GLOBAL STABILITY IN CYCLIC EPIDEMIC MODELS WITH DISEASE FATALITIES

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1 2

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CONTENTS

ABSTRACT

A general disease transmission model of SIRS type is formulated and analyzed. There is constant recruitment into the susceptible class, mass action incidence, and stage age in the removed class. Disease fatalities occur in the infective class and the removed stages. Sufficient conditions are given for the endemic equilibrium to be globally asymptotically stable. For example, if the disease confers permanent immunity, then global stability of the endemic equilibrium (for parameter values such that it exists) is assured. Other examples are given that exhibit this same assured behavior.

1. INTRODUCTION

In most classical epidemic models, the total population is assumed to be constant. Anderson and May [1] formulated one of the first o.d.e. epidemic models that includes population dynamics, thus the total population varies. They modeled the spread of *Pasteurella muris* in laboratory mice. The recruitment rate of mice was constant, and the rate at which mice acquired the infection was found to be proportional to the number of encounters between susceptible and infective mice (the law of mass action). This disease causes some fatalities, but other infective mice recover with temporary immunity. Thus the model is of SIRS type. Anderson and May [1] gave a condition for the disease to remain endemic, and showed that in this case the disease decreases the population. This model was further analyzed by Mena-Lorca and Hethcote [6, Section 2] and using a Lyapunov function they proved that the endemic equilibrium (when it exists) is globally asymptotically stable if there is no disease fatality or if immunity to the disease is permanent.

The SIRS model introduced by Anderson and May assumes that removed (recovered) individuals lose immunity at a rate proportional to their number, corresponding to an exponentially distributed time in the removed class. In other epidemic models a more general probability of remaining removed is assumed. For example, Hethcote *et al.* [4] derived two SIRS models in a constant population that can exhibit Hopf bifurcation giving rise to periodic solutions for some parameter values. One model, [4, Sections 2, 3] has a fixed period of temporary immunity, which corresponds to a step function probability. The other model [4, Section 4] has a chain of $n \geq 3$ removed stages corresponding to a gamma distribution. For $n = 1, 2$, the endemic equilibrium is known to be globally asymptotically stable [3, 9].

In a complementary study on the constant population SIRS model, Stech and Williams [9] used a result of Londen [5] to find conditions on the probability function that imply global stability of the endemic equilibrium. This result was used by Castillo-Chavez and Thieme [2, Section 3.5] in a variable population SIRS model with a distributed length of the removed period and no disease fatality. This latter assumption means that the system has the same asymptotic behavior as that of an easier limit system.

Motivated by HIV/AIDS studies, Simon and Jacquez [7] analyzed o.d.e. SI models with subpopulations and a chain of infective stages. Under the assumption that each subpopulation is isolated (restricted mixing), Simon and Jacquez [7, Section 6] used a Lyapunov function to find sufficient conditions for the endemic equilibrium to be globally asymptotically stable. These conditions are more readily satisfied

when the natural death rate is large compared with the rate of passing from one infective stage to the next.

Our aim is to use the method of Stech and Williams [9] to prove global convergence to the endemic equilibrium (for parameter values such that it exists) in a variable population SIRS model with disease fatalities. We base our model on that of [1], but we include stage age for those individuals in the removed class. Our model system is formulated in Section 2, where the notation and assumptions are given. Further a standard threshold condition is derived for stability of the disease-free equilibrium versus existence of an endemic equilibrium. In Section 3, the system is transformed into a scalar integro-differential equation and the result of Stech and Williams [9] is used to give sufficient conditions for convergence to the endemic equilibrium. Section 4 continues with conditions for arbitrarily distributed time in the removed class. Each of Sections 5 and 6 considers a special case of the model system with several exponentially distributed removed stages. The model in Section 5 has one primary removed stage through which all individuals pass, and then an individual passes into one of several secondary removed stages that may be permanent or transient to the susceptible class. A limiting case of this model reduces to the SIRS model analyzed by Anderson and May [1] and by Mena-Lorca and Hethcote [6, Section 2]. The model in Section 6 assumes that all individuals pass through a chain of two removed stages, then either return to the susceptible class or become permanently immune. Global asymptotic stability of the endemic equilibrium (whenever it exists) is proved for each of these o.d.e. models as well as for a chain of removed stages with permanent immunity (Section 4). Thus there is a sharp threshold, with the disease dying out below the threshold, and tending to the endemic level above the threshold. This is in contrast to the model with a chain of at least three removed stages through which all individuals pass before losing immunity, which can have solutions that oscillate about the endemic level [4, Section 4]. The models that we consider in Sections 5 and 6 need no extra parameter conditions for global convergence to the endemic equilibrium, this is in contrast to the models analyzed by Simon and Jacquez [7] with multiple infective stages. As kind of a trade-off, the method we present does not work if there is more than one infective stage, and it also does not work if an exposed class is included in the model (for diseases with a latent period). However, global stability of equilibria is preserved under small perturbations (Smith and Waltman [8]): so global stability of the endemic equilibrium still holds when the latency period is sufficiently small, although this is difficult to quantify.

2. The model

A population of size N is divided into susceptible, infective, and removed (or recovered) classes, with the number of individuals in each class given by S, I, R, respectively, and

$$N(t) = S(t) + I(t) + R(t).$$

Infection is modeled according to the law of mass action, thus

$$I'(t) = \kappa S(t)I(t) - (\mu + \epsilon + \gamma)I(t).$$

Here κ denotes the transmission coefficient, μ denotes the *per capita* natural death rate constant, ϵ denotes the extra *per capita* disease mortality rate constant for infectives, and γ denotes the *per capita* removal (or recovery) rate constant of infectives.

Substituting the first into the second equation gives

$$I'(t) = \kappa(N(t) - I(t) - R(t))I(t) - (\mu - \epsilon + \gamma)I(t). \tag{2.1}$$

In order to get a handle on N we formulate the following differential equation

$$N'(t) = \Lambda - \mu N(t) - \epsilon I(t) - M_R(t). \tag{2.2}$$

Here Λ is the constant recruitment rate into the population (actually into its susceptible class since vertical transmission is ignored). The remaining expressions on the right hand side are various components of the population mortality rate: μN is the mortality rate due to natural causes. ϵI is the extra mortality rate for infectives due to the disease. and $M_R(t)$ denotes the extra mortality rate of removed (recovered) individuals due to the disease.

In the following we illustrate that it is possible to express R and M_R in terms of I. To this end we stratify the removed individuals according to their stage age.

$$R(t) = \int_0^\infty \rho(t, a)da. \tag{2.3}$$

with the stage age a being the time since removal and $\rho(t, \cdot)$ the stage-age density at time t.

The stage age density ρ for the removed individuals relates to the stage input (which here is γI) and to the initial density ρ_0 in the usual way

$$\rho(t, a) = \begin{cases} \gamma I(t-a)\mathcal{F}(a), & t > a, \\ \rho_0(a-t)\frac{\mathcal{F}(a)}{\mathcal{F}(a-t)}, & t < a, \end{cases} \tag{2.4}$$

where $\mathcal{F}(a)$ is the probability to be still in the removed class a time units after removal from the infective class. This probability factorizes into three parts:

$$\mathcal{F}(a) = \epsilon^{-\mu a}\mathcal{F}_R(a)Q(a). \tag{2.5}$$

Here $\epsilon^{-\mu a}$ is the probability of not having died from natural causes in the time interval $[0, a]$. $\mathcal{F}_R$ is the survivorship of removed individuals with respect to the disease. *i.e.*, $\mathcal{F}_R(a)$ is the probability of not having died from disease-related causes in the time from the moment of removal until a time units later. and Q describes the duration of the removed class. *i.e.*, $Q(a)$ is the probability of not having returned to the susceptible class a time units after removal from the infective class. If the removed period has a finite maximum length L. then $Q(a) = 0$ for $a > L$. If the disease confers permanent immunity. then $Q(a) \equiv 1$.

It follows from the interpretation that both $\mathcal{F}_R$ and Q are non-negative. non-increasing functions on $[0, \infty)$ that have the value 1 at $a = 0$. For any function of this type. *e.g.*, for $\mathcal{F}$. we make the convention that

$$\frac{\mathcal{F}(a)}{\mathcal{F}(a-t)} = 0, \quad \text{whenever } a > t \text{ and } \mathcal{F}(a) = 0.$$

Another natural assumption states that the number of removed individuals is finite in the beginning and their density is non-negative. so $\rho_0 \in L^1[0, \infty)$. *i.e.*,

$$\int_0^\infty \rho_0(a)da < \infty.$$

In order to close our model, we have for the extra death rate of removed individuals, M_R, that

$$M_R(t) = -\int_0^\infty \frac{\rho(t,a)}{\mathcal{F}_R(a)}\mathcal{F}_R(da) \tag{2.6}$$

with the last integral being a Stieltjes integral.

The fastest way to understand the Stieltjes integral is to assume for a moment that $\mathcal{F}_R$ is differentiable. Then

$$\delta(a) = -\frac{\mathcal{F}_R'(a)}{\mathcal{F}_R(a)}$$

is the per capita extra mortality rate at which removed individuals die from the disease, and the integral

$$\int_0^\infty \rho(t,a)\delta(a)da$$

gives the associated population rate.

We substitute (2.4) and (2.5) into (2.3) and obtain that

$$R(t) = \int_0^t I(t-a)e^{-\mu a}g(a)da + e^{-\mu t}u(t)$$

with

$$g(a) = \mathcal{F}_R(a)Q(a), \quad \text{thus} \quad g(0) = 1, \tag{2.7}$$

and

$$u(t) = \int_t^\infty \rho_0(a-t)\frac{\mathcal{F}_R(a)Q(a)}{\mathcal{F}_R(a-t)Q(a-t)}da.$$

We have

$$u(t) \le \int_0^\infty \rho_0(a)da = u_0 < \infty.$$

We also substitute (2.4) and (2.5) into (2.6) obtaining

$$M_R(t) = \int_0^t I(t-a)e^{-\mu a}f(da) + e^{-\mu t}V(t).$$

with

$$f(a) = -\int_0^a Q(r)\mathcal{F}_R(dr), \quad a > 0, \qquad f(0) = 0. \tag{2.8}$$

and

$$V(t) = -\int_t^\infty \rho_0(a-t)\frac{Q(a)}{Q(a-t)\mathcal{F}_R(a-t)}\mathcal{F}_R(da).$$

We claim that $V \in L^1[0,\infty)$. Indeed,

$$\begin{aligned}
\int_0^t V(s)ds &\le -\int_0^t\int_s^\infty \rho_0(a-s)\frac{1}{\mathcal{F}_R(a-s)}\mathcal{F}_R(da)ds \\
&\le -\int_0^t\int_0^a \rho_0(a-s)\frac{1}{\mathcal{F}_R(a-s)}ds\mathcal{F}_R(da) \\
&= -\int_0^t\int_0^a \rho_0(s)\frac{1}{\mathcal{F}_R(s)}ds\mathcal{F}_R(da) \\
&\le \int_0^t \rho_0(a)da.
\end{aligned}$$

In the last step we have used integration by parts for Stieltjes integrals. Remember that we have assumed that $\rho_0 \in L^1[0,\infty)$, hence $V \in L^1[0,\infty)$.

Summarizing, we have obtained the following model:

$$\begin{aligned} I'(t) &= \kappa(N(t) - I(t) - R(t))\, I(t) - (\mu + \epsilon + \gamma) I(t), \\ N'(t) &= \Lambda - \mu N(t) - \epsilon I(t) - M_R(t), \\ R(t) &= \gamma \int_0^t I(t-a) e^{-\mu a} g(a) da + e^{-\mu t} u(t) \\ M_R(t) &= \gamma \int_0^t I(t-a) e^{-\mu a} f(da) + e^{-\mu t} V(t). \end{aligned} \tag{2.9}$$

In view of our derivation (recall (2.7) and (2.8)) we make the following assumptions.

Assumptions 2.1. All parameters are non-negative, $\mu > 0$.

- $g : [0,\infty) \to [0,1]$ is non-increasing.
- $f : [0,\infty) \to [0,1]$ is non-decreasing, and $f(0) = 0$.
- $u : [0,\infty) \to [0,\infty)$ is continuous and bounded.
- $V : [0,\infty) \to [0,\infty)$, $V \in L^1[0,\infty)$.

With the above assumptions, the model given by (2.9) is well posed, and solutions with nonnegative initial conditions remain nonnegative, while $S = N - I - R$ remains non-negative as well if it is non-negative initially. The system always has the disease free equilibrium, namely $N = S = \Lambda/\mu$, $I = R = 0$. The basic reproduction number, defined as

$$\mathcal{R}_0 = \frac{\Lambda \kappa}{\mu(\mu + \epsilon + \gamma)}. \tag{2.10}$$

is the product of the population size at the disease-free equilibrium, the transmission coefficient, and the mean infective period. The number $\mathcal{R}_0$ acts as a threshold parameter in the familiar way.

When $\mathcal{R}_0 \le 1$, the disease free equilibrium is the only nonnegative equilibrium. Applying Proposition 2.2 from Thieme [10] to the first equation in (2.9) shows that the disease-free equilibrium is globally asymptotically stable when $\mathcal{R}_0 \le 1$. When $\mathcal{R}_0 > 1$, system (2.9) has a unique endemic equilibrium with $I_\epsilon > 0$ and $S_\epsilon = N_\epsilon - I_\epsilon - R_\epsilon = \Lambda/(\mu \mathcal{R}_0)$ from the first equation. Solving the second equation for N_ϵ and equating to $S_\epsilon - I_\epsilon - R_\epsilon$, gives the number of infectives at the endemic equilibrium as

$$I_\epsilon \left[\mu + \epsilon + \gamma \mu \int_0^\infty e^{-\mu a} g(a)\, da + \gamma \int_0^\infty e^{-\mu a} f(da) \right] = \Lambda(\mathcal{R}_0 - 1)/\mathcal{R}_0. \tag{2.11}$$

We focus on the endemic equilibrium, and our aim is to give sufficient conditions so that all solutions of (2.9) with $\mathcal{R}_0 > 1$ and having a positive number of initial infectives are attracted to this endemic equilibrium.

3. Reduction to a scalar integro-differential equation

Our strategy consists in transforming the system (2.9) into a scalar integro-differential equation for I and in proceeding as in [9]. In order to find N we integrate the second equation in (2.9) and obtain

$$N(t) = N_0 e^{-\mu t} + \frac{\Lambda}{\mu}(1 - e^{-\mu t}) - \epsilon \int_0^t I(t-s) e^{-\mu s} ds - \int_0^t M_R(s) e^{-\mu(t-s)} ds.$$

From the last equation in (2.9),

$$\begin{aligned}\int_0^t M_R(s)e^{-\mu(t-s)}ds &= \gamma\int_0^t\int_0^s I(s-a)e^{-\mu a}f(da)e^{-\mu(t-s)}ds \\ &\quad +\epsilon e^{-\mu t}\int_0^t V(s)ds.\end{aligned}$$

Thus by changing the order of integration

$$\begin{aligned}\int_0^t M_R(s)e^{-\mu(t-s)}ds - \epsilon e^{-\mu t}\int_0^t V(s)ds &= \gamma\int_0^t\int_a^t I(s-a)e^{-\mu(t-a-s)}dsf(da) \\ &= \gamma\int_0^t\int_0^{t-a} I(s)e^{-\mu(t-s)}dsf(da) \\ &= \gamma\int_0^t I(t-a)e^{-\mu a}f(a)da.\end{aligned}$$

The last equality follows from integration by parts, recall $f(0)=0$. Summarizing, we have

$$N(t) = \frac{\Lambda}{\mu} - \int_0^t I(t-s)e^{-\mu s}\left(\epsilon+\gamma f(s)\right)ds - e^{-\mu t}v(t)$$

with a bounded continuous function v.

We substitute this equation and the third equation of (2.9) into the first equation of (2.9):

$$I'(t) = -(\mu+\epsilon+\gamma)I(t) + \kappa I(t)\left(\frac{\Lambda}{\mu} - I(t) - e^{-\mu t}w(t) - \int_0^t I(t-s)P(s)ds\right)$$

with a bounded continuous function $w = v + u$ and

$$P(s) = e^{-\mu s}(\epsilon+\gamma f(s)+\gamma g(s)). \tag{3.1}$$

To bring this equation to the same form as equation (1.4) in [9], we introduce

$$I(t) = \frac{\Lambda}{\mu}x(t)$$

and obtain

$$x'(t) = -(\mu-\epsilon+\gamma)x(t) + \beta x(t)\left(1 - x(t) - e^{-\mu t}z(t) - \int_0^t x(t-s)P(s)ds\right) \tag{3.2}$$

with

$$\beta = \kappa\frac{\Lambda}{\mu}$$

and a bounded function $z(t)$.

We call the endemic equilibrium *globally asymptotically stable* if it is locally asymptotically stable and attracts all solutions of (3.2) with $x(0) > 0$. Here local asymptotic stability is formulated as in [9, Lemma 4.1]; see Sections 4, 5. Before we formulate our first global stability result, recall the definition of the Laplace transform of P, namely

$$\hat{P}(\lambda) = \int_0^\infty e^{-\lambda s}P(s)ds.$$

Proposition 3.1. *Let* $-\hat{P}'(0) < \infty$ *and*

$$1 + \Re\hat{P}(\imath\nu) > 0 \quad \forall \nu > 0.$$

Then the endemic equilibrium of (3.2), whenever it exists, is globally asymptotically stable.

Proof: It follows from [9, Theorem 2.1] that the endemic equilibrium attracts all solutions of (3.2) with $x(0) > 0$. Local asymptotic stability follows from [9, Lemma 4.1] and a similar continuation argument as in the proof of [2, Theorem 5.2]. □

Notice that this condition does not involve the parameter β (the parameters γ and ϵ are hidden in P), although $\beta > \mu+\epsilon+\gamma$ is needed for the endemic equilibrium to exist, see (2.10). This indicates that this condition may not be optimal. Stech and Williams [9, Theorem 3.1], show that it is sharp in the following sense. If $-\hat{P}'(0) < \infty$, and

$$1 + \Re\hat{P}(\imath\nu) < 0 \quad \exists \nu > 0,$$

then there exists some $\beta > 0$ such that the endemic equilibrium exists and is unstable.

By (3.1),

$$\hat{P}(\lambda) = \frac{\epsilon}{\lambda+\mu} + \gamma \int_0^\infty e^{-(\lambda-\mu)a}(f(a) + g(a))da.$$

Hence

$$-\hat{P}'(0) = \frac{\epsilon}{\mu^2} + \gamma \int_0^\infty e^{-\mu a} a(f(a) + g(a))da.$$

Since f and g take values between 0 and 1, the condition $-\hat{P}'(0) < \infty$ is satisfied, and so Proposition 3.1 translates into the following result.

Theorem 3.1. *Let the Assumptions 2.1 be satisfied and*

$$1 + \frac{\epsilon\mu}{\mu^2+\nu^2} + \gamma\Re\widehat{(f+g)}(\mu+\imath\nu) > 0 \quad \forall \nu > 0.$$

Then the endemic equilibrium of (2.9), whenever it exists, is globally asymptotically stable.

The following corollaries of the above result are useful for applications.

Corollary 3.1. *Let the Assumptions 2.1 be satisfied and*

$$\int_0^\infty e^{-\mu a}(f(a) + g(a))da \le \frac{1}{\gamma}.$$

Then the endemic equilibrium of (2.9), whenever it exists, attracts all solutions with $I(0) > 0$.

Corollary 3.2. *Let the Assumptions 2.1 be satisfied and the function* $f+g$ *be non-increasing and convex on* $[0, \infty)$. *Then the endemic equilibrium of (2.9), whenever it exists, attracts all solutions with* $I(0) > 0$.

Proof:

$$\Re\widehat{(f+g)}(\mu+\imath\nu) = \int_0^\infty (f-g)(s)e^{-\mu s}\cos(\nu s)ds.$$

Since the product of two non-negative, non-increasing, convex functions has the same properties, then

$$h(s) = (f-g)(s)e^{-\mu s}$$

is non-increasing and convex. Without restricting the generality, it can be assumed that h is differentiable. Otherwise it is possible to find a sequence of differentiable non-increasing convex functions h_j such that

$$\int_0^\infty |h_j(s) - h(s)ds|ds \to 0, \quad j \to \infty.$$

Integrating by parts,

$$\widehat{\Re(f+g)}(\mu+\imath\nu) = -\frac{1}{\nu}\int_0^\infty \sin(\nu s)h'(s)ds.$$

Since $-h'$ is non-negative and non-increasing, the last integral is non-negative as can see be seen by splitting up the integral into appropriate pieces and comparing them. □

4. Some general results

In this section we look at the general case that the sojourn in the removed class is arbitrarily distributed. At the endemic equilibrium, the stage age distribution of the removed class is given by (2.4),

$$\rho_e(a) = \gamma I_e \mathcal{F}(a).$$

The endemic equilibrium is called *locally stable* if for every $\eta > 0$ there exists a $\tilde{\eta} > 0$ such that, for any solution of (2.1)–(2.6)

$$|N(t) - N_e| + |I(t) - I_e| + \int_0^\infty |\rho(t,a) - \rho_e(a)|da < \eta \quad \forall t \geq 0$$

whenever

$$|N(0) - N_e| + |I(0) - I_e| + \int_0^\infty |\rho(0,a) - \rho_e(a)|da < \tilde{\eta}.$$

The endemic equilibrium is globally asymptotically stable if it is locally stable and attracts all solutions with $I(0) > 0$. This notion of global asymptotic stability is equivalent to the one used in the previous section.

From (2.7) and (2.8), since Q and $\mathcal{F}_R$ are monotone non-increasing,

$$\begin{aligned} f(a) - g(a) &= \mathcal{F}_R(a)Q(a) - \int_0^a Q(r)\mathcal{F}_R(dr) \\ &\geq \mathcal{F}_R(a)Q(a) - \int_0^a Q(a)\mathcal{F}_R(dr) \\ &= Q(a). \end{aligned}$$

From Corollary 3.1 we obtain the following result.

Theorem 4.1. *Assume that*

$$\int_0^\infty e^{-\mu a}Q(a)da \leq \frac{1}{\gamma}.$$

Then the endemic equilibrium, whenever it exists, is globally asymptotically stable.

Recall that

$$D_R = \int_0^\infty Q(a)da$$

is the average duration of the removed class, while $1/\gamma$ is the average duration of the infective class. Hence the endemic equilibrium attracts all nontrivial solutions

if the average duration of the removed class does not exceed the average duration of the infective class.

In order to apply Corollary 3.4, we integrate by parts and obtain

$$f(a) - g(a) = 1 + \int_0^a \mathcal{F}_R(r)Q(dr).$$

which shows that $f + g$ is non-increasing.

Theorem 4.2. *Let*

$$\int_0^a \mathcal{F}_R(r)Q(dr)$$

be a convex function of a. Then the endemic equilibrium of (2.9), whenever it exists, is globally asymptotically stable.

If Q is differentiable, then the condition in Theorem 4.2 is satisfied if Q' has a representative such that $\mathcal{F}_R(a)Q'(a)$ is a non-decreasing function of a. Since $\mathcal{F}_R$ is non-increasing and Q' is non-positive, it is sufficient that Q' is non-decreasing. If Q is convex, but not necessarily differentiable, a sequence Q_j of convex differentiable functions can be chosen such that

$$\int_0^a \mathcal{F}_R(r)Q(dr) = \lim_{j\to\infty} \int_0^a \mathcal{F}_R(r)Q_j(dr)$$

pointwise in a. By the preceding considerations the assumptions of Theorem 4.2 are satisfied if Q is convex.

Corollary 4.1. *Let Q be convex. Then the endemic equilibrium of (2.9), whenever it exists, is globally asymptotically stable.*

The conditions of Corollary 4.1 are satisfied, for example, if the length of the removed period is exponentially distributed. In particular, the endemic equilibrium attracts all nontrivial disease dynamics if the disease induces permanent immunity ($Q \equiv 1$) even if disease-related deaths are arbitrarily distributed over the removed class. This includes a model with a chain of exponentially distributed removed stages with no return to the susceptible class.

5. One primary and several secondary exponentially distributed removed stages

We now consider a cyclic model of

$$\begin{array}{ccccccc} & & & \nearrow & R_1 & \searrow & \\ \rightarrow S & \rightarrow I & \rightarrow R_0 & \rightarrow & \vdots & \rightarrow & S \\ & & & \searrow & R_n & \nearrow & \end{array}$$

type where a removed individual first enters a primary removed stage where it is still prone to disease-related death and later one of several secondary removed stages where it is safe from disease-related death. The various secondary stages may have different durations: in particular it is possible that there is a stage where permanent immunity is acquired, but individuals in other secondary stages lose immunity and return to the susceptible class. The primary removed stage could be a quarantine period where the individual is still infective, but prevented from transmitting the disease. The total population size N splits into

$$N = S - I - R, \quad \text{with} \quad R = R_0 - R_1 - \cdots - R_n. \tag{5.1}$$

where $R_0, \ldots, R_n$ are the number of individuals in the various stages of the removed class. In terms of $S, I, R_0, \ldots, R_n$ the model takes the following form:

$$\begin{aligned} S' &= \Lambda - \mu S - \kappa SI + \sigma_1 R_1 + \cdots + \sigma_n R_n. \\ I' &= \kappa SI - (\mu + \epsilon + \gamma)I. \\ R_0' &= \gamma I - (\mu + \delta + \rho)R_0. \qquad \rho = \rho_1 + \cdots + \rho_n. \\ R_j' &= \rho_j R_0 - (\mu + \sigma_j)R_j. \quad j = 1, \ldots, n. \end{aligned} \tag{5.2}$$

Here $1/\rho$ and $1/\sigma_j$ are the mean durations of the primary removed stage and of the secondary removed stages: the jth secondary removed stage is associated with permanent immunity if $\sigma_j = 0$. The extra *per capita* mortality rate constant in the primary removed stage due to the disease is denoted by δ.

For this o.d.e. system, local stability of the endemic equilibrium is defined in the usual sense, and its global asymptotic stability means that it is locally stable and attracts all solutions with $I(0) > 0$. It is possible, but cumbersome to rewrite this model in the form of Section 2, in particular to determine $\mathcal{F}_{\mathcal{R}}$. This is why we determine the functions f and g instead.

Adding the differential equations in (5.2) yields

$$N' = \Lambda - \mu N - \epsilon I - \delta R_0. \tag{5.3}$$

Set

$$g_0(a) = e^{-(\delta+\rho)a}.$$

Then

$$R_0(t) = R_0(0)e^{-\mu t}g_0(t) + \gamma \int_0^t I(t-s)e^{-\mu s}g_0(s)ds.$$

We identify from (5.3) and the last equation in (2.9) that

$$f(a) = \frac{\delta}{\delta + \rho}(1 - g_0(t)). \tag{5.4}$$

Set

$$g_j(t) = \rho_j e^{-\sigma_j t}. \quad j = 1, \ldots, n. \tag{5.5}$$

For convenience we recall the convolution notation

$$(g_0 * g_j)(t) = \int_0^t g_0(s)g_j(t-s)ds.$$

Solving the differential equations for R_j, $j = 1, \ldots, n$, we obtain

$$R_j(t) = \frac{R_j(0)}{\rho_j}e^{-\mu t}g_j(t) + R_0(0)e^{-\mu t}(g_0 * g_j)(t) + \gamma \int_0^t I(t-s)e^{-\mu s}(g_0 * g_j)(s)ds.$$

Since $R = R_0 + \cdots + R_n$ we identify from the third equation in (2.9) that

$$g(a) = (g_0 + g_0 * (g_1 + \cdots + g_n))(a).$$

By (5.4),

$$\begin{aligned} f(a) + g(a) &= \frac{\delta}{\delta + \rho}(1 - g_0(a)) + g_0(a) + \left(g_0 * \left(\sum_{j=1}^n g_j\right)\right)(a) \\ &= \frac{\delta}{\delta + \rho} + \frac{\rho}{\delta + \rho}g_0(a) + \left(g_0 * \left(\sum_{j=1}^n g_j\right)\right)(a). \end{aligned}$$

By (5.5) and the convolution theorem for Laplace transforms,

$$\begin{aligned}\widehat{(f+g)}(\mu+\imath\nu) &= \frac{\delta}{\delta+\rho}\frac{1}{\mu+\imath\nu}+\frac{\rho}{\delta-\rho}frac1\mu+\imath\nu+\delta+\rho \\ &\quad +\frac{1}{\mu+\imath\nu+\delta+\rho}\left(\sum_{j=1}^{n}\frac{\rho_j}{\mu+\imath\nu+\sigma_j}\right).\end{aligned}$$

Multiplying by conjugates,

$$\begin{aligned}\widehat{(f+g)}(\mu+\imath\nu) &= \frac{\delta}{\delta+\rho}\frac{\mu-\imath\nu}{\mu^2+\nu^2}+\frac{\rho}{\delta+\rho}\frac{\mu+\delta+\rho-\imath\nu}{(\mu+\delta+\rho)^2+\nu^2} \\ &\quad +\frac{\mu+\delta+\rho-\imath\nu}{(\mu+\delta+\rho)^2+\nu^2}\left(\sum_{j=1}^{n}\rho_j\frac{\mu+\sigma_j-\imath\nu}{(\mu+\sigma_j)^2+\nu^2}\right).\end{aligned}$$

Taking real parts,

$$\begin{aligned}&\Re\widehat{(f+g)}\ (\mu+\imath\nu) \\ &= \frac{\delta}{\delta+\rho}\frac{\mu}{\mu^2+\nu^2}+\frac{\rho}{\delta+\rho}\frac{\mu+\delta+\rho}{(\mu+\delta+\rho)^2+\nu^2} \\ &\quad +\frac{\mu+\delta+\rho}{(\mu+\delta+\rho)^2+\nu^2}\left(\sum_{j=1}^{n}\rho_j\frac{\mu+\sigma_j}{(\mu+\sigma_j)^2+\nu^2}\right) \\ &\quad -\frac{\nu}{(\mu+\delta+\rho)^2+\nu^2}\left(\sum_{j=1}^{n}\rho_j\frac{\nu}{(\mu+\sigma_j)^2+\nu^2}\right) \\ &\geq \frac{1}{(\mu+\delta+\rho)^2+\nu^2}\left(\rho\frac{\mu+\delta-\rho}{\delta+\rho}-\left(\sum_{j=1}^{n}\rho_j\frac{\nu^2}{(\mu+\sigma_j)^2+\nu^2}\right)\right).\end{aligned}$$

Recalling that ρ is the sum of the ρ_j, $\Re\widehat{(f+g)}(\mu-\imath\nu)\geq 0$, and Theorem 3.1 gives the following result.

Theorem 5.1. *The endemic equilibrium of model (5.2), whenever it exists, is globally asymptotically stable.*

The SIRS formulated by Anderson and May [1] and analyzed by Mena-Lorca and Hethcote [6] as described in the Introduction is easily seen as a limiting case of the model of this section (with the mean durations of all secondary removed stages being 0). There is a unique removed stage with no disease mortality, thus stages $R_1,\cdots,R_n$ are absent, $\sum_{j=1}^{n}\sigma_jR_j$ is replaced by ρR_0 where ρ is the loss of immunity rate constant, and $\delta=0$. The endemic equilibrium is then given by

$$(S_e, I_e, R_{0e}) = (\Lambda/(\mu\mathcal{R}_0),\ I_e,\ \cdot I_e/(\mu+\rho))$$

where $\mathcal{R}_0$ is defined in (2.10) and

$$I_e = \frac{\Lambda-\mu S_e}{\epsilon+\mu(1+\cdot/(\mu-\rho))}$$

from (2.11). Theorem 5.1 shows that if $\mathcal{R}_0>1$, then this endemic equilibrium is globally asymptotically stable. This completes the global stability analysis of the endemic equilibrium in Mena-Lorca and Hethcote [6, Section 2].

6. Three subsequent removed stages with the last being permanent

In this section we consider a model of

$$\begin{array}{ccccccc} & & & & & \nearrow & R_2 \\ \rightarrow & S & \rightarrow & I & \rightarrow & R_0 \rightarrow R_1 & \\ & & & & & \searrow & S \end{array}$$

type where some removed individuals return into the susceptible class, but others become permanently immune. The total population size N splits into

$$N = S + I + R, \quad \text{with} \quad R = R_0 + R_1 + R_2, \tag{6.1}$$

where R_0, R_1, R_2 are the number of individuals in the various stages of the removed class. In these terms, the model takes the following form:

$$\begin{aligned} S' &= \Lambda - \mu S - \kappa SI + \sigma_1 R_1, \\ I' &= \kappa SI - (\mu + \epsilon + \gamma)I, \\ R_0' &= \gamma I - (\mu + \delta_0 + \rho_0)R_0, \\ R_1' &= \rho_0 R_0 - (\mu + \delta_1 + \rho_1 + \sigma_1)R_1, \\ R_2' &= \rho_1 R_1 - (\mu + \delta_2)R_2. \end{aligned} \tag{6.2}$$

The parameters $\delta_j \geq 0$ are the extra *per capita* mortality rate constants in the jth removed stage, $1/\rho_j$ are the mean durations in the jth removed stage, and σ_1 is the return rate constant into the susceptible class. We define

$$g_0(s) = e^{-(\delta_0+\rho_0)s}, \quad g_1(s) = \rho_0 e^{-(\delta_1+\rho_1+\sigma_1)s}, \quad g_2(s) = \rho_1 e^{-\delta_2 s}.$$

Integration of the equations in (6.2) and comparison with (2.9) yields

$$g = g_0 - g_0 * g_1 + g_0 * g_1 * g_2$$

and

$$f'(s) = \delta_0 g_0(s) - \delta_1 (g_0 * g_1)(s) + \delta_2 (g_0 * g_1 * g_2)(s).$$

Now

$$g'(s) = -\delta_0 g_0(s) - (\delta_1 - \sigma_1)(g_0 * g_1)(s) - \delta_2 (g_0 * g_1 * g_2)(s).$$

Hence

$$f'(s) - g'(s) = -\sigma_1 (g_0 * g_1)(s).$$

This implies that

$$f(s) + g(s) = 1 - \sigma_1 \int_0^s (g_0 * g_1)(s) ds.$$

By the convolution theorem for the Laplace transform,

$$\widehat{(f-g)}(\mu + \imath\nu) = \frac{1}{\mu - \imath\nu}(1 - \alpha)$$

with

$$\alpha = \frac{\sigma_1}{\delta_0 + \rho_0 + \mu + \imath\nu} \frac{\rho_0}{\delta_1 + \rho_1 + \sigma_1 + \mu + \imath\nu}.$$

Thus $\Re\widehat{(f+g)}(\mu + \imath\nu) \geq 0$ if

$$1 - \Re\alpha \geq 0, \quad \Im\alpha \leq 0.$$

Now

$$\alpha = \sigma_1 \rho_0 \frac{\delta_0 + \rho_0 + \mu - \imath\nu}{(\delta_0 + \rho_0 + \mu)^2 + \nu^2} \frac{\delta_1 + \rho_1 + \sigma_1 + \mu - \imath\nu}{(\delta_1 + \rho_1 + \sigma_1 + \mu)^2 + \nu^2}.$$

Obviously $\Im\alpha \leq 0$. Further

$$\begin{aligned}\Re\alpha &= \sigma_1\rho_0\frac{(\delta_0+\rho_0+\mu)(\delta_1-\rho_1+\sigma_1+\mu)-\nu^2}{[(\delta_0+\rho_0+\mu)^2+\nu^2][(\delta_1-\rho_1-\sigma_1-\mu)^2-\nu^2]}\\ &\leq \rho_0\frac{(\delta_0+\rho_0-\mu)(\delta_1+\rho_1-\sigma_1-\mu)}{(\delta_0+\rho_0+\mu)^2(\delta_1+\rho_1+\sigma_1-\mu)}\\ &\leq 1.\end{aligned}$$

From Theorem 3.1 we obtain the following result.

Theorem 6.1. *Whenever the endemic equilibrium of (6.2) exists, it is globally asymptotically stable.*

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