

## On vaccination controls for a time-varying SEIR epidemic model with asymptotic removal of the infection

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**Abstract**—This paper is devoted to a vaccination control strategy for a time-varying SEIR (susceptible plus infected plus infectious plus removed populations) epidemic model. The model of true mass action type, i.e. it takes into account the whole population as a refrain action to the disease propagation. The control objective is the asymptotically tracking the joint susceptible plus the removed-by-immunity population what is fully equivalent to the asymptotic removal of the infection.

**Keywords**—epidemic models; control; infection removal; SEIR time-varying models; tracking objective; vaccination controls; positivity; stability.

### I. INTRODUCTION

Important control problems nowadays are those of population evolution models (like, for instance, Beverton-Holt model, Hassell model, Ricker model etc.) which are solvable 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, oscillatory behaviors, permanence and control through the manipulation of the carrying capacity (see, for instance, [1-5]). On the other hand, the literature about epidemic mathematical models is exhaustive in several books and papers. A list of references is given in this manuscript, cf. [6-14]. The sets of models include the most basic ones, [6-7]:

- 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 [8], impulsive [12], discrete – time etc., incorporating point or distributed delays [12-13], oscillatory behaviors [14] etc.

Also, some variants of such models become considerably simpler for the illness transmission among plants [6-7]. In this paper, a continuous-time vaccination control strategy is proposed for a time-varying SEIR epidemic model of non-constant total population which makes the infection to be asymptotically removed.

### II. MODEL

Let  $S(t)$  be the “susceptible” population of infection at time  $t$ ,  $E(t)$  the “infected” (i.e. those which incubate the illness but do not still have any symptoms) at time  $t$ ,  $I(t)$  is the “infectious” (or “infective”) population at time  $t$ , and  $R(t)$  is the “removed by immunity” (or “immune”) population at time  $t$ . Consider the SEIR-type epidemic model:

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

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

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

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

subject to initial conditions  $S_0 = S(0) \geq 0$ ,  $E_0 = E(0) \geq 0$ ,  $I_0 = I(0) \geq 0$  and  $R_0 = R(0) \geq 0$  under the vaccination function  $V: \mathbf{R}_{0+} \rightarrow \mathbf{R}_{0+}$ . 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,  $\mu$  is the rate of deaths from causes unrelated to the infection,  $\omega$  is the rate of losing immunity,  $\beta$  is the transmission constant (with the total number of infections per unity of time at time  $t$  being  $\beta \frac{S(t)I(t)}{N(t)}$ ),  $\sigma^{-1}$  and  $\gamma^{-1}$  are, respectively, the average durations of the latent and infective periods. All the above parameters are nonnegative. The parameter  $\omega$  is that of 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:

$$\begin{aligned} \dot{N}(t) &= \dot{S}(t) + \dot{E}(t) + \dot{I}(t) + \dot{R}(t) \\ &= \mu(N(t) - S(t) - E(t) - I(t) - R(t)) = 0; \quad \forall t \in \mathbf{R}_{0+} \\ \Rightarrow N(t) &:= S(t) + E(t) + I(t) + R(t) = N(0) = N_0 = N > 0 \end{aligned}$$

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:

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

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

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

Note that (5) is identically zero if  $\nu - \mu = \rho = 0$ .

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

$$\begin{aligned} S(t) + R(t) &= e^{-\mu t} (S(0) + R(0)) \\ &+ \int_0^t e^{-\mu(t - \tau)} \left( \nu N(\tau) + \left( \gamma(1 - \rho) - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) \right) d\tau \end{aligned} \quad (8)$$

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

In order to further solve (8), an integration by parts procedure is performed as follows:

$$\begin{aligned} \int_0^t p(\tau) dq(t, \tau) &= \int_0^t p(\tau) \dot{q}(t, \tau) d\tau \\ &\equiv \int_0^t N(\tau) e^{-\mu(t - \tau)} d\tau \\ &= N(\tau) q(t, \tau) \Big|_0^t - \int_0^t q(t, \tau) \dot{N}(\tau) d\tau \end{aligned} \quad (10)$$

where

$$\begin{aligned} \bar{q}(t) &:= \int_0^t e^{-\mu(t - \tau)} d\tau = \frac{e^{-\mu(t - \tau)}}{\mu} \Big|_0^t = q(t, \tau) \Big|_0^t \\ &= \frac{1 - e^{-\mu t}}{\mu} = q(t, t) - q(t, 0) \end{aligned} \quad (11)$$

so that  $q(t, t) = 1/\mu$  and  $q(t, 0) = e^{-\mu t}/\mu$  and then using (5) in (10) yields

$$\int_0^t N(\tau) e^{-\mu(t-\tau)} d\tau = \frac{1}{\mu} \left( N(t) - e^{-\mu t} N(0) \right) - \frac{1}{\mu} \int_0^t e^{-\mu(t-\tau)} \left( (\nu - \mu) N(\tau) - \rho \gamma I(\tau) \right) d\tau$$

which, after grouping identical terms, leads to

$$\int_0^t N(\tau) e^{-\mu(t-\tau)} d\tau = \frac{1}{\nu} \left( N(t) - e^{-\mu t} N(0) + \rho \gamma \int_0^t e^{-\mu(t-\tau)} I(\tau) d\tau \right) \quad (12)$$

Thus, combining (8)-(9) and (12) yields:

$$S(t) + R(t) - N(t) = - \left( E(t) + I(t) \right) = e^{-\mu t} \times \left( S(0) + R(0) - N(0) + \int_0^t e^{\mu\tau} \left( \gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right) = - e^{-\mu t} \left( E(0) + I(0) - \int_0^t e^{\mu\tau} \left( \gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right) \quad (13)$$

### III. MAIN RESULTS

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  $S(t) = \gamma N(t) / \beta$ ;  $\forall t \in \mathbf{R}_{0+}$  with a

vaccination control in  $[0, 1]$  for all time. Then, the SEIR model (1)-(4) is positive for all time. Furthermore,

$$S(t) + R(t) - N(t) = - \left( E(t) + I(t) \right) = - e^{-\mu t} \left( E(0) + I(0) \right) \quad (14)$$

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

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

As a result,

$$R(t) = N(t) - S(t) - e^{-\mu t} \left( E(0) + I(0) \right) = \frac{\beta - \gamma}{\beta} N(t) - e^{-\mu t} \left( E(0) + I(0) \right) = \frac{\beta - \gamma}{\beta} N(t) + e^{-\mu t} \left( R(0) - \frac{\beta - \gamma}{\gamma} S(0) \right) \leq \frac{\beta - \gamma}{\beta} N(t); \quad \forall t \in \mathbf{R}_{0+} \text{ and } R(t) \rightarrow \frac{\beta - \gamma}{\beta} N(t) \text{ as } t \rightarrow \infty$$

Furthermore, the following two limits exist:

$$\lim_{t \rightarrow \infty} \left( S(t) + R(t) - N(t) \right) = \lim_{t \rightarrow \infty} \left( E(t) + I(t) \right) = 0 \quad (15)$$

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

$$N(t) = N(0) = N = \lim_{t \rightarrow \infty} \left( S(t) + R(t) \right);$$

$$\lim_{t \rightarrow \infty} E(t) = \lim_{t \rightarrow \infty} I(t) = 0 \quad (16)$$

**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, Eqs. 14-15 follow directly from (13) and

$S(t) = \gamma N(t) / \beta$  for all time. Eqs. 16 follow from (14)-(15) since  $\nu - \mu = \rho = 0$  imply  $N(t) \equiv N(0)$ ,  $\dot{N}(t) \equiv 0$  from (5).

□

An associate stability result follows:

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

1) The SEIR model is globally stable if  $0 \leq \nu \leq \mu$  and the vaccination law fulfills  $V: \mathbf{R}_{0+} \rightarrow [0, 1]$ .

2) If  $S(t) = \gamma N(t) / \beta$  and  $\nu > \mu \geq 0$  then the following conditions are jointly necessary for global stability under Theorem 1

$$\mu < \nu < \mu + \rho\gamma; \rho\gamma > 0 \quad N(0) = \rho\gamma \int_0^\infty e^{-(\nu-\mu)\tau} I(\tau) d\tau, \\ \lim_{t \rightarrow \infty} N(t) = 0$$

If  $\nu > \mu \geq 0$  and  $I(t) = \frac{(\nu-\mu)}{\rho\gamma} N(t)$  ;

$\forall t \geq t_0$  (finite)  $\in \mathbf{R}_{0+}$  then global stability of the SEIR-model (1)-(4) is guaranteed if  $V: \mathbf{R}_{0+} \rightarrow [0, 1]$  . If

$\nu > \mu \geq 0$ ,  $V: \mathbf{R}_{0+} \rightarrow [0, 1]$  and  $I(t) = \frac{(\nu-\mu)}{\rho\gamma} N(t)$  is

replaced with the weaker condition

$\left| I(t) - \frac{(\nu-\mu)}{\rho\gamma} N(t) \right| = o(e^{-\alpha t})$  for some  $\alpha \in \mathbf{R}_+$  then the

SEIR – model (1) –(4) is globally stable.

**Proof:**

1) If  $0 \leq \nu \leq \mu$  and  $\rho\gamma \geq 0$  then  $\dot{N}(t) = (\nu - \mu)N(t) - \rho\gamma I(t) \leq (\nu - \mu)N(t) \leq 0$  ;  $\forall t \in \mathbf{R}_{0+}$  so that  $N(t) \leq N(0) < \infty$ ;  $\forall t \in \mathbf{R}_{0+}$ . Since the SEIR – model is positive if  $V: \mathbf{R}_{0+} \rightarrow [0, 1]$  then all the populations are nonnegative and upper-bounded by  $N(0)$ .

2) 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  $\nu > \mu \geq 0$  . Also,

$N(t) < \infty$ ;  $\forall t \in \mathbf{R}_{0+}$  only if  $\dot{N}(t) \leq 0$  on a non-necessarily connected set of infinite Lebesgue measure. Thus, there is a finite sufficiently large finite time “ t ” such that :

$$I(t) \geq \frac{\nu - \mu}{\mu + \rho\gamma - \nu} (S(t) + E(t) + R(t))$$

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 [Eq. (14)] 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.

If  $I(t) = \frac{(\nu-\mu)}{\rho\gamma} N(t)$  with  $\nu > \mu$  after some finite time  $t_0$  then  $N(t) = N(t_0) < \infty$ ;  $\forall t \geq t_0$  and the SEIR – model is positive since  $V: \mathbf{R}_{0+} \rightarrow [0, 1]$ . Thus, global stability follows.

If  $\left| I(t) - \frac{(\nu-\mu)}{\rho\gamma} N(t) \right| = o(e^{-\alpha t})$  replaces the above stronger condition  $I(t) = \frac{(\nu-\mu)}{\rho\gamma} N(t)$

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. □

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 for all time to any of the subsequent equivalent identities below:

$$N(t) = \gamma N(t) / \beta + E(t) + I(t) + R(t)$$

$$\Leftrightarrow R(t) = \frac{\beta - \gamma}{\beta} N(t) - E(t) - I(t) \quad (17)$$

which requires as necessary condition  $\beta > \gamma \geq 0$ . Although unrelated to the physical problem at hand, the necessary condition will be also accomplished with  $\beta < 0$  and  $\gamma \leq 0$  with  $S(t) = \gamma N(t) / \beta$ . From Theorem 1, Eqs. 17 imply that

$\lim_{t \rightarrow \infty} (S(t) + R(t) - N(t)) = \lim_{t \rightarrow \infty} (E(t) + I(t)) = 0$  The solution of (7) is:

$$E(t) + I(t) = e^{-\mu t} \times \left[ E(0) + I(0) - \int_0^t e^{\mu\tau} \left( \gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right] \quad (18)$$

Then, the solution of (4) matches (17) for all time if and only if:

$$R(t) = \frac{\beta - \gamma}{\beta} N(t) - E(t) - I(t) = e^{-(\mu + \omega)t}$$

$$\times \left( R(0) + \int_0^t e^{(\mu + \omega)\tau} (\gamma(1 - \rho)I(\tau) + \nu N(\tau)V(\tau)) d\tau \right) \quad (19)$$

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

$$h(t) = h(0) + \int_0^t (\gamma(1 - \rho)I(\tau) + \nu N(\tau)V(\tau)) d\tau$$

such that a vaccination law is implemented as follows:

$$\dot{h}(t) = \gamma(1 - \rho)I(t) + \nu N(t)V(t) \Leftrightarrow$$

$$V(t) = \frac{1}{\nu N(t)} (\dot{h}(t) - \gamma(1 - \rho)I(t)) \quad (20)$$

for all time so that the last right-hand – side additive term in (19) becomes after integration by parts:

$$e^{-(\mu + \omega)t} \int_0^t e^{(\mu + \omega)\tau} \dot{h}(\tau) d\tau = e^{-(\mu + \omega)t}$$

$$\times \left( e^{(\mu + \omega)t} h(t) - h(0) - (\mu + \omega) \int_0^t e^{(\mu + \omega)\tau} h(\tau) d\tau \right) \quad (21)$$

The replacement of (21) into (19) yields:

$$\frac{\beta - \gamma}{\beta} e^{(\mu + \omega)t} N(t) - e^{\omega t} \times \left[ E(0) + I(0) - \int_0^t e^{\mu\tau} \left( \gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right]$$

$$= R(0) + e^{(\mu + \omega)t} h(t) - h(0) - (\mu + \omega) \int_0^t e^{(\mu + \omega)\tau} h(\tau) d\tau \quad (22)$$

and equivalently, and since  $S(t) = \gamma N(t) / \beta$  for all time:

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

$$= \frac{\beta - \gamma}{\beta} N(t) + (\mu + \omega) \int_0^t e^{-(\mu + \omega)(t - \tau)} h(\tau) d\tau + e^{-\mu t} \left( e^{-\omega t} (h(0) - R(0)) - E(0) - I(0) \right) \quad (23)$$

generated from:

$$\dot{h}(t) = \frac{\beta - \gamma}{\beta} [(v - \mu)N(t) - \rho\gamma I(t)]$$

$$- (\mu + \omega) e^{-(\mu + \omega)t} (h(0) - R(0)) + \mu e^{-\mu t} (E(0) + I(0))$$

$$- (\mu + \omega)^2 \int_0^t e^{-(\mu + \omega)(t - \tau)} h(\tau) d\tau + (\mu + \omega)h(t)$$

(24)

so that

$$\dot{h}(t) - \gamma(1 - \rho)I(t) = \frac{(\beta - \gamma)(v - \mu)}{\beta} N(t)$$

$$+ \gamma \left( \frac{\gamma\rho}{\beta} - 1 \right) I(t) - (\mu + \omega) e^{-(\mu + \omega)t} (h(0) - R(0)) + \mu e^{-\mu t} (E(0) + I(0)) - (\mu + \omega)^2$$

$$\times \int_0^t e^{-(\mu + \omega)(t - \tau)} h(\tau) d\tau + (\mu + \omega)h(t) \quad (25)$$

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

$$V(t) = \begin{cases} \bar{V}(t) & \text{if } \bar{V}(t) \in [0, 1] \\ 1 & \text{if } \bar{V}(t) > 1 \\ 0 & \text{if } \bar{V}(t) < 0 \end{cases} \quad (26)$$

where:

$$\bar{V}(t) = \dot{h}(t) - \gamma(1 - \rho)I(t) \quad (27)$$

Define the indicator function  $i(t)$  as follows:

$$i(t) = 0 \text{ if } \bar{V}(t) \in [0, 1] \text{ and } i(t) = 1, \text{ otherwise} \quad (28)$$

Then, one has instead of (13)

$$S(t) + R(t) - N(t) = -(E(t) + I(t)) = e^{-\mu t}$$

$$\times \left( S(0) + R(0) - N(0) + \int_0^t e^{-\mu\tau} \left( \gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) i(\tau) d\tau \right) \quad (29)$$

which coincides with (13) for all time if the indicator function is identically zero, that is, if  $\dot{h}(t)$  ism such that the auxiliary vaccination law (27) is in  $[0, 1]$  for all time. Also, for any given real  $\varepsilon > 0$  and  $T = T(\varepsilon)$  such that  $T = \frac{1}{\mu} \ln \left( \frac{N(0) - S(0) - R(0)}{\varepsilon} \right)$  and one gets from (13):

$$N(t) - S(t) - R(t) \leq \varepsilon$$

$$+ \int_0^t e^{-\mu(t-\tau)} \left( \beta \frac{S(\tau)}{N(\tau)} - \gamma \right) I(\tau) i(\tau) d\tau ; \forall t \geq T \quad (30)$$

and the right-hand-side integral takes into account the tracking deterioration if there is a time interval of nonzero Lebesgue measure such that  $V(t) \neq \bar{V}(t)$ ;  $\forall t \in \mathbf{R}_{0+}$ . 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 since the SEIR- model is positive since  $V(t) \in [0, 1]$ ;  $\forall t \in \mathbf{R}_{0+}$  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 and one has:

**Theorem 3.** The vaccination law (24), (26)-(27) makes the SEIR – model (1-4) positive and globally stable under Theorem 2. Furthermore, as  $t \rightarrow \infty$ :

$$N(t) - S(t) - R(t) \leq \limsup_{t \rightarrow \infty} \int_0^t e^{-\mu(t-\tau)} \left( \beta \frac{S(\tau)}{N(\tau)} - \gamma \right) I(\tau) i(\tau) d\tau \quad \square$$

Work is in progress to extend the above results to the adaptive case when the parameterization is not fully known by using former tools in [15-19]. For such a purpose, the SEIR epidemic model is rewritten in an equivalent form as a dynamic system whose state vector  $x(t)$  is formed by the partial populations with components ordered in the same order as in the SEIR- model (1)-(4) and the “measurable output” is the whole population what is expressed as follows:

$$\dot{x}(t) = A_i(x(t), t)x(t) + b_a y(t)V(t) + \zeta y(t) ; i=1,2,3,4$$

$$= A_i(x(t), t)x(t) + v N(t) u(t) \\ = A_i^0(x(t), t)x(t) + b_a y(t) V(t)$$

$$y(t) \equiv N(t) = c^T x(t)$$

where

$$b_a = (-v, 0, 0, v)^T ; \zeta := v e_1 = (v, 0, 0, 0)^T ;$$

$$c = (1, 1, 1, 1)^T$$

$$u(t) = (1 - V(t), 0, 0, V(t))^T$$

$$= (1 - V(t)) e_1 + e_4 V(t) = e_1 + (e_4 - e_1) V(t)$$

with  $e_i$  ( $1 \leq i \leq 4$ ) being the unit fourth dimensional Euclidean vector with i-th component being one and the matrix of dynamics being any of the subsequent ones:

$$A_1(x(t), t) = \begin{bmatrix} -\left( \mu + \frac{\beta I(t)}{N(t)} \right) & 0 & 0 & \omega \\ \frac{\beta I(t)}{N(t)} & -(\mu + \sigma) & 0 & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

$$A_2(x(t), t) = \begin{bmatrix} -\mu & 0 & -\frac{\beta S(t)}{N(t)} & \omega \\ 0 & -(\mu + \sigma) & \frac{\beta S(t)}{N(t)} & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

$$A_3(x(t), t) = \begin{bmatrix} -\mu & 0 & -\frac{\beta S(t)}{N(t)} & \omega \\ \frac{\beta I(t)}{N(t)} & -(\mu + \sigma) & 0 & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

$$A_4(x(t), t) = \begin{bmatrix} -\left(\mu + \frac{\beta I(t)}{N(t)}\right) & 0 & 0 & \omega \\ 0 & -(\mu + \sigma) & \frac{\beta S(t)}{N(t)} & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

$$A_1^0(x(t), t) = A_1(x(t), t) + \zeta c^T c^T x(t)$$

$$= \begin{bmatrix} -\left(\mu + \frac{\beta I(t)}{N(t)} - \nu\right) & \nu & \nu & \omega + \nu \\ \frac{\beta I(t)}{N(t)} & -(\mu + \sigma) & 0 & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

$$A_2^0(x(t), t) = A_2(x(t), t) + \zeta c^T c^T x(t)$$

$$= \begin{bmatrix} \nu - \mu & \nu & \nu - \frac{\beta S(t)}{N(t)} & \omega + \nu \\ 0 & -(\mu + \sigma) & \frac{\beta S(t)}{N(t)} & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

$$A_3^0(x(t), t) = A_3(x(t), t) + \zeta c^T c^T x(t)$$

$$= \begin{bmatrix} \nu - \mu & \nu & \nu - \frac{\beta S(t)}{N(t)} & \omega + \nu \\ \frac{\beta I(t)}{N(t)} & -(\mu + \sigma) & 0 & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

$$A_4^0(x(t), t) = A_4(x(t), t) + \zeta c^T c^T x(t)$$

$$= \begin{bmatrix} -\left(\mu + \frac{\beta I(t)}{N(t)} - \nu\right) & \nu & \nu & \omega + \nu \\ 0 & -(\mu + \sigma) & \frac{\beta S(t)}{N(t)} & 0 \\ 0 & \sigma & -(\mu + \gamma) & 0 \\ 0 & 0 & \gamma(1 - \rho) & -(\mu + \omega) \end{bmatrix}$$

An observer of can is intended to be built to estimate the partial populations as follows:

$$\dot{\hat{x}}(t) = \hat{A}(t)\hat{x}(t) + \hat{b}_a y(t)V(t) + \zeta C(x(t) - \hat{x}(t))$$

where  $\hat{x}(t) := (\hat{S}(t), \hat{E}(t), \hat{I}(t), \hat{R}(t))^T$  and  $\zeta$  is a design stabilizing vector gain of the order being compatible with the output matrix C which is identical to either the unit Euclidean vector  $e_3^T$  (to pick out the “measurable output” from the state the infectious population as a measurable output) or  $C = \begin{bmatrix} e_3^T \\ 1 \ 1 \ 1 \ 1 \end{bmatrix}$  (to pick up as a built two-dimensional output, both the infectious population and the total one N(t) if both of them are known with good accuracy for all time as it occurs in many practical situations). The observer-based vaccination law is similar to the proposed ones (20) or (26)-(27) by replacing the total and infectious populations by their estimates provided by the observer.

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