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GLOBAL STABILITY OF AN SIS EPIDEMIC MODEL WITH A FINITE INFECTIOUS PERIOD

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Abstract. Assuming a general distribution for the sojourn time in the infectious class, we consider an SIS type epidemic model formulated as a scalar integral equation. We prove that the endemic equilibrium of the model is globally asymptotically stable whenever it exists, solving the conjecture of Hethcote and van den Driessche (1995) for the case of nonfatal diseases.

1. Introduction

In the paper [7], Hethcote and van den Driessche formulate an SIS type epidemic model and analyze its qualitative properties. The model has a disease related death rate, which affects the size of the total population. The sojourn time of the infectious states is assumed to follow a general probability density function, though the authors elaborate the case of a constant infectious period. In Theorem 5.1 in the paper [7], the authors show that the endemic equilibrium is asymptotically stable when the disease related death rate is zero and subsequently mention global stability of the endemic equilibrium as an open problem. See also [8] for a study of a similar SIS epidemic model, where the assumed population demography is different from [7].

The problem of global stability does not seem to be fully solved up to now. In the recent paper [9] the authors analyze monotonicity of the semiflow induced by the model proposed in [7]. It is shown that the solution semiflow is monotone with respect to the initial function when a key parameter, namely the basic reproduction number R_0, is greater than two. Then the author of

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[10] proves that many solutions, but not all solutions, converge to the stable endemic equilibrium if $R_0 > 2$. In those papers, to derive those results, a constant infectious period is assumed in the model. Note that in [9, 10] the long time behavior of the solutions for $1 < R_0 \leq 2$ is not studied even for the case of constant delay.

The aim of this paper is to prove that the endemic equilibrium is indeed globally asymptotically stable for the epidemic model proposed by Hethcote and van den Driessche in [7, 8] for the case of nonfatal diseases. We prove that all positive solutions tend to the endemic equilibrium if $R_0 > 1$, thus the endemic equilibrium is *always* globally asymptotically stable. Our proof allows any probability function which the sojourn time of the infectious state follows.

This paper is organized as follows. In Section 2, we introduce an SIS epidemic model, corresponding to the model considered in [7, 8] for the case of nonfatal diseases. The model is formulated as a scalar integral equation describing time evolution of the infectious population. In Section 3, we prove global stability of the disease free equilibrium. In Section 4, we show that the endemic equilibrium is asymptotically stable analyzing the corresponding characteristic equation. Here, an elementary proof for persistence of the solution is also given. We then prove global attractivity of the endemic equilibrium. In Section 5, we discuss our results.

2. Endemic model

Following [7], we introduce the SIS epidemic model of which we analyze its global dynamics. Denote by $\mathcal{F}(a)$ the probability that infective individuals are infective up to infection-age a (time elapsed since infection). From the biological interpretation, $\mathcal{F} : [0, h] \to [0, 1]$ is nonincreasing with

$$\mathcal{F}(0) = 1, \quad \mathcal{F}(h) = 0,$$

where $h < \infty$ is the maximum infectious period. Without loss of generality we assume that $\mathcal{F}(a) > 0$ for $0 < a < h$.

Let $S(t)$ and $I(t)$ be the proportions of the susceptible population and the infective population at time t, respectively, so that

$$1 = S(t) + I(t), \tag{2.1}$$

holds for any t. The density of infective individuals at time t with respect to infection-age a is given as

$$i(t, a) = \beta S(t - a) I(t - a) \mathcal{F}(a) e^{-\mu a}, \tag{2.2}$$

where μ is the natural mortality rate and β is the constant transmission coefficient. Note that the density of newly infective individuals appearing in the host population at time t is

$$i(t,0) = \beta S(t)I(t).$$

Integrating both sides of (2.2) we obtain the following renewal equation

$$I(t) = \beta \int_0^h S(t-a)I(t-a)\mathcal{F}(a)e^{-\mu a}da, \tag{2.3}$$

see also the integral equation (2.2) in [7].

We scale the time so that the maximum infectious period becomes 1 and then subsequently we recall that (2.1) holds for $t \geq -1$ (so $I(t) \leq 1$ for $t \geq -1$). Then we get a scalar renewal equation for the proportion of infective population:

$$I(t) = \beta \int_0^1 (1 - I(t-a))\, I(t-a)\mathcal{F}(a)e^{-\mu a}da, \tag{2.4}$$

from (2.3). Since $\mathcal{F}$ is a monotone function, $\mathcal{F}$ is a bounded variation function such that

$$-\int_0^1 d\mathcal{F}(a) = \mathcal{F}(0) - \mathcal{F}(1) = 1,$$

holds. The proportion of individuals who obtain susceptibility per unit time at time t is given as

$$-\beta \int_0^1 S(t-a)I(t-a)e^{-\mu a}d\mathcal{F}(a),$$

where the integral is Riemann-Stieljes integral. Differentiating the equation (2.4) one also obtains the following delay differential equation

$$\frac{d}{dt}I(t) = \beta(1-I(t))I(t) + \beta \int_0^1 (1-I(t-a))I(t-a)e^{-\mu a}d\mathcal{F}(a) - \mu I(t). \tag{2.5}$$

Equations (2.4) and (2.5) with

$$\mathcal{F}(a) = \begin{cases} 1, & 0 \leq a < 1 \\ 0, & a = 1, \end{cases} \tag{2.6}$$

can be found in [7, 8] for the case of no disease induced death rate.

Denote by $C([-1,0],\mathbb{R})$ the Banach space of continuous functions mapping the interval $[-1,0]$ into $\mathbb{R}$ equipped with the sup-norm. The initial function

is chosen from the subset of continuous functions:

$$Y := \{\phi \in C([-1,0],[0,1]) \,|\phi(0) = G(\phi)\},$$

where $G : C([-1,0],[0,1]) \to \mathbb{R}$ is defined as

$$G(\phi) := \beta \int_0^1 (1-\phi(-a))\,\phi(-a)\mathcal{F}(a)e^{-\mu a}da.$$

The initial function for (2.4), and for (2.5), is given as

$$I(\theta) = \psi(\theta),\ \theta \in [-1,0], \tag{2.7}$$

with $\psi \in Y$. We introduce a standard notation $I_t : [-1,0] \to \mathbb{R}_+$ defined via the relation

$$I_t(\theta) = I(t+\theta) \ \text{ for } \theta \in [-1,0].$$

It is straightforward to see that the set Y is forward invariant under the semiflow induced by (2.4) with the initial condition (2.7) i.e., $I_t \in Y,\ t > 0$.

3. Global stability of the disease free equilibrium

The basic reproduction number is easily computed as

$$R_0 = \beta \int_0^1 \mathcal{F}(a)e^{-\mu a}da.$$

We here prove global stability of the disease free equilibrium when $R_0 \le 1$ holds, by using similar ideas as in the proof of Theorem 4.2 in [7] for the case that $\mathcal{F}$ is given by (2.6).

Theorem 1. *Let us assume that $R_0 \le 1$ holds. Then the disease free equilibrium is globally asymptotically stable in Y.*

Proof. Consider a sequence $\{M_n\}_{n=0}^{\infty}$ determined by

$$M_n = R_0 M_{n-1}(1 - M_{n-1}),$$

with $M_0 = \frac{1}{4}$. It holds that M_n monotonically decreases and that

$$\lim_{n\to\infty} M_n = 0,$$

if $R_0 \le 1$ holds. From the equation (2.4), we have

$$I(t) \le \frac{1}{4}R_0 \le \frac{1}{4}, \quad t \in [0,1].$$

One can see that $I(t) \le M_n,\ t \in [n, n+1]$, thus, we get $\lim_{t\to\infty} I(t) = 0$. Stability of the disease free equilibrium follows from the estimation above. □

4. Global stability of the endemic equilibrium

An endemic equilibrium emerges if $R_0 > 1$ holds. In Theorem 5.1 in [7] the endemic equilibrium is shown to be asymptotically stable when $\mathcal{F}$ is given by (2.6), see also Theorem 4 in [8]. In the following proposition we show that the endemic equilibrium is asymptotically stable for any $\mathcal{F}$.

Let us write $\hat{p}$ to denote the constant function in Y satisfying $\hat{p}(\theta) = p$ for $\theta \in [-1, 0]$. We then define $Y_+ := Y \setminus \left\{\hat{0}\right\}$. In the following, to generate a positive solution, we assume $\psi \in Y_+$.

Proposition 2. *Let us assume that $R_0 > 1$ holds. There exists a unique endemic equilibrium $\hat{I^*} \in Y_+$, where*

$$I^* = 1 - \frac{1}{R_0}. \tag{4.1}$$

The endemic equilibrium is asymptotically stable.

Proof. Let $R_0 > 1$ hold. The endemic equilibrium satisfies the following equation:

$$1 = (1 - I)\,\beta \int_0^1 \mathcal{F}(a) e^{-\mu a} da = R_0\,(1 - I)\,,$$

so we get (4.1).

We apply the principle of linearized stability established in [1] for Volterra functional equations. The Fréchet derivative of $G : C\left([-1, 0], [0, 1]\right) \to \mathbb{R}$ evaluated at the endemic equilibrium $\hat{I^*} \in Y_+$ can be computed as

$$DG(\hat{I^*})\phi = (1 - 2I^*)\,\beta \int_0^1 \phi(-a)\mathcal{F}(a) e^{-\mu a} da.$$

Thus, the characteristic equation is

$$1 = (1 - 2I^*)\,\beta \int_0^1 e^{-\lambda a}\mathcal{F}(a) e^{-\mu a} da,\ \lambda \in \mathbb{C}. \tag{4.2}$$

Denote

$$\tilde{\mathcal{F}}(a) = \mathcal{F}(a) e^{-\mu a}.$$

Using the partial integration

$$\int_0^1 e^{-\lambda a}\tilde{\mathcal{F}}(a) da = \frac{1}{\lambda}\Big(1 + \int_0^1 e^{-\lambda a} d\tilde{\mathcal{F}}(a)\Big),$$

one can deduce a priori bounds for the roots of the characteristic equation. We now show that the real part of all roots of (4.2) is negative. First, it can be easily seen that the characteristic equation (4.2) does not have a root with

positive real part for small $I^* > 0$. Suppose that there exists a root $\lambda = i\omega$ with $\omega > 0$. We get the following two equations

$$1 = (1 - 2I^*)\,\beta \int_0^1 \tilde{\mathcal{F}}(a)\cos(\omega a)\,da. \tag{4.3a}$$

$$0 = \int_0^1 \tilde{\mathcal{F}}(a)\sin(\omega a)\,da. \tag{4.3b}$$

Integrating by parts we have

$$\begin{aligned} 0 &= \int_0^1 \tilde{\mathcal{F}}(a)\sin(\omega a)da = \frac{1}{\omega}\Big(\Big[-\tilde{\mathcal{F}}(a)\cos(\omega a)\Big]_0^1 + \int_0^1 \cos(\omega a)d\tilde{\mathcal{F}}(a)\Big) \\ &= \frac{1}{\omega}\Big(1 + \int_0^1 \cos(\omega a)d\tilde{\mathcal{F}}(a)\Big), \end{aligned}$$

thus,

$$\int_0^1 \cos(\omega a)\,d\tilde{\mathcal{F}}(a) = -1,$$

follows. Noting that

$$\Big(\int_0^1 \cos(\omega a)\,d\tilde{\mathcal{F}}(a)\Big)^2 + \Big(\int_0^1 \sin(\omega a)\,d\tilde{\mathcal{F}}(a)\Big)^2 \le 1,$$

holds, we see

$$\int_0^1 \sin(\omega a)\,d\tilde{\mathcal{F}}(a) = 0,$$

holds. Since one has that

$$\begin{aligned} \int_0^1 \tilde{\mathcal{F}}(a)\cos(\omega a)\,da &= \frac{1}{\omega}\Big(\Big[\tilde{\mathcal{F}}(a)\sin(\omega a)\Big]_0^1 - \int_0^1 \sin(\omega a)\,d\tilde{\mathcal{F}}(a)\Big) \\ &= -\frac{1}{\omega}\int_0^1 \sin(\omega a)\,d\tilde{\mathcal{F}}(a), \end{aligned}$$

we finally obtain

$$\int_0^1 \tilde{\mathcal{F}}(a)\cos(\omega a)\,da = 0.$$

Therefore, we get a contradiction to the equality in (4.3a). Consequently, in the complex plane the characteristic roots do not cross the imaginary axis. □

Next, we show persistence of the solution when $R_0 > 1$.

Proposition 3. *Let $R_0 > 1$ holds. Then*

$$\liminf_{t\to\infty} I(t) > 0.$$

Proof. We can choose a $q \in (0,1)$ such that $qR_0 > 1$ holds. Assume that there is a solution with $\psi(0) > 0$ such that $\lim_{t\to\infty} I(t) = 0$. Then there is a T such that for $t > T$, $I(t) < \frac{1}{2}$ and $1 - I(t) > q$ hold. There is a sequence

$$t_n \to \infty \quad (n \to \infty),$$

such that

$$I(t_n) = \min\{I(t) : t \in [t_n - 1, t_n]\},$$

and $\lim_{n\to\infty} I(t_n) = 0$. Then, for $t_n > T + 1$, we have

$$I(t_n) = \beta \int_0^1 I(t_n - a)(1 - I(t_n - a))\mathcal{F}(a)e^{-\mu a}da,$$

and from the monotonicity of the quadratic map $x \mapsto x(1-x)$ on $[0, \frac{1}{2}]$, we obtain

$$I(t_n) \geq \beta \int_0^1 I(t_n)(1 - I(t_n))\mathcal{F}(a)e^{-\mu a}da = R_0 I(t_n)(1 - I(t_n)).$$

Since we have $1 - I(t_n) > q$, dividing by $I(t_n)$, we find the contradiction $1 > qR_0$. □

We now introduce the notations

$$\underline{I} = \liminf_{t\to\infty} I(t), \quad \overline{I} = \limsup_{t\to\infty} I(t).$$

From Proposition 3, one can easily see that $0 < \underline{I} \leq \overline{I} \leq 1$. The proof for the global attractivity of the endemic equilibrium is divided into two cases: $1 < R_0 \leq 2$ and $2 < R_0$. Using the monotonicity of the quadratic map $x \mapsto x(1-x)$ on the two intervals $\left[0, \frac{1}{2}\right]$ and $\left[\frac{1}{2}, 1\right]$ for the two cases respectively, we show that $\underline{I} = \overline{I} = I^*$ holds.

First, let us assume that $1 < R_0 \leq 2$ holds. We define the subspace

$$Y_1 := \left\{\phi \in Y : 0 \leq \phi(\theta) \leq \frac{1}{2},\ \theta \in [-1, 0]\right\},$$

and first prove that Y_1 attracts all positive solutions.

Lemma 4. *Let us assume that $1 < R_0 \leq 2$. Then $I(t) \leq \frac{1}{2}$, $t \geq 0$. thus, $I_t \in Y_1$, $t > 1$ for any $\psi \in Y_+$.*

Proof. Since $(1-x)x \leq \frac{1}{4}$ for $x \in [0,1]$, we can estimate the equation (2.4) as $I(t) \leq \frac{1}{4}R_0 \leq \frac{1}{2}$. Then solution $I_t,\ t>1$ satisfies

$$0 \leq I_t(\theta) = I(t+\theta) \leq \frac{1}{2}$$

for $\theta \in [-1,0]$. □

It is easy to see that $I^* = 1 - \frac{1}{R_0} \leq \frac{1}{2}$, when $1 < R_0 \leq 2$ holds. To show global attractivity, we use the monotonicity of the quadratic function:

$$0 \leq x \leq y \leq \frac{1}{2} \to (1-x)x \leq (1-y)y.$$

Proposition 5. *Let us assume that* $1 < R_0 \leq 2$. *Then*

$$\lim_{t\to\infty} I(t) = I^* \quad \textit{for any } \psi \in Y_+.$$

Proof. From Proposition 3 and Lemma 4, it holds that $0 < \underline{I} \leq \overline{I} \leq \frac{1}{2}$. It then holds that

$$\underline{I} \geq G(\hat{\underline{I}}) = R_0 \underline{I}\,(1-\underline{I})\,,$$

while

$$\overline{I} \leq G(\hat{\overline{I}}) = R_0 \overline{I}\,\left(1-\overline{I}\right).$$

Therefore, we get the following inequality

$$R_0\,(1-\underline{I}) \leq 1 \leq R_0\left(1-\overline{I}\right),$$

which implies $\overline{I} = \underline{I} = I^* = 1 - \frac{1}{R_0}$. □

Next, we assume that $R_0 > 2$ holds. It will be shown that all positive solutions are attracted to the set

$$Y_2 = \left\{\phi \in Y : \frac{1}{2} \leq \phi(\theta) \leq 1,\ \theta \in [-1,0]\right\}.$$

In Iggidr et al. [9], it is shown that Y_2 is an invariant set and that the semiflow is monotone in Y_2 when $\mathcal{F}$ is the step function (2.6).

Lemma 6. *Let us assume that* $R_0 > 2$ *holds. For any* $\psi \in Y_+$ *there exists* τ *such that* $I_t \in Y_2$, $t > \tau$.

Proof. First let us show that there exists no solution that is bounded by $\frac{1}{2}$ from above. To derive a contradiction, suppose that there exists a solution such that $I(t) \leq \frac{1}{2}$ for any $t \geq 0$. Then

$$0 < \underline{I} \leq \overline{I} \leq \frac{1}{2}, \tag{4.4}$$

holds. From (2.4) one sees that $\underline{I} \geq G(\hat{\underline{I}}) = R_0\underline{I}(1-\underline{I})$, which implies $\underline{I} \geq I^* = 1 - \frac{1}{R_0} > \frac{1}{2}$. Thus, we obtain a contradiction to (4.4), so the solution can not stay in Y_1 and leaves the set Y_1 eventually. Now consider a solution that oscillates about $\frac{1}{2}$. We show that the solution never returns to the set Y_1 once it crosses $\frac{1}{2}$. To see this we compute the differentiation of $I(t)$ when $I(t) = \frac{1}{2}$ holds. From (2.5), we get

$$\begin{aligned} I'(t) &= \beta\,(1-I(t))\,I(t) + \beta\int_0^1 (1-I(t-a))\,I(t-a)e^{-\mu a}d\mathcal{F}(a) - \mu I(t) \\ &= \frac{1}{4}\beta + \beta\int_0^1 (1-I(t-a))\,I(t-a)e^{-\mu a}d\mathcal{F}(a) - \frac{1}{2}\mu. \end{aligned}$$

Since for any nonnegative solutions it holds that

$$\int_0^1 (1-I(t-a))\,I(t-a)e^{-\mu a}d\mathcal{F}(a) \geq \frac{1}{4}\int_0^1 e^{-\mu a}d\mathcal{F}(a),$$

it follows

$$\begin{aligned} I'(t) &\geq \frac{1}{4}\beta + \frac{1}{4}\beta\int_0^1 e^{-\mu a}d\mathcal{F}(a) - \frac{1}{2}\mu \\ &= \frac{1}{2}\mu\Big\{\frac{1}{2}\frac{\beta}{\mu}\Big(1+\int_0^1 e^{-\mu a}d\mathcal{F}(a)\Big) - 1\Big\}. \end{aligned}$$

Since

$$\frac{\beta}{\mu}\Big(1+\int_0^1 e^{-\mu a}d\mathcal{F}(a)\Big) = \beta\int_0^1 e^{-\mu a}\mathcal{F}(a)da = R_0,$$

holds, we obtain

$$I'(t) \geq \frac{1}{2}\mu\Big(\frac{1}{2}R_0 - 1\Big) > 0,$$

which implies that if the solution once crosses $\frac{1}{2}$ then it is bounded below from $\frac{1}{2}$. □

Proposition 7. *Let us assume that $R_0 > 2$ holds. Then*

$$\lim_{t\to\infty} I(t) = I^* \quad \textit{for any } \psi \in Y_+.$$

Proof. From Lemma 6 it is sufficient to consider a solution in Y_2. Consider a sequence $\{p_n\}_{n=1}^{\infty}$ such that $I(p_n) \to \underline{I}$ as $n \to \infty$. We apply the fluctuation lemma to the equation (2.5) to get

$$0 = \beta(1-\underline{I})\underline{I} + \beta\lim_{n\to\infty}\int_0^1 (1-I(p_n-a))\,I(p_n-a)e^{-\mu a}d\mathcal{F}(a) - \mu\underline{I}$$

$$\geq \beta(1-\underline{I})\underline{I} + \beta(1-\underline{I})\underline{I}\int_0^1 e^{-\mu a}d\mathcal{F}(a) - \mu\underline{I}$$
$$= \mu\underline{I}\Big\{\frac{\beta}{\mu}\Big(1+\int_0^1 e^{-\mu a}d\mathcal{F}(a)\Big)(1-\underline{I}) - 1\Big\}.$$

From Proposition 3, we have $\underline{I} > 0$. Thus, $0 \geq R_0(1-\underline{I}) - 1$, which implies that $\underline{I} \geq I^*$. Similarly we can apply the fluctuation lemma for the sequence of a solution tending to $\overline{I}$. Then we obtain $\overline{I} \leq I^*$. Consequently, $\underline{I} \geq I^* \geq \overline{I}$ holds and we obtain the conclusion. □

Finally, we obtain the following result, combining the results of global attractivity of the endemic equilibrium established in Propositions 5 and 7 with local stability shown in Proposition 2.

Theorem 8. *Let us assume that $R_0 > 1$ holds. The endemic equilibrium is globally asymptotically stable in Y_+.*

5. Discussion

In the paper [7], Hethcote and van den Driessche propose an SIS type epidemic model with disease induced death rate. The model developed in [7] allows a general description for the distribution of the infectious period among individuals. To proceed the mathematical analysis it is then specified as a step function (2.6), implying that for every infective individual the infectious period is exactly same. The authors in [7] study stability of the disease free equilibrium and the endemic equilibrium. In Theorem 5.1 in [7], it is shown that the endemic equilibrium is asymptotically stable if there is no disease induced death rate. We solve the open problem mentioned in the paper: the endemic equilibrium is *globally* asymptotically stable if there is no disease induced death rate. Moreover, the global stability holds for the model with any distribution of the infectious period. The equation (2.4) is also derived from the model considered in [8] for the case of nonfatal diseases. In the first model considered in [8] the authors assume constant recruitment for the total population, differently from the model in [7].

In the paper [5], Gripenberg studied a similar integral equation describing disease transmission dynamics motivated by the study in [3]. Conditions for global attractivity of the equilibria are obtained. It involves technical conditions concerning kernels denoting variable infectivity and distribution for the sojourn period. The model considered in [3] is also an SIS type epidemic model, where individual's infectivity varies according to the progression of the infection-age (the time elapsed since the infection). The authors in [3]

deduce a characteristic equation for an endemic equilibrium and show that destabilization of the endemic equilibrium is possible. In those papers [3, 5], the integral equation is formulated in terms of newly infectives per unit time at time t.

Here, we assume that the maximum infectious period is finite. The assumption facilitates our analysis as we have the equation with *finite* delay [1]. The global stability results would be extended to the case that the maximum infectious period is infinite i.e., $h = \infty$, using the fading memory space [2, 6], see also [4, 11] for the treatment of such cases in epidemiological models.

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