

On the properties of some epidemic models

M. De la Sen , and S. Alonso-Quesada UPV/ EHU, POBox 644-Bilbao-SPAIN

Abstract - In this paper, we discuss the properties of some simple SI, SR, SIR and SEIR epidemic models where their parameterizing functions (such as per-capita death rate, disease transmission, removal rate etc.) might be eventually time-varying but either time-integrable or not.

Keywords— Epidemic models, SI (susceptible/infectious), SR (susceptible/immune), SIR (susceptible/infectious/immune) and SEIR (susceptible/ infected/infectious/immune) epidemic models.

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 (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 (see, for instance, [1-5]). 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, cf. [6-14] (see also the references listed therein). 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 behaviours [14] etc. . On the other hand, some ‘ad- hoc’ variants of such models are known to become considerably simpler for the illness transmission among plants [6-7]. It is also well-known that robust control is a powerful tool to deal with stabilization and control in the presence of unmodeled dynamics and perturbations (see , for instance [15-18]). In [19], a control point of view of a vaccination strategy in continuous- time has been proposed for the true mass action (namely, the whole population numbers influence the rate of disease transmission) so-called SEIR (i.e. susceptible/infected/ infectious and immune populations) epidemic model under constant whole population assumption. This model generalizes simpler SIR epidemic models where infected (ie. those still without symptoms) and infectious (i.e. those already with disease symptoms) are not mutually distinguished. The vaccination strategy involves an auxiliary control being proportional to either the susceptible or to the whole population so that the unsuitable dynamics is removed and replaced for an asymptotically stabilizing term of the susceptible dynamics. In this paper, we discuss four elementary epidemic models of respective types as follows: SI (susceptible/infectious), SR (susceptible/ immune) and SIR(susceptible / infected/ immune) models whose parameterizing functions (per-capita death rate, disease transmission etc.) might be eventually time-varying but either time-integrable or not.

II. A SIMPLE TIME-VARYING SI EPIDEMIC - MODEL

Bernoulli proposed in 1760 a simple epidemic model where the infection is removed instantaneously so that all the population passes from susceptible to removed by immunity (the simplest SR model), [20] . The model was assumed in particular for instantaneous infective effect via inoculation of the smallpox. Since then a lot of investigation has been devoted to epidemic models including the incorporation of infected and infectious populations (SIR and SEIR epidemic models), the presence of delays in the disease transmission etc. The following simple one-parameter time-varying model is a generalization to the time- varying one of the simpler time- invariant SI (susceptible/infectious) epidemic model:

$$N = S(t) + I(t) \quad (1)$$

$$\dot{I}(t) = \beta(t)S(t)I(t) \quad (2)$$

$$= \beta(t)S(t)(N - S(t)) = \beta(t)I(t)(N - I(t)) \quad (3)$$

with initial conditions $N \geq S(0) = S_0 \geq 0$, $N \geq I(0) = I_0 = N - S_0 \geq 0$ such that the total population $N(t) = S(t) + I(t) = S_0 + I_0 = N(0) = N_0$ is constant for all time and the disease transmission function $\beta: \mathbf{R}_{0+} \rightarrow \mathbf{R}_{0+}$ with $\mathbf{R}_{0+} := \mathbf{R}_+ \cup \{0\}$. Thus, one gets for $N > 0$:

$$\frac{dI(t)}{I(t)(N-I(t))} = \left(\frac{1}{I(t)} + \frac{1}{N-I(t)} \right) \frac{dI(t)}{N}$$

$$= -\frac{dS(t)}{S(t)(N-S(t))} = -\left(\frac{1}{S(t)} + \frac{1}{N-S(t)} \right) \frac{dS(t)}{N} = \beta(t) dt \quad (4)$$

so that

$$\ln \frac{I(t)}{N-I(t)} - \ln \frac{I(0)}{N-I(0)} = \ln \frac{S(0)}{N-S(0)} - \ln \frac{S(t)}{N-S(t)} = N \bar{\beta}(t)$$

$$; \forall t \in \mathbf{R}_{0+} \quad (5)$$

where $\bar{\beta}: \mathbf{R}_{0+} \rightarrow cl \mathbf{R}_{0+}$, i.e., the image is the closure of the nonnegative real numbers so that the $+\infty$ -point is added, in is defined by $\bar{\beta}(t) := \int_0^t \beta(\tau) d\tau \leq \bar{\beta}_\infty$ with $0 \leq \bar{\beta}_\infty < \infty$ if

$\beta \in L^1(\mathbf{R}_{0+}, \mathbf{R}_{0+})$ and $\bar{\beta}_\infty = +\infty$, otherwise. The solution of (1)-(2) is obtained from (5) as follows:

$$I(t) = \frac{N I(0)}{I(0) + (N - I(0)) e^{-N \bar{\beta}(t)}}$$

$$S(t) = \frac{N(N - I(0)) e^{-N \bar{\beta}(t)}}{I(0) + (N - I(0)) e^{-N \bar{\beta}(t)}} = \frac{N - I(0)}{I(0)} I(t) e^{-N \bar{\beta}(t)}$$

$$; \forall t \in \mathbf{R}_{0+} \quad (6)$$

which are nonnegative for all time, so that (1)-(3) is a positive dynamic system (see [15-17]), and have finite nonnegative limits as $t \rightarrow \infty$ which is a global attractor of the trajectory-solution and it is also a globally asymptotically stable endemic (in the sense that the disease propagates) equilibrium point:

$$I(\infty) = \frac{N I(0)}{I(0) + (N - I(0)) e^{-N \bar{\beta}_\infty}} \in [0, N] \quad (7.a)$$

$$S(\infty) = \frac{N(N - I(0)) e^{-N \bar{\beta}_\infty}}{I(0) + (N - I(0)) e^{-N \bar{\beta}_\infty}}$$

$$= \frac{N - I(0)}{I(0)} I(\infty) e^{-N \bar{\beta}_\infty} = N - I(\infty) \in [0, N] \quad (7.b)$$

which becomes in particular if $\bar{\beta}_\infty = +\infty$ the following strongly endemic (in the sense that the whole population becomes infectious) equilibrium point:

$$I(\infty) = N ; \quad S(\infty) = 0 \quad \text{if } I(0) \neq 0$$

and

$$I(\infty) = I(t) = I(0) = 0 ; \quad S(\infty) = S(t) = S(0) = N \quad \text{if } I(0) = 0 ; \forall t \in \mathbf{R}_{0+} \quad (8)$$

Thus, the solution of (1)-(2) is nonnegative for all time if the initial conditions are nonnegative and converge asymptotically to a stable equilibrium point for any given nonnegative initial conditions satisfying a constant population constraint $N = S(0) + I(0)$. Simple calculations yield:

$$\frac{dI(\infty)}{dI(0)} = \frac{N^2 e^{-N \bar{\beta}_\infty}}{\left(I(0) + (N - I(0)) e^{-N \bar{\beta}_\infty} \right)^2}$$

$$\frac{dS(\infty)}{dI(0)} = -\frac{dI(\infty)}{dI(0)} = -\frac{N^2 e^{-N \bar{\beta}_\infty}}{\left(I(0) + (N - I(0)) e^{-N \bar{\beta}_\infty} \right)^2} \quad (9)$$

what leads to $\frac{dS(\infty)}{dI(\infty)} = -1$ and the following cases can occur:

1) If $0 \leq \bar{\beta}_\infty < \infty$ then $\frac{dI(\infty)}{dI(0)} > 0$, $\frac{dS(\infty)}{dI(0)} < 0$. Thus, if $I(0)$ increases (decreases) then the susceptible limit decreases (increases) and infected limit increases (decreases).

2) If $\bar{\beta}_\infty = +\infty$ or if $N = 0$ (leading to the trivial solution of (1)-(2)) then

$\frac{dI(\infty)}{dI(0)} = 0$, $\frac{dS(\infty)}{dI(0)} = 0$. Then, the equilibrium point coincides with the initial conditions.

3) If $N > 1$ and $\bar{\beta}_\infty = 0$ then $\frac{dI(\infty)}{dI(0)} > 0$, $\frac{dS(\infty)}{dI(0)} < 0$. Thus, if $I(0)$ increases (decreases) then the limit infected increases (decreases) and the limit susceptible decreases (increases).

The solution of (1)-(2) may be alternatively written as follows with given upper-bounding functions:

$$e^{\bar{\beta}(t) \left(\begin{smallmatrix} N - \max_{\tau \in [0, t]} I(\tau) \\ \tau \in [0, t] \end{smallmatrix} \right)} I(0) \leq I(t) = e^{\int_0^t \beta(\tau) (N - I(\tau)) d\tau} I(0)$$

$$\leq e^{\bar{\beta}(t) \left(\begin{smallmatrix} N - \min_{\tau \in [0, t]} I(\tau) \\ \tau \in [0, t] \end{smallmatrix} \right)} I(0) ; \forall t \in \mathbf{R}_{0+} \quad (10)$$

$$N - e^{\bar{\beta}(t) \left(\begin{smallmatrix} N - \min_{\tau \in [0, t]} I(\tau) \\ \tau \in [0, t] \end{smallmatrix} \right)} I(0) \leq S(t) = \left(1 - e^{\int_0^t \beta(\tau) (N - I(\tau)) d\tau} \right) N$$

$$+ e^{\int_0^t \beta(\tau) (N - I(\tau)) d\tau} S(0) \leq N - e^{\bar{\beta}(t) \left(\begin{smallmatrix} N - \max_{\tau \in [0, t]} I(\tau) \\ \tau \in [0, t] \end{smallmatrix} \right)} I(0)$$

$$; \forall t \in \mathbf{R}_{0+} \quad (11)$$

Also, one gets from (6):

$$\frac{dI(t)}{dI(0)} = \frac{N^2 e^{-N\bar{\beta}(t)}}{\left(I(0) + (N - I(0))e^{-N\bar{\beta}(t)}\right)^2}$$

$$\frac{dI(t)}{dt} = \frac{N^2 I(0)(N - I(0))e^{-N\bar{\beta}(t)}\beta(t)}{\left(I(0) + (N - I(0))e^{-N\bar{\beta}(t)}\right)^2}; \forall t \in \mathbf{R}_{0+} \quad (12)$$

Thus, the infected population at any time t increases (decreases) when I (0) is increased (decreased) . The susceptible population behaves in the contrary sense. That is $I'(t) > I(t)$ and $S'(t) < S(t)$ at any time if $I'(0) > I(0)$ and conversely,

Also, the infected (susceptible) population is a monotone strictly increasing (decreasing) function for all time for any initial condition in $(0, N]$.

III. A SIMPLE TIME-VARYING SR- EPIDEMIC MODEL

A simple SR (susceptible/ immune –also called removed by immunity-) time-varying epidemic model extending its time-invariant counterpart is (see [20]):

$$\dot{N}(t) = -\mu(t)N(t) \quad (13)$$

$$\dot{S}(t) = -(\mu(t) + \beta(t))S(t) \quad (14)$$

$$\dot{R}(t) = \dot{N}(t) - \dot{S}(t) = -\mu(t)R(t) + \beta(t)S(t) \quad (15)$$

under initial conditions $N(0) = N_0 = S(0) + R(0) \geq 0$, $N_0 \geq S(0) = S_0$; $R(0) = R_0 = N_0 - S_0 \geq 0$ from which two differential equations are independent. The transmission function is $\beta: \mathbf{R}_{0+} \rightarrow \mathbf{R}_{0+}$ and

$\mu: \mathbf{R}_{0+} \rightarrow \mathbf{R}_{0+}$ is the per capita death ratio at time t . The unique solution of (13)-(15) is:

$$S(t) = e^{-\int_0^t (\mu(\tau) + \beta(\tau))d\tau} S(0)$$

$$N(t) = e^{-\int_0^t \mu(\tau)d\tau} N(0); \forall t \in \mathbf{R}_{0+} \quad (16.a)$$

$$R(t) = N(t) - S(t) = e^{-\int_0^t \mu(\tau)d\tau} \left(N(0) - e^{-\int_0^t \beta(\tau)d\tau} S(0) \right)$$

$$; \forall t \in \mathbf{R}_{0+} \quad (16.b)$$

which take nonnegative real values for all time. Define

$$cl \mathbf{R}_{0+} \ni \bar{\mu}(t) := \int_0^t \mu(\tau)d\tau;$$

$$\bar{\beta}(t) := \int_0^t \beta(\tau)d\tau \in cl \mathbf{R}_{0+} \text{ with } 0 < \bar{\mu}(t) \leq \bar{\mu}_\infty \leq \infty \text{ and}$$

$$0 < \bar{\beta}(t) \leq \bar{\beta}_\infty \leq \infty; \forall t \in \mathbf{R}_{0+} \text{ with } \bar{\mu}_\infty := \lim_{t \rightarrow +\infty} \bar{\mu}(t) < \infty$$

if and only if $\mu \in L^1(\mathbf{R}_{0+}, \mathbf{R}_{0+})$ (otherwise, $\bar{\mu}_\infty = +\infty$),

and $\bar{\beta}_\infty := \lim_{t \rightarrow +\infty} \bar{\beta}(t) < \infty$ if and only if

$\beta \in L^1(\mathbf{R}_{0+}, \mathbf{R}_{0+})$ (otherwise, $\bar{\beta}_\infty = +\infty$). From (16), the following properties hold:

- 1) If $\bar{\mu}_\infty = +\infty$ then $N(\infty) = S(\infty) = R(\infty) = 0$ irrespective of the initial conditions so that the whole and the two partial populations asymptotically extinguish.
- 2) If $\bar{\beta}_\infty = +\infty$ then $S(\infty) = 0$ and

$R(\infty) = N(\infty) = e^{-\bar{\mu}_\infty} N(0)$ so that the susceptible population asymptotically extinguish and the whole one is asymptotically immune identical to a finite limit which depends on the initial total population and the value.

$\bar{\mu}_\infty$ If $\bar{\mu}_\infty = +\infty$ then such a limit is zero so that the whole population again asymptotically extinguishes as in the above case 1.

- 3) It follows from (13)-(15) that

$$d\dot{N}(t) / dN(t) = -\mu(t) \leq 0,$$

$$d\dot{S}(t) / dS(t) = -(\mu(t) + \beta(t)) \leq 0$$

$$d\dot{R}(t) / dR(t) = -\mu(t) \leq 0, \quad d\dot{R}(t) / dS(t) = \beta(t) \geq 0$$

Thus, the whole population and the susceptible and immune populations are monotone decreasing functions so that they have a finite limits. Also, the immune population increases / decreases as the susceptible one increases (decreases).

An equivalent result to (16.b) for the immune population is calculated directly from (15) and (16.a) as follows $\forall t \in \mathbf{R}_{0+}$:

$$R(t) = e^{-\int_0^t \mu(\tau)d\tau} R(0) + \int_0^t e^{-\int_0^\tau \mu(\tau')d\tau'} \beta(t-\tau) S(t-\tau) d\tau$$

$$= e^{-\int_0^t \mu(\tau)d\tau} R(0) + \left(\int_0^t e^{-\int_0^\tau \mu(\tau')d\tau'} \beta(t-\tau) e^{-\int_0^{t-\tau} (\mu(\tau') + \beta(\tau'))d\tau'} d\tau \right) S(0)$$

$$= e^{-\int_0^t \mu(\tau)d\tau} R(0) + \left(\int_0^t e^{-\int_0^\tau \mu(\tau')d\tau'} \beta(t-\tau) e^{-\int_0^{t-\tau} (\mu(\tau') + \beta(\tau'))d\tau'} d\tau \right) (N(0) - R(0))$$

$$+ \left(\int_0^t e^{-\int_0^\tau \mu(\tau')d\tau'} \beta(t-\tau) e^{-\int_0^{t-\tau} (\mu(\tau') + \beta(\tau'))d\tau'} d\tau \right) N(0)$$

$$= \left(e^{-\bar{\mu}(t)} - \int_0^t e^{-(\bar{\mu}(\tau) + \bar{\mu}(t-\tau) + \bar{\beta}(t-\tau))} \beta(t-\tau) \right) R(0)$$

$$+ \left(\int_0^t e^{-(\bar{\mu}(\tau) + \bar{\mu}(t-\tau) + \bar{\beta}(t-\tau))} \beta(t-\tau) d\tau \right) N(0)$$

$$\begin{aligned}
 &= e^{-\bar{\mu}(t)} \left(1 - e^{-\bar{\beta}(t)} \right) \left(\int_0^t e^{-\bar{\beta}(\tau)} \beta(t-\tau) \right) R(0) \\
 &+ \left(e^{-\bar{\mu}(t)+\bar{\beta}(t)} \int_0^t e^{\bar{\beta}(\tau)} \beta(t-\tau) d\tau \right) N(0) \\
 &= e^{-\bar{\mu}(t)} R(0) \\
 &+ \left(e^{-\bar{\mu}(t)+\bar{\beta}(t)} \int_0^t e^{\bar{\beta}(\tau)} \beta(t-\tau) d\tau \right) S(0) \quad (17)
 \end{aligned}$$

$$\begin{aligned}
 R(\infty) &:= e^{-\bar{\mu} \infty} R(0) \\
 &+ \left(e^{-\bar{\mu} \infty + \bar{\beta} \infty} \int_0^\infty e^{\bar{\beta}(\tau)} \beta(t-\tau) d\tau \right) S(0) \\
 &= e^{-\bar{\mu} \infty} R(0) + \left(\int_0^\infty e^{\bar{\beta}(\tau)} \beta(t-\tau) d\tau \right) S(\infty) \\
 &= e^{-\bar{\mu} \infty} (N(0) - S(0)) \\
 &+ \left(\int_0^\infty e^{\bar{\beta}(\tau)} \beta(t-\tau) d\tau \right) S(\infty)
 \end{aligned}$$

$$\begin{aligned}
 &= N(\infty) + \left(\int_0^\infty e^{\bar{\beta}(\tau)} \beta(t-\tau) d\tau \right) S(\infty) - e^{-\bar{\mu} \infty} S(0) \left(e^{-\int_0^t \beta(\tau) I(\tau) d\tau} - 1 \right) S(0) \leq 0 \leq I(0) + R(0); \forall t \in \mathbf{R}_{0+} \quad (26) \\
 &\quad (18)
 \end{aligned}$$

IV. A SIMPLE TIME-VARYING SIR-EPIDEMIC MODEL

A simple SIR (susceptible/infectious/immune) time-varying epidemic model extending its time-invariant counterpart (Kermack-McKendrick model - 1927), [20] is:

$$\dot{S}(t) = -\beta(t)S(t)I(t) \quad (19)$$

$$\dot{I}(t) = \beta(t)S(t)I(t) - \gamma(t)I(t) \quad (20)$$

$$\dot{R}(t) = \gamma(t)I(t) \quad (21)$$

where $\gamma: \mathbf{R}_{0+} \rightarrow \mathbf{R}_{0+}$ is the removal rate with initial conditions $S(0) = S_0 \geq 0, I(0) = I_0 \geq 0, R(0) = R_0 \geq 0$ and where the new parameterizing function right hand-sides of (19)-(21) yields a constant total population $N(0) = N_0 = S_0 + I_0 + R_0$. The use of (21) in (19)

yields $\dot{S}(t) = -\frac{\beta(t)\dot{R}(t)}{\gamma(t)}S(t)$ which together with (19)

yields the two equivalent expressions for the susceptible:

$$\begin{aligned}
 S(t) &= e^{-\int_0^t \beta(\tau) I(\tau) d\tau} S(0) = e^{-\int_0^t (\beta(\tau) \dot{R}(\tau) / \gamma(\tau)) d\tau} S(0) \\
 &; \forall t \in \mathbf{R}_{0+} \quad (22)
 \end{aligned}$$

Eq. 20 might be rewritten equivalently as $\dot{I}(t) = (\beta(t)S(t) - \gamma(t))I(t)$ what leads to the following solution:

$$\begin{aligned}
 I(t) &= e^{\int_0^t (\beta(\tau)S(\tau) - \gamma(\tau)) d\tau} I(0) \geq 0; \forall t \in \mathbf{R}_{0+} \quad (23) \\
 &\text{which is well-posed if}
 \end{aligned}$$

$$\begin{aligned}
 &e^{\int_0^t (\beta(\tau)S(\tau) - \gamma(\tau)) d\tau} I(0) \leq N = S(0) + I(0) + R(0) \\
 &; \forall t \in \mathbf{R}_{0+} \quad (24)
 \end{aligned}$$

or, equivalently, if

$$\left(e^{\int_0^t (\beta(\tau)S(\tau) - \gamma(\tau)) d\tau} - 1 \right) I(0) \leq S(0) + R(0); \forall t \in \mathbf{R}_{0+} \quad (25)$$

which holds irrespective of any nonnegative values of the initial conditions if $e^{\int_0^t (\beta(\tau)S(\tau) - \gamma(\tau)) d\tau} \leq 1; \forall t \in \mathbf{R}_{0+}$. That is guaranteed if $\beta(t) \leq \gamma(t) / S(t); \forall t \in \mathbf{R}_{0+}$. Looking now at the susceptible population given by (22), one gets that if $\beta(t) \leq \gamma(t) / S(t); \forall t \in \mathbf{R}_{0+}$, guaranteeing non-negativity for all time of the infectious population then

so that the susceptible population is also nonnegative for all time under the same sufficiency-type condition as the infectious one is nonnegative, that is, $\beta(t) \leq \gamma(t) / S(t)$ for all time. On the other hand, it also follows directly from integration of (22)-(23) through time that:

$$\begin{aligned}
 R(t) &= R(0) + \int_0^t \gamma(\tau) I(\tau) d\tau \\
 &= R(0) + \left(\int_0^t \gamma(\tau) e^{\int_0^\tau (\beta(\tau')S(\tau') - \gamma(\tau')) d\tau'} d\tau \right) I(0); \forall t \in \mathbf{R}_{0+} \quad (27)
 \end{aligned}$$

which is nonnegative for all time if the infectious population is also nonnegative for all time which is guaranteed if the disease transmission function is sufficiently small to satisfy the upper-bounding condition $\beta(t) \leq \gamma(t) / S(t); \forall t \in \mathbf{R}_{0+}$. Then, it follows as a global result that if $\beta(t) \leq \gamma(t) / S(t); \forall t \in \mathbf{R}_{0+}$ then $0 \leq S(t), I(t), R(t) \leq N$ for all time. Since this condition is always guaranteed for $t=0$, it follows by complete induction that if the stronger condition $\beta(t) \leq \gamma(t) / N; \forall t \in \mathbf{R}_{0+}$ holds then $0 \leq S(t), I(t), R(t) \leq N$ for all time for any set of well-posed initial conditions so that the given SIR-model is positive. On the other hand, it follows by observing (27) that the condition $\beta(t) \geq \gamma(t) / N; \forall t \in \mathbf{R}_{0+}$ implies that $R(t) \rightarrow +\infty$ if $\gamma(t) \in \mathbf{R}_+$ for all time what makes the epidemic mathematical model to be not well-posed. However, those conditions can fail on time intervals of finite measures and the model to be still well-posed.

A necessary condition for well-posed model is $R(t) \leq N = S(0) + I(0) + R(0); \forall t \in \mathbf{R}_{0+}$ for any given initial

conditions what in view of (27) translates into the following constraint:

$$\int_0^t \gamma(\tau) e^{\int_0^\tau (\beta(\tau')S(\tau') - \gamma(\tau')) d\tau'} d\tau - 1 \leq S(0) / I(0); \quad \forall t \in \mathbf{R}_{0+} \quad (28)$$

The worst case of (28) is when $S(0) = 0 \Rightarrow \left(S(t) = 0 \wedge I(t) = e^{-\int_0^t \gamma(\tau) d\tau} I(0) \right); \forall t \in \mathbf{R}_{0+}$

from (22)–(23) so that the necessary condition, irrespective of the disease transmission function, for well-posed model for the worst-case of (28), and then valid for any set of initial conditions, is

$$\int_0^t \gamma(\tau) e^{-\int_0^\tau \gamma(\tau') d\tau'} d\tau \leq 1; \forall t \in \mathbf{R}_{0+} \quad (29)$$

what is guaranteed in particular with an upper-bounding function of exponential order $Ke^{-\alpha t}$ of the left-hand-side of (29) if there exist constants $\alpha \in \mathbf{R}_{0+}, K(\leq \alpha) \in \mathbf{R}_+$ such that

$$\alpha \leq \min_{t \in \mathbf{R}_{0+}} (1/t) \ln(K / \gamma(t)) + \int_0^t \gamma(\tau) d\tau \quad (30)$$

The combination of (19) and (20) leads to:

$$\dot{I}(t) = -\gamma(t)I(t) - \dot{S}(t) \quad (31)$$

so that

$$0 \leq I(0) + S(0) - (I(t) + S(t)) = \int_0^t \gamma(\tau) I(\tau) d\tau = \int_0^t \dot{R}(\tau) d\tau = R(t) - R(0); \forall t \in \mathbf{R}_{0+} \quad (32)$$

provided that the model is well-posed so that the infectious population is nonnegative for all time what implies:

$$I(0) + S(0) \geq I(t) + S(t); \\ N(0) = I(0) + S(0) + R(0) = N(t) = I(t) + S(t) + R(t) \text{ (as expected); } \forall t \in \mathbf{R}_{0+}$$

so that the joint susceptible plus infected population is a monotone decreasing real function independent of initial conditions and the whole population is constant (the constant property of the whole population was already known from simple inspection of (19)–(21). Equivalently, (20) may be integrated via integration by parts as follows by also using (19):

$$I(t) = e^{-\int_0^t \gamma(\tau) d\tau} I(0) - \int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} \dot{S}(t-\tau) d\tau = e^{-\int_0^t \gamma(\tau) d\tau} I(0) - e^{-\int_0^t \gamma(\tau') d\tau'} S(t-\tau) \Big|_{\tau=0}^{\tau=t}$$

$$+ \int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} \gamma(\tau) S(t-\tau) d\tau = e^{-\int_0^t \gamma(\tau) d\tau} (I(0) + S(t)) - S(0) - \left(\int_0^t \int_0^\tau e^{-\int_0^\tau \gamma(\tau') d\tau'} e^{-\int_0^{t-\tau} \beta(\tau') I(\tau') d\tau'} \gamma(\tau') d\tau' d\tau \right) S(0) \quad (33)$$

; $\forall t \in \mathbf{R}_{0+}$. Then, under any of the conditions $\beta(t) \leq \gamma(t) / S(t); \forall t \in \mathbf{R}_{0+}$ or $\beta(t) \leq \gamma(t) / N; \forall t \in \mathbf{R}_{0+}$ guaranteeing that the mathematical model is positive, it follows that :

$$\frac{e^{-\int_0^t \gamma(\tau) d\tau} + \int_0^t \int_0^\tau e^{-\int_0^\tau \gamma(\tau') d\tau'} e^{-\int_0^{t-\tau} \beta(\tau') I(\tau') d\tau'} \gamma(\tau') d\tau' d\tau}{e^{-\int_0^t \gamma(\tau) d\tau}} \leq \frac{I(0)}{S(0)} ; \forall t \in \mathbf{R}_{0+} \quad (34)$$

irrespective of any well-posed set of initial conditions. Now, one can easily obtain from (19) to (21):

$$\dot{S}(t) + \dot{I}(t) = -\dot{R}(t) = -\gamma(t) (N - S(t) - R(t)) ; \forall t \in \mathbf{R}_{0+} \quad (35)$$

Then, $\dot{R}(t) = -\gamma(t)R(t) + \gamma(t)(N - S(t)); \forall t \in \mathbf{R}_{0+}$ (36) which has the following solution by using (22):

$$R(t) = e^{-\int_0^t \gamma(\tau) d\tau} R(0) + \int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} \gamma(t-\tau) (N - S(t-\tau)) d\tau = e^{-\int_0^t \gamma(\tau) d\tau} R(0) + \int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} \left(N - e^{-\int_0^{t-\tau} \beta(\tau') I(\tau') d\tau'} S(0) \right) \gamma(t-\tau) d\tau = e^{-\int_0^t \gamma(\tau) d\tau} R(0) + \int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} \left(S(0) + I(0) + R(0) - e^{-\int_0^{t-\tau} \beta(\tau') I(\tau') d\tau'} S(0) \right) \gamma(t-\tau) d\tau = \left(\int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} d\tau \right) I(0) + \left[\int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} \left(1 - e^{-\int_0^{t-\tau} \beta(\tau') I(\tau') d\tau'} \right) d\tau \right] S(0) + \left(e^{-\int_0^t \gamma(\tau) d\tau} + \int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} d\tau \right) R(0) \geq 0, \quad \forall t \in \mathbf{R}_{0+} \quad (37)$$

If $\beta(t) \leq \gamma(t)/S(t); \forall t \in \mathbf{R}_{0+}$ or $\beta(t) \leq \gamma(t)/N; \forall t \in \mathbf{R}_{0+}$ for any set of well-posed initial conditions. This leads to the following integral constraint:

$$\int_0^t e^{-\int_0^\tau \gamma(\tau') d\tau'} \left(1 - e^{-\int_0^{\tau'} \beta(\tau'') I(\tau'') d\tau''} \right) d\tau \geq 0 \quad (38)$$

what follows directly by contradiction arguments by choosing initial conditions $S(0) = N, I(0) = R(0) = 0$ so that if (38) is false for some time t then $R(t) < 0$ under the positivity constraint for the model (19)-(21) $\beta(t) \leq \gamma(t)/S(t); \forall t \in \mathbf{R}_{0+}$ or $\beta(t) \leq \gamma(t)/N; \forall t \in \mathbf{R}_{0+}$ what is impossible. Some simple concerns with the spreading or not of the disease are now discussed.

- 1) From (20) and (23), $I(0) = 0 \Rightarrow (\dot{I}(0) = 0 \wedge I(t) = \dot{I}(t) = 0; \forall t \in \mathbf{R}_{0+})$ and the disease does not spread through time.
- 2) Assume that $I(0) > 0$ and $S(t) = \gamma(t)/\beta(t); \forall t \in \mathbf{R}_{0+}$ (a necessary condition being $\beta(t) \in \mathbf{R}_+$). Then, one gets $\dot{I}(t) = 0$, so that $I(t) = I(0)$ and $\dot{S}(t) = -\gamma(t)I(t); \forall t \in \mathbf{R}_{0+}$ and the disease still does not spread out through time so that

$$S(t) = \gamma(t)/\beta(t) = S(0) - \int_0^t \gamma(\tau)I(\tau) d\tau = \gamma(0)/\beta(0) - I(0) \int_0^t \gamma(\tau) d\tau; \forall t \in \mathbf{R}_{0+}$$

from (19)-(20). The above equation is equivalent to the subsequent rule for the disease transmission function:

$$\beta(t) = \frac{\gamma(t)}{\gamma(0)\beta^{-1}(0) - I(0) \int_0^t \gamma(\tau) d\tau}; \forall t \in \mathbf{R}_{0+} \quad (39)$$

since the denominator of (39) cannot be negative at any time. It is necessary that $\int_0^t \gamma(\tau) d\tau \leq \frac{\gamma(0)}{\beta(0)I(0)}; \forall t \in \mathbf{R}_{0+}$ so that it is also required as a result $\gamma \in L^1(\mathbf{R}_{0+}, \mathbf{R}_{0+})$ (needing in addition $\gamma(t) \rightarrow 0$ as $t \rightarrow +\infty$) with sufficiently small bound for the integral on \mathbf{R}_{0+} depending on the initial infectious population and the initial values of the average initial disease removal rate and initial disease transmission function value. In this case, it follows from (21) that the immune population is given by:

$$R(t) = R(0) + I(0) \int_0^t \gamma(\tau) d\tau; \forall t \in \mathbf{R}_{0+} \quad (40)$$

which introduced an additional constraint on the average removal rate of the disease which together with the former one deriving from (39) yields the stronger necessary constraint for non-propagation of the disease under initial nonzero infected population which remains constant for all time:

$$\int_0^t \gamma(\tau) d\tau \leq \frac{1}{I(0)} \min\left(\frac{\gamma(0)}{\beta(0)}\right); \forall t \in \mathbf{R}_{0+} \quad (41)$$

One has also from (20)-(21) that

$$dI(t)/dR(t) = \frac{\beta(t)S(t)}{\gamma(t)} - 1 \leq 0; \forall t \in \mathbf{R}_{0+}$$

so that the infected population is a monotone decreasing function (eventually being constant) with respect to the immune one.

- 3) The disease still does not spread if $I(0) > 0$ and $S(t) \leq \gamma(t)/\beta(t); \forall t \in \mathbf{R}_{0+}$ what implies $\dot{I}(t) \leq 0; \forall t \in \mathbf{R}_{0+}$ so that $I(t) \leq I(0); \forall t \in \mathbf{R}_{0+}$. Then,

$$\gamma(t)/\beta(t) \geq S(t) \geq S(0) - \int_0^t \gamma(\tau)I(\tau) d\tau; \forall t \in \mathbf{R}_{0+}$$

so that, one has instead of (39),

$$\beta(t) \leq \frac{\gamma(t)}{S(0) - I(0) \int_0^t \gamma(\tau) d\tau}; \forall t \in \mathbf{R}_{0+} \quad (42)$$

which requires the necessary condition by taking also into account (40)

$$\int_0^t \gamma(\tau) d\tau \leq \frac{1}{I(0)} \min(S(0)); \forall t \in \mathbf{R}_{0+} \quad (43)$$

This condition is weaker than (41) but still guarantees that the disease does not spread with the infectious population being a monotone decreasing function including eventually to be a constant function defined by the initial conditions.

- 4) The disease spreads through time if $I(0) > 0$ and $S(t) \geq \gamma(t)/\beta(t); \forall t \in \mathbf{R}_{0+}$ and, furthermore, $S(t) > \gamma(t)/\beta(t); \forall t \in IT \subset \mathbf{R}_{0+}$ with the interval IT being some non necessarily connected subset of \mathbf{R}_{0+} of infinite measure. Thus, $\dot{I}(t) > 0; \forall t \in IT$ so that $I: \mathbf{R}_{0+} \rightarrow \mathbf{R}_{0+}$ is monotone increasing. Then,

$$S(t) \leq S(0) - \int_0^t \gamma(\tau)I(\tau) d\tau \geq R_p := \gamma(t)/\beta(t); \forall t \in \mathbf{R}_{0+}$$

$$S(t) \leq S(0) - \int_0^t \gamma(\tau)I(\tau) d\tau > \gamma(t)/\beta(t); \forall t \in IT$$

what is guaranteed under the necessary condition (43) if

$$\beta(t) \geq \frac{\gamma(t)}{S(0) - I(0) \int_0^t \gamma(\tau) d\tau}; \forall t \in \mathbf{R}_{0+}$$

$$\beta(t) > \frac{\gamma(t)}{S(0) - I(0) \int_0^t \gamma(\tau) d\tau}; \forall t \in IT \quad (44)$$

and $R_p := \gamma(t)/\beta(t)$ is said to be the basic reproduction ration of the disease at time t which allows its propagation. This condition implies also from (20)-(21) that

$$dI(t)/dR(t) = \frac{\beta(t)S(t)}{\gamma(t)} - 1 \geq 0; \forall t \in \mathbf{R}_{0+}$$

so that the infected population is a monotone increasing function with

respect to the immune one. Since the above derivative is strictly positive on the time interval IT then the infected population is a strictly monotone increasing function with respect to the immune on the time interval IT .

5) The susceptible population can be calculated through time independent of the other populations as follows. One gets combining (19) and (21) by using (23):

$$\begin{aligned} dS(t)/S(t) &= -\frac{\beta(t)}{\gamma(t)}dR(t) = -\frac{\beta(t)}{\gamma(t)}\dot{R}(t)dt \\ \Rightarrow S(t) &= S(0) e^{-\int_0^t \beta(\tau)I(\tau)d\tau} \\ &= S(0) e^{-I(0)\int_0^t \beta(\tau)e^{\int_0^\tau (\beta(\tau')S(\tau')-\gamma(\tau'))d\tau'} d\tau} \\ &; \forall t \in \mathbf{R}_{0+}. \end{aligned}$$

V. SEIR EPIDEMIC MODEL

The following SEIR- model distinguishes as tow separate populations the “infected” $E(t)$ which do not still have external disease symptoms from the “infectious” $I(t)$ (also so-called “infective”) which exhibit already such symptoms. 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:

$$\dot{S}(t) = -\mu S(t) + \omega R(t) - \beta \frac{S(t)I(t)}{N(t)} + \nu N(t)(1-V(t)) \quad (45)$$

$$\dot{E}(t) = \beta \frac{S(t)I(t)}{N(t)} - (\mu + \sigma)E(t) \quad (46)$$

$$\dot{I}(t) = -(\mu + \gamma)I(t) + \sigma E(t) \quad (47)$$

$$\dot{R}(t) = -(\mu + \omega)R(t) + \gamma(1-\rho)I(t) + \nu N(t)V(t) \quad (48)$$

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, 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 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,

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

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 (45)-(48). Furthermore, (45) and (48) and (46) and (47) 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:

$$\begin{aligned} \dot{N}(t) &= (\nu - \mu)N(t) - \rho\gamma I(t) \\ \dot{S}(t) + \dot{R}(t) & \end{aligned} \quad (49)$$

$$= -\mu(S(t) + R(t)) + \left(\gamma(1-\rho) - \beta \frac{S(t)}{N(t)} \right) I(t) + \nu N(t) \quad (50)$$

$$\dot{E}(t) + \dot{I}(t) = -\mu(E(t) + I(t)) - \left(\gamma - \beta \frac{S(t)}{N(t)} \right) I(t) \quad (51)$$

Note that (49) is identically zero if $\nu - \mu = \rho = 0$ and

$$\begin{aligned} N(t) &= e^{(\nu - \mu)t} N(0) - \rho\gamma \int_0^t e^{(\nu - \mu)(t - \tau)} I(\tau) d\tau \\ S(t) + R(t) &= e^{-\mu t} (S(0) + R(0)) \\ &+ \int_0^t e^{-\mu(t - \tau)} \left(\nu N(\tau) + \left(\gamma(1-\rho) - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) \right) d\tau \end{aligned} \quad (52)$$

$$\begin{aligned} E(t) + I(t) &= e^{-\mu t} (E(0) + I(0)) \\ &- \int_0^t e^{-\mu(t - \tau)} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \end{aligned} \quad (53)$$

In order to further solve (52), an integration by parts is performed as follows:

$$\begin{aligned} \int_0^t p(\tau) dq(t, \tau) &= \int_0^t p(\tau) \dot{q}(t, \tau) d\tau \\ &\equiv \int_0^t N(\tau) e^{-\mu(t - \tau)} d\tau \\ &= N(\tau) q(t, \tau) \Big|_0^t - \int_0^t q(t, \tau) \dot{N}(\tau) d\tau \end{aligned} \quad (54)$$

where

$$\bar{q}(t) := \int_0^t e^{-\mu(t-\tau)} d\tau = \frac{e^{-\mu(t-\tau)} \Big|_0^t}{\mu} = q(t, \tau) \Big|_0^t$$

$$= \frac{1 - e^{-\mu t}}{\mu} = q(t, t) - q(t, 0) \tag{55}$$

so that $q(t, t) = 1/\mu$ and $q(t, 0) = e^{-\mu t}/\mu$ and then using (49) in (54) yields

$$\int_0^t N(\tau) e^{-\mu(t-\tau)} d\tau = \frac{1}{\mu} (N(t) - e^{-\mu t} N(0))$$

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

which, after grouping identical terms, leads to

$$\int_0^t N(\tau) e^{-\mu(t-\tau)} d\tau$$

$$= \frac{1}{\nu} \left(N(t) - e^{-\mu t} N(0) + \rho\gamma \int_0^t e^{-\mu(t-\tau)} I(\tau) d\tau \right) \tag{56}$$

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

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

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

$$= -e^{-\mu t} \left(E(0) + I(0) - \int_0^t e^{\mu\tau} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right) \tag{57}$$

VI. 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 $S(t) = \gamma N(t) / \beta$; $\forall t \in \mathbf{R}_{0+}$ with a vaccination control in $[0, 1]$ for all time. Then, the SEIR model (45)-(49) is positive for all time. Furthermore,

$$S(t) + R(t) - N(t) = -(E(t) + I(t))$$

$$= e^{-\mu t} (S(0) + R(0) - N(0))$$

$$= -e^{-\mu t} (E(0) + I(0)) \tag{58}$$

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

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

As a result,

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

$$= \frac{\beta - \gamma}{\beta} N(t) - e^{-\mu t} (E(0) + I(0))$$

$$= \frac{\beta - \gamma}{\beta} N(t) + e^{-\mu t} \left(R(0) - \frac{\beta - \gamma}{\gamma} S(0) \right) \leq \frac{\beta - \gamma}{\beta} N(t);$$

$$\forall t \in \mathbf{R}_{0+} \text{ and } R(t) \rightarrow \frac{\beta - \gamma}{\beta} N(t) \text{ as } t \rightarrow \infty$$

Furthermore, the following two limits exist:

$$\lim_{t \rightarrow \infty} (S(t) + R(t) - N(t)) = \lim_{t \rightarrow \infty} (E(t) + I(t)) = 0 \tag{59}$$

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

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

$$\lim_{t \rightarrow \infty} E(t) = \lim_{t \rightarrow \infty} I(t) = 0 \tag{60}$$

Proof: The mathematical SEIR- model (45)-(49) 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. 58-59 follow directly from (57) and $S(t) = \gamma N(t) / \beta$ for all time. Eqs. 16 follow from (58)-(59) since $\nu - \mu = \rho = 0$ imply

$$N(t) \equiv N(0), \dot{N}(t) \equiv 0 \text{ from (49).} \quad \square$$

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 $0 \leq \nu \leq \mu$ and the vaccination law fulfills $V : \mathbf{R}_{0+} \rightarrow [0, 1]$.

(ii) 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

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

$$\lim_{t \rightarrow \infty} N(t) = 0$$

(iii) If $v > \mu \geq 0$ and $I(t) = \frac{(v-\mu)}{\rho\gamma} N(t)$; $\forall t \geq t_0$ (finite) $\in \mathbf{R}_{0+}$ then global stability of the SEIR-model (45)-(49) is guaranteed if $V: \mathbf{R}_{0+} \rightarrow [0, 1]$. If $v > \mu \geq 0$, $V: \mathbf{R}_{0+} \rightarrow [0, 1]$ and $I(t) = \frac{(v-\mu)}{\rho\gamma} N(t)$ is replaced with the weaker condition $\left| I(t) - \frac{(v-\mu)}{\rho\gamma} N(t) \right| = o(e^{-\alpha t})$ for some $\alpha \in \mathbf{R}_+$ then the SEIR – model (45) –(48) is globally stable.

Proof: (i) If $0 \leq v \leq \mu$ and $\rho\gamma \geq 0$ then $\dot{N}(t) = (v-\mu)N(t) - \rho\gamma I(t) \leq (v-\mu)N(t) \leq 0$; $\forall t \in \mathbf{R}_{0+}$ 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 $N(0)$.

(ii) On the other hand, the solution of (49) for any initial conditions is

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

which is uniformly bounded for all time only if $N(0) = \rho\gamma \int_0^\infty e^{-(v-\mu)\tau} I(\tau) d\tau$ since $v > \mu \geq 0$. 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 :

$$\begin{aligned} I(t) &\geq \frac{(v-\mu)}{\rho\gamma} N(t) = \frac{(v-\mu)}{\rho\gamma} (S(t) + E(t) + I(t) + R(t)) \\ \Leftrightarrow \left(1 - \frac{v-\mu}{\rho\gamma} \right) I(t) &\geq \frac{v-\mu}{\rho\gamma} (S(t) + E(t) + R(t)) \\ \Leftrightarrow I(t) &\geq \frac{v-\mu}{\mu + \rho\gamma - v} (S(t) + E(t) + R(t)) \end{aligned}$$

which requires the parametrical conditions $\rho\gamma > 0$ and $\mu < v < \mu + \rho\gamma$. Since $I(t)$ is of exponential order of at most $(-\mu)$ from Theorem 1 [Eq. (58)] 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 $I(t) = \frac{(v-\mu)}{\rho\gamma} N(t)$ with $v > \mu$ 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 $\left| I(t) - \frac{(v-\mu)}{\rho\gamma} N(t) \right| = o(e^{-\alpha t})$ replaces the above stronger condition $I(t) = \frac{(v-\mu)}{\rho\gamma} N(t)$ 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. \square
Note that the case $v > \mu$ 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:

$$\begin{aligned} N(t) &= \gamma N(t) / \beta + E(t) + I(t) + R(t) \\ \Leftrightarrow \left(\frac{\beta-\gamma}{\beta} \right) N(t) &= E(t) + I(t) + R(t) \\ \Leftrightarrow N(t) &= \frac{\beta}{\beta-\gamma} (E(t) + I(t) + R(t)) \\ \Leftrightarrow R(t) &= \frac{\beta-\gamma}{\beta} N(t) - E(t) - I(t) \end{aligned} \tag{61}$$

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. 50-51 imply that $\lim_{t \rightarrow \infty} (S(t) + R(t) - N(t)) = \lim_{t \rightarrow \infty} (E(t) + I(t)) = 0$ The solution of (51) is:

$$\begin{aligned} E(t) + I(t) &= e^{-\mu t} \\ \times \left[E(0) + I(0) - \int_0^t e^{\mu\tau} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right] \end{aligned} \tag{62}$$

Then, the solution of (48) matches (61) for all time if and only if:

$$\begin{aligned} R(t) &= \frac{\beta-\gamma}{\beta} N(t) - E(t) - I(t) = \frac{\beta-\gamma}{\beta} N(t) \\ &- e^{-\mu t} \left[E(0) + I(0) - \int_0^t e^{\mu\tau} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right] \\ &= e^{-(\mu+\omega)t} \\ &\times \left(R(0) + \int_0^t e^{(\mu+\omega)\tau} (\gamma(1-\rho)I(\tau) + vN(\tau)V(\tau)) d\tau \right) \end{aligned} \tag{63}$$

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

$$\begin{aligned} \dot{h}(t) &= \gamma(1-\rho)I(t) + \nu N(t)V(t) \\ \Leftrightarrow V(t) &= \frac{1}{\nu N(t)} (\dot{h}(t) - \gamma(1-\rho)I(t)) \end{aligned} \quad (64)$$

for all time so that the last right-hand – side additive term in (63) becomes after integration by parts:

$$\begin{aligned} e^{-(\mu+\omega)t} \int_0^t e^{(\mu+\omega)\tau} \dot{h}(\tau) d\tau &= e^{-(\mu+\omega)t} \\ \times \left(e^{(\mu+\omega)t} h(t) - h(0) - (\mu+\omega) \int_0^t e^{(\mu+\omega)\tau} h(\tau) d\tau \right) \end{aligned} \quad (65)$$

The replacement of (65) into (63) yields:

$$\begin{aligned} &\frac{\beta-\gamma}{\beta} e^{(\mu+\omega)t} N(t) - e^{\omega t} \\ &\times \left[E(0) + I(0) - \int_0^t e^{\mu\tau} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right] \\ &= R(0) + \int_0^t e^{(\mu+\omega)\tau} (\gamma(1-\rho)I(\tau) + \nu N(\tau)V(\tau)) d\tau \\ &= R(0) + e^{(\mu+\omega)t} h(t) - h(0) - (\mu+\omega) \int_0^t e^{(\mu+\omega)\tau} h(\tau) d\tau \end{aligned} \quad (66)$$

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

$$\begin{aligned} h(t) &= \frac{\beta-\gamma}{\beta} N(t) + e^{-(\mu+\omega)t} \\ &\times (h(0) - R(0)) + (\mu+\omega) \int_0^t e^{-(\mu+\omega)(t-\tau)} h(\tau) d\tau \\ &\quad - e^{-\mu t} \left[E(0) + I(0) - \int_0^t e^{\mu\tau} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) d\tau \right] \\ &= \frac{\beta-\gamma}{\beta} N(t) + (\mu+\omega) \int_0^t e^{-(\mu+\omega)(t-\tau)} h(\tau) d\tau \\ &\quad + e^{-\mu t} (e^{-\omega t} (h(0) - R(0)) - E(0) - I(0)) \end{aligned} \quad (67)$$

generated from:

$$\begin{aligned} \dot{h}(t) &= \frac{\beta-\gamma}{\beta} [(v-\mu)N(t) - \rho\gamma I(t)] \\ &\quad - (\mu+\omega)e^{-(\mu+\omega)t} (h(0) - R(0)) + \mu e^{-\mu t} (E(0) + I(0)) \\ &\quad - (\mu+\omega)^2 \int_0^t e^{-(\mu+\omega)(t-\tau)} h(\tau) d\tau + (\mu+\omega)h(t) \end{aligned} \quad (68)$$

so that

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

$$\begin{aligned} &+ \gamma \left(\frac{\gamma\rho}{\beta} - 1 \right) I(t) - (\mu+\omega)e^{-(\mu+\omega)t} (h(0) - R(0)) \\ &+ \mu e^{-\mu t} (E(0) + I(0)) - (\mu+\omega)^2 \\ &\times \int_0^t e^{-(\mu+\omega)(t-\tau)} h(\tau) d\tau + (\mu+\omega)h(t) \end{aligned} \quad (69)$$

The vaccination law which ensures the positivity of the mathematical SEIR- model (45) – (48) is generated as follows:

$$V(t) = \begin{cases} \bar{V}(t) & \text{if } \bar{V}(t) \in [0, 1] \\ 1 & \text{if } \bar{V}(t) > 1 \\ 0 & \text{if } \bar{V}(t) < 0 \end{cases} \quad (70)$$

where

$$\bar{V}(t) = \dot{h}(t) - \gamma(1-\rho)I(t) \quad (71)$$

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

$$i(t) = 0 \text{ if } \bar{V}(t) \in [0, 1] \text{ and } i(t) = 1, \text{ otherwise} \quad (72)$$

Then, one has instead of (57)

$$\begin{aligned} S(t) + R(t) - N(t) &= -(E(t) + I(t)) = e^{-\mu t} \\ &\times \left(S(0) + R(0) - N(0) + \int_0^t e^{\mu\tau} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) i(\tau) d\tau \right) \\ &= -e^{-\mu t} \\ &\times \left(E(0) + I(0) - \int_0^t e^{\mu\tau} \left(\gamma - \beta \frac{S(\tau)}{N(\tau)} \right) I(\tau) i(\tau) d\tau \right) \end{aligned} \quad (73)$$

which coincides with (57) for all time if the indicator function is identically zero, that is, if $\dot{h}(t)$ ism such that the auxiliary vaccination law (71) 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 $\forall t \geq T$, one gets from (57):

$$\begin{aligned} N(t) - S(t) - R(t) &\leq \varepsilon \\ &+ \int_0^t e^{-\mu(t-\tau)} \left(\beta \frac{S(\tau)}{N(\tau)} - \gamma \right) I(\tau) i(\tau) d\tau \end{aligned} \quad (74)$$

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 (49). However, the whole susceptible plus immune does not asymptotically track the whole population. In summary, one has:

Theorem 3. The vaccination law (68), (70)-(71) makes the SEIR – model (1-4) positive and globally stable under Theorem 2. Furthermore,

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

□

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