

# A Mathematical Model of *Schistosoma mansoni* in *Biomphalaria glabrata* with Control Strategies

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## Abstract

We describe and analyze a mathematical model for schistosomiasis in which infected snails are distinguished from susceptible through increased mortality and no reproduction. We based the model on the same derivation as Anderson and May [3, 17, 10], but used logistic growth both in human and snail hosts. We introduce a parameter  $r$ , the effective coverage of medical treatment/prevention to control the infection. We determine a reproductive number for the disease directly related to its persistence and extinction. Finally, we obtain a critical value for  $r$  that indicates the minimum treatment effort needed in order to clear out the disease from the population.

## 1 Introduction

Schistosomiasis is a family of diseases caused by flatworms of the *Schistosoma*. Schistosomes are digenetic trematodes that spend their adult life in humans and a previous stage in aquatic snails [13]. Schistosomiasis is possibly the most widespread public health problem in the world. There are about 200 million people infected worldwide, and more than 650 million people live in endemic areas [29]. *Schistosoma mansoni* is one of three most common schistosomes and affects large geographical areas in several countries. Its prevalence is estimated to be 8-10 million people in Brazil alone [30].

Mathematical modeling of schistosomiasis has been done by many researchers [16, 19, 6, 2, 4, 5, 1, 14, 20, 21, 22, 10]. Macdonald [16] was the first to use simple mathematical models to study the transmission dynamics of schistosomiasis. Näsell [19] established a hybrid (stochastic-deterministic) model to study the transmission of schistosomiasis in a community. Anderson and May [2, 3, 4, 17] studied the regulation and stability of host-parasite interaction from an infinite system of differential equations inspired by Kostizin [15], and found that overdispersion of parasites in the human hosts is the key for parasites to regulate and stabilize their numbers. Adler and Kretzschmar [1, 14] further revealed that

the stability of the endemic equilibrium is not mediated by aggregation but by dispersion, which is measured by the variance-to-mean ratio. Recently, Pugliese and Rosà [20, 21] generalized the idea of Adler and Kretzschmar [1, 14] to a larger system including the larval stage of intermediate hosts, found periodic solutions and estimated the period of such oscillations. Moreover, they compared individual-based stochastic model with the deterministic model to study the host cycle and extinction [22].

However, all the pioneering work mentioned above is built on simplifications of the complicated indirect-cycle dynamics of schistosomiasis. In fact, the life cycle of schistosomes consists of adults in human hosts and larvae in aquatic snails, and it is not adequate to omit any stage. Dobson [7] explored the dynamics of the interaction between parasites and their hosts using phase plane analysis for a coupled system of differential equations for human hosts, intermediate snail hosts, adult parasites, and two larval stages of parasites. Analysis of their models suggests that both asexual reproduction of the parasite within a host and parasite-induced reduction in host fecundity may be stabilizing mechanisms of parasites with indirect life cycles when they occur in the intermediate hosts [7]. Castration of *Biomphalaria glabrata* infected with *Schistosoma mansoni* was first reported by Gérard and Théron [12]; other studies then corroborated this phenomenon [17, 25, 24]. Feng and Milner [10] introduced a model with infected snails that are non-reproductive and have a higher death risk. Moreover, they incorporated the fact that in the real world host population growth will be limited by, among other factors, intraspecific competition for finite resources [3] and, therefore, they assumed logistic growth of snails. Furthermore, they simply assumed the number of cercariae is linearly proportional to the number of infected snails and the number of miracidia is linearly proportional to the number of adult parasites [10]. This assumption is based on laboratory experiments for *Biomphalaria glabrata* infected with *Schistosoma mansoni*. Théron [27] noticed that in the case of recent infections of less than 4 or 5 months, productivity of cercariae doubles between monomiracidial and bimiracidial infections. For more than 2 miracidia there is practically no increase in productivity. Similarly, for infections older than 5 months there is no discernible difference in productivity between monomiracidial and plurimiracidial infections. One of the main purposes of Feng and Milner's work [10] was to study the regulation of human hosts by parasitism, so they made same assumption of exponential growth of human hosts as Anderson and May [3]. However, that assumption is not appropriate [20, 21, 22] when the interest is in long-term dynamics.

In this paper, we extend the model by Anderson and May [3, 17] in the way of Feng and Milner [10] and we analyze the existence of equilibria and their stability. Our model is derived for the system of *Schistosoma mansoni* and *Biomphalaria glabrata* snails. Though no carrying capacity for either host is proposed in literature, it is common sense that the resources are limited and we may assume a number large enough that the human (or snail) population can never reach it. Experiments [27, 26] show that the cercariae productivity in *Biomphalaria glabrata* is more or less independent of dose of miracidia exposure; therefore our assumption about the production of cercariae  $C = \beta I$  is more re-

alistic than  $\lambda P(t)H(t)/(H_0 + H(t))$  described in [3]. One of our purposes is to analyze how the logistic growth of both hosts can affect the transmission dynamics of schistosomiasis. For certain parameter ranges our model shows multiple endemic equilibria. Moreover, we introduce the effective treatment/prevention parameter  $r$  for people in endemic areas, and we show that the epidemic reproductive number,  $\mathcal{R}_0$ , is a decreasing function of  $r$  that goes to zero. This means that the disease can be eradicated if the coverage/treatment is large enough—a positive message for public health.

## 2 Derivation of model equations

We define  $H(t)$  and  $P(t)$  to be the sizes of the host and parasite populations, respectively,  $S(t)$  and  $I(t)$  to be the sizes of the susceptible and infected snails, respectively, and  $M(t)$  and  $C(t)$  to be the sizes of the miracidia and cercariae populations, respectively, at time  $t$ . Since [27] showed that cercariae production of *Schistosoma mansoni* has no discernible difference related to the level of miracidial exposure of the snail host *Biomphalaria glabrata*, we simply assume that the number of cercariae is linearly proportional to the number of infected snails,

$$C = \beta I. \quad (1)$$

In general, parasites tend to reduce intermediate host reproduction [17]. For some species the magnitude of this reduction may be high, up to two orders of magnitude, as is, for example, for *Biomphalaria pfeifferi* infected with *Schistosoma mansoni* (Sambon) [25, 17] and adult *Biomphalaria glabrata* infected with *Schistosoma mansoni* [12]. The parasite may even completely eliminate the reproduction of the intermediate host as is the case, for example, for juvenile *Biomphalaria glabrata* infected with *Schistosoma mansoni* [12, 24]. For simplicity, we ignore in our model the reproduction of infected snails, and we also assume the snail population grows logistically in the absence of parasites,

$$\begin{cases} S' = [b_s - \mu_{s0} - \mu_{s1}(S + I)]S - \rho MS, \\ I' = \rho MS - [\mu_{s0} + \mu_{s1}(S + I) + d_s]I, \end{cases} \quad (2)$$

where  $b_s$  is the *per capita* birth rate of snails;  $\mu_{s0}$  is *per capita* natural death rate of snails;  $\mu_{s1}$  is *per capita* crowding-induced logistic death rate of snails;  $d_s$  is parasite-induced death rate of snails;  $\rho$  is the infectious contact rate (per snail) of uninfected snails with miracidia. Since the snail population is now bounded by its carrying capacity  $L_s = (b_s - \mu_{s0})/\mu_{s1}$ , we may omit the saturation factor appearing in [10] in the equation describing the dynamics of that population and simply use mass action law to model the infection process.

We make the same assumptions as in Anderson and May [3] that the rate of parasite-induced host mortality is linearly proportional to the number of parasites a host harbors and that the distribution of parasites in human beings is a

negative binomial with a constant clumping parameter  $\kappa$ . This type of distribution is shown to be a reasonable approximation in real life, e.g. Feng. *et. al.* [9], though the parameter  $\kappa$  may not be a constant for all time [20, 21, 22]. In the absence of effective vaccination, the current control programs for schistosome infections have primarily relied on chemotherapy [23]. Since Praziquantel reliably cures 60 to 90 percent of patients and substantially decreases the worm burden and egg production in those treated who are not cured [23], we make a further assumption that control of schistosomiasis only results from the treatment of human hosts and the reduction rate of parasites is given by

$$(rH)\frac{P}{H} = rP,$$

where  $r$  is the effective treatment rate and  $P/H$  is mean parasite load per host.

Many authors [3, 20, 21, 16, 7] simplified the model by omitting the differential equation related to the rate of change of human hosts and assumed the population size of human beings as a constant based on the different time scales in the dynamics of schistosomes and humans. One of our purposes in this paper is to study the reduction of the logistic growth of humans in the system. The dynamics of the human and adult parasite populations are described by:

$$\begin{cases} H' = (b_h - \mu_{h0} - \mu_{h1}H)H - \alpha P, \\ P' = \zeta HC - \alpha\left(\frac{\kappa+1}{\kappa}\right)\left(\frac{P^2}{H}\right) - (\mu_{h0} + \mu_{h1}H + \mu_p + \alpha + r)P, \end{cases} \quad (3)$$

where  $b_h$  is *per capita* birth rate of human hosts;  $\mu_{h0}$  is *per capita* natural death rate of human hosts;  $\mu_{h1}$  is *per capita* crowding-induced logistic death rate of human hosts;  $\zeta$  is “efficacy” of cercariae in infecting humans;  $\alpha$  is parasite-induced death rate of human hosts per parasite;  $\kappa$  is the clumping parameter of negative binomial distribution;  $\mu_p$  is *per capita* death rate of parasites;  $r$  is the effective treatment rate of human hosts. We assume that  $b_h - \mu_{h0}$  and  $b_s - \mu_{s0}$  are positive, which indicates that the hosts asymptotically approach their carrying environmental capacities in the absence of parasites. Since the human population  $H$  is bounded by its carrying capacity  $L_h = (b_h - \mu_{h0})/\mu_{h1}$ , once again the saturation factor can be omitted and a mass action law is enough to describe the infection process.

One more relation between miracidia  $M$  and adult parasites  $P$  is needed in order to close the system. Here we make the same assumption as in [10], that the number of miracidia is linearly proportional to the number of adult parasites

$$M = b_p P, \quad (4)$$

where  $b_p$  is mean number of eggs (miracidia) laid per parasite.

### 3 Well-Posedness

For convenience, we can combine Eq. (1), Eq. (2), Eq. (3), Eq. (4) into the following system,

$$\begin{cases} H' = (b_h - \mu_{h0} - \mu_{h1}H)H - \alpha P, \\ P' = \zeta HC - \alpha\left(\frac{\kappa+1}{\kappa}\right)\left(\frac{P^2}{H}\right) - (\mu_{h0} + \mu_{h1}H + \mu_p + \alpha + r)P, \\ S' = [b_s - \mu_{s0} - \mu_{s1}(S + I)]S - \rho MS, \\ dI = \rho MS - [\mu_{s0} + \mu_{s1}(S + I) + d_s]I, \\ M = b_p P, C = \beta I. \end{cases} \quad (5)$$

At first glance it may seem that System (5) has singularity at  $H = 0$ , that is when humans go to extinction due to overwhelming parasitism. Even though our assumptions will guarantee the positivity of solutions if we start from positive initial data, the mathematical model should allow us to study the limiting case where  $H = 0$ . To see that this can indeed be done, instead of looking at the rate of change of the parasite number, we investigate the rate of change of the mean parasite load per person,  $R = P/H$ , and we shall see that not only are the parasites eradicated with the extinction of human beings, but also the mean parasite load goes to zero. In the following reformulation of our model, the equation for the uninfected snails will be replaced by one for the total population of snails,  $T = S + I$ . It is easy to see that  $R$  and  $T$  satisfy the following equations:

$$\begin{cases} R' = \left(\frac{P}{H}\right)' = \frac{P'H - PH'}{H^2} = \zeta C - \frac{\alpha}{\kappa}R^2 - (b_h + \mu_p + \alpha + r)R, \\ T' = S' + I' = -(d_s + \mu_{s0} + \mu_{s1}T)T + (b_s + d_s)S. \end{cases}$$

Notice that the miracidia population  $M$  and the cercariae population  $C$  are directly proportional to the parasite population  $P = HR$  and to the infected snail population  $I = T - S$ , respectively. Therefore, System (5) can be written in terms of just  $H, R, S, T$  as follows:

$$\begin{cases} H' = (b_h - \mu_{h0} - \mu_{h1}H)H - \alpha HR, \\ R' = \zeta\beta(T - S) - \frac{\alpha}{\kappa}R^2 - (b_h + \mu_p + \alpha + r)R, \\ S' = (b_s - \mu_{s0} - \mu_{s1}T)S - \rho b_p HRS, \\ T' = -(d_s + \mu_{s0} + \mu_{s1}T)T + (b_s + d_s)S. \end{cases} \quad (6)$$

It is easy to prove that the positive cone is invariant for System (6).

**Lemma 3.1.** *If  $H(0)$ ,  $R(0)$ , and  $S(0)$  are positive and  $T(0) > S(0)$ , then  $H$ ,  $R$ , and  $S$ , are positive and  $T > S$  as long as they exist.*

*Proof.* First note that, subtracting Eq. (6.iii) from Eq. (6.iv), we have

$$(T - S)' = -(d_s + \mu_{s0} + \mu_{s1}T)(T - S) + \rho b_p HRS. \quad (7)$$

Therefore, when  $H(0) > 0$  and  $S(0) > 0$ , if either  $R(0) > 0$  or  $T(0) > S(0)$ , then for small  $\varepsilon > 0$  we certainly have  $H$ ,  $R$ ,  $S$ , and  $T - S$  positive on  $(0, \varepsilon)$ . It is clear that Eq. (6.i) gives the positivity of  $H$ , Eq. (6.iii) gives the positivity of  $S$ , and then Eq. (6.iv) gives the positivity of  $T$  as long as they exist. Hence, it suffices to show that  $T - S$  must remain positive as long as it exists, since that is sufficient (in fact, equivalent) to establishing the positivity of  $R$ .

Suppose that  $T - S$  vanishes for some positive time, and let  $\bar{t}$  be the smallest such time. Then,  $T - S$  is positive on  $[0, \bar{t})$  and  $T(\bar{t}) = S(\bar{t})$ . It follows from Eq. (6.ii) that  $R$  is positive on  $[0, \bar{t}]$  and then Eq. (7) implies that  $T - S$  is positive on  $[0, \bar{t}]$ , contradicting  $T(\bar{t}) = S(\bar{t})$ . Thus  $T - S$  remains positive as long as it exists, and so does  $R$ .  $\square$

**Remark 3.1.** *Note that the positivity of solutions of System (5) can be deduced directly from the above lemma, since  $I = T - S$  and  $P = RH$ .*

**Remark 3.2.** *If  $T(0) = S(0)$  and  $R(0) = 0$ , System (6) shows that  $T = S$  and  $R = 0$  for all time, while  $H$  and  $S$  are solutions of decoupled logistic equations, as should be the case when no parasites exist initially in any form (miracidia, cercariae, or adults).*

**Remark 3.3.** *The well-posedness of System (5) is equivalent to the well-posedness of System (6), but the latter is easier to establish.*

**Lemma 3.2.** *System (6) admits a unique solution for all time.*

*Proof.* From the theory of systems of ordinary differential equations we immediately have local existence and uniqueness of solutions for any non-negative initial values. Using very standard techniques, one can derive *a priori* the exponential boundedness of solutions, from which the unique existence of a global solution follows.  $\square$

## 4 Equilibria

For convenience, let us define the carrying capacity of human hosts and snail hosts as:

$$L_h = (b_h - \mu_{h0})/\mu_{h1}, \quad L_s = (b_s - \mu_{s0})/\mu_{s1}.$$

It is clear that the System (6) admits the following four parasite-free steady states

$$\begin{cases} E_0 & = & (H_0, R_0, S_0, T_0) & = & (0, 0, 0, 0), \\ E_1 & = & (H_1, R_1, S_1, T_1) & = & (0, 0, L_s, L_s), \\ E_2 & = & (H_2, R_2, S_2, T_2) & = & (L_h, 0, 0, 0), \\ E_{DFE} & = & (H_{DFE}, R_{DFE}, S_{DFE}, T_{DFE}) & = & (L_h, 0, L_s, L_s), \end{cases}$$

where  $E_{DFE}$  represents  $(H, P, S, I) = (L_h, 0, L_s, 0)$  for System (5).  $E_0$  is the trivial equilibrium, while  $E_1$  and  $E_2$  are semi-trivial in that they represent, respectively, the ultimate state of a logistic population of snails and of humans in the absence of parasitism.

Let us turn to the existence of nontrivial equilibria, i.e. constant solutions of System (6) for which  $R > 0$ .

It follows easily from Eq. (6.i), Eq. (6.iii), and Eq. (6.iv) that, at equilibrium,

$$\left\{ \begin{array}{l} R = \frac{b_h - \mu_{h0}}{\alpha} \left(1 - \frac{H}{L_h}\right), \\ T = \frac{b_s - \mu_{s0} - \rho b_p H R}{\mu_{s1}}, \\ T - S = \frac{(b_s - \mu_{s0} - \mu_{s1} T) T}{(b_s + d_s)} = \frac{\rho b_p (b_s - \mu_{s0} - \rho b_p H R) H R}{\mu_{s1} (b_s + d_s)}. \end{array} \right.$$

Substituting  $T - S$  into Eq. (6.ii) we have

$$\frac{\zeta \beta \rho b_p (b_s - \mu_{s0} - \rho b_p H R) H R}{\mu_{s1} (b_s + d_s)} - \frac{\alpha}{\kappa} R^2 - (b_h + \mu_p + \alpha + r) R = 0. \quad (8)$$

Obviously,  $R = 0$  is a solution to the above equation, and the two semi-trivial equilibria  $E_0$  and  $E_2$  can be retrieved from here.

For simplicity, we introduce now the following notation:

$$C_0 = \frac{\zeta \beta \rho b_p}{\mu_{s1} (b_s + d_s)}.$$

Then, for  $R \neq 0$ , Eq. (8) can be rewritten as

$$(b_s + \mu_{s0}) C_0 H - \rho b_p C_0 H^2 R - \frac{\alpha}{\kappa} R - (b_h + \mu_p + \alpha + r) = 0.$$

Substituting  $R$  into the above equation, we have

$$(b_s - \mu_{s0}) C_0 H - \rho b_p C_0 \frac{b_h - \mu_{h0}}{\alpha} \left(1 - \frac{H}{L_h}\right) H^2 - \frac{b_h - \mu_{h0}}{\kappa} \left(1 - \frac{H}{L_h}\right) - (b_h + \mu_p + \alpha + r) = 0.$$

After simplifying the expression above, it turns into the cubic equation

$$H^3 + a_2 H^2 + a_1 H + a_0 = 0, \quad (9)$$

where

$$\left\{ \begin{array}{l} a_2 = -L_h, \\ a_1 = \frac{(b_s - \mu_{s0}) \alpha}{\rho b_p \mu_{h1}} + \frac{\alpha}{\rho b_p C_0 \kappa}, \\ a_0 = -\frac{(b_h - \mu_{h0}) \alpha}{\kappa \mu_{h1} C_0 \rho b_p} - \frac{\alpha (b_h + \mu_p + \alpha + r)}{\mu_{h1} C_0 \rho b_p}. \end{array} \right. \quad (10)$$

Now identifying the equilibria becomes equivalent to identifying the positive real roots of a cubic equation. We recall a lemma that states the type of roots of cubic polynomials in terms of their discriminant, so-called Cubic Formula, which can be found in many algebra books, e.g. [8].

**Lemma 4.1.** *Let  $x^3 + c_2x^2 + c_1x + c_0$  be a third order polynomial and define its discriminant as*

$$\bar{D} = \left( \frac{3c_1 - c_2^2}{9} \right)^3 + \left( \frac{9c_1c_2 - 27c_0 - 2c_2^3}{54} \right)^2.$$

*If  $\bar{D} > 0$ , one root of the polynomial is real and two are complex conjugates; if  $\bar{D} = 0$ , all roots are real and at least two are equal; and if  $\bar{D} < 0$ , all roots are real and unequal.*

Now let us introduce some new notation:

$$\begin{aligned} Q &= (3a_1 - a_2^2)/9, \\ R &= (9a_1a_2 - 27a_0 - 2a_2^3)/54, \\ D &= Q^3 + U^2. \end{aligned} \tag{11}$$

where  $a_1, a_2, a_3$  are defined in Eq. (10). Then,  $D$  is the discriminant of Eq. (9).

Since  $a_0$  in Eq. (10) is negative, Eq. (9) has at least one positive real root. It is easy to prove the following theorem about positive solutions of Eq. (9).

**Theorem 4.2.** *Let  $D$  be defined in Eq. (11), where  $a_0, a_1, a_2$  are defined in Eq. (10), and consider  $D = D(r)$  and  $U = U(r)$  as functions of the treatment rate  $r$ .*

- i) If  $Q > 0$  or if  $Q < 0$  with  $U(0) > 0$  and  $D(0) > 0$ , then Eq. (9) admits exactly one positive real root for any  $r$ ;*
- ii) If  $Q < 0$  and  $D(0) < 0$ , then as  $r$  increases from 0 to  $\infty$ , Eq. (9) admits first three, then two, and finally one positive real root;*
- iii) If  $Q < 0$  with  $U(0) < 0$  and  $D(0) > 0$ , then as  $r$  increases from 0 to  $\infty$ , Eq. (9) admits first one, then two, then three, then again two, and finally one positive real root.*

*Proof.* Looking at the coefficients in Eq. (9), we know that the polynomial tends to infinity as  $H$  increases without bound, and it goes to negative infinity as  $H$  approaches negative infinity. Moreover,  $a_0 < 0$  implies that the  $H$ -intercept is negative;  $a_1 > 0$  implies that the polynomial is increasing at  $H = 0$ ;  $a_2 < 0$  implies that the polynomial is concave downward at  $H = 0$ . These conditions imply that all real roots of the polynomial lie on the positive  $H$ -axis. By Lemma 3.1, we know that if  $D > 0$ , there is only one real root, and it is positive; if  $D = 0$ , there are three real positive roots and at least two of them are equal; if  $D < 0$ , there are three distinct real roots and they are all positive.

Also, looking at Eq. (10), we see that only  $a_0$  depends on  $r$ . It is easy to see that  $U$  (and *a fortiori* also  $D$ ) increases with  $r$ , and

$$\lim_{r \rightarrow \infty} U = +\infty$$

which implies  $D > 0$  for  $r$  large enough.  $\square$

Note that a positive real solution of Eq. (9),  $H^*$ , leads to a positive equilibrium of Eq. (6) if, and only if,  $H^* < L_h$  (so the equilibrium value for  $R$  is positive) and  $H^*(L_h - H^*) < (b_s - \mu_{s0})\alpha L_h / (\rho b_p (b_h - \mu_{h0}))$  (so the equilibrium value for  $T$  is positive). Numerical simulations suggest that these conditions may always hold for  $H^* > 0$ , though we have not proved it.

## 5 Stability and the Reproduction Number $\mathcal{R}_0$

Concerning the stability of the equilibria, we shall use the Jacobian matrices of Systems (6) and (5) according to which is more convenient. Regarding the trivial equilibria  $E_0$ ,  $E_1$  and  $E_2$ , it is easier to use the Jacobian matrix of System (6), which at an equilibrium  $E = (H, R, S, T)$  is

$$J_6(E) = \begin{pmatrix} j_{11} & -\alpha H & 0 & 0 \\ 0 & j_{22} & -\zeta\beta & \zeta\beta \\ -\rho b_p R S & -\rho b_p H S & j_{33} & -\mu_{s1} S \\ 0 & 0 & (b_s + d_s) & j_{44} \end{pmatrix},$$

where

$$\begin{aligned} j_{11} &= b_h - \mu_{h0} - 2\mu_{h1}H - \alpha R, \\ j_{22} &= -\frac{2\alpha}{\kappa}R - (b_h + \mu_p + \alpha + r), \\ j_{33} &= b_s - \mu_{s0} - \mu_{s1}T - \rho b_p H R, \\ j_{44} &= -\mu_{s0} - d_s - 2\mu_{s1}T. \end{aligned}$$

**Theorem 5.1.**  $E_0$ ,  $E_1$ , and  $E_2$  are unstable.

*Proof.* The Jacobian at  $E_0$  is

$$J_6(E_0) = \begin{pmatrix} b_h - \mu_{h0} & 0 & 0 & 0 \\ 0 & -(b_h + \mu_p + \alpha + r) & -\zeta\beta & \zeta\beta \\ 0 & 0 & b_s - \mu_{s0} & 0 \\ 0 & 0 & (b_s + d_s) & -(\mu_{s0} + d_s) \end{pmatrix}.$$

Then  $b_h - \mu_{h0} > 0$  is an eigenvalue of  $J_6(E_0)$  so that  $E_0$  is unstable.

The Jacobian at  $E_1$  is

$$J_6(E_1) = \begin{pmatrix} b_h - \mu_{h0} & 0 & 0 & 0 \\ 0 & -(b_h + \mu_p + \alpha + r) & -\zeta\beta & \zeta\beta \\ 0 & 0 & -(b_s - \mu_{s0}) & -(b_s - \mu_{s0}) \\ 0 & 0 & (b_s + d_s) & -(\mu_{s0} + d_s) \end{pmatrix}.$$

Then  $b_h - \mu_{h0} > 0$  is an eigenvalue of  $J_6(E_1)$  too so that  $E_1$  is unstable.

The Jacobian at  $E_2$  is

$$J_6(E_2) = \begin{pmatrix} -(b_h - \mu_{h0}) & -\alpha L_h & 0 & 0 \\ 0 & -(b_h + \mu_p + \alpha + r) & -\zeta\beta & \zeta\beta \\ 0 & 0 & b_s - \mu_{s0} & 0 \\ 0 & 0 & (b_s + d_s) & -(\mu_{s0} + d_s) \end{pmatrix}.$$

Then  $b_s - \mu_{s0} > 0$  is an eigenvalue of  $J_6(E_2)$  so that  $E_2$  is unstable.  $\square$

**Remark 5.1.** *If the snail population exists initially, it will persist forever under this model. Parasitism only affects what proportion of the carrying capacity of the environment for snails will be ultimately present, albeit always a positive fraction of  $L_s$ .*

In order to analyze the stability of the equilibrium  $E_{DFE}$ , it is easier to use the Jacobian of System (5), which at an equilibrium  $E = (H, P, S, I)$  is

$$J_5(E) = \begin{pmatrix} (b_h - \mu_{h0} - 2\mu_{h1}H) & -\alpha & 0 & 0 \\ a_{21} & a_{22} & 0 & \beta\zeta H \\ 0 & -\rho b_p S & a_{33} & -\mu_{s1} S \\ 0 & \rho b_p S & \rho b_p P - \mu_{s1} I & a_{44} \end{pmatrix},$$

where

$$\begin{cases} a_{21} = \beta\zeta I + \left(\frac{\kappa+1}{\kappa}\right) \alpha \left(\frac{P}{H}\right)^2 - \mu_{h1} P, \\ a_{22} = -\alpha \left(\frac{\kappa+1}{\kappa}\right) \left(\frac{2P}{H}\right) - (\mu_{h0} + \mu_{h1} H + \mu_p + \alpha + r), \\ a_{33} = b_s - \mu_{s0} - \mu_{s1}(2S + I) - \rho b_p P, \\ a_{44} = -(\mu_{s0} + \mu_{s1}(S + 2I) + d_s). \end{cases}$$

Define now

$$\mathcal{R}_0 = \frac{\beta\zeta L_h \rho b_p L_s}{(b_s + d_s)(b_h + \mu_p + \alpha + r)},$$

the basic reproduction number of the epidemic.

**Theorem 5.2.** *If  $\mathcal{R}_0 < 1$ , then  $E_{DFE}$  is locally asymptotically stable; if  $\mathcal{R}_0 > 1$  then  $E_{DFE}$  is unstable.*

*Proof.* The Jacobian at this equilibrium is

$$J_5(E_{DFE}) = \begin{pmatrix} -(b_h - \mu_{h0}) & -\alpha & 0 & 0 \\ 0 & -(b_h + \mu_p + \alpha + r) & 0 & \beta\zeta L_h \\ 0 & -\rho b_p L_s & -(b_s - \mu_{s0}) & -(b_s - \mu_{s0}) \\ 0 & \rho b_p L_s & 0 & -(b_s + d_s) \end{pmatrix}.$$

The characteristic equation of the above matrix is

$$(\lambda + b_h - \mu_{h0})\{(\lambda + b_h + \mu_p + \alpha + r)(\lambda + b_s - \mu_{s0})[\lambda + (b_s + d_s)] - \beta\zeta\rho b_p L_h L_s (\lambda + b_s - \mu_{s0})\} = 0,$$

i.e.

$$(\lambda + b_h - \mu_{h0})(\lambda + b_s - \mu_{s0})\{(\lambda + b_h + \mu_p + \alpha + r)[\lambda + (b_s + d_s)] - \beta\zeta\rho b_p L_h L_s\} = 0.$$

The first two factors have negative real roots. Consider now the last factor in the above expression,

$$\begin{aligned} & (\lambda + b_h + \mu_p + \alpha + r)[\lambda + (b_s + d_s)] - \beta\zeta\rho b_p L_h L_s \\ &= \lambda^2 + (b_h + \mu_p + \alpha + r + b_s + d_s)\lambda + \delta(b_s + d_s) - \beta\zeta\rho b_p L_h L_s. \end{aligned}$$

The discriminant of this quadratic equation is

$$\Delta = (b_h + \mu_p + \alpha + r - b_s - d_s)^2 + 4\beta\zeta\rho b_p L_h L_s > 0.$$

Therefore, there are two real roots. In addition, the coefficient of the linear term is positive. Thus, if

$$(b_s + d_s)(b_h + \mu_p + \alpha + r) - \beta\zeta\rho b_p L_h L_s > 0,$$

or, equivalently,

$$\frac{\beta\zeta\rho b_p L_h L_s}{(b_s + d_s)(b_h + \mu_p + \alpha + r)} = \mathcal{R}_0 < 1,$$

the other two roots of the characteristic equation are also negative, which means  $E_{DFE}$  is locally asymptotically stable. On the other hand, if  $\mathcal{R}_0 > 1$ , the quadratic above has one positive and one negative real root, which means that  $E_{DFE}$  is unstable.  $\square$

**Remark 5.2.** *The expression for  $\mathcal{R}_0$  can be derived from the second equation of the System (6) and from Eq. (7). When  $\mathcal{R}_0 < 1$ , numerical simulations suggest that  $E_{DFE}$  is not just locally but actually globally stable, though we have not proved it. Ignoring the effect of the second term in the Eq. (6.ii), a necessary condition for the persistence of parasitism is the satisfaction of a minimum net birth rate condition for the parasites,  $T - S < (\rho b_p L_h L_s)/(b_s + d_s)$ .*

Figure 1 shows that if  $\mathcal{R}_0 > 1$ , parasitism persists, if  $\mathcal{R}_0 < 1$ , parasitism disappears.

**Remark 5.3.** *In terms of designing a strategy to eradicate the parasitism, a classical approach is to increase treatment rate to the point of lowering the reproduction number  $\mathcal{R}_0$  below unity. Note that  $\mathcal{R}_0$  is decreasing with respect to  $r$ , which means we can estimate the smallest treatment rate to eradicate the parasitism by solving for  $r$  the equation  $\mathcal{R}_0=1$ ,*

$$\tilde{r} = \frac{\beta\zeta L_h L_s \rho b_p}{b_s + d_s} - b_h - \mu_p - \alpha.$$

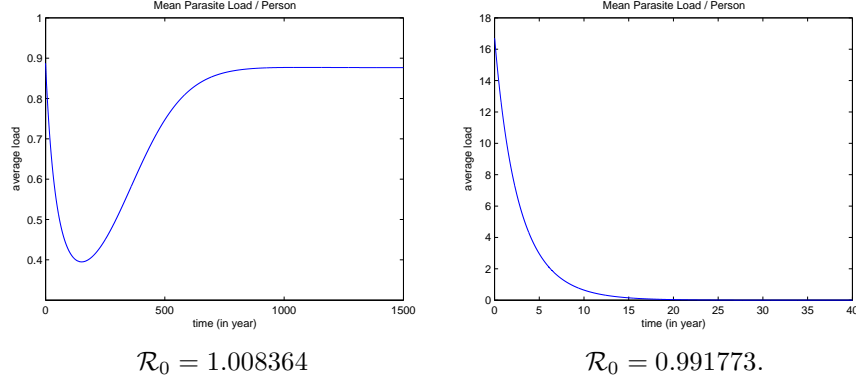


Figure 1: Mean parasite load as a function of time as the reproduction number  $\mathcal{R}_0$  changes from just above unity to just below unity. Parameters are chosen as in Section 5 with  $L_h = 800$ .

**Remark 5.4.** *The proof of Theorem 4.2 can also be done by analyzing the Jacobian matrix  $J_6(E_{DFE})$  of System (6) given by*

$$\begin{pmatrix} -(b_h - \mu_{h0}) & -\alpha L_h & 0 & 0 \\ 0 & -(b_h + \mu_p + \alpha + r) & -\zeta\beta & \zeta\beta \\ 0 & -\rho b_p L_h L_s & -(b_s - \mu_{s0}) & -(b_s - \mu_{s0}) \\ 0 & 0 & (b_s + d_s) & -(b_s - \mu_{s0}) - (b_s + d_s) \end{pmatrix}.$$

*The characteristic polynomial of the above Jacobian is*

$$\begin{aligned} f(\lambda) = & (\lambda + b_h - \mu_{h0}) \{ \lambda^3 + [b_h + \mu_p + \alpha + r + b_s - \mu_{s0} + (b_s + d_s)]\lambda^2 \\ & + [(b_s - \mu_{s0} + b_s + d_s)(b_h + \mu_p + \alpha + r) + (b_s - \mu_{s0})(b_s + d_s) - \rho b_p L_h L_s \zeta\beta]\lambda \\ & + (b_s - \mu_{s0})[(b_s + d_s)(b_h + \mu_p + \alpha + r) - \rho b_p L_h L_s \zeta\beta] \}. \end{aligned}$$

*The Routh-Hurwitz criterion can be used to see that  $\mathcal{R}_0 < 1$  implies that all roots of this polynomial have negative real part, and also that  $\mathcal{R}_0 > 1$  implies that at least one of its roots has positive real part. We want to stress, though, that this process is much more cumbersome than the one presented in the proof of Theorem 4.2 for the Jacobian matrix of System (5).*

In previous section, we have shown that the System (5) and System (6) may have multiple positive equilibria. Even though we can write explicit expressions for all the interior equilibria and their corresponding Jacobian matrices in terms of the model parameters, it seems hopeless to be able to study analytically the stability of these equilibria through the roots of their characteristic polynomials. Instead, based on the results of many numerical experiments, we make the following conjecture that amounts to a bifurcation diagram in terms of the parameters  $r$  and  $L_h = -a_2$ . Let  $\tilde{r}$  be the unique positive value of  $r$  for which  $\mathcal{R}_0 = 1$  (given in Remark 4.3), and let  $\bar{r}$  and  $\hat{r}$  be the two real roots of  $D(r) = 0$

(that is  $[U(r)]^2 = -Q^3$ ),

$$\begin{aligned}\bar{r} &= -\frac{b_h - \mu_{h0}}{\kappa} + \frac{\mu_{h1}C_0\rho b_p}{\alpha} \left[ -\frac{1}{3}a_1a_2 + \frac{2}{27}a_2^3 - \sqrt{-Q^3} \right] - b_h - \mu_p - \alpha, \\ \hat{r} &= -\frac{b_h - \mu_{h0}}{\kappa} + \frac{\mu_{h1}C_0\rho b_p}{\alpha} \left[ -\frac{1}{3}a_1a_2 + \frac{2}{27}a_2^3 + \sqrt{-Q^3} \right] - b_h - \mu_p - \alpha.\end{aligned}$$

**Conjecture 5.1.** *Let  $H_1 \leq H_2 \leq H_3$  denote the real roots of Eq. (9) and denote by  $(H_i, P_i, S_i, I_i)$  ( $1 \leq i \leq 3$ ) the resulting steady states of System (5).*

- i) If  $Q > 0$  or if  $Q \leq 0$ ,  $U(0) > 0$ , and  $D(0) > 0$ , then for  $r < \bar{r}$  we have  $H_1 = H_2 = H_3$ ,  $(H_1, P_1, S_1, I_1)$  is the only interior equilibrium of (9) and it is globally stable. If  $r > \bar{r}$ , then  $E_{DFE}$  is the only non-trivial equilibrium of (9) and it is globally stable.*
- ii) If  $Q < 0$  and  $D(0) < 0$ , then  $\bar{r} < 0$  and there may exist  $r_{osc} > 0$  such that periodic solutions exist for  $r < r_{osc}$ , three distinct positive equilibria exist for  $r_{osc} < r < \min\{\bar{r}, \hat{r}\}$  with  $(H_1, P_1, S_1, I_1)$  and  $(H_3, P_3, S_3, I_3)$  locally asymptotically stable and  $(H_2, P_2, S_2, I_2)$  unstable, while  $(H_1, P_1, S_1, I_1)$  is the only positive equilibrium for  $\hat{r} < r < \bar{r}$  and it is globally stable; finally, for  $r > \bar{r}$   $E_{DFE}$  is globally stable.*
- iii) If  $Q < 0$ ,  $U(0) < 0$ , and  $D(0) > 0$ , then for  $0 \leq r < \bar{r}$  we have  $H_1 = H_2 = H_3$ ,  $(H_1, P_1, S_1, I_1)$  is the only interior equilibrium of (9) and it is globally stable; for  $\bar{r} < r < \min\{\bar{r}, \hat{r}\}$  three distinct positive equilibria exist with  $(H_1, P_1, S_1, I_1)$  and  $(H_3, P_3, S_3, I_3)$  locally asymptotically stable and  $(H_2, P_2, S_2, I_2)$  unstable; for  $\hat{r} < r < \bar{r}$   $(H_1, P_1, S_1, I_1)$  is the only positive equilibrium and it is globally stable; finally, for  $r > \bar{r}$   $E_{DFE}$  is globally stable.*

Figure 2 shows the parameter regions resulting from Conjecture 5.1 in terms of the number and stability of positive equilibria for  $r > 0$  and  $L_h > 0$  while the other biological and demographic parameters are chosen based on the estimates found in [9, 11]. We choose  $\mu_{h0} = 1/70$  (average life span of a human being is 70 years),  $b_h = 3/140$ , (then Malthusian parameter of human beings is  $b_h - \mu_{h0} = 1/140$ ),  $\beta = 4000$ ,  $\alpha = 0.00001$ ,  $\zeta = 0.000027$ ,  $\kappa = 0.243$ ,  $\mu_p = 0.2$  (average life span of a parasite is 5 years),  $\mu_{s0} = 0.5$  (average life span of a snail is 2 years),  $b_s = 80$  (then Malthusian parameter of snails is  $b_s - \mu_{s0} = 79.5$ ),  $L_s = 20000$ ,  $\rho = 0.00004$ ,  $d_s = 6.0$ ,  $b_p = 20$ .

In region I we have  $\mathcal{R}_0 < 1$ , there is no positive equilibrium, and  $E_{DFE}$  is globally stable; in region II, there is only one positive equilibrium and it is globally stable ( $E_{DFE}$  is unstable); in region III, there are three positive equilibria and those corresponding to the largest and the smallest root of Eq. (9) are locally asymptotically stable, while that corresponding to middle root together with  $E_{DFE}$  are unstable; in region IV, there are also three positive equilibria but those corresponding to two consecutive roots of Eq. (9) are unstable and,

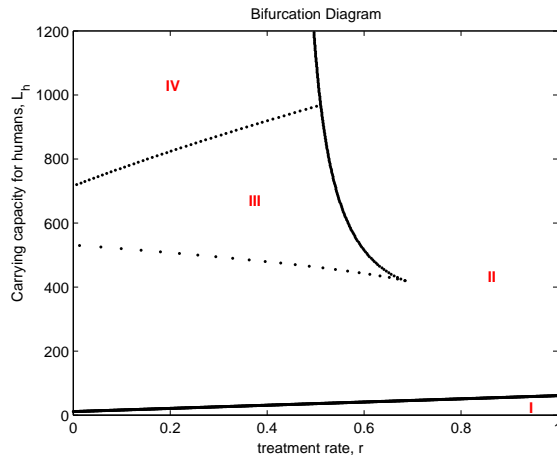


Figure 2: Regions with different numbers of equilibria or stability changes.

therefore, oscillatory solutions may happen. Numerical simulations show that periodic solutions do indeed occur.

We show next in Figures 3 and 4 the existence of periodic solutions for System (5) through numerical simulations.

## 6 Discussion and Conclusions

Castration in *Biomphalaria glabrata* infected by *Schistosoma mansoni* has been documented in many papers [17, 25, 24, 12]. Human infection by *Schistosoma mansoni* still prevails as a big threat to health care in developing countries [23]. As a matter of fact, chemoprophylaxis using Praziquantel, Oxamniquine, and Artemeter are among the best solutions to control schistosomiasis due to lack of a vaccine and the negative effect to the environment through aquatic modification [23] or the use of molluscicides. Since there is not too much we can do to limit the prevalence of snails, the best course of action seems to treat people who are already infected and to prevent new people from acquiring infection in highly endemic areas. Classical models of schistosomiasis [2, 3, 17, 20, 21, 22, 7] do not consider the medical interaction into the dynamic system of schistosomiasis. We have considered treatment in our modeling in order to make more accurate prediction and possible suggestions. The discrepancy in reproduction of susceptible and infected snails as well as the effective medical treatment in the endemic areas of schistosomiasis introduced in our model are quite necessary since they impact the dynamics of the system.

In contrast with the model of Feng and Milner [10], the starting demographic point is logistic growth for both human and snail hosts instead of exponential

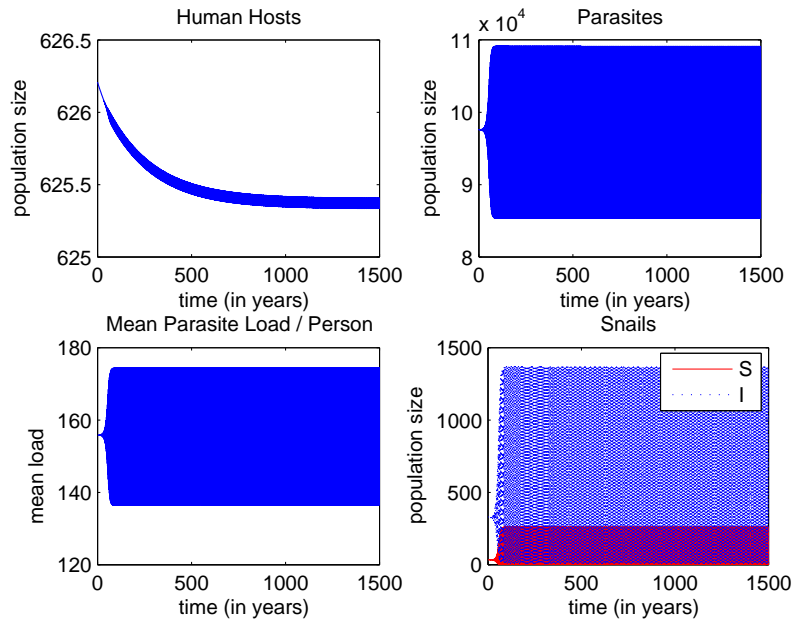


Figure 3: Periodic solution corresponding to  $L_h = 800$  and  $r = 0$ .

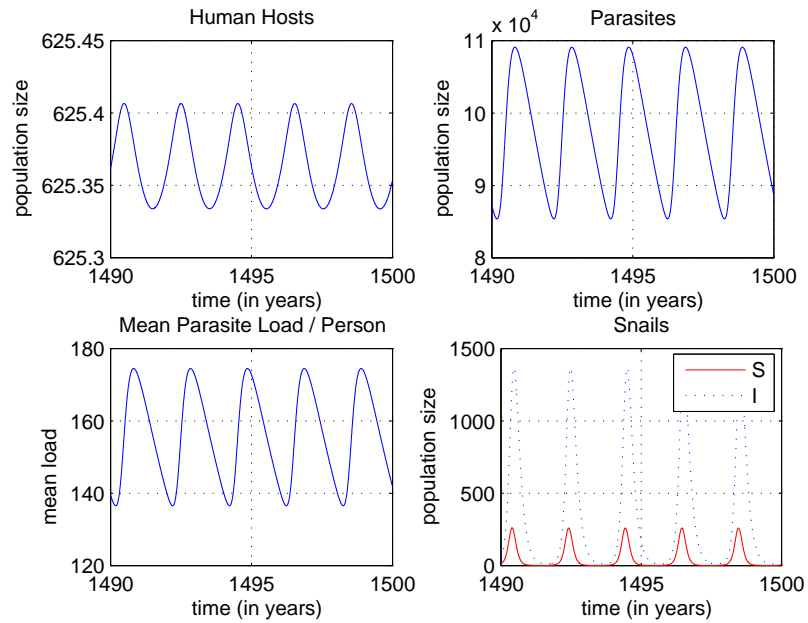


Figure 4: Short-time depiction of periodic solution with  $L_h = 800$  and  $r = 0$ .

growth of humans. An important epidemiological consequence is that in our model the mean parasite load at equilibrium is not a priori independent of the treatment rate as it is in [10]. Of course, effective treatment should lead to a reduction of that mean, not just to a redistribution of parasites among the hosts. A precise carrying capacity of any species is hard to get in the real world, but we can assign a number that is large enough in practice. Moreover, we can assume that the human hosts have reached to late phase of logistic growth now and an approximation of carrying capacity can be found by fitting the data surveyed for an interested area. Another important modification to the model of Feng and Milner's [10] is the way we treat the extra mortality of snails due to the schistosome infection. The natural death rates are same for susceptible and infected snails. Mathematical richness of our model is enhanced in the way that the system may have more than one local endemic equilibria. Unfortunately, no field observation of such phenomena was ever reported and it is impossible to check in reality. The multiple endemic equilibria may be artificial and due to the chosen system of differential equations. However, their number and stability are determined by the parameters and these parameters lie in certain ranges which has been estimated and reported by several authors [9, 11]. Thus, we can make some good estimates of the dynamics of the real-life system.

Even though we do not have a analytical proof, numerical simulations show that the mean parasite load is a decreasing function of the effective treatment rate  $r$ , even for small values of  $r$ , which is a desirable property in view of the high efficacy of Praziquantel. Moreover, the reproduction number  $\mathcal{R}_0$  is a decreasing function of  $r$ , and this shows that infection could be finally eradicated with a sufficiently large treatment rate. Numerical simulations suggest that the dynamics may naturally show oscillatory behavior. With the epidemiological parameters chosen in a realistic range we observed that for a small population of approximately 625 humans in an environment with a carrying capacity of 800, there is a periodic limit cycle with a period of approximately 2 years and the peaks of the uninfected snail population approximately 4 months ahead of those of the parasite population, with those for infected snails and for humans lying in between these. The oscillations are driven by a disproportionately high snail population peaking at 1600 with 1300 infected snails that is almost driven to extinction by the overwhelming presence of parasites but then recovers. This property is an artifact of deterministic models and it would be interesting to see whether periodic solutions also exist with all populations staying bounded well away from zero.

Our model itself is just an attempt to mimic the real situation as much as possible. There are other factors playing important roles in spreading and control of schistosomiasis, and there are mathematical and laboratory works done related to these factors, such as the inclusion of age of hosts [11, 28], spatial distribution of hosts and parasites [18], different species of schistosomes [24, 26], drug resistance of schistosomes [23]. The model presented in this paper tells us that the parasitism can be controlled if there is sufficient treatment of infected individuals and any treatment will reduce mean parasite load. Moreover, it can be eradicated if the effective treatment rate is large enough,  $r > \tilde{r}$ . This is

a positive message for public health officials in affected areas, who should be encouraged to attempt reaching such treatment rates.

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