Rubrique

SCHISTOSOMIA INFECTION

A mathematical analysis of a model with mating structure

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ABSTRACT. Drug treatment, snail control, cercariae control, improved sanitation and health education are the effective strategies which are used to control the schistosomiasis. In this paper, we consider a deterministic model for schistosomiasis transmission dynamics in order to explore the role of the several control strategies. The global stability of a schistosomiasis infection model that involves mating structure including male schistosomes, female schistosomes, paired schistosomes and snails is studied by constructing appropriate Lyapunov functions. We derive the basic reproduction number $\mathcal{R}_0$ for the deterministic model, and establish that the global dynamics are completely determined by the values of $\mathcal{R}_0$. We show that the disease can be eradicated when $\mathcal{R}_0 \leq 1$; otherwise, the system is persistent when $\mathcal{R}_0 > 1$.

RÉSUMÉ. Le traitement médicamenteux, le traitement par les molluscicides, l'amélioration de l'assainissement et l'éducation sanitaire sont les stratégies efficaces qui sont utilisés pour contrôler la schistosomiase. Dans cet article, nous considérons un modèle déterministe pour la dynamique de transmission de la schistosomiase dans le but d'explorer le rôle des différentes stratégies de contrôle. La stabilité globale d'un modèle d'infection de la schistosomiase qui incorpore une structure d'appariement et une dynamique des schistosomes mâles, femelles, pairs et des escargots est étudiée par la construction de fonctions de Lyapunov appropriées. Nous calculons le taux de reproduction de base $\mathcal{R}_0$ pour le modèle déterministe, et établissons que la dynamique globale est complètement déterminée par les valeurs de $\mathcal{R}_0$. Nous montrons que la maladie peut être éradiquée quand $\mathcal{R}_0 \leq 1$; par ailleurs, le système est persistant lorsque $\mathcal{R}_0 > 1$.

KEYWORDS : Epidemic models; Nonlinear dynamical systems; Global stability; Reproduction number; Schistosomiasis.

MOTS-CLÉS : Modèles épidémiologiques; systèmes dynamiques nonlinèaires; Stabilité globale; Taux de reproduction de base; Bilharziose.

1. Introduction

Schistosomiasis (also known as bilharzia, bilharziasis or snail fever) is a vector-borne disease caused by infection of the intestinal or urinary venous system by trematode worms of the genus Schistosoma. More than 207 million people are infected worldwide, with an estimated 700 million people at risk in 74 endemic countries [12]. Schistosomiasis is prevalent in tropical and subtropical areas, especially in poor communities without access to safe drinking water and adequate sanitation. Of the 207 million people with schistosomiasis, 85% live in Africa [12]. Of the tropical diseases, only malaria accounts for a greater global burden than schistosomiasis [11]. Therefore, it is vital to prevent and control the schistosomiasis transmission.

Schistosoma requires the use of two hosts to complete its life cycle: the definitive hosts and the intermediate snail hosts. In definitive hosts, schistosoma has two distinct sexes. Mature male and female worms pair and migrate either to the intestines or the bladder where eggs production occurs. One female worm may lay an average of 200 to $2,000$ eggs per day for up to twenty years. Most eggs leave the blood stream and body through the intestines. Some of the eggs are not excreted, however, and can lodge in the tissues. It is the presence of these eggs, rather than the worms themselves, that causes the disease. These eggs pass in urine or feces into fresh water into miracidia which infect the intermediate snail hosts. In snail hosts, parasites undergo further asexual reproduction, ultimately yielding large numbers of the second free-living stage, the cercaria. Free-swimming cercariae leave the snail host and move through the aquatic or marine environment, often using a whip-like tail, though a tremendous diversity of tail morphology is seen. Cercariae are infective to the second host and turn it into single schistosoma, and infection may occur passively (e.g., a fish consumes a cercaria) or actively (the cercaria penetrates the fish) and terminates the life cycle of the parasite.

Many effective strategies are used in the real world, such as: based on preventive treatment, snail control, cercariae control, improved sanitation and health education. The WHO strategy for schistosomiasis control focuses on reducing disease through periodic, targeted treatment with praziquantel. This involves regular treatment of all people in at-risk groups [12]. Over the past few decades, different mathematical models [3], [5], [13], [10] have been constructed to describe the transmission dynamics involving two-sex problems. In [3], [5], [13], a mathematical model is developed for a schistosomiasis infection that involves pair-formation models and studied the existence, uniqueness and the stabilities of exponential solutions. We note that in [5], [13] authors formulate three forms of pair-formation functions (also known as mating functions) that are the harmonic mean function, the geometric mean function and the minimum function. In [16], Xu et al. have proposed a multi-strain schistosome model with mating structure. Their goal was to study the effect of drug treatment on the maintenance of schistosome genetic diversity. However, in their model they only consider the adult parasite populations. Castillo-Chavez et al. [3] have considered a time delay model but also do not include the snails dynamics. But it is important to take into account the snail dynamics as it is shown in the life cycle of schistosoma. In fact, the parasite offspring is produced directly by infected snails but not by paired parasites as is related in [10].

Recently, Qi et al. [10] have formulated a deterministic mathematical model to study the transmission dynamics of schistosomiasis with a linear mating function incorporating these snail dynamics. This paper gave the expression of a threshold number (and not the basic reproduction number) with a local stability analysis of the disease free equilibrium.

However, no work has been done to investigate the global stability of the equilibria which is more in interest. Here, we take this deterministic schistosomiasis model with mating structure [10] and we propose a complete mathematical analysis. A stability analysis is provided to study the epidemiological consequences of control strategies. We compute the basic reproduction number and we show that when it is less or equal to one then the disease free equilibrium (DFE) is the unique equilibrium of the system and it is globally asymptotically stable, while when the basic reproduction number is greater than one we show that the disease persists. This paper is organized as follows. Model formulation is carried out and the basic properties are shown in the next section. In Section 3, we determine the basic reproductive number $\mathcal{R}_0$ of the model and also establish global stability of the disease-free equilibrium. In the end of this section we show that the disease is uniformly persistent when $\mathcal{R}_0 > 1$. A general conclusion is given in the last section.

2. Mathematical Model

The model that we consider has been presented in [10]. It describes the time evolution of a population divided in three parasites sub-populations and two intermediate snail host sub-populations. The state variables of the model are:

– $X_m(t)$ the male schistosoma population size.

– $X_f(t)$ the female schistosoma population size.

– $X_p(t)$ the pair schistosoma population size.

– $X_s(t)$ the susceptible (uninfected) snail host population size.

– $X_i(t)$ the infected snail host population size.

The time evolution of the different populations is governed by the following system of equations:

$$\begin{cases} \frac{dX_m}{dt} = & k_m\, X_i - (\mu_m + \epsilon_m)\, X_m - \rho\, X_f, \\ \frac{dX_f}{dt} = & k_f\, X_i - (\mu_f + \epsilon_f)\, X_f - \rho\, X_f, \\ \frac{dX_p}{dt} = & \rho\, X_f - (\mu_p + \epsilon_p)\, X_p, \\ \frac{dX_s}{dt} = & \Lambda - (\mu_s + \epsilon_s)\, X_s - \beta\, X_p\, X_s, \\ \frac{dX_i}{dt} = & \beta\, X_p\, X_s - (\mu_s + \epsilon_s + \alpha_s)\, X_i. \end{cases} \tag{1}$$

The different parameters are:

– k_m and k_f are the recruitment rates of male schistosoma and female schistosoma respectively. α_s is the disease-induced death rate of snail hosts.

– μ_m, μ_f, μ_p, and μ_s denote the natural death rate for male, female, pair and snail hosts respectively.

– ρ represents the effective mating rate.

– Λ is the recruitment rate of snail hosts.

– β is the transmission rate from pairs parasite to susceptible snails.

– ϵ_m, ϵ_f, ϵ_p and ϵ_s are the elimination rates of male shistosoma, female schistosoma, paired schistosoma and snails respectively. These elimination rates represent the control strategies.

As it has been done in [10], we shall denote

$$\mu_m + \epsilon_m = \mu_{m\epsilon}, \qquad \mu_f + \epsilon_f = \mu_{f\epsilon},$$
$$\mu_p + \epsilon_p = \mu_{p\epsilon}, \qquad \mu_s + \epsilon_s = \mu_{s\epsilon}.$$

2.1. Basic Properties

In this section, we give some basic results concerning solutions of system (1) that will be subsequently used in the proofs of the stability results.

Proposition 2.1. *The set* $\Gamma = \{M_{sc} \geq F_{sc} \geq 0,\ P_{sc} \geq 0,\ S_{sn} \geq 0,\ I_{sn} \geq 0\}$ *is a positively invariant set for system (1).*

Proof. The vector field given by the right-hand side of system (1) points inward on the boundary of $\mathbb{R}^5_+$. For example, if $X_s = 0$, then, $\dot{X}_s = \Lambda > 0$. In an analogous manner, the same can be shown for the other system components. □

Proposition 2.2. *All solutions of system (1) are forward bounded.*

Proof. Let us define $N_X = X_m + X_f + X_p$ and $N_Y = X_s + X_i$. Using system (1), we have $\dfrac{dN_Y}{dt} = \Lambda - \mu_{s\epsilon}\, N_Y - \alpha_s\, X_i \leq \Lambda - \mu_{s\epsilon}\, N_Y$. This implies that the set $\{N_Y \leq \dfrac{\Lambda}{\mu_{s\epsilon}}\}$ is positively invariant and attracts all the solutions of (1).

We also have:

$$\begin{aligned}\frac{dN_X}{dt} &= (k_m + k_f)\, X_i - \mu_{m\epsilon}\, X_m - (\mu_{f\epsilon} + \rho)\, X_f - \mu_{p\epsilon}\, X_p \\ &\leq (k_m + k_f)\, \frac{\Lambda}{\mu_{s\epsilon}} - \min\{\mu_{m\epsilon}, \mu_{f\epsilon}, \mu_{p\epsilon}\}\, N_X - \rho\, X_f.\end{aligned}$$

Hence, the set $\left\{N_X \leq \dfrac{(k_m + k_f)\Lambda}{\mu_{s\epsilon}\,\gamma}\right\}$, where $\gamma = \min\{\mu_{m\epsilon}, \mu_{f\epsilon}, \mu_{p\epsilon}\}$, is positively invariant set and attracts all the solutions of (1). □

Therefore all feasible solutions of system (1) enter the region

$$\Omega = \left\{(X_m, X_f, X_p, X_s, X_i) \in \mathbb{R}^5_+ : X_s + X_i \leq \frac{\Lambda}{\mu_{s\epsilon}},\ X_m + X_f + X_p \leq \frac{(k_m + k_f)\Lambda}{\mu_{s\epsilon}\,\gamma}\right\},$$

and the set Ω is a compact positively invariant set for system (1). It is then sufficient to consider solutions in Ω.

3. The basic reproduction number and the disease-free Equilibrium

The disease-free equilibrium of system (1) is $\mathcal{E}^0 = \left(0, 0, 0, X_s^0, 0\right) = \left(0, 0, 0, \dfrac{\Lambda}{\mu_{s\epsilon}}, 0\right)$. Using the notations of [15] for the model system (1), the matrices F and V for the new infection terms and the remaining transfer terms are, respectively, given by

$$F = \begin{pmatrix} 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & \beta\dfrac{\Lambda}{\mu_{s\epsilon}} & 0 \end{pmatrix} \quad \text{and} \quad V = \begin{pmatrix} -k_m & \mu_{m\epsilon} & \rho & 0 \\ 0 & \rho+\mu_{f\epsilon} & 0 & -k_f \\ 0 & -\rho & \mu_{p\epsilon} & 0 \\ 0 & 0 & & \mu_{s\epsilon}+\alpha_s \end{pmatrix}$$

The basic reproduction number $\mathcal{R}_0$ is equal to the spectral radius of the matrix $F\,V^{-1}$, a simple computation gives:

$$\mathcal{R}_0 = \frac{\beta\,\rho\,k_f\,\Lambda}{\mu_{s\epsilon}\,\mu_{p\epsilon}\,(\mu_{f\epsilon}+\rho)\,(\mu_{s\epsilon}+\alpha_s)} = \frac{\beta\,\rho\,k_f\,X_s^0}{\mu_{p\epsilon}\,(\mu_{f\epsilon}+\rho)\,(\mu_{s\epsilon}+\alpha_s)}.$$

One can remark that there is a mistake in the formula for $\mathcal{R}_0$ provided in [10].

The basic reproductive number for system (1) measures the average number of new infections generated by a single infected individual in a completely susceptible population.

As it is well known (see, for instance, [15]), the local asymptotic stability of the disease-free equilibrium is completely determined by the value of $\mathcal{R}_0$ compared to unity, i.e., The disease-free equilibrium $\mathcal{E}^0$ of the system (1) is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Hence $\mathcal{R}_0$ determines whether the disease will be prevalent in the given population or will go extinct.

Next, we discuss the global stability of infection-free equilibrium by using suitable Lyapunov function and LaSalle invariance principle for system (1). In recent years, the method of Lyapunov functions has been a popular technique to study global properties of population models. However, it is often difficult to construct suitable Lyapunov functions.

Theorem 3.1. *The disease-free equilibrium $\mathcal{E}^0$ of system (1) is globally asymptotically stable (GAS) on the nonnegative orthant $\mathbb{R}^5_+$ whenever $\mathcal{R}_0 \leq 1$.*

Proof. See Appendix A. □

Biologically speaking, Theorem 3.1 implies that schistosomiasis may be eliminated from the community if $\mathcal{R}_0 \leq 1$. One can remark that $\mathcal{R}_0$ does not depend on $\mu_{m\epsilon} = \mu_m + \epsilon_m$. Hence it is not helpful to try to control the the male schistosoma population and then one can take $\epsilon_m = 0$. Therefore the only way to eliminate schistosomiasis is to increase the killing rates of female schistosoma (ϵ_f), paired schistosoma (ϵ_p) and snails (ϵ_s) in order to have $\mathcal{R}_0 \leq 1$.

In the rest of this section, we show that the disease persists when $\mathcal{R}_0 > 1$. The disease is endemic if the infected fraction of the population persists above a certain positive level. The endemicity of a disease can be well captured and analyzed through the notion of uniform persistence. System (1) is said to be uniformly persistent in Ω if there exists constant $c > 0$, independent of initial conditions in $\overset{\circ}{\Omega}$ (the interior of Ω), such that all solutions $(X_m(t), X_f(t), X_p(t), X_s(t), X_i(t))$ of system (1) satysfy

$$\liminf_{t\to\infty} X_m(t) \geq c, \quad \liminf_{t\to\infty} X_f(t) \geq c, \quad \liminf_{t\to\infty} X_p(t) \geq c,$$

$$\liminf_{t\to\infty} X_s(t) > c, \quad \liminf_{t\to\infty} X_i(t) \geq c,$$

provided $(X_m(0), X_f(0), X_p(0), X_s(0), X_i(0)) \in \overset{\circ}{\Omega}$, (see [14], [2]).

Theorem 3.2. *System (1) is uniformly persistent in* Ω *if and only if* $\mathcal{R}_0 > 1$.

Proof. See Appendix B □

4. Numerical simulation

In this section, we use numerical simulations to illustrate the asymptotic stability and persistent results. Parameter values have been chosen in such a way that they are realist and at the same time obey the conditions for stability or persistent. Figure 1 illustrates the convergence of the dynamic of the system to the disease-free point.

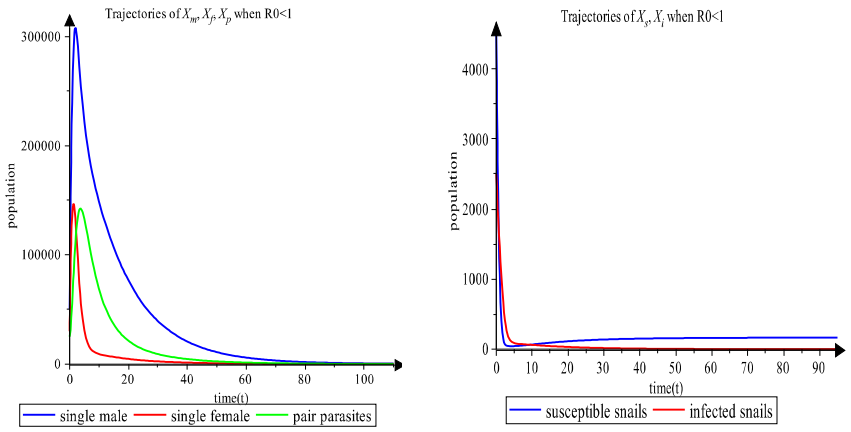

Figure 1. *Solutions of the schistosomiasis model (1) with parameter values defined as follows:* $k_f = 100$, $k_m = 145$, $\Lambda = 150$, $\beta = 0.000018$, $\alpha_s = 0.5$, $\mu_{f\epsilon} = 0.3$, $\mu_{m\epsilon} = 0.1$, $\mu_{p\epsilon} = 0.2$, $\rho = 0.467$, $\mu_{s\epsilon} = 0.9$. *These parameters correspond to* $\mathcal{R}_0 = 0.6$. *The initial condition is* $X_m = 50000$, $X_f = 30000$, $X_p = 25000$, $X_s = 4500$, $X_i = 2500$.

Figure 2 presents how the system persists and approaches the endemic point.

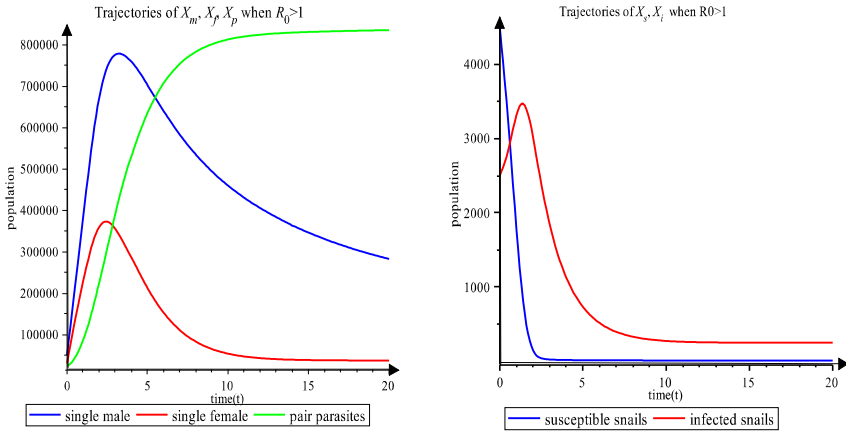

Figure 2. *Solutions of the schistosomiasis model (1) with parameter values defined as follows:* $k_f = 100$, $k_m = 145$, $\Lambda = 150$, $\beta = 0.000018$, $\alpha_s = 0.5$, $\mu_{f\epsilon} = 0.2$, $\mu_{m\epsilon} = 0.1$, $\mu_{p\epsilon} = 0.02$, $\rho = 0.467$, $\mu_{s\epsilon} = 0.1$. *These parameters correspond to* $\mathcal{R}_0 = 157.5$. *The initial condition is* $X_m = 50000$, $X_f = 30000$, $X_p = 25000$, $X_s = 4500$, $X_i = 2500$.

5. CONCLUSION

In this paper, we have investigated the dynamical properties of a schistosomiasis model with mating structure which incorporates some control strategies and uses the minimum mating function. When the basic reproductive number $\mathcal{R}_0$ is less than 1, we have proved the global asymptotic stability of the disease free equilibrium $\mathcal{E}_0$. When the basic reproductive number $\mathcal{R}_0$ is greater than 1, the persistent of the endemic equilibrium $\mathcal{E}_h$ has been obtained.

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Appendix A. Proof of Theorem 3.1

Proof. We shall use the following notations: $x = (X_m, X_f, X_p, X_s, X_i)$, and $X_s^0 = \dfrac{\Lambda}{\mu_{s\epsilon}}$. To show the global stability of infection-free equilibrium of system (1), we use the following candidate Lyapunov function:

$$V(x) = \frac{\mu_{s\epsilon} + \alpha_s}{k_f} X_f + \frac{(\mu_{s\epsilon} + \alpha_s)(\mu_{f\epsilon} + \rho)}{k_f \rho} X_p + \int_{X_s^0}^{X_s} \frac{X_\tau - X_s^0}{X_\tau} d X_\tau + X_i \quad (2)$$

This function satisfies: $V(x) \geq 0$ for all $x \in \Omega$, and $V(x) = 0$ if and only if $x = (X_m, 0, 0, X_s^0, 0)$.

Taking the time derivative of the function V (defined by 2), along the solutions of system (1), we obtain

$$\begin{aligned}
\dot{V} &= \left(1 - \frac{X_s^0}{X_s}\right)(\Lambda - \mu_{s\epsilon} X_s - \beta X_s X_p) + (\beta X_s X_p - (\mu_{s\epsilon} + \alpha_s) X_i) \\
&+ \frac{(\mu_{s\epsilon} + \alpha_s)}{k_f}(k_f X_i - (\mu_{f\epsilon} + \rho)) X_f + \frac{(\mu_{s\epsilon} + \alpha_s)(\mu_{f\epsilon} + \rho)}{k_f \rho}(\rho X_f - \mu_{p\epsilon} X_p)
\end{aligned}$$

Using $\Lambda - \mu_{s\epsilon} X_s^0 = 0$, we get

$$\begin{aligned}
\dot{V} &= \left(1 - \frac{X_s^0}{X_s}\right)(-\mu_{s\epsilon} X_s + \mu_{s\epsilon} X_s^0) + \left[\beta X_s^0 X_p - \frac{(\mu_{s\epsilon} + \alpha_s)(\mu_{f\epsilon} + \rho)}{k_f \rho} \mu_{p\epsilon} X_p\right] \\
&= \mu_{s\epsilon} X_s^0 \left(1 - \frac{X_s^0}{X_s}\right)\left(1 - \frac{X_s}{X_s^0}\right) + \frac{\beta \Lambda}{\mu_{s\epsilon}}\left[1 - \frac{(\mu_{s\epsilon} + \alpha_s)(\mu_{f\epsilon} + \rho)\ \mu_{m\epsilon}\mu_{p\epsilon}}{k_f \rho \Lambda \beta}\right] X_p \\
&= \mu_{s\epsilon} X_s^0 \left(1 - \frac{X_s^0}{X_s}\right)\left(1 - \frac{X_s}{X_s^0}\right) + \frac{\beta \Lambda}{\mu_{s\epsilon}}\left[1 - \frac{1}{\mathcal{R}_0}\right] X_p \quad (3) \\
&= -\frac{\mu_{s\epsilon}}{X_s}(X_s^0 - X_s)^2 + \frac{\beta \Lambda}{\mu_{s\epsilon}}\left[1 - \frac{1}{\mathcal{R}_0}\right] X_p
\end{aligned}$$

Hence, $\dot{V} \leq 0$ if $\mathcal{R}_0 \leq 1$, and

$$\Omega \cap \{\dot{V} = 0\} = \begin{cases} \{x \in \Omega : x = (X_m, X_f, 0, X_s^0, X_i)\} \text{ if } \mathcal{R}_0 < 1 \\ \{x \in \Omega : x = (X_m, X_f, X_p, X_s^0, X_i)\} \text{ if } \mathcal{R}_0 = 1 \end{cases}$$

We will show that the largest invariant set $\mathcal{L}$ contained in $\Omega \cap \{\dot{V} = 0\}$ is reduced to the disease-free equilibrium $\mathcal{E}^0$.

Let $x = (X_m, X_f, X_p, X_s, X_i) \in \mathcal{L}$ and $x(t) = (X_m(t), X_f(t), X_p(t), X_s(t), X_i(t))$ the solution of (1) issued from this point. By invariance of $\mathcal{L}$, we have $X_s(t) \equiv X_s^0$ which imlies $\dot{X}_s(t) = 0 = \Lambda - \mu_s\, X_s(t) - \beta\, X_p(t)\, X_s(t) = \Lambda - \mu_s\, X_s^0 - \beta\, X_p(t)\, X_s^0$ and hence $X_p(t) = 0$ for all t. But, $X_p(t) \equiv 0$ implies that $\dot{X}_p(t) = 0$ for all t which implies, using system (1), that $X_f(t) = 0$ for all t. In the same way, it can be proved that $X_i(t) = 0$ for all t. Reporting in the first equation of system (1), one obtains that, in $\mathcal{L}$,

$$\dot{X}_m(t) = -\mu_{m\epsilon}\, X_m(t) \qquad \forall t$$

Thus the solution of (1) issued from $x = (X_m, X_f, X_p, X_s, X_i) \in \mathcal{L}$ is given by $x(t) = (X_m\, e^{-\mu_{m\epsilon}\, t}, 0, 0, X_s^0, 0)$ which clearly leaves Ω and hence $\mathcal{L}$ for $t < 0$ if $X_m \neq 0$. Therefore $\mathcal{L} = \{\mathcal{E}^0\}$ and hence $\mathcal{E}^0$ is a globally asymptotically stable equilibrium state for system (1) on the compact set Ω thanks to LaSalle invariance principle [7], (one can also see [1], Theorem 3.7.11, page 346). Since the set Ω is an attractive set, the DFE is actually GAS on the nonnegative orthant $\mathbb{R}^5_+$. □

Appendix B. Proof of Theorem 3.2

Proof. When $\mathcal{R}_0 \leq 1$, the infection-free equilibrium $\mathcal{E}^0$ is globally asymptotically stable which precludes any sort of persistence and hence $\mathcal{R}_0 > 1$ is a necessary condition for persistence. In order to show that $\mathcal{R}_0 > 1$ is a sufficient condition for uniform persistence, it suffices to verify conditions (1) and (2) of Theorem 4.1 in [6] (one can also see [8], Theorem 3.5).

We use the notations of [6] with $\mathscr{X} = \Omega$ and $\mathscr{Y} = \partial\Omega$. Let M be the largest invariant compact set in $\mathscr{Y}$. We have already seen that $M = \{\mathcal{E}^0\}$, and so M is isolated. To show that $\mathcal{W}^s(M)$ (the stable set of M) is contained in $\mathscr{Y} = \partial\Omega$, we use the following function:

$$\mathcal{F} = \frac{\mu_{s\epsilon} + \alpha_s}{k_f}\, X_f + \frac{(\mu_{s\epsilon} + \alpha_s)\,(\mu_{f\epsilon} + \rho)}{k_f\, \rho}\, X_p + X_i$$

The time derivative of $\mathcal{F}$ along the solutions of system (1) is given by

$$\begin{aligned}
\dot{\mathcal{F}} &= \beta\, X_s\, X_p - \frac{(\mu_{s\epsilon} + \alpha_s)\,(\mu_{f\epsilon} + \rho)}{k_f\, \rho}\, \mu_{p\epsilon}\, X_p \\
&= \left(\beta\, X_s - \frac{(\mu_{s\epsilon} + \alpha_s)\,(\mu_{f\epsilon} + \rho)}{k_f\, \rho}\, \mu_{p\epsilon}\right) X_p \\
&= \frac{\mu_{p\epsilon}\,(\mu_{s\epsilon} + \alpha_s)\,(\mu_{f\epsilon} + \rho)}{k_f\, \rho} \left(\beta\, X_s\, \frac{k_f\, \rho}{\mu_{p\epsilon}\,(\mu_{s\epsilon} + \alpha_s)\,(\mu_{f\epsilon} + \rho)} - 1\right) X_p \\
&= \frac{\mu_{p\epsilon}\,(\mu_{s\epsilon} + \alpha_s)\,(\mu_{f\epsilon} + \rho)}{k_f\, \rho} \left(\mathcal{R}_0\, \frac{X_s}{X_s^0} - 1\right) X_p
\end{aligned}$$

Since $\mathcal{R}_0 > 1$, we have $\dot{\mathcal{F}} > 0$ for $X_p > 0$ and $\dfrac{X_s^0}{\mathcal{R}_0} < X_s \leq X_s^0$. Therefore $\dot{\mathcal{F}} > 0$ in a neighborhood N of $\mathcal{E}^0$ relative to $\Omega \setminus \partial\Omega$. This implies that any solution starting in N must leave N at finite time and hence the stable set of M, $\mathcal{W}^s(M)$ is contained in $\partial\Omega$. □