S(t), \quad t \ne (n+l-1)T, \ t \ne nT,$$

$$\Delta S(t) = -\theta S(t), \quad t = (n+l-1)T,$$

$$\Delta S(t) = \mu, \quad t = nT.$$
(58)

By Lemma 1, there exists $T_1 > t_0 + \tau$ so that for $t > T_1$

$$S(t) > \frac{\mu(1-\theta) e^{-(\beta\eta m^*+b)T}}{1-(1-\theta) e^{-(\beta\eta m^*+b)T}} - \varepsilon \equiv S_{\Delta}.$$
 (59)

Similarly, from the second and the fourth equations of (4), we have

$$\frac{dV(t)}{dt} \ge -\left(\delta\beta\eta m^* + \gamma_1 + b\right)V(t), \quad t \neq (n+l-1)T,$$

$$\Delta V(t) = \theta S(t), \quad t = (n+l-1)T,$$
(60)

and for $t > T_1$,

$$V(t) \geq \frac{\mu \theta e^{-(\beta(\delta+l)\eta m^* + \gamma_1 + b + bl)T}}{\left(1 - e^{-(\delta\beta\eta m^* + \gamma_1 + b)T}\right)\left(1 - (1 - \theta) e^{-(\beta\eta m^* + b)T}\right)} - \varepsilon \equiv V_{\Delta}.$$
(61)

Then, by (50), for $t \ge T_1$,

$$\begin{split} \dot{U}(t) &= \beta e^{-b\tau} \left(S^{p-1}(t) + S^{p-2}(t) S^* + \cdots \right. \\ &+ S(t) \left(S^* \right)^{p-2} + \left(S^* \right)^{p-1} \right) \\ &\times \left(S(t) - S^* \right) I(t - \tau) \\ &+ \delta \beta e^{-b\tau} \left(V^{q-1}(t) + V^{q-2}(t) V^* + \cdots \right. \\ &+ V(t) \left(V^* \right)^{q-2} + \left(V^* \right)^{q-1} \right) \\ &\times \left(V(t) - V^* \right) I(t - \tau) \\ &> p \beta e^{-b\tau} \left(S^* \right)^{p-1} \left(S_\Delta - S^* \right) I(t - \tau) \\ &+ q \delta \beta e^{-b\tau} \left(V^* \right)^{q-1} \left(V_\Delta - V^* \right) I(t - \tau) . \end{split}$$

$$(62)$$

Let

$$I_L = \min_{t \in [T_1, T_1 + \tau]} I(t) .$$
(63)

We can prove that $I(t) \ge I_L$ for all $t \ge T_1$. Otherwise, there exists a nonnegative constant T_2 such that $I(t) \ge I_L$ for $t \in [T_1, T_1 + \tau + T_2]$, $I(T_1 + \tau + T_2) = I_L$, and $\dot{I}(T_1 + \tau + T_2) \le 0$.

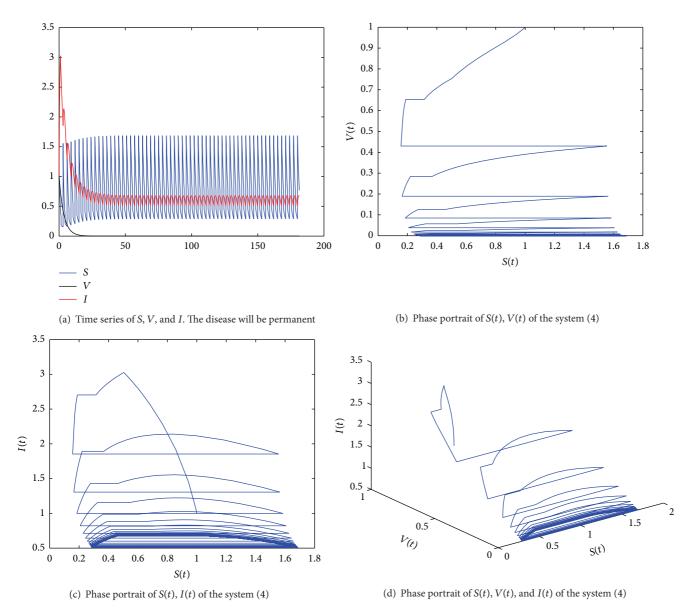


FIGURE 1: The results of numerical simulation on the threshold values $\Re_2 = 2.6155 > 1$, where p = 1.5, q = 1.25.

Then from the second equation of (4) and (37), we easily see that

÷ (m

$$\begin{split} &P(I_{1} + \tau + I_{2}) \\ &\geq \left(\beta e^{-b\tau}S^{p}(t) + \delta\beta e^{-b\tau}V^{q}(t) - (\gamma + b + \alpha)\right)I_{L} \\ &= \left(\gamma + b + \alpha\right)\left(\frac{\beta e^{-b\tau}S^{p}(t)}{\gamma + b + \alpha} + \frac{\delta\beta e^{-b\tau}V^{q}(t)}{\gamma + b + \alpha} - 1\right)I_{L} \\ &> \left(\gamma + b + \alpha\right)\left(\left(\frac{S_{\Delta}}{S^{*}}\right)^{p} + \frac{\gamma_{1} + b}{\gamma + b + \alpha}\left(\frac{V_{\Delta}}{V^{*}}\right)^{q} - 1\right)I_{L} \\ &> 0, \end{split}$$

which is a contradiction. Hence $I(t) \ge I_L > 0$ for all $t \ge T_1$. Equation (62) implies

$$\frac{dU(t)}{dt} > p\beta e^{-b\tau} (S^*)^{p-1} (S_{\Delta} - S^*) I(t - \tau)
+ q\delta\beta e^{-b\tau} (V^*)^{q-1} (V_{\Delta} - V^*) I(t - \tau)
> 0.$$
(65)

It then follows that $U(t) \rightarrow +\infty$ as $t \rightarrow +\infty$. This is a contradiction to $U(t) \leq (\alpha + \gamma + \gamma_1 + 2b)\tau + 2$. Therefore, for any positive constant t_0 , the inequality $I(t) < \eta m^*$ cannot hold for all $t \geq t_0$.

Step II. From Step I, we only need to consider the followng: (i) $I(t) > \eta m^*$ for all t large enough and (ii) I(t) oscillates

(64)

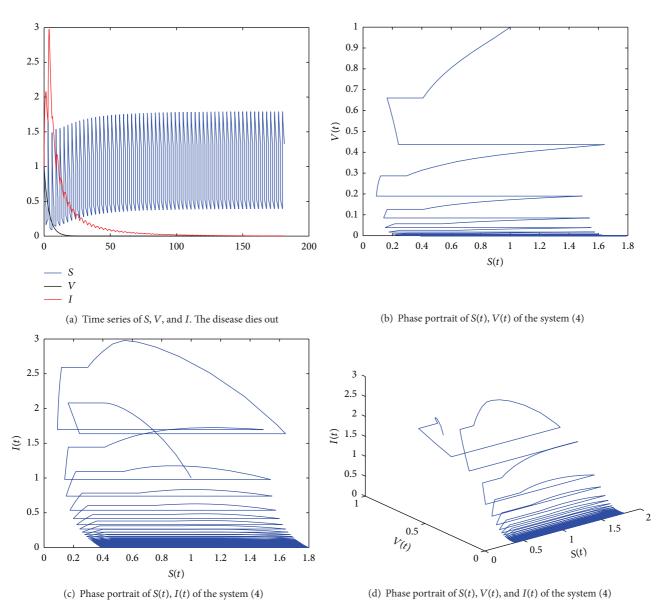


FIGURE 2: The results of numerical simulation on the threshold values $\Re_1 = 0.0339 < 1$, where p = 1.5, q = 1.25.

about ηm^* for all large *t*. However, Case (i) is obvious in the result of this theorem, so we only need to consider Case (ii), in which we will show that $I(t) \ge m_1$ for all large *t* where

$$m_1 = \min\left\{\frac{\eta m^*}{2}, \eta m^* e^{-(\gamma+b+\alpha)\vartheta}\right\}.$$
 (66)

First, we notice there exist two positive constants \overline{t} , φ such that

$$I(\overline{t}) = I(\overline{t} + \varphi) = I^*,$$

$$I(t) < \eta m^*, \quad \text{for } \overline{t} < t < \overline{t} + \varphi.$$
(67)

Second, because I(t) is bounded continuous function and I(t) has no pulse, we can get that I(t) is uniformly continuous. Therefore there exists a constant T_3 (with $0 < T_3 < \varpi$ and T_3 is independent of the choice of \bar{t}) such that $I(t) > \eta m^*/2$ for all $\bar{t} \le t \le \bar{t} + T_3$.

If $\varphi \leq T_3$, our aim is obtained.

If $T_3 < \varphi \leq \omega$, from the second equation of (4) we have that $\dot{I}(t) \geq -(\gamma + b + \alpha)I(t)$ for $\bar{t} < t \leq \bar{t} + \varphi$. Then we have $I(t) \geq \eta m^* e^{-(\gamma + b + \alpha)\omega}$ for $\bar{t} < t \leq \bar{t} + \varphi \leq \bar{t} + \omega$ since $I(\bar{t}) = \eta m^*$. It is clear that $I(t) \geq m_1$ for $\bar{t} < t \leq \bar{t} + \varphi$.

If $\varphi \ge \omega$, then we have $I(t) \ge m_2$ for $\overline{t} < t \le \overline{t} + \omega$. We then can easily prove $I(t) \ge m_1$ for $\overline{t} + \omega \le t \le \overline{t} + \varphi$. Since the interval $[\overline{t}, \overline{t} + \varphi]$ is arbitrarily chosen, we know that $I(t) \ge m_1$ holds for *t* large enough. Finally, noticing the choice of m_1 is independent of the positive solution of (4), we completed our proof.

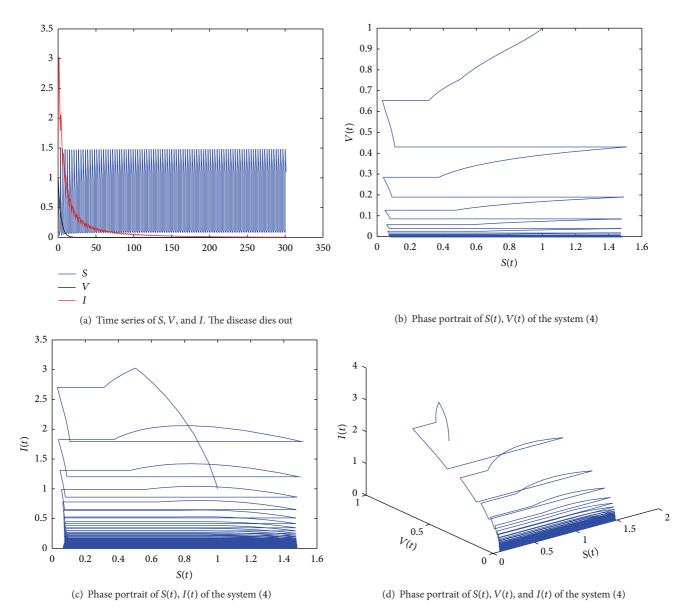


FIGURE 3: The results of numerical simulation on the threshold values $\Re_1 = 0.0449 < 1$, where p = 1.5, q = 1.25.

Theorem 9. Let $1 \le q \le p$, if $\mathcal{R}_2 > 1$, and then system (4) is permanent.

Proof. Suppose that X(t) = (S(t), V(t), I(t)) is a positive solution of system (4) with initial conditions (5). Then from system (4), we have

$$\begin{aligned} \frac{dS(t)}{dt} &\geq -\left(b+\beta\right)S(t),\\ \frac{dV(t)}{dt} &\geq -\left(\delta\beta+\gamma_1+b\right)V(t),\\ t &\neq (n+l-1)T, \quad t \neq nT, \quad n \in N,\\ \Delta S(t) &= -\theta S(t), \quad \Delta V(t) = \theta S(t), \end{aligned}$$

$$t = (n+l-1)T, \quad n \in N,$$

$$\Delta S(t) = \mu, \quad \Delta V(t) = 0, \quad t = nT, \quad n \in N.$$
(68)

As what we did in the proof of Theorem 5, we can prove that there exist *t* large enough and $\varepsilon > 0$ small enough such that

$$S(t) \geq \frac{\mu (1-\theta) e^{-(b+\beta)T}}{1-(1-\theta) e^{-(b+\beta)T}} - \varepsilon = m_3,$$

$$V(t) \geq \frac{\mu \theta e^{-(b+\gamma_1+\delta\beta+(b+\beta)l)T}}{(1-(1-\theta) e^{-(b+\beta)T})(1-e^{-(b+\gamma_1+\delta\beta)T})}$$

$$-\varepsilon_2 = m_4.$$
(69)

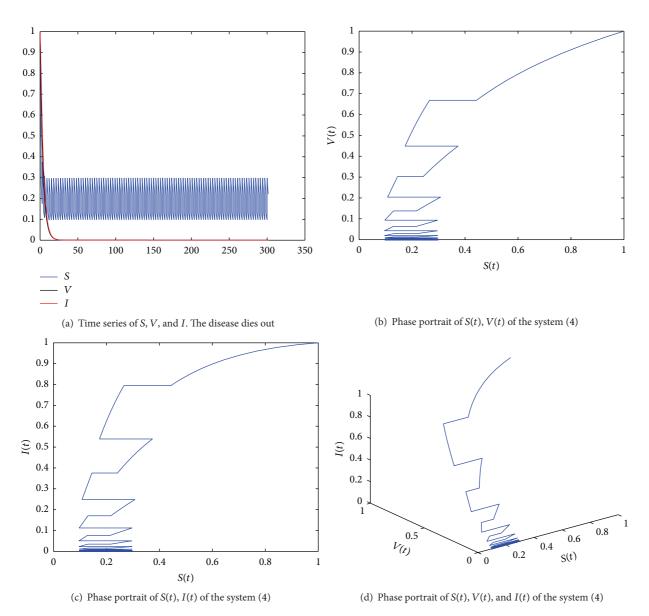


FIGURE 4: The results of numerical simulation on the threshold values $\Re_1 = 0.0352 < 1$, where p = 1.5, q = 1.25.

Then for $\mathcal{D} = \{(S, V, I) \in R^3_+ \mid S(t) + V(t) + I(t) \le 1\}$, by Theorem 8, we have

$$m_3 \le S(t) \le 1,$$
 $m_1 \le I(t) \le 1,$ $m_4 \le V(t) \le 1$
(70)

for *t* large enough. Thus the system (4) is uniformly permanent. \Box

5. Numerical Simulations and Discussions

Next, we carry out numerical simulations to illustrate the theoretical results obtained in the previous sections. We first set the parameters as follows: b = 0.2, $\beta = 0.5$, $\alpha = 0.05$, $\gamma = 0.04$, $\delta = 0.02$, $\gamma_1 = 0.06$, p = 1.5, q = 1.25, T = 1.5, $\omega = 1$, $\tau = 1$, $\theta = 0.4$, and $\mu = 1.4$. Straightforward

calculation shows $\Re_2 = 2.6155 > 1$. Then by Theorem 8, the disease will be permanent (please see Figures 1(a), 1(b), 1(c), and 1(d)). In order to show the effect of τ , we decrease τ to 4, and other parameters are the same with those in Figure 1, and the infection-free periodic solution of system (4) is globally attractive. This phenomenon is also seen from our theoretical analysis as in this case $\Re_1 = 0.0339 < 1$ and then according to Theorem 5, the disease will be eradicated; please see Figure 2(a).

If we keep $\tau = \omega = 1$ and $\mu = 1$, as the same with those in Figure 1, but increase vaccination proportion of susceptible persons θ to 0.9, then the disease will be eradicated; see Figure 3(a). If we keep $\tau = \omega = 1$ and $\theta = 0.4$ and decrease μ to 0.2, then the disease also will be eradicated; see Figure 4(a).

And if we keep $\tau = \omega = 4$, $\mu = 1$ but decrease θ to 0.1, then the disease will be permanent; see Figure 5. If we keep $\tau = \omega =$

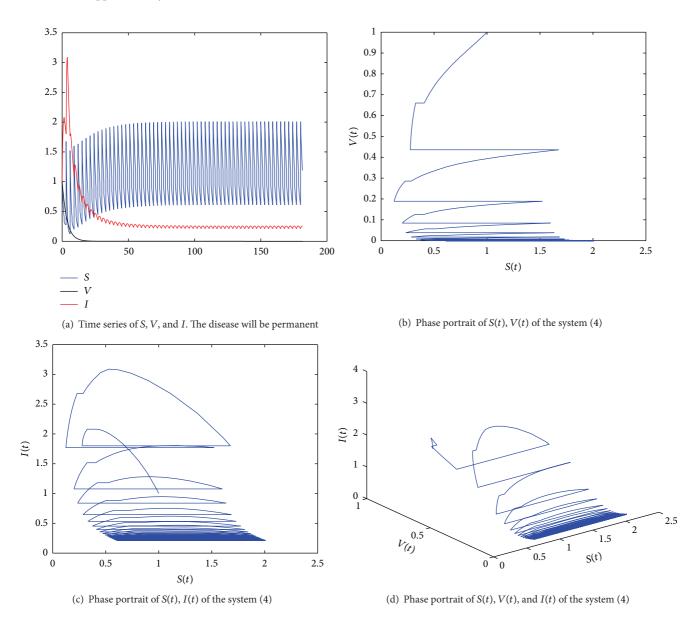


FIGURE 5: The results of numerical simulation on the threshold values $\Re_2 = 1.1036 > 1$, where p = 1.5, q = 1.25.

				TABLE 1	
ω	τ	θ	μ	\mathscr{R}_i	Status of the disease
1	1	0.4	1.4	$\mathcal{R}_2 = 2.6155 > 1$	Permanence
4	4	0.4	1.4	$\mathcal{R}_1=0.0339<1$	Eradication
1	1	0.9	1.4	$\mathcal{R}_1=0.0449<1$	Eradication
1	1	0.4	0.2	$\mathcal{R}_1=0.0352<1$	Eradication
4	4	0.1	1.4	$\mathcal{R}_2 = 1.1036 > 1$	Permanence
4	4	0.4	2	$\mathcal{R}_2 = 2.3121 > 1$	Permanence

4 and θ = 0.4 and increase μ to 2, then the disease also will be permanent; see Figure 6. For details please see Table 1.

Lastly, we conclude our paper as follows. In this paper, we proposed an SVEIRS model, which is a new epidemic model with periodic pulse vaccination and pulse population input at two different fixed moments. Our primary result is to investigate the effect of impulsive vaccination, pulse population input, and time delays to the dynamics of population model. With the help of comparison theorems, we proved the existence of the "infection-free" periodic solution and obtained the conditions for global attractivity of the "infection-free" periodic solution and the conditions for the permanence of the system. All the theoretical results show that we believe it might be helpful in disease control: people can select appropriate vaccination rate and population input rate according to our theoretical results to control diseases.

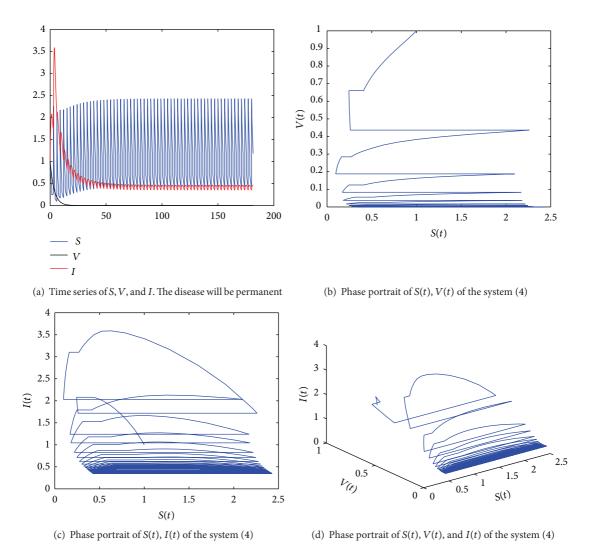


FIGURE 6: The results of numerical simulation on the threshold values $\Re_2 = 2.3121 > 1$, where p = 1.5, q = 1.25.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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