Fluctuations in a SIS epidemic model with variable size population

Abderrahman Iggidr, Khadija Niri, Elkhomeini Ould Moulay Ely

Fluctuations in a SIS epidemic model with variable size population

A. Iggidr[a] K. Niri[b*] E. Ould Moulay Ely[b]

[a]INRIA Nancy - Grand Est and LMAM UMR CNRS 7122,
I.S.G.M.P. Bat. A, Ile du Saulcy
University of Metz, 57045 Metz Cedex 01, France.
phone : +33 3 87 54 72 80, Fax: +33 3 87 54 72 77
e-mail: iggidr@loria.fr, iggidr@univ-metz.fr

[b]Université Hassan II, Faculté des Sciences Aïn chock
Département de Mathématiques et Informatique,
Casablanca, Maroc.
e-mail: khniri@yahoo.fr

February 23, 2010

Abstract

In an epidemiological model, time spent in one compartment is often modeled by a delay in the model. In general the presence of delay in differential equations can change the stability of an equilibrium to instability and causes the appearance of oscillatory solutions.

In this paper we consider a SIS epidemiological model with demographic effects: birth, mortality and mortality caused by infection. The delay is the period of infection. We define the concept of oscillation in the sense that solutions of the model studied fluctuate around a steady state. Our goal is to show that in this model, there are oscillating solutions for certain parameters values. We determine a large set of initial data for which solutions of this model are slowly oscillating.

Keywords: Retarded Differential Equation, Oscillation, equilibrium, basic reproduction number.

1 Introduction

In an epidemiological model, time spent in one compartment is often modeled by a delay in the model.

Often the presence of delay in differential equations can change the stability of an equilibrium to instability and causes the appearance of fluctuating solutions. The best known (especially among physicists) are periodic solutions.

*Corresponding Author

The existence of periodic solutions in the epidemiological models whose formulation contains a delay has been the subject of several works [2, 7, 15, 16]

However, it appears that little work in mathematical epidemiology has used the concept of oscillation in the sense that the solutions of the model studied fluctuate around a steady state without necessarily being periodic.

The oscillatory properties in the case of delay differential equations have been the subject of several publications. Without being exhaustive, we can cite [1, 3, 4, 5, 6, 18, 19, 20, 22, 23]. An important reference in this field is the book of Gyori [13].

In this paper we consider a SIS epidemiological model with demographic effects: birth, natural mortality and mortality due to infection. The total size of the population is not constant. The formulation of the model leads to a delay differential equation in which the delay corresponds to the duration of infection.

Our goal is to show first, for certain values of the parameters of this model, there are solutions oscillating around the endemic equilibrium independently of the choice of initial data.

Secondly we will make a qualitative analysis of the global behavior of the model. It appears that this model is monotone; that is the order between the initial data is preserved by the solutions corresponding to them. This monotonicity property can already move us towards the type of initial data set for which the solutions are oscillating: initial data located above or below the equilibrium gives a solution which is also in the same situation. Therefore, initial data crossing the endemic equilibrium once during an interval of time equal to the duration of infection, can give a solution oscillating around the equilibrium. In this case, we calculate the first peak and the first zero of fluctuation. We show that the distance between two consecutive zeros is greater than the duration of infection, this is called slowly oscillating solution.

2 Formulation of the model

We study in this section the SIS model described in [16] where a population of size N(t) is divided into susceptible and infective individuals, with numbers denoted by $S(t)$, $I(t)$, respectively. Thus

$$N(t) = S(t) + I(t) \tag{2.1}$$

All new born are assumed to be susceptible. The birth rate as well as the natural death and the disease-induced rate are all assumed to be constant, and are respectively denoted b, d, and δ. The death outflow from the susceptible class is then given by dS and death outflow from the infective class is $(d+\delta)I$. The force of infection is $\beta I/N$ with $\beta > 0$ being the effective contact rate of an infective individual. Thus the individuals leave the susceptible class at rate $\beta SI/N$. It is assumed that the disease confers no immunity, so that infective individuals return to the susceptible class after recovery. Therefore we shall use an SIS model. For $t \geq 0$, let $P(t)$ be the probability for an individual to remain in the infective class at least t time units before returning to the susceptible class. The probability $P(t)$ is assumed to be nonnegative, nonincreasing with $P(0^+) = 1$ and $\int_0^\infty P(u)du = \omega$, the mean length of infection, which is assumed to be positive and finite. The SIS model is formulated with a general $P(t)$ satisfying the above assumptions.

For $t \geq 0$, the integral equation describing the evolution of the number of infective individuals is

$$I(t) = I_0(t) + \int_0^t \beta \frac{S(u)I(u)}{N(u)} P(t-u) \exp\{-(d+\delta)(t-u)\}\, du \tag{2.2}$$

The quantity $I_0(t)$ represents the number of initially infected individuals that are still infected at time t. The integral in (2.2) is the summation up to time t of individuals who became infected at time u and who have neither recovered back to susceptible status nor died. The total population varies according to the differential equation

$$N'(t) = (b-d)N(t) - \delta I(t), \tag{2.3}$$

Defining respectively the proportions of susceptible and infective individuals in the population by $s(t) = S(t)/N(t)$, $i(t) = I(t)/N(t)$, equation (2.1) gives

$$s(t) + i(t) = 1 \tag{2.4}$$

Equation (2.3) gives

$$N'(t) = (b - d - \delta i(t))N(t), \tag{2.5}$$

which integrates to

$$N(t) = N(0) \exp\left\{(b-d)t - \delta \int_0^t i(p)dp\right\}, \tag{2.6}$$

Using the expression (2.6) with $i_0(t) = I_0(t)/N(t)$, equation (2.2) gives

$$i(t) = i_0(t) + \int_0^t \beta \left[1 - i(u)\right] i(u) P(t-u) \exp\left\{-(d+\delta)(t-u) + \delta \int_u^t i(p)dp\right\} du. \tag{2.7}$$

This is an integral equation for $i(t)$. The local existence, uniqueness and continuation were proved in [23]. It was shown, in [22], that the solution remains in the interval $[0,1]$ so it exists for all $t \geq 0$.
In the case when the length of infection is equal to a constant $\omega > 0$, then $P(t)$ is a step function, namely

$$P(t) = \begin{cases} 1 & \text{on } [0,\omega] \\ 0 & \text{on } (\omega, \infty). \end{cases}$$

For this step function $P(t)$, the initial infective individuals must have recovered by time ω, so $i_0(t)$ is zero for $t \geq \omega$. The integral equation (2.7) gives

$$i(t) = \int_{t-\omega}^t \beta \left[1 - i(u)\right] i(u) \exp\left\{-(b+\delta)(t-u) + \delta \int_u^t i(p)dp\right\} du \tag{2.8}$$

For $t \geq \omega$ the integral equation (2.8) is equivalent to the following delay-integro-differential equation

$$\begin{aligned} i'(t) = \; & \beta\left[1 - i(t)\right] i(t) - \beta\left[1 - i(t-\omega)\right] i(t-\omega) \exp\left\{-(b+\delta)\omega + \delta \textstyle\int_{t-\omega}^t i(p)dp\right\} \\ & -(b+\delta)i(t) + \delta i^2(t). \end{aligned} \tag{2.9}$$

Using the notation $\theta = \beta \dfrac{1 - \exp\left(-(b+\delta)\omega\right)}{b+\delta}$, it has been proved in [22] that the the disease free state $(s,i) = (1,0)$ is always an equilibrium for equation (2.9). This equilibrium is stable if $\theta < 1$, unstable if $\theta > 1$ and globally asymptotically stable if $\delta\omega \leq \theta \leq 1$. A unique endemic equilibrium exists if and only if $\theta > 1$.
When $\delta = 0$ (i.e., there is no disease-related death), the equation (2.9) is a delay-differential-equation. So, for $\theta > 1$, the endemic equilibrium is explicitly given by $(s^*, i^*) = (1/\theta, 1 - 1/\theta)$, and it is asymptotically stable ([4]).

3 Monotonicity of the model and existence of oscillating solutions

3.1 Monotonicity of the equation

In this section, we shall show that equation (2.9) is monotone: the order established between two initial functions is preserved by the corresponding solutions. We then use this to prove afterward that equation (2.9) has oscillating solutions about the endemic equilibrium. The notion of oscillations defined here is linked to the monotonicity in the following manner: we shall say that a function $x(t)$ oscillates about $y(t)$ if $x(t)$ and $y(t)$ are never comparable in the sense of the usual order in $C([-\omega, 0], I\!R^{+})$. In particular, a solution $x(t)$ of (2.9) is oscillating about i^* if we do not have $x(t) \leq i^*$ nor $x(t) \geq i^*$ for $t > t_0$ for some t_0.
Cooperative systems and many compartmental models satisfy the monotonicity property. The oscillating properties of delay scalar differential equation solutions have been used by J. Mallet-Paret in the elaboration of Morse's theory for delay equation [21]. (see also works of Yullin Cao [10]).
In the case of differential delay equation the study of the monotonicity properties has been done, first by P. Seguier [5], then by O. Arino and P. Seguier [6]. More recently, H. Smith has developed the theory of monotone dynamics systems for delay differential equations [24, 25, 26].
The study of oscillations for monotone systems has also been the topic of the thesis [23] and has been considered in [3].

Here, we are interested in the behavior of solutions of (2.9) in a neighborhood of the steady solution $x(t) \equiv i^*$. The following three assumptions on the parameters will be considered:

$$[H_1] : \beta \left[\frac{1 - e^{-(b+\delta/2)\omega}}{b + \delta/2} \right] < 2 \ , \quad [H_2] : \beta \left[\frac{1 - e^{-(b+\delta/2)\omega}}{b + \delta/2} \right] > 2 \ , \quad [H_3] : \beta \left[\frac{1 - e^{-b\omega}}{b + \delta/2} \right] > 2$$

Proposition 3.1 *Consider equation (2.9) and let $i(t)$ be the solution of (2.9) corresponding to an initial function φ.*

1. *Suppose that $[H_1]$ is verified. Then the endemic equilibrium satisfies $i^* < 1/2$.*
2. *Suppose that $[H_2]$ is verified. Then the endemic equilibrium satisfies $i^* > 1/2$.*
3. *Suppose that $[H_3]$ is verified. Then, $\frac{1}{2} \leq \varphi(t) \leq 1 \Longrightarrow \frac{1}{2} \leq i(t) \leq 1$.*

Remark: $[H_3]$ implies $[H_2]$.
Proof. We recall the expression of the threshold θ:

$$\theta = \beta \, \frac{1 - \exp\left(-(b+\delta)\omega\right)}{b + \delta}.$$

First, one can notice that $\theta = \theta(\delta)$ is a decreasing function of δ.

1. Suppose $[H_1]$ is satisfied. The endemic equilibrium satisfies the equation:

$$F(i^*) = 0, \tag{3.1}$$

where

$$F(i) = -1 + \frac{\beta(1-i)\left(1 - e^{-(b+(1-i)\delta)\omega}\right)}{b + (1-i)\delta} \tag{3.2}$$

The map $i \mapsto F(i)$ is decreasing. Moreover we have $F(0) = -1 + \dfrac{\left(1-e^{(-b-\delta)\omega}\right)\beta}{b+\delta} = -1+\theta > 0$, $F(1/2) = -1 + \dfrac{\left(1-e^{\left(-b-\frac{\delta}{2}\right)\omega}\right)\beta}{2\left(b+\frac{\delta}{2}\right)} < 0$ thanks to $[H_1]$, and $F(1) = -1 < 0$. Thus there is a unique nontrivial equilibrium i^* and it satisfies $i^* < 1/2$.

2. The proof is similar to case H_1.

3. Suppose that the condition $[H_3]$ is satisfied. We assume that $\frac{1}{2} < \varphi(t) < 1$ for all $t \in [-\omega, 0]$ and we prove that $\frac{1}{2} < i(t) < 1$ for all $t \geq 0$.

   Suppose there exists a time t such that $i(t) = \frac{1}{2}$. Let t^* be the first time for which $i(t^*) = \frac{1}{2}$. The time t^* satisfies $i(t) > \frac{1}{2}$ if $t < t^*$ and $i(t) < \frac{1}{2}$ if $t^* < t < t^* + \eta$, for some $\eta > 0$. In particular, we would have $i(t^* - \omega) > \frac{1}{2}$ and $i'(t^*) \leq 0$. But, from equation (2.9), we have

   $i'(t^*) \geq \dfrac{\beta}{4} - \dfrac{\beta}{4}e^{-b\omega} - \dfrac{b+\delta}{2} + \delta/4 \geq (2b+\delta)\left[\dfrac{\beta}{2}\left(\dfrac{1-e^{-b\omega}}{b+\delta/2}\right) - 1\right] > 0$, which is in contradiction with $i'(t^*) \leq 0$. Thus $i(t) \geq 1/2$ for all $t \geq 0$. ■

The following theorem shows that the order established between two initial functions is preserved by the corresponding solutions of equation (2.9) when $\delta = 0$.

Theorem 3.1 *Suppose $\delta = 0$ and $[H_3]$ is fulfilled. Then, the equation (2.9) is monotone; that is, for each pair of initial conditions φ and ψ in $C([-\omega, 0], [1/2, 1])$, with $\varphi(t) \leq \psi(t)$, for every $t \in [-\omega, 0]$, if $x(t)$ (resp. $y(t)$) is the solution of (2.9) verifying $x_0 = \varphi$ (resp. $y_0 = \psi$) then $x(t) \leq y(t)$, for $t \geq 0$.*

Proof. Equation (2.9) can be written in the following condensed form:

$$\begin{cases} i'(t) = g(i(t)) - \beta f(t, i_t) \quad for \quad t \geq 0 \\ \\ i_0(t) = \varphi(t) \quad for \quad -\omega \leq t \leq 0. \end{cases} \tag{3.3}$$

where $g(u) = \beta(1-u)u - bu$.
i_t is the function defined on $[-\omega, 0]$ by $i_t(\theta) = i(t+\theta)$ for every t.
$f(t, u) = [1 - u(-\omega)]\, u(-\omega) \exp(-b\omega)$
Let φ and ψ be two initial functions in $C([-\omega, 0], [1/2, 1])$, and suppose that $\varphi(t) \leq \psi(t)$. Let x (respectively y) be the corresponding solution with initial functions $\varphi(t)$ (respectively $\psi(t)$). We will show that for all $t \geq 0$, one has $x(t) \leq y(t)$. Thanks to Assumption $[H_3]$ and Proposition 3.1, it is actually sufficient to compare $x(t)$ and $y(t)$ on $[0, \omega]$.
It is convenient, for the comparison, to substitute for y, the solution of a perturbed problem which keeps the same properties as the initial problem, but which makes it possible to obtain strict comparisons. For $\epsilon > 0$, we denote by $y\epsilon$ the solution of perturbed equation:

$$\begin{cases} \frac{dy^\epsilon}{dt} = g(y^\epsilon(t)) - \beta f(t, y_t^\varepsilon) + \epsilon \quad for \quad t \geq 0 \\ \\ y^\epsilon(t) = \psi(t) \quad for \quad -\omega \leq t \leq 0. \end{cases} \tag{3.4}$$

Equation (2.9) is the non perturbed equation and $y^0 = y$. We shall use the following lemma relating the solutions of (3.4) to those of (2.9).

Lemma 3.1 *There exists $\varepsilon_0 > 0$, such that for ε, $0 \leq \varepsilon \leq \varepsilon_0$, and for $T > 0$, y^ε exists on $[0, T]$. Moreover y^ε converges uniformly on $[0, T]$ to y, solution of (2.9).*

The proof of this lemma is in ([23], page 33).
Let us now compare y^ε and x on $[0, T]$. We have:

$$\begin{aligned}(y^\varepsilon)'(t) - x'(t) &= g(y^\varepsilon(t)) - \beta f(t, y_t^\epsilon) - g(x(t)) + \beta f(t, x_t) + \epsilon \\ &= g(y^\varepsilon(t)) - g(x(t)) + \beta\,[f(t, x_t) - f(t, y_t^\epsilon)] + \epsilon\end{aligned}$$

We introduce the following functions:
$A(t) = g(y^\varepsilon(t)) - g(x(t))$.
$B(t) = \beta\,[f(t, x_t)) - f(t, y_t^\epsilon)]$.
We have $B(t) \geq 0$ for $t \in [0, \omega]$ thanks to $[H_3]$ and to the fact that the map $v \mapsto (1-v)v$ is decreasing on $[1/2, 1]$. On the other hand, we can write $A(t) = [y^\varepsilon(t) - x(t)]\,h(t)$. We then have:
$\frac{d}{dt}(y^\varepsilon(t) - x(t)) - [y^\varepsilon(t) - x(t)]\,h(t) = B(t) + \varepsilon$
$\frac{d}{dt}\left\{[y^\varepsilon(t) - x(t)] \exp\left(-\int_0^t h(s))ds\right)\right\} = [B(t) + \varepsilon] \exp\left(-\int_0^t h(s)ds\right)$
We define $z(t) = [y^\varepsilon(t) - x(t)]\,exp\left(-\int_0^t h(s)ds\right)$, $z(t)$ verifies the equation:

$$\frac{d}{dt}z(t) = [B(t) + \varepsilon] \exp\left(-\int_0^t h(s)ds\right).$$

We prove that $z(t) > 0$ for all t. Suppose that this is not true. Let t_0 be the first value of t such that the inequality $z(t) > 0$ ceases being satisfied. Then, $z(t_0) = 0$, $z(t) > 0$ for $t < t_0$, and $z(t) < 0$ if $t_0 < t < t_0 + \eta$, for some $\eta > 0$. We have $\frac{d}{dt}z(t) = [B(t) + \varepsilon] \exp\left(-\int_0^t h(s)ds\right) > 0$.
So, $z'(t_0) > 0$, and since $z(t_0) = 0$, we must have $z(t) > 0$ for $t_0 < t < t_0 + \eta'$ with $\eta' > 0$. Hence we reach a contradiction. We deduce that $y^\varepsilon(t) > x(t)$ $\forall t \geq 0$. Lemma (3.1) allows to finish the proof of Theorem (3.1). ■

As a consequence of Theorem 3.1, we have the following result which characterizes the global behavior of solutions of (2.9).

Proposition 3.2 *Consider equation (2.9) with $\delta = 0$, and suppose that $[H_3]$ is fulfilled. Let φ be an initial function in $C\left([-\omega, 0], \left[\frac{1}{2}, 1\right]\right)$, then:*

1. *if $\varphi(t) \geq i^*$, then the corresponding solution $i(t)$ is such that $i(t) \geq i^*$ for all $t \geq 0$;*
2. *if $\frac{1}{2} \leq \varphi(t) \leq i^*$, then the corresponding solution $i(t)$ is such that $\frac{1}{2} \leq i(t) \leq i^*$ for all $t \geq 0$.*

4 Existence of oscillating solutions:

4.1 Existence of oscillating solutions

We give now some definitions of the oscillation concept.

Definition 4.1 *Let x be a continuous function defined on some infinite interval $[a, \infty)$. The function x is said to oscillate or to be oscillatory about zero if x has arbitrarily large zeros. That is, for every $b > a$ there exists a point $c > b$ such that $x(c) = 0$. Otherwise x is called non-oscillatory.*

Definition 4.2 *Let x be a continuous function defined on some infinite interval $[a, \infty)$. The function x is said to oscillate or to be oscillatory about a steady state x^* if $x - x^*$ oscillates about zero in the sense of Definition 4.1.*

The monotonicity of equation (2.9) defined in Paragraph 3.1 plays an important role in the existence of oscillating solutions about the endemic equilibrium. The following theorem illustrates the relation between these two concepts.

Theorem 4.1 *Consider equation (2.9) with $\delta = 0$, and suppose that $[H_3]$ is fulfilled. Choose φ and ψ two initial functions in $C([-\omega, 0], I\!R^+)$ such that $\frac{1}{2} \leq \varphi \leq i^* \leq \psi < 1$, $\varphi \neq i^*$, $\psi \neq i^*$, φ and ψ being linearly independent.*
Then, among the family of convex combinations of φ and ψ, $(1-\lambda)\varphi + \lambda\psi$, there is at least one $\overline{\lambda}$, $0 \leq \overline{\lambda} \leq 1$, such that the solution of (2.9) starting from $(1-\overline{\lambda})\varphi + \overline{\lambda}\psi$ is oscillating about the endemic equilibrium i^*

Proof: A similar proof for a particular case of equation (2.9) has been made in ([3]).
We denote by $i(t, \psi)$ a solution of (2.9) with initial function ψ. Let us define the sets :

$$\Lambda^+ = \{0 \leq \lambda \leq 1 : i(t, (1-\lambda)\varphi + \lambda\psi) \geq i^*,\ i(t, (1-\lambda)\varphi + \lambda\psi) \not\equiv i^*\}.$$

$$\Lambda^- = \{0 \leq \lambda \leq 1 : i(t, (1-\lambda)\varphi + \lambda\psi) \leq i^*,\ i(t, (1-\lambda)\varphi + \lambda\psi) \not\equiv i^*\}.$$

We observe readily that $1 \in \Lambda^+$, $0 \in \Lambda^-$, and by monotonicity of the equation (2.9), Λ^+ and Λ^- are intervals.
If $\Lambda^+ \cup \Lambda^-$ is strictly contained in $[0, 1]$, the conclusion of the theorem is verified. So, let us consider the situation where $\Lambda^+ \cup \Lambda^- = [0, 1]$. Noting that $\Lambda^+ \cap \Lambda^- = \emptyset$, except if we had $i(t) = i^*$ for t large which is excluded in the definition of Λ^+ and Λ_-. We then have two possibilities either, $\Lambda^- = [0, a)$ and $\Lambda^+ = [a, 1]$, or $\Lambda^- = [0, a]$ and $\Lambda^+ = (a, 1]$. In both cases we have $0 < a < 1$.
Let us study the first case. The other one will follow the same line. Set

$$z(t) = i(t, (1-a)\varphi + a\psi),\ a \in \Lambda^+.$$

By definition of Λ^+, we have $z(t) > i^*$ for $t \geq 0$. But the continuity of the solution implies that, for some $\rho > 0$, and for λ such that $a - \rho < \lambda \leq a$, we still have $i(t, (1-\lambda)\varphi + \lambda\psi) \geq i^*, \neq i^*$, for all $t \geq 0$. This implies that $]a - \rho, a] \subset \Lambda^+$, in contradiction with the definition of a. So, $\Lambda^+ \cup \Lambda^- \neq [0, 1]$, which yields the desired conclusion ■

4.2 Sufficient conditions of existence of oscillating solutions

Our goal in this section is to show that under sufficient conditions for certain values of the parameters of this model, there are solutions oscillating around the endemic equilibrium independently of the choice of initial data.
Recall the equation (2.9) :

$$\begin{aligned} i'(t) = \; & \beta\,[1 - i(t)]\,i(t) - \beta\,[1 - i(t-\omega)]\,i(t-\omega)\exp\left(-(b+\delta)\omega + \delta\int_{t-\omega}^{t} i(p)dp\right) \\ & -(b+\delta)i(t) + \delta i^2(t). \end{aligned} \tag{4.1}$$

Equation (4.1) can be written in the form:

$$i'(t) = \alpha\,[K - i(t)]\,i(t) - \beta\exp\left(-(b+\delta)\omega\right)[1 - i(t-\omega)]\,i(t-\omega)\exp\left(\delta\int_{t-\omega}^{t} i(p)dp\right) \tag{4.2}$$

with $\alpha = \beta - \delta$, $K = 1 - \dfrac{b}{\beta - \delta}$

Theorem 4.2 *Consider the equation (4.2) and suppose that i^* is asymptotically stable. Then,*
if $\alpha > 0$, the condition

$$\frac{K}{2} < i^* < \frac{1}{2} - \frac{e^{(b+\delta)\omega}}{2\beta e\omega}$$

is sufficient so that all solutions of equation (4.2) are oscillating.

Proof:
The principle of this proof is to compare our model to a linear differential equation with delay for which necessary and sufficient conditions for oscillations are known. We particularly use the following famous results whose complete proofs are done in ([13]: Theorems 2.2.3 and 3.2.2):
1) The equation $y'(t) + py(t-\omega) = 0$ is oscillating iff $p\omega > \frac{1}{e}$
2) For $p > 0, \omega > 0$, the following statements are equivalent:

- *The delay differential equation $y'(t) + py(t-\omega) = 0$ has a positive solution.*
- *The delay differential inequality $y'(t) + py(t-\omega) \leq 0$ has a positive solution.*

Assume $i(t)$ is a solution of (4.2) such that $i(t) > i^*$

and let $v(t) = i(t) - i^* > 0$. Then $0 < v(t) < 1$, and $v(t)$ is solution of

$$\begin{aligned} v'(t) &= \alpha\,[K - 2\,i^* - v(t)]\,v(t) - \beta_1\,[1 - 2i^* - v(t-\omega)]\,v(t-\omega)\exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right) \\ &+\alpha\,[K - i^*]\,i^* - \beta_1\,[1 - i^*]\,i^* \exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right) \end{aligned}$$

With $\beta_1 = \beta e^{-(b+\delta)\omega} e^{\delta\omega i^*}$
This can be written

$$\begin{aligned} 0 = \;& v'(t) - \alpha\,[K - 2\,i^* - v(t)]\,v(t) + \beta_1\,[1 - 2i^* - v(t-\omega)]\,v(t-\omega)\exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right) \\ & -\alpha\,[K - i^*]\,i^* + \beta_1\,[1 - i^*]\,i^* \exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right) \end{aligned}$$

Since i^* is an equilibrium of equation (4.2), we have $0 = \alpha\,[K - i^*]\,i^* - \beta_1\,[1 - i^*]\,i^*$. So $\alpha\,[K - i^*] > 0$, and

$$\begin{aligned} &-\alpha\,[K - i^*]\,i^* + \beta_1\,[1 - i^*]\,i^* \exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right) \\ &= \alpha\,[K - i^*]\,i^* \left(\exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right) - 1\right) > 0. \end{aligned}$$

Since $\alpha > 0$ and $i^* > \frac{K}{2}$ we have $\alpha\,[K - 2\,i^* - v(t)]\,v(t) < 0$.
So we deduce $0 > v'(t) + \beta_1\,[1 - 2i^* - v(t-\omega)]\,v(t-\omega)\exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right)$

On the other hand we have $0 < v(t) < 1$ which implies
$\beta_1\,[1 - 2i^* - v(t-\omega)]\,v(t-\omega)\exp\left(\delta \int_{t-\omega}^{t} v(p)dp\right) > \beta_1\,[1 - 2i^* - v(t-\omega)]\,v(t-\omega)$
Therefore,
$0 > v'(t) + \beta_1[1 - 2i^* - v(t-\omega)]v(t-\omega)$

On the other hand if i^* is asymptotically stable then $lim_{t\to\infty} v(t) = 0$. So
$\forall \varepsilon > 0, \exists A > 0 : \forall t > A + \omega, 1 - 2i^* - v(t-\omega) > 1 - 2i^* - \varepsilon$
and then,

$0 \geq v'(t) + \beta_1[1 - 2i^* - \varepsilon]v(t - \omega)$,

For $0 < \varepsilon < 1 - 2i^* - \dfrac{1}{\omega e \beta_1}$, we deduce that inequality $v'(t) + \beta_1[1 - 2i^* - \varepsilon]v(t - \omega) < 0$ has a positive solution.

But the condition $\dfrac{K}{2} < i^* < \dfrac{1}{2} - \dfrac{e^{(b+\delta)\omega}}{\omega e \beta}$ implies $\omega\beta_1[1 - 2i^* - \varepsilon] > \dfrac{1}{e}$

This is contradictory with the result cited at the begining of our proof.

Therefore, the assumption $i(t) > i^*$ is false.

■

4.3 Existence of slowly oscillating solutions when there is no disease-related death:

Our aim in this section is to define a notion of slow oscillations and to prove in the case $\delta = 0$ the existence of a sufficiently large set of initial functions which are transformed into slowly oscillating solutions by the flow.

Definition 4.3 *Let x be a function defined on some interval $[t_0, +\infty)$. We will say that x is* **slowly oscillating** *if x is oscillating in the sense of Definition 4.1, x is alternatively positive and negative between its zeros and the distance between two successive zeros is not less than ω.*

Definition 4.3 eliminates the case where the solution is vanishing as from a certain time. Let Γ be the cone defined by

$$\Gamma = \Big\{\varphi \in C\left([-\omega, 0], I\!R^+\right), \;\; such \;\; that \;\; \exists \gamma \in [-\omega, 0], \varphi(\gamma) = i^*,$$
$$\varphi(s) < i^* \text{ for } s < \gamma, \text{ and } i^* \leq \varphi(s) \leq \varphi(0) \text{ for } \gamma < s \leq 0\Big\}.$$

When $\delta = 0$, equation (2.9) becomes:

$$i'(t) = \beta\left[K - i(t)\right]i(t) - \beta\exp(-b\omega)\left[1 - i(t - \omega)\right]i(t - \omega) \tag{4.3}$$

with $K = 1 - \dfrac{b}{\beta}$

In the following theorem we prove that there exist slowly oscillating solutions of (4.3). More precisely we state that solutions of (4.3) corresponding to initial functions φ in the cone Γ return to Γ at a sequence of time t_k whose distance is larger than the delay 2ω.

Theorem 4.3 *Let i be a solution of equation (4.3), with φ as initial function. Assume that $\varphi \in \Gamma$. Then, the solution i is slowly oscillating about the endemic equilibrium.*

To prove Theorem 4.3, we need to prove first some technical lemmas that we give hereafter. We begin by doing two changes of variable:

The first change of variable is $i(t) = x(t) + i^*$. The map $t \longrightarrow x(t)$ is then a solution of:

$$x'(t) = \beta x(t)\left[K_0 - x(t)\right] - \beta\exp\left(-(b\omega)\right)\left[K_1 - x(t - \omega)\right]x(t - \omega) \tag{4.4}$$

where $K_0 = K - 2\,i^*$ and $K_1 = 1 - 2\,i^*$.

The second change of variable is $y(t) = x(t)e^{-\beta\displaystyle\int_0^t (K_0 - x(s))ds} = x(t)p(t)$, where $p(t) = e^{-\beta\displaystyle\int_0^t (K_0 - x(s))ds}$.

So we have:

$$i(t) = i^* \Longleftrightarrow x(t) = 0 \Longleftrightarrow y(t) = 0$$

We will study the slowly oscillations of y about zero which is equivalent to studying the slow oscillations of i about i^*.
The map $t \longrightarrow y(t)$ is the solution of:

$$\begin{aligned} y'(t) &= -\beta\, e^{-b\omega} p(t) \frac{y(t-\omega)}{p(t-\omega)} \left[K_1 - \frac{y(t-\omega)}{p(t-\omega)} \right] \\ &= -\beta\, e^{-b\omega} \frac{p(t)}{p(t-\omega)} y(t-\omega) \Big(K_1 - \frac{y(t-\omega)}{p(t-\omega)} \Big) \end{aligned}$$

This can be written in a condensed form

$$y'(t) = -\sigma P(t) Q\left(t-\omega, y(t-\omega)\right) \tag{4.5}$$

where:
$\sigma = \beta \exp\left(-b\omega\right)$,
$P(t) = \dfrac{p(t)}{p(t-\omega)}$,
$Q(t,u) = u(K_1 - \dfrac{u}{p(t)})$.

Lemma 4.1 *the functions P and Q satisfy*

1. $\forall t,\ 0 < P(t) < e^{(-\sigma(1-i^*)+\beta)\omega}$,
2. $Q(t,0) = 0, \ \ \forall t$
3. $Q(t,u) < 0$ *for* $u < 0, K_1 > 0$ *and* $\forall t$,
4. $Q(t,u) > 0$ *for* $u > 0, K_1 > 0, u < K_1 p(t)$ *and* $\forall t$,
5. $Q(t,u) < u$ *for* $u > 0$ *and* $\forall t$.

Proof 2), 3) and 4) are obvious.

1. We have

   $$K - i^* - 1 \leq K_0 - x \leq K_0 + i^* = K - i^*$$

   i^* satisfies

   $$\beta\left(K - i^*\right) = \beta e^{-b\omega}\left(1 - i^*\right) = \sigma\left(1 - i^*\right)$$

   So

   $$-\sigma\left(1 - i^*\right) \leq -\beta(K_0 - x) \leq -\sigma\left(1 - i^*\right) + \beta$$

   $$e^{-\sigma\left(1 - i^*\right)\omega} \leq e^{-\beta \int_{t-\omega}^{t} \left(K_0 - x(s)\right) ds} \leq e^{\left(-\sigma\left(1 - i^*\right) + \beta\right)\omega}$$

   $$e^{-\sigma\left(1 - i^*\right)\omega} \leq P(t) \leq e^{\left(-\sigma\left(1 - i^*\right) + \beta\right)\omega} \leq e^{\beta\omega}$$

5. For $u > 0$, we have $\dfrac{Q(t,u)}{u} = K_1 - \dfrac{u}{p(t)} = 1 - 2\,i^* - \dfrac{u}{p(t)} < 1.$ ∎

Lemma 4.2 *Suppose that* $be^{b\omega} > \beta$ *and* $i^* < \dfrac{1}{2}$.
Let φ *an initial function and* $y(t)$ *the corresponding solution of equation (4.5).*
If $\varphi < K_1 e^{-\beta\omega}$ *then* $y(t) < K_1 p(t)$

Proof: $i^* < \dfrac{1}{2} \Longrightarrow K_1 > 0$.
We suppose that $\varphi < K_1$ and we prove that the solution of (4.4) verifies $x(t) < K_1$. We deduce that $y(t) < K_1 p(t)$.

Suppose there exists a first time t_0 such that $x(t_0) = K_1$. Then, $x(t) < K_1$ if $t < t_0$ and $x(t_0) > K_1$ if $t_0 < t < t_0 + \eta$, for some $\eta > 0$. In particular, we would have $x(t_0 - \omega) < K_1$ and $x'(t_0) > 0$.
But, from equation (4.4), we have

$$
\begin{aligned}
& x'(t_0) = \beta K_1 [K_0 - K_1] - \sigma x(t_0 - \omega) [K_1 - x(t_0 - \omega)] \\
& = \beta K_1 [K_0 - K_1] - \sigma K_1 x(t_0 - \omega) + \sigma x^2(t_0 - \omega) \\
& = \beta K_1 \left[\frac{-b}{\beta} \right] - \sigma K_1 x(t_0 - \omega) + \sigma x^2(t - \omega) \\
& < -b\, K_1 + \sigma K_1^2 \\
& = (-b + \sigma K_1)\, K_1 \\
& = (-b + \sigma\, [1 - 2\, i^*])\, K_1 \\
& < (-b + \sigma)\, K_1 = K_1\, [-b + \beta\, \exp(-b\omega)] < 0.
\end{aligned}
$$

■

Since we are studying the slowly oscillations of y about zero and because the properties in the lemma (4.2), we consider the following cone Γ_0 instead of the cone Γ:

$$
\begin{aligned}
\Gamma_0 = \quad & \Big\{ \varphi \in C\left([-\omega, 0], I\!R^+\right), \ \ \textit{such that} \ \exists \gamma \in [-\omega, 0], \varphi(\gamma) = 0, \\
& \varphi(s) < 0 \text{ for } s < \gamma, \text{ and } 0 \le \varphi(s) \le K_1 e^{-\beta\omega} \text{ for } \gamma \le s \le 0 \Big\}.
\end{aligned}
$$

We prove the following preliminary lemmas.
We give in lemma (4.3) the first peak above the endemic equilibrium of the solution, in lemma (4.4) the first zero of the solution and in lemma (4.5) the first peak of the solution below the endemic equilibrium.

Lemma 4.3 *Let* $\varphi \in \Gamma_0$, *and* $t_0^* = \gamma + \omega$.
The solution $y(t)$ *of the equation (4.5) corresponding to the initial function* φ, *is increasing on the interval* $[0, t_0^*]$, *non-increasing on an interval on the right of* t_0^* *and* $y'(t_0^*) = 0$.

Proof:
At the point t_0^*, we have $y'(t_0^*) = -\sigma P(t_0^*) Q(\gamma, y(\gamma)) = -\sigma P(t_0^*) Q(\gamma, \varphi(\gamma)) = -\sigma P(t_0^*) Q(\gamma, 0) = 0$.
For $0 < t < t_0^*$, we have $-\omega \le t - \omega < \gamma$, hence $\varphi(t - \omega) < 0$.
Lemma (4.1) implies $Q(t - \omega, \varphi(t - \omega)) < 0$
And so $y'(t) = -\sigma P(t - \omega) Q(t - \omega, y(t - \omega)) = -\sigma P(t - \omega) Q(t - \omega, \varphi(t - \omega)) > 0$.
For $t_0^* < t < \omega$, we have $\gamma \le t - \omega < 0$. thus $\varphi(t - \omega) > 0$
$\varphi \in \Gamma_0 \Longrightarrow \varphi(t - \omega) \le K_1 e^{-\beta\omega} \Longrightarrow Q(t - \omega, \varphi(t - \omega)) > 0$ then $y'(t) < 0$.
We deduce that $y(t_0^*)$ is the maximum of the values of y over an interval containing t_0^*. ■

Lemma 4.4 *Let $y(t)$ be the solution of the equation (4.5) corresponding to the initial function $\varphi \in \Gamma_0$ and suppose $\frac{K}{2} = \frac{1}{2}(1 - \frac{b}{\beta}) \leq i^* < \frac{1}{2}$. Then, there exists a first finite positive time $t_1 \geq t_0^* + \omega$ such that $y(t_1) = 0$. Moreover, $y(t)$ is non-increasing on the interval $[t_0^*, t_1]$.*

Proof: We prove that $y(t)$ is non-increasing on $[t_0^*, t_1 + \omega]$. Indeed, for $t \in [t_0^*, t_1 + \omega]$, we have $\gamma \leq t - \omega \leq t_1$. So, $y(t - \omega)) \geq 0$ for each $t \in [t_0^*, t_1 + \omega]$.
Since $\varphi \in \Gamma_0 \implies y(t - \omega) \leq K_1 p(t - \omega)$ by lemma 4.2. We have $y'(t) = -\sigma P(t) Q\left(t - \omega, y(t - \omega)\right)\Big) \leq 0$.

We show that t_1 is finite: Ad Absurdum, suppose that $y(t) > 0$ for all $t \geq t_0^*$ or equivalently $i(t) > i^*$ for all $t \geq t_0^*$. On the other hand we have $i(t) > i^*$ for all $\gamma < t \leq t_0^*$ thanks to Lemma 4.3. Thus, for $t \geq t_0^*$
we have $p'(t) = -\beta(K_0 - x(t))\, p(t)$.
$K_0 - x(t) = K - 2i^* - (i(t) - i^*) = K - (i(t) + i^*) < K - 2i^* \leq 0$ since $i^* > \frac{K}{2}$. Therefore the function $t \mapsto p(t)$ is increasing, and hence $p(t) > p(t - \omega)$ for all $t \geq t_0^*$. This implies $P(t) > 1$ for all $t \geq t_0^*$.

Now $y'(t) = -\sigma\, P(t)\, Q\left(t - \omega, y(t - \omega)\right) < -\sigma\, Q\left(t - \omega, y(t - \omega)\right)$
$Q\left(t - \omega, y(t - \omega)\right) = (K_1 - x(t - \omega))\, y(t - \omega)$. $x(t - \omega) \to 0$ as $t \to \infty$. So $x(t - \omega) \leq K_1 - \frac{1}{\sigma\,\omega}$, for $t - \omega \geq T$ for some $T > 0$.
So, for $t \geq T + \omega$, $y'(t) < -\frac{1}{\omega}\, y(t - \omega)$. Since y is decreasing, we have $y(T + \omega) \leq y(t - \omega) \leq y(T)$ for $T + \omega \leq t \leq T + 2\omega$. Hence, $y'(t) < -\frac{1}{\omega}\, y(T + \omega)$ for $T + \omega \leq t \leq T + 2\omega$. Integrating, we get $y(T + 2\omega) - y(T + \omega) < -y(T + \omega)$ which implies $y(T + 2\omega) < 0$ which is in contradiction to the assumption $y(t) > 0$ for $t > t_0^*$.

On the other hand, using 1), 5) of Lemma 4.1, and the fact that $y(t_0^*)$ is the maximum of y on $[t_0^*, t_1 + \omega]$, we have:
$y'(t) = -\sigma P(t) Q\left(t - \omega, y(t - \omega)\right) > -\beta e^{-\sigma(1 - i^*)\omega}\ y(t - \omega) > -\beta e^{-\sigma(1 - i^*)\omega} y(t_0^*), \forall t \in [t_0^*, t_1 + \omega]$.
Integrating on the interval $[t_0^*, t]$ ($t \in [t_0^*, t_1 + \omega]$) yields:
$y(t) \geq y(t_0^*)\left[1 - \beta e^{-\sigma(1 - i^*)\omega}(t - t_0^*)\right]$.
For $t = t_1$, we deduce that
$0 \geq 1 - \beta e^{-\sigma(1 - i^*)\omega}(t_1 - t_0^*)$, which implies that $t_1 - t_0^* \geq \dfrac{1}{\beta e^{-\sigma(1 - i^*)\omega}} > \omega$.
Then $t_1 \geq t_0^* + \omega$. ∎

Lemma 4.5 *Let $t_1^* = t_1 + \omega$, the solution $y(t)$ of the equation (4.1) is non-increasing on $[t_1, t_1^*,]$ and $y'(t_1^*) = 0$.*

Proof: For $t \in [t_1, t_1^*]$, $t_1 - \omega \leq t - \omega \leq t_1$.
In view of the inequality in Lemma 4.4, $t_0^* \leq t - \omega \leq t_1$, so: $y(t - \omega) > 0$ for $t \in [t_1, t_1^*]$ and then,
$y'(t) = -\sigma K P(t) Q\left(t - \omega, y(t - \omega)\right) < 0, \forall t \in [t_1, t_1^*]$ $y(t_1^* - \omega) = y(t_1) = 0 \Rightarrow y'(t_1^*) = 0$ ∎

Proof of Theorem 4.3: Let t_1 be as defined in Lemma 4.4 and define $\psi(t) = y(t + t_1 + \gamma)$ for $t \in [-\omega, 0]$.
Then, the function ψ has a zero on the interval $[-\omega, 0]$.
Precisely, we have $\psi(-\gamma) = y(t_1) = 0$. So, $\psi \in -\Gamma$.
We can see that the same technique that we used in lemmas (4.1)-(4.5) works if we assume $\varphi \in -\Gamma$, with the changes: non-decreasing to non-increasing, and non-increasing to non-decreasing. If $\varphi \in -\Gamma$, we have $\psi \in \Gamma$,

So, starting from $\varphi \in \Gamma$, the solution y is non-increasing on $[t_0^*, t_1^*]$, then it is non-decreasing on $[t_1^*, t_2]$, etc.
We obtain a sequence t_j^*, t_j, verifying $t_j^* - t_{j-1}^* \geq \omega$, $t_j^* - \omega \leq t_j \leq t_j^*$, such that $(-1)^j y(t)$ is non-decreasing on $[t_{j-1}^*, t_j^*]$ and $y'(t_j^*) = 0 = y(t_{j+1})$, for $j \geq 0$.
The distance between two successive zeros is not less than ω. ∎
The behavior of φ and y over the interval $[-\omega, t_2]$ is illustrated in Figure 1.

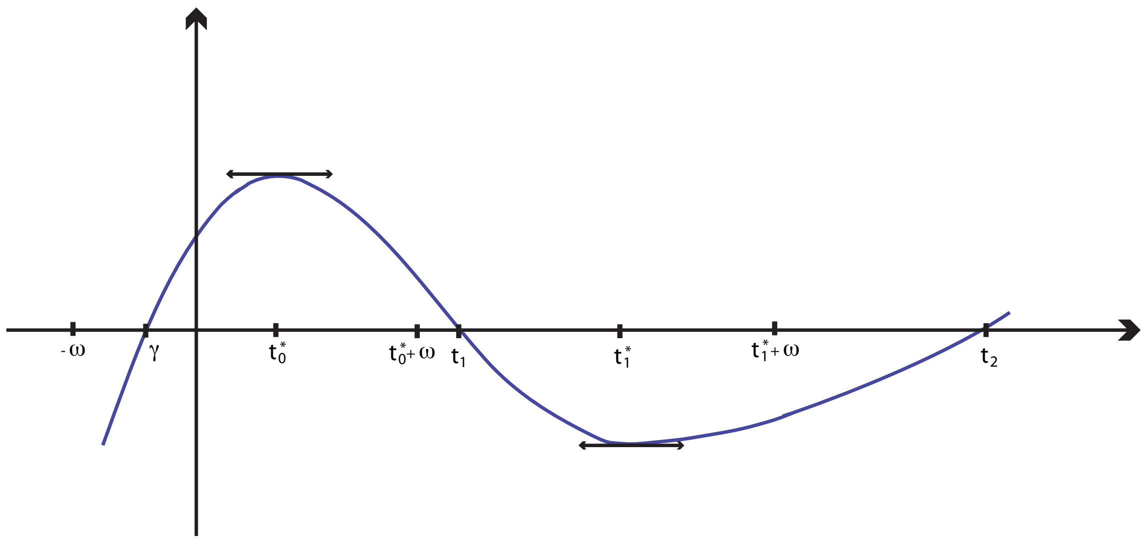

Figure 1: Behaviour of an initial function φ and its corresponding solution y

The following lemma shows that the solution does not degenerate and the peaks don't collapse.

Lemma 4.6 *Let y be a solution of equation 4.5, with φ as initial function.*
a) Suppose that φ is such that: $\varphi(\gamma) = 0$ for all $\gamma \in [-\omega, 0]$. Then, $y(t) = 0$, for all $t \geq 0$.
b)Suppose that $\varphi \in \Gamma$. Suppose that there exists $t_0 \geq 0$ such that $y(t) = 0$ for $t \geq t_0$. Then, $y(t) = 0$ for all $t \geq 0$, and φ is such that $\varphi(\gamma) = 0$ for all $\gamma \in [-\omega, 0]$.
c)Suppose that $\varphi \in \Gamma$, and consider the sequence $(t_i^*)_{i \geq 0}$ as in lemma 4.3.
Then, we have $\mid y(t_i^*) \mid > 0$ for all $i \geq 0$.

Proof: The properties a) an b) are obvious. If the delay ω in equation (2.9) is not constant, then there exist other solutions than $y = 0$ which die out eventually, see [22].
c)At t_0^*, we have, $\varphi \in \Gamma \Longrightarrow \varphi(-\omega) < 0 \Longrightarrow y'(0^+) > 0 \Longrightarrow y(t_0^*) > 0$.
At t_1^*, we have $y(t_1^*) < 0$.
Otherwise $y(t_1^*) = 0$, this implies that y is constant on $[t_1, t_1^*]$, therefore $y = 0$ on $[t_1, t_1^*]$.
We can deduce by the form of equation (4.5) that $y(t) = 0$ for $t \geq t_1$. So by property b) $y(t) = 0$ for all t, in contradiction to $\varphi \in \Gamma$.
We complete the proof of the theorem as in Lemma 4.6 by defining a new initial data $\psi(t) = y(t - t_1^*)$. We obtain $y(t_2^*) > 0$ and $y(t_3^*) < 0$ and so on. ∎

References

[1] O.Arino, I.Gy*öri*, and A.Jawhari, Oscillation criteria in delay equations, J.Differential Equations, pp.115-123, (1984).

[2] O.Arino, K.P.Hadeler and M.L.Hbid, *Existence of periodic solutions for delay-differential equations with state-depending delay.* J.Diff.Equat.144,vol.2,pp.263-301 (1998).

[3] O.Arino and K.Niri. Oscillations in vector spaces: A comparison result for monotone delay differential systems. *J. Math. Anal. Appl.*, 160(1):267–283, 1991.

[4] O.Arino and K.Niri. Subdominant behavior in positive semigroups. The case of a class of delay differential equations. *Differ. Equ. Dyn. Syst.*, 4(1):99–111, 1996.

[5] O.Arino and P.Seguier. Existence of oscillating solutions for certain differential equations with delay. Functional differential equations and approximation of fixed points, Proc., Bonn 1978, Lect. Notes Math. 730, 46-64 (1979). Springer, Berlin, 1979.

[6] O.Arino and P.Seguier, Thèses de Doctorat d'Etat, Bordeaux 1, No.667, and Pau, No.35, (1980).

[7] J.Arino, C.C.McCluskey and Van Den Driessche, Global results for an epidemic model with vaccination that exhibits backward bifurcation, SIAM J.Appl.Math., 64, pp.260-276, (2003)

[8] N.T.J.Bayley, *The mathematical Theory of Infectious diseases*, 2nd ed.,Herner,New york, (1975).

[9] F.Brauer and C.Castillo-Chavez, *Mathematical Models in Population Biology and Epidemiology*, Spring-Verlag, New York Inc. (2001).

[10] Y.Cao. The oscillation and exponential decay rate of solutions of differential delay equations. Oscillation and dynamics in delay equations, Proc. Spec. Sess. AMS, San Francisco/CA (USA) 1991, Contemp. Math. 129, 43-54 (1992)., 1992.

[11] O.Diekman and J.A.P.Heesterbeek, Mathematical epidemiology of infectious diseases: Model Building Analysis and Interpretation. *Wiley series in Mathematical and computational Biology*, Wiley, London, (2000).

[12] I.Györi, Connections between compartmental systems with pipes and integro-differential equations,Math.Modeling, 7,pp.1215-1238, (1986).

[13] I. Győri and G. Ladas. *Oscillation theory of delay differential equations.* Oxford Mathematical Monographs. The Clarendon Press Oxford University Press, New York, 1991. With applications, Oxford Science Publications.

[14] J. K. Hale and S. M. V. Lunel. *Introduction to Functional Differential Equations,* Springer-Verlag, New York Inc, 1991.

[15] H.W.Hethecote,H.W.Stech, P.van den Drieesshe,Periodicity and stability in epidemic models: a survey, In differential Equations and Applications in Ecology, Epidemic and Population Problems, (Edited by S.N.Busenbery and K.L..Cooke), Academic Press, New York, (1981)

[16] H.W.Hethecote, P.van den Drieesshe, An SIS epidemic model with variable population size and a delay, J.Maths.Biol. 34, pp 177-194, (1995)

[17] M.W.Hirsch, Systems of differential equations which are competitive or cooperative, SIAM J.Math.Anal. 16 (1965), pp.423-439

[18] B.B.Hunt and J.A.Yorke, When all solutions of $x'(t) = -\sum_{i=1}^{n} x(t - T_i(t))$ oscillate, J.Differential Equations, 53,pp.138-145, (1984).

[19] G.Ladas, Y.G Sficas and I.P.Stavroulakis, Necessary and sufficient conditions for oscillations, Amer.Maths.Monthly, 90, pp.637,(1983)

[20] G.Ladas and I.P.Stavroulakis, Oscillations caused by several retarded and advanced arguments, J.Differential Equations, 44, pp 134-152, (1982)

[21] J. Mallet-Paret. Morse decompositions for delay-differential equations. *J. Differ. Equations*, 72(2):270–315, 1988.

[22] K.Niri, Oscillations in Differential Equations with State-Dependent Delay, *J.Nonlin Oscillations*, 6, pp.250-257, (2003) .

[23] K.Niri, Etudes des propriétés oscillatoires de systèmes diffèrentiels à retard de type monotone , thèse de 3ème Cycle de l'Université de Pau, (1988).

[24] H.W.Smith, Monotone semiflow generated by functional differential equations, J.Differential Equations 66 (1987), 420-442

[25] H.W.Smith, systems of ordinary differential equations which generate an order-preserving flow: a survey of results, SIAM Rev.30 , pp.87-113, (1988)

[26] H.W.Smith, Monotone dynamical systems: An Introduction to the Theory of competitive and cooperative Systems, Mathematical Surveys and Monographs, Vol.41, Amer.Math.Soc., Providence, (1995)

[27] H.R.Thieme, Epidemic and demographic interaction in the spread of potentially fatal disease in governing populations, *Math.Biosci.* (111)(1992) 99-130.