ON A DELAYED EPIDEMIC MODEL WITH NON-INSTANTANEOUS IMPULSES

Dedicated to professor Tomás Caraballo on the occasion of his 60th birthday

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Abstract. We introduce a non-instantaneous pulse vaccination model. Non-instantaneous impulsive nonlinear differential equations provide an adequate biomathematical model of some medical problems. In this paper we study some basic properties such as the attractiveness of the infection-free periodic solution and the permanence of some sub-population for a vaccine model where a constant fraction of the susceptible population is vaccinated in some periodic way. Our model is a system of nonlinear differential equations with impulses.

1. Introduction. In classical epidemiological models, for example [7, 9], the total population \( N \) is usually divided into three groups, susceptible \( (S) \), infected \( (I) \) and recovered \( (R) \). This is the traditional SIR model,

\[
\begin{align*}
S'(t) &= -bS(t)I(t) \\
I'(t) &= bS(t)I(t) - aI(t) \\
R'(t) &= aI(t),
\end{align*}
\]

(1)

where \( b \) is the transmission contact rate and \( a \) is the recovery rate. In addition, \( S(t) + I(t) + R(t) \) is assumed to be constant.

One variant is to introduce a new group into the population. It is the group of individuals that carries the disease but does not show symptoms because the disease is in the incubation period. This group is called exposed \( (E) \).

A strategy to control infectious diseases is vaccination. The question we can ask is how many individuals within the population need to be vaccinated in order to prevent an epidemic. A vaccination campaign is usually started late, when the
disease is already in the population. The strategy that is often used is constant vaccination. Another strategy, called Pulse Vaccination Strategy (PVS), has been revealed adequate against some diseases (see [17]). It consists of periodic repetitions of impulsive vaccinations in a population. This method is based on performing periodic vaccinations in a population. A constant fraction of susceptible people is vaccinated in each vaccination period.

Impulses are usually assumed to be instantaneous due to the abrupt nature of the changes in the state of the system. However, in some real biological medical problems, the change takes a very short time and hence the state of the system is not modified instantly or in an impulsive manner, but in a non-instantaneous way. Non-instantaneous impulsive differential equations were introduced by Hernández and O'Regan in [12] motivated by the study of the hemodynamical equilibrium of a human being. For example, the introduction of a drug or a vaccine and the absorption for the body is a gradual process, then one is forced to consider the vaccine as a non-instantaneous impulse since it starts abruptly but remains active on a finite interval of time. Some recent results on non-instantaneous impulsive differential equations can be found in [1, 3, 4, 11, 23, 20, 24, 6, 14] and in monograph [2]. Further technical details are given in Section 2.

The paper is organized as follows: First, we introduce some classical models and the new model subjected to non-instantaneous impulses. In Section 3 some basic properties of the model are presented. Then it is shown the global attractiveness of the infection-free periodic solution and the permanence of the infected population. Some numerical simulations are presented to reveal the interest of our model. Finally, we present some conclusions in the last section. Some proofs, due to their technical difficulties, are included as an Appendix.

2. Models. In [8] it was investigated an epidemic model with a latent period of the disease and an immune period of the population. The model is as follows:

\[
\begin{align*}
S'(t) &= bN(t) - bS(t) - \frac{\beta S(t)I(t)}{N(t)} + \gamma I(t - \tau)e^{-b\tau} \\
E(t) &= \int_{t-\omega}^{t} \frac{\beta S(u)I(u)}{N(u)} e^{b(t-u)} du \\
I'(t) &= \frac{\beta S(t - \omega)I(t - \omega)}{N(t - \omega)} e^{-b\omega} - (b + \gamma)I(t) \\
R(t) &= \int_{t-\tau}^{t} \gamma I(u)e^{-b(t-u)} du,
\end{align*}
\]

where \(b\) is the natural birth rate and death rate of the population, \(\beta\) is average number of adequate contacts of an infectious individuals per unit time, \(\gamma\) is the recovery rate of infectious individuals, \(\omega\) is the latent period of the disease and \(\tau\) is the immune period of the population. All coefficients are assumed to be positive constants.

We now recall a model very similar to the previous one. In [10] the Pulse Vaccination Strategy was introduced in a model identical to (2). We consider a very
similar model. We take $Z^+ = \mathbb{N} \cup \{0\}$.

\[
\begin{align*}
S'(t) &= b - bS(t) - \frac{\beta S(t)I(t)}{1 + \alpha S(t)} + \gamma I(t - \tau)e^{-\beta \tau} \\
E(t) &= \int_{t-\tau}^{t} \frac{\beta S(u)I(u)}{1 + \alpha S(t)} e^{-b(t-u)} du \\
I'(t) &= \frac{\beta e^{-b\omega}S(t-\omega)I(t-\omega)}{1 + \alpha S(t-\omega)} - (b + \gamma)I(t) \\
R(t) &= \int_{t-\tau}^{t} \gamma I(u)e^{-b(t-u)} du \\
S(t^+) &= (1 - \theta)S(t^-) \\
E(t^+) &= E(t^-) \\
I(t^+) &= I(t^-) \\
R(t^+) &= R(t^-) + \theta S(t^-)
\end{align*}
\]

(3)

where $\theta \in (0, 1)$ denotes the proportion of those vaccinated satisfactorily.

Incidence rate plays a very important role in the research of epidemiological models. In most epidemic models, bilinear incidence rate $\beta SI$ and standard incidence rate $\beta SI/N$ are used. In this model, the incidence rate is supposed to be saturated with the susceptible population, of the form $\beta SI/(1 + \alpha S)$, where $\alpha$ is called saturation and it is a positive constant.

We assume that the total population is $N(t) = S(t) + E(t) + I(t) + R(t) = 1$ for all $t$. It suffices to take initial conditions verifying the equations and $N(0) = 1$. To study this problem, we see that neither $E$ nor $R$ appears in the first and third equations. Therefore, instead of studying the system (3), we study the following subsystem

\[
\begin{align*}
S'(t) &= b - bS(t) - \frac{\beta S(t)I(t)}{1 + \alpha S(t)} + \gamma I(t - \tau)e^{-\beta \tau} \\
I'(t) &= \frac{\beta e^{-b\omega}S(t-\omega)I(t-\omega)}{1 + \alpha S(t-\omega)} - (b + \gamma)I(t) \\
S(t^+) &= (1 - \theta)S(t^-) \\
I(t^+) &= I(t^-) \\
& t = kT, k \in Z^+.
\end{align*}
\]

(4)

A similar model was considered in [16]. We study the previous model under the assumption that the impulses are non-instantaneous, that is,

\[
\begin{align*}
S'(t) &= b - bS(t) - \frac{\beta S(t)I(t)}{1 + \alpha S(t)} + \gamma I(t - \tau)e^{-\beta \tau}, \quad t \in [kT + p, (k + 1)T) \\
I'(t) &= \frac{\beta e^{-b\omega}S(t-\omega)I(t-\omega)}{1 + \alpha S(t-\omega)} - (b + \gamma)I(t), \quad t \neq kT, k \in Z^+ \\
S(t) &= g(t, S(kT)), \quad t \in [kT, kT + p), \ k \in Z^+ \\
I(t^+) &= I(t^-), \quad t = kT, k \in Z^+.
\end{align*}
\]

(5)

with $0 < p < T$ and $g \in \mathcal{C}([0, \infty) \times [0, 1], [0, 1])$, $g(\cdot, u)$ $T$-periodic for all $u \in [0, 1]$, $g(T, u) = u$, $g(T + p, u) = (1 - \theta)u$, $g(t, u) \in [(1 - \theta)g(T, u), g(T, u)]$ and $g$ monotonically decreasing on the second variable when $t \in [kT, kT + p)$. We shall refer to all of the above assumptions on $g$ as condition (g).
We will give a brief description of the solution \((S(t), I(t))\) of (5) with initial conditions. The function \(I(t)\) is continuous, because it verifies the differential equation outside the points \(t = kT\) and \(I(kT^+) = I(kT^-)\). The function \(S(t)\) is also continuous, and

- on the interval \([0, p]\), \(S(t)\) satisfies \(S(t) = g(t, S(0))\), that is, \(S\) is completely determined by the function \(g\) and the value \(S(0)\), which are known data.
- on the interval \([p, T]\), \(S(t)\) satisfies the differential equation with the initial condition \(S(p) = g(p, S(0))\).
- on the interval \([T, T + p]\), \(S(t)\) satisfies \(S(t) = g(t, S(T))\), similarly to the first step.
- on the interval \([T + p, 2T]\), \(S(t)\) satisfies the differential equation with the initial condition \(S(T + p) = g(T + p, S(T))\).

and so on.

Graphically this means that \(S(t)\) follows the following behavior:

![Graph](image)

The solution satisfies the equation with \(g\) on the red intervals and the differential equation on the blue intervals.

An example of a function \(g\) verifying condition \((g^*)\) is

\[
g(t, u) = \begin{cases} 
  u - \frac{\theta(t - kT)u}{p}, & t \in [kT, kT + p), \\
  u + \frac{\theta(t - (k + 1)T)u}{T - p}, & t \in [kT + p, (k + 1)T),
\end{cases}
\]

The study of the local stability of differential equations with delays and impulses (instantaneous or non-instantaneous) is difficult.

For some results on the theory of impulsive differential equations we refer the reader to [5, 18, 15] and for delay differential equations to [19].

Sufficient conditions will be given for the disease to disappear. In addition, other conditions will be provided guaranteeing the permanence of the disease.

3. Preliminaries. The initial conditions for problems with delays are functions, that is, the initial conditions are

\((\phi_1, \phi_2) : [-l, 0] \rightarrow [0, \infty) \times [0, \infty)\)

continuous, with \(l = \max\{\tau, \omega\}\). A solution of system (5) is a continuous function verifying the equation, and for fixed initial conditions this solution is unique.

**Lemma 3.1.** Let \((S(t), I(t))\) be a solution of the system (5) with non-negative initial conditions \((\phi_1, \phi_2)\). Then \(S(t), I(t) \geq 0\) \(\forall t \geq 0\), that is, the set

\[\Omega = \{(S, I) \in \mathbb{R}^2 : S \geq 0, I \geq 0\}\]

is positively invariant.

**Proof.** Let \((S(t), I(t))\) be a solution of (5) with non-negative initial conditions \((\phi_1, \phi_2)\).

- If \(S(0) = 0\), then \(S'(0) = b + \gamma I(t - \tau)e^{-b\tau} > 0\).
- If \(I(0) = 0\), then \(I'(0) = \frac{\beta e^{-b\phi_1(-\omega)}\phi_2(-\omega)}{1 + \alpha \phi_1(-\omega)} \geq 0\).

Then it is proved that \(\Omega\) is positively invariant. \(\square\)
Corollary 1. If the initial conditions verify $N(0) = 1$.

**Definition 3.2.** The system (5) is uniformly persistent if there exists $\nu > 0$, independent of the initial conditions, such that any solution $(S(t), I(t))$ of the system with non-negative initial conditions and $S(0), I(0) > 0$ verifies
\[ \liminf_{t \to \infty} S(t) \geq \nu \quad \text{and} \quad \liminf_{t \to \infty} I(t) \geq \nu. \]

**Lemma 3.3.** Consider the system
\[
\begin{align*}
u'(t) &= a - bu(t), \quad t \in [kT + p, (k + 1)T), \quad k \in Z^+ \\
u(t) &= g(t, u(kT)), \quad t \in [kT, kT + p), \quad k \in Z^+,
\end{align*}
\]
with $g \in C([0, \infty) \times [0, 1], [0, 1])$ verifying condition $(g^*)$, $a$ and $b$ positive. Then there exists a unique positive $T$-periodic solution which is globally asymptotically stable.

**Lemma 3.4.** Consider the delay differential equation $x'(t) = a_1 x(t - \omega) - a_2 x(t)$, with $a_1, a_2, \omega > 0$ and $\phi : [-\omega, 0] \to (0, \infty)$ an initial condition. If a function $x : [-\omega, +\infty) \to \mathbb{R}$ is a solution, then
\[ \begin{align*} &\cdot \text{ If } a_1 < a_2, \text{ then } \lim_{t \to \infty} x(t) = 0. \\
&\cdot \text{ If } a_2 < a_1, \text{ then } \lim_{t \to \infty} x(t) = \infty. \end{align*} \]

The proof of this result can be found on [22].

4. **Global attractiveness of infection-free periodic solution.** Depending on the value of the parameters we show that the infection-free solution is an attractor. Indeed, suppose that there are no infected people, that is, $I(t) = 0$ $\forall t \geq -l$. Then system (5) becomes
\[
\begin{align*}
S'(t) &= b - hS(t), \quad t \in [kT + p, (k + 1)T), \quad k \in Z^+ \\
S(t) &= g(t, S(kT)), \quad t \in [kT, kT + p), \quad k \in Z^+.
\end{align*}
\]
By Lemma 3.3, we know that there exists a positive and periodic solution which is globally asymptotically stable. We denote that solution by $S_c(t)$.

**Theorem 4.1.** The infection-free periodic solution $(S_c, 0)$ is globally attractive provided that $R^* < 1$, where
\[ R^* = \frac{(\beta e^{-bw} - \alpha (b + \gamma)) \left(1 + \frac{\gamma}{b} e^{-b\tau} \right) (1 - e^{-b(T-p)})}{(1 - (1 - \theta)e^{-b(T-p)}) (b + \gamma)}. \]

The proof of this result is given on the Appendix. Denote
\[ \theta^* = 1 - \frac{(b + \gamma)e^{b(T-p)} - (\beta e^{-bw} - \alpha (b + \gamma)) \left(1 + \frac{\gamma}{b} e^{-b\tau} \right) (e^{b(T-p)} - 1)}{b + \gamma}, \]
\[ \omega^* = -\frac{1}{b} \ln \left[ \frac{b + \gamma}{\beta} \left(1 - (1 - \theta)e^{-b(T-p)} \right) \left(1 + \frac{\gamma}{b} e^{-b\tau} \right) (1 - e^{-b(T-p)}) + \alpha \right]. \]

**Corollary 1.** If $\omega > \omega^*$ or $\theta > \theta^*$, then $(S_c, 0)$ is globally attractive.
5. Permanence of the infected population. If a factor depending on the parameters of the system is large, then we show that the infected population remains above some lower threshold.

Definition 5.1. We will say that a system is permanent if there exists \( m, M \) such that for any solution \( x \) and \( t \) sufficiently large then \( 0 < m \leq x(t) \leq M \).

Denote

\[
R_* = \frac{(\beta e^{-b\omega} - \alpha (b + \gamma)) (1 - \theta) (1 - e^{-b(T - p)})}{(b + \gamma) (1 - (1 - \theta) e^{-b(T - p)})} \quad \text{and} \quad I^* = \frac{b}{\beta} (R_* - 1).
\]

Theorem 5.2. Suppose that \( R_* > 1 \). Then there is a positive constant \( q > 0 \) such that each positive solution \((S(t), I(t))\) of (5) satisfies \( I(t) \geq q \) for \( t \) large enough.

The proof of this result can be found on the Appendix.

Theorem 5.3. If \( R_* > 1 \) then the system is permanent.

Proof. Let \((S(t), I(t))\) be a solution of the system. If \( t \in [kT + p, (k + 1)T] \) for some \( k \), then we have that

\[
S'(t) = b - bS(t) - \frac{\beta S(t)I(t)}{1 + \alpha S(t)} + \gamma I(t - \tau)e^{-b\tau} > b - bS(t) - \beta S(t)I(t) > b - bS(t) - \beta S(t)
\]

Using the comparison theorem in a similar way as the proof of Theorem 4.1 we have that \( \liminf_{t \to \infty} S(t) \geq \kappa \), with

\[
\kappa = \frac{b}{b + \beta} \frac{(1 - \theta) (1 - e^{-(b + \beta)(T - p)})}{1 - (1 - \theta) e^{-b(T - p)}} - \varepsilon_1,
\]

and \( \varepsilon_1 > 0 \) small. Then we conclude that for any solution \((S(t), I(t))\) of (5) we have \( S(t) \geq \kappa, I(t) \geq q \) for \( t \) large enough.

Consider \( \theta_* \) and \( \omega_* \) given by

\[
\theta_* = 1 - \frac{(b + \gamma)e^{b(T - p)}}{(\beta e^{-b\omega} - \alpha (b + \gamma)) (e^{b(T - p)} - 1) + (b + \gamma)},
\]

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

As a consequence of the previous results, if \( \theta < \theta_* \) or \( \omega < \omega_* \), then the system is permanent.

6. Simulations. In this section, using Mathematica, we make two numerical simulations of the model (5). These simulations support the results obtained in previous sections. We plot the numerical solutions of the model (5) under different parameters.

On the first figure, we take \( \beta = 14, b = 3.1, \omega = 0.3, \tau = 0.2, \alpha = 0.2, \gamma = 4.5, \theta = 0.3, p = 1, T = 10 \) with initial conditions \((\phi_1(t), \phi_2(t)) = (0.7, 0.09)\). Then \( S(0) + E(0) + I(0) + R(0) \approx 1 \) and \( R^* < 1 \). Theorem 4.1 implies that the infection-free solution is an attractor, i.e., \( I(t) \to 0 \) as \( t \to \infty \). The numerical solution \((S(t), I(t))\) of the model (5) has been plotted in Figure 1, where the vertical lines represent the time where the non-instantaneous impulses occur.
Figure 1. Simulation with $R^* < 1$, infection-free solution

Figure 2. Simulation with $R_* > 1$, permanence of infected population

On the second figure, we take $\beta = 14, b = 1, \omega = 0.5, \tau = 0.4, \alpha = 0.2, \gamma = 0.2, \theta = 0.1, p = 1, T = 10$ with initial conditions $(\phi_1(t), \phi_2(t)) = (0.63, 0.09)$. Then $S(0) + E(0) + I(0) + R(0) \approx 1$ and $R_* > 1$. Theorems 5.2 and 5.3 imply that the infected population remains above a certain threshold. The numerical solution $(S(t), I(t))$ has been plotted in Figure 2.

Remark 1. We note that we have used the initial condition $(\phi_1(t), \phi_2(t))$ in both figures.

7. Conclusions. In some processes such as the introduction of a substance in the blood stream, an impulsive action starts abruptly and stays active during a short time but still a finite time interval. The mathematical formulation of this phenomena leads to non-instantaneous impulses. We have developed a biomathematical model of non-instantaneous impulsive vaccination and study the qualitative properties of the model such as the attractiveness of the infection-free periodic solution depending of the values of some parameters associated to the epidemic model as
well as the permanence of some groups of the population (susceptible, exposed, infected, recovered). We have shown that:

| $\theta < \theta_*$ | $\theta_* \leq \theta \leq \theta^*$ | $\theta^* < \theta$ |
|---------------------|---------------------------------|----------------------|
| $\omega < \omega_*$ | $\omega_* \leq \omega \leq \omega^*$ | $\omega^* < \omega$ |

Permanence | Infection-free attractiveness

In particular, the results indicate that a large latent period of the disease ($\omega$) or a large percentage of vaccinated population ($\theta$) imply the eradication of the disease.

There are two main directions of further study. Firstly, the study of the qualitative properties of the biomathematical model and secondly the implementation of the model to develop new strategies of vaccination.

The results obtained are a generalization on the results obtained for the instantaneous impulsive model in [10]. In fact, if we take $p = 0$ we recover the results contained there.

**Appendix.**

**Proof of Lemma 3.3.** Fix $k \in \mathbb{Z}^+$. We first solve the differential equation on $[kT + p, (k + 1)T]$. We obtain that the solution is $u(t) = a/b + ce^{-bt}$, with $c \in \mathbb{R}$ a constant to be determined. We want $u(kT + p)$ to be equal $(1 - \theta)u(kT)$. In this case,

$$\frac{a}{b} + ce^{-b(kT+p)} = (1 - \theta)u(kT) \implies ce^{-b(kT+p)} = (1 - \theta)u(kT) - \frac{a}{b}$$

So $c = \left( (1 - \theta)u(kT) - \frac{a}{b} \right) e^{b(kT+p)}$.

Then $u(t) = a/b + [(1 - \theta)u(kT) - a/b] e^{-b(t-(kT+p))}$ when $t \in [kT + p, (k + 1)T]$. We are trying to find $u(t)$ such that $u((k + 1)T) = u(kT)$. We define the map $f(x) = a/b + [(1 - \theta)x - a/b] e^{-b(T-p)}$. Finding $u(kT)$ such that $u((k + 1)T) = u(kT)$ is equivalent to find the fixed points of $f$. Computing the derivative we obtain that $f'(x) = (1 - \theta)e^{-b(T-p)} \in [0, 1)$, so we can assure that $f$ is a contraction and using the contraction mapping principle we know that there exists a unique fixed point $\tilde{x}$, which is globally asymptotically stable. The expression for $\tilde{x}$ is

$$f(x) = x \implies \frac{a}{b} + \left( (1 - \theta)x - \frac{a}{b} \right) e^{-b(T-p)} = x$$

$$\implies \frac{a}{b} + (1 - \theta)xe^{-b(T-p)} - \frac{a}{b}e^{-b(T-p)} = x$$

$$\implies \frac{a}{b} \left( 1 - e^{-b(T-p)} \right) = x - (1 - \theta)e^{-b(T-p)}x = \left( 1 - (1 - \theta)e^{-b(T-p)} \right) x$$

$$\implies x = \frac{a(1 - e^{-b(T-p)})}{b(1 - (1 - \theta)e^{-b(T-p)})} \equiv \tilde{x}$$

We define

$$\tilde{u}(t) = \begin{cases} g(t, \tilde{x}), & t \in [kT, kT + p], k \in \mathbb{Z}^+ \\ \frac{a}{b} + \left( (1 - \theta)\tilde{x} - \frac{a}{b} \right) e^{-b(t-(kT+p))}, & t \in [kT + p, (k + 1)T], k \in \mathbb{Z}^+, \end{cases}$$

which is a positive and $T$-periodic function. Furthermore it is globally asymptotically stable.
Let $x(t)$ be another solution of (6) and suppose $x(0) > \tilde{u}(0)$. We define $y(t) = x(t) - \tilde{u}(t)$ and fix $\varepsilon > 0$. After some calculations we get

$$y(t) = \begin{cases} g(t, (1 - \theta)^k e^{-bk(T-p)} y(0)), & t \in [kT, kT + p), k \in \mathbb{Z}^+ \\ (1 - \theta)^{k+1} e^{-bk(T-p)} e^{-b(t+kT-p)} y(0), & t \in [kT + p, (k + 1)T), k \in \mathbb{Z}^+ \end{cases}$$

We know that $\lim_{u \to 0} g(t, u) = 0$ if $t \in [0, p]$, so there exists $k \in \mathbb{N}$ sufficiently large such that $0 \leq (1 - \theta)^k e^{-bk(T-p)} y(0) < \delta$, so if $k_1 \geq k$ then

$$t \in [k_1T, k_1T + p] \implies g(t, (1 - \theta)^{k_1} e^{-bk_1(T-p)} y(0)) < \varepsilon$$

On the other hand, if $k_1 \geq k$ then

$$(1 - \theta)^{k_1+1} e^{-bk_1(T-p)} y(0) e^{-b(t-k_1T-p)} \leq (1 - \theta)^{k_1} e^{-bk_1(T-p)} y(0) < \delta < \varepsilon$$

So if $t$ is sufficiently large, then $|y(t)| < \varepsilon$.

**Proof of Theorem 4.1.** Consider the function

$$f : \delta \in (0, +\infty) \mapsto \frac{\beta e^{-b\omega \delta}}{1 + \alpha \delta} \in \mathbb{R},$$

which is a strictly increasing and continuous function.

$$R^* < 1 \iff \beta e^{-b\omega h} \left( \frac{1 + \frac{\gamma}{b} e^{-bT}}{1 - (1 - \theta) e^{-b(T-p)}} \right) - \alpha (b + \gamma) \left( \frac{1 + \frac{\gamma}{b} e^{-bT}}{1 - (1 - \theta) e^{-b(T-p)}} \right) < b + \gamma$$

$$\iff \beta e^{-b\omega h} < (b + \gamma)(1 + \alpha h) \iff \beta e^{-b\omega h} h < b + \gamma \iff f(h) < b + \gamma$$

We know that $f(h)$ is less than $b + \gamma$, so there exists $\varepsilon_0 > 0$ such that $f(h + \varepsilon_0) < b + \gamma$. Let $\delta = h + \varepsilon_0$, then

$$\delta = \frac{\left( 1 + \frac{\gamma}{b} e^{-bT} \right) (1 - e^{-b(T-p)})}{1 - (1 - \theta) e^{-b(T-p)}} + \varepsilon_0$$

If $t \in (kT + p, (k + 1)T)$, then

$$S'(t) = b - bS(t) - \frac{\beta S(t) I(t)}{1 + \alpha S(t)} + \gamma I(t - \tau) e^{-brT} \leq b + \gamma e^{-brT} - bS(t).$$

Consider the system

$$\begin{cases} x'(t) = (b + \gamma e^{-brT}) - bx(t), & t \in [kT, kT + (k + 1)T), k \in \mathbb{Z}^+ \\ x(t) = g(t, x(kT)), & t \in [kT, kT + p), k \in \mathbb{Z}^+ \end{cases}$$

(9)
This system has a periodic and positive solution by Lemma 3.3, which is
\[
\tilde{x}(t) = \begin{cases} 
  g(t, \tilde{x}_T) & t \in [kT, kT + p) \\
  1 + \gamma \beta e^{-b\tau} + \left(1 - \theta \right) \tilde{x}_T - 1 - \frac{\gamma \beta e^{-b\tau}}{1 + \alpha S(t)} & t \in [kT + p, (k+1)T).
\end{cases}
\]
Furthermore this solution is globally asymptotically stable, where
\[
\tilde{x}_T = \left(1 + \frac{\gamma \beta e^{-b\tau}}{1 - (1 - \theta)e^{-b(T-p)}} \right) \left(1 - e^{-b(T-p)}\right).
\]

Let \((S(t), I(t))\) be a solution of the system (5) and \(S_0 = S(0)\). We want to prove that \(\delta\) as an upper bound of \(S(t)\) for sufficiently big \(t\).

We choose \(x(t)\) a solution of (9) with \(x(0) = S_0\) as an initial condition. By the comparison theorem, we can say that \(S(t) \leq x(t)\) \(\forall t \geq 0\). Furthermore, \(\tilde{x}\) is a globally asymptotically stable solution, so there exist \(k_1 \in \mathbb{N}\) such that if \(t > k_1 T\), then \(x(t) < \tilde{x}(t) + \varepsilon_0\). Thus \(S(t) < \tilde{x}(t) + \varepsilon_0\) for all \(t > k_1 T\).

The maximum of \(\tilde{x}\) on \([kT, (k+1)T]\) is reached on its endpoints. Then if \(t\) is greater than \(k_1 T\) we have that
\[
S(t) < \tilde{x}(t) + \varepsilon_0 \leq \tilde{x}((k+1)T) + \varepsilon_0 = \delta.
\]

We can deduce that
\[
I'(t) \leq \frac{\beta e^{-b\omega\delta}}{1 + \alpha \delta} I(t - \omega) - (b + \gamma) I(t) \quad \forall t > kT + \omega, k > k_1.
\]
(10)

We consider the problem
\[
y'(t) = \frac{\beta e^{-b\omega\delta}}{1 + \alpha \delta} y(t - \omega) - (b + \gamma) y(t)
\]
(11)

We know \(\frac{\beta e^{-b\omega\delta}}{1 + \alpha \delta} < b + \gamma\). By Lemma 3.4 we have that \(y(t) \to 0\) when \(t\) goes to \(\infty\) for an arbitrary solution.

We take \((S(t), I(t))\) the solution of (5) with initial conditions \((\phi_1, \phi_2)\). We want to prove that \(\lim_{t \to \infty} I(t) = 0\).

Take \(y(t)\) the solution of (11) which is equal to \(I(t)\) on an interval of length \(\omega\) where (10) is verified. By the comparison principle, \(I(t) \leq y(t)\) for all \(t\) sufficiently large. So we have that
\[
\lim \sup_{t \to \infty} I(t) \leq \lim \sup_{t \to \infty} y(t) = 0.
\]

Furthermore, by Lemma 3.1 we know that \(I(t) \geq 0\) for all \(t\) positive, then \(\lim_{t \to \infty} I(t) = 0\). Therefore there exists an integer \(k_2 \in \mathbb{N}\) with \(k_2 > k_1\) and \(k_2 T > k_1 T + \omega\) such that \(I(t) < \varepsilon_0\) for all \(t > k_2 T\).

Finally we prove that \((S_\varepsilon, 0)\) is globally asymptotically stable. For any \(t > k_2 T + \tau\) we have
\[
S'(t) = b - bS(t) - \beta \frac{S(t)}{1 + \alpha S(t)} I(t) + \gamma I(t - \tau) e^{-b\tau}
\geq b - bS(t) - \beta I(t) \geq (b - \beta \varepsilon_0) - bS(t)
\]
\[
S'(t) = b - bS(t) - \beta \frac{S(t)}{1 + \alpha S(t)} I(t) + \gamma I(t - \tau) e^{-b\tau}
\leq b - bS(t) + \gamma I(t - \tau) e^{-b\tau}
\]
Consider the following systems for \( t > k_2 T + \tau \),
\[
\begin{aligned}
  z_1'(t) &= (b - \beta \varepsilon_0) - bz_1(t), \quad t \in [kT + p, (k + 1)T), \ k \in \mathbb{Z}^+ \\
  z_1(t) &= g(t, z_1(kT)), \quad t \in [kT, kT + p), \ k \in \mathbb{Z}^+ \\
  z_2'(t) &= (b + \gamma e^{-br} \varepsilon_0) - bz_2(t), \quad t \in [kT + p, (k + 1)T), \ k \in \mathbb{Z}^+ \\
  z_2(t) &= g(t, z_2(kT)), \quad t \in [kT, kT + p), \ k \in \mathbb{Z}^+.
\end{aligned}
\] (12)

By Lemma 3.3, there exist positive and periodic solutions of the above systems.

Let \( (S, I) \) a solution of (5) and take \( k_3 \) such that \( k_3 T > k_2 T + \tau \). Denote \( S^0 = S(k_3 T) \). Let \( z_1 \) the solution of (12) with \( z_1(k_3 T) = S^0 \) and \( z_2 \) the solution of (13) with \( z_2(k_3 T) = S^0 \). We know:

- \( z_1(t) \leq S(t) \leq z_2(t) \) for \( t > k_3 T \) by the comparison theorem.
- There exists \( k_4 \in \mathbb{N} \) with \( k_4 T > k_2 T + \omega \) such that
  \[
  t > k_4 T \implies \tilde{z}_{1,e}(t) - \varepsilon_0 < z_{1,e}(t) < \tilde{z}_{1,e}(t) + \varepsilon_0, \quad i \in \{1, 2\},
  \]
where \( \tilde{z}_{i,e} \) is the positive and periodic solution given by Lemma 3.3 for (12) and (13).

Using the above properties we know that there exists \( t > k_4 T \) such that

- \( S(t) \leq z_2(t) < \tilde{z}_{2,e}(t) + \varepsilon_0 \).
- \( S(t) \geq z_1(t) > \tilde{z}_{1,e}(t) + \varepsilon_0 \).

As a consequence, if \( t \in [kT + p, (k + 1)T] \) for some \( k \in \mathbb{Z}^+ \), we get
\[
\lim_{\varepsilon_0 \to 0^+} \tilde{z}_{2e}(t) = 1 + \left( 1 - \theta \frac{1 - e^{-b(T - t)}}{1 - \theta e^{-b(T - t)}} - 1 \right) e^{-b(t - (kT + p))} = S_e(t)
\]
\[
\lim_{\varepsilon_0 \to 0^+} \tilde{z}_{1e}(t) = 1 + \left( 1 - \theta \frac{1 - e^{-b(T - t)}}{1 - \theta e^{-b(T - t)}} - 1 \right) e^{-b(t - (kT + p))} = S_e(t)
\]
Furthermore if \( t \notin [kT + p, (k + 1)T] \), then \( z_{1,e}(t) \) depends on \( z_{1,e}(kT) \) for some \( k \). Using the fact that \( g \) is continuous, we can conclude that \( S_e \) is globally asymptotically stable.

Therefore, the infection-free periodic solution \((S_e, 0)\) is globally attractive.

**Proof of Theorem 5.2.** First we have
\[
I'(t) = \frac{\beta e^{-bw} S(t - \omega) I(t - \omega)}{1 + \alpha S(t - \omega)} - (b + \gamma) I(t)
\]
\[
= \frac{\beta e^{-bw} S(t) I(t)}{1 + \alpha S(t)} - (b + \gamma) I(t) - \beta e^{-bw} \left( \frac{S(t) I(t)}{1 + \alpha S(t)} - \frac{S(t - \omega) I(t - \omega)}{1 + \alpha S(t - \omega)} \right)
\]
\[
= I(t) \left( \frac{\beta e^{-bw} S(t)}{1 + \alpha S(t)} - (b + \gamma) \right) - \beta e^{-bw} \frac{d}{dt} \int_{t-\omega}^{t} \frac{S(u) I(u)}{1 + \alpha S(u)} \, du
\]
Let \((S(t), I(t))\) be a positive solution of (5). Define
\[
V(t) = I(t) + \beta e^{-bw} \int_{t-\omega}^{t} \frac{S(u) I(u)}{1 + \alpha S(u)} \, du.
\]
Computing the derivative we get

\[ V'(t) = I'(t) + \beta e^{-bw} \frac{d}{dt} \int_{t-\omega}^{t} \frac{S(u)I(u)}{1 + \alpha S(u)} \, du \]

\[ = I(t) \left( \beta e^{-bw}S(t) + (b + \gamma) \right) - \beta e^{-bw} \frac{d}{dt} \int_{t-\omega}^{t} \frac{S(u)I(u)}{1 + \alpha S(u)} \, du \]

\[ + \beta e^{-bw} \frac{d}{dt} \int_{t-\omega}^{t} \frac{S(u)I(u)}{1 + \alpha S(u)} \, du \]

\[ = I(t) \left( \beta e^{-bw}S(t) + (b + \gamma) \right) = (b + \gamma) I(t) \left( \frac{\beta e^{-bw}S(t)}{b + \gamma} \frac{S(t)}{1 + \alpha S(t)} - 1 \right) \]

Furthermore we know that \( R_* > 1 \) implies \( I^* > 0 \).

Consider the family of functions \( f_a(\delta) = a\delta/(1 + a\delta) \), with \( \delta > 0 \), which depends on the parameter \( a > \alpha \). Each function is strictly increasing because its derivative is positive. We will find the value of \( \delta \) such that \( f_a(\delta) = 1 \).

\[ a \frac{\delta}{1 + a\delta} = 1 \Rightarrow a\delta = 1 + a\delta \Rightarrow (a - \alpha)\delta = 1 \Rightarrow \delta = \frac{1}{a - \alpha}. \]

We want to prove that \( \frac{\beta e^{-bw}}{b + \gamma} \frac{\delta}{1 + a\delta} \) is greater than 1, with

\[ \delta = \frac{b}{b + \beta I^*} \left( 1 - \theta \right) \frac{1 - e^{-(b + \beta I^*)(T-p)}}{1 - (1 - \theta)e^{-(b + \beta I^*)(T-p)}}. \]  \hspace{1cm} (14)

Taking \( a = \frac{\beta e^{-bw}}{b + \gamma} \), we know that \( f_a \left( \frac{1}{a - \alpha} \right) = 1 \).

\[ \frac{1}{a - \alpha} = \frac{b + \gamma}{\beta e^{-bw} - a(b + \gamma)} = \delta^* \]

In order to prove that \( \frac{\beta e^{-bw}}{b + \gamma} \frac{\delta}{1 + a\delta} \) is greater than 1 it suffices to prove that

\[ \frac{b}{b + \beta I^*} \left( 1 - \theta \right) \frac{1 - e^{-(b + \beta I^*)(T-p)}}{1 - (1 - \theta)e^{-(b + \beta I^*)(T-p)}} \]  > \( \delta^* \).

We check that the previous equation is true.

\[ \frac{b}{b + \beta I^*} \left( 1 - \theta \right) \frac{1 - e^{-(b + \beta I^*)(T-p)}}{1 - (1 - \theta)e^{-(b + \beta I^*)(T-p)}} \]

\[ = \frac{1}{R_*} \left( 1 - \theta \right) e^{-bR_*(T-p)(1 - \theta)} (1 - \theta) \left( 1 - e^{-(bR_*)(T-p)} \right) \]

\[ = \frac{(b + \gamma) (1 - (1 - \theta)e^{-b(T-p)}) (1 - \theta) (1 - e^{-(bR_*)(T-p)})}{(\beta e^{-bw} - a(b + \gamma))(1 - (1 - \theta)e^{-(bR_*)(T-p)}) \left( 1 - \theta \right) (1 - \theta) e^{-(bR_*)(T-p)} \} \]

\[ = \frac{\beta e^{-bw} - a(b + \gamma)}{(1 - (1 - \theta)e^{-(bR_*)(T-p)}) \left( 1 - \theta \right) (1 - \theta) e^{-(bR_*)(T-p)})} \]

\[ = \delta^* \]

\[ h \]
If \( h \) is greater than 1, then the result will be proved.

\[
\begin{align*}
    h &= 1 - e^{-(bR_\ast)(T-p)} - (1-\theta)e^{-b(T-p)} + (1-\theta)e^{-b(T-p)}e^{b(T-p)R_\ast} \\
    &= 1 - e^{-(b(T-p))R_\ast} - e^{-b(T-p)} + \theta e^{-b(T-p)} + (1-\theta)e^{-b(T-p)(1+R_\ast)} \\
    &= \frac{\tilde{h} + \theta e^{-b(T-p)}}{\tilde{h} + e^{-b(T-p)R_\ast}} = \frac{\tilde{h} + c_1}{\tilde{h} + c_2}
\end{align*}
\]

We know that this last quantity is greater than 1 because \( c_1 \) is greater than \( c_2 \) \((R_\ast \text{ is greater than } 1)\).

It is proved that \( \frac{\beta e^{-bw}}{x+y} \frac{\delta}{1+\delta} \) is greater than 1, with \( \delta \) given by (14). There exists \( \varepsilon > 0 \) such that \( f_u(\delta - \varepsilon) > 1 \) because \( f_u \) is continuous. Denote \( \delta_1 = \delta - \varepsilon \).

We want to prove that for any \( t_0 > 0 \), it is impossible that \( I(t) < I^* \) for all \( t \geq t_0 \). Suppose that there exists \( t_0 > 0 \) such that \( I(t) < I^* \) for all \( t \geq t_0 \).

Given \( t \geq t_0 \), if \( t \in [KT + p, (k+1)T] \) for some \( k \), then

\[
S'(t) = b - bS(t) - \frac{\beta S(t)I(t)}{1 + \alpha S(t)} + \gamma I(t-\tau)e^{-br} > b - bS(t) - \beta \frac{S(t)}{1 + \alpha S(t)} I^*
\]

\[
\geq b - bS(t) - \beta S(t)I^* = b - (b + \beta I^*)S(t)
\]

Consider the non-instantaneous impulsive differential equation

\[
\begin{align*}
    u'(t) &= b - (b + \beta I^*)u(t), & t \in [KT + p, (k+1)T) \\
    u(t) &= g(t, u(KT)), & t \in [KT, KT + p).
\end{align*}
\]

This system has a positive and periodic solution \( \tilde{u}_\varepsilon \), which is globally asymptotically stable as an application of Lemma 3.3.

Let \( k_5 \in \mathbb{N} \) such that \( k_5T > t_0 \), \( S_0 = S(k_5T) > 0 \) and \( u(t) \) a solution of (15) with \( u(k_5T) = S_0 \). Then \( u(t) \leq S(t) \) for all \( t \) greater than \( k_5T \) by the comparison theorem. There exists \( t_1 > 0 \), \( t_1 > t_0 + \omega \) such that

\[
t > t_1 \implies \tilde{u}_\varepsilon(t) - \varepsilon < u(t) < \tilde{u}_\varepsilon(t) + \varepsilon,
\]

because \( \tilde{u}_\varepsilon \) is global asymptotically stable. Then we have that if \( t \) is greater than \( t_1 \), then \( S(t) > \tilde{u}_\varepsilon(t) - \varepsilon \). The minimum of \( \tilde{u}_\varepsilon \) on \([KT, (k+1)T]\) is reached on \( KT + p \), and that value is \((1-\theta)u_T\), where \( u_T \) is given by Lemma 3.3. If \( t > t_1 \) then

\[
S(t) > (1-\theta)u_T - \varepsilon = \delta_1.
\]

Then we can ensure that if \( t \) is greater than \( t_1 \) we have

\[
V'(t) > (b + \gamma)I(t) \left( \frac{\beta e^{-bw}}{b + \gamma} \frac{\delta_1}{1 + \alpha \delta_1} - 1 \right)
\]

Take \( I_t = \min\{I(t) : t \in [t_1, t_1 + \omega]\} \). We know that \( I_t > 0 \) because \((S(t), I(t))\) is a positive solution. We will prove that \( t > t_1 \implies I(t) \geq I_t \). Suppose it is false. Then there exists \( T_0 \geq 0 \) such that

\[
I(t) > I_t \quad \forall t \in [t_1, t_1 + \omega + T_0], \quad I(t_1 + \omega + T_0) = I_t, \quad I'(t_1 + \omega + T_0) \leq 0
\]
However,
\[
I'(t_1 + \omega + T_0) = \frac{\beta e^{-b\omega}S(t_1 + T_0)I(t_1 + T_0) - (b + \gamma)I(t_1 + \omega + T_0)}{1 + \alpha S(t_1 + T_0)} \\
\geq \frac{\beta e^{-b\omega}S(t_1 + T_0)I_t - (b + \gamma)I_t}{1 + \alpha S(t_1 + T_0)} = \left( \frac{\beta e^{-b\omega}S(t_1 + T_0)}{1 + \alpha S(t_1 + T_0)} - (b + \gamma) \right) I_t \\
= \left( \frac{\beta e^{-b\omega}S(t_1 + T_0)}{b + \gamma + 1 + \alpha S(t_1 + T_0)} - 1 \right) (b + \gamma) I_t \\
\geq \left( \frac{\beta e^{-b\omega}}{b + \gamma + 1 + \alpha S} - 1 \right) (b + \gamma) I_t > 0
\]

We arrive at a contradiction, so \( t > t_1 \) implies \( I(t) \geq I_t \). Then \( V'(t) > (b + \gamma)I_t \left( \frac{\beta e^{-b\omega}}{b + \gamma + 1 + \alpha S} - 1 \right) > 0 \) for all \( t \) greater than \( t_1 \). We can conclude that \( \lim_{t \to \infty} V(t) = +\infty \). But
\[
V(t) = I(t) + \beta e^{-b\omega} \int_{t-\omega}^t S(u)I(u) \, du \leq 1 + \beta e^{-b\omega} \int_{t-\omega}^t 1 \, du = 1 + \beta e^{-b\omega} \omega,
\]
arriving at a contradiction. Therefore we have just proved that
\[
I(t) \not\in I^* \quad \forall t \geq t_0.
\]

We have to prove that there exists \( q > 0 \) such that \( I(t) \geq q \) for \( t \) large enough. We have to consider two cases.

- There exists \( \tilde{t} > 0 \) such that \( t > \tilde{t} \implies I(t) \geq I^* \).
- \( I(t) \) oscillates about \( I^* \) for \( t \) large enough.

Define \( q = \min \{ I^*/2, q^* \} \), with \( q^* = I^*e^{-(b+\gamma)\omega} \). We will prove that \( I(t) \geq q \) for \( t \) large enough. The first case is obvious. We will check the second.

Let \( t^* \) and \( \xi \) be positive numbers such that \( I(t^*) = I^* = I(t^* + \xi), \ t \in (t^*, t^* + \xi) \implies I(t) < I^* \) and \( S(t) > \delta_1 \ \forall t \in (t^*, t^* + \xi) \).

\[
|I'(t)| = \frac{\beta e^{-b\omega}S(t-\omega)I(t-\omega)}{1 + \alpha S(t-\omega)} + (b + \gamma)I(t) \leq \beta e^{-b\omega} + (b + \gamma).
\]

As a consequence we have that \( I(t) \) is uniformly continuous. Hence, there is a \( \lambda > 0 \), \( \lambda < \omega \), \( \lambda \) independent of \( t^* \) such that \( t \in [t^*, t^* + \lambda] \implies I(t) > I^*/2 \). We study the following cases.

- \( \xi \leq \lambda \). There is nothing to prove, \( I(t) > I^*/2 \geq q \ \forall t \in [t^*, t^* + \xi] \).
- \( \lambda < \xi \leq \omega \). We know that \( I'(t) \geq -(b + \gamma)I(t) \) and \( I(t^*) = I^* \), so

\[
I(t) \geq I^*e^{-(b+\gamma)\omega} = q^* \quad \forall t \in [t^*, t^* + \omega].
\]

So \( I(t) \geq q \ \forall t \in [t^*, t^* + \xi] \).

- \( \omega < \xi \). As before, \( I(t) \geq q \ \forall t \in [t^*, t^* + \omega] \). Following the same argument that was used to prove that \( I(t) \geq I_t \), it is checked that \( I(t) \geq q \ \forall t \in [t^* + \omega, t^* + \xi] \).

The interval \([t^*, t^* + \xi]\) was chosen in an arbitrary way (we only need \( t^* \) to be large). Therefore we can conclude that \( I(t) \geq q \) for \( t \) large enough. In addition, \( q \) does not depend on the chosen solution (it only depends on \( I^* \), \( b \), \( \omega \) and \( \gamma \), which are data), then any positive solution \( I \) verifies \( I(t) \geq q \) for \( t \) large enough.
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