

# A THEORETICAL STUDY ON SCHISTOSOMIASIS INFECTION MODEL : APPLICATION OF BIOLOGICAL OPTIMAL CONTROL

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**Abstract** A general mathematical model for schistosomiasis is formulated that incorporates the miracidia and cercariae dynamics, since parasites play an important role in the transmission dynamics of schistosomiasis. This model is an extension of the study undertaken in Diaby etc [6] concerning the evolution of a schistosomiasis infection. Meanwhile, optimal control theory is applied to the proposed model. In the first part of our analysis we describe and propose a complete mathematical analysis of a new mathematical model for schistosomiasis infection with fixed control for both drug and biological treatment. It also includes a net inflow of competitor snails into the aquatic region at the rate  $u$  per unit of time as control term. Schistosomiasis is associated with water resource development such as dams and irrigation schemes, where the snail is the intermediate host of the parasite breeds. The snail intermediate host breeds in slow-flowing or stagnant water. We establish a deterministic model to explore the role of biological control strategy. We derive the basic reproduction number  $\mathcal{R}_0$  and establish that the global dynamics are completely determined by the values of  $\mathcal{R}_0$ . It is shown that the disease can be eradicated when  $\mathcal{R}_0 \leq 1$ . In the case where  $\mathcal{R}_0 > 1$ , we prove the existence, uniqueness and global asymptotic stability of an endemic equilibrium. We also show how the control  $u$  can be chosen in order to eradicate the disease. In the second part, we take the controls as time dependent and obtain the optimal control strategy to minimize both infected humans and snails populations. All the analytical results are verified by simulation works. Some important conclusions are given at the end of the paper.

**Keywords** Schistosomiasis model, stability analysis, basic reproduction number, optimal control.

**MSC(2010)** 34D23, 37M05, 49K15.

## 1. Introduction

Schistosomiasis is a chronic, parasitic disease caused by blood flukes (trematode worms) of the genus schistosoma. More than 229 million people required preventive treatment in 2018, with an estimated 2290.8 million people at risk in 78 endemic

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countries [26]. Schistosomiasis is prevalent in tropical and subtropical areas, especially among poor communities without access to safe drinking water and adequate sanitation. Of the people with schistosomiasis, 90% lives in Africa [26]. Schistosomiasis continues to be a significant public health threat in the world. In the area of parasitic disease, it is widely considered second only to malaria as a health problem, with an incalculable drain on the economy [26]. Therefore, it is an important and urgent task to prevent and control the schistosoma infection. Schistosomes rely on an intermediate host (snails in most cases) to complete their life cycle: they pass the egg stage to miracidia and then to cercariae stage to finally become adult flukes. Unlike direct parasites as hookworms, schistosomes have two stages of reproduction: sexual reproduction in humans and asexual amplification in snails.

In fact, eggs passed in the feces must be deposited in water if they are to hatch and release miracidia, which invade suitable water snails and develop through primary and secondary sporocysts to become cercariae. When the cercariae fully develop, they leave the snail and swim freely in the water, where they stay alive for several hours. Ruminants are generally infected when cercariae penetrate the skin, although it has been shown that infection can be acquired orally when drinking. During penetration, cercariae become schistosomula, which are transported via the lymph and blood to their favorite sites.

Dynamical behavior of schistosomiasis infection models have been investigated by many researchers since the first paper by MacDonald [18] in 1965. Numerous subsequent studies have been done to provide a better understanding of the schistosomiasis control and transmission process (see Anderson and May [2, 3], Chiyaka etc [5], Kalinda etc [13], Guiro etc [9], Zhang etc [27], Liu etc [17], Diaby etc [6], Qi etc [20], Li etc [16], Ding etc [7]).

In [1], a mathematical model for a schistosomiasis infection based on a simplified life cycle of the parasite is developed. The model involves human and intermediate snail hosts, as well as an additional mammalian host and a competitor snail species. In fact, in [4] (1980), researchers reported schistosomiasis infection in wild rats and mice and it is well known that *Thiara granifera* is a snail which competes with the intermediate host snail of schistosomes *Biomphalaria glabrata* (see [1]). Moreover, in [1], values for the parameters in the model are estimated. Results of the simulations indicate that invading competing snail species can change the dynamics of a schistosomiasis infection. Diaby etc [6] have studied the deterministic model developed by Allen and Victory [1] and have established threshold conditions to discuss the effectiveness of the biological control. The authors also dealt with the global stability of the equilibria of the deterministic model.

However, the built model in [1] is based on simplifications of the complicated indirect-cycle dynamics of schistosomiasis. In fact, the life cycle of schistosomes consists of adults in human hosts and different larval forms assumed by the parasite in aquatic snails, and it is more realistic to adequately incorporate these stages in the mathematical modeling.

Schistosomiasis is considered to be a complex disease involving two different types of host (molluscs, mammalian), at least five different stages of parasite development (egg, miracidium, mother spore, cercaria, adult) and two different periods of reproduction (within the mammal and within the snail). Indeed, mathematical study of schistosomiasis model is so complicated that models like Allen's [1] have taken only certain aspects of the disease by omitting the stage of parasite development that is essential in its life cycle.

In this paper, our model is a natural extension of those in [1] and [6], in which improvement relates to the cercariae and the miracidia dynamics modeling. In this sense, this new model can aid in designing control strategy like the reduction in worm burden. In addition, it also includes a net inflow of competitor snails into aquatic region at the rate  $u$  per unit time as control term. We divide the population into humans (including uninfected and infected humans), host snails (including uninfected, latent and infected snails), mammals (including uninfected and infected mammals), as well as the cercariae and the miracidia.

A mathematical model is derived that describes the interaction between the different populations. One of our purposes is to propose a complete mathematical analysis of that deterministic model, to analyze how the biological control can be effective and then to determine the potential impact of the introduction of the dynamics of cercariae and miracidia. Among others we will show that miracidia and cercariae elimination is better than cure for controlling the infection.

This paper is organized as follows. We analyze the dynamics of the model with constant controls in the next section 2 and establish conditions for global asymptotic stability of the disease free equilibrium and the endemic equilibrium by using the Krasnoselskii sub-linearity tricks and the theory of  $K$ -monotone systems. In Section 3 some discussions are given about our theoretical results. Section 4 is devoted to the optimal control of the system with time dependent controls and simulations on optimal control are given in Section 5. Finally, we present some discussions and conclusions in Section 6. To be self-contained, we collect a brief theoretical background material that helped us to analyze our model in Appendix A.

## 2. Analysis of the systems for fixed controls

### 2.1. Model and preliminaries

In this section we present basic facts on the biological control strategy on the life cycle of the schistosome parasite. In what follows we describe a dynamical model for schistosomiasis derived from the model of [1] and based on biological assumptions and on the available data in [1].

We divide the human population, snail population and a second mammalian host into subgroups in respect to the infection status: four definite mammalian host sub-populations, three intermediate snail host sub-populations, a population of resistant competitor snails, cercariae and miracidia populations are also considered.

It is assumed that infected snails and infected mammals do not recover from schistosomiasis as their life span are short in comparison to that for humans and also, that infected mammal has the same contribution as an infected individual for the simplicity of the model. In addition, the population of snails as well as mammals are assumed to be competitive. We denote by  $b_i$  and  $d_i$  the natural birth and death rate of the various sub-populations respectively.

For an infected human, eggs leave the body and hatch into miracidia at the rate  $\gamma_m$  into the fresh water, and the infected snails release cercariae at the rate  $\gamma_p$ .

The dynamical compartments of the model are:

- $H_s(t)$  : the susceptible (uninfected) human population size,  
 $H_i(t)$  : the infected human population size,  
 $P_m(t)$  : the miracidia population size,  
 $S_s(t)$  : the susceptible snail host population size,  
 $S_e(t)$  : the population size of the infected snails which are not yet shedding cercariae,  
 $S_i(t)$  : the infected and shedding snail population size (shedding population size),  
 $S_{rc}(t)$  : the competitor snail population size (resistant to infection),  
 $M_s(t)$  : the susceptible mammal population size,  
 $M_i(t)$  : the infected mammal population size,  
 $P_c(t)$  : the cercariae population size.

The transmission parameters for the model are:

- $t_{110}$  := Composite parameter being the rate at which a susceptible human becomes infected with cercariae released by the snails,  
 $t_{39}$  := The rate at which miracidia causes potentially successful penetration into to susceptible snail,  
 $t_{710}$  := Composite parameter being the rate at which a susceptible mammal becomes infected with cercariae released by the snails.

Competition parameters are defined for the populations:

- $c_{33}$  is the competition parameter between  $S_s$  and  $S_s, S_e, S_i$ ,  
 $c_{44}$  and  $c_{55}$  are the competition parameters between  $S_e$  and  $S_i$ , respectively, and  $S_s$ ,  
 $S_e$ , and  $S_i$ ,  
 $c_{36}$  is the competition parameter for snails  $S_{rc}$  with snails  $S_s$ ,  
 $c_{46}$  and  $c_{56}$  are defined analogously,  
 $c_{64}$  is the competition parameter for snails  $S_s, S_e$  and  $S_i$  with  $S_{rc}$ ,  
 $c_{66}$  is the competition parameter for  $S_{rc}$  with  $S_{rc}$ ,  
 $c_{77}$  and  $c_{88}$  are the competition parameter for the mammals populations.

Also,  $r_{12}$  the rate that infected humans recover (both natural and treatment recovery) and

- $r_{54}$  denotes the rate that the latent snail population  $S_e$  becomes shedding  $S_i$ .

The following system of equations relate the evolution of various populations :

$$\left\{ \begin{array}{l} \frac{dH_s}{dt} = -t_{110} P_c H_s + r_{12} H_i; \\ \frac{dH_i}{dt} = t_{110} P_c H_s - r_{12} H_i; \\ \frac{dS_s}{dt} = b_3 (S_s + S_e + S_i) - t_{39} P_m S_s - d_3 S_s - c_{33} S_s (S_s + S_e + S_i) - c_{36} S_s S_{rc}; \\ \frac{dS_e}{dt} = t_{39} P_m S_s - d_4 S_e - c_{44} S_e (S_s + S_e + S_i) - c_{46} S_e S_{rc} - r_{54} S_e; \\ \frac{dS_i}{dt} = r_{54} S_e - d_5 S_i - c_{55} S_i (S_s + S_e + S_i) - c_{56} S_i S_{rc}; \\ \frac{dS_{rc}}{dt} = u + b_6 S_{rc} - c_{64} S_{rc} (S_s + S_e + S_i) - c_{66} S_{rc}^2 - d_6 S_{rc}; \\ \frac{dM_s}{dt} = b_7 (M_s + M_i) - t_{710} P_c M_s - c_{77} M_s (M_s + M_i) - d_7 M_s; \\ \frac{dM_i}{dt} = t_{710} P_c M_s - d_8 M_i - c_{88} M_i (M_s + M_i); \\ \frac{dP_m}{dt} = \gamma_m (H_i + M_i) - d_9 P_m; \\ \frac{dP_c}{dt} = \gamma_p S_i - d_{10} P_c; \end{array} \right. \quad (2.1)$$

the real number  $u \geq 0$  represents the rate of an external inflow of the competitor snail population and it is considered as a control term.

It is assumed for simplicity that  $c_{33} = c_{44} = c_{55}$ ,  $c_{77} = c_{88}$  and  $c_{46} = c_{56} = c_{36}$ . Furthermore, the death rate of different sub-populations of mammals and intermediate host snails will be assumed to be equal, i.e  $d_3 = d_4 = d_5$  and  $d_7 = d_8$ . We shall assume that, for each subpopulation, the death rate  $d_i$  is less than the birth rate  $b_i$ , that is  $d_i < b_i$ , and we shall use the notation

$$a_i = b_i - d_i.$$

The total population of humans ( $H_s + H_i$ ) is constant and denoted by  $N_H$ . The total mammal population is  $N_M = M_s + M_i$  and it satisfies the equation

$$\frac{dN_M}{dt} = (b_7 - d_7) N_M - c_{77} N_M^2 = \left( \frac{a_7}{c_{77}} - N_M \right) c_{77} N_M.$$

The total no resistant snails population is denoted  $N_{S_i} = S_s + S_e + S_i$ . Its time-evolution is governed by

$$\frac{dN_{S_i}}{dt} = (b_3 - d_3) N_{S_i} - c_{33} N_{S_i}^2 - c_{36} S_{rc} N_{S_i}.$$

It follows that

$$\frac{dN_{S_i}}{dt} \leq (b_3 - d_3) N_{S_i} - c_{33} N_{S_i}^2 = \left( \frac{a_3}{c_{33}} - N_{S_i} \right) c_{33} N_{S_i}.$$

We also have

$$\frac{dS_{rc}}{dt} = u + (b_6 - d_6) S_{rc} - c_{66} S_{rc}^2 - c_{64} S_{rc} (S_s + S_e + S_i) \leq u + \left( \frac{a_6}{c_{66}} - S_{rc} \right) c_{66} S_{rc}.$$

Thus, for a given control  $u$ , the feasible region for the system 2.1 is

$$\begin{aligned} \mathcal{D} = \{ & (H_s, H_i, S_s, S_e, S_i, P_m, P_c, S_{rc}, M_s, M_i) \in \mathbb{R}_+^{10} : \\ & H_s + H_i = N_H, N_{S_i} \leq \frac{a_3}{c_{33}}, N_M \leq \frac{a_7}{c_{77}}, S_{rc} \leq \frac{a_6 + \sqrt{a_6^2 + 4c_{66}u}}{2c_{66}}, P_c \leq \frac{\gamma_p N_{S_i}}{d_{10}}, \\ & P_m \leq \frac{\gamma_m (N_H + N_M)}{d_9} \}. \end{aligned}$$

In Appendix B, we prove the following proposition.

**Proposition 2.1.** *The compact set  $\mathcal{D}$  is a positively invariant and attracting set for system 2.1.*

Thanks to Proposition 2.1, it is sufficient to study the system on the compact set  $\mathcal{D}$ .

## 2.2. Reduction model

To derive the dynamical properties of the model, we shall use the variables  $N_{S_i}$  and  $N_M$  instead of  $S_s$  and  $M_s$  since  $S_s = N_{S_i} - S_e - S_i$  and  $M_s = N_M - M_i$ . Moreover we can skip the equation of  $H_s$  since  $H_s = N_H - H_i$  and  $N_H$  is assumed to be constant.

Using the assumptions on the parameters:  $c_{44} = c_{55} = c_{33}$ ,  $c_{46} = c_{56} = c_{36}$ ,  $c_{88} = c_{77}$ ,  $d_4 = d_5 = d_3$ , and  $d_8 = d_7$ , we get the following equivalent differential system:

$$\left\{ \begin{aligned} \frac{dH_i}{dt} &= t_{110} (N_H - H_i) P_c - r_{12} H_i, \\ \frac{dS_e}{dt} &= t_{39} P_m (N_{S_i} - S_e - S_i) - S_e (c_{33} N_{S_i} + c_{36} S_{rc} + r_{54} + d_3), \\ \frac{dS_i}{dt} &= r_{54} S_e - S_i (c_{33} N_{S_i} + c_{36} S_{rc} + d_3), \\ \frac{dM_i}{dt} &= t_{710} P_c (N_M - M_i) - M_i (c_{77} N_M + d_7), \\ \frac{dP_m}{dt} &= \gamma_m (H_i + M_i N_M) - d_9 P_m, \\ \frac{dP_c}{dt} &= \gamma_p N_{S_i} S_i - d_{10} P_c, \\ \frac{dS_{rc}}{dt} &= u + a_6 S_{rc} - c_{64} S_{rc} N_{S_i} - c_{66} S_{rc}^2 = F_2(N_{S_i}, S_{rc}), \\ \frac{dN_{S_i}}{dt} &= a_3 N_{S_i} - c_{33} N_{S_i}^2 - c_{36} S_{rc} N_{S_i} = F_1(N_{S_i}, S_{rc}), \\ \frac{dN_M}{dt} &= a_7 N_M - c_{77} N_M^2. \end{aligned} \right. \quad (2.2)$$

The last three equations do not depend on the variables  $H_i$ ,  $P_c$ ,  $P_m$ ,  $S_e$ ,  $S_i$ ,  $M_i$ .

We will then first study the following sub-system:

$$\begin{cases} \frac{dN_{Si}}{dt} = a_3 N_{Si} - c_{33} N_{Si}^2 - c_{36} S_{rc} N_{Si} = F_1(N_{Si}, S_{rc}); \\ \frac{dS_{rc}}{dt} = u + a_6 S_{rc} - c_{64} S_{rc} N_{Si} - c_{66} S_{rc}^2 = F_2(N_{Si}, S_{rc}); \\ \frac{dN_M}{dt} = a_7 N_M - c_{77} N_M^2; \end{cases} \quad (2.3)$$

### 2.3. Equilibria of system (2.3)

The equilibria of system (2.3) are: the trivial equilibrium  $(0, 0, 0)$ , two boundary equilibria ( $E_1$  and  $E_2$ ), and two possible interior equilibria  $E^*$  and  $E^{**}$ . The coordinates of these possible equilibria are:

$$E_1 = \left( \frac{a_3}{c_{33}}, 0, \frac{a_7}{c_{77}} \right) \text{ exists only when } u = 0, \quad E_2 = \left( 0, \frac{a_6 + \sqrt{a_6^2 + 4c_{66}u}}{2c_{66}}, \frac{a_7}{c_{77}} \right),$$

$$E^* = (N_{Si}^*, S_{rc}^*, N_M^*), \text{ and } E^{**} = (N_{Si}^{**}, S_{rc}^{**}, N_M^{**}) \text{ with}$$

$$\begin{cases} N_{Si}^* = \frac{2a_3c_{33}c_{66} - a_3c_{36}c_{64} - a_6c_{33}c_{36} - c_{36}\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2c_{33}(c_{33}c_{66} - c_{36}c_{64})}, \\ S_{rc}^* = \frac{a_6c_{33} - a_3c_{64} + \sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2(c_{33}c_{66} - c_{36}c_{64})}, \\ N_M^* = \frac{a_7}{c_{77}}. \end{cases} \quad (2.4)$$

$$\begin{cases} N_{Si}^{**} = \frac{2a_3c_{33}c_{66} - a_3c_{36}c_{64} - a_6c_{33}c_{36} + c_{36}\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2c_{33}(c_{36}c_{64} - c_{33}c_{66})} \\ = \frac{-2a_3c_{33}c_{66} + a_3c_{36}c_{64} + a_6c_{33}c_{36} - c_{36}\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2c_{33}(c_{33}c_{66} - c_{36}c_{64})}, \\ S_{rc}^{**} = \frac{a_3c_{64} - a_6c_{33} + \sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2(c_{36}c_{64} - c_{33}c_{66})} \\ = \frac{(a_6c_{33} - a_3c_{64}) - \sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2(c_{33}c_{66} - c_{36}c_{64})}, \\ N_M^{**} = \frac{a_7}{c_{77}}. \end{cases} \quad (2.5)$$

Hereafter we shall discuss the possible existence of two positive equilibria  $E^*$  and  $E^{**}$ .

### Existence and positiveness of $E^*$ :

1st case:  $c_{33}c_{66} - c_{36}c_{64} > 0$ :

$$S_{rc}^* = \frac{(a_6c_{33} - a_3c_{64}) \left( 1 + \frac{|a_6c_{33} - a_3c_{64}|}{a_6c_{33} - a_3c_{64}} \sqrt{1 + \frac{4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}{(a_6c_{33} - a_3c_{64})^2}} \right)}{2(c_{33}c_{66} - c_{36}c_{64})}.$$

This shows that  $S_{rc}^*$  is always positive.

$$\begin{aligned} llN_{Si}^* &= \frac{2a_3c_{33}c_{66} - a_3c_{36}c_{64} - a_6c_{33}c_{36} - c_{36}\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2c_{33}(c_{33}c_{66} - c_{36}c_{64})} \\ &= \frac{2c_{33}(a_3c_{66} - a_6c_{36}) + c_{36}(a_6c_{33} - a_3c_{64}) - c_{36}\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2c_{33}(c_{33}c_{66} - c_{36}c_{64})}. \end{aligned} \quad (2.6)$$

So  $N_{Si}^* > 0$  iff

$$\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})} < \frac{2c_{33}(a_3c_{66} - a_6c_{36}) + c_{36}(a_6c_{33} - a_3c_{64})}{c_{36}}$$

iff

$$(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64}) < \left( \frac{2c_{33}(a_3c_{66} - a_6c_{36}) + c_{36}(a_6c_{33} - a_3c_{64})}{c_{36}} \right)^2$$

iff

$$u < \frac{1}{4c_{33}(c_{33}c_{66} - c_{36}c_{64})} \left( \left( \frac{2c_{33}(a_3c_{66} - a_6c_{36}) + c_{36}(a_6c_{33} - a_3c_{64})}{c_{36}} \right)^2 - (a_6c_{33} - a_3c_{64})^2 \right).$$

Hence

$$N_{Si}^* > 0 \text{ iff } u < \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2} \text{ and so, } a_3c_{66} - a_6c_{36} > 0.$$

2nd case:  $c_{33}c_{66} - c_{36}c_{64} < 0$ : In this case  $E^* \in \mathbb{R}^3$  if  $u \leq \frac{(a_6c_{33} - a_3c_{64})^2}{4c_{33}(c_{36}c_{64} - c_{33}c_{66})}$ .

But  $S_{rc}^*$  is always negative. So when  $c_{33}c_{66} - c_{36}c_{64} < 0$ , the equilibrium  $E^*$  does not belong to the positive orthant. Therefore,  $E^* = (N_{Si}^*, S_{rc}^*, N_M^*)$  exists and belongs to the positive orthant iff

$$c_{33}c_{66} - c_{36}c_{64} > 0, a_3c_{66} - a_6c_{36} > 0 \text{ and } u < \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}.$$

### Existence and positiveness of $E^{**}$ :

1st case:  $c_{33}c_{66} - c_{36}c_{64} > 0$ :

$$S_{rc}^{**} = - \frac{(a_3c_{64} - a_6c_{33}) \left( 1 + \frac{|a_3c_{64} - a_6c_{33}|}{a_3c_{64} - a_6c_{33}} \sqrt{1 + \frac{4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}{(a_3c_{64} - a_6c_{33})^2}} \right)}{2(c_{33}c_{66} - c_{36}c_{64})}.$$

This shows that  $S_{rc}^{**}$  is always negative. In this case the equilibrium  $E^{**} = (N_{Si}^{**}, S_{rc}^{**}, N_M^{**}) \in \mathbb{R}^3$ , for  $u > 0$ , but it does not belong to the positive orthant.



2nd case:  $c_{33}c_{66} - c_{36}c_{64} < 0$ :

In this case  $S_{rc}^{**}$  is always positive, and  
 $N_{Si}^{**} > 0$  iff

$$\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})} < \frac{-2c_{33}(a_3c_{66} - a_6c_{36}) - c_{36}(a_6c_{33} - a_3c_{64})}{c_{36}}$$

iff

$$(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64}) < \left( \frac{-2c_{33}(a_3c_{66} - a_6c_{36}) - c_{36}(a_6c_{33} - a_3c_{64})}{c_{36}} \right)^2.$$

Since  $c_{33}c_{66} - c_{36}c_{64} < 0$ , this implies

$$u > \frac{1}{4c_{33}(c_{33}c_{66} - c_{36}c_{64})} \left( \left( \frac{-2c_{33}(a_3c_{66} - a_6c_{36}) - c_{36}(a_6c_{33} - a_3c_{64})}{c_{36}} \right)^2 - (a_6c_{33} - a_3c_{64})^2 \right).$$

Hence

$$N_{Si}^{**} > 0 \text{ iff } u > \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}.$$

Therefore,  $E^{**} = (N_{Si}^{**}, S_{rc}^{**}, N_M^{**})$  exists and belongs to the positive orthant iff

$$c_{33}c_{66} - c_{36}c_{64} < 0, \text{ and}$$

$$\frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2} < u < \frac{(a_6c_{33} - a_3c_{64})^2}{4c_{33}(c_{36}c_{64} - c_{33}c_{66})}.$$

The existence conditions for the interior equilibria can then be summarized as follows:

**Proposition 2.2.** *The coexistence of two interior equilibria  $E^{**}$  and  $E^*$  can not hold: if  $c_{33}c_{66} - c_{36}c_{64} < 0$  then the unique positive equilibrium is  $E^{**} = (N_{Si}^{**}, S_{rc}^{**}, N_M^{**})$  with this following additional requirement  $\frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2} < u < \frac{(a_6c_{33} - a_3c_{64})^2}{4c_{33}(c_{36}c_{64} - c_{33}c_{66})}$ . Else, the unique positive equilibrium is  $E^* = (N_{Si}^*, S_{rc}^*, N_M^*)$  under conditions  $a_3c_{66} - a_6c_{36} > 0$  and  $u < \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}$ .*

## 2.4. Stability of the equilibria of system (2.3)

The trivial equilibrium  $(0, 0, 0)$  is unstable (US): three positive eigenvalues  $a_3$ ,  $a_6$ , and  $a_7$ .

$$E_1 = \left( \frac{a_3}{c_{33}}, 0, \frac{a_7}{c_{77}} \right) \text{ is associated to eigenvalues } -a_3, -a_7, \text{ and } a_6 - \frac{a_3c_{64}}{c_{33}} = \frac{a_6c_{33} - a_3c_{64}}{c_{33}}.$$

Hence, when it exists (i.e., for  $u = 0$ ), it is asymptotically stable (AS) iff  $a_6c_{33} - a_3c_{64} < 0$ .

$$E_2 = \left( 0, \frac{a_6 + \sqrt{a_6^2 + 4c_{66}u}}{2c_{66}}, \frac{a_7}{c_{77}} \right) \text{ is associated with two negative eigenvalues } -\sqrt{a_6^2 + 4c_{66}u}, -a_7, \text{ and a third eigenvalue } \lambda_{E_2} = a_3 - \frac{c_{36}(a_6 + \sqrt{a_6^2 + 4c_{66}u})}{2c_{66}} = \frac{2a_3c_{66} - c_{36}(a_6 + \sqrt{a_6^2 + 4c_{66}u})}{2c_{66}}.$$

It can be shown that the equilibrium  $E_2$  is asymptotically stable ( $\lambda_{E_2} < 0$ ) iff

$$a_6 c_{33} - a_3 c_{64} < 0 \quad \text{or} \quad u > \frac{a_3(a_3 c_{66} - a_6 c_{36})}{c_{36}^2}.$$

Moreover using the Poincaré-Bendixson theorem on  $\Gamma = [0, \frac{b_3 - d_3}{c_{33}}] \times [0, \frac{b_6 - d_6}{c_{66}}]$  one can prove the global stability of  $E_2$  iff  $a_6 c_{33} - a_3 c_{64} < 0$  or  $u > \frac{a_3(a_3 c_{66} - a_6 c_{36})}{c_{36}^2}$ .

Let  $\rho(N_{Si}, S_{rc}) = \frac{1}{N_{Si} S_{rc}}$  defined on  $\Gamma_1 = ]0, \frac{b_3 - d_3}{c_{33}}[ \times ]0, \frac{b_6 - d_6}{c_{66}}[$ .

We have  $\frac{\partial(\rho F_1)}{\partial N_{Si}} + \frac{\partial(\rho F_2)}{\partial S_{rc}} = -\left(\frac{c_{33}}{S_{rc}} + \frac{c_{66}}{N_{Si}} + \frac{u}{N_{Si} S_{rc}^2}\right) < 0$ .

By Dulac criterion, we conclude that there is no periodic orbit for the system (2.3) lying entirely in  $\Gamma_1$ . The set  $\Gamma \setminus \Gamma_1$  can not contain a periodic since it is just the union of two segments.

Therefore there are no periodic orbits in  $\Gamma$ .

Because of the local stability of the equilibrium  $E_2$  for  $a_6 c_{33} - a_3 c_{64} < 0$  or  $u > \frac{a_3(a_3 c_{66} - a_6 c_{36})}{c_{36}^2}$ , the equilibrium  $E_2$  is globally asymptotically stable (GAS).

It remains to explore the stability of  $E^*$  and  $E^{**}$ . The Jacobian matrix of system (2.3) is given by:

$$J_{(N_{Si}, X_6, N_M)} = \begin{pmatrix} a_3 - 2 c_{33} N_{Si} - c_{36} S_{rc} & -c_{36} N_{Si} & 0 \\ -c_{64} S_{rc} & a_6 - c_{64} N_{Si} - 2 c_{66} S_{rc} & 0 \\ 0 & 0 & a_7 - 2 c_{77} N_M \end{pmatrix}.$$

For all the equilibria, the third coordinate is given by  $N_M^* = \frac{a_7}{c_{77}}$  and is associated with the negative eigenvalue  $-a_7$ . Hence, we only need to study at each equilibrium the  $2 \times 2$  matrix:

$$J_E = \begin{pmatrix} a_3 - 2 c_{33} N_{Si} - c_{36} S_{rc} & -c_{36} N_{Si} \\ -c_{64} S_{rc} & a_6 - c_{64} N_{Si} - 2 c_{66} S_{rc} \end{pmatrix}.$$

1. 1st case:  $c_{33}c_{66} - c_{36}c_{64} > 0$ .

In this case the only positive equilibrium is  $E^* = (N_{Si}^*, S_{rc}^*, N_M^*)$ . We will show that the existence of  $E^*$  implies that  $E^*$  is asymptotically stable (AS) and that  $E_2$  is unstable.

Indeed, the Jacobian at  $E^*$  is

$$J_{E^*} = \begin{pmatrix} a_3 - 2 c_{33} N_{Si}^* - c_{36} S_{rc}^* & -c_{36} N_{Si}^* \\ -c_{64} S_{rc}^* & a_6 - c_{64} N_{Si}^* - 2 c_{66} S_{rc}^* \end{pmatrix}.$$

Using the relations at the equilibria:

$$\begin{cases} a_3 = c_{33} N_{Si}^* + c_{36} S_{rc}^*, \\ a_6 = -u + c_{64} N_{Si}^* + c_{66} S_{rc}^*, \end{cases} \tag{2.7}$$

we obtain

$$\begin{aligned}
\text{Tr}(J_{E^*}) &= a_3 + a_6 - 2c_{33} N_{Si}^* - c_{64} N_{Si}^* - c_{36} S_{rc}^* - 2c_{66} S_{rc}^* \\
&= -c_{33} N_{Si}^* - c_{66} S_{rc}^* - u < 0, \\
\text{Det}(J_{E^*}) &= (a_3 - 2c_{33} N_{Si}^*)(a_6 - c_{64} N_{Si}^*) - (a_6 c_{36} \\
&\quad + 2c_{66} (a_3 - 2c_{33} N_{Si}^*)) S_{rc}^* + 2c_{36} c_{66} S_{rc}^{*2} \\
&= N_{Si}^* (-c_{36} c_{64} S_{rc}^* + c_{33} (u + c_{66} S_{rc}^*)) \\
&= N_{Si}^* ((c_{33} c_{66} - c_{36} c_{64}) S_{rc}^* + c_{33} u).
\end{aligned}$$

So  $\text{Det}(J_{E^*}) > 0$  since  $c_{33} c_{66} - c_{36} c_{64} > 0$  and  $u \geq 0$ .

Moreover, in this case  $E_2$  is unstable since

$$\begin{aligned}
2c_{66} \lambda_{E_2} &= 2a_3 c_{66} - c_{36} \left( a_6 + \sqrt{a_6^2 + 4c_{66} u} \right) \\
&> 2a_3 c_{66} - c_{36} \left( a_6 + \sqrt{a_6^2 + 4c_{66} \frac{a_3(a_3 c_{66} - a_6 c_{36})}{c_{36}^2}} \right) \\
&\text{since } u < \frac{a_3(a_3 c_{66} - a_6 c_{36})}{c_{36}^2} \\
&> 2a_3 c_{66} - c_{36} a_6 - \sqrt{c_{36}^2 a_6^2 + 4c_{66} a_3(a_3 c_{66} - a_6 c_{36})} \\
&> 2a_3 c_{66} - c_{36} a_6 - \sqrt{(2c_{66} a_3 - c_{36} a_6)^2} = 0 \\
&\text{since } a_3 c_{66} - a_6 c_{36} > 0.
\end{aligned}$$

Hence  $\lambda_{E_2} > 0$ .

2. 2nd case:  $c_{33} c_{66} - c_{36} c_{64} < 0$ .

In this case the only positive equilibrium is  $E^{**}$ .

The boundary equilibrium  $E_1$  is AS when it exists, i.e., when  $u = 0$ . Indeed,  $c_{33} c_{66} - c_{36} c_{64} < 0$  and  $a_3 c_{66} - a_6 c_{36} > 0$  imply that  $a_6 c_{33} - a_3 c_{64} < 0$ . Hence, if moreover  $u = 0$  then  $E_1$  is AS.

The second boundary equilibrium  $E_2$  is stable since

$$\lambda_{E_2} < 2a_3 c_{66} - c_{36} a_6 - \sqrt{(2c_{66} a_3 - c_{36} a_6)^2} = 0.$$

We have

$$\begin{aligned}
\text{Det}(J_{E^{**}}) &= N_{Si}^{**} ((c_{33} c_{66} - c_{36} c_{64}) S_{rc}^{**} + c_{33} u) > 0 \\
&\Leftrightarrow (c_{33} c_{66} - c_{36} c_{64}) S_{rc}^{**} + c_{33} u > 0 \\
&\Leftrightarrow a_6 c_{33} - a_3 c_{64} + 2c_{33} u - \sqrt{(a_6 c_{33} - a_3 c_{64})^2 + 4c_{33} (-c_{36} c_{64} + c_{33} c_{66})} u > 0 \\
&\Leftrightarrow u > \frac{a_3 c_{64} - a_6 c_{33} + c_{33} c_{66} - c_{36} c_{64}}{c_{33}}.
\end{aligned}$$

Hence,  $E^{**}$  is AS iff  $c_{33}c_{66} - c_{36}c_{64} < 0$ , and

$$u_m := \max \left\{ \frac{a_3 (a_3 c_{66} - a_6 c_{36})}{c_{36}^2}, \frac{a_3 c_{64} - a_6 c_{33} + c_{33} c_{66} - c_{36} c_{64}}{c_{33}} \right\}$$

$$< u < \frac{(a_6 c_{33} - a_3 c_{64})^2}{4 c_{33} (c_{36} c_{64} - c_{33} c_{66})}.$$

The existence and stability of different equilibria are summarized in the following table 1.

We shall assume that  $E_1$  and  $E_2$  are unstable which implies that

$$a_6 c_{33} - a_3 c_{64} > 0 \quad \text{and} \quad a_3 c_{66} - a_6 c_{36} > 0 \quad \text{and} \quad u < \frac{a_3 (a_3 c_{66} - a_6 c_{36})}{c_{36}^2}. \quad (2.8)$$

This implies

$$c_{33} c_{66} - c_{36} c_{64} > 0, \quad \text{and} \quad u < \frac{a_3 (a_3 c_{66} - a_6 c_{36})}{c_{36}^2}. \quad (2.9)$$

Therefore, with relation (2.9),  $E^*$  is the unique positive equilibrium and it is asymptotically stable: eigenvalues with negative real part.

Let

$$V = (N_{Si} - N_{Si}^* \log N_{Si}) + d (S_{rc} - S_{rc}^* \log S_{rc}).$$

Then

$$\dot{V} = (N_{Si} - N_{Si}^*) (a_3 - c_{33} N_{Si} - c_{36} S_{rc}) + d (S_{rc} - S_{rc}^*) (a_6 + \frac{u}{S_{rc}} - c_{64} N_{Si} - c_{66} S_{rc}).$$

Using equilibria relations, we obtain:

$$\begin{aligned} \dot{V} &= (N_{Si} - N_{Si}^*) (c_{33} N_{Si}^* + c_{36} S_{rc}^* - c_{33} N_{Si} - c_{36} S_{rc}) + d (S_{rc} - S_{rc}^*) (c_{64} N_{Si}^* \\ &\quad + c_{66} S_{rc}^* - c_{64} N_{Si} - c_{66} S_{rc} - \frac{u}{S_{rc}} + \frac{u}{S_{rc}^*}) \\ &= -c_{33} (N_{Si} - N_{Si}^*)^2 - d c_{66} (S_{rc} - S_{rc}^*)^2 - c_{36} (N_{Si} - N_{Si}^*) (S_{rc} - S_{rc}^*) \\ &\quad - d c_{64} (N_{Si} - N_{Si}^*) (S_{rc} - S_{rc}^*) + d u (S_{rc} - S_{rc}^*) (\frac{1}{S_{rc}} - \frac{1}{S_{rc}^*}) \\ &= -c_{33} (N_{Si} - N_{Si}^*)^2 - d c_{66} (S_{rc} - S_{rc}^*)^2 - (c_{36} + d c_{64}) (N_{Si} - N_{Si}^*) (S_{rc} - S_{rc}^*) \\ &\quad + d u (S_{rc} - S_{rc}^*) (\frac{1}{S_{rc}} - \frac{1}{S_{rc}^*}). \end{aligned}$$

We choose  $d = \frac{c_{66} a_3^2}{c_{33} a_6^2}$ . With this and using (2.9) we can show

$$(c_{36} + d c_{64})^2 - 4 d c_{33} c_{66} < 0, \quad (2.10)$$

then  $\dot{V}$  is definite negative and hence the equilibrium  $(N_{Si}^*, S_{rc}^*, N_M^*)$  is GAS (globally asymptotically stable).

Then, under the condition (2.9),  $(N_{Si}^*, S_{rc}^*, N_M^*)$  is GAS.

**Remark.** It is also possible to prove the GAS of  $(N_{Si}^*, S_{rc}^*)$  by using Dulac criterion with the function  $\rho(N_{Si}, S_{rc}) = \frac{1}{N_{Si} S_{rc}}$  defined on  $\Omega = ]0, \frac{b_3 - d_3}{c_{33}}[ \times ]0, \frac{b_6 - d_6}{c_{66}}[$ .

We have  $\frac{\partial(\rho F_1)}{\partial N_{Si}} + \frac{\partial(\rho F_2)}{\partial S_{rc}} = - \left( \frac{c_{33}}{S_{rc}} + \frac{c_{66}}{N_{Si}} + \frac{u}{N_{Si} S_{rc}^2} \right) < 0$ .

Thanks to Theorem A.1 (see Appendix A), we will reduce the stability analysis of (2.1), to the study of a smaller and simpler system.

Therefore, under the assumption (2.9), the stability properties of system (2.2) on the set  $\mathcal{D}$  are the same as those of the following reduced system :

$$\left\{ \begin{array}{l} \frac{dH_i}{dt} = t_{110}(N_H - H_i) P_c - r_{12} H_i, \\ \frac{dS_e}{dt} = t_{39} P_m (N_{Si}^* - S_e - S_i) - S_e(c_{33} N_{Si}^* + c_{36} S_{rc} + r_{54} + d_3), \\ \frac{dS_i}{dt} = r_{54} S_e - S_i (c_{33} N_{Si}^* + c_{36} S_{rc} + d_3), \\ \frac{dM_i}{dt} = t_{710} P_c (N_M^* - M_i) - M_i (c_{77} N_M^* + d_7), \\ \frac{dP_m}{dt} = \gamma_m (H_i + M_i N_M^*) - d_9 P_m, \\ \frac{dP_c}{dt} = \gamma_p N_{Si}^* S_i - d_{10} P_c. \end{array} \right. \quad (2.11)$$

Using the equilibria relations related to  $S_{rc}^*$ ,  $N_{Si}^*$ , and  $N_M^*$ :

$$\begin{aligned} u + a_6 S_{rc}^* - c_{64} S_{rc}^* N_{Si}^* - c_{66} S_{rc}^{*2} = 0, \quad a_3 N_{Si} - c_{33} N_{Si}^{*2} - c_{36} S_{rc} N_{Si}^* = 0, \\ \text{and } a_7 N_M^* - c_{77} N_M^{*2} = 0, \end{aligned}$$

with  $a_i = b_i - d_i$ , we obtain the following system:

$$\left\{ \begin{array}{l} \frac{dH_i}{dt} = t_{110} (N_H - H_i) P_c - r_{12} H_i; \\ \frac{dS_e}{dt} = t_{39} P_m (N_{Si}^* - S_e - S_i) - (b_3 + r_{54}) S_e; \\ \frac{dS_i}{dt} = r_{54} S_e - b_3 S_i; \\ \frac{dM_i}{dt} = t_{710} P_c (N_M^* - M_i) - b_7 M_i; \\ \frac{dP_m}{dt} = \gamma_m (H_i + M_i N_M^*) - d_9 P_m; \\ \frac{dP_c}{dt} = \gamma_p N_{Si}^* S_i - d_{10} P_c \end{array} \right. \quad (2.12)$$

defined on the set

$$\mathcal{D}_1 = \{(H_i, P_m, P_c, S_e, S_i, M_i) \in \mathbb{R}_+^6 : H_i \leq N_H, P_m \leq \frac{\gamma_m(N_H + N_M^*)}{d_9}, P_c \leq \frac{\gamma_p N_{Si}^*}{d_{10}}\}.$$

## 2.5. Reproduction number and local stability of the disease free equilibrium of system (2.12)

In this section, we give an analytic expression for  $\mathcal{R}_0$  the basic reproductive number of the system and completely answer the stability question for the disease-free equi-

librium (DFE). As usual  $\rho(M)$  and  $s(M)$  denote respectively the spectral radius and the stability modulus of the matrix  $M$ .

The basic reproduction number,  $\mathcal{R}_0$ , is defined as the number of secondary infections produced by one infectious individual during his or her entire infectious period in a completely susceptible population [23].

It can be easily seen that system (2.12) admits the disease free equilibrium (DFE)

$$E_0 = (0, 0, 0, 0, 0, 0)$$

on the boundary of  $\mathcal{D}_1$ .

The Jacobian matrix at  $E_0$  is

$$J_0 = \begin{pmatrix} -r_{12} & 0 & 0 & 0 & 0 & N_H t_{110} \\ 0 & -(b_3 + r_{54}) & 0 & 0 & N_{S_i}^* t_{39} & 0 \\ 0 & r_{54} & -b_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & -b_7 & 0 & N_M^* t_{710} \\ \gamma_m & 0 & 0 & \gamma_m N_M^* & -d_9 & 0 \\ 0 & 0 & \gamma_p N_{S_i}^* & 0 & 0 & -d_{10} \end{pmatrix}$$

$J_0$  is Metzler matrix and  $J_0 = F + V$  with

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & N_H t_{110} \\ 0 & 0 & 0 & 0 & N_{S_i}^* t_{39} & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & N_M^* t_{710} \\ \gamma_m & 0 & 0 & \gamma_m N_M^* & 0 & 0 \\ 0 & 0 & \gamma_p N_{S_i}^* & 0 & 0 & 0 \end{pmatrix},$$

$$V = \begin{pmatrix} -r_{12} & 0 & 0 & 0 & 0 & 0 \\ 0 & -(b_3 + r_{54}) & 0 & 0 & 0 & 0 \\ 0 & r_{54} & -b_3 & 0 & 0 & 0 \\ 0 & 0 & 0 & -b_7 & 0 & 0 \\ 0 & 0 & 0 & 0 & -d_9 & 0 \\ 0 & 0 & 0 & 0 & 0 & -d_{10} \end{pmatrix}.$$

We have  $F > 0$  and  $V$  is Metzler stable. Thanks to Varga's theorem [24]: The matrix  $J_0$  is stable if only if  $\rho(-FV^{-1}) < 1$ . A straightforward calculus give :

$$\mathcal{R}_0 = \rho(-FV^{-1}) = \sqrt[4]{\frac{\gamma_m \gamma_p r_{54} t_{39} N_{S_i}^{*2} (b_7 t_{110} N_H + r_{12} t_{710} N_M^{*2})}{b_3 b_7 d_9 d_{10} r_{12} (b_3 + r_{54})}} = T_0^{1/4}.$$

Then  $E_0$  is LAS if  $T_0 \leq 1$  and is unstable if  $T_0 > 1$ .

## 2.6. Global Stability of the disease free equilibrium:

**Theorem 2.1.** *If  $T_0 \leq 1$  then the DFE is GAS.*

**Proof.** Consider this following Lyapunov function :

$$V = \frac{r_{54} t_{39} N_{Si}^*}{r_{12}(b_3 + r_{54})} H_i + \frac{d_9 r_{54}}{\gamma_m (b_3 + r_{54})} S_e + \frac{d_9}{\gamma_m} S_i + \frac{r_{54} t_{39} N_M^* N_{Si}^*}{b_7 (b_3 + r_{54})} M_i \\ + \frac{t_{39} r_{54} N_{Si}^*}{\gamma_m (b_3 + r_{54})} P_m + \frac{b_3 d_9}{\gamma_p N_{Si}^* \gamma_m} P_c.$$

Its derivative along trajectories of (2.12) satisfy:

$$\dot{V} = \frac{r_{54} t_{39} N_{Si}^*}{r_{12}(b_3 + r_{54})} [t_{110} (N_H - H_i) P_c - r_{12} H_i] \\ + \frac{d_9 r_{54}}{\gamma_m (b_3 + r_{54})} [t_{39} P_m (N_{Si}^* - S_e - S_i) - (b_3 + r_{54}) S_e] \\ + \frac{d_9}{\gamma_m} [r_{54} S_e - b_3 S_i] + \frac{r_{54} t_{39} N_M^* N_{Si}^*}{b_7 (b_3 + r_{54})} [t_{710} P_c (N_M^* - M_i) - b_7 M_i] \\ + \frac{t_{39} r_{54} N_{Si}^*}{\gamma_m (b_3 + r_{54})} [\gamma_m (H_i + M_i N_M^*) - d_9 P_m] + \frac{b_3 d_9}{\gamma_p N_{Si}^* \gamma_m} [\gamma_p N_{Si}^* S_i - d_{10} P_c] \\ = - \frac{r_{54} t_{39} N_{Si}^*}{r_{12} (b_3 + r_{54})} t_{110} H_i P_c - \frac{d_9 r_{54}}{\gamma_m (b_3 + r_{54})} t_{39} P_m (S_e + V_5) \\ - \frac{r_{54} t_{39} N_M^* N_{Si}^*}{b_7 (b_3 + r_{54})} t_{710} P_c M_i + P_m \left[ \frac{d_9 r_{54} N_{Si}^*}{\gamma_m (b_3 + r_{54})} t_{39} - \frac{t_{39} r_{54} N_{Si}^*}{\gamma_m (b_3 + r_{54})} d_9 \right] \\ + P_c \left[ \frac{r_{54} t_{39} N_{Si}^*}{r_{12}(b_3 + r_{54})} t_{110} N_H + \frac{\gamma_m r_{54} t_{39} N_M^* N_{Si}^*}{b_7 d_9 (b_3 + r_{54})} t_{710} N_M^* - \frac{b_3 d_9}{\gamma_p N_{Si}^* \gamma_m} d_{10} \right] \\ + S_i \left[ \frac{d_9}{\gamma_m} b_3 + \frac{b_3 d_9}{\gamma_p N_{Si}^* \gamma_m} \gamma_p N_{Si}^* \right] + S_e \left[ - \frac{d_9 r_{54}}{\gamma_m (b_3 + r_{54})} (b_3 + r_{54}) + \frac{d_9}{\gamma_m} r_{54} \right] \\ + M_i \left[ - \frac{r_{54} t_{39} N_M^* N_{Si}^*}{b_7 (b_3 + r_{54})} b_7 + \frac{t_{39} r_{54} N_{Si}^*}{\gamma_m (b_3 + r_{54})} \gamma_m N_M^* \right] \\ + H_i \left[ - \frac{r_{54} t_{39} N_{Si}^*}{r_{12}(b_3 + r_{54})} r_{12} + \frac{t_{39} N_{Si}^* r_{54}}{\gamma_m (b_3 + r_{54})} \gamma_m \right].$$

Then,

$$\dot{V} \leq P_c \frac{b_3 d_9}{\gamma_p N_{Si}^* \gamma_m} d_{10} \left[ \frac{\gamma_m \gamma_p N_H N_{Si}^{*2} r_{54} t_{39} t_{110}}{b_3 d_9 d_{10} r_{12} (b_3 + r_{54})} + \frac{\gamma_m \gamma_p N_M^* N_{Si}^{*2} r_{54} t_{39} t_{710}}{b_3 b_7 d_9 d_{10} (b_3 + r_{54})} - 1 \right] \\ \leq \left( \frac{\gamma_m \gamma_p N_{Si}^{*2} r_{54} t_{39} (b_7 N_H t_{110} + N_M^{*2} r_{12} t_{710})}{b_3 b_7 d_9 d_{10} r_{12} (b_3 + r_{54})} - 1 \right) \frac{b_3 d_9}{\gamma_p N_{Si}^* \gamma_m} d_{10} P_c \\ \leq P_c \frac{b_3 d_9}{\gamma_p N_{Si}^* \gamma_m} d_{10} (T_0 - 1).$$

Its follows that

$$\dot{V} \leq 0 \quad \text{if } T_0 \leq 1.$$

It can be shown that the largest invariant set contained in  $\dot{V} = 0$  is reduced to the DFE. Hence, thanks to Lasalle Invariance Principle [15] we conclude.  $\square$

### 2.7. Existence and uniqueness of the endemic equilibrium

We shall present here a result concerning the existence and the uniqueness of the point of endemic equilibrium of the model (2.12). In what follows, we will prove the existence of a unique endemic equilibrium of system (2.12) when  $\mathcal{R}_0 > 1$ . For this purpose, we express the problem as a fixed point problem and we use Theorem A.2 ([10], theorem 2.1, see Appendix A).

Let us define  $\hat{E}^* = (H_i^*, P_m^*, P_c^*, S_e^*, S_i^*, M_i^*)$  an equilibrium point. We can define a multi-variable function with respect in  $(H_i, S_e, M_i)$  as follows ( see Appendix D) :

$$\mathcal{U} = \mathcal{F}(\mathcal{U}),$$

where

$$\mathcal{U} = \begin{pmatrix} H_i \\ S_e \\ M_i \end{pmatrix},$$

$$\mathcal{F} = \begin{pmatrix} \mathcal{F}_1 := \frac{\gamma_p N_H N_{S_i}^* r_{54} t_{110} S_e}{b_3 d_{10} \left( r_{12} + \frac{\gamma_p N_{S_i}^* r_{54} t_{110} S_e}{b_3 d_{10}} \right)} \\ \mathcal{F}_2 := \frac{\gamma_m t_{39} N_{S_i}^* (H_i + N_M^* M_i)}{d_9 \left( b_3 + r_{54} + \frac{\gamma_m \left( 1 + \frac{r_{54}}{b_3} \right) t_{39} S_e (H_i + N_M^* M_i)}{d_9} \right)} \\ \mathcal{F}_3 := \frac{\gamma_p N_{S_i}^* r_{54} t_{710} N_M^* S_e}{b_3 d_{10} \left( b_7 + \frac{\gamma_p N_{S_i}^* r_{54} t_{710} S_e}{b_3 d_{10}} \right)} \end{pmatrix}.$$

Then the equilibrium points  $(H_i^*, S_e^*, M_i^*)$  are fixed point of  $\mathcal{F}$  given by  $\mathcal{U} = \mathcal{F}(\mathcal{U})$  and it is from this formulation that we shall prove the existence and the uniqueness of the point of endemic equilibrium  $(H_i^*, S_e^*, S_i^*, P_m^*, P_c^*)$ .

$\mathcal{F}(\mathcal{U})$  is continuous, bounded function which maps into the non-negative orthant  $\mathbb{R}_+^3$  into itself and infinitely differentiable with Jacobian as follows

$$\mathcal{J}_e = \begin{pmatrix} 0 & \frac{b_3 \gamma_p d_{10} N_H N_{S_i}^* r_{12} r_{54} t_{110}}{(b_3 d_{10} r_{12} + \gamma_p N_{S_i}^* r_{54} t_{110} S_e)^2} & 0 \\ \frac{b_3^2 \gamma_m d_9 t_{39} N_{S_i}^*}{(b_3 + r_{54})(b_3 d_9 + \gamma_m t_{39} S_e (H_i + N_M^* M_i))^2} & 0 & \frac{b_3^2 \gamma_m d_9 N_M^* t_{39} N_{S_i}^*}{(b_3 + r_{54})(b_3 d_9 + \gamma_m t_{39} S_e (H_i + N_M^* M_i))^2} \\ 0 & \frac{b_3 b_7 \gamma_p d_{10} N_{S_i}^* r_{54} t_{710} N_M^*}{(b_3 b_7 d_{10} + \gamma_p N_{S_i}^* r_{54} t_{710} S_e)^2} & 0 \end{pmatrix}$$

where the off-diagonal elements are non-negative. Thus, function  $\mathcal{F}(\mathcal{U})$  is monotone non-decreasing and  $\mathcal{F}(0) = 0$ . Note that  $\rho(\mathcal{F}'(0)) = T_0^{1/2} > 1$ . Thanks to the graph theory, we claim that  $\mathcal{F}'(0)$  is irreducible because the associated graph of the matrix is strongly connected.

Let us now prove that  $\mathcal{F}$  is strictly sub linear in  $\Omega$ , i.e.,  $\mathcal{F}(r\mathcal{U}) > r\mathcal{F}(\mathcal{U})$ , for any  $\mathcal{U} \in \Omega$  with  $\mathcal{U} > 0$ , and  $r \in (0, 1)$ .



Few computations provide:

$$\begin{aligned} \frac{r_1 \mathcal{F}_1(\mathcal{U})}{\mathcal{F}_1(r_1 \mathcal{U})} &= \frac{\frac{r_{12} + r_1 \gamma_p N_H N_{Si}^* r_{54} t_{110} S_e}{b_3 d_{10}}}{r_{12} + \frac{\gamma_p N_H N_{Si}^* r_{54} t_{110} S_e}{b_3 d_{10}}} = \frac{r_{12} + r_1 \gamma_p N_H N_{Si}^* r_{54} t_{110} S_e}{r_{12} + \gamma_p N_H N_{Si}^* r_{54} t_{110} S_e} < 1. \\ \frac{r_2 \mathcal{F}_2(\mathcal{U})}{\mathcal{F}_2(r_2 \mathcal{U})} &= \frac{b_3 + r_{54} + \frac{r_2 \gamma_m \left(1 + \frac{r_{54}}{b_3}\right) t_{39} S_e (H_i + N_M^* M_i)}{d_9}}{b_3 + r_{54} + \frac{\gamma_m \left(1 + \frac{r_{54}}{b_3}\right) t_{39} S_e (H_i + N_M^* M_i)}{d_9}} < 1. \\ \frac{r_3 \mathcal{F}_3(\mathcal{U})}{\mathcal{F}_3(r_3 \mathcal{U})} &= \frac{r_3 \gamma_p N_{Si}^* r_{54} t_{710} N_M^* S_e}{b_3 d_{10} \left(b_7 + \frac{\gamma_p N_{Si}^* r_{54} t_{710} S_e}{b_3 d_{10}}\right)} \frac{b_3 d_{10} \left(b_7 + \frac{r_3 \gamma_p N_{Si}^* r_{54} t_{710} S_e}{b_3 d_{10}}\right)}{r_3 \gamma_p N_{Si}^* r_{54} t_{710} N_M^* S_e}. \\ \frac{r_3 \mathcal{F}_3(\mathcal{U})}{\mathcal{F}_3(r_3 \mathcal{U})} &= \frac{b_7 + \frac{r_3 \gamma_p N_{Si}^* r_{54} t_{710} S_e}{b_3 d_{10}}}{b_7 + \frac{\gamma_p N_{Si}^* r_{54} t_{710} S_e}{b_3 d_{10}}} < 1. \end{aligned} \tag{2.13}$$

So the function  $\mathcal{F}(\mathcal{U})$  is strictly sub-linear with  $r = \min(r_1, r_2, r_3)$ . In this way we have proved the following theorem

**Theorem 2.2.** *If  $\mathcal{R}_0 \leq 1$ , the only equilibrium point of the system is the DFE. If  $\mathcal{R}_0 > 1$ , there is also a unique endemic equilibrium point  $\hat{E}^*$  in  $\text{int}(\mathcal{D}_1)$ .*

## 2.8. Local Stability of the Endemic Equilibrium

In this section, the local stability of the endemic equilibrium will be proved when  $\mathcal{R}_0 > 1$ . To do so, we are going to follow the method given by Hethcote and Thieme [10], which is based on a Krasnoselkii technique.

Let us consider the system of differential equations:

$$\bar{x}' = f(\bar{x}). \tag{2.14}$$

A way in which we can show the local asymptotic stability of an equilibrium point  $\bar{x}_0$  of system 2.14 is to prove that the linearized equation

$$\bar{Z}' = Df(\bar{x}_0)\bar{Z} \tag{2.15}$$

has no solutions of the form

$$\bar{Z}(t) = \bar{Z}_0 \exp(w t) \tag{2.16}$$

with  $\bar{Z}_0 \in \mathbb{C}^n \setminus \{0\}$ ,  $w \in \mathbb{C}$  and  $\mathcal{R}_e w \geq 0$ , where  $\mathbb{C}$  denotes the complex numbers i.e.,  $w \bar{Z} = Df(\bar{x}_0) \bar{Z}$  with  $\bar{Z} \in \mathbb{C}^n \setminus \{0\}$ ,  $w \in \mathbb{C}^n$  implies  $\mathcal{R}_e w < 0$ .

**Theorem 2.3.** *If  $\mathcal{R}_0 > 1$ , then the endemic equilibrium labeled  $\hat{E}^*$  of the system (2.12) is locally asymptotically stable (LAS).*

The proof of Theorem 2.3 is given in Appendix C.

## 2.9. Global Stability of the Endemic Equilibrium

In this section we will establish the global stability of the unique endemic equilibrium point when  $\mathcal{R}_0 > 1$ . We shall use Theorem A.3, stated in the Appendix A for convenience to prove the following result.

**Theorem 2.4.** *If  $\mathcal{R}_0 > 1$ , Then the endemic positive equilibrium (EEP) of the model is globally asymptotically stable in the interior of the set  $\mathcal{D}_1$ .*

The detailed proof is shown in Appendix D.

## 3. Biological control

By using a competitor resistant snail species, capable of eliminating the population of the intermediate host snails, we found that the biological control can ultimately eradicate the disease. The first concerns the way to eradicate the disease by excluding completely the intermediate host snails. This means that system (2.3) admits

$E_2 = \left( 0, \frac{a_6 + \sqrt{a_6^2 + 4c_{66}u}}{2c_{66}}, \frac{a_7}{c_{77}} \right)$  as a globally asymptotically stable equilibrium

state. This equilibrium corresponds to the absence of the intermediate host snails:  $N_{Si} = 0$ . According to the computations done in Paragraph 2.4, the parameters must satisfy  $c_{66}a_3 - c_{36}a_6 < 0$  or the control  $u$  must satisfy  $u > \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}$

and the other equilibrium  $E_1 = \left( \frac{a_3}{c_{33}}, 0, \frac{a_7}{c_{77}} \right)$  (equilibrium corresponding to the absence of competitor snails) must be unstable which implies that we must have  $c_{33}a_6 - c_{64}a_3 > 0$ . It is worth noting that when the two above conditions are satisfied then the coexistence of positive equilibrium ( $E^*$  and  $E^{**}$ ) does not exist.

Well, just to recap, the population of the intermediate host snails can be eliminated if the parameters satisfy the following listed conditions

$$c_{66}a_3 - c_{36}a_6 < 0 \text{ or } u > \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}. \quad (3.1)$$

Another way to control the disease without completely eliminating the intermediate host snails is to choose a competitor resistant snail species that keep the size of the snail population below a certain threshold. We have to make a control mechanism,  $u$ , so as to reduce the basic reproduction number  $\mathcal{R}_0$  to a value less than one. Recall that

$$\mathcal{R}_0^4 = \frac{\gamma_m \gamma_p r_{54} t_{39} N_{Si}^{*2} (b_7 t_{110} N_H + r_{12} t_{710} N_M^{*2})}{b_3 b_7 d_9 d_{10} r_{12} (b_3 + r_{54})}.$$

In the expression of  $\mathcal{R}_0$ , the only quantity that depends on the competitor resistant snail species is  $N_{Si}^*$  since (by relation (2.4))

$$N_{Si}^* = \frac{2a_3c_{33}c_{66} - a_3c_{36}c_{64} - a_6c_{33}c_{36} - c_{36}\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2c_{33}(c_{33}c_{66} - c_{36}c_{64})}$$

and the other terms do not depend on the competitor.

We can remark that the introduction of a competitor reduces the value of  $\mathcal{R}_0$  since the value of the steady state size of the intermediate host snail in the absence

of the competitor (which is equal to  $\frac{a_3}{c_{33}}$ ) is larger than its value in the presence of the competitor.

Now,  $\mathcal{R}_0 \leq 1$  iff

$$N_{Si}^{*2} = \left( \frac{2a_3c_{33}c_{66} - a_3c_{36}c_{64} - a_6c_{33}c_{36} - c_{36}\sqrt{(a_6c_{33} - a_3c_{64})^2 + 4c_{33}u(c_{33}c_{66} - c_{36}c_{64})}}{2c_{33}(c_{33}c_{66} - c_{36}c_{64})} \right)^2$$

$$\leq \frac{b_3 b_7 d_9 d_{10} r_{12} (b_3 + r_{54})}{\gamma_m \gamma_p r_{54} t_{39} (b_7 N_H t_{110} + N_M^{*2} r_{12} t_{710})} := \Gamma_0.$$

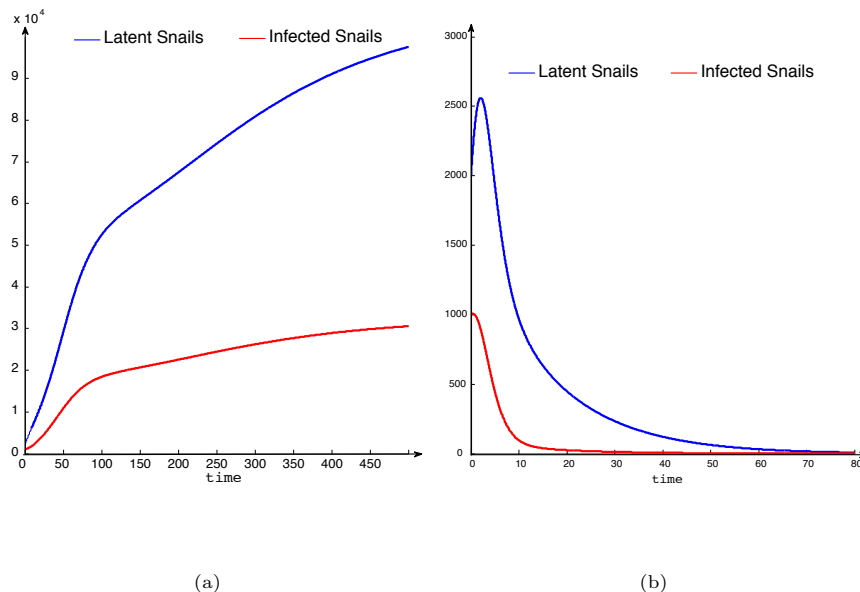
This implies

$$u \geq \frac{(a_3 - c_{33}\Gamma_0^{1/2})(a_3c_{66} - a_6c_{36} - c_{33}c_{66}\Gamma_0^{1/2} + c_{36}c_{64}\Gamma_0^{1/2})}{c_{36}^2}. \quad (3.2)$$

$\Gamma_0$  is a function of the disease characteristics and related parameters such as human, mammal and intermediate snail demographic parameters. Thus, in order to eradicate the disease, the control  $u$  has to satisfy the inequality (3.2). This situation is illustrated in Fig. 1.

Consequently, the critical value of the control rate  $u$  above which schistosomiasis can be eradicated is  $u_c = \frac{(a_3 - c_{33}\Gamma_0^{1/2})(a_3c_{66} - a_6c_{36} - c_{33}c_{66}\Gamma_0^{1/2} + c_{36}c_{64}\Gamma_0^{1/2})}{c_{36}^2}$ .

It has a significant effect in reducing intermediate snail hosts to sufficient low levels to combat schistosomiasis in the long term.



**Figure 1.** Evolution of the latent  $S_e(t)$  and infected  $S_i(t)$  snails when the control  $u = 0$  (Figure (a)) and when the control  $u$  satisfies relation (3.2) (Figure (b)). The parameter values are taken in table 2.

## 4. The optimal control problem

In the previous sections we have analyzed the model with two controls, one is drug treatment and other is the release of competitor snails and throughout the analysis we consider their fixed value. But in the reality these parameters should be time dependent. In this section we formulate the optimal control problem applied to system (2.1). We want to minimize the drug treatment cost, as well as the cost of production and release of competitor snails. For this end we consider as control variables:

1. The increase in the recovery rate by drug treatment investment denoted by  $u_1(t)$ , and
2. The investment in production and release of competitor snails denoted by  $u_2(t)$ .

The control  $u_1$  describes the effects of the chemotherapeutic treatment only on the humans, meanwhile  $u_2$  is related to the number of competitor snails,  $S_{rc}$ , that should be released at time  $t$ .

Further, we want to minimize the number of infected humans. For this end, we consider the following performance index

$$J[u_1, u_2] = \frac{1}{2} \int_0^T (c_1 u_1^2 + c_2 u_2^2 + c_3 H_i^2 - c_4 S_{rc}^2) dt \quad (4.1)$$

and the control set  $\Delta = \{(u_1(t), u_2(t)) | u_i(t) \text{ is Lebesgue on } [0, T], 0 \leq u_1(t) \leq 1, 0 \leq u_2(t) \leq U_b\}$ , where the upper bound of the control  $u_2(t)$  is defined by  $U_b$ .

The costs and benefits of the controls should be weighed and both epidemiological and economic goals considered.

This is taken into account in the objective functional (4.1) that includes the costs which relate to the resources that is needed for applying drug treatment  $\frac{1}{2} c_1 u_1^2$  and releasing competitor snails  $\frac{1}{2} c_2 u_2^2$ . The quantities  $c_3$  and  $c_4$  respectively represent the associated with minimizing infected human population  $H_i$  and competitor snails population  $S_{rc}$ .

In the control problem, we assume fixed final time, and free dynamical variables at this time. Further, we assume a quadratic functional cost [14] since we believe that the performance index is a nonlinear function. The quadratic terms act as a penalization [12, 22], amplifying the effects of great variations of the variables. Each quadratic term is multiplied by a coefficient,  $c_i$ ;  $i = 1, \dots, 4$ , which establishes the relative importance of the term on schistosomiasis control cost. Notice that when we minimize the performance index,  $J$ , the competitor snails population is maximized.

Mathematically, the optimal control problem is formulated as the minimization of the functional (4.1) subject to the system

$$\left\{ \begin{array}{l} \frac{dH_s}{dt} = -t_{110} P_c H_s + r_{12} u_1 H_i; \\ \frac{dH_i}{dt} = t_{110} P_c H_s - r_{12} u_1 H_i; \\ \frac{dS_s}{dt} = b_3 (S_s + S_e + S_i) - t_{39} P_m S_s - d_3 S_s - c_{33} S_s (S_s + S_e + S_i) - c_{36} S_s S_{rc}; \\ \frac{dS_e}{dt} = t_{39} P_m S_s - d_4 S_e - c_{44} S_e (S_s + S_e + S_i) - c_{46} S_e S_{rc} - r_{54} S_e; \\ \frac{dS_i}{dt} = r_{54} S_e - d_5 S_i - c_{55} S_i (S_s + S_e + S_i) - c_{56} S_i S_{rc}; \\ \frac{dS_{rc}}{dt} = u_2 + b_6 S_{rc} - c_{64} S_{rc} (S_s + S_e + S_i) - c_{66} S_{rc}^2 - d_6 S_{rc}; \\ \frac{dM_s}{dt} = b_7 (M_s + M_i) - t_{710} P_c M_s - c_{77} M_s (M_s + M_i) - d_7 M_s; \\ \frac{dM_i}{dt} = t_{710} P_c M_s - d_8 M_i - c_{88} M_i (M_s + M_i); \\ \frac{dP_m}{dt} = \gamma_m (H_i + M_i) - d_9 P_m; \\ \frac{dP_c}{dt} = \gamma_p S_i - d_{10} P_c; \end{array} \right. \quad (4.2)$$

where  $H_s(0), H_i(0), S_s(0), S_e(0), S_i(0), S_{rc}(0), M_s(0), M_i(0), P_m(0), P_c(0)$  are given and the control variables  $u_1$ , and  $u_2$  are non-negatives. This scenario assumes that control mechanisms are introduced in a steady state of the individu population at time  $t = 0$ .

Since one of our objectives is to control the introduction of competitor snails,  $S_{rc}$ , the constant rate  $u_2$  in (2.1) is replaced by the control function  $u_2$ . The insecticide control  $u_1$  in (4.2) appears as the fraction of infected humans  $H_i$  that are submitted to treatment.

#### 4.1. Characterization of the optimal control problem

We use the Pontryaguin Maximum Principle [8] to determine the formulation of our optimal control  $u_1^*$  and  $u_2^*$ . To this end, we note that the Hamiltonian for our problem is given by

$$\begin{aligned} H = & \frac{1}{2} (c_1 u_1^2 + c_2 u_2^2 + c_3 H_i^2 - c_4 S_{rc}^2) + \lambda_1 \frac{dH_m}{dt} + \lambda_2 \frac{dH_i}{dt} + \lambda_3 \frac{dS_s}{dt} \\ & + \lambda_4 \frac{dS_e}{dt} + \lambda_5 \frac{dS_i}{dt} + \lambda_6 \frac{dS_{rc}}{dt} + \lambda_7 \frac{dM_s}{dt} + \lambda_8 \frac{dM_i}{dt} + \lambda_9 \frac{dP_m}{dt} + \lambda_{10} \frac{dP_c}{dt}. \end{aligned} \quad (4.3)$$

In (4.3),  $\lambda_i, i = 1, \dots, 10$ , are the adjoint variables; they determine the adjoint system which, together with the state system (2.1), gives the optimality system. We

shall consider all possible non-negative values for the control variables, including the case  $u_1 = u_2 = 0$ .

Pontryaguin Maximum Principle [8] states that the unconstrained optimal variables  $u_1^*$ , and  $u_2^*$  satisfy

$$\frac{\partial H}{u_1^*} = \frac{\partial H}{u_2^*} = 0.$$

We find  $\frac{\partial H}{u_i^*}$ , and solve for  $u_i^*$ ,  $i = 1, 2$ , by setting the partial derivatives of  $H$  equal to zero. Thus, from

$$\begin{cases} \frac{dH}{du_1^*} = r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i - c_1 u_1^* \\ \frac{dH}{du_2^*} = \lambda_6 + c_2 u_2^*, \end{cases}$$

we have

$$\begin{cases} u_1^* = \frac{r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i}{c_1} \\ u_2^* = -\frac{\lambda_6}{c_2}. \end{cases} \quad (4.4)$$

Using the property of the control space, we obtain

$$u_1^* = \begin{cases} 0, & \text{if } \frac{r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i}{c_1} \leq 0 \\ \frac{r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i}{c_1}, & \text{if } \frac{r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i}{c_1} \in (0, 1) \\ 1, & \text{if } \frac{r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i}{c_1} \geq 1. \end{cases} \quad (4.5)$$

Those can be rewritten in compact notation

$$\begin{cases} u_1^* = \min \left\{ 1, \max \left\{ 0, \frac{r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i}{c_1} \right\} \right\} \\ u_2^* = -\frac{\lambda_6}{c_2}. \end{cases} \quad (4.6)$$

The Pontryagin Maximum Principle establishes that the following equations

$$\begin{aligned} \frac{d\lambda}{dt} &= -\frac{\partial H}{\partial x}, \\ H(x(t), u^*(t), \lambda(t), t) &= \max_{u \in U} H(x(t), u(t), \lambda(t), t) \end{aligned} \quad (4.7)$$

are necessary conditions that must be satisfied by the optimal control  $u(t)$  and the state variable  $x(t)$ . System (4.7) is referred as the adjoint system. In our problem it becomes

$$\begin{aligned} \lambda'_1 &= -\frac{dH}{dH_s}, \lambda'_2 = -\frac{dH}{dH_i}, \lambda'_3 = -\frac{dH}{dS_s}, \lambda'_4 = -\frac{dH}{dS_e}, \lambda'_5 = -\frac{dH}{dS_i}, \\ \lambda'_6 &= -\frac{dH}{dS_{rc}}, \lambda'_7 = -\frac{dH}{dM_s}, \lambda'_8 = -\frac{dH}{dM_i}, \lambda'_9 = -\frac{dH}{dP_m}, \lambda'_{10} = -\frac{dH}{dP_c}. \end{aligned} \quad (4.8)$$

Taking the partial derivatives of  $H$  in (4.3) and substituting them above we obtain

$$\left\{ \begin{array}{l} \lambda'_1 = t_{110} \lambda_1 P_c - t_{110} \lambda_2 P_c; \\ \lambda'_2 = -c_3 H_i - b_9 \lambda_9 - r_{12} \lambda_1 u_1 + r_{12} \lambda_2 u_1; \\ \lambda'_3 = \lambda_3 (- (b_3 - c_{33} (S_e + S_i + S_s)) - c_{36} S_{rc} - c_{33} S_s - d_3 - t_{39} P_m) \\ \quad - \lambda_4 (t_{39} P_m - c_{44} S_e) + c_{55} \lambda_5 S_i + c_{64} \lambda_6 S_{rc}; \\ \lambda'_4 = \lambda_3 (- (b_3 - c_{33} S_s)) - \lambda_4 (-c_{44} (S_e + S_i + S_s) - c_{44} S_e - c_{46} S_{rc} - d_4 - r_{54}) \\ \quad - \lambda_5 (r_{54} - c_{55} S_i) + c_{64} \lambda_6 S_{rc}; \\ \lambda'_5 = \lambda_3 (- (b_3 - c_{33} S_s)) - \lambda_5 (-c_{55} (S_e + S_i + S_s) - c_{55} S_i - c_{56} S_{rc} - d_5) \\ \quad + c_{44} \lambda_4 S_e + c_{64} \lambda_6 S_{rc} - \gamma_p \lambda_{10}; \\ \lambda'_6 = -\lambda_6 (b_6 - c_{64} (S_e + S_i + S_s) - 2 c_{66} S_{rc} - d_6) + c_{46} \lambda_4 S_e \\ \quad + c_{56} \lambda_5 S_i + c_{36} \lambda_3 S_s + c_4 S_{rc}; \\ \lambda'_7 = \lambda_7 (- (b_7 - c_{77} (M_i + M_s)) - c_{77} M_s - t_{710} P_c - d_7) - \lambda_8 (t_{710} P_c - c_{88} M_i); \\ \lambda'_8 = \lambda_7 (- (b_7 - c_{77} M_s)) - \lambda_8 (-c_{88} (M_i + M_s) - c_{88} M_i - d_8) - \gamma_m \lambda_9; \\ \lambda'_9 = d_9 \lambda_9 + t_{39} \lambda_3 S_s - t_{39} \lambda_4 S_s; \\ \lambda'_{10} = d_{10} \lambda_{10} + t_{110} \lambda_1 H_s - t_{110} \lambda_2 H_s + t_{710} \lambda_7 M_s - t_{710} \lambda_8 M_s; \end{array} \right. \quad (4.9)$$

Finally we analyze the transversality conditions for the adjoint variables. Since in our problem there are not terminal values for the state variables, these conditions are given at the final time  $T$  by

$$\lambda_i(T) = 0, i = 1, \dots, 10. \quad (4.10)$$

## 4.2. The optimality system

The optimality system describes how the system behaves under the application of the controls that minimize  $J$ . It is obtained taking the state system (4.2), with the adjoint system (4.9), the optimal control  $u_1$ , and  $u_2$  (4.6), the initial conditions, and the transversality conditions (4.10), which gives:

$$\begin{aligned} \frac{dH_s}{dt} &= -t_{110} P_c H_s + r_{12} u_1 H_i; \\ \frac{dH_i}{dt} &= t_{110} P_c H_s - r_{12} u_1 H_i; \\ \frac{dS_s}{dt} &= b_3 (S_s + S_e + S_i) - t_{39} P_m S_s - d_3 S_s - c_{33} S_s (S_s + S_e + S_i) - c_{36} S_s S_{rc}; \\ \frac{dS_e}{dt} &= t_{39} P_m S_s - d_4 S_e - c_{44} S_e (S_s + S_e + S_i) - c_{46} S_e S_{rc} - r_{54} S_e; \\ \frac{dS_i}{dt} &= r_{54} S_e - d_5 S_i - c_{55} S_i (S_s + S_e + S_i) - c_{56} S_i S_{rc}; \end{aligned}$$

$$\begin{aligned}
\frac{dS_{rc}}{dt} &= u_2 + b_6 S_{rc} - c_{64} S_{rc}(S_s + S_e + S_i) - c_{66} S_{rc}^2 - d_6 S_{rc}; \\
\frac{dM_s}{dt} &= b_7 (M_s + M_i) - t_{710} P_c M_s - c_{77} M_s(M_s + M_i) - d_7 M_s; \\
\frac{dM_i}{dt} &= t_{710} P_c M_s - d_8 M_i - c_{88} M_i (M_s + M_i); \\
\frac{dP_m}{dt} &= \gamma_m (H_i + M_i) - d_9 P_m; \\
\frac{dP_c}{dt} &= \gamma_p S_i - d_{10} P_c; \\
\frac{d\lambda_1}{dt} &= t_{110} \lambda_1 P_c - t_{110} \lambda_2 P_c; \\
\frac{d\lambda_2}{dt} &= -c_3 H_i - b_9 \lambda_9 - r_{12} \lambda_1 u_1 + r_{12} \lambda_2 u_1; \\
\frac{d\lambda_3}{dt} &= \lambda_3 (- (b_3 - c_{33} (S_e + S_i + S_s)) - c_{36} S_{rc} - c_{33} S_s - d_3 - t_{39} P_m) \\
&\quad - \lambda_4 (t_{39} P_m - c_{44} S_e) + c_{55} \lambda_5 S_i + c_{64} \lambda_6 S_{rc}; \\
\frac{d\lambda_4}{dt} &= \lambda_3 (- (b_3 - c_{33} S_s)) - \lambda_4 (-c_{44} (S_e + S_i + S_s) - c_{44} S_e - c_{46} S_{rc} - d_4 - r_{54}) \\
&\quad - \lambda_5 (r_{54} - c_{55} S_i) + c_{64} \lambda_6 S_{rc}; \\
\frac{d\lambda_5}{dt} &= \lambda_3 (- (b_3 - c_{33} S_s)) - \lambda_5 (-c_{55} (S_e + S_i + S_s) - c_{55} S_i - c_{56} S_{rc} - d_5) \\
&\quad + c_{44} \lambda_4 S_e + c_{64} \lambda_6 S_{rc} - \gamma_p \lambda_{10}; \\
\frac{d\lambda_6}{dt} &= -\lambda_6 (b_6 - c_{64} (S_e + S_i + S_s) - 2 c_{66} S_{rc} - d_6) + c_{46} \lambda_4 S_e \\
&\quad + c_{56} \lambda_5 S_i + c_{36} \lambda_3 S_s + c_4 S_{rc}; \\
\frac{d\lambda_7}{dt} &= \lambda_7 (- (b_7 - c_{77} (M_i + M_s)) - c_{77} M_s - t_{710} P_c - d_7) - \lambda_8 (t_{710} P_c - c_{88} M_i); \\
\frac{d\lambda_8}{dt} &= \lambda_7 (- (b_7 - c_{77} M_s)) - \lambda_8 (-c_{88} (M_i + M_s) - c_{88} M_i - d_8) - \gamma_m \lambda_9; \\
\frac{d\lambda_9}{dt} &= d_9 \lambda_9 + t_{39} \lambda_3 S_s - t_{39} \lambda_4 S_s; \\
\frac{d\lambda_{10}}{dt} &= d_{10} \lambda_{10} + t_{110} \lambda_1 H_s - t_{110} \lambda_2 H_s + t_{710} \lambda_7 M_s - t_{710} \lambda_8 M_s; \\
u_1^* &= \frac{r_{12} \lambda_2 H_i - r_{12} \lambda_1 H_i}{c_1}; \\
u_2^* &= -\frac{\lambda_6}{c_2}; \\
\lambda_i(T) &= 0, i = 1, \dots, 10.
\end{aligned}$$

## 5. Numerical results

In this section we discuss the method to solve numerically the optimality system (20), and we present the obtained results.

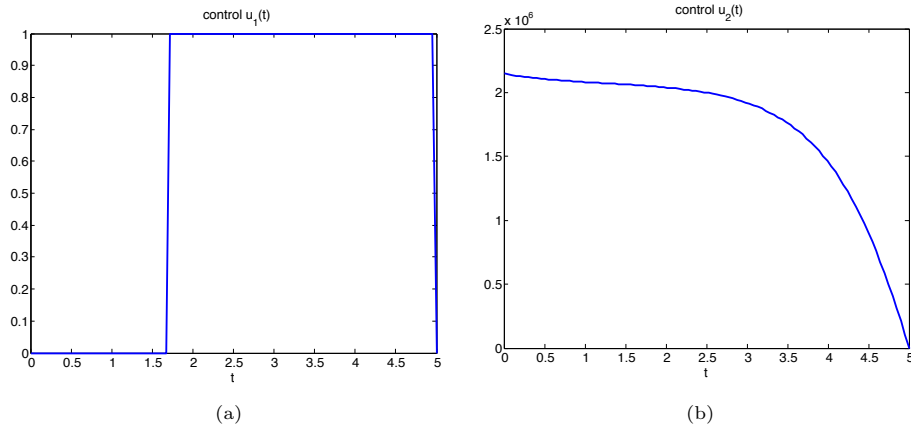
The numerical method deals with a two-point boundary-value problem with separated boundary conditions at time  $t = 0$  and  $t = T$ . In our simulations we use



a period of  $T = 5$  years. This value was chosen to represent the time (in years) at which the release strategy of snails is applied.

Our aim is to understand the effect of two conflicting mechanisms of control, named, drug treatment and the release of competitor snails. For the epidemiological and demographic parameters in all simulations, we use the values given in [1] (see Table 2); the initial conditions for the state variables are given by  $H_s = 8 * 10^3$ ,  $H_i = 450$ ,  $S_s = 8500$ ,  $S_e = 2 * 10^3$ ,  $S_i = 1 * 10^3$ ,  $S_{rc} = 0$ ,  $M_s = 2400$ ,  $M_i = 1000$ ,  $P_m = 7000$ ,  $P_c = 4000$ .

Interestingly, Fig. 2 shows that it is optimal to apply a drug treatment on the maximum rate after one and half year, while the competitor snails must be released at upper bound at the beginning after which it declines steadily to 0. This means that competitor snails releasing is more important in the beginning of disease outbreak. On the other hand, drug treatment is more important while the disease prevails.



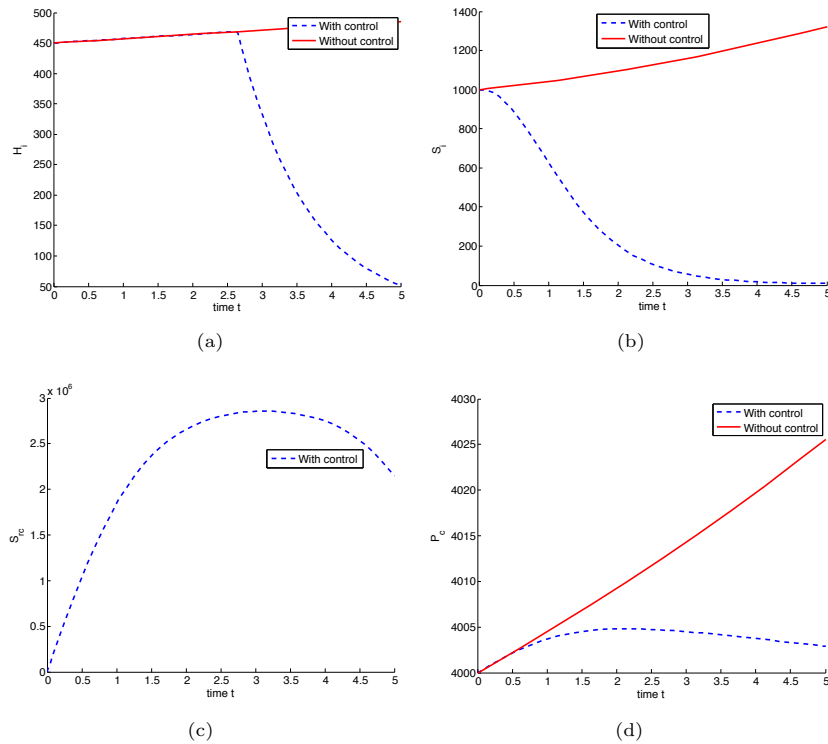
**Figure 2.** Optimal control trajectories for insecticide application (Figure (a)), and release of sterile male snails (Figure (b)) when all the costs are proportionally equal ( $c_1 = c_2 = c_3 = c_4 = 1$ ). The parameter values are taken in table 2.

Figs. 3 present the trajectories of the infected humans, infected snails, competitor snails and cercaria population. The dashed line show the evolution of the sub-populations resulting from control, while the solid line show the evolution resulting from no control. Others figures are not shown to avoid repetition. We can observe that the prevalence of the disease increases and stays very high if there is no additional control measures employed.

As was expected, the population of the resistant and competitor snails follows the same pattern than the control  $u_2$ . On the other hand, if the strategy which apply simultaneously  $u_2$  and  $u_1$  is made to treat the schistosomiasis infection, the prevalence comes down at faster rate in snails population (Figure 3(b)), and larvae population (Figure 3(d)) and at slowly rate in humans population (Figure 3(a)).

This study and observations show that with only chemotherapeutic drug control there is a little change in the nature of infected humans evolution while with only competitor snails releasing there is a remarkable change in infected snails and cercaria evolution. But using both controls together we can get the best result as it lowers the growth level of infected humans and eliminates infected snails and

cercaria population.



**Figure 3.** The evolution for the state variables showing the impact of the controls strategy : Infected humans (a), Infected Snails (b), Competitor snails (c) and Cercaria (d). The parameter values are taken in table 2.

## 6. Summary and conclusions

In this paper, we have described and completely analyzed a deterministic model for the transmission dynamics of a schistosomiasis infection including miracidia and cercariae dynamics.

We have considered treatment with drug and biological control in our modeling. This work highlights also the significance of optimal control theory as a tool to design effective ways of controlling schistosomiasis in the community. Ten sub-population sizes were modeled: human host susceptible and infected, snail intermediate host susceptible, latent, and shedding, resistant competitor snail, mammal host susceptible and infected, miracidia and cercariae. The snails competition is needed to study the control of the infection by biological control. Our model itself is just an attempt to mimic the real situation as much as possible.

First we examine the dynamic behavior of the epidemic system for fixed controls. The reproductive number  $\mathcal{R}_0$  is calculated. We proved that the disease-free steady state  $E_0$  is globally asymptotically stable if  $\mathcal{R}_0 \leq 1$  and it is unstable if  $\mathcal{R}_0 > 1$ . We proved also the existence and uniqueness of the endemic equilibrium  $\hat{E}^*$  in the case where  $\mathcal{R}_0 > 1$  as well as its global asymptotic stability. Also some discussions

are done to support our analytic results and it is also observed that our system may reach to its disease free equilibrium by the successful application of controls.

After investigating the dynamic behavior of the system with fixed controls we study the dynamics of the disease if the controls become time dependent. In this situation our objective is to get maximum disease control by using minimum cost. So we form the optimal control problem and solve it by using Pontryagin's maximum principle. The main conclusion based on the results is that high application of competitor snails releasing is needed at the beginning of the control, with a small decay as well as high application of drug treatment after a while. As such one of the limitations of this study is that it proposes and analyzes a non-spatial model. An interesting futur work can consist to explore the influence of river velocity on miracidia and cercariae transmission dynamics.

## Appendix A Theoretical background

In this appendix, we outline general mathematical frameworks that have been used in this paper.

We start by recalling a reduction theorem for stability results given by Vidyasagar [25]. The author proved the following statement which give criteria for stability in the case of a finite dimensional non-autonomous system in triangular form.

**Theorem A.1** (Theorem 3.1, [25]). *Consider the following  $\mathbb{C}^1$  system*

$$\begin{cases} \dot{x} = f(x); & x \in \mathbb{R}^n & y \in \mathbb{R}^m, \\ \dot{y} = g(x, y); \\ \text{with a equilibrium point, } (x^*, y^*) \text{ i.e,} \\ f(x^*) = 0 \text{ and } g(x^*, y^*) = 0. \end{cases} \quad (\text{A.1})$$

*If  $x^*$  is globally asymptotically stable (GAS) in  $\mathbb{R}^n$  for the system  $\dot{x} = f(x)$ , and if  $y^*$  is GAS in  $\mathbb{R}^m$ , for the system  $\dot{y} = g(x^*, y)$ , then  $(x^*, y^*)$  is (locally) asymptotically stable for (A.1).*

*Moreover, if all the trajectories of (A.1) are forward bounded, then  $(x^*, y^*)$  is GAS for (A.1).*

After that, we notice a theorem due to Hethcote and Thieme ([10], Theorem 2.1) for the existence and uniqueness of a positive fixed point of a multi-variable function.

**Theorem A.2** (Theorem 2.1, Hethcote and Thieme [10]).

*Let  $F(x)$  be a continuous, monotone non-decreasing, strictly sub linear, bounded function which maps the non-negative orthant  $\mathbb{R}_+^n = [0, \infty)$  into itself. Let  $F(0) = 0$  and  $F'(0)$  exists and be irreducible. Then  $F(x)$  does not have a non-trivial fixed point on the boundary of  $\mathbb{R}_+^n$ . Moreover,  $F(x)$  has a positive fixed point iff  $\rho(F'(0)) > 1$ . If there is a positive fixed point, then it is unique.*

Finally, we point out the properties of K-monotone systems for the analysis of our system (see [21]). To that end, let us first look the definition of K-monotone systems. Let

$$\dot{x} = f(x) \quad (\text{A.2})$$

where  $f$  is a continuously differentiable function defined on a convex, open set  $U$  in  $\mathbb{R}^n$ . We seek sufficient conditions for the flow associated with (A.2) to preserve a partial ordering on  $\mathbb{R}^n$  generated by an orthant. More precisely, let  $m = (m_1, \dots, m_n)$ ,  $m_i \in \{0, 1\}$ ,  $1 \leq i \leq n$ , and  $K_m = \{x \in \mathbb{R}^n : (-1)^{m_i} x_i \geq 0, 1 \leq i \leq n\}$ . We say that the solution operator  $\phi(t)$  of (A.2) preserves the partial ordering  $\leq$  (for  $t \geq 0$ ) and (A.2) is type  $K_m$  monotone if whenever  $x, y \in U$  with  $x \leq_{K_m} y$  then  $\phi_t(x) \leq_{K_m} \phi_t(y)$  for all  $t \geq 0$  for which both  $\phi_t(x)$  and  $\phi_t(y)$  are defined.

The following lemma gives necessary and sufficient conditions for (A.2) to be a type  $K_m$  monotone system in the case that  $f \in \mathcal{C}^1(U)$  for an open convex set  $U \in \mathbb{R}^n$ .

**Lemma A.1** (Lemma 2.1, Smith [21]). *If  $f \in \mathcal{C}^1(U)$  where  $U$  is open and convex in  $\mathbb{R}^n$  then  $\phi_t$  preserves the partial ordering  $\leq_{K_m}$  for  $t \geq 0$  if and only if  $P_m \mathcal{D}f(x) P_m$  has non-negative off-diagonal elements for every  $x \in U$ , where  $P_m = \text{diag}((-1)^{m_1}, \dots, (-1)^{m_n})$ .*

We assume that  $f$  is strongly monotone flow in ordered space  $X$ .

We now highlight below a result concerning convergence properties of strongly monotone systems.

**Theorem A.3** (Theorem 10.3, Hirsh [11]). *Suppose  $X$  is an open subset of a strongly ordered topological vector space. Let  $W \subset X$  be an open set of points with compact orbit closures, and assume that there is a unique equilibrium  $p$  in  $\bigcup_{x \in W} \omega(x)$ . Then  $x.t \rightarrow p$  for all  $x \in W$ .*

## Appendix B Proof of Proposition 2.1

It is sufficient to show that on the border of  $\mathcal{D}$ , the vector field associated to system 2.1 is pointing inside  $\mathcal{D}$ .

Consider the system on the faces of  $\mathcal{D}$  and to show that for each face, the vector fields associated to the system point into the set  $\mathcal{D}$ .

$$\text{If } N_{S_i} = 0 \text{ then } \frac{dN_{S_i}}{dt} = 0.$$

$$\text{If } N_{S_i} = \frac{a_3}{c_{33}} \text{ then } \frac{dN_{S_i}}{dt} \leq 0.$$

$$\text{If } N_M = 0 \text{ then } \frac{dN_M}{dt} = 0.$$

$$\text{If } N_M = \frac{a_7}{c_{77}} \text{ then } \frac{dN_M}{dt} \leq 0.$$

$$\text{If } S_{rc} = 0 \text{ then } \frac{dS_{rc}}{dt} = u \geq 0.$$

$$\text{If } S_{rc} = \frac{a_6 + \sqrt{a_6^2 + 4c_{66}u}}{2c_{66}} \text{ then } \frac{dS_{rc}}{dt} = -c_{64} S_{rc}(S_s + S_e + S_i) \leq 0.$$

$$\text{If } P_c = 0 \text{ then } \frac{dP_c}{dt} = \gamma_p S_i \geq 0.$$

$$\text{If } P_c = \frac{\gamma_p N_{S_i}}{d_{10}} \text{ then } \frac{dP_c}{dt} \leq \gamma_p N_{S_i} - \gamma_p N_{S_i} = 0.$$

$$\text{If } P_m = 0 \text{ then } \frac{dP_m}{dt} = \gamma_m (H_i + M_i) \geq 0.$$

$$\text{If } P_m = \frac{\gamma_m (N_H + N_M)}{d_9} \text{ then } \frac{dP_m}{dt} \leq \gamma_m (N_H + N_M) - d_9 \frac{\gamma_m (N_H + N_M)}{d_9} = 0.$$

## Appendix C Proof of Theorem 2.3

By replacing a solution of the form (2.16) in the linearized equation of the endemic equilibrium, one can get the following linear equations.

$$\left\{ \begin{array}{l} w \bar{Z}_1 = -(t_{110} P_c^* + r_{12}) \bar{Z}_1 + t_{110} (N_H - H_i^*) \bar{Z}_3, \\ w \bar{Z}_2 = \gamma_m \bar{Z}_1 - d_9 \bar{Z}_2 + \gamma_m N_M^* \bar{Z}_6, \\ w \bar{Z}_3 = -d_{10} \bar{Z}_3 + \gamma_p N_{Si}^* \bar{Z}_5, \\ w \bar{Z}_4 = t_{39} (N_{Si}^* - S_e^* - S_i^*) \bar{Z}_2 + (-b_3 - r_{54} - t_{39} P_m^*) \bar{Z}_4 - t_{39} P_m^* \bar{Z}_5, \\ w \bar{Z}_5 = r_{54} \bar{Z}_4 - b_3 \bar{Z}_5, \\ w \bar{Z}_6 = t_{710} (N_M^* - M_i^*) \bar{Z}_3 + (t_{710} P_c^* - b_7) \bar{Z}_6. \end{array} \right. \quad (C.1)$$

Solving for  $\bar{Z}_5$  from the fifth equation of (C.1), and substituting at the same time as simplifying the result into the rest of the equations, we have the equivalent system :

$$\left\{ \begin{array}{l} \left(1 + \frac{w + t_{110} P_c^*}{r_{12}}\right) \bar{Z}_1 = \frac{t_{110} (N_H - H_i^*)}{r_{12}} \bar{Z}_3, \\ \left(1 + \frac{w}{d_9}\right) \bar{Z}_2 = \frac{\gamma_m}{d_9} \bar{Z}_1 + \frac{\gamma_m N_M^*}{d_9} \bar{Z}_6, \\ \left(1 + \frac{w}{d_{10}}\right) \bar{Z}_3 = \frac{\gamma_p N_{Si}^*}{d_{10}} \bar{Z}_5, \\ \left(1 + \frac{w}{b_3 + r_{54}} + \frac{t_{39} P_m^*}{b_3 + r_{54}} \left(1 + \frac{r_{54}}{w + b_3}\right)\right) \bar{Z}_4 = \frac{t_{39} (N_{Si}^* - S_e^* - S_i^*)}{b_3 + r_{54}} \bar{Z}_2, \\ \left(1 + \frac{w}{d_3}\right) \bar{Z}_5 = \frac{r_{54}}{b_3} \bar{Z}_4, \\ \left(1 + \frac{w + t_{710} P_c^*}{b_7}\right) \bar{Z}_6 = \frac{t_{710} (N_M^* - M_i^*)}{b_7} \bar{Z}_3. \end{array} \right. \quad (C.2)$$

Let us define

$$\begin{aligned} G_1(w) &= \frac{w + t_{110} P_c^*}{r_{12}}, & G_2(w) &= \frac{w}{d_9} \\ G_3(w) &= \frac{w}{d_{10}}, & G_4(w) &= \frac{w}{b_3 + r_{54}} + \frac{t_{39} P_m^*}{b_3 + r_{54}} \left(1 + \frac{r_{54}}{w + b_3}\right), \\ G_5(w) &= \frac{w}{d_3}, & G_6(w) &= \frac{w + t_{710} P_c^*}{b_7}. \end{aligned}$$

We get the following system :

$$\begin{cases} [1 + G_1(w)] \bar{Z}_1 = (L \bar{Z})_3; \\ [1 + G_2(w)] \bar{Z}_2 = (L \bar{Z})_6; \\ [1 + G_3(w)] \bar{Z}_3 = (L \bar{Z})_5; \\ [1 + G_4(w)] \bar{Z}_4 = (L \bar{Z})_2; \\ [1 + G_5(w)] \bar{Z}_5 = (L \bar{Z})_4; \\ [1 + G_6(w)] \bar{Z}_6 = (L \bar{Z})_3; \end{cases} \tag{C.3}$$

with

$$L = \begin{pmatrix} 0 & 0 & \frac{t_{110}(N_H - H_i^*)}{r_{12}} & 0 & 0 & 0 \\ \frac{\gamma_m}{d_9} & 0 & 0 & 0 & 0 & \frac{\gamma_m}{d_9} N_M^* \\ 0 & 0 & 0 & 0 & \frac{\gamma_p N_{Si}^*}{d_{10}} & 0 \\ 0 & \frac{t_{39}(N_{Si}^* - S_e^* - S_i^*)}{b_3 + r_{54}} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & \frac{r_{54}}{b_3} & 0 & 0 \\ 0 & 0 & \frac{t_{710}(N_M^* - M_i^*)}{b_7} & 0 & 0 & 0 \end{pmatrix}.$$

Note that the notation  $L(\bar{Z})_i$  (with  $i = 1, \dots, 4$ ) denote the  $i$ th coordinate of the vector  $L(\bar{Z})$ . It should further be noted that the matrix  $L$  has non-negative entries, and the equilibrium  $\hat{E}^* = (H_i^*, P_c^*, P_m^*, S_e^*, S_i^*, M_i^*)$  satisfies  $\hat{E}^* = L \hat{E}^*$ . Furthermore, since the coordinates of  $\hat{E}^*$  are all positive, its follows that if  $\bar{Z}$  is a solution of (C.3), then it is possible to find a minimal positive real numbers  $s$ , depending on  $\bar{Z}$ , such that

$$\|\bar{Z}\| \leq s \hat{E}^*, \tag{C.4}$$

where  $\|\bar{Z}\| = (\|\bar{Z}_1\|, \|\bar{Z}_2\|, \|\bar{Z}_3\|, \|\bar{Z}_4\|)$  with the lexicographic order, and  $\|\cdot\|$  is a norm in  $\mathbb{C}$ . Now we want to show that  $Re w < 0$ . Deny it, we distinguish two cases :  $w = 0$  and  $w \neq 0$ .

In the first case, the determinant of the homogeneous linear system (C.1) in the variable  $\bar{Z}_i$  ( $i = 1, \dots, 6$ ) corresponds to that of the Jacobian of the matrix

$$\begin{pmatrix} -1 - G_1(0) & 0 & \frac{t_{110}(N_H - H_i^*)}{r_{12}} & 0 & 0 & 0 \\ \frac{\gamma_m}{d_9} & -1 - G_2(0) & 0 & 0 & 0 & \frac{\gamma_m}{d_9} N_M^* \\ 0 & 0 & -1 - G_3(0) & 0 & \frac{\gamma_p N_{Si}^*}{d_{10}} & 0 \\ 0 & \frac{t_{39}(N_{Si}^* - S_e^* - S_i^*)}{b_3 + r_{54}} & 0 & -1 - G_4(0) & 0 & 0 \\ 0 & 0 & 0 & \frac{r_{54}}{b_3} & -1 - G_5(0) & 0 \\ 0 & 0 & \frac{t_{710}(N_M^* - M_i^*)}{b_7} & 0 & 0 & -1 - G_6(0) \end{pmatrix},$$

which is given by

$$\begin{aligned} \Delta &= (-1 - G_6(0)) ((1 + G_1(0) + G_2(0) + G_1(0)G_2(0)) (-1 - G_3(0)) (-1 - G_4(0)) (-1 - G_5(0)) \\ &\quad + \frac{\gamma_m \gamma_p N_{S_i}^* r_{54} t_{39} t_{110} (N_H - H_i^*) (N_{S_i}^* - S_e^* - S_i^*)}{b_3 d_9 d_{10} r_{12} (b_3 + r_{54})}) \\ &\quad + \frac{\gamma_m \gamma_p (-1 - G_1(0)) N_M^* N_{S_i}^* r_{54} t_{39} t_{710} (N_{S_i}^* - S_e^* - S_i^*) (N_M^* - M_i^*)}{b_3 b_7 d_9 d_{10} (b_3 + r_{54})}. \end{aligned} \quad (\text{C.5})$$

Since  $G_2(0) = G_3(0) = G_5(0) = 0$ ,

$$\begin{aligned} \Delta &= (-1 - G_6(0)) (1 + G_1(0)) (-1 - G_4(0)) \\ &\quad + (-1 - G_6(0)) \frac{\gamma_m \gamma_p N_{S_i}^* r_{54} t_{39} t_{110} (N_H - H_i^*) (N_{S_i}^* - S_e^* - S_i^*)}{b_3 d_9 d_{10} r_{12} (b_3 + r_{54})} \\ &\quad + \frac{\gamma_m \gamma_p (-1 - G_1(0)) N_M^* N_{S_i}^* r_{54} t_{39} t_{710} (N_{S_i}^* - X_4^* - S_i^*) (N_M^* - M_i^*)}{b_3 b_7 d_9 d_{10} (b_3 + r_{54})} \\ &= (-1 - G_6(0)) (1 + G_1(0)) (-1 - G_4(0)) \\ &\quad - \frac{1}{P_m^*} \left( (1 + G_6(0)) \frac{\gamma_m H_i^*}{d_9} + (1 + G_1(0)) \frac{\gamma_m N_M^* M_i^*}{d_9} \right). \end{aligned}$$

Let  $\alpha = \max\{1 + G_1(0), 1 + G_6(0)\}$ , we have

$$\begin{aligned} \Delta &> 1 + G_1(0) + G_4(0) + G_1(0) G_4(0) + G_6(0) + G_1(0) G_6(0) \\ &\quad + G_4(0) G_6(0) + G_1(0) G_4(0) G_6(0) - \alpha. \end{aligned}$$

Then if  $\alpha = 1 + G_1(0)$ , we have

$$\Delta > G_4(0) + G_1(0)G_4(0) + G_6(0) + G_1(0) G_6(0) + G_4(0) G_6(0) + G_1(0) G_4(0) G_6(0) > 0.$$

Else  $\alpha = 1 + G_6(0)$ , and

$$\begin{aligned} \Delta &> G_1(0) + G_4(0) + G_1(0) G_4(0) + G_1(0) G_6(0) \\ &\quad + G_4(0) G_6(0) + G_1(0) G_4(0) G_6(0) > 0, \end{aligned}$$

since  $G_1(0)$ ,  $G_2(0)$ ,  $G_4(0)$  are also positive.

Thus, for  $w = 0$ , the unique solution of the system (C.3) is the trivial solution which implies that  $w \neq 0$ . Let us suppose now that  $w \neq 0$ , and that  $\mathcal{R}_e w \geq 0$ . Let  $G(w) = \min\{|1 + G_i(w)|, i = 1, \dots, 4\}$ . It is easy to prove that in the case  $|1 + G_i(w)| > 1$  for all  $i$ , and then  $G(w) > 1$ . Taking norms on both sides of (C.3), and using the fact that  $L$  is positive, we obtain the following inequality:

$$G(w) \|\bar{Z}\| \leq L \|\bar{Z}\|. \quad (\text{C.6})$$

Using (C.4) and (C.6), we find

$$G(w) \|\bar{Z}\| \leq s L \hat{E}^* = s \hat{E}^*.$$

That implies

$$\|\bar{Z}\| \leq \frac{s}{G(w)} \hat{E}^* < s \hat{E}^*,$$

but this contradicts the minimality of  $s$ . Therefore  $\mathcal{R}_e w < 0$ .

## Appendix D Proof of Existence of multi-variable function $\mathcal{F}$

Let us define  $\hat{E}^* = (H_i^*, P_m^*, P_c^*, S_e^*, S_i^*, M_i^*)$  an equilibrium point. Then the positive equilibrium point (equilibrium with  $H_i, P_m, P_c, S_e, S_i, M_i > 0$ ) maybe obtained by solving the equations of the second member of the system (2.12) equal zero.

$$t_{110} (N_H - H_i) P_c - r_{12} H_i = 0; \quad (D.1)$$

$$\gamma_m (H_i + M_i N_M^*) - d_9 P_m = 0; \quad (D.2)$$

$$\gamma_p N_{S_i}^* S_i - d_{10} P_c = 0; \quad (D.3)$$

$$t_{39} P_m (N_{S_i}^* - S_e - S_i) - (b_3 + r_{54}) S_e = 0; \quad (D.4)$$

$$r_{54} S_e - b_3 S_i = 0; \quad (D.5)$$

$$t_{710} P_c (N_M^* - M_i) - b_7 M_i = 0; \quad (D.6)$$

Using Equation (D.3) we have

$$P_c = \frac{\gamma_p N_{S_i}^*}{d_{10}} S_i.$$

Equation (D.5) gives

$$S_e = \frac{b_3}{r_{54}} S_i.$$

Also, Equation (D.2) produces

$$P_m = \frac{\gamma_m (H_i + M_i N_M^*)}{d_9}.$$

And, Equation (D.1) gives

$$H_i = \frac{\gamma_p N_H N_{S_i}^* r_{54} t_{110} S_e}{b_3 d_{10} \left( r_{12} + \frac{\gamma_p N_{S_i}^* r_{54} t_{110} S_e}{b_3 d_{10}} \right)}$$

with Equation (D.4) we get

$$S_e = \frac{\gamma_m N_{S_i}^* t_{39} (H_i + N_M^* M_i)}{d_9 \left( b_3 + r_{54} + \frac{\gamma_m \left( 1 + \frac{r_{54}}{b_3} \right) S_e t_{39} (H_i + N_M^* M_i)}{d_9} \right)}$$

And, Equation (D.6) gives

$$M_i = \frac{\gamma_p N_{S_i}^* r_{54} t_{710} N_M^* S_e}{b_3 d_{10} \left( b_7 + \frac{\gamma_p N_{S_i}^* r_{54} t_{710} S_e}{b_3 d_{10}} \right)}$$

So, we can define a multi-variable function with respect in  $(H_i, S_e, M_i)$  as follows:

$$\mathcal{U} = \mathcal{F}(\mathcal{U}),$$



where

$$u = \begin{pmatrix} H_i \\ S_e \\ M_i \end{pmatrix}, \quad \mathcal{F} = \begin{pmatrix} \mathcal{F}_1 := \frac{\gamma_p N_H N_{S_i}^* r_{54} t_{110} S_e}{b_3 d_{10} \left( r_{12} + \frac{\gamma_p N_{S_i}^* r_{54} t_{110} S_e}{b_3 d_{10}} \right)} \\ \mathcal{F}_2 := \frac{\gamma_m t_{39} N_{S_i}^* (H_i + N_M^* M_i)}{d_9 \left( b_3 + r_{54} + \frac{\gamma_m \left( 1 + \frac{r_{54}}{b_3} \right) t_{39} S_e (H_i + N_M^* M_i)}{d_9} \right)} \\ \mathcal{F}_3 := \frac{\gamma_p N_{S_i}^* r_{54} t_{710} N_M^* S_e}{b_3 d_{10} \left( b_7 + \frac{\gamma_p N_{S_i}^* r_{54} t_{710} S_e}{b_3 d_{10}} \right)} \end{pmatrix}.$$

## Appendix E Proof of Theorem 2.4

Let us rewrite the system (2.12) in terms of variables  $(H_i, P_m, P_c, S_s, S_i, M_i)$  for more convenience. We get the following system :

$$\left. \begin{cases} \frac{dH_i}{dt} = t_{110} (N_H - H_i) P_c - r_{12} H_i; \\ \frac{dP_m}{dt} = \gamma_m (H_i + M_i N_M^*) - d_9 P_m; \\ \frac{dP_c}{dt} = \gamma_p N_{S_i}^* S_i - d_{10} P_c; \\ \frac{dS_s}{dt} = b_3 - (t_{39} P_m + b_3) S_s; \\ \frac{dS_i}{dt} = r_{54} S_s - b_3 S_i; \\ \frac{dM_i}{dt} = t_{710} S_s (N_M^* - M_i) - b_7 M_i; \end{cases} \right\} := f(H_i, P_m, P_c, S_s, S_i, M_i) = f(x) \quad (\text{E.1})$$

with Jacobian

$$Df(x) = \begin{pmatrix} -r_{12} - t_{110} P_c & 0 & t_{110} (N_H - H_i) & 0 & 0 & 0 \\ \gamma_m & -d_9 & 0 & 0 & 0 & \gamma_m N_M^* \\ 0 & 0 & -d_{10} & 0 & \gamma_p N_{S_i}^* & 0 \\ 0 & -t_{39} S_s & 0 & -b_3 - t_{39} P_m & 0 & 0 \\ 0 & 0 & 0 & -r_{54} & -b_3 - r_{54} & 0 \\ 0 & 0 & t_{710} (N_M^* - M_i) & 0 & 0 & -b_7 - t_{710} P_c \end{pmatrix}.$$

We choose the matrix  $T$  as

$$T = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}.$$

Then from the matrix  $T$  and the Jacobian given, we get

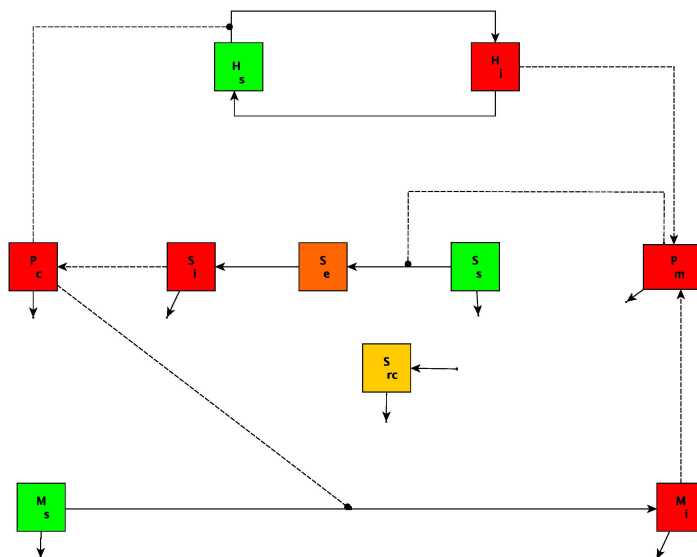
$$T (Df(x)) T = \begin{pmatrix} -r_{54} - t_{110} P_c & 0 & t_{110} (N_H - H_i) & 0 & 0 & 0 \\ \gamma_m & -d_9 & 0 & 0 & 0 & \gamma_m N_M^* \\ 0 & 0 & -d_{10} & 0 & \gamma_p N_{S_i}^* & 0 \\ 0 & t_{39} S_s & 0 & -b_3 - t_{39} P_m & 0 & 0 \\ 0 & 0 & 0 & r_{54} & -b_3 - r_{54} & 0 \\ 0 & 0 & t_{710} (N_M^* - M_i) & 0 & 0 & -b_7 - t_{710} P_c \end{pmatrix}.$$

It is observed that the system is  $K$ -monotone in  $\mathcal{D}_1$  with respect to the partial ordering defined by the orthant  $K = \{(H_i, S_s, S_i, M_i) \in \mathbb{R}^4 : H_i \geq 0, S_s \leq 0, S_i \geq 0, M_i \geq 0\}$ . Moreover it is strongly monotone with respect to the orthant  $K$  because  $Df(x)$  is irreducible.

Thanks to Hirsch's theorem A.3 and the fact that we have only one endemic equilibrium  $E^*$  which is locally asymptotically stable in  $\mathcal{D}_1$  when  $\mathcal{R}_0 > 1$  we state that  $E^*$  is globally asymptotically stable in  $\mathcal{D}_1$  when  $\mathcal{R}_0 > 1$ .

**Table 1.** Existence and stability of equilibria of system (2.3)

	$E_1$	$E_2$	$E^*$	$E^{**}$
$c_{33}c_{66} - c_{36}c_{64} > 0$	AS iff $u = 0$ and $a_6c_{33} - a_3c_{64} < 0$	GAS iff $a_3c_{66} - a_6c_{36} < 0$ or $u > \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}$	AS if $u < \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}$ , and $a_3c_{66} - a_6c_{36} > 0$	does not exist
$c_{33}c_{66} - c_{36}c_{64} < 0$	AS iff $u = 0$ and $a_6c_{33} - a_3c_{64} < 0$	GAS iff $a_3c_{66} - a_6c_{36} < 0$ or $u > \frac{a_3(a_3c_{66} - a_6c_{36})}{c_{36}^2}$	does not exist	AS if $u_m < u < \frac{(a_6c_{33} - a_3c_{64})^2}{4c_{33}(c_{36}c_{64} - c_{33}c_{66})}$



**Figure 4.** Compartmental diagram for the mathematical model. The dashed lines indicate the transmission paths for disease between sub-populations.

**Table 2.** Values selected for the parameters.

Parameters	Estimated values per day	Source
$r_{12}$	$4.47 \times 10^{-4}$	[1]
$d_3, d_4, d_5$	$8.86 \times 10^{-3}$	[1]
$d_7, d_8$	$5.00 \times 10^{-3}$	[1]
$d_6$	$8.86 \times 10^{-3}$	[1]
$b_6$	$6.60 \times 10^{-2}$	[1]
$c_{33}, c_{44}, c_{55}$	$5.11 \times 10^{-7}$	[1]
$c_{77}, c_{88}$	$7.00 \times 10^{-8}$	[1]
$c_{66}$	$2.50 \times 10^{-7}$	[1]
$b_3$	$6.00 \times 10^{-2}$	[1]
$r_{54}$	$2.50 \times 10^{-2}$	[1]
$t_{39}$	$1.05 \times 10^{-9}$	[19]
$\gamma_m$	0.696	[19]
$\gamma_p$	2.6	[19]
$d_9$	2	[19]
$d_{10}$	1	[19]
$b_7$	$1.20 \times 10^{-2}$	[1]
$t_{710}$	$2.0 \times 10^{-6}$	Estimated
$t_{110}$	$2.23 \times 10^{-7}$	Estimated

## References

- [1] E. Allen and H. Victory Jr, *Modelling and simulation of a schistosomiasis infection with biological control*, Acta Tropica, 2003, 87(2), 251–267.

- [2] R. Anderson and R. May, *Prevalence of schistosome infections within molluscan populations: observed patterns and theoretical predictions*, *Parasitology*, 1979, 79(1), 63–94.
- [3] R. M. Anderson and R. M. May, *Regulation and stability of host-parasite population interactions: I. regulatory processes*, *The journal of animal ecology*, 1978, 219–247.
- [4] J. N. Behrman et al., *Tropical diseases—responses of pharmaceutical companies.*, American Enterprise Institute for Public Policy Research, 1980.
- [5] E. T. Chiyaka and W. GARIRA, *Mathematical analysis of the transmission dynamics of schistosomiasis in the human-snail hosts*, *Journal of Biological Systems*, 2009, 17(03), 397–423.
- [6] M. Diaby, A. Iggidr, M. Sy and A. Sene, *Global analysis of a schistosomiasis infection model with biological control*, *Applied Mathematics and Computation*, 2014, 246, 731–742.
- [7] C. Ding, Y. Sun and Y. Zhu, *A schistosomiasis compartment model with incubation and its optimal control*, *Mathematical Methods in the Applied Sciences*, 2017, 40(14), 5079–5094.
- [8] W. Fleming and P.-L. Lions, *Stochastic Differential Systems, Stochastic Control Theory and Applications: Proceedings of a Workshop, held at IMA, June 9-19, 1986*, 10, Springer Science & Business Media, 2012.
- [9] A. Guiro, D. Ngom and D. Ouedraogo, *Stability analysis for a class of discrete schistosomiasis models with general incidence*, *Advances in Difference Equations*, 2017, 2017(1), 1–16.
- [10] H. W. Hethcote and H. R. Thieme, *Stability of the endemic equilibrium in epidemic models with subpopulations*, *Mathematical Biosciences*, 1985, 75(2), 205–227.
- [11] M. W. Hirsch, *Stability and convergence in strongly monotone dynamical systems*, *Journal fur die reine und angewandte Mathematik*, 1988, 383.
- [12] H. R. Joshi, *Optimal control of an hiv immunology model*, *Optimal control applications and methods*, 2002, 23(4), 199–213.
- [13] C. Kalinda, S. Mushayabasa, M. J. Chimbari and S. Mukaratirwa, *Optimal control applied to a temperature dependent schistosomiasis model*, *Biosystems*, 2019, 175, 47–56.
- [14] D. Kirschner, S. Lenhart and S. Serbin, *Optimal control of the chemotherapy of hiv*, *Journal of mathematical biology*, 1997, 35(7), 775–792.
- [15] J. LaSalle and Z. Artstein, *The stability of dynamical systems/jp lasalle*, Appendix A, Limiting Equations and Stability of Nonautonomous Ordinary Differential Equations, Society for Industrial and Applied Mathematics, Philadelphia, 1976.
- [16] Y. Li, Z. Teng, S. Ruan et al., *A mathematical model for the seasonal transmission of schistosomiasis in the lake and marshland regions of china*, *Mathematical Biosciences & Engineering*, 2017, 14(5&6), 1279.
- [17] Y. Liu, Y. He, S. Yan and S. Gao, *A class of nonautonomous schistosomiasis transmission model with incubation period*, *Applied Mathematics*, 2019, 10(3), 159–172.

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- [18] G. Macdonald et al., *The dynamics of helminth infections, with special reference to schistosomes.*, Transactions of the Royal Society of Tropical Medicine and Hygiene, 1965, 59(5), 489–506.
- [19] T. D. Mangal, S. Paterson and A. Fenton, *Predicting the impact of long-term temperature changes on the epidemiology and control of schistosomiasis: a mechanistic model*, PLoS one, 2008, 3(1), e1438.
- [20] L.-x. Qi, Y. Tang and S.-j. Tian, *Parameter estimation of modeling schistosomiasis transmission for four provinces in china*, 2018.
- [21] H. L. Smith, *Systems of ordinary differential equations which generate an order preserving flow. a survey of results*, SIAM review, 1988, 30(1), 87–113.
- [22] R. F. Stengel, R. Ghigliazza, N. Kulkarni and O. Laplace, *Optimal control of innate immune response*, Optimal control applications and methods, 2002, 23(2), 91–104.
- [23] P. Van den Driessche and J. Watmough, *Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission*, Mathematical biosciences, 2002, 180(1-2), 29–48.
- [24] R. S. Varga, *Matrix iterative analysis*, 27, Springer Science & Business Media, 1999.
- [25] M. Vidyasagar, *Decomposition techniques for large-scale systems with nonadditive interactions: Stability and stabilizability*, IEEE transactions on automatic control, 1980, 25(4), 773–779.
- [26] WHO, *Schistosomiasis*, <https://www.who.int/en/news-room/fact-sheets/detail/schistosomiasis>, 2020.
- [27] F. Zhang, S. Gao, H. Cao and Y. Luo, *Dynamical analysis of a schistosomiasis japonicum model with time delay*, Journal of Applied Mathematics and Physics, 2019, 7(4), 948–967.