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Analysis of a delayed epidemic model with pulse vaccination and saturation incidence

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Abstract

Pulse vaccination is an important strategy for the elimination of infectious diseases. An SEIRS epidemic model with time delays and pulse vaccination is formulated in this paper. Using the discrete dynamical system determined by the stroboscopic map, we obtain the exact infection-free periodic solution of the impulsive epidemic system and prove that the infection-free periodic solution is globally attractive if the vaccination rate is larger than θ^*. Moreover, we show that the disease is uniformly persistent if the vaccination rate is less than θ_*. The permanence of the model is investigated analytically. Our results indicate that a long latent period of the disease is sufficient condition for the extinction of the disease.

Keywords: Time delay; Pulse vaccination; SEIRS epidemic model; Global attractivity; Permanence

1. Introduction

In the classical epidemiological model [1–7], the total population N is divided into three groups:

- The susceptibles (S)
- The infectives (I)
- The removed group (R)

If death or isolation may occur, $R(t)$ represents all removed individuals from the population (including immunes, deaths and isolates). In the model, an infected individual becomes immediately infected. The infectives have a constant probability per unit of time to become removed, i.e., the infectious period has an exponential distribution with parameter a. This leads to the SIR model

$$\begin{cases} \dot{S}(t) = -bS(t)I(t), \\ \dot{I}(t) = bS(t)I(t) - aI(t), \\ \dot{R}(t) = aI(t), \end{cases}$$

where b, a are positive parameters, b is the infection parameter or the transmission contact rate, a is the removal parameter giving the rate at which infectives become immune. The initial population are $S(0), I(0)$ positive and $R(0) = 0$. Obviously, $S(0) + I(0) + R(0) = N$. It is known that $S(t) + I(t) + R(t) = N$ is constant. Dividing S, I and R by N we may assume that $N = 1$ without loss of generality.

An important parameter is the relative removal rate

$$c = a/b$$

A major outbreak occurs only if the initial number of suceptibles $S(0) > c$. This is known as the Threshold Theorem, c being such a threshold.

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Kermack and McKendrick deduced form the model that some susceptibles survive the epidemic free from infection. Indeed, if $S(0)$ exceeds the relative removal rate by a small quantity e, but the initial number of infectives $I(0)$ is small (relative to e), then the final number of susceptibles left in the population is approximately $c - e$. Moreover, the number in the remainder group approach to $2e$. This is known as the Second Threshold Theorem.

For many diseases an infected individual becomes immediately infectious, but for many there is a latent period, i.e., the period of time between becoming infected and becoming infectious. For example, measles has an 8–13 day latent period and the incubation time for AIDS is anything from a few months to years after the patient has got antibodies to the human immunodeficiency virus (VIH). To include the latent period it is necessary to consider a new group in the population.

- The exposed but not yet infectious (E)

Exposed individuals E undergo an average incubation period, asymptomatic and uninfectious of $1/d$ units of time before progressing to the infectious class I. The new model is the so-called SEIR model:

$$\begin{cases} \dot{S}(t) = -bS(t)I(t), \\ \dot{E}(t) = bS(t)I(t) - dE(t), \\ \dot{I}(t) = dE(t) - aI(t), \\ \dot{R}(t) = aI(t). \end{cases}$$

In Fig. 1, we represent the flow of individuals between epidemiological classes.

Infectious diseases have tremendous influence on human life. Every year millions of human being suffer or die of various infectious diseases. Controlling infectious diseases has been an increasingly complex issue in recent year. A strategy to control infectious diseases is vaccination. One can investigate under what conditions a given agent can invade a (partially) vaccinated population, i.e., how large a fraction of the population do we have to keep vaccinated in order to prevent the agent from establishing. However, in practical situations one usually has to start a vaccination campaign when the agent has become endemic. In such a case, will the vaccination effort sufficient to eliminate the agent? What is the adequate strategy? Constant vaccination is the conventional strategy. Recently a new strategy denominated Pulse Vaccination Strategy (PVS) has been revealed adequate against poliomyelitis and measles. The effectiveness of constant and pulse vaccination policies are compared theoretically and numerically in [8].

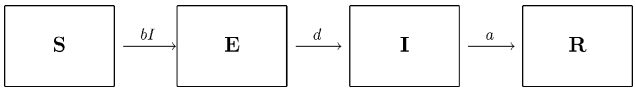

Fig. 1. The flow of individuals between epidemiological classes.

A usual recommendation for measles immunization is to apply a first vaccination dose to all infants of 15 months of age and a second dose at 6 years. However, it was hypothesized [9] that measles epidemics can be more efficiently controlled when the natural temporal process of the epidemics is antagonized by another temporal process, that is, by a vaccination effort that is pulsed in time rather than uniform and continuous. We call this policy pulse vaccination and it was shown theoretically that if children aged one to seven years are immunized once every 5 years, that may suffice for preventing the epidemics [9].

The strategy of pulse vaccination (PVS) consists of periodical repetitions of impulsive vaccinations in a population, on all the age cohorts [10,11]. At each vaccination time a constant fraction of the susceptible population is vaccinated. Some theoretical considerations, practical advantages, and examples of the PVS are presented in [11–14]. For example, some successes against poliomyelitis and measles have been attributed to repeated PVS [15]. As indicated in [16], models have clearly shown the advantages of a mass campaign approach in rapidly achieving high measles population immunity and interrupting measles virus circulation.

Mathematical models that use age-specific incidence rates, vaccination coverage data, and population-based serological surveys have provided useful insights for developing and refining of the measles eradication vaccination strategies [16–18]. When the total population is divided into four distinct epidemiological subclasses of individuals which are susceptible (S), exposed (E), infectious (I), and recovered (R) we have a SEIR model [19]. For a schematic representation of the flow of individuals between the four epidemiological subclasses, see [20] where the authors model the course of an Ebola outbreak via an SEIR model. SEIR models have been used, as indicated above, to study Ebola outbreaks, measles, polio, dengue [21,22], or transmission of varicella-zoster virus [23]. Other authors have used SEIR epidemic modelling techniques to examine herpesvirus in Australian pilchards (*Sardinops sagax*) [24], and to two retroviruses of domestic cats (*Felis catus*) and to the rabies virus for red foxes (*Vulpes*) [25].

Different vaccination policies and strategies combining PVS, treatment, pre-outbreak vaccination or isolation are now been introduced [14,26–28].

Another, totally different and at distinct level, pulse strategy in vaccination is electrotansfer, a suitable electric pulses delivered to the muscle after DNA injections, and electroporation [29–31].

A SEIR spatially-structured model of measles is considered in [32]. A PVS has been considered to study hepatitis, but it is in Chinese [33]. Some other interesting are [34,35].

2. Models, definitions and preliminaries

Standard epidemiological models use a bilinear incidence rate βIS based on the law of mass action [36,37]. However, as

the number of susceptibles is large, it is unreasonable to consider the bilinear incidence owing to the number of susceptibles with which every infective contact within a certain time is limited. If the population is saturated with infectives, there are three kinds of incidence forms that are used in epidemiological model: the proportionate mixing incidence $\beta IS/N$ [37–39], nonlinear incidence $\beta I^p S^q$ [40,41] and saturation incidence $\beta IS/(1+\alpha S)$ [37,42] or $\beta I^l S/(1+\alpha I^h)$ [43].

Cooke and Driessche [38] investigated an SEIRS model with the latent period and the immune period. The consideration of the latent period and the immune period gives rise to models with the incorporation of delays and integral equation formulations. By neglecting disease-related rate, the model which proposed in [38] yields:

$$\begin{cases} \dot{S}(t) = bN(t) - bS(t) - \dfrac{\beta S(t)I(t)}{N(t)} + \gamma I(t-\tau)\mathrm{e}^{-b\tau}, \\ E(t) = \int_{t-\omega}^{t} \dfrac{\beta S(u)I(u)}{N(u)}\mathrm{e}^{-b(t-u)}\mathrm{d}u, \\ \dot{I}(t) = \dfrac{\beta S(t-\omega)I(t-\omega)}{N(t-\omega)}\mathrm{e}^{-b\omega} - (b+\gamma)I(t), \\ R(t) = \int_{t-\tau}^{t} \gamma I(u)\mathrm{e}^{-b(t-u)}\mathrm{d}u, \end{cases} \tag{2.1}$$

where b is the natural birth rate and death rate of the population, β is average number of adequate contacts of an infectious individuals per unit time, γ is the recovery rate of infectious individuals, ω is the latent period of the disease, τ is the immune period of the population. All coefficients are positive constants. Wang [39] studied the model (2.1) and presented sufficient conditions for local stability and global stability of endemic equilibrium.

Comparing with bilinear and proportionate mixing incidence, saturating contact rate is a kind of contact rate, which it may be more suitable for our real world. Instead of the proportionate mixing incidence in model (2.1), we consider saturation incidence in this paper, and assume saturating contact rate is $U(S) = \frac{\beta S(t)}{1+\alpha S(t)}$. Hence we have $U(S) \to \frac{\beta}{\alpha}$ as $S \to \infty$, where α and β are positive constants. It is easy to obtain from (2.1) that the total population is constant. For convenience, we assume that $N(t) = S(t) + E(t) + I(t) + R(t) = 1$ for all $t \geq 0$. Therefore, we investigate the SEIRS epidemic model with time delays and saturation incidence:

$$\begin{cases} \dot{S}(t) = b - bS(t) - \dfrac{\beta S(t)I(t)}{1+\alpha S(t)} + \gamma I(t-\tau)\mathrm{e}^{-b\tau}, \\ E(t) = \int_{t-\omega}^{t} \dfrac{\beta S(u)I(u)}{N(u)}\mathrm{e}^{-b(t-u)}\,\mathrm{d}u, \\ \dot{I}(t) = \dfrac{\beta\mathrm{e}^{-b\omega}S(t-\omega)I(t-\omega)}{1+\alpha S(t-\omega)} - (b+\gamma)I(t), \\ R(t) = \int_{t-\tau}^{t} \gamma I(u)\mathrm{e}^{-b(t-u)}\,\mathrm{d}u. \end{cases} \tag{2.2}$$

Further we consider PVS in model (2.2) and assume that the impulsive vaccination is applied every $T(>0)$ years and $\theta(0<\theta<1)$ denote the proportion of those vaccinated successfully. Incorporating with pulse vaccination, model (2.2) yields

$$\left.\begin{cases} \dot{S}(t) = b - bS(t) - \dfrac{\beta S(t)I(t)}{1+\alpha S(t)} + \gamma I(t-\tau)\mathrm{e}^{-b\tau}, \\ E(t) = \int_{t-\omega}^{t} \dfrac{\beta S(u)I(u)}{N(u)}\mathrm{e}^{-b(t-u)}\,\mathrm{d}u, \\ \dot{I}(t) = \dfrac{\beta\mathrm{e}^{-b\omega}S(t-\omega)I(t-\omega)}{1+\alpha S(t-\omega)} - (b+\gamma)I(t), \\ R(t) = \int_{t-\tau}^{t} \gamma I(u)\mathrm{e}^{-b(t-u)}\,\mathrm{d}u, \end{cases}\right\} \quad t \neq kT, k \in Z^+$$

$$\left.\begin{cases} S(t^+) = (1-\theta)S(t^-), \\ E(t^+) = E(t^-), \\ I(t^+) = I(t^-), \\ R(t^+) = R(t^-) + \theta S(t^-), \end{cases}\right\} \quad t = kT,\ k \in Z^+, \tag{2.3}$$

where $Z^+ = \{0, 1, 2, \ldots\}$, $N(t) = S(t) + E(t) + I(t) + R(t) = 1$ for all $t \geq 0$. Note that the variables E and R do not appear in the first and third equations of system (2.3). This allows us to attack (2.3) by studying the subsystem:

$$\left.\begin{cases} \dot{S}(t) = b - bS(t) - \dfrac{\beta S(t)I(t)}{1+\alpha S(t)} + \gamma I(t-\tau)\mathrm{e}^{-b\tau}, \\ \dot{I}(t) = \dfrac{\beta\mathrm{e}^{-b\omega}S(t-\omega)I(t-\omega)}{1+\alpha S(t-\omega)} - (b+\gamma)I(t), \end{cases}\right\} \quad t \neq kT,\ k \in Z^+$$

$$\left.\begin{cases} S(t^+) = (1-\theta)S(t^-), \\ I(t^+) = I(t^-), \end{cases}\right\} \quad t = kT,\ k \in Z^+. \tag{2.4}$$

It is difficulty to study local stability of periodic solution of impulsive equations with time delays. Hence the main purpose of this paper is to establish sufficient conditions that the disease dies out, and the second purpose of this paper is to show that the disease is uniformly persistent if the latent period of the disease is less than ω_*, that is, there is a positive constant q (independent of the choice of the solution) such that $I(t) \geq q$ for all large t.

In the following, we introduce some notations and definitions and state two results which will be useful in subsequent sections.

Let $R_+ = [0, \infty)$, $R_+^2 = \{Z \in R^2 : Z \geq 0\}$. Denote $f = (f_1, f_2)^{\mathrm{T}}$ the map defined by the right hand of the first and second equations of system (2.4).

Set $l = \max\{\tau, \omega\}$. Let C be the space of continuous functions on $[-l, 0]$ with uniform norm. The initial conditions for (2.4) are

$$(\phi_1(\zeta), \phi_2(\zeta)) \in C_+ = C([-l, 0], R_+^2), \phi_i(0) > 0, i = 1, 2. \tag{2.5}$$

The solution of system (2.4) is a piecewise continuous function $Z : R_+ \to R_+^2$, $Z(t)$ is continuous on $(kT, (k+1)T]$, $k \in Z^+$ and $Z(kT^+) = \lim_{t \to kT^+} Z(t)$ exists. Obviously the smooth properties of f guarantee the global existence and uniqueness of solutions of system (2.4) (See [44,45] for details on funda-

mental properties of impulsive systems.). Since $\dot{S}(t)|_{S=0} > 0$, and $\dot{I}(t) = 0$ whenever $I(t) = 0$, for $t \neq kT, k \in Z^+$. Moreover, $S(kT^+) = (1-\theta)S(kT^-)$, $I(kT^+) = I(kT^-)$ for $k \in Z^+$. Therefore we have the following lemma.

Lemma 2.1. *Suppose $Z(t)$ is a solution of system (2.4) with initial conditions (2.5), then $Z(t) \geq 0$ for all $t \geq 0$.*

Denote $\Omega = \{(S, I) \in R^2 | S \geq 0, I \geq 0, S + I \leq 1\}$,

Using the fact that $S(t) + E(t) + I(t) + R(t) \equiv 1$, it is easy to show that Ω is positively invariant with respect to (2.4).

Definition 2.1. System (2.4) is said to be uniformly persistent if there is an $\eta > 0$ (independent of the initial conditions) such that every solution $(S(t), I(t))$ with initial conditions (2.5) of system (2.4) satisfies

$$\liminf_{t\to\infty} S(t) \geq \eta, \quad \liminf_{t\to\infty} I(t) \geq \eta.$$

Definition 2.2. System (2.4) is said to be permanent if there exists a compact region $\Omega_0 \in int\Omega$ such that every solution of system (2.4) with initial conditions (2.5) will eventually enter and remain in region Ω_0.

To prove our main results we state two lemmas which will be essential to our proofs.

Lemma 2.2. *Let us consider the following impulsive system*

$$\begin{cases} \dot{u}(t) = a - bu(t), & t \neq kT, \\ u(t^+) = (1-\theta)u(t^-), & t = kT. \end{cases} \tag{2.6}$$

where $a > 0$, $b > 0$, $0 < \theta < 1$. Then there exists a unique positive periodic solution of system (2.6)

$$\tilde{u}_e(t) = \frac{a}{b} + (u^* - \frac{a}{b})e^{-b(t-kT)}, \quad kT < t \leq (k+1)T,$$

which is globally asymptotically stable, where $u^* = \frac{(a/b)(1-\theta)(1-e^{-bT})}{1-(1-\theta)e^{-bT}}$.

Proof. Integrating and solving the first equation of system (2.6) between pulses

$$u(t) = \frac{a}{b} + \left(u(kT) - \frac{a}{b}\right) e^{-b(t-kT)}, \quad kT < t \leq (k+1)T,$$

where $u(kT)$ be the initial value at time kT. Using the second equation of system (2.6), we deduce the stroboscopic map such that

$$u((k+1)T) = (1-\theta)\left(\frac{a}{b} + \left(u(kT) - \frac{a}{b}\right) e^{-bT}\right) \doteq f(u(kT)), \tag{2.7}$$

where $f(u) = (1-\theta)[\frac{a}{b} + (u - \frac{a}{b})e^{-bT}]$. It is easy to know that system (2.7) has a unique positive equilibrium $u^* = \frac{(a/b)(1-\theta)(1-e^{-bT})}{1-(1-\theta)e^{-bT}}$. Since $f(u)$ is a straight line with slope less than 1, we obtain that u^* is globally asymptotically stable. It implies that the corresponding periodic solution of system (2.6)

$$\tilde{u}_e(t) = \frac{a}{b} + \left(u^* - \frac{a}{b}\right) e^{-b(t-kT)}, \quad kT < t \leq (k+1)T,$$

is globally asymptotically stable. The proof of Lemma 2.2 is complete. □

The following lemma is a direct consequence of the monotonicity results of [46].

Lemma 2.3. *Consider the following equation*

$$\dot{x}(t) = a_1 x(t-\omega) - a_2 x(t),$$

where $a_1, a_2, \omega > 0$; $x(t) > 0$ for $-\omega \leq t \leq 0$. We have:

(i) *if $a_1 < a_2$, then $\lim_{t\to\infty} x(t) = 0$;*
(ii) *if $a_1 > a_2$, then $\lim_{t\to\infty} x(t) = +\infty$.*

3. Global attractivity of infection-free periodic solution

In this section, we begin the analysis (2.4) by first demonstrating the existence of an infection-free periodic solution, in which infectious individuals are entirely absent from the population permanently, i.e. $I(t) = 0$ for all $t \geq 0$. Under this condition, the growth of susceptible individuals must satisfy:

$$\begin{cases} \dot{S}(t) = b - bS(t), & t \neq kT, \\ S(t^+) = (1-\theta)S(t^-), & t = kT. \end{cases} \tag{3.1}$$

We will show that the susceptible population S oscillates with period T, in synchronization with the periodic pulse vaccination.

By Lemma 2.2, we know that periodic solution of system (3.1)

$$\tilde{S}_e(t) = 1 - \frac{\theta}{1-(1-\theta)e^{-bT}} e^{-b(t-kT)}, \quad kT < t \leq (k+1)T, \tag{3.2}$$

is globally asymptotically stable.

In this section that follows we determine the global attractivity condition of the infection-free periodic solution $(\tilde{S}_e(t), 0)$ of model (2.4).

Theorem 3.1. *The infection-free periodic solution $(\tilde{S}_e(t), 0)$ of system (2.4) is globally attractive provided that $R^* < 1$, where*

$$R^* = \frac{(\beta e^{-b\omega} - \alpha(b+\gamma))(1 + (\gamma/b)e^{-bT})(1 - e^{-bT})}{(b+\gamma)(1-(1-\theta)e^{-bT})}.$$

Proof. Since $R^* < 1$, we can choose $\epsilon_0 > 0$ sufficiently small such that

$$\frac{\beta e^{-b\omega}\delta}{1+\alpha\delta} < b+\gamma, \tag{3.3}$$

where $\delta = \frac{(1+(\gamma/b)e^{-bT})(1-e^{-bT})}{1-(1-\theta)e^{-bT}} + \epsilon_0$. From the first equation of system (2.4), we have $\dot{S}(t) < (b+\gamma e^{-b\tau}) - bS(t)$. Then we consider the following comparison system with pulses

$$\begin{cases} \dot{x}(t) = (b+\gamma e^{-b\tau}) - bx(t), & t \neq kT, \\ x(t^+) = (1-\theta)x(t^-), & t = kT. \end{cases} \tag{3.4}$$

In view of Lemma 2.2, we know that the unique periodic solution of system (3.4) is of form

$$\tilde{x}_e(t) = \left(1+\frac{\gamma}{b}e^{-b\tau}\right)\left(1-\frac{\theta}{1-(1-\theta)e^{-bT}}e^{-b(t-kT)}\right),$$
$$kT < t \le (k+1)T,$$

and it is globally asymptotically stable.

Let $(S(t), I(t))$ be the solution of system (2.4) with initial values (2.5) and $S(0^+) = S_0 > 0$, $x(t)$ be the solution of system (3.4) with initial value $x(0^+) = S_0$. By the comparison theorem in impulsive differential equation [44,45], there exists an integer $k_1 > 0$ such that for $t > k_1 T$

$$S(t) < \tilde{x}_e(t) + \epsilon_0,$$

thus,

$$S(t) < \frac{(1+(\gamma/b)e^{-bT})(1-e^{-bT})}{1-(1-\theta)e^{-bT}} + \epsilon_0 = \delta,$$
$$kT < t \le (k+1)T,\ k > k_1. \tag{3.5}$$

Further, from the second equation of system (2.4), we know that (3.5) implies

$$\dot{I}(t) \le \frac{\beta e^{-b\omega}\delta}{1+\alpha\delta} I(t-\omega) - (b+\gamma)I(t), \quad t > kT+\omega, k > k_1.$$

Consider the following comparison system

$$\dot{y}(t) = \frac{\beta e^{-b\omega}\delta}{1+\alpha\delta} y(t-\omega) - (b+\gamma)y(t),$$
$$t > kT+\omega, k > k_1. \tag{3.6}$$

According to (3.3) and Lemma 2.3, we have $\lim_{t\to\infty} y(t) = 0$.

Let $(S(t), I(t))$ be the solution of system (2.4) with initial values (2.5) and $I(\zeta) = \varphi(\zeta) > 0$ $(\zeta \in [-\omega, 0])$, $y(t)$ be the solution of system (3.6) with initial value $y(\zeta) = \varphi(\zeta)(\zeta \in [-\omega, 0])$. By the comparison theorem, we have $\lim_{t\to\infty} \sup I(t) \le \lim_{t\to\infty} \sup y(t) = 0$. Incorporating into the positivity of $I(t)$, we know that $\lim_{t\to\infty} I(t) = 0$. Therefore, there exists an integer $k_2 > k_1$ (where $k_2 T > k_1 T + \omega$) such that $I(t) < \epsilon_0$ for all $t > k_2 T$.

For the first equation of system (2.4), we have

$$\dot{S}(t) > (b-\beta\epsilon_0) - bS(t), \quad \text{for} \quad t > k_2 T + \tau,$$

and

$$\dot{S}(t) < (b+\gamma e^{-b\tau}\epsilon_0) - bS(t), \quad \text{for} \quad t > k_2 T + \tau.$$

Consider comparison impulsive differential equations for $t > k_2 T + \tau$ and $k > k_2$,

$$\begin{cases} \dot{z}_1(t) = (b-\beta\epsilon_0) - bz_1(t), & t \neq kT, \\ z_1(t^+) = (1-\theta)z_1(t^-), & t = kT, \end{cases} \tag{3.7}$$

and

$$\begin{cases} \dot{z}_2(t) = (b+\gamma e^{-b\tau}\epsilon_0) - bz_2(t), & t \neq kT, \\ z_2(t^+) = (1-\theta)z_2(t^-), & t = kT. \end{cases} \tag{3.8}$$

By Lemma 2.2, we have that the unique periodic solution of system (3.7)

$$\tilde{z}_{1_e}(t) = \left(1-\frac{\beta\epsilon_0}{b}\right)\left(1-\frac{\theta e^{-b(t-kT)}}{1-(1-\theta)e^{-bT}}\right),$$
$$kT < t \le (k+1)T,$$

and the unique periodic solution of system (3.8)

$$\tilde{z}_{2_e}(t) = \left(1+\frac{\gamma e^{-b\tau}\epsilon_0}{b}\right)\left(1-\frac{\theta e^{-b(t-kT)}}{1-(1-\theta)e^{-bT}}\right),$$
$$kT < t \le (k+1)T,$$

are globally asymptotically stable.

Let $(S(t), I(t))$ be the solution of system (2.4) with initial values (2.5) and $S(0^+) = S^0 > 0$, $z_1(t)$ and $z_2(t)$ be the solutions of system (3.7) and (3.8) with initial value $z_1(0^+) = z_2(0^+) = S^0$, respectively. According to the comparison theorem in impulsive differential equation, there exists an integer $k_3 > k_2$ such that $k_3 T > k_2 T + \tau$ and

$$\tilde{z}_{1_e}(t) - \epsilon_0 < S(t) < \tilde{z}_{2e}(t) + \epsilon_0,$$
$$kT < t \le (k+1)T, \quad k > k_3. \tag{3.9}$$

Because ϵ_0 is arbitrarily small, it follows from (3.9) that

$$\tilde{S}_e(t) = 1 - \frac{\theta}{1-(1-\theta)e^{-bT}}e^{-b(t-kT)}, \quad kT < t \le (k+1)T$$

is globally attractive. Therefore, infection-free periodic solution $(\tilde{S}_e(t), 0)$ is globally attractive. The proof is complete. □

Denote

$$\theta^* = 1 - \frac{(b+\gamma)e^{bT} - (\beta e^{-b\omega} - \alpha(b+\gamma)) \times (1+(\gamma/b)e^{-bT})(e^{bT}-1)}{b+\gamma}$$

and

$$\omega^* = -\frac{1}{b}\ln\left[\frac{b+\gamma}{\beta}\left(\frac{1-(1-\theta)\mathrm{e}^{-bT}}{(1+(\gamma/b)\mathrm{e}^{-bT})(1-\mathrm{e}^{-bT})}+\alpha\right)\right].$$

According to Theorem 3.1 we can easily obtain the following result.

Corollary 3.1. *The infection-free periodic solution* $(\tilde{S}_e(t), 0)$ *is globally attractive provided that* $\theta > \theta^*$ *or* $\omega > \omega^*$.

Theorem 3.1 determines the global attractivity of (2.4) in Ω for the case $R^* < 1$. Its epidemiological implication is that the infectious population vanishes so the disease dies out. Corollary 3.1 implies that the disease will disappear if the vaccination rate is larger than θ^* or the length of latent period of disease is larger than ω^*.

4. Permanence

In this section we say the disease is endemic if the infectious population persists above a certain positive level for sufficiently large time.

Denote two quantities

$$R_* = \frac{(\beta\mathrm{e}^{-b\omega}-\alpha(b+\gamma))(1-\theta)(1-\mathrm{e}^{-bT})}{(b+\gamma)(1-(1-\theta)\mathrm{e}^{-bT})}$$

and

$$I^* = \frac{b}{\beta}\left[\frac{(\beta\mathrm{e}^{-b\omega}-\alpha(b+\gamma))(1-\theta)(1-\mathrm{e}^{-bT})}{(b+\gamma)(1-(1-\theta)\mathrm{e}^{-bT})}-1\right].$$

Theorem 4.1. *Suppose* $R_* > 1$. *Then there is a positive constant* q *such that each positive solution* $(S(t), I(t))$ *of system (2.4) satisfies*

$$I(t) \geq q, \quad \text{for } t \text{ large enough}$$

Proof. Note that the second equation of (2.4) can be rewritten as

$$\begin{aligned}\dot{I}(t) &= \frac{\beta\mathrm{e}^{-b\omega}S(t)I(t)}{1+\alpha S(t)} - (b+\gamma)I(t) - \beta\mathrm{e}^{-b\omega}\left(\frac{S(t)I(t)}{1+\alpha S(t)} - \frac{S(t-\omega)I(t-\omega)}{1+\alpha S(t-\omega)}\right)\\ &= I(t)\left(\frac{\beta\mathrm{e}^{-b\omega}S(t)}{1+\alpha S(t)} - (b+\gamma)\right) - \beta\mathrm{e}^{-b\omega}\frac{\mathrm{d}}{\mathrm{d}t}\int_{t-\omega}^{t}\frac{S(u)I(u)}{1+\alpha S(u)}\,\mathrm{d}u.\end{aligned} \tag{4.1}$$

Let us consider any positive solution $(S(t), I(t))$ of system (2.4). According to this solution, we define

$$V(t) = I(t) + \beta\mathrm{e}^{-b\omega}\int_{t-\omega}^{t}\frac{S(u)I(u)}{1+\alpha S(u)}\,\mathrm{d}u.$$

According to (4.1), we calculate the derivative of V along the solutions of (2.4)

$$\dot{V}(t) = (b+\gamma)I(t)\left(\frac{\beta\mathrm{e}^{-b\omega}}{b+\gamma}\frac{S(t)}{1+\alpha S(t)} - 1\right). \tag{4.2}$$

Since $R_* > 1$, we easily see that $I^* > 0$, and there exists sufficiently small $\epsilon > 0$ such that

$$\frac{\beta\mathrm{e}^{-b\omega}}{b+\gamma}\frac{\delta_1}{1+\alpha\delta_1} > 1, \tag{4.3}$$

where $\delta_1 = \frac{b}{b+\beta I^*}\frac{(1-\theta)(1-\mathrm{e}^{-(b+\beta I^*)T})}{1-(1-\theta)\mathrm{e}^{-(b+\beta I^*)T}} - \epsilon$. We claim that for any $t_0 > 0$, it is impossible that $I(t) < I^*$ for all $t \geq t_0$. Suppose that the claim is not valid. Then there is a $t_0 > 0$ such that $I(t) < I^*$ for all $t \geq t_0$. It follows from the first equation of (2.4), that for $t \geq t_0$,

$$\begin{aligned}\dot{S}(t) &> b - bS(t) - \beta I^* S(t)\\ &= b - (b+\beta I^*)S(t)\end{aligned}$$

Consider the following comparison impulsive system for $t \geq t_0$,

$$\begin{cases}\dot{u}(t) = b - (b+\beta I^*)u(t), & t \neq kT,\\ u(t^+) = (1-\theta)u(t^-), & t = kT,\end{cases} \tag{4.4}$$

By Lemma 2.2, we obtain that

$$\tilde{u}_e(t) = \frac{b}{b+\beta I^*} + \left(u^* - \frac{b}{b+\beta I^*}\right)\mathrm{e}^{-(b+\beta I^*)(t-kT)},$$
$$kT < t \leq (k+1)T,$$

is the unique positive periodic solutions of (4.4), which is globally asymptotically stable, where

$$u^* = \frac{b}{b+\beta I^*}\frac{(1-\theta)(1-\mathrm{e}^{-(b+\beta I^*)T})}{1-(1-\theta)\mathrm{e}^{-(b+\beta I^*)T}}.$$

Let $(S(t), I(t))$ be the solution of system (2.4) with initial values (2.5) and $S(0^+) = \bar{S}_0 > 0$, $u(t)$ be the solution of system (4.4) with initial value $u(0^+) = \bar{S}_0$. By comparison theorem for impulsive differential equation, we know that, there exists $t_1 (> t_0 + \omega)$ such that the following inequality

holds for $t \geq t_1$

$$S(t) > \tilde{u}_e(t) - \epsilon.$$

Thus,

$$S(t) > u^* - \epsilon = \delta_1 \quad \text{for} \quad t \geq t_1. \tag{4.5}$$

By (4.2), (4.3) and (4.5), we have

$$\dot{V}(t) > (b+\gamma)I(t) \times \left(\frac{\beta e^{-b\omega}}{b+\gamma}\frac{\delta_1}{1+\alpha\delta_1} - 1\right) > 0 \quad \text{for} \quad t \geq t_1. \tag{4.6}$$

Set

$$I_l = \min_{t\in[t_1,t_1+\omega]} I(t).$$

We will show that $I(t) \geq I_l$ for all $t \geq t_1$. Suppose the contrary. Then there is a $T_0 \geq 0$ such that $I(t) \geq I_l$ for $t_1 \leq t \leq t_1+\omega+T_0$, $I(t_1+\omega+T_0) = I_l$ and $\dot{I}(t_1+\omega+T_0) \leq 0$. However, the second equation of system (2.4) and (4.5) imply that

$$\begin{aligned}\dot{I}(t_1+\omega+T_0) &\geq \left(\beta e^{-b\omega}\frac{S(t_1+T_0)}{1+\alpha S(t_1+T_0)} - (b+\gamma)\right) I_l \\ &> (b+\gamma)\left(\frac{\beta e^{-b\omega}}{b+\gamma}\frac{\delta_1}{1+\alpha\delta_1} - 1\right) I_l > 0,\end{aligned}$$

This is a contradiction. Thus, $I(t) \geq I_l$ for all $t \geq t_1$. As a consequence, (4.6) leads to

$$\dot{V}(t) > (b+\gamma)\left(\frac{\beta e^{-b\omega}}{b+\gamma}\frac{\delta_1}{1+\alpha\delta_1} - 1\right) I_l \quad \text{for} \quad t \geq t_1,$$

which implies that as $t \to \infty$, $V(t) \to \infty$. This contradicts $V(t) \leq 1 + \beta e^{-b\omega}$. Hence, the claim is proved.

By the claim, we are left to consider two cases. First, $I(t) \geq I^*$ for t large enough. Second, $I(t)$ oscillates about I^* for t large enough. Define

$$q = \min\left\{\frac{I^*}{2}, q^*\right\} \quad \text{and} \quad q^* \triangleq I^* e^{-(b+\gamma)\omega}.$$

We hope to show that $I(t) \geq q$ for t large enough. The conclusion is evident in the first case. For the second case, let $t^* > 0$ and $\xi > 0$ satisfy

$$I(t^*) = I(t^*+\xi) = I^*,$$

and

$$I(t) < I^* \quad \text{for} \quad t^* < t < t^*+\xi,$$

where t^* is sufficiently large such that

$$S(t) > \delta_1 \quad \text{for} \quad t^* < t < t^*+\xi.$$

$I(t)$ is uniformly continuous since the positive solutions of (2.4) are ultimately bounded and $I(t)$ is not effected by impulses. Hence, there is a $\lambda (0 < \lambda < \omega$, and λ is independent of the choice of t^*) such that $I(t) > \frac{I^*}{2}$ for $t^* \leq t \leq t^*+\lambda$. If $\xi \leq \lambda$, there is nothing to prove. Let us consider the case where $\lambda < \xi \leq \omega$, since $\dot{I}(t) > -(b+\gamma)I(t)$, and $I(t^*) = I^*$, it is obvious that $I(t) \geq q$ for $t^* < t < t^*+\lambda$. If $\xi > \omega$, by the second equation of (2.4), we obtain $I(t) \geq q$ for $t \in [t^*, t^*+\omega]$. Then, proceeding exactly as the proof for above claim, we see that $I(t) \geq q$ for $t \in [t^*+\omega, t^*+\xi]$. Since this kind of interval $[t^*, t^*+\xi]$ is chosen in an arbitrary way (we only need t^* to be large), we conclude that $I(t) \geq q$ for all large t in the second case. In view of our above discussions, the choices of q is independent of the positive solution, and we have proved that any positive solution of (2.4) satisfies $I(t) \geq q$ for sufficiently large t. The proof of Theorem 4.1 is complete. □

Remark. Denote

$$\theta_* = 1 - \frac{(b+\gamma)e^{bT}}{(\beta e^{-b\omega} - \alpha(b+\gamma))(e^{bT}-1) + b + \gamma}$$

and

$$\omega_* = -\frac{1}{b}\ln\left[\frac{b+\gamma}{\beta}\left(\frac{1-(1-\theta)e^{-bT}}{(1-\theta)(1-e^{-bT})} + \alpha\right)\right].$$

It follows Theorem 4.1 that the disease is uniformly persistent provided that $\theta < \theta_*$ or $\omega < \omega_*$.

Theorem 4.2. *System (2.4) is permanent provided that* $R_* > 1$.

Proof. Denote $(S(t), I(t))$ be any solution of system (2.4). From the first equation of system (2.4), we have

$$\dot{S}(t) \geq b - (b+\beta)S(t).$$

By the similar arguments as those in the proof of Theorem 3.1, we have that

$$\lim_{t\to\infty} S(t) \geq p, \tag{4.7}$$

where $p = \frac{b}{b+\beta}\frac{(1-\theta)(1-e^{-(b+\beta)T})}{1-(1-\theta)e^{-(b+\beta)T}} - \epsilon_1$ ($\epsilon_1 > 0$ is sufficiently small).

We let $\Omega_0 = \{(S, I) | p \leq S, q \leq I, S+I \leq 1\}$. From Theorem 4.1 and inequality (4.7), we know that the set Ω_0 is a global attractor in Ω, and of course, every solution of system (2.4) with initial conditions (2.5) will eventually enter and remain in region Ω_0. Therefore, system (2.4) is permanent. The proof of Theorem 4.2 is complete. □

From Theorem 4.2, we also easily obtain the following result.

Corollary 4.1. *Assume that* $\theta < \theta_*$ *or* $\omega < \omega_*$. *Then system (2.4) is permanent.*

5. Conclusion

We have considered an SEIRS epidemic model with time delays and pulse vaccination. We have shown that $\theta < \theta_*$ or $\omega < \omega_*$ implies that the disease will be uniformly persistent, whereas $\theta > \theta^*(\theta_* < \theta^*)$ or $\omega > \omega^*(\omega_* < \omega^*)$ implies that the disease will fade out. We have also established sufficient condition for the permanence of the epidemic model. Our results indicate that a long latent period of the disease will lead to eradication of the disease.

In this paper, we have only discussed two cases: (*i*) $\theta > \theta^*$ (or $\omega > \omega^*$); (*ii*) $\theta < \theta_*$ (or $\omega < \omega_*$). But for $\theta \in [\theta_*, \theta^*]$ (or $\omega \in [\omega_*, \omega^*]$), the dynamical behavior of model (2.4) has not been studied, and the threshold parameter for the vaccination rate (or the latent period of the disease) between the extinction of the disease and the uniform persistence of the disease has not been obtained. These issues will be considered in our future research.

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