An Observer-Based Vaccination Law for a SEIR Epidemic Model

M. De la Sen, S. Alonso-Quesada, A. Ibeas, and R. Nistal

***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 of the removed-by-immunity population to the total population while achieving simultaneously the remaining population tends to zero.**

***Index Terms*—Control, SEIR epidemic models, stability.**

I. 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 have been investigated at the levels of stability, cycle-oscillatory behavior, permanence and control through the manipulation of the carrying capacity [1], [2]. 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 [3]-[8] (see also the references listed therein). The sets of models include the most basic ones, [3], [4]:

- SI-models where not removed-by-immunity population is assumed. In other words, only susceptible and infected populations are assumed.
- SIR-models, which include susceptible plus infected plus removed-by-immunity populations.
- SEIR-models where the infected populations is split into two ones. Namely, 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 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 [5], impulsive [6], discrete-time etc., incorporating point or distributed delays [6], [7], oscillatory behaviours [8] and so on. In this paper, a continuous-time vaccination observer-based control strategy is given for a SEIR epidemic model which takes directly the estimated susceptible, infected, infectious and immune populations to design the vaccination strategy. It is not required either the knowledge through time of the true partial populations of susceptible, infected, infectious and immune or the knowledge of the true parameters. It is assumed that the total population is known and equal to the total estimated population and that it remains constant through time, so that the illness transmission is not critical. Moreover, the SEIR-model is of the above mentioned true-mass action type. Some important issues about the stability and positivity of the combined SEIR-model and its observer are discussed.

II. SEIR Epidemic Model

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

$$\begin{aligned}
\dot{S}(t) &= -\mu S(t) + \omega R(t) - \beta \frac{S(t)I(t)}{N} + \mu N\left(1 - V(t)\right) \\
\dot{E}(t) &= \beta \frac{S(t)I(t)}{N} - (\mu + \sigma)E(t) \\
\dot{I}(t) &= -(\mu + \gamma)I(t) + \sigma E(t) \\
\dot{R}(t) &= -(\mu + \omega)R(t) + \gamma I(t) + \mu N V(t)
\end{aligned} \tag{1}$$

subject to initial conditions $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$ and $R(0) \geq 0$ under the constraint:

$$\begin{aligned}
N = N(0) &= S(t) + E(t) + I(t) + R(t) \\
&= S(0) + E(0) + I(0) + R(0)
\end{aligned} \tag{2}$$

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$\forall t \in \mathbb{R}_{0+}$ and the vaccination function $V : \mathbb{R}_{0+} \to \mathbb{R}_{0+}$, with $\mathbb{R}_{0+} \triangleq \{z \in \mathbb{R} | z \geq 0\}$. In the above SEIR-model, N 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 $\beta S(t)I(t)/N$), σ^{-1} and γ^{-1} are finite and, respectively, the average durations of the latent and infective periods. All the above parameters are assumed to be nonnegative. This model has been studied in [9] from the point of view of equilibrium points in the free-vaccination case and control. Two vaccination auxiliary controls being respectively proportional to the susceptible or to the whole population so that the whole population is asymptotically immune have been proposed. The model proposed assumes that the parameters of the SEIR-model are known. The current paper does not require such a perfect parametrical knowledge since an observer is incorporated.

III. Observed-Based Vaccination

It turns out that while the assumption of the knowledge of the total population N is not quite restrictive in practice, the knowledge of partial populations of susceptible, infected, infectious and immune may be considered severely restrictive. It turns out that if the partial initial populations are unknown then their evolution through time cannot be computed in a closed form from the differential system (1). A practical solution to circumvent the problem might be to estimate them based on percentages of the total population through time from experimental knowledge of the disease propagation. Another solution may be to estimate them online by using an on-line observer. This solution is focused on in the current manuscript by using a SEIR-estimation algorithm (observer) of the SEIR-model (1) which estimates through time the individual populations being involved. The vaccination strategy is obtained as a control strategy from the date supplied by the observer through time. Such a strategy does not require the knowledge of the partial populations to organize and perform the vaccination strategy. The estimates of the various individual populations are denoted by the same notations as the real populations with hat superscripts, namely, $\hat{S}(t)$, $\hat{E}(t)$, $\hat{I}(t)$ and $\hat{R}(t)$. Thus, consider the SEIR-type observer for the SEIR-model (1) as follows:

$$\begin{aligned}
\dot{\hat{S}}(t) &= -\hat{\mu}\hat{S}(t) + \hat{\omega}\hat{R}(t) - \hat{\beta}\frac{\hat{S}(t)\hat{I}(t)}{N} + \hat{\mu}N\left(1 - V(t)\right) \\
\dot{\hat{E}}(t) &= \hat{\beta}\frac{\hat{S}(t)\hat{I}(t)}{N} - (\hat{\mu} + \hat{\sigma})\hat{E}(t) \\
\dot{\hat{I}}(t) &= -(\hat{\mu} + \hat{\gamma})\hat{I}(t) + \hat{\sigma}\hat{E}(t) \\
\dot{\hat{R}}(t) &= -(\hat{\mu} + \hat{\omega})\hat{R}(t) + \hat{\gamma}\hat{I}(t) + \hat{\mu}NV(t)
\end{aligned} \tag{3}$$

subject to initial conditions $\hat{S}(0) \geq 0$, $\hat{E}(0) \geq 0$, $\hat{I}(0) \geq 0$ and $\hat{R}(0) \geq 0$ under the constant through time estimated population constraint equalizing the true one, i.e.,

$$\begin{aligned}
N = N(0) &= \hat{S}(t) + \hat{E}(t) + \hat{I}(t) + \hat{R}(t) \\
&= \hat{S}(0) + \hat{E}(0) + \hat{I}(0) + \hat{R}(0)
\end{aligned} \tag{4}$$

$\forall t \in \mathbb{R}_{0+}$ and the vaccination law $V : \mathbb{R}_{0+} \to \mathbb{R}_{0+}$ given by:

$$V(t) = \frac{1}{\hat{\mu}N}\left(k_1\hat{S}(t) + k_2\hat{E}(t) + k_3\hat{I}(t) + k_4\hat{R}(t) + k_5\hat{S}(t)\hat{I}(t) + gN\right). \tag{5}$$

In the above estimated SEIR-model, $\hat{\mu}$ is the estimated rate of deaths from causes unrelated to the infection, $\hat{\omega}$ is the estimated rate of losing immunity, $\hat{\beta}$ is the estimated transmission constant (with the total number of infections per unity of time at time t being $\hat{\beta}\hat{S}(t)\hat{I}(t)/N$), $\hat{\sigma}^{-1}$ and $\hat{\gamma}^{-1}$ are finite and, respectively, the estimated average durations of the latent and infective periods. The above parameter estimates can be done, through the use of available "a priori" knowledge, to be identical to the true values if those ones are known or estimated on-line from data measurements. Through this manuscript, we assume that those estimated parameters are fixed but not necessarily identical to the true parameters and all of them are nonnegative. The substitution of (5) in (3) yields the following combined observer-controller for the SEIR-model:

$$\dot{\hat{x}}(t) = \hat{A}(t)\hat{x}(t) + \hat{b} \tag{6}$$

where

$$\hat{x}(t) = \left[\hat{S}(t) \;\; \hat{E}(t) \;\; \hat{I}(t) \;\; \hat{R}(t)\right]^T, \tag{7}$$

$$\hat{b} = \left[(\hat{\mu} - g)N \;\; 0 \;\; 0 \;\; gN\right]^T \text{ and} \tag{8}$$

$$\hat{A}(t) = \begin{bmatrix}
-\left(\hat{\mu} + k_1 + (\hat{\beta}_1 + k_5)\hat{I}(t)\right) & -k_2 & -k_3 & \hat{\omega} - k_4 \\
\hat{\beta}_1\hat{I}(t) & -(\hat{\mu} + \hat{\sigma}) & 0 & 0 \\
0 & \hat{\sigma} & -(\hat{\mu} + \hat{\gamma}) & 0 \\
k_1 + k_5\hat{I}(t) & k_2 & \hat{\gamma} + k_3 & -(\hat{\mu} + \hat{\omega} - k_4)
\end{bmatrix} \tag{9}$$

with $\hat{\beta}_1 = \hat{\beta}/N$. The substitution of (5) into (1) yields the following SEIR observer-based vaccination controlled SEIR-model:

$$\dot{x}(t) = A(t)x(t) + B(t)\hat{x}(t) + b \tag{10}$$

where

$$x(t) = \left[S(t) \;\; E(t) \;\; I(t) \;\; R(t)\right]^T, \tag{11}$$

$$b = \left[\left(1 - \frac{g}{\hat{\mu}}\right)\mu N \;\; 0 \;\; 0 \;\; \frac{g\mu N}{\hat{\mu}}\right]^T, \tag{12}$$

$$A(t)=\begin{bmatrix} -(\mu+\beta_1 I(t)) & 0 & 0 & \omega \\ \beta_1 I(t) & -(\mu+\sigma) & 0 & 0 \\ 0 & \sigma & -(\mu+\gamma) & 0 \\ 0 & 0 & \gamma & -(\mu+\omega) \end{bmatrix} \quad (13)$$

with $\beta_1 = \beta / N$ and

$$B(t)=\left(\frac{\mu}{\hat{\mu}}\right)\begin{bmatrix} -\left(k_1+k_5\hat{I}(t)\right) & -k_2 & -k_3 & -k_4 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ k_1+k_5\hat{I}(t) & k_2 & k_3 & k_4 \end{bmatrix}. \quad (14)$$

The systems (6)-(9) and (10)-(14) may be compacted as an extended system as follows:

$$\dot{\bar{x}}(t)=\bar{A}(t)\bar{x}(t)+\bar{b} \quad (15)$$

where

$$\bar{x}(t)=\left[\hat{x}^T(t) \;\; \tilde{x}^T(t)\right]^T, \quad (16)$$

$$\bar{b}=\left[\hat{b}^T \;\; \tilde{b}^T\right]^T \text{ and} \quad (17)$$

$$\bar{A}(t)=\left[\begin{array}{c|c} \hat{A}(t) & 0 \\ \hline A(t)-\hat{A}(t)+B(t) & A(t) \end{array}\right] \quad (18)$$

with $\tilde{x}(t)=x(t)-\hat{x}(t)$ being the observation error and $\tilde{b}$ a parametrical error defined by:

$$\tilde{b}=b-\hat{b}=\left(\frac{\mu}{\hat{\mu}}-1\right)N\left[\hat{\mu}-g \;\; 0 \;\; 0 \;\; g\right]^T. \quad (19)$$

It is direct to see that $\|\tilde{b}\|\le\varepsilon$ for any given real $\varepsilon>0$, with $\|\tilde{b}\|=|(\mu/\hat{\mu})-1|\,N\sqrt{(\hat{\mu}-g)^2+g^2}$ being the Euclidean norm of $\tilde{b}$, if $|\mu-\hat{\mu}|\le\hat{\mu}\varepsilon/\left(N\sqrt{(\hat{\mu}-g)^2+g^2}\right)$. Decompose

$$\begin{aligned} &A(t)=A_0+\Delta A(t) \;\; ; \;\; \hat{A}(t)=\hat{A}_0+\Delta\hat{A}(t) \\ &A(t)-\hat{A}(t)+B(t)=B_0+\Delta B(t) \end{aligned} \quad (20)$$

where A_0, $\hat{A}_0$ and B_0 are constant matrices and the non-unique decompositions (20) are as follows:

$$A_0=\begin{bmatrix} -(\mu+\beta_1 I_r) & 0 & 0 & \omega \\ 0 & -(\mu+\sigma) & 0 & 0 \\ 0 & \sigma & -(\mu+\gamma) & 0 \\ 0 & 0 & \gamma & -(\mu+\omega) \end{bmatrix}, \quad (21)$$

$$\hat{A}_0=\begin{bmatrix} -\left(\hat{\mu}+k_1+(\hat{\beta}_1+k_5)\hat{I}_r\right) & -k_2 & -k_3 & \hat{\omega}-k_4 \\ 0 & -(\hat{\mu}+\hat{\sigma}) & 0 & 0 \\ 0 & \hat{\sigma} & -(\hat{\mu}+\hat{\gamma}) & 0 \\ k_1+k_5\hat{I}_r & k_2 & \hat{\gamma}+k_3 & -(\hat{\mu}+\hat{\omega}-k_4) \end{bmatrix}, \quad (22)$$

$$\Delta A(t)=\begin{bmatrix} \beta_1\left(I_r-I(t)\right) & 0 & 0 & 0 \\ \beta_1 I(t) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{bmatrix} \text{ and} \quad (23)$$

$$\Delta\hat{A}(t)=\begin{bmatrix} (\hat{\beta}_1+k_5)\left(\hat{I}_r-\hat{I}(t)\right) & 0 & 0 & 0 \\ \hat{\beta}_1\hat{I}(t) & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ k_5\left(\hat{I}(t)-\hat{I}_r\right) & 0 & 0 & 0 \end{bmatrix} \quad (24)$$

for any given prefixed constant values $I_r \ge 0$ and $\hat{I}_r \ge 0$. Moreover,

$$\begin{aligned} \Delta B(t) &= A(t)-\hat{A}(t)+B(t)-B_0 \\ &= \begin{bmatrix} -\tilde{\mu}-f_1(t)+f_2(t)-b_{011} & k_2' & k_3' & \tilde{\omega}+k_4' \\ f_1(t)-b_{021} & -\tilde{\mu}-\tilde{\sigma} & 0 & 0 \\ 0 & \tilde{\sigma} & -\tilde{\mu}-\tilde{\gamma} & 0 \\ -f_2(t) & -k_2' & \tilde{\gamma}-k_3' & -\tilde{\mu}-\tilde{\omega}-k_4' \end{bmatrix} \end{aligned} \quad (25)$$

with $f_1(t)=\beta_1 I(t)-\hat{\beta}_1\hat{I}(t)$, $f_2(t)=\left(1-(\mu/\hat{\mu})\right)\left(k_1+k_5\hat{I}(t)\right)$, $k_i'=\left(1-(\mu/\hat{\mu})\right)k_i$, for $i=2, 3, 4$, $\tilde{\mu}=\mu-\hat{\mu}$, $\tilde{\sigma}=\sigma-\hat{\sigma}$, $\tilde{\gamma}=\gamma-\hat{\gamma}$, $\tilde{\omega}=\omega-\hat{\omega}$ and, b_{011} and b_{012} being, respectively, the coefficients in the first and the second raw of the first column of matrix $B_0\in\mathbb{R}^{4\times4}$. The rest of the coefficients of such a matrix are identically zero.

In this way, $\bar{A}(t)$ is decompose as follows:

$$\bar{A}(t)=\bar{A}_0+\tilde{\bar{A}}_0(t) \text{ with} \quad (26)$$

$$\bar{A}_0=\begin{bmatrix} \hat{A}_0 & 0 \\ B_0 & A_0 \end{bmatrix} \text{ and } \tilde{\bar{A}}_0(t)=\begin{bmatrix} \Delta\hat{A}(t) & 0 \\ \Delta B(t) & \Delta A(t) \end{bmatrix}. \quad (27)$$

If A_0 and $\hat{A}_0$ are stability (or Hurwitz) matrices then the block triangular matrix $\bar{A}_0$ is also a stability matrix with stability abscissa $(-\rho)$ subject to the constraint $\max\left\{\mathrm{Re}\left(\lambda_i(A_0)\right),\mathrm{Re}\left(\lambda_i(\hat{A}_0)\right)\right\}\le-\rho<0$ where the first inequality is non strict if there is some multiple eigenvalue of $\bar{A}_0$.

IV. Stability

A simple inspection shows that A_0 is a stability matrix if $\det(sI_4 - A_0) = (s+\mu+\beta_1 I_r)(s+\mu+\sigma)(s+\mu+\gamma)(s+\mu+\omega)$, where I_4 denotes the 4-order identity matrix, is Hurwitz. Also, $\hat{A}_0$ is a stability matrix if $\det(sI_4 - \hat{A}_0) = \hat{d}(s) + (k_1 + k_5\hat{I}_r)\hat{n}(s)$ has all its zeros in $\mathrm{Re}(s) < 0$ where:

$$\begin{aligned} \hat{n}(s) &= (k_4 - \hat{\omega})(s + \hat{\mu} + \hat{\sigma})(s + \hat{\mu} + \hat{\gamma}) \\ \hat{d}(s) &= \left(s + \hat{\mu} + k_1 + (\hat{\beta}_1 + k_5)\hat{I}_r\right)\cdot \\ &\quad (s + \hat{\mu} + \hat{\sigma})(s + \hat{\mu} + \hat{\gamma})(s + \hat{\mu} + \hat{\omega} - k_4) \end{aligned} \quad .(28)$$

Assume that $\hat{d}(s)$ is a Hurwitz polynomial, that is, $k_4 < \hat{\mu} + \hat{\omega}$, $\hat{\mu} + k_1 + (\hat{\beta}_1 + k_5)\hat{I}_r > 0$, $\hat{\mu} + \hat{\sigma} > 0$ and $\hat{\mu} + \hat{\gamma} > 0$ and define $\hat{h}(s) \triangleq (k_1 + k_5\hat{I}_r)\hat{n}(s)/\hat{d}(s)$. Note that:

$$\begin{aligned} & det(sI_4 - \hat{A}_0) = \hat{d}(s) + (k_1 + k_5\hat{I}_r)\hat{n}(s) = 0 \\ & \Leftrightarrow \quad 1 + \hat{h}(s) = 0 \end{aligned} \quad (29)$$

has all its solutions in $\mathrm{Re}(s) < 0$ if and only if $\|\hat{h}\|_\infty < 1$ since $\hat{d}(s)$ is a Hurwitz polynomial, where $\|\hat{h}\|_\infty$ is the H_∞-norm of the transfer function $\hat{h}(s)$. Since $\bar{A}_0$ is block-triangular and constant then the following result is direct.

Assertion 1. $\bar{A}_0$ is a stability matrix if and only if $\mu + \beta_1 I_r > 0$, $\mu + \sigma > 0$, $\mu + \gamma > 0$, $\mu + \omega > 0$ and $\hat{h} \in \mathbf{RH}_\infty$ (i.e. $k_4 < \hat{\mu} + \hat{\omega}$, $\hat{\mu} + k_1 + (\hat{\beta}_1 + k_5)\hat{I}_r > 0$, $\hat{\mu} + \hat{\sigma} > 0$ and $\hat{\mu} + \hat{\gamma} > 0$) with $\|\hat{h}\|_\infty < 1$. ***

From Assertion 1 and Gronwall's Lemma [10] the following follows.

Assertion 2. The matrix function $\bar{A}(t)$ is stable if $\bar{A}_0$ is a stability matrix and, furthermore, $\rho > \sup_{t \in \mathbb{R}_{0+}} \left\{ \left\| \tilde{\bar{A}}_0(t) \right\| \right\}$ where $(-\rho) < 0$ is the stability abscissa of the matrix $\bar{A}_0$. ***

Note that the Euclidean norm of $\bar{b}$ may be directly calculated from those of $\hat{b}$ and $\tilde{b}$ using (8) and (19) leading to:

$$\|\bar{b}\| \le \frac{\left(\hat{\mu} + |\mu - \hat{\mu}|\right) N}{\hat{\mu}} \sqrt{(\hat{\mu} - 2g)\hat{\mu} + 2g^2} \quad . \quad (30)$$

Note that $\rho_0 \triangleq \rho - \sup_{t \in \mathbb{R}_{0+}} \left\{ \left\| \tilde{\bar{A}}_0(t) \right\| \right\} > 0$ so that $(-\rho_0) < 0$ is larger than the maximum of the stability abscissas of $\bar{A}(t)$ for $t \in \mathbb{R}_{0+}$ if Assertion 2 holds.

Assertion 3. If Assertion 2 holds then any solution of the forced system (15)-(27) satisfies the following inequality:

$$\begin{aligned} \|\bar{x}(t)\| &\le M(t) = k_0 e^{-\rho_0 t}\left(\|\bar{x}(0)\| + \|\bar{b}\|\int_0^t e^{\rho_0 \tau} d\tau\right) \\ &\to \frac{k_0}{\rho_0}\frac{\left(\hat{\mu} + |\mu - \hat{\mu}|\right) N}{\hat{\mu}} \sqrt{(\hat{\mu} - 2g)\hat{\mu} + 2g^2} \end{aligned} \quad (31)$$

as $t \to \infty$, for some real constant $k_0 \ge 1$, and the corresponding sub-states of $\bar{x}(t)$ satisfy:

$$\begin{aligned} \|\hat{x}(t)\| &\le \hat{M}(t) = k_0 e^{-\rho_0 t}\left(\|\hat{x}(0)\| + \|\hat{b}\|\int_0^t e^{\rho_0 \tau} d\tau\right) \\ &\to \frac{k_0}{\rho_0} N \sqrt{(\hat{\mu} - 2g)\hat{\mu} + 2g^2} \end{aligned} \quad (32)$$

and

$$\begin{aligned} \|\tilde{x}(t)\| &\le \tilde{M}(t) = k_0 e^{-\rho_0 t}\left(\|\tilde{x}(0)\| + \|\tilde{b}\|\int_0^t e^{\rho_0 \tau} d\tau\right) \\ &\to \frac{k_0}{\rho_0}\frac{|\mu - \hat{\mu}| N}{\hat{\mu}} \sqrt{(\hat{\mu} - 2g)\hat{\mu} + 2g^2} \end{aligned} \quad (33)$$

as $t \to \infty$. ***

Note that $\|\tilde{x}(t)\| \to 0$ as $t \to \infty$ either if $\hat{\mu} = \mu$ (and then $\|\hat{x}(t)\| \to \frac{k_0}{\rho_0} N\sqrt{(\mu - 2g)\mu + 2g^2}$ as $t \to \infty$ and, if in addition, $g = 0$ then $\|\hat{x}(t)\| \to \frac{k_0 \mu N}{\rho_0}$ as $t \to \infty$) or if $\hat{\mu} = g = 0$ (and then $\|\hat{x}(t)\| \to 0$ as $t \to \infty$).

Finally, $x(t)$ satisfy:

$$\begin{aligned} \|x(t)\| &\le \|M(t)\| \to \\ &\to \frac{k_0}{\rho_0}\frac{\left(\hat{\mu} + |\mu - \hat{\mu}|\right) N}{\hat{\mu}} \sqrt{(\hat{\mu} - 2g)\hat{\mu} + 2g^2} \end{aligned} \quad (34)$$

as $t \to \infty$ from the definition of b in (12). However, this upper-bound can be improved if a version of Assertion 2 applied to the matrix function $A(t)$ leads to a smaller ratio of its corresponding constants than the ratio k_0/ρ_0 of the whole extended system.

V. Positivity

Positive systems are those having nonnegative solutions in the sense that all the state components are nonnegative for all time provided that the initial condition and control are both nonnegative [11]. Because of the nature of the SEIR epidemic model (1), it is required that it be a positive system for the implemented vaccination law. The extended SEIR system has a unique solution for each initial state given by:

$$\bar{x}(t) = e^{\bar{A}_0 t}\left(\bar{x}(0) + \int_0^t e^{-\bar{A}_0 \tau}\left(\tilde{\bar{A}}_0(\tau)\bar{x}(\tau) + \bar{b}\right)d\tau\right). \quad (35)$$

From (6) and (10) the SEIR solution and its estimate through the observer are uniquely given by:

$$\hat{x}(t) = e^{\hat{A}_0 t}\left(\hat{x}(0) + \int_0^t e^{-\hat{A}_0 \tau}\left(\Delta\hat{A}(\tau)\hat{x}(\tau) + \hat{b}\right)d\tau\right) \quad (36)$$

and

$$x(t) = e^{A_0 t}\left(x(0) + \int_0^t e^{-A_0 \tau}\left(\Delta A(\tau)x(\tau) + B(\tau)\hat{x}(\tau) + b\right)d\tau\right) \quad (37)$$

respectively. In principle, it is apparently non necessary to require in addition that the estimation algorithm or the extended system be positive. The following notation is used for the theoretical results in this section.

Notation. $x \in \mathbb{R}^n_{0+}$ is a positive real n-vector in the usual sense that all its components are nonnegative . This can be also denoted by $x > 0$ if $x \neq 0$. In the same way, $A \in \mathbb{R}^{n\times n}_{0+}$ (or $A > 0$) is a positive real n-matrix in the usual sense that all its entries are nonnegative. A square real matrix A is a Metzler matrix if and only if all its off-diagonal entries are nonnegative and then its associate exponential matrix function is positive. ***

Assertion 4. The following properties hold:

(i) Assume that A_0 and $\hat{A}_0$ are Metzler matrices, $\Delta A(t) > 0$, $b + B(t)\hat{x}(t) \geq 0$ and $\Delta\hat{A}(t) > 0$ $\forall t \in \mathbb{R}_{0+}$, and $b > 0$ and $\hat{b} > 0$ then $\left[x^T(0) \;\; \hat{x}^T(0)\right]^T > 0$ implies that $x(t) > 0$ and $\hat{x}(t) > 0$ $\forall t \in \mathbb{R}_{0+}$. In other words, the extended system of state $\left[x^T(t) \;\; \hat{x}^T(t)\right]^T$ is positive.

(ii) Assume that in Property (i) $\hat{A}_0$ fails to be a Metzler matrix because of the value k_1 or k_5 in its (4,1) entry. Then, for initial conditions $\hat{x}(0) > 0$ which make $\hat{x}(t)$ to be non positive, $x(t)$ can fail to be positive for all time for some $x(0) > 0$ and some such k_1 or k_5 with sufficiently large absolute values. ***

Remarks 1. It is required for modeling coherency that both the epidemic SEIR-model and its observer be positive dynamic systems. The condition of nonnegative of $b + B(t)\hat{x}(t) \geq 0$ $\forall t \in \mathbb{R}_{0+}$ in Assertion 4 requires $g \geq 0$ and $(\hat{\mu} - g)N \geq \left(k_1 + k_5\hat{I}(t)\right)\hat{S}(t) + k_2\hat{E}(t) + k_3\hat{I}(t) + k_4\hat{R}(t) \geq -gN$ $\forall t \in \mathbb{R}_{0+}$, which may be guaranteed by choosing the controller gains under the knowledge $N = \sum_{i=1}^{4}\hat{x}_i(t)$ $\forall t \in \mathbb{R}_{0+}$. The requirement that $\hat{A}_0$ be a Metzler matrix is guaranteed if $k_2 = 0$, $-\hat{\gamma} \leq k_3 \leq 0$, $0 \leq k_4 \leq \hat{\omega}$ and $k_1 + k_5\hat{I}_r \geq 0$. The condition that $\hat{b} > 0$ is guaranteed if $0 \leq g \leq \hat{\mu}$. Finally, $\min_{t\in\mathbb{R}_{0+}}\left\{\Delta\hat{A}(t)\right\} > 0$ is guaranteed if k_5 is such that $(\hat{\beta}_1 + k_5)\left(\hat{I}_r - \max_{t\in\mathbb{R}_{0+}}\left\{\hat{I}(t)\right\}\right) \geq 0$ and $k_5\left(\min_{t\in\mathbb{R}_{0+}}\left\{\hat{I}(t)\right\} - \hat{I}_r\right) \geq 0$ are fulfilled. Such conditions require that $0 \geq k_5 \geq -\hat{\beta}_1$. In this way the observer is a positive system.

This restricts the generality of the choice of the gains in the vaccination control law (5). However, if the requirement for the observer to be positive is removed then it is only needed that the SEIR-model (1) be positive under a modified vaccination law (5) by requiring the weaker condition that $0 \leq g \leq \hat{\mu}$ and $\min\{\sigma, \omega, \gamma\} \geq 0$ and $I_r \geq \max_{t\in\mathbb{R}_{0+}}\{I(t)\}$. ***

Note that while Assertion 4(i) is of sufficiency-type to guarantee positivity, the lack of all the joint above conditions in Assertion 4 (ii) refer to a necessary condition for positivity in such cases. Note also that positive and total population equal to N for all time implies necessary global stability so that we have directly the following:

Assertion 5. If Assertion 4 (i) holds then the extended SEIR-model (i.e. the combined SEIR-model plus its observer) is globally stable if all the initial populations and their estimates are nonnegative. Furthermore all the susceptible, infected, infectious and immune populations and their estimates are upper-bounded by N and the sum of all the populations and that of their estimates is equal to N at any time. The converse is not true, in general, so that if the extended SEIR-model is stable under Assertion 2 then such a model is not necessarily positive.
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VI. Simulation Example

This section illustrates through a simulation example the theoretical results previously stated for the combined SEIR control-observer model. The SEIR-model is described by the following parameters taken from an influenza outbreak [3]: $\mu^{-1} = 25550$ days (d), $\sigma^{-1} = \gamma^{-1} = 2.2$ d, $\omega^{-1} = 15$ d and $\beta^{-1} = 1.66$ d. The initial conditions are given by, $S(0) = 400$, $E(0) = 150$, $I(0) = 250$ and $R(0) = 200$ individuals so that the total population is $N = N(0) = 1000$ individuals. The observer (3) is used to estimate the partial populations for all time since they are not measurable. The initial estimates are $\hat{S}(0) = 250$, $\hat{E}(0) = \hat{I}(0) = 150$ and $\hat{R}(0) = 450$ individuals. Moreover, an estimation of the values of the unknown true model parameters is used to parameterize the observer. Such estimates are: $\hat{\mu}^{-1} = 23500$ d, $\hat{\sigma}^{-1} = \hat{\gamma}^{-1} = 2$ d, $\hat{\omega}^{-1} = 14$ d and $\hat{\beta}^{-1} = 1.46$ d. A vaccination strategy given by (5) is introduced in the system. The following values have been used for the control gains: $k_1 = 1$, $k_2 = -0.1$, $k_3 = -\hat{\gamma}$, $k_4 = 0.95\hat{\omega}$, $k_5 = -\hat{\beta}_1$ and $g = \hat{\mu}$. Fig. 1 shows the time-evolution of the populations.

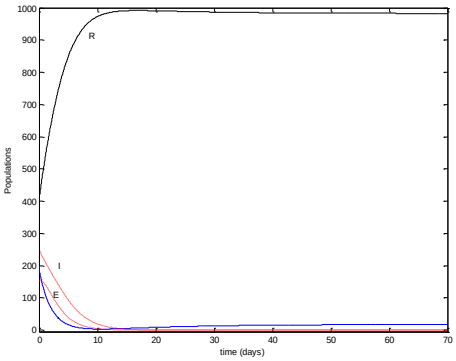

Fig.1. Evolution of the populations with vaccination-based observer.

Fig. 2 shows the error between the observation and the real states.

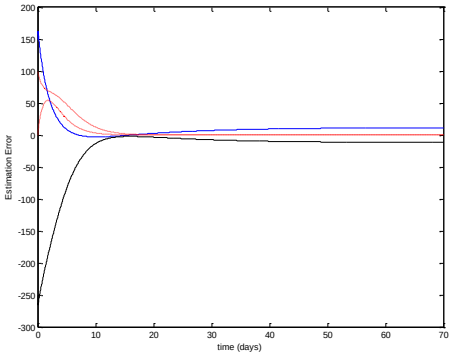

Fig. 2. Evolution of the observation error with vaccination.

Fig. 1 not only shows that the SEIR-model is globally stable regardless the observation error depicted in Fig. 2 but also that the observer-based control law eradicates the infective and infectious while the immune almost reaches to be the total population N. A small number of susceptible still appear in the steady-state. However, this behavior is much better than that obtained with the combined SEIR-model and observer system without vaccination where a number of infective and infectious appear as it can be seen in Fig. 3.

In summary, this example points out the improvement in the eradication of an infection disease if a vaccination control law based on an observer for the SEIR-model is applied compared with the results obtained in a free vaccination case.

Note also that the true partial populations are bounded for all time, i.e., the combined SEIR control-observer model is stable. However, it is not a positive system since the control gain $k_2 = -0.1$ makes $\hat{A}_0$ not be a Metzler matrix, so the observer is not a positive system (Remark 1). This fact is according to the theoretical result pointed out in Assertion 5.

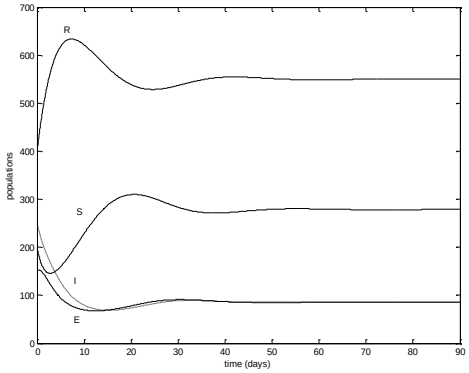

Fig. 3. Evolution of the actual populations through time in the vaccination-free case.

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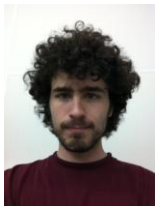

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