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A Lyapunov functional for a SIRI model with nonlinear incidence of infection and relapse

Paul Georgescu [a,*], Hong Zhang [b]

[a] Department of Mathematics, Technical University of Iaşi, Bd. Copou 11, 700506 Iaşi, Romania
[b] Department of Mathematics, Jiangsu University, Zhenjiang, Jiangsu 212013, PR China

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ABSTRACT

We analyze the dynamics of a disease propagation model with relapse under the assumption that the incidence of infection is given in an abstract, possibly bi-nonlinear form. Sufficient conditions for the local stability of equilibria are obtained by means of Lyapunov's second method and it is shown that global stability can be attained under suitable monotonicity conditions. The persistence of the system is then investigated and it is established that the basic reproduction number R_0 is a threshold parameter for the stability of the system. Alternate Lyapunov functionals are also introduced, being observed that the originating functional template generalizes both quadratic and Volterra functionals.

1. Introduction

To model the propagation of a human or animal disease, it is often convenient to subdivide the total population, depending on disease status, into a small, tractable group of epidemiological classes, or compartments, the result being called a compartmental model. Among the most often considered compartments are the class of susceptible individuals (S), the class of infective individuals (I) and the class of recovered individuals (R), while other classes may be added for increased accuracy. Upon contracting the disease, the susceptible individuals enter the infective class and then, after their infective period ends, enter the recovered class.

However, in diseases such as herpes and human and bovine tuberculosis, recovered individuals may experience relapse and reenter the infective class. For herpes (see, for instance, Blower et al. [1] or Wildy et al. [26]), it has been observed that an individual, once infected, remains infected all his life, passing regularly through episodes of relapse of infectiousness. For tuberculosis, relapse can be caused by incomplete treatment or by latent infection, being observed that HIV-positive patients are significantly more likely to relapse than HIV-negative patients, although it is often difficult to differentiate relapse from reinfection (see Cox et. al. [2]). Also, it has been observed in [27] that the dominant force for attenuating the decline in tuberculosis incidence in Hong Kong is endogenous reactivation of latent infection, being also noted that public health interventions focusing solely on reducing transmission may not ease the burden caused by endogenous reactivation in the short and medium term.

A SIRI model for the spread of herpes with bilinear incidence and constant population size has been introduced by Tudor [23], being shown that the basic reproduction number is a threshold parameter for the stability of the system. Further, it has been observed in [23] that this model is also appropriate for the propagation of pseudorabies in swine. The results of [23] have been extended by Moreira and Wang [20] to allow for the use of an incidence term featuring a more general dependence on the size of the susceptible class, use being made of Lyapunov's direct method and of an analysis of Liénard's

* Corresponding author.
E-mail addresses: v.p.georgescu@gmail.com (P. Georgescu), hongzhang@ujs.edu.cn (H. Zhang).

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equation to establish a similar global stability threshold. A more general SIRI model, formulated as a integrodifferential system with the fraction $P(t)$ of recovered individuals remaining in the recovered class t time units after the recovery expressed in an abstract form has been proposed and analyzed in van den Driessche and Zou [5], certain threshold stability results being obtained by particularizing $P(t)$. See also van den Driessche et al. [3] for an analysis of a related SEIRI model.

Lyapunov's second method is a robust tool which has been used to establish the local or global stability of equilibria for large classes of models arising in mathematical biology and mathematical epidemiology, including certain models of predator–prey interaction and disease transmission. A Lyapunov functional of type $V(x,y) = c_1\left(x - x^* - x^* \ln\frac{x}{x^*}\right) + c_2\left(y - y^* - y^* \ln\frac{y}{y^*}\right)$ has been first used by Volterra in [25] to discuss the stability of a predator–prey ecosystem. To relate the specific form of this functional with our subsequent analysis, note here that V can be expressed under the equivalent form $V(x,y) = c_1\int_{x^*}^{x}\frac{\tau - x^*}{\tau}d\tau + c_2\int_{y^*}^{y}\frac{\tau - y^*}{\tau}d\tau$. This approach (and Lyapunov functional) has been vastly generalized by Harrison in [10], who discussed the stability of a predator–prey interaction of a very general form using a Lyapunov functional which is neither logarithmic, like Volterra's, nor quadratic.

In recent years, a systematic study regarding the use of Lyapunov's second method to discuss the stability of various models of disease propagation and predation has been made by Korobeinikov and his coworkers. See, for instance, Korobeinikov [12–14], Korobeinikov and Maini [15], Melnik and Korobeinikov [19]. See also Guo et al. [9] for a graph theoretic approach to the task of constructing suitable functionals, McCluskey [16–18] for a stability analysis of delayed SIR and SIRS models, Georgescu and Hsieh [8] for an analysis of a SEIV model with nonlinear incidence of infection and removal expressed in an abstract form, Yuan and Wang [28] for the study of a SEIR model with nonlinear incidence and group mixing. For a survey on the use of Lyapunov functionals to establish the stability of disease propagation models, see also Fall et. al. [6]. However, Lyapunov's second method has been comparatively less successful for models with relapse or loss of immunity than for models lacking these features.

We consider a compartmental model which divides the total population into susceptible individuals (S), infective individuals (I) and recovered individuals (R) and describes the transmission of a contagious disease with relapse, in the form

$$\begin{aligned}\frac{dS}{dt} &= n(S) - c(S)f(I),\\ \frac{dI}{dt} &= c(S)f(I) - c_1\varphi(I) + k_1\gamma(R),\\ \frac{dR}{dt} &= c_2\varphi(I) - k_2\gamma(R).\end{aligned} \tag{1}$$

The intrinsic growth rate of the susceptible class, which includes recruitment due to birth and immigration, as well as losses due to natural death, is given by $n(S)$. The incidence rate of infection is given by $c(S)f(I)$, where $c(S)$ is a contact function and $f(I)$ represents the force of infection. The progression of infectious individuals to the recovered class is given by $c_2\varphi(I)$, while $c_1\varphi(I)$ represent the total movement of infectious individuals outside of the infective class due to their progression to the recovered class, death due to natural causes and disease-related death. The displacement of recovered individuals to the infective class due to relapse is given by $k_1\gamma(R)$, while the total movement of recovered individuals outside of the recovered class due to relapse and to death due to natural causes is given by $k_2\gamma(R)$. For obvious biological reasons, it is assumed that $c_1 > c_2$ and $k_2 > k_1$.

For $n(S) = \Lambda - \mu S, c(S) = S, f(I) = \beta I, \varphi(I) = I, \gamma(R) = R, c_1 = \alpha + \kappa + \mu, c_2 = \kappa, k_1 = \gamma, k_2 = \gamma + \mu$, one obtains the model

$$\begin{aligned}\frac{dS}{dt} &= \Lambda - \mu S - \beta SI,\\ \frac{dI}{dt} &= \beta SI - (\alpha + \kappa + \mu)I + \gamma R,\\ \frac{dR}{dt} &= \kappa I - (\mu + \gamma)R,\end{aligned}$$

which has been discussed by Vargas-deLeón in [24]. In the above model, Λ is the constant recruitment rate of susceptibles due to birth and immigration, μ is the natural death rate of the population, α is the disease-induced death rate, γ is the relapse rate and β is the average number of adequate contacts for an infective individual. Also, for $n(S) = \mu - \mu S, f(I) = I, \varphi(I) = I, \gamma(R) = R, c_1 = \kappa + \mu, c_2 = \kappa, k_1 = \gamma, k_2 = \gamma + \mu$, one obtains the model

$$\begin{aligned}\frac{dS}{dt} &= \mu - \mu S - c(S)I,\\ \frac{dI}{dt} &= c(S)I - (\kappa + \mu)I + \gamma R,\\ \frac{dR}{dt} &= \kappa I - (\mu + \gamma)R,\end{aligned}$$

analyzed by Moreira and Wang in [20], the meaning of the parameters being as indicated above.

2. The well-posedness of the model

In this section, we shall discuss the global existence of the solutions of (1) and their positivity for suitable initial data, establishing the well-posedness of the model in a biological sense. To this purpose, we assume that c, f, φ, γ, n are real C^1 functions defined at least on $[0,\infty)$ which satisfy the following positivity and growth conditions

(P) $c(0) = f(0) = \varphi(0) = \gamma(0) = 0, n(0) > 0, c(t), f(t), \varphi(t), \gamma(t) > 0$ for $t > 0$.

(G) $\varphi(I) \leqslant c_\varphi I$ for $I \geqslant 0, \gamma(R) \leqslant c_\gamma R$ for $R \geqslant 0, n(S) \leqslant \Lambda - c_n S$ for $S \geqslant 0, \int_{0+}^{1} \frac{1}{f(s)} ds = +\infty$, where $\Lambda, c_n, c_\varphi, c_\gamma > 0$.

Note that (G) also implies that $\int_{0+}^{1} \frac{1}{\varphi(s)} ds = \int_{0+}^{1} \frac{1}{\gamma(s)} ds = +\infty$. Also, we assume that the equation $n(S) = 0$ has a single solution S_0 and the following sign conditions are satisfied

(SGN) $(n(S) - n(S_0))(S - S_0) < 0, (c(S) - c(S_0))(S - S_0) > 0$ for all $S \neq S_0, S \geqslant 0$.

It is easy to see that conditions (SGN) are satisfied provided that n and c are strictly decreasing and strictly increasing, respectively. Due to the sign and positivity conditions (SGN) and (P), it is easily seen that (1) admits a single disease-free equilibrium $(S_0, 0, 0)$, which will be denoted by $\mathbf{E_0}$.

First, since Nagumo's tangency condition (see, for instance, Pavel [21] for details) is satisfied on the boundary of $[0,\infty)^3$, the system (1) has a unique solution (S, I, R) for positive initial data, which remains positive on its maximal interval of existence.

Let us now choose $1 < \alpha < \frac{c_1 k_2}{c_2 k_1}$ and define

$$G : \mathbb{R}^3 \to \mathbb{R}, \quad G(S, I, R) = S + I + \frac{c_1}{\alpha c_2} R.$$

It follows that

$$\frac{dG}{dt} \leqslant \Lambda - c_n S - c_1 \left(1 - \frac{1}{\alpha}\right) c_\varphi I - \left(\frac{c_1}{c_2} \frac{k_2}{\alpha} - 1\right) c_\gamma R,$$

and consequently

$$\frac{dG}{dt} + dG \leqslant \Lambda,$$

where

$$d = \min\left(c_n, c_1 \left(1 - \frac{1}{\alpha}\right) c_\varphi, \left(\frac{c_1}{c_2} \frac{k_2}{\alpha} - 1\right) c_\gamma\right). \tag{2}$$

This implies that

$$F = \left\{(S, I, R) \in [0,\infty)^3, G(S, I, R) \leqslant \frac{\Lambda}{d}\right\},$$

is a feasible domain for (1) which also attracts all solutions starting in $[0,\infty)^3$. Note that $G(\mathbf{E_0}) = G(S_0, 0, 0) = S_0$ and, by (SGN) and the continuity of n, $n(S_0) = 0$. From (G) and (2), one sees that

$$0 = n(S_0) \leqslant \Lambda - c_n S_0 \leqslant \Lambda - d S_0,$$

and consequently $G(\mathbf{E_0}) \leqslant \frac{\Lambda}{d}$, which implies that $\mathbf{E_0} \in F$.

In what follows, we shall consider only the behavior of solutions starting (and remaining) in this feasible domain. Obviously, such solutions are *a priori* bounded. Also, it is seen that $(0,\infty)^3 \cap F$ is an invariant set for (1) and the only ω-limit point of (1) on the boundary of F is $\mathbf{E_0}$.

Let us also define the basic reproduction number R_0 by

$$R_0 = \frac{k_2}{c_1 k_2 - c_2 k_1} c(S_0) \frac{f'(0)}{\varphi'(0)}.$$

In this regard, the derivation of R_0 can be performed by means of the next generation method as in [4], noting that

$$\frac{d}{dt}\begin{pmatrix} I \\ R \\ S \end{pmatrix} = \begin{pmatrix} c(S) f(I) \\ 0 \\ 0 \end{pmatrix} - \begin{pmatrix} c_1 \varphi(I) - k_1 \gamma(R) \\ -c_2 \varphi(I) + k_2 \gamma(R) \\ c(S) f(I) - n(S) \end{pmatrix} = \mathcal{F} - \mathcal{V}.$$

At the disease-free equilibrium $\mathbf{E_0}$, one has

$$D\mathcal{F}(\mathbf{E_0}) = \begin{pmatrix} F & O_{2,1} \\ O_{1,2} & 0 \end{pmatrix}, \quad D\mathcal{V}(\mathbf{E_0}) = \begin{pmatrix} V & O_{2,1} \\ J_1 & J_2 \end{pmatrix},$$

where the infection matrix F and the transition matrix V are given by

$$F = \begin{pmatrix} c(S_0)f'(0) & 0 \\ 0 & 0 \end{pmatrix}, \quad V = \begin{pmatrix} c_1\varphi'(0) & -k_1\gamma'(0) \\ -c_2\varphi'(0) & k_2\gamma'(0) \end{pmatrix},$$

and

$$J_1 = \begin{pmatrix} c(S_0)f'(0) & 0 \end{pmatrix}, \quad J_2 = -n'(S_0).$$

Consequently,

$$FV^{-1} = \frac{1}{c_1k_2 - c_2k_1}\frac{f'(0)}{\varphi'(0)}\begin{pmatrix} c(S_0)k_2 & c(S_0)k_1 \\ 0 & 0 \end{pmatrix},$$

and since R_0 is the leading eigenvalue of FV^{-1}, the conclusion follows.

For a biological interpretation of the quantities used in the definition of R_0, one sees that $\frac{1}{c_1\varphi'(0)}$ is the average time spent by an individual in the infective class in the first pass (an infective individual may return to the infective class after relapse) if the second equation is replaced by its linearization near the disease-free equilibrium. Since the probability of surviving the infective class is $\frac{c_2}{c_1}$ and the probability of surviving the recovered class is $\frac{k_1}{k_2}$, the average time spent by an individual in the infective class (on multiple passes) is

$$T_I = \frac{1}{c_1\varphi'(0)} + \frac{1}{c_1\varphi'(0)}\frac{c_2k_1}{c_1k_2} + \frac{1}{c_1\varphi'(0)}\left(\frac{c_2k_1}{c_1k_2}\right)^2 + \ldots = \frac{k_2}{c_1k_2 - c_2k_1}\frac{1}{\varphi'(0)}.$$

Then the number of secondary infections caused by I infectives in a totally susceptible population ($S = S_0$) on multiple passes is $c(S_0)f(I)T_I$ and consequently the number of new infections caused by a single infective is

$$c(S_0)\frac{f(I)}{I}\frac{k_2}{c_1k_2 - c_2k_1}\frac{1}{\varphi'(0)}.$$

Passing to limit as $I \to 0$, one deduces the expression of R_0 which is indicated above.

3. The stability of the disease-free equilibrium

In what follows, we shall be concerned with the stability of the disease-free equilibrium $\mathbf{E_0}$.

We consider the Lyapunov functional

$$U_1(S,I,R) = \int_{S_0}^{S}\frac{c(\tau) - c(S_0)}{c(\tau)}d\tau + I + \frac{k_1}{k_2}R.$$

Due to the sign condition (C), it is seen that U_1 increases whenever any of $|S - S_0|, I, R$ increases and $U_1(S,I,R) \geqslant 0$, with $U_1(S,I,R) = 0$ if and only if $(S,I,R) = \mathbf{E_0}$, that is, $\mathbf{E_0}$ is a minimum point for U_1. Also $\lim_{S\to 0}U_1(S,I,R) = +\infty$, due to the growth conditions (G), and consequently the level sets of U_1 do not have limit points on the boundary of $(0,\infty)^3$. We now compute the time derivative of U_1 along the solutions of (1).

Lemma 3.1. *The time derivative of U_1 along the solutions of (1) is*

$$\dot{U}_1 = \left(\frac{c(S) - c(S_0)}{c(S)}\right)(n(S) - n(S_0)) + \frac{c_1k_2 - c_2k_1}{k_2}\left(R_0f(I)\frac{\varphi'(0)}{f'(0)} - \varphi(I)\right). \tag{3}$$

Proof. By direct computations, it is seen that

$$\begin{aligned}\dot{U}_1 &= \left(\frac{c(S) - c(S_0)}{c(S)}\right)(n(S) - c(S)f(I)) + (c(S)f(I) - c_1\varphi(I) + k_1\gamma(R)) + \frac{k_1}{k_2}(c_2\varphi(I) - k_2\gamma(R)) \\ &= \left(\frac{c(S) - c(S_0)}{c(S)}\right)n(S) - c(S_0)f(I) - \frac{c_1k_2 - c_2k_1}{k_2}\varphi(I).\end{aligned}$$

Since $n(S_0) = 0$, we may deduce that

$$\dot{U}_1 = \left(\frac{c(S) - c(S_0)}{c(S)}\right)(n(S) - n(S_0)) + \frac{c_1k_2 - c_2k_1}{k_2}\left(\frac{k_2c(S_0)}{c_1k_2 - c_2k_1}f(I) - \varphi(I)\right),$$

from which the conclusion follows. □

We are now ready to establish our first stability result, which gives an estimation for the domain of attraction associated with the disease-free equilibrium $\mathbf{E_0}$.

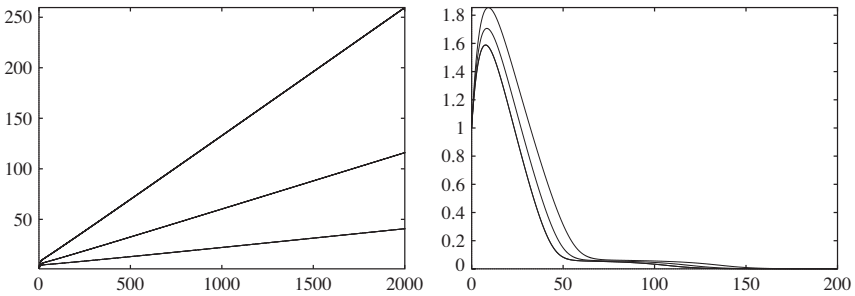

Fig. 1. I as a function of t for $r_f \in \{2,3,4\}$, respectively for $r_f \in \{10,11,12\}$.

Theorem 3.1. *Suppose that there is $I_{DF} > 0$ such that*

$$\frac{f(I)}{\varphi(I)} \leqslant \frac{f'(0)}{\varphi'(0)} \frac{1}{R_0} \quad \text{for } I \in (0, I_{DF}) \tag{4}$$

and let $m = U_1(S_0, I_{DF}, 0)$. Then the disease-free equilibrium $\mathbf{E_0}$ is locally asymptotically stable and its domain of attraction includes the set

$$D_m^1 = \{(S,I,R) \in (0,\infty) \times [0,\infty)^2; U_1(S,I,R) < m\}.$$

Proof. First, due to the sign conditions (SGN), it is seen that $\dot{U}_1(S,I,R) \geqslant 0$ for $I \in (0, I_{DF})$, with equality if and only if $S = S_0$ and either $I = 0$ or the equality holds in (4). Also, for $I \geqslant I_{DF}, \dot{U}_1(S,I,R) \geqslant U_1(S_0, I_{DF}, 0) = m$. Consequently, if $(S,I,R) \in D_m^1$, then $I < I_{DF}$, which implies that $\dot{U}_1(S,I,R) \leqslant 0$ on D_m^1.

We now find the invariant subsets within

$$\tilde{P}^1 = \left\{(S,I,R) \in D_m^1; \dot{U}_1(S,I,R) = 0\right\}.$$

It is easily seen that if $(S,I,R) \in \tilde{P}^1$ then $S = S_0$ and consequently $I = 0$ and the only invariant subset of $\tilde{P}^1$ is $\{(S_0,0,0)\}$. The use of LaSalle's invariance principle (see, for instance, Khalil [11]) concludes the proof. □

Although Theorem 3.1 is seemingly a local stability result, it will be seen in what follows that it ensures the global stability of the disease-free equilibrium under a suitable monotonicity condition.

Corollary 3.1. *Suppose that $R_0 \leqslant 1$ and the following monotonicity condition holds*
(M1) $\frac{f}{\varphi}$ is decreasing.
Then the disease-free equilibrium $\mathbf{E_0}$ is globally asymptotically stable.

Proof. Since $\frac{f}{\varphi}$ is decreasing, one sees that

$$\frac{f(I)}{\varphi(I)} \leqslant \lim_{I \to 0} \frac{f(I)}{\varphi(I)} = \frac{f'(0)}{\varphi'(0)} \quad \text{for all } I > 0,$$

which implies that (4) is satisfied for all $I > 0$. Consequently, I_{DF} and m can be chosen arbitrarily large and $\mathbf{E_0}$ is globally asymptotically stable. □

Note that condition (M1) is trivially satisfied if f and φ are linear functions, case in which $\frac{f}{\varphi}$ is a constant function. Also, (M1), which assumes that the functional quotient between the force of infection and the removal rate of infectives is decreasing, is a natural prerequisite for the global stability of the disease-free equilibrium. Note that the stability conditions employed in Corollary 3.1 do not depend explicitly on γ, although R_0 does depend on the functional quotient $\frac{k_1}{k_2}$ between the displacement of the infectives to the recovered class, $k_1\gamma$, and the removal rate of the recovered, $k_2\gamma$.

It also appears, from numerical simulations, that condition (M1) may have a significant impact on the dynamics of the solutions when $R_0 \leqslant 1$. In this regard, let us consider $n(S) = \Lambda - \mu S, f(I) = \frac{\beta I}{1+r_f I}, \varphi(I) = \frac{I}{1+r_\varphi I}, \gamma(R) = \frac{I}{1+r_\gamma R}, c_1 = \alpha + \kappa + \mu, c_2 = \kappa, k_1 = \gamma, k_2 = \gamma + \mu$, with $\Lambda = 2.5, \mu = 0.2, \beta = 0.04, \alpha = 0.2, \kappa = 0.6, r_f \in \{2,3,4\}, r_\varphi = 8, r_\gamma = 8$. In this situation, $R_0 = 0.714 < 1$ and $\frac{f}{\varphi}(I) = \frac{1+r_\varphi I}{1+r_f I}$, which is increasing, rather than decreasing, as condition (M1) requires. We have represented on the Fig. 1 below the graph of I as a function of t for $r_f = 2$ (the fastest growth), $r_f = 3$ and $r_f = 4$ and (the slowest growth) and the initial data $S(0) = 100, I(0) = 1, R(0) = 0$. Also, it is useful to note that graph of R shares the same quasi-linear shape and that $I(10000) = 1276.4$ (for $r_f = 2$), respectively $I(10000) = 564.8$ (for $r_f = 3$) and $I(10000) = 191.8$ (for $r_f = 4$), that is,

the size of the infected class continues to grow. However, changing the value of r_f to $r_f \in \{10, 11, 12\}$ drastically alters the shape of the graph of I, as seen from the figure below, in which $r_f = 12$ corresponds to the fastest decay, and $r_f = 10$ corresponds to the slowest decay, even though the value of R_0 does not change.

4. The existence of the endemic equilibrium and the persistence of infection

We shall now discuss the existence of an endemic equilibrium, denoted in what follows by $\mathbf{E}^*$, where $\mathbf{E}^* = (S^*, I^*, R^*)$. To this purpose, we assume that the following strict monotonicity and limit conditions are satisfied, in addition to the positivity and growth conditions (P) and (G) mentioned above

(SM) c, γ, f are strictly increasing, $\frac{f}{\varphi}$ is decreasing, n is strictly decreasing

$$\text{(LI)} \lim_{R\to\infty}\gamma(R) > \frac{c_2 n(0)}{c_1 k_2 - k_2 c_1}, \lim_{I\to\infty} f(I) > \frac{n}{c}\left(c^{-1}\left(\frac{1}{R_0}c(S_0)\right)\right).$$

Note that the limit conditions (LI) are trivially satisfied if $\lim_{R\to\infty}\gamma(R) = \lim_{I\to\infty} f(I) = +\infty$, as it is the case for models with bilinear incidence of infection and constant relapse rate.

To ensure the existence of $\mathbf{E}^*$, the following equilibrium relations need to be satisfied

$$n(S^*) - c(S^*)f(I^*) = 0, \quad c(S^*)f(I^*) - c_1\varphi(I^*) + k_1\gamma(R^*) = 0, \tag{5}$$

$$c_2\varphi(I^*) = k_2\gamma(R^*).$$

Consequently, necessarily

$$n(S^*) - c(S^*)f(I^*) = 0, \quad c(S^*)f(I^*) - \frac{c_1k_2 - c_2k_1}{k_2}\varphi(I^*) = 0. \tag{6}$$

Theorem 4.1. *Suppose that conditions (SM) and (LI) are satisfied. Then (1) admits an endemic equilibrium $\mathbf{E}^*$ if and only if $R_0 > 1$.*

Proof. Let us note first that if $R_0 \leqslant 1$, then there is no endemic equilibrium. Indeed, suppose that (S^*, I^*, R^*) verifies (5). Then, since $\frac{\varphi}{f}$ is increasing,

$$c(S^*) = \frac{c_1k_2 - c_2k_1}{k_2}\frac{\varphi(I^*)}{f(I^*)} \geqslant \frac{c_1k_2 - c_2k_1}{k_2}\frac{\varphi'(0)}{f'(0)} = \frac{1}{R_0}c(S_0) \geqslant c(S_0),$$

and, since c is strictly increasing, $S^* \geqslant S_0$. Since f is strictly increasing, $f(0) = 0$ and

$$f(I^*) = \frac{n(S^*)}{c(S^*)} \leqslant \frac{n(S_0)}{c(S_0)} = 0,$$

this yields a contradiction and consequently there is no endemic equilibrium if $R_0 \leqslant 1$.

Suppose now that $R_0 > 1$ and let us define

$$F_1(S, I) = n(S) - c(S)f(I), \quad F_2(S, I) = c(S)f(I) - \frac{c_1k_2 - c_2k_1}{k_2}\varphi(I).$$

We first discuss the solvability of the equation $F_1(S, I) = 0$. For fixed I,

$$F_1(0, I) = n(0) > 0, \quad F_1(S_0, I) = -c(S_0)I < 0.$$

Since $\frac{n}{c}$ is strictly decreasing, it then follows that the equation $F_1(S, I) = 0$ can be uniquely solved with respect to S as a function of I. That is, there is $S = \psi_1(I)$ such that $F_1(S, I) = 0$. Also, since $\frac{n}{c}$ is strictly decreasing, it follows that ψ_1 is strictly decreasing. It is seen that $\psi_1(0) = S_0$ and

$$\lim_{I\to\infty}\frac{n(\psi_1(I))}{c(\psi_1(I))} = \lim_{I\to\infty} f(I) > \frac{n}{c}\left(c^{-1}\left(\frac{1}{R_0}c(S_0)\right)\right),$$

which, since $\frac{n}{c}$ is strictly decreasing, implies the existence of $I_0 > 0$ such that

$$\psi_1(I_0) < c^{-1}\left(\frac{1}{R_0}c(S_0)\right).$$

We now discuss the solvability of the equation $F_2(S, I) = 0$. It is seen that

$$F_2(0, I) < 0,$$

$$F_2(S_0, I) = c(S_0)f(I) - \frac{c_1k_2 - c_2k_1}{k_2}\varphi(I) = \frac{c_1k_2 - c_2k_1}{k_2}f(I)\left(R_0\frac{\varphi'(0)}{f'(0)} - \frac{\varphi(I)}{f(I)}\right).$$

Since $R_0 > 1$ and $\lim_{I\to 0}\frac{\varphi(I)}{f(I)} = \frac{\varphi'(0)}{f'(0)}$, $F_2(S_0, I) > 0$ for I small enough, and consequently the equation $F_2(S, I) = 0$ can be solved with respect to S as a function of I for I small enough. That is, there is $S = \psi_2(I)$ such that $F_2(S, I) = 0$. Since $\frac{\varphi}{f}$ is increasing, ψ_2 is increasing. Note that

$$c(\psi_2(I)) = \frac{1}{R_0}c(S_0)\frac{f'(0)}{\varphi'(0)}\frac{\varphi(I)}{f(I)},$$

and consequently

$$c(\psi_2(0)) = \operatorname*{limc}_{I\to 0} c(\psi_2(I)) = \frac{1}{R_0}c(S_0), \quad c(\psi_1(0)) = c(S_0).$$

Since c is strictly increasing and $R_0 > 1$, it follows that $0 < \psi_2(0) < \psi_1(0)$. Noting that ψ_1 and ψ_2 have positive values, ψ_1 is strictly decreasing, ψ_2 is increasing and $\psi_1(I_0) < \psi_2(I_0)$, it follows that the graphs of ψ_1 and ψ_2 have a single common point (S^*, I^*). That is, there are unique S^*, I^* such that (6) are satisfied. Also, since γ is strictly increasing and (LI) is satisfied, there is a unique R^* such that (S^*, I^*, R^*) verifies (5), which establishes the existence and uniqueness of the endemic equilibrium. □

We continue by analyzing the persistence of infection. Naturally, if $R_0 > 1$, then each infected individual causes in average more than one secondary infection and consequently the infection is expected to remain endemic. In this regard, the infection is said to be uniformly persistent, or permanent, if there is $\varepsilon_0 > 0$ such that $\liminf_{t\to\infty} I(t) \geqslant \varepsilon_0$ for any solution of (1) which starts with strictly positive initial data. Note that the permanence of the infection excludes the stability of the disease-free equilibrium.

We now introduce the notion of an uniform repeller for a semidynamical system, which is an useful mathematical tool to establish the permanence of infection.

Let π_1 be a semidynamical system defined on a closed subset F of a locally compact metric space (X, d). It is then said that a subset S of F is a uniform repeller if there is $\eta > 0$ such that for each $x \in F \setminus S$, $\liminf_{t\to\infty} d(\pi_1(x, t), S) > \eta$.

The following remarkable result of Fonda [7, Corollary 1] provides a characterization of uniform repellers for semidynamical systems on abstract metric spaces in terms of a seemingly weaker condition which is also easily verifiable in concrete situations. See also Smith and Thieme [22] for a comprehensive overview of persistence theory for dynamical systems with applications in mathematical biology.

Lemma 4.1. *Let π be a semidynamical system defined on a locally compact metric space X and let Σ be a compact subset of X such that $X \setminus \Sigma$ is positively invariant. A necessary and sufficient condition for Σ to be a uniform repeller is that there exists a neighborhood U of Σ and a continuous function $P : X \to \mathbb{R}_0^+$ satisfying*

(1) *$P(x) = 0$ if and only if $x \in \Sigma$.*
(2) *For all $x \in U \setminus \Sigma$ there is a $T_x > 0$ such that $P(\pi(x, T_x)) > P(x)$.*

We are now ready to discuss the permanence of infection.

Theorem 4.2. *Suppose that condition (SM) is satisfied and $R_0 > 1$. Then the infection is permanent.*

Proof. We shall prove that the set $\Sigma = \{(S, I, R) \in F; I = 0\}$ is an uniform repeller, which is equivalent to the infection being permanent. We denote $\pi(x, t) = (S(t), I(t), R(t))$, where (S, I, R) is the unique solution of (1) with initial data $(S(0), I(0), R(0)) = x$.

First, it has been seen that F is compact and $F \setminus \Sigma$ is positively invariant. Let us define the function $P : F \to [0, \infty)$ by $P(S, I, R) = I$ and the neighborhood $U \subset F$ of Σ by

$$U = \{(S, I, R) \in F; P(S, I, R) < \rho\},$$

where ρ is small enough, so that

$$c\left(\left(\frac{n}{c}\right)^{-1}(f(\rho))\right)\inf_{0<\tau\leqslant\rho}\frac{f(\tau)}{\varphi(\tau)}\frac{k_2}{c_1k_2 - k_1c_2} > 1.$$

Note that

$$\operatorname*{limc}_{\rho\to 0}\left(\left(\frac{n}{c}\right)^{-1}(f(\rho))\right)\inf_{0<\tau\leqslant\rho}\frac{f(\tau)}{\varphi(\tau)}\frac{k_2}{c_1k_2 - k_1c_2} = c(S_0)\frac{f'(0)}{\varphi'(0)}\frac{k_2}{c_1k_2 - c_2k_1} = R_0,$$

so the above choice of ρ is feasible. Suppose by contradiction that there is $z \in U \setminus \Sigma$ such that for all $t > 0$ one has $P(\pi(z, t)) \leqslant P(z) < \rho$ and let us consider the auxiliary function $\xi : [0, \infty) \to [0, \infty)$ defined by

$$\xi(t) = I(t) + \frac{k_1}{k_2}(1 - \rho^*)R(t),$$

where ρ^* is small enough, so that

$$\delta = c\left(\left(\frac{n}{c}\right)^{-1}(f(\rho))\right)\inf_{0<\tau\leqslant\rho}\frac{f(\tau)}{\varphi(\tau)}\frac{k_2}{c_1k_2-k_1c_2(1-\rho^*)} > 1.$$

One then has

$$\xi'(t) = \varphi(I)\frac{c_1k_2-k_1c_2(1-\rho^*)}{k_2}\left[c(S)\frac{f(I)}{\varphi(I)}\frac{k_2}{c_1k_2-k_1c_2(1-\rho^*)}-1\right]+k_1\rho^*\gamma(R).$$

It is also seen form the first equation of (1) that, since $\frac{dS}{dt}\leqslant n(S)$,

$$\liminf_{t\to\infty}S(t) \geqslant \left(\frac{n}{c}\right)^{-1}(f(\rho)),$$

and consequently

$$\xi'(t) \geqslant c_\varphi\frac{c_1k_2-k_1c_2(1-\rho^*)}{k_2}(\delta-1)I+k_1c\gamma R.$$

As a result, $\xi'(t)\geqslant C\xi(t)$ for some sufficiently small C and consequently $\xi(t)\to\infty$ as $t\to\infty$, which contradicts the boundedness of S,I,R. Consequently, for all $z\in U\setminus\Sigma$ there is $T_z>0$ such that $P(\pi(z,T_z))>P(z)$. From Lemma 4.1, Σ is an uniform repeller, which ends the proof of our permanence result. □

5. The stability of the endemic equilibrium

In this section, we *a priori* assume the existence of an endemic equilibrium $\mathbf{E}^*$ satisfying (5) rather than assume the supplementary hypotheses (SM) and (LI) mentioned in the previous section, as these hypotheses seem to be sufficient for the existence of the endemic equilibrium, but not necessary, and discuss its stability. We assume instead that the following sign conditions similar to those employed in Section 2 are satisfied

$$\begin{aligned}&(\mathrm{PE})(c(S)-c(S^*))(S-S^*)>0 \quad \text{for } S\neq S^*,\ S\geqslant 0;\\ &(f(I)-f(I^*))(I-I^*)>0 \quad \text{for } I\neq I^*,\ I\geqslant 0;\\ &(\gamma(R)-\gamma(R^*))(R-R^*)>0 \quad \text{for } R\neq R^*,\ R\geqslant 0,\end{aligned}$$

and

$$(\mathrm{NE})(n(S)-n(S^*))(S-S^*)<0 \quad \text{for } S\neq S^*, S\geqslant 0.$$

Obviously, (PE) and (NE) are satisfied if c,f,γ are strictly increasing and n is strictly decreasing.

We consider the Lyapunov functional

$$U_2(S,I,R) = \int_{S^*}^{S}\frac{c(\tau)-c(S^*)}{c(\tau)}d\tau+\int_{I^*}^{I}\frac{f(\tau)-f(I^*)}{f(\tau)}d\tau+\frac{k_1}{k_2}\int_{R^*}^{R}\frac{\gamma(\tau)-\gamma(R^*)}{\gamma(\tau)}d\tau.$$

Due to (PE) and (NE), it is seen that U_2 increases whenever any of $|S-S^*|,|N-N^*|,|R-R^*|$ increases and $U_2(S,I,R)\geqslant 0$, with $U_2(S,I,R)=0$ if and only if $(S,I,R)=(S^*,I^*,R^*)$. Consequently, $\mathbf{E}^*$ is a minimum point for U_2. Also, due to the growth conditions (G), it is seen that $U_2(S,I,R)\to\infty$ whenever any of S,I,R tend to 0 and consequently the level sets of U_2 do not have limit points on the boundary of $(0,\infty)^3$.

We now compute the time derivative of U_2 along the solutions of (1).

Lemma 5.1. *The time derivative of U_2 along the solutions of (1) is*

$$\begin{aligned}\dot U_2 = {}& \left(\frac{c(S)-c(S^*)}{c(S)}\right)(n(S)-n(S^*))+n(S^*)\left(2-\frac{c(S^*)}{c(S)}-\frac{c(S)}{c(S^*)}\right)\\ &+k_1\gamma(R^*)\left[3-\frac{f(I^*)}{f(I)}\frac{\gamma(R)}{\gamma(R^*)}-\frac{\varphi(I)}{\varphi(I^*)}\frac{\gamma(R^*)}{\gamma(R)}-\frac{\varphi(I^*)}{\varphi(I)}\frac{f(I)}{f(I^*)}\right]\\ &+c_1\left(\frac{\varphi(I^*)}{f(I^*)}-\frac{\varphi(I)}{f(I)}\right)(f(I)-f(I^*))\\ &+\frac{k_1\gamma(R^*)}{f(I^*)}\left(\frac{f(I^*)}{\varphi(I^*)}-\frac{f(I)}{\varphi(I)}\right)(\varphi(I)-\varphi(I^*)).\end{aligned} \tag{7}$$

If the inequality

$$\begin{aligned}&c_1\left(\frac{\varphi(I^*)}{f(I^*)}-\frac{\varphi(I)}{f(I)}\right)(f(I)-f(I^*))\\ &\quad+\frac{k_1\gamma(R^*)}{f(I^*)}\left(\frac{f(I^*)}{\varphi(I^*)}-\frac{f(I)}{\varphi(I)}\right)(\varphi(I)-\varphi(I^*))\leqslant 0,\end{aligned} \tag{8}$$

holds true for $I \in (I_L, I_R)$, then $\dot{U}_2(S,I,R) \leqslant 0$ for $I \in (I_L, I_R)$, a necessary condition for the equality to hold being

$$\frac{f(I)}{f(I^*)} = \frac{\varphi(I)}{\varphi(I^*)} = \frac{\gamma(R)}{\gamma(R^*)}.$$

Proof. By direct computations, it is seen that

$$\begin{aligned}\dot{U}_2 &= \left(1-\frac{c(S^*)}{c(S)}\right)(n(S)-c(S)f(I)) + \left(1-\frac{f(I^*)}{f(I)}\right)(c(S)f(I)-c_1\varphi(I)+k_1\gamma(R)) \\ &\quad + \frac{k_1}{k_2}(c_2\varphi(I)-k_2\gamma(R))\left(1-\frac{\gamma(R^*)}{\gamma(R)}\right) = \left(1-\frac{c(S^*)}{c(S)}\right)n(S) + c(S^*)f(I) - c(S)f(I^*) - c_1\varphi(I)\left(1-\frac{f(I^*)}{f(I)}\right) \\ &\quad - \frac{f(I^*)}{f(I)}k_1\gamma(R) + \frac{k_1}{k_2}c_2\varphi(I) - \frac{k_1}{k_2}c_2\varphi(I)\frac{\gamma(R^*)}{\gamma(R)} + k_1\gamma(R^*).\end{aligned}$$

Using the equilibrium relations (5), it follows that

$$\begin{aligned}\dot{U}_2 &= \left(1-\frac{c(S^*)}{c(S)}\right)(n(S)-n(S^*)) + n(S^*)\left(2-\frac{c(S^*)}{c(S)}-\frac{c(S)}{c(S^*)}\right) \\ &\quad + c(S^*)f(I) - c_1\varphi(I)\left(1-\frac{f(I^*)}{f(I)}\right) - \frac{f(I^*)}{f(I)}k_1\gamma(R) + \frac{k_1}{k_2}c_2\varphi(I) \\ &\quad - \frac{k_1}{k_2}c_2\varphi(I)\frac{\gamma(R^*)}{\gamma(R)} + k_1\gamma(R^*) - n(S^*) \\ &= \left(1-\frac{c(S^*)}{c(S)}\right)(n(S)-n(S^*)) + n(S^*)\left(2-\frac{c(S^*)}{c(S)}-\frac{c(S)}{c(S^*)}\right) \\ &\quad + c_1\left(\frac{\varphi(I^*)}{f(I^*)}-\frac{\varphi(I)}{f(I)}\right)(f(I)-f(I^*)) - k_1\gamma(R^*)\frac{f(I)}{f(I^*)} - \frac{f(I^*)}{f(I)}k_1\gamma(R) \\ &\quad + \frac{k_1}{k_2}c_2\varphi(I) - \frac{k_1}{k_2}c_2\varphi(I)\frac{\gamma(R^*)}{\gamma(R)} + 2\gamma(R^*).\end{aligned}$$

This implies that

$$\begin{aligned}\dot{U}_2 &= \left(1-\frac{c(S^*)}{c(S)}\right)(n(S)-n(S^*)) + n(S^*)\left(2-\frac{c(S^*)}{c(S)}-\frac{c(S)}{c(S^*)}\right) \\ &\quad + c_1\left(\frac{\varphi(I^*)}{f(I^*)}-\frac{\varphi(I)}{f(I)}\right)(f(I)-f(I^*)) \\ &\quad + k_1\gamma(R^*)\left[3-\frac{f(I^*)}{f(I)}\frac{\gamma(R)}{\gamma(R^*)}-\frac{\varphi(I)}{\varphi(I^*)}\frac{\gamma(R^*)}{\gamma(R)}-\frac{\varphi(I^*)}{\varphi(I)}\frac{f(I)}{f(I^*)}\right] \\ &\quad + k_1\gamma(R^*)\frac{\varphi(I)}{\varphi(I^*)} - k_1\gamma(R^*)\frac{f(I)}{f(I^*)} - k_1\gamma(R^*) + k_1\gamma(R^*)\frac{\varphi(I^*)}{\varphi(I)}\frac{f(I)}{f(I^*)},\end{aligned}$$

which in turn implies (7). Now, from the sign conditions (PE) and (NE), it is seen that

$$\left(1-\frac{c(S^*)}{c(S)}\right)(n(S)-n(S^*)) \leqslant 0 \quad \text{for } S>0,$$

with equality if and only if $S = S^*$. Also, from the AM–GM inequality, which says that the arithmetic mean is not smaller than the geometric mean, it is seen that

$$2-\frac{c(S^*)}{c(S)}-\frac{c(S)}{c(S^*)} \leqslant 0 \quad \text{for } S>0,$$

with inequality if and only if $\frac{c(S^*)}{c(S)} = \frac{c(S)}{c(S^*)}$, that is $c(S) = c(S^*)$, or $S = S^*$.

Using again the AM–GM inequality, it is seen that

$$3-\frac{f(I^*)}{f(I)}\frac{\gamma(R)}{\gamma(R^*)}-\frac{\varphi(I)}{\varphi(I^*)}\frac{\gamma(R^*)}{\gamma(R)}-\frac{\varphi(I^*)}{\varphi(I)}\frac{f(I)}{f(I^*)} \leqslant 0,$$

with equality if and only if

$$\frac{f(I)}{f(I^*)} = \frac{\varphi(I)}{\varphi(I^*)} = \frac{\gamma(R)}{\gamma(R^*)}. \tag{9}$$

It then follows that if the inequality (8) holds true for $I \in (I_L, I_R)$, then $\dot{U}_2(S,I,R) \leqslant 0$ for $I \in (I_L, I_R)$. Note that $\dot{U}_2(S,I,R) = 0$ if and only if $S = S^*$, (9) holds and the equality holds in (8). □

Using the setup for LaSalle's invariance principle provided by the above lemma, one may now obtain an estimation for the domain of attraction associated with the endemic equilibrium.

Theorem 5.1. *Suppose that there are $I_L < I^* < I_R$ such that (8) holds for $I \in (I_L, I_R)$ and let us define $m = \min(U_2(S^*, I_L, R^*), U_2(S^*, I_R, R^*))$. Then $\mathbf{E}^*$ is locally asymptotically stable and its domain of attraction includes the set*

$$D_m^2 = \{(S,I,R) \in (0,\infty)^3; U_2(S,I,R) < m\}.$$

Proof. First, it is seen that for I outside (I_L, I_R),

$$U_2(S,I,R) \geqslant \min(U_2(S,I_L,R), U_2(S,I_R,R)) \geqslant \min(U_2(S^*,I_L,R^*), U_2(S^*,I_R,R^*)) = m.$$

Consequently, if $(S,I,R) \in D_m^2$, then $I \in (I_L, I_R)$, which implies that $\dot{U}_2(S,I,R) \leqslant 0$ on D_m^2. We now find the invariant subsets within

$$\tilde{P}^2 = \{(S,I,R) \in D_m^2; \dot{U}_2(S,I,R) = 0\}.$$

Since necessarily $S = S^*$, it follows that $\frac{dS}{dt} = c(S^*)(f(I^*) - f(I))$, and then $\frac{dS}{dt} = 0$ if and only if $I = I^*$. Since (9) holds, it also follows that $R = R^*$. The conclusion then follows using LaSalle's invariance principle. □

Note that if $\varphi = \lambda f, \lambda \in \mathbb{R}$, then the left-hand side of (8) is null and consequently (8) is satisfied for all I. Then, as it has already been the case with Theorem 3.1, one easily obtains the global stability of the endemic equilibrium under suitable hypotheses of the functional coefficients of the model, as seen from the following result.

Corollary 5.1. *Suppose that $\varphi = \lambda f$, the system (1) admits an endemic equilibrium $\mathbf{E}^*$ and the sign conditions (PE) and (NE) hold true. Then $\mathbf{E}^*$ is globally asymptotically stable.*

One also obtains from the same inequality (8) that the endemic equilibrium of the system without relapse ($k_1 = 0$) is globally asymptotically stable under a suitable monotonicity condition.

Corollary 5.2. *Suppose that $k_1 = 0$, the system (1) admits an endemic equilibrium $\mathbf{E}^*$, the sign conditions (PE) and (NE) hold true and condition (M1) holds. Then the endemic equilibrium $\mathbf{E}^*$ is globally asymptotically stable.*

Note that a monotonicity condition of type (M1) would not suffice anymore for the global stability of the system with relapse.

In the above, to discuss the stability of the equilibria, use has been made of the following functionals

$$U_1(S,I,R) = \int_{S_0}^{S} \frac{c(\tau) - c(S_0)}{c(\tau)} d\tau + I + \frac{k_1}{k_2} R,$$
$$U_2(S,I,R) = \int_{S^*}^{S} \frac{c(\tau) - c(S^*)}{c(\tau)} d\tau + \int_{I^*}^{I} \frac{f(\tau) - f(I^*)}{f(\tau)} d\tau + \frac{k_1}{k_2} \int_{R^*}^{R} \frac{\gamma(\tau) - \gamma(R^*)}{\gamma(\tau)} d\tau.$$

If c, f and φ are linear functions, then U_1 and U_2 reduce to

$$U_1(S,I,R) = S - S_0 - S_0 \ln \frac{S}{S_0} + I + \frac{k_1}{k_2} R,$$
$$U_2(S,I,R) = S - S^* - S^* \ln \frac{S}{S^*} + I - I^* - I^* \ln \frac{I}{I^*} - \frac{k_1}{k_2} \left(R - R^* - R^* \ln \frac{R}{R^*} \right),$$

that is, to logarithmic functionals of Volterra type.

Another set of Lyapunov functionals which may be used to establish the stability of the equilibria are slightly modified versions of the above functionals obtained by changing their respective S-parts, of the form

$$V_1(S,I,R) = \int_{S_0}^{S} \frac{c(\tau) - c(S_0)}{c(S_0)} d\tau + I + \frac{k_1}{k_2} R,$$
$$V_2(S,I,R) = \int_{S^*}^{S} \frac{c(\tau) - c(S^*)}{c(S^*)} d\tau + \int_{I^*}^{I} \frac{f(\tau) - f(I^*)}{f(\tau)} d\tau + \frac{k_1}{k_2} \int_{R^*}^{R} \frac{\gamma(\tau) - \gamma(R^*)}{\gamma(\tau)} d\tau,$$

in which case

$$\dot{V}_1 = \left(\frac{c(S) - c(S_0)}{c(S_0)} \right) (n(S) - n(S_0)) - \frac{(c(S) - c(S_0))^2}{c(S_0)} f(I) + \frac{c_1 k_2 - c_2 k_1}{k_2} \left(R_0 f(I) \frac{\varphi'(0)}{f'(0)} - \varphi(I) \right),$$
$$\dot{V}_2 = -\frac{(c(S) - c(S^*))^2}{c(S^*)} f(I) + \frac{(n(S) - n(S^*))(c(S) - c(S^*))}{c(S^*)} + k_1 \gamma(R^*) \left[3 - \frac{f(I^*)}{f(I)} \frac{\gamma(R)}{\gamma(R^*)} - \frac{\varphi(I)}{\varphi(I^*)} \frac{\gamma(R^*)}{\gamma(R)} - \frac{\varphi(I^*)}{\varphi(I)} \frac{f(I)}{f(I^*)} \right]$$
$$+ c_1 \left(\frac{\varphi(I^*)}{f(I^*)} - \frac{\varphi(I)}{f(I)} \right) (f(I) - f(I^*)) + \frac{k_1 \gamma(R^*)}{f(I^*)} \left(\frac{f(I^*)}{\varphi(I^*)} - \frac{f(I)}{\varphi(I)} \right) (\varphi(I) - \varphi(I^*)),$$

the stability results being obtained via similar arguments. Note that if c, f and φ are linear functions, then V_1 and V_2 reduce to

$$V_1(S,I,R) = \frac{(S-S_0)^2}{2S_0} + I + \frac{k_1}{k_2}R$$
$$V_2(S,I,R) = \frac{(S-S^*)^2}{2S^*} + I - I^* - I^* \ln\frac{I}{I^*} - \frac{k_1}{k_2}\left(R - R^* - R^* \ln\frac{R}{R^*}\right),$$

featuring both logarithmic and quadratic terms. That is, purely logarithmic or logarithmic-quadratic functionals are actually originating from similar integral templates.

For $n(S) = \Lambda - \mu S, c$ an increasing C^1 function, $f(I) = \beta I, \varphi(I) = I, \gamma(R) = R, c_1 = \alpha + \kappa + \mu, c_2 = \kappa, k_1 = \gamma, k_2 = \gamma + \mu$, one obtains the model

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \mu S - \beta c(S) I \\ \frac{dI}{dt} &= \beta c(S) I - (\alpha + \kappa + \mu) I + \gamma R \\ \frac{dR}{dt} &= \kappa I - (\mu + \gamma) R, \end{aligned} \tag{10}$$

its basic reproduction number being

$$\hat{R}_0 = \frac{(\mu+\gamma)\beta c\left(\frac{\Lambda}{\mu}\right)}{(\mu+\lambda)(\mu+\alpha) + \kappa\mu}.$$

We can therefore use the discussion previously laid out and obtain the following result which enlarges both Theorems 2.1 and 2.2 in [24] and Theorem 1 in [20].

Corollary 5.3

(1) *If* $\hat{R}_0 < 1$, *then the disease-free equilibrium* $\mathbf{E_0}$ *of the system (10) is globally asymptotically stable in* $(0,\infty)^3$ *and there is no endemic equilibrium* $\mathbf{E}^*$ *of (10).*
(2) *If* $\hat{R}_0 > 1$, *then the disease-free equilibrium* $\mathbf{E_0}$ *of (10) is unstable, the infection remains endemic and there is a unique endemic equilibrium* $\mathbf{E}^*$ *of (10) which is globally asymptotically stable in* $(0,\infty)^3$.

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References

[1] S. Blower, T.C. Porco, G. Darby, Predicting and preventing the emergence of antiviral drug resistance in HSV-2, Nat. Med. 4 (1998) 673.
[2] H. Cox, Y. Kebeda, S. Allamuratova, G. Ismailov, Z. Davletmuratova, G. Byrnes, C. Stone, S. Niemann, S. Rüsch-Gerdes, L. Blok, D. Doshetov, Tuberculosis recurrence and mortality after successful treatment: impact of drug resistance, PLoS Med. 3 (2006) 1836–1843.
[3] P. van den Driessche, L. Wang, X. Zou, Modeling diseases with latency and relapse, Math. Biosci. Eng. 4 (2007) 205–219.
[4] P. van den Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (2002) 29–48.
[5] P. van den Driessche, X. Zou, Modeling relapse in infectious diseases, Math. Biosci. 207 (2007) 89–103.
[6] A.A. Fall, A. Iggidr, G. Sallet, J.J. Tewa, Epidemiological models and Lyapunov functions, Math. Model. Nat. Phenom. 2 (2006) 55–71.
[7] A. Fonda, Uniformly persistent dynamical systems, Proc. Am. Math. Soc. 104 (1998) 111–116.
[8] P. Georgescu, Y.-H. Hsieh, Global stability for a virus dynamics model with nonlinear incidence of infection and removal, SIAM J. Appl. Math. 67 (2006) 337–353.
[9] H. Guo, M.Y. Li, Z. Shuai, A graph-theoretic approach to the method of Lyapunov functions, Proc. Am. Math. Soc. 136 (2008) 2793–2802.
[10] G.W. Harrison, Global stability of predator–prey interactions, J. Math. Biol. 8 (1979) 159–171.
[11] H. Khalil, Nonlinear Systems, Prentice Hall, Upper Saddle River, New Jersey, NY, 2002.
[12] A. Korobeinikov, Global properties of basic virus dynamics models, Bull. Math. Biol. 66 (2004) 879–883.
[13] A. Korobeinikov, Lyapunov functions and global properties for SEIR and SEIS epidemic models, Math. Med. Biol. 21 (2004) 75–83.
[14] A. Korobeinikov, Lyapunov functions and global stability for SIR and SIRS epidemiological models with non-linear transmission, Bull. Math. Biol. 30 (2006) 615–626.
[15] A. Korobeinikov, P.K. Maini, Non-linear incidence and stability of infectious disease models, Math. Med. Biol. 22 (2005) 113–128.
[16] C. McCluskey, Global stability for an SIR epidemic model with delay and nonlinear incidence, Nonlinear Anal. Real World Appl. 11 (2010) 3106–3109.
[17] C. McCluskey, Complete global stability for an SIR epidemic model with delay – distributed or discrete, Nonlinear Anal. Real World Appl. 11 (2010) 55–59.
[18] C. McCluskey, Global stability for an SEIR epidemiological model with varying infectivity and infinite delay, Math. Biosci. Eng. 6 (2009) 603–610.

[19] A.V. Melnik, A. Korobeinikov, Global asymptotic properties of staged models with multiple progression pathways for infectious diseases, Math. Biosci. Eng. 8 (2011) 1019–1034.
[20] H.N. Moreira, Y. Wang, Global stability in a $S \to I \to R \to I$ model, SIAM Rev. 39 (1997) 497–502.
[21] N.H. Pavel, Differential equations flow invariance and applications, Pitman Research Notes in Mathematics, vol. 113, Pitman, London, 1984.
[22] H.L. Smith, H.R. Thieme, Dynamical Systems and Population Persistence, Graduate Studies in Mathematics, vol. 118, American Mathematical Society, Providence, RI, 2011.
[23] D. Tudor, A deterministic model for herpes infections in human and animal populations, SIAM Rev. 32 (1990) 136–139.
[24] C. Vargas de León, On the global stability of infectious disease models with relapse, in press.
[25] V. Volterra, Leçons sur la Theorie Mathematique de la Lutte pour la Vie, Gauthier-Villars, Paris, 1931.
[26] P. Wildy, H.J. Field, A.A. Nash, Classical herpes latency revisited, in: B.W.J. Mahy, A.C. Minson, G.K. Darby (Eds.), Virus Persistence Symposium, vol. 33, Cambridge University Press, Cambridge, 1982, pp. 133–168.
[27] P. Wu, E.H.Y. Lau, B.J. Cowling, C.C. Leung, C.M. Tam, The transmission dynamics of tuberculosis in a recently developed Chinese city, PLoS One 5 (2010) e10468.
[28] Z. Yuan, L. Wang, Global stability of epidemiological models with group mixing and nonlinear incidence rates, Nonlinear Anal. Real World Appl. 11 (2010) 995–1004.