

## A NOTE ON GLOBAL STABILITY FOR MALARIA INFECTIONS MODEL WITH LATENCIES

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**ABSTRACT.** A recent paper [Y. Xiao and X. Zou, *On latencies in malaria infections and their impact on the disease dynamics*, Math. Biosci. Eng., 10(2) 2013, 463-481.] presented a mathematical model to investigate the spread of malaria. The model is obtained by modifying the classic Ross-Macdonald model by incorporating latencies both for human beings and female mosquitoes. It is realistic to consider the new model with latencies differing from individuals to individuals. However, the analysis in that paper did not resolve the global malaria disease dynamics when  $\mathfrak{R}_0 > 1$ . The authors just showed global stability of endemic equilibrium for two specific probability functions: exponential functions and step functions. Here, we show that if there is no recovery, the endemic equilibrium is globally stable for  $\mathfrak{R}_0 > 1$  without other additional conditions. The approach used here, is to use a direct Lyapunov functional and Lyapunov- LaSalle invariance principle.

**1. Introduction.** In this note, we consider a mathematical model for spread of malaria:

$$\begin{aligned} S_1'(t) &= d_1 - ae_1mS_1(t)I_2(t) - d_1S_1(t), \\ I_1'(t) &= - \int_0^t ae_1mS_1(\xi)I_2(\xi)e^{-d_1(t-\xi)}D_tP_1(t-\xi)d\xi - d_1I_1(t), \\ S_2'(t) &= d_2 - ae_2S_2(t)I_1(t) - d_2S_2(t), \\ I_2'(t) &= - \int_0^t ae_2S_2(\xi)I_1(\xi)e^{-d_2(t-\xi)}D_tP_2(t-\xi)d\xi - d_2I_2(t), \end{aligned} \quad (1)$$

which is presented and studied in [17].  $S_1(t)$  and  $I_1(t)$  represent the sub-population of the susceptible and infectious classes of human hosts, respectively.  $S_2(t)$  and  $I_2(t)$  are the respective sub-populations of the susceptible and infectious classes of female mosquitoes. Denote the size of the population of human beings by  $N(t)$  and that of the female mosquitoes by  $M(t)$ . The natural birth rates  $d_1$  and  $d_2$  of humans and female mosquitoes are assumed to equal the respective birth rates of

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human and mosquitoes so that the total human and female mosquito populations remain constants (that is,  $N(t) = N$  and  $M(t) = M$ ). Thus,  $m = \frac{M}{N}$  represents the average mosquito number per person. The integrals are in the Riemann-Stieltjes sense.  $D_t P_i(t - \xi) = \frac{dP_i(t - \xi)}{dt}$ ,  $i = 1, 2$ , whenever the derivative exists. The constant  $a$  denote the mosquito biting rate and  $e_1$  be the probability that a biting by an infectious mosquito to a susceptible person will cause infection to the person, and  $e_2$  be the probability that a biting by a susceptible mosquito to an infectious human individual will cause infection to the mosquito.

As pointed in [17],  $P_1(t)$  denote the probability (without taking death into account) that a latent host individual still remains in the latent class  $t$  time units after entering the latent class (i.e., being infected). And similarly,  $P_2(t)$  be the probability that a latent vector individual still remains in the latent class  $t$  time after entering the latent class. It is biologically reasonable to assume that  $P_1(t)$  and  $P_2(t)$  satisfy the following properties [16, 17]:

(H<sub>1</sub>)  $P : [0, \infty) \rightarrow [0, 1]$  are non-increasing, piecewise continuous with possibly finitely many jumps and satisfies  $P(0^+) = 1$ ;  $\lim_{t \rightarrow \infty} P(t) = 0$  with  $\int_0^\infty P(t)dt$  is positive and finite.

Note that (1) may not have an endemic equilibrium (EE) for finite time  $t$ . According to [11], if (1) has an EE, then the EE must satisfy the limiting system given by

$$\begin{aligned} S_1'(t) &= d_1 - ae_1mS_1(t)I_2(t) - d_1S_1(t), \\ I_1'(t) &= - \int_0^\infty ae_1mS_1(t - \xi)I_2(t - \xi)e^{-d_1\xi}D_\xi P_1(\xi)d\xi - d_1I_1(t), \\ S_2'(t) &= d_2 - ae_2S_2(t)I_1(t) - d_2S_2(t), \\ I_2'(t) &= - \int_0^\infty ae_2S_2(t - \xi)I_1(t - \xi)e^{-d_2\xi}D_\xi P_2(\xi)d\xi - d_2I_2(t). \end{aligned} \tag{2}$$

Since the limiting system (2) contains an infinite delay, its associated initial condition needs to be restricted in an appropriate fading memory space [1, 4, 13].

Let

$$Q_i := - \int_0^\infty e^{-d_i\xi}D_\xi P_i(\xi)d\xi, \quad i = 1, 2. \tag{3}$$

It can be verified that  $Q_i \in (0, 1)$  for all  $i = 1, 2$ . Define

$$J_i(t) := - \int_t^\infty e^{-d_i\xi}D_\xi P_i(\xi)d\xi, \quad i = 1, 2,$$

then  $J_i(t) \geq 0, \forall t > 0$  and  $J_i(0) = Q_i > 0$ .

Using  $Q_i, i = 1, 2$ , the basic reproduction number for the model (1) can then be defined as

$$\mathfrak{R}_0 = m \frac{ae_1}{d_1} \cdot Q_1 \cdot \frac{ae_2}{d_2} \cdot Q_2, \tag{4}$$

which accounts for the average number of secondary infections that a single infectious human being (female mosquito), once introduced into fully susceptible populations of mosquitoes and humans, is expected to cause to the humans (female mosquitoes) during the infection period.

Model system (1) has a disease free equilibrium  $E_0$ , given by  $E_0 = (S_1^0, 0, S_2^0, 0) = (1, 0, 1, 0)$ . When  $\mathfrak{R}_0 > 1$ , in addition to the disease free equilibrium, (2) also admits an endemic equilibrium  $E^* = (S_1^*, I_1^*, S_2^*, I_2^*)$ , where  $S_1^*, I_1^*, S_2^*, I_2^* > 0$  satisfy the

following equilibrium equations

$$\begin{aligned} d_1 &= ae_1mS_1^*I_2^* + d_1S_1^*, \\ d_1I_1^* &= Q_1ae_1mS_1^*I_2^*, \\ d_2 &= ae_2S_2^*I_1^* + d_2S_2^*, \\ d_2I_2^* &= Q_2ae_2S_2^*I_1^*. \end{aligned} \tag{5}$$

After simple calculation, we have

$$S_1^* = \frac{d_1d_2 + ae_2d_1Q_1}{ae_2(d_1 + ae_1mQ_2)Q_1}, \quad I_1^* = \frac{d_1d_2(\mathfrak{R}_0 - 1)}{ae_2(d_1 + ae_1mQ_2)}, \tag{6}$$

$$S_2^* = \frac{d_1d_2 + ae_1md_2Q_2}{ae_1m(d_2 + ae_2Q_1)Q_2}, \quad I_2^* = \frac{d_1d_2(\mathfrak{R}_0 - 1)}{ae_1m(d_2 + ae_2Q_1)}. \tag{7}$$

The authors in [17] gave a through analysis of model (1), but leaving out only the elusive global stability of endemic equilibrium of (2). This provides us with one motivation to conduct our work. The object of this note is to show that the endemic equilibrium  $E^*$  of (2) is always globally asymptotically stable whenever it exists, which implies that possibility of Hopf bifurcations is therefore ruled out. The approach here is to use a Lyapunov functional, which was adopted recently in [6, 7, 8, 9, 12, 13, 15] to get the global properties of epidemiological models.

The paper is organized as follows. In section 2 we describe previous results by Xiao and Zou from [17] providing the context where this paper is to be read. The global stability of the corresponding equilibria for  $\mathfrak{R}_0 > 1$  is shown in section 3—the key results of this paper.

**2. Previous results.** By a careful analysis of the characteristic equation, and using the Fluctuation Lemma [5], the Lebesgue-Fatou Lemma [14] together with the theory of asymptotically autonomous systems [2], the authors of [17] proved that the disease free equilibrium is globally asymptotically stable provided that the basic reproduction number  $\mathfrak{R}_0 < 1$ . When  $\mathfrak{R}_0 > 1$  and there is no recovery for human beings, the authors of [17] were able to show that the endemic equilibrium  $E^*$  is globally asymptotically stable when the two probability functions are either exponential functions or step functions. In this note, we still assume that there is no recovery, but we will show that  $E^*$  is globally asymptotically stable for general latency probability functions  $P_1(t)$  and  $P_2(t)$  satisfying  $(\mathbf{H}_1)$ . To achieve this goal, we first need some results from [17].

Define

$$\begin{aligned} \Omega := \{ &(S_1, I_1, S_2, I_2) \in \mathbb{R}^4 : S_1 > 0, I_1 \geq 0, S_1 + I_1 \leq 1 \\ &S_2 > 0, I_2 \geq 0, S_2 + I_2 \leq 1 \}, \end{aligned}$$

which is obviously positively invariant for (1).

**Lemma 2.1.** *If  $(S_1(0), I_1(0), S_2(0), I_2(0)) \in \Omega$  satisfies  $S_1(0) + I_1(0) = 1$  and  $S_2(0) + I_2(0) = 1$ , then system (1) has a unique solution  $(S_1(t), I_1(t), S_2(t), I_2(t))$  satisfying the initial conditions, which remains in  $\Omega$  for all  $t \geq 0$ . Moreover, if  $I_1(0) + I_2(0) > 0$ , then  $I_1(t) > 0$  and  $I_2(t) > 0$  for  $t > 0$ .*

**Theorem 2.2.** *If  $\mathfrak{R}_0 < 1$ , then  $E_0$  is globally asymptotically stable in  $\Omega$ ; if  $\mathfrak{R}_0 > 1$ , then  $E_0$  becomes unstable.*

3. **Main results.** In what follows, we make use of the function

$$H(u) = u - 1 - \ln u, \quad \forall u > 0. \tag{8}$$

Obviously,  $H : \mathbb{R}^+ \rightarrow \mathbb{R}/\mathbb{R}_-$  attains its strict global minimum at  $u = 1$  and  $H(1) = 0$ . Here we prove the global asymptotic stability of the endemic equilibrium by means of Lyapunov functional.

**Theorem 3.1.** *If  $\mathfrak{R}_0 > 1$ , then  $E^*$  is globally asymptotically stable for system (2).*

*Proof.* Consider a Lyapunov functional

$$\begin{aligned} L_1 = & Q_2 a e_2 S_2^* I_1^* \left[ Q_1 S_1^* H\left(\frac{S_1(t)}{S_1^*}\right) + I_1^* H\left(\frac{I_1(t)}{I_1^*}\right) \right] \\ & + Q_1 a e_1 m S_1^* I_2^* \left[ Q_2 S_2^* H\left(\frac{S_2(t)}{S_2^*}\right) + I_2^* H\left(\frac{I_2(t)}{I_2^*}\right) \right] + L_+ + L_-, \end{aligned}$$

where

$$L_+ = a e_1 m S_1^* I_2^* Q_2 a e_2 S_2^* I_1^* \int_0^\infty J_1(\xi) H\left(\frac{S_1(t-\xi)I_2(t-\xi)}{S_1^* I_2^*}\right) d\xi,$$

and

$$L_- = Q_1 a e_1 m S_1^* I_2^* a e_2 S_2^* I_1^* \int_0^\infty J_2(\xi) H\left(\frac{S_2(t-\xi)I_1(t-\xi)}{S_2^* I_1^*}\right) d\xi.$$

Differentiating  $L_+$  and  $L_-$  along the solution of system (2) respectively, and using integration by parts, we obtain

$$\begin{aligned} L'_+ = & a e_1 m S_1^* I_2^* Q_2 a e_2 S_2^* I_1^* \int_0^\infty J_1(\xi) \frac{\partial}{\partial t} H\left(\frac{S_1(t-\xi)I_2(t-\xi)}{S_1^* I_2^*}\right) d\xi \\ = & - a e_1 m S_1^* I_2^* Q_2 a e_2 S_2^* I_1^* \int_0^\infty J_1(\xi) \frac{\partial}{\partial \xi} H\left(\frac{S_1(t-\xi)I_2(t-\xi)}{S_1^* I_2^*}\right) d\xi \\ = & - a e_1 m S_1^* I_2^* Q_2 a e_2 S_2^* I_1^* J_1(\xi) H\left(\frac{S_1(t-\xi)I_2(t-\xi)}{S_1^* I_2^*}\right) \Big|_{\xi=0}^\infty \\ & + a e_1 m S_1^* I_2^* Q_2 a e_2 S_2^* I_1^* \int_0^\infty H\left(\frac{S_1(t-\xi)I_2(t-\xi)}{S_1^* I_2^*}\right) dJ_1(\xi) \\ = & Q_1 a e_1 m S_1^* I_2^* Q_2 a e_2 S_2^* I_1^* H\left(\frac{S_1(t)I_2(t)}{S_1^* I_2^*}\right) \\ & + a e_1 m S_1^* I_2^* Q_2 a e_2 S_2^* I_1^* \int_0^\infty D_\xi P_1(\xi) e^{-d_1 \xi} H\left(\frac{S_1(t-\xi)I_2(t-\xi)}{S_1^* I_2^*}\right) d\xi \\ = & Q_1 a e_1 m Q_2 a e_2 S_2^* I_1^* \left( S_1(t)I_2(t) - S_1^* I_2^* \ln \frac{S_1(t)I_2(t)}{S_1^* I_2^*} \right) \\ & + a e_1 m Q_2 a e_2 S_2^* I_1^* \times \\ & \int_0^\infty D_\xi P_1(\xi) e^{-d_1 \xi} \left[ S_1(t-\xi)I_2(t-\xi) - S_1^* I_2^* \ln \frac{S_1(t-\xi)I_2(t-\xi)}{S_1^* I_2^*} \right] d\xi. \tag{9} \end{aligned}$$

And similarly, we have

$$\begin{aligned} L'_- = & Q_1 a e_1 m S_1^* I_2^* Q_2 a e_2 \left( S_2(t)I_1(t) - S_2^* I_1^* \ln \frac{S_2(t)I_1(t)}{S_2^* I_1^*} \right) \\ & + Q_1 a e_1 m S_1^* I_2^* a e_2 \times \\ & \int_0^\infty D_\xi P_2(\xi) e^{-d_2 \xi} \left[ S_2(t-\xi)I_1(t-\xi) - S_2^* I_1^* \ln \frac{S_2(t-\xi)I_1(t-\xi)}{S_2^* I_1^*} \right] d\xi. \tag{10} \end{aligned}$$

Set  $c_1 = Q_2 a e_2 S_2^* I_1^*$  and  $c_2 = Q_1 a e_1 m S_1^* I_2^*$  for simplicity in calculation. Thus the derivative of  $L_1$  is given as

$$\begin{aligned} L'_1 = & c_1 \left[ Q_1 \left( 1 - \frac{S_1^*}{S_1(t)} \right) \left( a e_1 m S_1^* I_2^* + d_1 S_1^* - a e_1 m S_1(t) I_2(t) - d_1 S_1(t) \right) \right. \\ & \left. + \left( 1 - \frac{I_1^*}{I_1(t)} \right) \left( - \int_0^\infty a e_1 m S_1(t - \xi) I_2(t - \xi) e^{-d_1 \xi} D_\xi P_1(\xi) d\xi - d_1 I_1(t) \right) \right] \\ & + c_2 \left[ Q_2 \left( 1 - \frac{S_2^*}{S_2(t)} \right) \left( a e_2 S_2^* I_1^* + d_2 S_2^* - a e_2 S_2(t) I_1(t) - d_2 S_2(t) \right) \right. \\ & \left. + \left( 1 - \frac{I_2^*}{I_2(t)} \right) \left( - \int_0^\infty a e_2 S_2(t - \xi) I_1(t - \xi) e^{-d_2 \xi} D_\xi P_2(\xi) d\xi - d_2 I_2(t) \right) \right] \\ & + L'_+ + L'_-. \end{aligned}$$

Combining the above equations (9) and (10), we get

$$\begin{aligned} L'_1 = & c_1 \left[ 2c_2 + Q_1 d_1 S_1^* \left( 2 - \frac{S_1(t)}{S_1^*} - \frac{S_1^*}{S_1(t)} \right) - c_2 \frac{S_1^*}{S_1(t)} + Q_1 a e_1 m S_1^* I_2(t) \right. \\ & \left. + \frac{I_1^*}{I_1(t)} \int_0^\infty a e_1 m S_1(t - \xi) I_2(t - \xi) D_\xi P_1(\xi) e^{-d_1 \xi} d\xi - d_1 I_1(t) \right] \\ & + c_2 \left[ 2c_1 + Q_2 d_2 S_2^* \left( 2 - \frac{S_2(t)}{S_2^*} - \frac{S_2^*}{S_2(t)} \right) - c_1 \frac{S_2^*}{S_2(t)} + Q_2 a e_2 S_2^* I_1(t) \right. \\ & \left. + \frac{I_2^*}{I_2(t)} \int_0^\infty a e_2 S_2(t - \xi) I_1(t - \xi) D_\xi P_2(\xi) e^{-d_2 \xi} d\xi - d_2 I_2(t) \right] \\ & - c_1 c_2 \ln \frac{S_1(t) I_2(t)}{S_1^* I_2^*} - \frac{c_1 c_2}{Q_1} \int_0^\infty D_\xi P_1(\xi) e^{-d_1 \xi} \ln \frac{S_1(t - \xi) I_2(t - \xi)}{S_1^* I_2^*} d\xi \\ & - c_1 c_2 \ln \frac{S_2(t) I_1(t)}{S_2^* I_1^*} - \frac{c_1 c_2}{Q_2} \int_0^\infty D_\xi P_2(\xi) e^{-d_2 \xi} \ln \frac{S_2(t - \xi) I_1(t - \xi)}{S_2^* I_1^*} d\xi \\ = & c_1 Q_1 d_1 S_1^* \left( 2 - \frac{S_1(t)}{S_1^*} - \frac{S_1^*}{S_1(t)} \right) + c_2 Q_2 d_2 S_2^* \left( 2 - \frac{S_2(t)}{S_2^*} - \frac{S_2^*}{S_2(t)} \right) \\ & + \left( Q_1 Q_2 a^2 e_1 e_2 m S_1^* I_2(t) S_2^* I_1^* - Q_1 a e_1 m S_1^* I_2^* d_2 I_2(t) \right) \\ & + \left( Q_1 Q_2 a^2 e_1 e_2 m S_1^* I_2^* S_2^* I_1(t) - Q_2 a e_2 S_2^* I_1^* d_1 I_1(t) \right) \\ & + c_1 c_2 \left[ - H \left( \frac{S_1^*}{S_1(t)} \right) + \frac{1}{Q_1} \int_0^\infty D_\xi P_1(\xi) e^{-d_1 \xi} H \left( \frac{I_1^* S_1(t - \xi) I_2(t - \xi)}{I_1(t) S_1^* I_2^*} \right) d\xi \right. \\ & \left. - H \left( \frac{S_2^*}{S_2(t)} \right) + \frac{1}{Q_2} \int_0^\infty D_\xi P_2(\xi) e^{-d_2 \xi} H \left( \frac{I_2^* S_2(t - \xi) I_1(t - \xi)}{I_2(t) S_2^* I_1^*} \right) d\xi \right]. \end{aligned}$$

Recall that equilibrium of (2) satisfy equilibrium equations (5) and it follows from the properties of  $H(u)$  in (8) that positive-define functional  $L_1(t)$  has non-positive derivative  $L'_1(t)$ . Let  $M$  be the largest invariant subset of (2) contained in the set of

$$\{(S_1(t), I_1(t), S_2(t), I_2(t)) | L'_1 = 0\}.$$

In what follows we determine  $M$ . In order to have  $L'_1$  equal to zero it is necessary to have  $S_1(t) = S_1^* = S_1(t - \xi)$ ,  $S_2(t) = S_2^* = S_2(t - \xi)$ ,  $I_1(t) = I_1^* = I_1(t - \xi)$  and  $I_2(t) = I_2^* = I_2(t - \xi)$ . Thus, at each point in  $M$ , we have  $S_1(t) = S_1^*$  and

$S_2(t) = S_2^*$  and therefore  $S_1'(t) = 0$  and  $S_2'(t) = 0$  in  $M$ , from the first and third equations of (2), it has

$$\begin{aligned} S_1'(t) &= d_1 - ae_1mS_1^*I_2(t) - d_1S_1^*, \\ S_2'(t) &= d_2 - ae_2S_2^*I_1(t) - d_2S_2^*, \end{aligned}$$

for all  $t$ , which implies that  $I_1(t) = I_1^*$  and  $I_2(t) = I_2^*$  for all  $t$ . Hence,  $M = \{E^*\}$ . By LaSalle invariance principle [3, 10], every positive solution of (2) tends to the endemic equilibrium  $E^*$ , proving that  $E^*$  is globally asymptotically stable. The proof is completed.  $\square$

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