ON VACCINATION CONTROLS FOR THE SEIR EPIDEMIC MODEL WITH SUSCEPTIBLE PLUS IMMUNE POPULATIONS TRACKING THE WHOLE POPULATION

M. De la Sen, S. Alonso-Quesada
Department of Electricity and Electronics, Faculty of Science and Technology, University of the Basque Country
Campus of Leioa, 48940-Leioa, Bizkaia, Spain

A. Ibeas
Departmento de Telecomunicación e Ingeniería de Sistemas, Escuela Técnica Superior de Ingeniería
Universitat Autònoma, Barcelona, Spain

Keywords: Epidemic models, Control, SEIR epidemic models, Tracking objective, Vaccination control, Positivity stability.

Abstract: This paper presents a simple continuous-time linear vaccination-based control strategy for a SEIR (susceptible plus infected plus infectious plus removed populations) propagation disease model. The model takes into account the total population amounts as a refrain for the illness transmission since its increase makes more difficult contacts among susceptible and infected. The control objective is the asymptotically tracking the joint susceptible plus the removed-by-immunity population to the total population while achieving simultaneously the remaining population (i.e. infected plus infectious) to asymptotically tend to zero.

1 INTRODUCTION

Important control problems nowadays related to Life Sciences are the control of ecological models like, for instance, those of population evolution (Beverton-Holt model, Hassell model, Ricker model etc.) via the online adjustment of the species environment carrying capacity, that of the population growth or that of the regulated harvesting quota as well as the disease propagation via vaccination control. In a set of papers, several variants and generalizations of the Beverton-Holt model (standard time-invariant, time-varying parameterized, generalized model or modified generalized model) have been investigated at the levels of stability, cycle-oscillatory behavior, permanence and control through the manipulation of the carrying capacity (De la Sen, 2008a, 2008b, De la Sen and Alonso-Quesada, 2008a, 2008b, 2009). The design of related control actions has been proved to be important in those papers at the levels, for instance, of aquaculture exploitation or plague fighting. On the other hand, the literature about epidemic mathematical models is exhaustive in many books and papers. A non-exhaustive list of references is given in this manuscript (Erturk and Momani, 2008, Keeling and Rohani, 2008, Khan et al., 2009, Mollison, 2003, Mukhopadhyay and Battacharyya, 2007, Ortega et al., 2003, Song et al., 2009, Yildirim and Cherruault, 2009, Zhang et al., 2009). The sets of models include the most basic ones (Keeling and Rohani, 2008, Mollison, 2003):

- SI models where not removed-by-immunity population is assumed. i.e., only susceptible and infected populations are assumed,
- SIR models, which include susceptible, infected and removed-by-immunity populations, and
- SEIR models where the infected populations is split into the "infected", which incubate the disease but do not still have any disease symptoms, and the "infectious" or "infective", which do have the external disease symptoms.

Those models have also two major variants, namely, the so-called "pseudo-mass action models", where the total population is not taken into account

De la Sen M., Alonso-Quesada S. and Ibeas A..
ON VACCINATION CONTROLS FOR THE SEIR EPIDEMIC MODEL WITH SUSCEPTIBLE PLUS IMMUNE POPULATIONS TRACKING THE WHOLE POPULATION .
DOI: 10.5220/0003152901650172
In *Proceedings of the International Conference on Bioinformatics Models, Methods and Algorithms* (BIOINFORMATICS-2011), pages 165-172
ISBN: 978-989-8425-36-2

as a relevant disease contagious factor and the so-called "true-mass action models", where the total population is more realistically considered as an inverse factor of the disease transmission rates. There are many variants of the above models, for instance, including vaccination of different kinds: constant (Yildirim and Cherruault, 2009), impulsive (Song et al., 2009, Zhang et al., 2009), discrete-time etc., incorporating point or distributed delays (Song et al., 2009), oscillatory behaviors (Mukhopadhyay and Battacharyya, 2007) and so on. In this paper, a continuous-time vaccination control strategy is given for a SEIR epidemic model which makes directly the susceptible plus removed- by-immunity populations to asymptotically track the whole population. It is assumed that the total population remains uniformly bounded through time while being nonnegative as they are all the partial populations of susceptible, infected, infectious and immune. Thus, the disease transmission is not critical, and the SEIR-model is of the above mentioned true-mass action type. Note that although all the partial populations and the total one are all nonnegative for all time in the real problem under study, the property has to be guaranteed for the mathematical SEIR-model (1)-(4) as well.

2 SEIR EPIDEMIC MODEL

Let S(t) be the "susceptible" population of infection, E(t) the "infected", I(t) the "infectious" population, and R(t) the "removed by immunity" (or "immune") population at time t. Consider the SEIR-type epidemic model:

$$\dot{S}(t) = -\mu S(t) + \omega R(t) - \beta\frac{S(t)I(t)}{N(t)} + \nu N(t)\left(1 - V(t)\right) \quad (1)$$

$$\dot{E}(t) = \beta\frac{S(t)I(t)}{N(t)} - (\mu + \sigma)E(t) \quad (2)$$

$$\dot{I}(t) = -(\mu + \gamma)I(t) + \sigma E(t) \quad (3)$$

$$\dot{R}(t) = -(\mu + \omega)R(t) + \gamma(1-\rho)I(t) + \nu N(t)V(t) \quad (4)$$

subject to initial conditions $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$ and $R(0) \geq 0$ under the vaccination function $V : \mathbb{R}_{0+} \to \mathbb{R}_{0+}$, with $\mathbb{R}_{0+} \triangleq \{z \in \mathbb{R} \,|\, z \geq 0\}$. The vaccination control is either the vaccination function itself or some appropriate four dimensional vector depending on it defined "ad-hoc" for some obtained equivalent representation of the SEIR-model as a dynamic system. In the above SEIR-model, N(t) is the total population, μ is the rate of deaths from causes unrelated to the infection, ω is the rate of losing immunity, β is the transmission constant (with the total number of infections per unity of time at time t being $\beta\frac{S(t)I(t)}{N(t)}$), σ^{-1} and γ^{-1} are, respectively, the average durations of the latent and infective periods. All the above parameters are nonnegative. The parameter ω means the rate of immunity lost since it makes the susceptible to increase and then the immune to decrease. The usual simplified SEIR-model is obtained with $\nu = \mu$ and $\rho = 0$. In that case,

$$\begin{aligned}\dot{N}(t) &= \dot{S}(t) + \dot{E}(t) + \dot{I}(t) + \dot{R}(t)\\ &= \mu\left[N(t) - S(t) - E(t) - I(t) - R(t)\right] = 0 \quad \forall t \in \mathbb{R}_{0+}\\ \Rightarrow\ N(t) &\triangleq S(t) + E(t) + I(t) + R(t) = N(0) = N > 0\end{aligned}$$

If $\nu > \mu$ then the new-born lost of maternal immunity is considered in the model. If $\nu < \mu$ then there is a considered mortality incidence by external causes to the illness. The parameter $\rho \in (0, 1]$ is the per-capita probability of dying from the infection. If either $\nu \neq \mu$ and $\rho = 0$ or $\nu = \mu$ and $\rho \neq 0$, and otherwise, $I(t) = \frac{(\nu - \mu)N(t)}{\rho\gamma}$ occurs eventually on a set of zero measure only, then the total population varies through time as obtained by correspondingly summing up both sides of (1)-(4). Furthermore, (1) and (4) and (2) and (3) might be separately summed up to obtain the evolution dynamics of the separate populations of joint susceptible and immune and joint infected and infectious. This leads to:

$$\dot{N}(t) = (\nu - \mu)N(t) - \rho\gamma I(t) \quad (5)$$

$$\begin{aligned}\dot{S}(t) + \dot{R}(t) &= -\mu\left[S(t) + R(t)\right]\\ &\quad + \left(\gamma(1-\rho) - \beta\frac{S(t)}{N(t)}\right)I(t) + \nu N(t)\end{aligned} \quad (6)$$

$$\dot{E}(t) + \dot{I}(t) = -\mu\left[E(t) + I(t)\right] - \left(\gamma - \beta\frac{S(t)}{N(t)}\right)I(t) \quad (7)$$

Note that (5) is identically zero if $\nu - \mu = \rho = 0$. From (5)-(7), it follows that:

$$N(t) = e^{(\nu-\mu)t}N(0) - \rho\gamma\int_0^t e^{(\nu-\mu)(t-\tau)}I(\tau)d\tau \quad (8)$$

$$\begin{aligned}S(t) + R(t) &= e^{-\mu t}\left[S(0) + R(0)\right]\\ &\quad + \int_0^t e^{-\mu(t-\tau)}\left[\nu N(\tau) + \left(\gamma(1-\rho) - \beta\frac{S(\tau)}{N(\tau)}\right)I(\tau)\right]d\tau\end{aligned} \quad (9)$$

$$\begin{aligned}E(t) + I(t) &= e^{-\mu t}\left[E(0) + I(0)\right]\\ &\quad - \int_0^t e^{-\mu(t-\tau)}\left(\gamma - \beta\frac{S(\tau)}{N(\tau)}\right)I(\tau)d\tau\end{aligned} \quad (10)$$

In order to further solve (9), an integration by parts is performed as follows:

$$\begin{aligned}\int_0^t p(\tau)dq(t,\tau) &= \int_0^t p(\tau)\dot{q}(t,\tau)d\tau \equiv \int_0^t N(\tau)e^{-\mu(t-\tau)}d\tau \\ &= \left[N(\tau)q(t,\tau)\right]_0^t - \int_0^t q(t,\tau)\dot{N}(\tau)d\tau\end{aligned} \tag{11}$$

where:

$$\begin{aligned}\bar{q}(t) &\triangleq \int_0^t e^{-\mu(t-\tau)}d\tau = \left[\frac{e^{-\mu(t-\tau)}}{\mu}\right]_0^t = \left[q(t,\tau)\right]_0^t \\ &= \frac{1-e^{-\mu t}}{\mu} = q(t,t) - q(t,0)\end{aligned} \tag{12}$$

so that $q(t,t) = 1/\mu$, $q(t,0) = e^{-\mu t}/\mu$ and then, using (5) in (11) yields:

$$\begin{aligned}\int_0^t N(\tau)e^{-\mu(t-\tau)}d\tau &= \frac{1}{\mu}\left[N(t) - e^{-\mu t}N(0)\right] \\ &-\frac{1}{\mu}\int_0^t e^{-\mu(t-\tau)}\left[(\nu-\mu)N(\tau) - \rho\gamma I(\tau)\right]d\tau\end{aligned} \tag{13}$$

which, after grouping identical terms, leads to:

$$\begin{aligned}&\int_0^t N(\tau)e^{-\mu(t-\tau)}d\tau \\ &= \frac{1}{\nu}\left[N(t) - e^{-\mu t}N(0) + \rho\gamma\int_0^t e^{-\mu(t-\tau)}I(\tau)d\tau\right]\end{aligned} \tag{14}$$

Thus, combining (9)-(10) and (14) yields:

$$\begin{aligned}&S(t) + R(t) - N(t) = -\left[E(t) + I(t)\right] \\ &= e^{-\mu t}\left[S(0) + R(0) - N(0) + \int_0^t e^{\mu\tau}\left(\gamma - \beta\frac{S(\tau)}{N(\tau)}\right)I(\tau)d\tau\right] \\ &= -e^{-\mu t}\left[E(0) + I(0) - \int_0^t e^{\mu\tau}\left(\gamma - \beta\frac{S(\tau)}{N(\tau)}\right)I(\tau)d\tau\right]\end{aligned} \tag{15}$$

3 VACCINATION CONTROL

If the control objective $S(t) = \gamma N(t)/\beta$ for all time is achieved with a positive vaccination control in $[0, 1]$, it is proven below that the whole population converges exponentially to the sum of the susceptible population plus the immune population while both the infectious and infective converge exponentially to zero. This is theoretically the ideal objective since the infection is collapsing as time increases while the susceptible plus the immune populations are approximately integrating the whole population for large time. Other alternative objective has been that the immune population be the whole one but this is a more restrictive practical objective since the whole susceptible population should asymptotically track the immune one even those of the susceptible who are not contacting the disease.

Theorem 1. Assume that $\beta > \gamma \geq 0$ and that the vaccination function is such that $S(t) = \gamma N(t)/\beta$ $\forall t \in \mathbb{R}_{0+}$ with a vaccination control in $[0, 1]$ for all time. Then, the SEIR model (1)-(4) is positive for all time. Furthermore,

$$\begin{aligned}&S(t) + R(t) - N(t) = -\left[E(t) + I(t)\right] \\ &= e^{-\mu t}\left[S(0) + R(0) - N(0)\right] = -e^{-\mu t}\left[E(0) + I(0)\right]\end{aligned} \tag{16}$$

for all time what implies the following constraint for the initial conditions:

$$S(0) = \frac{\gamma N(0)}{\beta} = \frac{\gamma}{\beta - \gamma}\left[E(0) + I(0) + R(0)\right] \tag{17}$$

As a result,

$$\begin{aligned}R(t) &= N(t) - S(t) - e^{-\mu t}\left[E(0) + I(0)\right] \\ &= \frac{\beta-\gamma}{\beta}N(t) - e^{-\mu t}\left[E(0) + I(0)\right] \\ &= \frac{\beta-\gamma}{\beta}N(t) + e^{-\mu t}\left[R(0) - \frac{\beta-\gamma}{\gamma}S(0)\right] \leq \frac{\beta-\gamma}{\beta}N(t)\end{aligned} \tag{18}$$

$\forall t \in \mathbb{R}_{0+}$. Then, $R(t) \to \frac{\beta-\gamma}{\beta}N(t)$ as $t \to \infty$.

Furthermore, the following two limits exist:

$$\lim_{t\to\infty}\left\{S(t) + R(t) - N(t)\right\} = \lim_{t\to\infty}\left\{E(t) + I(t)\right\} = 0 \tag{19}$$

If, in addition, $\nu - \mu = \rho = 0$ then

$$\begin{aligned}&N(t) = N(0) = N = \lim_{t\to\infty}\left\{S(t) + R(t)\right\} \\ &\lim_{t\to\infty}\left\{E(t)\right\} = \lim_{t\to\infty}\left\{I(t)\right\} = 0\end{aligned} \tag{20}$$

***Proof*:** The mathematical SEIR-model (1)-(4) is positive since the vaccination control is in $[0, 1]$ for all time so that no population takes negative values at any time. On the other hand, (16) and (19) follow directly from (15) and $S(t) = \gamma N(t)/\beta$ for all time. Finally, (20) follows from (16) and (19) since $\nu - \mu = \rho = 0$ implies $\dot{N}(t) \equiv 0$ $\forall t \in \mathbb{R}_{0+}$, i.e., $N(t) \equiv N(0)$ $\forall t \in \mathbb{R}_{0+}$ from (5). ***

An associate stability result follows:

Theorem 2. Assume that $\rho\gamma \geq 0$. Then, the following properties hold:

(i) The SEIR-model is globally stable if $0 \le \nu \le \mu$ and the vaccination law fulfils $V : \mathbb{R}_{0+} \to [0, 1]$.

(ii) If $S(t) = \gamma N(t)/\beta$ and $\nu > \mu \ge 0$ then the conditions

$\mu < \nu < \mu + \rho\gamma$ with $\rho\gamma > 0$

$N(0) = \rho\gamma \int_0^\infty e^{(\nu - \mu)\tau} I(\tau) d\tau$, $\lim_{t \to \infty} \{N(t)\} = 0$

are jointly necessary for global stability under Theorem 1.

(iii) If $\nu > \mu \ge 0$ and $I(t) = (\nu - \mu)N(t)/\rho\gamma$ $\forall t \ge t_0 (\text{finite}) \in \mathbb{R}_{0+}$ then global stability of the SEIR-model (1)-(4) is guaranteed if $V : \mathbb{R}_{0+} \to [0, 1]$. If $\nu > \mu \ge 0$, $V : \mathbb{R}_{0+} \to [0, 1]$ and $I(t) = (\nu - \mu)N(t)/\rho\gamma$ is replaced with the weaker condition $|I(t) - (\nu - \mu)N(t)/\rho\gamma| = o(e^{-\alpha t})$ for some $\alpha \in \mathbb{R}_+$ then the SEIR-model (1)-(4) is globally stable.

***Proof*:**

(i) If $0 \le \nu \le \mu$ and $\rho\gamma \ge 0$ then:

$$\dot{N}(t) = (\nu - \mu)N(t) - \rho\gamma I(t) \le (\nu - \mu)N(t) \le 0$$

$\forall t \in \mathbb{R}_{0+}$ so that $N(t) \le N(0) < \infty$ $\forall t \in \mathbb{R}_{0+}$. Since the SEIR-model is positive if $V : \mathbb{R}_{0+} \to [0, 1]$ then all the populations are nonnegative and upper-bounded by N(0).

(ii) On the other hand, the solution of (5) for any initial conditions is:

$$N(t) = e^{(\nu - \mu)t} \left[N(0) - \rho\gamma \int_0^t e^{-(\nu - \mu)\tau} I(\tau) d\tau \right]$$

which is uniformly bounded for all time only if $N(0) = \rho\gamma \int_0^\infty e^{-(\nu - \mu)\tau} I(\tau) d\tau$ since $\nu > \mu \ge 0$. Also, $N(t) < \infty$ $\forall t \in \mathbb{R}_{0+}$ only if $\dot{N}(t) \le 0$ on a non-necessarily connected set of infinite Lebesgue measure. Thus, there is a finite sufficiently large finite time "t" such that:

$$I(t) \ge \frac{\nu - \mu}{\rho\gamma} N(t) = \frac{\nu - \mu}{\rho\gamma} [S(t) + E(t) + I(t) + R(t)]$$

$$\Leftrightarrow \left(1 - \frac{\nu - \mu}{\rho\gamma}\right) I(t) \ge \frac{\nu - \mu}{\rho\gamma} [S(t) + E(t) + R(t)]$$

$$\Leftrightarrow I(t) \ge \frac{\nu - \mu}{\mu + \rho\gamma - \nu} [S(t) + E(t) + R(t)]$$

which requires the parametrical conditions $\rho\gamma > 0$ and $\mu < \nu < \mu + \rho\gamma$. Since I(t) is of exponential order of at most $-\mu$ from Theorem 1 [see (16)] then $S(t) + E(t) + R(t)$ is also of exponential of order of at most $-\mu$ so that N(t) extinguishes exponentially as they do all the populations of susceptible, infected, infectious and immune.

(iii) If $I(t) = \frac{\nu - \mu}{\rho\gamma} N(t)$ with $\nu > \mu$ after some finite time t_0 then $N(t) = N(t_0) < \infty$ $\forall t \ge t_0$ and the SEIR-model is positive since $V : \mathbb{R}_{0+} \to [0, 1]$. Thus, global stability follows. If $|I(t) - (\nu - \mu)N(t)/\rho\gamma| = o(e^{-\alpha t})$ replaces the above stronger condition $I(t) = (\nu - \mu)N(t)/\rho\gamma$ after a finite time then $\dot{N}(t)$ is of exponential order $-\alpha$ so that $N(t)$ is uniformly bounded for all time and the global stability still holds. ***

3.1 Control Law Synthesis

Note that the case $\nu > \mu$ is not feasible in practice for $\rho\gamma = 0$ since the population diverges. If $\rho\gamma > 0$, it requires a collapsing effect of the illness on the population which is also unfeasible in practical situations. It is now discussed how the vaccination law is generated to keep simultaneously the SEIR-model positivity plus the tracking objective of Theorem 1 which requires positivity. The tracking objective $S(t) = \gamma N(t)/\beta$ for all time is equivalent to any of the subsequent equivalent identities below:

$$\begin{aligned} & N(t) = \gamma N(t)/\beta + E(t) + I(t) + R(t) \\ & \Leftrightarrow \left(\frac{\beta - \gamma}{\beta}\right) N(t) = E(t) + I(t) + R(t) \\ & \Leftrightarrow N(t) = \frac{\beta}{\beta - \gamma} [E(t) + I(t) + R(t)] \\ & \Leftrightarrow R(t) = \frac{\beta - \gamma}{\beta} N(t) - E(t) - I(t) \end{aligned} \quad (21)$$

which requires as necessary condition $\beta > \gamma \ge 0$. Although unrelated to the physical problem at hand, the necessary condition will be also accomplished with $\beta < 0$ and $\gamma \le 0$ with $S(t) = \gamma N(t)/\beta$.

The solution of (4) matches (21) for all time if and only if:

$$\begin{aligned} R(t) &= \frac{\beta-\gamma}{\beta}N(t) - E(t) - I(t) = \frac{\beta-\gamma}{\beta}N(t) - e^{-\mu t}\left[E(0)+I(0)\right] \\ &= e^{-(\mu+\omega)t}\left(R(0) + \int_0^t e^{(\mu+\omega)\tau}\left[\gamma(1-\rho)I(\tau) + \nu N(\tau)V(\tau)\right]d\tau\right) \end{aligned} \quad (22)$$

where (10), with $S(t) = \gamma N(t)/\beta$, has been used.

Define an everywhere time-differentiable auxiliary function $h : \mathbb{R}_{0+} \to \mathbb{R}$ defined as:

$$h(t) = h(0) + \int_0^t \left[\gamma(1-\rho)I(\tau) + \nu N(\tau)V(\tau)\right]d\tau \quad (23)$$

such that,

$$\begin{aligned} &\dot{h}(t) = \gamma(1-\rho)I(t) + \nu N(t)V(t) \\ &\Leftrightarrow V(t) = \frac{1}{\nu N(t)}\left[\dot{h}(t) - \gamma(1-\rho)I(t)\right] \end{aligned} \quad (24)$$

for all time so that the last right-hand-side additive term in (23) becomes after integration by parts:

$$\begin{aligned} &e^{-(\mu+\omega)t}\int_0^t e^{(\mu+\omega)\tau}\dot{h}(\tau)d\tau \\ &= e^{-(\mu+\omega)t}\left[e^{(\mu+\omega)t}h(t) - h(0) - (\mu+\omega)\int_0^t e^{(\mu+\omega)\tau}h(\tau)d\tau\right] \end{aligned} \quad (25)$$

The replacement of (25) into (22) yields:

$$\begin{aligned} &\frac{\beta-\gamma}{\beta}e^{(\mu+\omega)t}N(t) - e^{\omega t}\left[E(0)+I(0)\right] \\ &= R(0) + \int_0^t e^{(\mu+\omega)\tau}\left[\gamma(1-\rho)I(\tau) + \nu N(\tau)V(\tau)\right]d\tau \\ &= R(0) + e^{(\mu+\omega)t}h(t) - h(0) - (\mu+\omega)\int_0^t e^{(\mu+\omega)\tau}h(\tau)d\tau \end{aligned} \quad (26)$$

and equivalently:

$$\begin{aligned} h(t) &= \frac{\beta-\gamma}{\beta}N(t) + e^{-(\mu+\omega)t}\left[h(0) - R(0)\right] \\ &\quad + (\mu+\omega)\int_0^t e^{-(\mu+\omega)(t-\tau)}h(\tau)d\tau - e^{-\mu t}\left[E(0)+I(0)\right] \\ &= \frac{\beta-\gamma}{\beta}N(t) + (\mu+\omega)\int_0^t e^{-(\mu+\omega)(t-\tau)}h(\tau)d\tau \\ &\quad + e^{-\mu t}\left(e^{-\omega t}\left[h(0) - R(0)\right] - E(0) - I(0)\right) \end{aligned} \quad (27)$$

generated from:

$$\begin{aligned} \dot{h}(t) &= \frac{\beta-\gamma}{\beta}\left[(\nu-\mu)N(t) - \rho\gamma I(t)\right] \\ &\quad - (\mu+\omega)e^{-(\mu+\omega)t}\left[h(0) - R(0)\right] + \mu e^{-\mu t}\left[E(0)+I(0)\right] \\ &\quad - (\mu+\omega)^2\int_0^t e^{-(\mu+\omega)(t-\tau)}h(\tau)d\tau + (\mu+\omega)h(t) \end{aligned} \quad (28)$$

so that:

$$\begin{aligned} \dot{h}(t) - \gamma(1-\rho)I(t) &= \frac{(\beta-\gamma)(\nu-\mu)}{\beta}N(t) + \gamma\left(\frac{\gamma\rho}{\beta} - 1\right)I(t) \\ &\quad - (\mu+\omega)e^{-(\mu+\omega)t}\left[h(0) - R(0)\right] + \mu e^{-\mu t}\left[E(0)+I(0)\right] \\ &\quad - (\mu+\omega)^2\int_0^t e^{-(\mu+\omega)(t-\tau)}h(\tau)d\tau + (\mu+\omega)h(t) \end{aligned} \quad (29)$$

The vaccination law which ensures the positivity of the mathematical SEIR-model (1)-(4) is generated as follows:

$$V(t) = \begin{cases} \bar{V}(t) & \text{if } \bar{V}(t) \in [0,\ 1] \\ 1 & \text{if } \bar{V}(t) > 1 \\ 0 & \text{if } \bar{V}(t) < 1 \end{cases} \quad (30)$$

where:

$$\bar{V}(t) = \frac{\dot{h}(t) - \gamma(1-\rho)I(t)}{\nu N(t)} \quad (31)$$

Define the indicator function i(t) as follows:

$$i(t) = \begin{cases} 0 & \text{if } \bar{V}(t) \in [0,\ 1] \\ 1 & \text{otherwise} \end{cases} \quad (32)$$

Then, one has instead of (15):

$$\begin{aligned} &S(t) + R(t) - N(t) = -\left[E(t) + I(t)\right] \\ &= e^{-\mu t}\left[S(0) + R(0) - N(0) + \int_0^t e^{\mu\tau}\left(\gamma - \beta\frac{S(\tau)}{N(\tau)}\right)I(\tau)i(\tau)d\tau\right] \\ &= -e^{-\mu t}\left[E(0) + I(0) - \int_0^t e^{\mu\tau}\left(\gamma - \beta\frac{S(\tau)}{N(\tau)}\right)I(\tau)i(\tau)d\tau\right] \end{aligned} \quad (33)$$

which coincides with (15) for all time if the indicator function is identically zero, that is, if $\dot{h}(t)$ is such that the auxiliary vaccination law (31) is in $[0,\ 1]$ for all time. Also, one gets from (15) that:

$$N(t) - S(t) - R(t) \le \varepsilon + \int_0^t e^{-\mu(t-\tau)}\left(\beta\frac{S(\tau)}{N(\tau)} - \gamma\right)I(\tau)i(\tau)d\tau \quad (34)$$

$\forall t \ge T(\varepsilon) \triangleq \frac{1}{\mu}\ln\left(\frac{N(0) - S(0) - R(0)}{\varepsilon}\right)$ for any given real $\varepsilon > 0$. The right-hand-side integral of (34) takes into account the tracking deterioration if there is a time interval of nonzero Lebesgue measure such that $V(t) \neq \bar{V}(t) \quad \forall t \in \mathbb{R}_{0+}$. The following result is important to discuss stability when the vaccination law $V(t) \in [0,\ 1]$ but it is not identically equal to $\bar{V}(t)$. In fact, the positivity part of Theorem 1 still holds because of the SEIR-model is positive since $V(t) \in [0,\ 1] \quad \forall t \in \mathbb{R}_{0+}$ and the whole population evolution is independent of the vaccination law according to (5). However, the whole susceptible plus immune does not asymptotically track the whole population. In summary, one has:

Theorem 3. The vaccination law (28), (30)-(31) makes the SEIR–model (1)-(4) positive and globally stable under Theorem 2. Furthermore,

$$\lim_{t\to\infty}\{N(t)-S(t)-R(t)\} \leq \lim_{t\to\infty}\sup\left[\int_0^t e^{-\mu(t-\tau)}\left(\beta\frac{S(\tau)}{N(\tau)}-\gamma\right)I(\tau)i(\tau)d\tau\right]$$

***

A more practical vaccination law is defined as follows:

$$V(t)=\begin{cases}\bar{V}(t) & \text{if } \begin{cases}\min\{S(t),\ R(t)\}>0 \text{ and}\\ \min\{E(t),\ I(t)\}\geq 0\end{cases}\\ V_{aux}(t) & \text{otherwise}\end{cases} \quad (35)$$

with $\bar{V}(t)$ given by (31) and $V_{aux}(t)$ obtained from:

$$V_{aux}(t)=\begin{cases}1 & \text{if } S(t)=0 \text{ and/or } R(t)=0\\ 0 & \text{otherwise}\end{cases} \quad (36)$$

Remark 1. The inclusion of the auxiliary function $V_{aux}(t)$ in (35) guarantees the non-negativity of the susceptible and remove-by-immunity populations. In this sense, note that large values of $|V(t)|$ could eventually do negative $S(t)$ or $R(t)$ from (1)-(4). This fact is avoided with such a construction of $V(t)$ since $V(t)=V_{aux}(t)$ at the time instants where $S(t)=0$ and/or $R(t)=0$ guarantees that $\dot{S}(t)\geq 0$ and $\dot{R}(t)\geq 0$ $\forall t\in\mathbb{R}_{0+}$. Moreover, the non-negativity for $S(t)$ and $R(t)$ guarantees the non-negativity of the infected and infectious populations from (2) and (3). Finally, note that the construction of the vaccination function (35)-(36) lets that $E(t)$ and $I(t)$ reach zero, which is the ideal objective for the eradication of the infection from the population. In summary, such an alternative control law guarantees the positivity property for the SEIR-epidemic model by the proper construction of the law. In this sense, the condition $V:\mathbb{R}_{0+}\to[0,\ 1]$ in Theorem 1 is a sufficient, but a non-necessary, condition to ensure the positivity of the system. ***

4 SIMULATION EXAMPLE

An example based on the rabbit hemorrhagic disease in United Kingdom is considered to illustrate the theoretical results presented in the paper. An initial population of $N(0)=1000$ rabbits is used. Such an epidemic can be described by the SEIR model (1)-(4) with the parameter values: $\mu=0.01$ per day (p. d.), $\nu=0.017$ p. d., $\beta=0.936$ p. d., $\omega=0.0333$ p. d., $\rho=0.9314$ and $\sigma=\gamma=0.025$ p. d.. Such values are commonly used in the literature (Keeling and Rohani, 2008, White et al., 2004). The main characteristic of such an infection is its high mortality, note the value of the probability of dying from the infection ($\rho=0.9314$) close to 1. The initial conditions for the individual populations are given by: $S(0)=800$, $E(0)=80$, $I(0)=50$ and $R(0)=70$.

The time evolution of the system in the free-vaccination case, i.e. if $V(t)=0$ $\forall t\in\mathbb{R}_{0+}$ is displayed in Figure 1. The population of rabbits disappears because of the high mortality of the infection as it can be seen in such a figure. As a consequence, a vaccination strategy has to be applied if the persistence of the rabbits is required. In this sense, Figure 2 displays the evolution of the total, the susceptible and the removed-by-immunity populations if the vaccination control law defined by (28), (31), (35) and (36), with the initial condition $h(0)=0$, is applied. On the other hand, the time evolution of the infected and the infectious population with such a vaccination strategy is shown in Figure 3. The total population of the rabbits monotonically grows through time as it can be seen from Figure 2. Moreover, the infected and infectious population decrease to zero as time grows as it is seen in Figure 3. In other words, the infection is eradicated after a time interval and then, the population of rabbits grows in a fast way, like it occurs in absence of disease. Finally, the time evolution of the vaccination function is displayed in Figure 4.

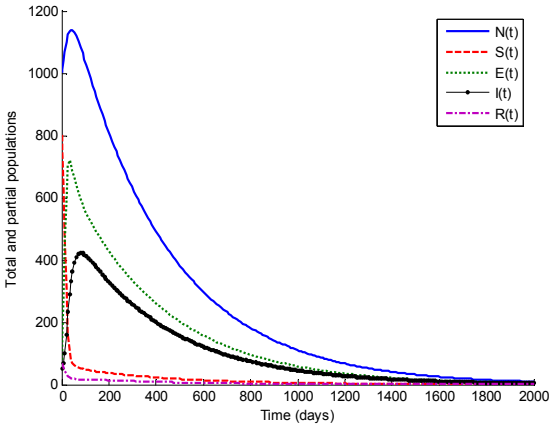

Figure 1: Time evolution of the total and individual populations without vaccination.

These simulation results point out the improvement of the use of a vaccination strategy in order to guarantee the suitable growth of a population against a high mortality infectious disease.

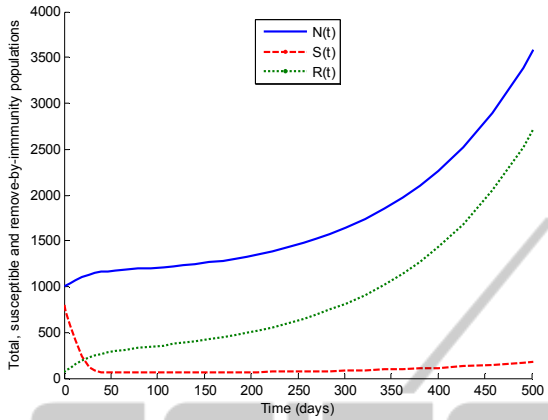

Figure 2: Time evolution of the total, susceptible and removed-by-immunity populations with the proposed vaccination control law.

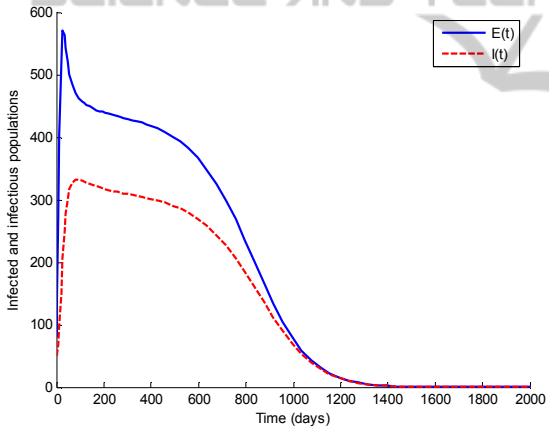

Figure 3: Time evolution of the infected and infectious populations with the proposed vaccination control law.

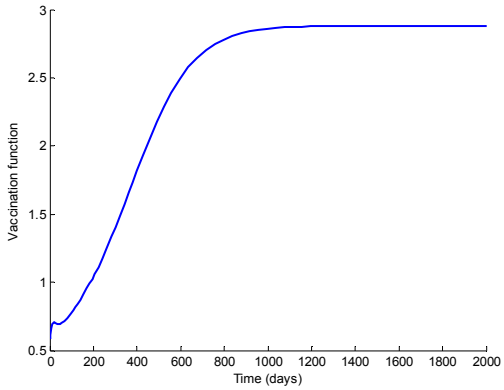

Figure 4: Time evolution of the vaccination associated to the control law.

5 CONCLUSIONS

A vaccination control strategy has been presented to eradicate the propagation of infectious diseases. The SEIR mathematical model has been used to design a control action via a vaccination strategy, which modifies suitably the system dynamics in order to get the disease eradication objective. The performance of such a vaccination strategy has been illustrated via some simulation results based on the rabbit hemorrhagic disease. Such results show that *a continuous-time vaccination through the population could be carried out in order to eradicate the epidemic*. Otherwise, the rabbits population extinguishes due to the high mortality associated to such an epidemic disease.

Future research is in progress to deal with more general models to describe propagations of diseases. Also, other types of control strategies based on impulsive or discrete-time vaccinations are going to be treated.

ACKNOWLEDGEMENTS

The authors thank to the Spanish Ministry of Education by its support of this work through Grant DPI2009-07197 and to the Basque Government by its support through Grants IT378-10, SAIOTEK SPE07UN04 and SAIOTEK SPE09UN12.

REFERENCES

De la Sen, M., 2008. About the properties of a modified generalized Beveron-Holt equation in ecology models. *Discrete Dynamics in Nature and Society 2008, Article ID 592950, 23 pages, doi: 10.1155/2008/592950.*

De la Sen, M., 2008. The generalized Beverton-Holt equation and the control of populations. *Applied Mathematical Modelling 32, pp. 2312-2328.*

De la Sen, M., Alonso-Quesada, S., 2008. A control theory point of view on Beverton-Holt equation in population dynamics and some of its generalizations. *Applied Mathematics and Computation 199, pp. 464-481.*

De la Sen, M., Alonso-Quesada, S., 2008. Model-matching-based control of the Beverton-Holt equation in Ecology. *Discrete Dynamics in Nature and Society 2008, Article ID 793512, 21 pages, doi: 10.1155/2008/793512.*

De la Sen, M., Alonso-Quesada, S., 2009. Control issues for the Beverton-Holt equation in ecology by locally monitoring the environment carrying capacity: Non-adaptive and adaptive cases. *Applied Mathematics and*

Computation 215, pp. 2616-2633.

Erturk, V. S., Momani, S., 2008. Solutions to the problem of prey and predator and the epidemic model via differential transform method, *Kybernetes 37, pp. 1180-1188*.

Keeling, M. J., Rohani, P., 2008. *Modeling Infectious Diseases in Humans and Animals*, Princeton University Press, Princeton and Oxford.

Khan, H., Mohapatra, R. N., Varajvelu, K., Liao, S. J., 2009. The explicit series solution of SIR and SIS epidemic models. *Applied Mathematics and Computation 215, pp. 653-669.*

Mollison, D., 2003. *Epidemic Models: Their Structure and Relation to Data*, Publications of the Newton Institute. Cambridge University Press.

Mukhopadhyay, B., Battacharyya, R., 2007. Existence of epidemic waves in a disease transmission model with two-habitat population. *International Journal of Systems Science 38, pp. 699-707.*

Ortega, N., Barros, L. C., Massad, E., 2003. Fuzzy gradual rules in epidemiology. *Kybernetes, 32, pp. 460-477.*

Song, X. Y., Jiang, Y., Wei, H. M., 2009. Analysis of a saturation incidence SVEIRS epidemic model with pulse and two time delays. *Applied Mathematics and Computation 214, pp. 381-390.*

White, P. J., Trout, R. C., Moss, S. R., Desai, A., Armesto, M., Forrester N. L., Gould, E. A., Hudson, P. J., 2004. Epidemiology of rabbit haemorrhagic disease virus in the United Kingdom: evidence for seasonal transmission by both virulent and avirulent modes of infection. *Epidemiology and Infection 132, pp. 555-567.*

Yildirim, A., Cherruault, Y., 2009. Anaytical approximate solution of a SIR epidemic model with constant vaccination strategy by homotopy perturbation method. *Kybernetes 38, pp. 1566-1575.*

Zhang, T. L., Liu, J. L., Teng, Z. D., 2009. Dynamic behaviour for a nonautonomous SIRS epidemic model with distributed delays. *Applied Mathematics and Computation 214, pp. 624-631.*