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Schistosomiasis mathematical model in a spatially heterogeneous environment

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ABSTRACT

Schistosomiasis is classified by WHO as a neglected tropical disease. Recent research works have shown that large-scale development projects involving massive population displacement and water irrigation, such as the construction of dams, lakes, and the development of agricultural areas, favour the proliferation of bilharzia. These observations motivate us to propose a reaction–diffusion model to assess the role of the displacements of humans, snails, cercaria, miracidia in the transmission dynamics of Schistosomiasis. The model incorporates a general non-linear contact functions and density-dependent parameters. The aim is to better understanding the role of spatial interactions on the spread of Schistosomiasis, in order to propose appropriate recommendations for the control of that silent threat. We characterize the basic reproduction number R_0 of the model. The uniform persistence theory, the maximum principle are used to conduct an in-depth analysis of both the homogeneous and heterogeneous models. Theoretical results are illustrated through numerical simulations.

1. Introduction

Schistosomiasis or Bilharzia is an endemic disease, existing in about 51 countries in the world, with a strong presence in the tropics and subtropics. It is the second most common parasitic disease after malaria [1]. Given its socio-economic impact, the WHO considers it to be a neglected tropical disease (NTD). Indeed, causing about 200,000 deaths per year worldwide, it is estimated that about 241.3 million people needed preventive treatment against schistosomiasis in 2020 [1]. The African continent pays the highest price for this disease with about 90% of infections [1].

Schistosomiasis is an acute and chronic parasitic disease caused by worms (trematodes) of the genus Schistosoma [2]. Human behaviour is the main cause of the spread of the disease. Poor hygiene, agricultural activities, fish farming, domestic activities, children's play, and the movement of people are key factors in the spread of the disease [3]. The transmission of schistosomiasis takes place in three stages. An infected individual releases eggs in his faeces and urine, which on contact with water, produce miracidia, which will then penetrate an intermediate host (aquatic mollusc), and after some time, produce cercaria. Human beings in contact with water contaminated by cercaria can be contaminated and the cycle starts again [2].

The WHO focuses its schistosomiasis control strategy on large-scale treatment of at-risk populations by various means: regular and targeted treatment with praziquantel, preventive chemotherapy for affected populations, access to safe drinking water, improved sanitation, health education and gastropod control [2].

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However, it is well documented that some human activities (storage, water irrigation and population migrations) can unconsciously become divers for fast spread of schistosomiasis [4]. For instance, in Cameroon, during the year 1982, the construction of the Lagdo dam and the Semry I, Semry II and Semry III projects in Yagoua, Maga and Kousseri, respectively, encouraged a strong migration of populations from neighbouring countries and other regions of the country for fishing and farming activities. These activities have increased the prevalence of the Schistosomiasis from 13% to almost 46% [5]. In Senegal, the construction of the Diama and Manantali dams in 1986 and 1988 respectively in the north have favoured the proliferation of cercaria. In the Pador district, the presence of irrigation canals has favoured the appearance of sites conducive to the emergence of molluscs, leading to the development of the disease. Moreover, in some villages, such as Aroudou, the prevalence of the disease increased from 6.8% before construction to 50.5% only two years after construction [6]. In Nigeria the construction of the Kainji dam in 1970 increased the prevalence from 20% to 62% in the surrounding villages [7]. In Ghana the construction of the Akoussomba dam in 1964, which led to the formation of Lake Volta, increased the prevalence from 10% to 62% [8]. In Burundi, the construction of the Rusizi valley in 1950 led to a major population influx, causing the prevalence to multiply after 15 years the number of cases by 30 [9]. All these examples give a clear indication that the displacements of people and their settling around constructed dams, as well as their movement around those dams for fishing play a crucial role in the exacerbated situation of schistosomiasis evolution. This calls for a mathematical assessment of people and molluscs displacements on the dynamics of schistosomiasis.

Numerous mathematical models have been formulated to understand the dynamics of the disease and to evaluate different control strategies. The very first model was that of Macdonald [10]. Subsequently, other authors have worked to improve this model. We can mention the works of [11–13] which introduced periods of maturation in infected individuals (humans and snails), to better reflect the transmission processes of the disease. We also have the works in [11,13] which dealt with age-structured models, aiming to better understand the processes of transmission of schistosomiasis by highlighting the fact that children of school age seem to be the most exposed. A handful of works considered climate change by accounting for seasonally forced periodic models [14–16]. However, very few mathematical models have taken into account the underlined displacement of populations and intermediate molluscs.

Models along these lines have begun to be formulated. We can mention the works in [17,18], where the human population is divided into two groups. They were further generalized in [19,20] by dividing the population into $n \geq 3$ groups (meta-population). However, the problem remains that in the different groups, it is assumed that the populations are uniformly distributed, and the heterogeneous feature of space is not accounted for. Hence the need to accurately describe the evolutionary dynamics of the disease by a reaction–diffusion model to really capture the displacements of humans, molluscs (snails), cercariae and miracidia.

In that regards, we propose here a reaction–diffusion model to describe dynamics of the disease, which additionally takes into account control strategies. The paper is structured as follows: Section 2 presents the construction of the reaction–diffusion model with space-dependent parameters and general incidence functions, and addresses the existence and uniqueness of a unique positive global solution for well-chosen initial conditions. In Section 3, we give a characterization of the basic reproduction number R_0 and prove the global attractiveness of the unique disease-free equilibrium for $R_0 < 1$. In Section 4, we prove the uniform persistence of the model by establishing that there are always a few infected individuals in the populations whenever $R_0 > 1$. Section 5 deals with the homogeneous model, with space-independent parameters. The basic reproduction number is explicitly computed and the existence and uniqueness of an endemic equilibrium, as well as its global asymptotic stability when $R_0 > 1$ are established. We perform some numerical simulations in Section 6 to support our theoretical results, and conclude the work in Section 7.

2. Model formulation and well-posedness

The development of the model is done based on the following main assumptions:

(H1) The susceptible humans (H_s) become infected through adequate contact with contaminated water containing cercariae (P) released from infected intermediate molluscs (M_i), and the disease incidence is modelled by the space-dependent function $H_s f(x, P)$. A human individual can die either naturally or due to the disease.

(H2) Susceptible molluscs (M_s) become infected by adequate contact with contaminated water containing miracidia (K), shed from faeces and urine of infected humans (H_i), and the disease incidence follows the space-dependent function $M_s g(x, K)$. The death of intermediate molluscs is only due to natural factors because the miracidia infection has no effect on them.

(H3) There are some control actions by humans on the disease represented by the treatment with praziquantel at rate σ per unit time.

(H4) Some awareness and sensitization programs are run by local authorities and health-care workers such that sick individuals who recovered will no longer exposed themselves to the disease.

(H5) The study domain (the human's living environment) is large enough so that no individual crosses its boundary, and snails (molluscs), cercaria, miracidia remain in the dams present in the area where people live and work.

To build our model, let $x \in \Omega$ and $t > 0$ be the position and time unit. We assume that the variation of susceptible human population at location x at time t, $H_s(x,t)$ with respect to time, is due to the diffusion process described by the term diffusion $\nabla.(d_1(x)\nabla H_s)$, in which the diffusion coefficient $d_1(x)$ depends on the location x, always with the aim of properly reflecting the non-homogeneity of the domain Ω, but also of the recruitment $\lambda_h(x)$, infection $H_s f(x, P)$ and natural death $\mu_h(x)H_s$. The model's variables and parameters, as well as their biological and epidemiological definitions are gathered in Table 1. We thus obtain the

Table 1
States variables and Model parameters.

Variable	Description
$H_s(x,t)$	Density of Susceptible human population at location x at time t
$H_i(x,t)$	Density of Infected human population at location x at time t
$K(x,t)$	Density or concentration of miracidia at location x at time t
$M_s(x,t)$	Density of Susceptible mollusc population at location x at time t
$M_i(x,t)$	Density of Infected mollusc population at location x at time t
$P(x,t)$	Density or concentration of cercariae population at location x at time t
Parameter	**Description**
$\lambda_h(x)$	Density-dependent per-capita recruitment rate of susceptible humans at location x
$\lambda_m(x)$	Density-dependent per-capita recruitment rate of susceptible molluscs at location x
$\mu_h(x)$	Density-dependent mortality rate from means other than disease in humans at location x
$\eta(x)$	Density-dependent mortality rate of infected humans due to the disease at location x
σ	Density-independent (homogeneous) recovery rate of infected humans
$\alpha_1(x)$	Density-dependent rate of production of miracidia by infected humans at location x
$\alpha_2(x)$	Density-dependent production rate of cercaria by infected molluscs at location x
$\mu_k(x)$	Density-dependent natural mortality rate of miracidia at location x
$\mu_p(x)$	Density-dependent natural mortality rate of cercaria at location x
$\mu_m(x)$	Density-dependent natural mortality rate of molluscs at location x

partial differential equation governing the dynamics of evolution of susceptible humans. We do the same for other components and we obtain the model.

$$\begin{cases} \frac{\partial H_s}{\partial t} &= \nabla.(d_1(x)\nabla H_s) + \lambda_h(x) - H_s f(x,P) - \mu_h(x)H_s, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial H_i}{\partial t} &= \nabla.(d_2(x)\nabla H_i) + H_S f(x,P) - (\mu_h(x) + \eta(x) + \sigma)H_i, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial K}{\partial t} &= \nabla.(d_3(x)\nabla K) + \alpha_1(x)H_i - \mu_k(x)K, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial M_s}{\partial t} &= \nabla.(d_4(x)\nabla M_s) + \lambda_m(x) - M_s g(x,K) - \mu_m(x)M_s \quad x \in \Omega, \quad t > 0, \\ \frac{\partial M_i}{\partial t} &= \nabla.(d_5(x)\nabla M_i) + M_s g(x,K) - \mu_m(x)M_i, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial P}{\partial t} &= \nabla.(d_6(x)\nabla P) + \alpha_2(x)M_i - \mu_p(x)P, \quad x \in \Omega, \quad t > 0, \\ \frac{\partial R}{\partial t} &= \nabla.(d_7(x)\nabla R) + \sigma H_i - \mu_h(x)R, \quad x \in \Omega, \quad t > 0, \end{cases} \tag{2.1}$$

By virtue of assumption (H5), System (2.1) is appended with the following boundary conditions (Neumann condition).

$$\frac{\partial H_s}{\partial n} = \frac{\partial H_i}{\partial n} = \frac{\partial K}{\partial n} = \frac{\partial M_s}{\partial n} = \frac{\partial M_i}{\partial n} = \frac{\partial P}{\partial n} = \frac{\partial R}{\partial n} = 0, \quad x \in \partial\Omega, \quad t > 0, \tag{2.2}$$

and the initial conditions :

$$\begin{aligned} H_s(x,0) &= H_s^0(x) > 0, H_i(x,0) = H_i^0(x) \geq 0, K(x,0) = K^0(x) \geq 0, \quad x \in \Omega, \\ M_s(x,0) &= M_s^0(x) > 0, M_i(x,0) = M_i^0(x) \geq 0, P(x,0) = P^0(x) \geq 0, \quad x \in \Omega. \end{aligned} \tag{2.3}$$

In our work, we make the following additional assumptions:

(A1): Ω is a bounded domain of $\mathbb{R}^n$ $n \geq 1$.

(A2): $d_{i=1\ldots7}(.)$, $\lambda_h(.)$, $\lambda_m(.)$, $\mu_h(.)$, $\eta(.)$, $\alpha_1(.)$, $\alpha_2(.)$, $\mu_k(.)$, $\mu_p(.)$, $\mu_m(.) \in C^2(\overline{\Omega})$ are positive and bounded on $\overline{\Omega}$.

(A3): $d_1(.) = d_2(.) := d(.)$ and $d_4(.) = d_5(.) := d'(.)$. This assumption supports that infection of individuals has no real impact on their movements.

(A4): $f(x,P) > 0$ and $g(x,K) > 0$ for all $x \in \overline{\Omega}$ and $P, K > 0$, $f(x,0) = 0$ et $g(x,0) = 0$ for $x \in \overline{\Omega}$.

(A5): $f(x,P)$ and $g(x,K)$ are twice differentiable with respect to $(x,P) \in \overline{\Omega} \times \mathbb{R}_+$ and $(x,K) \in \overline{\Omega} \times \mathbb{R}_+$, and $\frac{\partial f(x,P)}{\partial P} > 0$, $\frac{\partial g(x,K)}{\partial K} > 0$; $\frac{\partial^2 f(x,P)}{\partial P^2} \leq 0$, $\frac{\partial^2 g(x,K)}{\partial K^2} \leq 0$.

(A6): $f(x,P) \leq \frac{\partial f(x,0)}{\partial P} P$ and $g(x,K) \leq \frac{\partial g(x,0)}{\partial K} K$, for all $x \in \overline{\Omega}$.

Some common examples for the incidence functions f and g used the literature are as follows:

$$f_1(x,P) = \frac{\beta_1(x)P}{1 + \tau_1(x)P}; \; f_2(x,P) = \beta_1(x) \ln\left(1 + \frac{P}{1 + \tau_1(x)P}\right);$$

$$g_1(x,K) = \frac{\beta_2(x)K}{1 + \tau_2(x)K}; \; g_2(x,K) = \beta_2(x) \ln\left(1 + \frac{K}{1 + \tau_2(x)K}\right).$$

Assumptions (A4), (A5) and (A6) capture the fact that the force of infection of the disease maybe increasing but must saturate at some point in time and space.

In the rest of the paper, when we talk about the System (2.1), we refer to System (2.1) appended with the initial conditions given by (2.2) and the boundary conditions highlighted in (2.3).

We then show that System (2.1) has a unique global solution in time.

To do this, for $i \in \{1,2,\dots,7\}$ and $\varphi \in C^1(\overline{\Omega}) \cap C^2(\overline{\Omega})$, we define the operator A_i^0 by $A_i^0\varphi := \nabla.(d_i(.)\nabla\varphi)$, with the domain, $D(A_i^0) := \{\varphi \in C^2(\Omega) \cap C^1(\overline{\Omega}) : A_i^0\varphi \in C(\overline{\Omega}), \frac{\partial\varphi}{\partial n} = 0, x \in \partial\Omega\}$.

Then, for $i = 1,\dots,7$, the closure A_i of A_i^0 generates the C_0-semi-group $(T_i(t))_{t\geq 0}$, and the function $u_i(t) = T_i(t)\varphi$ is the solution of the equation $u_i'(t) = A_iu_i(t), t > 0$, with $u_i(0) = \varphi \in D(A_i)$, where $D(A_i) := \{\varphi \in C(\overline{\Omega}) : \lim_{t\to 0} \frac{(T_i(t) - Id)\varphi}{t} \ exist\}$. Here, Id is identity operator.

We now define the non-linear functions $F_i(x,r)$, $i = 1,\dots,7$ on $\overline{\Omega}\times\mathbb{R}^7$ as follows :

$$\begin{aligned}
F_1(x,r) &= \lambda_h(x) - r_1 f(x,r_6) - \mu_h(x)r_1,\\
F_2(x,r) &= r_1 f(x,r_6) - (\mu_h(x) + \eta(x) + \sigma)r_2,\\
F_3(x,r) &= \alpha_1(x)r_2 - \mu_k(x)r_3,\\
F_4(x,r) &= \lambda_m(x) - r_4(x)g(x,r_3) - \mu_m(x)r_4,\\
F_5(x,r) &= r_4 g(x,r_3(x)) - \mu_m(x)r_5,\\
F_6(x,r) &= \alpha_2(x)r_5 - \mu_p(x)r_6,\\
F_7(x,r) &= \sigma r_2 - \mu_h(x)r_7,\\
\text{where, } x \in \overline{\Omega},\ r &= (r_1,r_2,r_3,r_4,r_5,r_6,r_7) \in \mathbb{R}^7.
\end{aligned}$$

Let $X_i = C(\overline{\Omega},\mathbb{R})$, $X_i^+ = C(\overline{\Omega},\mathbb{R}^+), i = 1...7$, $X = \prod_{i=1}^7 X_i$, $X^+ = \prod_{i=1}^7 X_i^+$. The sets X and X^+ are equipped with following norm, $\forall\varphi \in X, \|\varphi\|_X = \max_{1\leq i\leq 7}\{\sup|\varphi_i(x)|, x \in \overline{\Omega}\}$.

For the sake of presentation, we define the function

$$F(x,r) = (F_1(x,r), F_2(x,r), F_3(x,r), F_4(x,r), F_5(x,r), F_6(x,r), F_7(x,r)), \quad (x,r) \in \overline{\Omega}\times\mathbb{R}^7,$$

and the operators

$$A := \prod_{i=1}^7 A_i, \quad D(A) := \prod_{i=1}^7 D(A_i), \quad T(t) := \prod_{i=1}^7 T_i(t), \quad t > 0.$$

For any continuous functions f defined from Ω to $\mathbb{R}$, let us defined $f^+ = \max\{f(x) : x \in \overline{\Omega}\} < +\infty, f^- = \min\{f(x) : x \in \overline{\Omega}\} < +\infty$.

With the above notations, System (2.1) takes the following compact form:

$$\begin{cases} u'(t) &= Au(t) + \mathcal{F}(u(t)), \quad t > 0,\\ u(0) &= \varphi \in D(A) \subset X, \end{cases}$$

where, $u(t) = (H_s(.,t), H_i(.,t), K(.,t), M_s(.,t), M_i(.,t), P(.,t), R(.,t)) \in X$, $\varphi = (H_s^0(.), H_i^0(.), K^0(.), M_s^0(.), M_i^0(.), P^0(.), R^0(.)) \in X$ and $\mathcal{F}(\varphi)(x) = F(x,\varphi(x)), \quad x \in \overline{\Omega}, \quad \varphi \in X$.

System (2.1) can also be written in the following integral form.

$$\begin{cases} u(t) &= T(t)\varphi + \int_0^t T(t-s)\mathcal{F}(u(s))ds, \quad t > 0,\\ u(0) &= \varphi \in X. \end{cases}$$

Using ([21] Corollary 7.3.2), we establish the following proposition, which guarantees the existence of the unique local solution of System (2.1).

Proposition 2.1. *Assume (A1)-(A6) hold, then for any $\varphi \in X^+$, System (2.1) admits a unique and continuous local solution $u(t) = u(.,t,\varphi) \in X^+$ defined on $[0,T_\varphi[$. Moreover, $u(t)$ is differentiable on $]0,T_\varphi[$, and if $T_\varphi < +\infty$, then $\|u(t)\|_X \to +\infty$ when $t \to T_\varphi$.*

The following lemma, whose proof can be seen in ([22], Lemma 1) is instrumental for the proof of the existence of a global solution of System (2.1).

Lemma 2.2. *Consider the following problem,*

$$\begin{cases} \dfrac{\partial u(x,t)}{\partial t} &= \nabla.(d(x)\nabla u(x,t)) + \beta(x) - \rho(x)u(x,t), \quad x \in \Omega, t > 0,\\ \dfrac{\partial u(x)}{\partial n} &= 0, \quad x \in \partial\Omega, t > 0. \end{cases} \tag{2.4}$$

If $\beta(.)$ and $\rho(.)$ are continuous and positive functions, then System (2.4) has a stationary solution $u_0(.)$, satisfying $\nabla.(d(x)\nabla u_0(x)) + \beta(x) - \rho(x)u_0(x) = 0, \quad x \in \Omega, \ \frac{\partial u_0(x)}{\partial n} = 0, \quad x \in \partial\Omega$, and which is globally asymptotically stable in X. If $\beta(.) = \beta$ and $\rho(.) = \rho$ then $u_0(.) = \frac{\beta}{\rho}$.

Theorem 2.3. *Assume (A1)-(A6) hold, then for all $\varphi \in X^+$, the System (2.1) has a unique global solution, $u(t) = u(.,t,\varphi) \in D(A)$, on $[0,+\infty[$ with $u(0) = \varphi(.)$.*

Proof. By Proposition 2.1, it suffices to show that $T_\varphi = +\infty,\ \ \varphi \in X^+$.

Let us assume by contradiction that $T_\varphi < +\infty$. Adding the first two equations of System (2.1) we have :

$$\frac{\partial H_s}{\partial t} + \frac{\partial H_i}{\partial t} \leq \nabla.(d(x)\nabla(H_s + H_i)) + \lambda_h(x) - \mu_h(x)(H_s + H_i).$$

Therefore, $H_s + H_i$ is a sub-solution of the following linear problem,

$$\begin{cases} u_t' &= \nabla.(d(x)\nabla u) + \lambda_h^+ - \mu_h^- u, \quad x \in \Omega, \\ \dfrac{\partial u}{\partial n} &= 0,\ x \in \partial\Omega, \\ u(0,x) &= H_s^0(x) + H_i^0(x),\ x \in \Omega. \end{cases} \tag{2.5}$$

According to the comparison theorem for parabolic equation, $H_s(t,x) + H_i(x,t) \leq v(x,t),\ \ x \in \overline{\Omega},\ \ t \in [0, T_\phi[$, where $v(x,t)$ is the solution of System (2.5).

By Lemma 2.2, $\lim_{t\to+\infty} v(x,t) = \lambda_h^+/\mu_h^-,\ \ x \in \overline{\Omega}$, then there exists a constant $M_1 > 0$ such that $H_s(t,x) + H_i(x,t) \leq M_1,\ \ x \in \overline{\Omega},\ \ t \in [0, T_\phi[$. This proves that H_s and H_i are bounded.

For the boundedness of the functions M_s and M_i, it suffices to see that,

$$\frac{\partial M_s}{\partial t} + \frac{\partial M_i}{\partial t} \leq \nabla.(d'(x)\nabla(M_s + M_i)) + \lambda_m(x) - \mu_m(x)(M_s + M_i),$$

and perform a similar proof as above to obtain the desired result. On the other hand, an analogous reasoning, using the boundedness of H_i, M_i, and M_s, already show, it is straightforward to prove the boundedness of K, P and R. Thus, all the trajectories are bounded.

Now according to ([21], Theorem 3.1), if $T_\varphi < +\infty$ then, $\|u(t)\|_X \to \infty$ when $t \to T_\varphi$, which is contradictory, so $T_\varphi = +\infty,\ \ \forall \varphi \in X^+$. ■

Corollary 2.4. *Assume (A1)–(A6) hold true, then for any solution $u(t) = (H_s(.,t), H_i(.,t), K(.,t), M_s(.,t), M_i(.,t), P(.,t), R(.,t)), t \geq 0$ of System (2.1) with the initial condition $\varphi \in X^+$, we have:* $\limsup_{t\to\infty} H_s(x,t) + H_i(x,t) \leq \dfrac{\lambda_h^+}{\mu_h^-}, \limsup_{t\to\infty} M_s(x,t) + M_i(x,t) \leq \dfrac{\lambda_m^+}{\mu_m^-}, \limsup_{t\to\infty} K(x,t) \leq \dfrac{\alpha_1^+\lambda_h^+}{\mu_k^-\mu_h^-}, \ \limsup_{t\to\infty} K(x,t) \leq \dfrac{\alpha_2^+\lambda_m^+}{\mu_p^-\mu_m^-}$, $\limsup_{t\to\infty} R(x,t) \leq \dfrac{\sigma\lambda_h^+}{(\mu_h^-)^2}$.

Proof. The proof is obtained from Theorem 2.3 and the comparison theorem by letting t go to ∞. ■

Corollary 2.5. *Assume (A1)-(A6) are satisfied. For any $\varphi \in X^+$, System (2.1) generates a semi-flow $\{\Phi_t\}_{t\geq 0} : X^+ \to X^+$, defined by $\Phi_t\varphi = u(t,\varphi), t \geq 0$. For any closed and bounded set $B \subset X^+$ then $\Phi_t B$ has compact closure in X^+.*

Proof. The proof follows directly from ([21], Theorem 3.3). ■

In the rest of the paper, we discard the recovered compartment R, since it does not appear in remaining equations.

In the next section, we characterize the basic reproduction ratio R_0 and prove the global attractiveness of the disease-free equilibrium when $R_0 < 1$.

3. Global attractiveness of the disease-free equilibrium

We start this section by characterizing the basic reproduction ratio, using the method developed in [23]. At the equilibrium point, we have, $H_i = M_i = K = P \equiv 0$, by substituting in the system we get,

$$\begin{cases} \nabla.(d_1(x)\nabla H_s) + \lambda_h(x) - \mu_h(x)H_s &= 0, \quad x \in \Omega, \\ \nabla.(d_4(x)\nabla M_s) + \lambda_m(x) - \mu_m(x)M_s &= 0, \quad x \in \Omega, \\ \dfrac{\partial H_s}{\partial n} = \dfrac{\partial M_s}{\partial n} &= 0, \quad x \in \partial\Omega. \end{cases} \tag{3.1}$$

Thanks to Lemma 2.2, and after decoupling System (3.1), one can see that it admits unique positive solution $(H_0(x), M_0(x))$, for all $x \in \Omega$,. Hence the existence of our unique disease-free equilibrium

$$E_0 = (H_0(.), 0, 0, M_0(.), 0, 0).$$

Let $u = (H_i, M_i, K, P, H_s, M_s)$. we define the functions, $\mathcal{F}(u) = (H_s f(x,P), M_s g(x,K), 0, 0, 0, 0)$, given the recruitment rate of newly infected individuals into the different compartments. Similarly, we define

$$\begin{aligned}\mathcal{V}(u) &= ((\mu_h(x)+\eta(x)+\sigma)H_i, \mu(x)M_i, \mu_k(x)K - \alpha_1(x)H_i, \mu_p(x)P\\ &- \alpha_2(x)M_i, \mu_h(x)H_s - \lambda_h(x), \mu_m(x)M_s - \lambda_m(x)),\end{aligned}$$

which gives the transfer rate of individuals into infected compartments by other means (e.g., births and immigrations), and the rate movement of individuals out of infected compartments (e.g., death and/or recovery). The Jacobian matrices of $\mathcal{F}$ and $\mathcal{V}$ around the disease-free equilibrium are respectively:

$$\mathcal{F}(x) = \begin{pmatrix} 0 & 0 & 0 & H_0\frac{\partial f(x,0)}{\partial P} & 0 & 0\\ 0 & 0 & M_0\frac{\partial g(x,0)}{\partial K} & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix} = \begin{pmatrix} F(x) & 0\\ 0 & 0 \end{pmatrix},$$

and

$$\mathcal{V}(x) = \begin{pmatrix} \mu_h(x)+\eta(x)+\sigma & 0 & 0 & 0 & 0 & 0\\ 0 & \mu_m(x) & 0 & 0 & 0 & 0\\ -\alpha_1(x) & 0 & \mu_k(x) & 0 & 0 & 0\\ 0 & -\alpha_2(x) & 0 & \mu_p(x) & 0 & 0\\ 0 & 0 & 0 & 0 & \mu_h(x) & 0\\ 0 & 0 & 0 & 0 & 0 & \mu_m(x) \end{pmatrix} = \begin{pmatrix} V(x) & 0\\ J(x) & -M^0(x) \end{pmatrix},$$

where,

$$F(x) = \begin{pmatrix} 0 & 0 & 0 & H_0\frac{\partial f(x,0)}{\partial P}\\ 0 & 0 & M_0\frac{\partial g(x,0)}{\partial K} & 0\\ 0 & 0 & 0 & 0\\ 0 & 0 & 0 & 0 \end{pmatrix}, \quad V(x) = \begin{pmatrix} \mu_h(x)+\eta(x)+\sigma & 0 & 0 & 0\\ 0 & \mu_m(x) & 0 & 0\\ -\alpha_1(x) & 0 & \mu_k(x) & 0\\ 0 & -\alpha_2(x) & 0 & \mu_p(x) \end{pmatrix}.$$

Following [23], we consider the semi-group $Y(t)$ of the linear system,

$$\begin{cases} \frac{\partial H_i}{\partial t} &= \nabla.(d_2(x)\nabla H_i) - (\mu_h(x)+\eta(x)+\sigma)H_i, \ \ x\in\Omega, \ \ t>0,\\ \frac{\partial M_i}{\partial t} &= \nabla.(d_5(x)\nabla M_i) - \mu_m(x)M_i, \ \ x\in\Omega, \ \ t>0,\\ \frac{\partial K}{\partial t} &= \nabla.(d_3(x)\nabla K) + \alpha_1(x)H_i - \mu_k(x)K, \ \ x\in\Omega, \ \ t>0,\\ \frac{\partial P}{\partial t} &= \nabla.(d_6(x)\nabla P) + \alpha_2(x)M_i - \mu_p(x)P, \ \ x\in\Omega, \ \ t>0. \end{cases} \tag{3.2}$$

Let $\mathbf{Y} = \prod_{i=1}^{4} X_i^+$, introducing the initial distribution of infective individuals described by $\varphi^0(x) = (H_i^0(x), M_i^0(x), K^0(x), P^0(x))^T \in \mathbf{Y}$, then $Y(t)\varphi^0(x)$ represents the internal evolution of this population over time t. Thus, $F(x)Y(t)\varphi^0(x)$ represents the distribution of new infective individuals at time t.

Define the operator, $L : \mathbf{Y} \to \mathbf{Y}$ as follows

$$L(\varphi)(x) := \int_0^{+\infty} F(x)Y(t)\varphi^0(x)dt,$$

representing the total distribution of new infective individuals at position $x \in \Omega$. Thus, R_0 is the spectral radius of L:

$$R_0 = \rho(L).$$

Now, we prove the global stability of our disease-free equilibrium if $R_0 < 1$.

For that, we consider the sub-model consisting only of the equations of the comportments with disease. That is:

$$\begin{cases} \frac{\partial H_i}{\partial t} &= \nabla.(d_2(x)\nabla H_i) + H_S f(x,P) - (\mu_h(x)+\eta(x)+\sigma)H_i, \ \ x\in\Omega, \ \ t>0,\\ \frac{\partial K}{\partial t} &= \nabla.(d_3(x)\nabla K) + \alpha_1(x)H_i - \mu_k(x)K, \ \ x\in\Omega, \ \ t>0,\\ \frac{\partial M_i}{\partial t} &= \nabla.(d_5(x)\nabla M_i) + M_s g(x,K) - \mu_m(x)M_i, \ \ x\in\Omega, \ \ t>0,\\ \frac{\partial P}{\partial t} &= \nabla.(d_6(x)\nabla P) + \alpha_2(x)M_i - \mu_p(x)P, \ \ x\in\Omega, \ \ t>0,\\ \frac{\partial H_i}{\partial n} &= \frac{\partial M_i}{\partial n} = \frac{\partial K}{\partial n} = \frac{\partial P}{\partial n} = 0, \ \ x\in\partial\Omega, \ \ t>0. \end{cases} \tag{3.3}$$

System (3.3) linearized at $(H_0, 0, 0, M_0, 0, 0)$ gives

$$\begin{cases} \frac{\partial H_i}{\partial t} &= \nabla.(d_2(x)\nabla H_i) + H_0\frac{\partial f(x,0)}{\partial P}P - (\mu_h(x)+\eta(x)+\sigma)H_i, \quad x\in\Omega, \quad t>0, \\ \frac{\partial K}{\partial t} &= \nabla.(d_3(x)\nabla K) + \alpha_1(x)H_i - \mu_k K, \quad x\in\Omega, \quad t>0, \\ \frac{\partial M_i}{\partial t} &= \nabla.(d_5(x)\nabla M_i) + M_0\frac{\partial g(x,0)}{\partial K}K - \mu_m(x)M_i, \quad x\in\Omega, \quad t>0, \\ \frac{\partial p}{\partial t} &= \nabla.(d_6(x)\nabla P) + \alpha_2(x)M_i - \mu_p(x)P, \quad x\in\Omega, \quad t>0, \\ \frac{\partial H_i}{\partial n} &= \frac{\partial M_i}{\partial n} = \frac{\partial K}{\partial n} = \frac{\partial P}{\partial n} = 0, \quad x\in\partial\Omega, \quad t>0. \end{cases} \tag{3.4}$$

By the principle of separation of variables, let us define

$$H_i(x,t) = e^{\lambda t}\psi_2(x), K(x,t) = e^{\lambda t}\psi_3(x), M_i(x,t) = e^{\lambda t}\psi_5(x), P(x,t) = e^{\lambda t}\psi_6(x),$$

where, $\lambda\in\mathbb{C}$ and $\psi_i (i = 2,3,5,6)$ are positive functions of the variables x.

Substituting in System (3.4), we obtain,

$$\begin{cases} \lambda\psi_2(x) &= \nabla.(d_2(x)\nabla\psi_2(x)) + H_0\frac{\partial f(x,0)}{\partial P}\psi_6(x) - (\mu_h(x)+\eta(x)+\sigma)\psi_2(x), \quad x\in\Omega, \\ \lambda\psi_3(x) &= \nabla.(d_3(x)\nabla\psi_3(x)) + \alpha_1(x)\psi_2(x) - \mu_k(x)\psi_3(x), \quad x\in\Omega, \\ \lambda\psi_5(x) &= \nabla.(d_5(x)\nabla\psi_5(x)) + M_0\frac{\partial g(x,0)}{\partial K}\psi_6(x) - \mu_m(x)\psi_5(x), \quad x\in\Omega, \\ \lambda\psi_6(x) &= \nabla.(d_6(x)\nabla\psi_6(x)) + \alpha_2\psi_5(x) - \mu_p(x)\psi_5(x), \quad x\in\Omega, \\ \frac{\partial\psi_3}{\partial n} &= \frac{\partial\psi_4}{\partial n} = \frac{\partial\psi_5}{\partial n} = \frac{\partial\psi_6}{\partial n} = 0, \quad x\in\partial\Omega. \end{cases} \tag{3.5}$$

System (3.5) takes the simplified form

$$[B+M]\begin{pmatrix}\psi_2\\ \psi_3\\ \psi_5\\ \psi_6\end{pmatrix} = \lambda\begin{pmatrix}\psi_2\\ \psi_3\\ \psi_5\\ \psi_6\end{pmatrix},$$

with

$$B = \begin{pmatrix} \nabla.(d_2(x)\nabla) & 0 & 0 & \\ 0 & \nabla.(d_3(x)\nabla) & 0 & 0 \\ 0 & 0 & \nabla.(d_5(x)\nabla) & 0 \\ 0 & 0 & 0 & \nabla.(d_6(x)\nabla) \end{pmatrix}, \quad \textit{and} \quad M = F - V.$$

Lemma 3.1. *System (3.5) has a principal eigenvalue, denoted λ_0, with the associated positive eigenfunction $\psi_0 = (\psi_2^0, \psi_3^0, \psi_5^0, \psi_6^0)$, of the same sign as $R_0 - 1$.*

Proof. Since $d_{i=1\ldots6}(.)$ are continuous, strictly positive and bounded on Ω, then there exists a positive constant d_0 such that $d_i(x) \geq d_0$, for all $x\in\overline{\Omega}$.

In addition, it is easily seen that the directed graph of M is strongly connected, by virtue of the graph theory, M is irreducible. Moreover, since the elements out of its diagonal are positive, it is also cooperative, for all $x\in\Omega$. Then, by ([23], Theorem 2.2), System (3.5) has a principal eigenvalue $\lambda_0 := s(B+M)$, corresponding to a positive eigenfunction $\psi_0 = (\psi_2^0, \psi_3^0, \psi_5^0, \psi_6^0)$.

On the other hand, according to ([23], Theorem 3.1), $R_0 - 1$ has the same sign as $\lambda_0 := s(B+M)$. ■

Theorem 3.2. *Assume (A1)-(A6) hold true. If $R_0 < 1$, then the disease-free equilibrium $(H_0(.), 0, 0, M_0(.), 0, 0) \in X^+$ is globally attractive.*

To do this, we show that if $R_0 < 1$ then,

$$\lim_{t\to+\infty}((H_s(x,t), H_i(x,t), K(x,t), M_s(x,t), M_i(x,t)), P(x,t)) = (H_0(x), 0, 0, M_0(x), 0, 0), \quad x\in\overline{\Omega}.$$

Proof. We have

$$\begin{cases} \frac{\partial H_s}{\partial t} &\leq \nabla.(d(x)\nabla H_s) + \lambda_h(x) - \mu_h(x)H_s, \\ \frac{\partial H_s}{\partial n} &= 0, \quad x\in\partial\Omega. \end{cases}$$

$$\begin{cases} \frac{\partial M_s}{\partial t} &\leq \nabla.(d(x)\nabla M_s) + \lambda_m(x) - \mu_m(x)M_s, \\ \frac{\partial M_s}{\partial n} &= 0, \quad x\in\partial\Omega. \end{cases}$$

Thanks to Lemma 2.2 and the comparison theorem, there exist H_0 and M_0 such that we have, $\limsup_{\to\infty} H_s(x,t) \leq H_0(x)$, $\limsup_{t\to\infty} M_s(x,t) \leq M_0(x)$, $x \in \overline{\Omega}$.

From hypothesis (A6), we have,

$$\begin{cases} \frac{\partial H_i}{\partial t} & \leq & \nabla.(d_2(x)\nabla H_i) + H_0\frac{\partial f(x,0)}{\partial P}P - (\mu_h(x)+\eta(x)+\sigma)H_i, \ \ x\in\Omega, \ \ t>0, \\ \frac{\partial K}{\partial t} & \leq & \nabla.(d_3(x)\nabla K) + \alpha_1(x)H_i - \mu_k(x)K, \ \ x\in\Omega, \ \ t>0, \\ \frac{\partial M_i}{\partial t} & \leq & \nabla.(d_5(x)\nabla M_i) + M_0\frac{\partial g(x,0)}{\partial K}K - \mu_m(x)M_i, \ \ x\in\Omega, \ \ t>0, \\ \frac{\partial p}{\partial t} & \leq & \nabla.(d_6(x)\nabla P) + \alpha_2(x)M_i - \mu_p(x)P, \ \ x\in\Omega, \ \ t>0. \end{cases} \tag{3.6}$$

Thus, (H_i, K, M_i, P) is a sub-solution of the following linear problem,

$$\begin{cases} \frac{\partial u_1}{\partial t} & = & \nabla.(d_2(x)\nabla u_1) + H_0\frac{\partial f(x,0)}{\partial P}u_4 - (\mu_h(x)+\eta(x)+\sigma)u_1, \ \ x\in\Omega, \ \ t>0, \\ \frac{\partial u_2}{\partial t} & = & \nabla.(d_3(x)\nabla u_2) + \alpha_1(x)u_1 - \mu_k(x)u_2, \ \ x\in\Omega, \ \ t>0, \\ \frac{\partial u_3}{\partial t} & = & \nabla.(d_5(x)\nabla u_3) + M_0\frac{\partial g(x,0)}{\partial K}u_2 - \mu_m(x)u_3, \ \ x\in\Omega, \ \ t>0, \\ \frac{\partial u_4}{\partial t} & = & \nabla.(d_6(x)\nabla u_4) + \alpha_2(x)u_3 - \mu_p(x)u_4, \ \ x\in\Omega, \ \ t>0, \\ \frac{\partial u_1}{\partial n} & = & \frac{\partial u_2}{\partial n} = \frac{\partial u_2}{\partial n} = \frac{\partial u_4}{\partial n} = 0, \ \ t>0, \ \ x\in\partial\Omega. \end{cases} \tag{3.7}$$

Moreover there exists a constant $M > 0$ such that

$$(H_i(x,0), K(x,0), M_i(x,0), P(x,0)) \leq M\psi_0(x), \ \ x\in\overline{\Omega},$$

and since $M\psi_0(x)e^{\lambda_0 t}$ is a solution of the linear System (3.7) and thus an super-solution of System (3.7). As such, by the comparison theorem we have:

$$(H_i(x,t), K(x,t), M_i(x,t), P(x,t)) \leq M\psi_0(x)e^{\lambda_0 t}, \ \ x\in\overline{\Omega}, \ \ t>0.$$

Since $R_0 < 1$ is equivalent to $\lambda_0 < 0$, so, for $t \to +\infty$ we have:

$$(H_i(x,t), K(x,t), M_i(x,t), P(x,t)) \to (0,0,0,0), \ \ x\in\overline{\Omega}.$$

Using assumption (A6) and the fact that P tends to 0, we then have for all $0 < \epsilon \leq \min_{x\in\overline{\Omega}} \lambda_h(x)$, there exists $T > 0$: $H_s f(x,P) \leq H_0\frac{\partial f(x,0)}{\partial P}P \leq \epsilon$, for all $x \in \overline{\Omega}$, $t > T$.

Then we have :

$$\frac{\partial H_s}{\partial t} \geq \nabla.(d(x)\nabla H_s) + \lambda_h(x) - \epsilon - \mu_h(x)H_s, \ \ x\in\overline{\Omega}, \ \ t>T,$$

and we show using Lemma 2.2 and the comparison theorem for parabolic PDEs that $H_s(x,t) \geq H_0^\epsilon(x)$, for all $x \in \overline{\Omega}$, $t > T$, where H_0^ϵ is the unique stationary solution of the System (3.8) below.

$$\begin{cases} \frac{\partial v}{\partial t} & = & \nabla.(d(x)\nabla v) + \lambda_h(x) - \epsilon - \mu_h(x)v \ \ x\in\Omega, \ \ t>T, \\ \frac{\partial v}{\partial n} & = & 0, \ \ x\in\partial\Omega. \end{cases} \tag{3.8}$$

We have shown that

$$H_0^\epsilon(x) \leq \liminf_{t\to\infty} H_s(x,t) \leq \limsup_{t\to+\infty} H_s(x,t) \leq H_0(x), \ \ x\in\overline{\Omega}. \tag{3.9}$$

Finally, by letting ϵ go to zero in (3.9), and use the fact that $\lim_{\epsilon\to 0} H_0^\epsilon(x) = H_0(x)$, we have $H_s \to H_0$ when $t \to +\infty$.

A similarly proof can be done to show that $M_s \to M_0$ when $t \to +\infty$. Thus,

$$\lim_{t\to+\infty}(H_s(x,t), H_i(x,t), K(x,t), M_s(x,t), M_i(x,t), P(x,t)) = (H_0(x), 0, 0, M_0(x), 0, 0), \ \ x\in\overline{\Omega}.$$

This ends the proof of the theorem. ■

Since, it very difficult (if not impossible) to compute explicitly the endemic equilibrium points, we alternatively establish the uniform persistence of our system when $R_0 > 1$.

4. Uniform persistence

Let $Y(t)$ be the semi-group defined by (3.2) and define $R_\epsilon = \rho(L(\epsilon))$, where

$$L(\epsilon)\varphi(x) = \int_0^{+\infty} F(x,\epsilon)Y(t)\varphi(x)dt, \quad x\in\overline{\Omega}, \varphi\in X,$$

and

$$F(x,\epsilon)=\begin{pmatrix} 0 & 0 & 0 & (H_0-\epsilon)\dfrac{\partial f(x,\epsilon)}{\partial P} \\ 0 & 0 & (M_0-\epsilon)\dfrac{\partial g(x,\epsilon)}{\partial K} & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix},$$

Then, by the continuity, if $R_0>1$, there exists a sufficiently small ϵ such that $R_\epsilon>1$.

Lemma 4.1. *Assume that $Z(.,t,\varphi)$ is a solution of System (2.1) with condition $Z(.,0,\varphi)=\varphi\in X^+$.*

1. *Then $\forall\varphi\in X^+$, we have $H_s(x,t,\varphi)>0$ and $M_s(x,t,\varphi)>0$, $\forall x\in\overline{\Omega}, t>0$ and there exists a constant $\rho>0$ such that, $\liminf_{t\to+\infty}H_s(x,t,\varphi)\geq\rho$ and $\liminf_{t\to+\infty}M_s(x,t,\varphi)\geq\rho$ uniformly for $x\in\overline{\Omega}$.*
2. *If there exists $t_1>0$ such that $H_i(.,t_1,\varphi)\neq 0$, $M_i(.,t_1,\varphi)\neq 0$, $K(.,t_1,\varphi)\neq 0$ and $P(.,t_1,\varphi)\neq 0$ then $H_i(x,t,\varphi)>0$, $M_i(x,t,\varphi)>0$, $K(x,t,\varphi)>0$ and $P(x,t,\varphi)>0$, $\forall x\in\overline{\Omega}, t>t_1$.*

Proof. It suffices to use Lemma 2.2 and the comparison theorem. ■

In the following, we pose:

$$\Omega_0=\{(\phi_1,\phi_2,\phi_3,\phi_4,\phi_5,\phi_6)\in X^+ : \phi_2\neq 0,\quad \phi_3\neq 0,\quad \phi_5\neq 0,\ \text{and}\ \phi_6\neq 0\},$$

$$\partial\Omega_0=\{(\phi_1,\phi_2,\phi_3,\phi_4,\phi_5,\phi_6)\in X^+ : \phi_2\equiv 0\ \text{or}\ \phi_3\equiv 0\ \text{or}\ \phi_5\equiv 0\ \text{or}\ \phi_6\equiv 0\}.$$

Ω_0 and $\partial\Omega_0$ are closed and convex subspaces of X^+ and $X^+=\Omega_0\cup\partial\Omega_0$; $\Omega_0\cap\partial\Omega_0=\varnothing$. By Lemma 4.1, Ω_0 is invariant under the flow of System (2.1). That is $\Phi_t(\Omega_0)\subseteq\Omega_0, t>0$.

Lemma 4.2. *Suppose that (A1)-(A6) hold. If $R_0>1$, $E_0=\{(H_0(.),0,0,M_0(.),0,0)\}$ is a uniform weak repeller for Ω_0, in the sense that there exists $\mu_0>0$ such that,*

$$\limsup_{t\to+\infty}\|\Phi_t\varphi-E_0\|_X\geq\mu_0,\quad\forall\varphi\in\Omega_0.$$

Proof. Let $\varepsilon>0$, by contradiction, assume that there exists $\varphi_0\in\Omega_0$ such that,

$$\limsup_{t\to+\infty}\|\Phi_t\varphi_0-E_0\|_X<\epsilon.$$

Then there exists $t_1>0$ such that, for any $t\geq t_1$ and for any $x\in\Omega$, we have:

$$H_0-\epsilon\leq H_s\leq H_0+\epsilon;\quad M_0-\epsilon\leq M_s(x,t)\leq M_0+\epsilon;\quad H_i(x,t)\leq\epsilon;\quad M_i(x,t)\leq\epsilon;\quad K(x,t)\leq\epsilon;\quad P(x,t)\leq\epsilon, \tag{4.1}$$

and consequently

$$\begin{cases} \dfrac{\partial H_i}{\partial t} & \geq & \nabla.(d_2(x)\nabla H_i)+(H_0-\epsilon)\dfrac{\partial f(x,\epsilon)}{\partial P}P-(\mu_h(x)+\eta(x)+\sigma)H_i,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial K}{\partial t} & \geq & \nabla.(d_3(x)\nabla K)+\alpha_1(x)H_i-\mu_k K,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial M_i}{\partial t} & \geq & \nabla.(d_5(x)\nabla M_i)+(M_0-\epsilon)\dfrac{\partial g(x,\epsilon)}{\partial K}K-\mu(x)M_i,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial P}{\partial t} & \geq & \nabla.(d_6(x)\nabla P)+\alpha_2(x)M_i-\mu_p P,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial H_i}{\partial n} & = & \dfrac{\partial K}{\partial n}=\dfrac{\partial M_i}{\partial n}=\dfrac{\partial P}{\partial n}=0,\quad x\in\partial\Omega,\quad t>t_1. \end{cases} \tag{4.2}$$

Let, $\psi_\lambda(\epsilon)=(\psi_{\lambda_1}(\epsilon),\psi_{\lambda_2}(\epsilon),\psi_{\lambda_3}(\epsilon),\psi_{\lambda_4}(\epsilon))$ be the principal eigenfunction associated with the principal eigenvalue $\lambda_0(\epsilon)$ of the following linearized system,

$$\begin{cases} \dfrac{\partial u_1}{\partial t} & = & \nabla.(d_2(x)\nabla u_1)+(H_0-\epsilon)\dfrac{\partial f(x,\epsilon)}{\partial P}u_4-(\mu_h(x)+\eta(x)+\sigma)u_1,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial u_2}{\partial t} & = & \nabla.(d_3(x)\nabla u_2)+\alpha_1(x)u_1-\mu_k(x)u_2,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial u_3}{\partial t} & = & \nabla.(d_5(x)\nabla u_3)+(M_0-\epsilon)\dfrac{\partial g(x,\epsilon)}{\partial K}u_2-\mu(x)u_2,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial u_4}{\partial t} & = & \nabla.(d_6(x)\nabla u_4)+\alpha_2(x)u_3-\mu_p(x)u_4,\quad x\in\Omega,\quad t>t_1, \\ \dfrac{\partial u_1}{\partial n} & = & \dfrac{\partial u_2}{\partial n}=\dfrac{\partial u_3}{\partial n}=\dfrac{\partial u_4}{\partial n}=0,\quad x\in\partial\Omega,\quad t>t_1. \end{cases} \tag{4.3}$$

Then, the function

$$v(x,t) = (v_1(x,t), v_2(x,t), v_3(x,t), v_4(x,t)) = e^{\lambda_0(\epsilon)t}\psi_\lambda(\epsilon)(x),$$

is a solution of System (4.3).

Moreover, since $W(x,t) = (H_i(t,x,\varphi_0), M_i(t,x,\varphi_0), K(t,x,\varphi_0), P(t,x,\varphi_0))$ is a super-solution of System (4.3), then there exists a constant $C > 0$, such that

$$(H_i(t,x,\varphi_0), M_i(t,x,\varphi_0), K(t,x,\varphi_0), P(t,x,\varphi_0)) \geq Ce^{\lambda_0(\epsilon)t}\psi_\lambda(\epsilon)(x), \quad x \in \Omega, \quad \geq t_1.$$

Since $R_0 > 1$ then $R_\epsilon > 1$, by similar argument as in Lemma 3.1, $\lambda_0(\epsilon) > 0$.

Letting t goes to $+\infty$ we get $H_i(t,x,\varphi_0) \to +\infty$, $M_i(t,x,\varphi_0) \to +\infty$, $K(t,x,\varphi_0) \to +\infty$ and $P(t,x,\varphi_0) \to +\infty$, $x \in \overline{\Omega}$. This contradicts (4.1). ■

Lemma 4.3. *Let*

$$M_\partial = \{\varphi \in \partial\Omega_0 : \Phi_t\varphi \in \partial\Omega_0, \quad \forall t \geq 0\}$$

and $w(\varphi)$, the omega-limit set of φ, then

$$\bigcup_{\varphi \in M_\partial} w(\varphi) = E_0 = \{(H_0(.), 0, 0, M_0(.), 0, 0)\}.$$

Proof. Let $\varphi \in M_\partial$, then $\Phi_t\varphi \in \partial\Omega_0$, $\forall t \geq 0$ and consequently, $H_i(.,t,\varphi) \equiv 0$ or $M_i(.,t,\varphi) \equiv 0$ or $K(.,t,\varphi) \equiv 0$ or $P(.,t,\varphi) \equiv 0$ $\forall t \geq 0$.

Suppose without lost of generality that $H_i(.,t,\varphi) \equiv 0$, $\forall t \geq 0$, substituting this into the third equation of System (2.1), we have

$$\begin{cases} \dfrac{\partial K}{\partial t} &= \nabla.(d_3(x)\nabla K) - \mu_k(x)K, \quad x \in \Omega, \quad t > 0, \\ \dfrac{\partial K}{\partial n} &= 0, \quad x \in \partial\Omega. \end{cases} \tag{4.4}$$

Then we deduce from Lemma 2.2 that,

$$\lim_{t\to+\infty} K(x,t) = 0, \quad x \in \overline{\Omega}.$$

The same is done to obtain

$$\lim_{t\to+\infty} M_i(x,t) = 0, \quad x \in \overline{\Omega}.$$

We then show that

$$\lim_{t\to+\infty} P(x,t) = 0, \quad x \in \overline{\Omega}.$$

Substituting all this into the System(2.1) we get from Lemma 2.2 that,

$$\lim_{t\to+\infty} H_s(x,t,\varphi) = H_0(x), \quad \lim_{t\to+\infty} M_s(x,t,\varphi) = M_0(x), \quad x \in \overline{\Omega}.$$

We there fore have

$$w(\varphi) = E_0.$$

Now suppose $H_i(x,t_1,\varphi) \neq 0$, then by Lemma 4.1, $H_i(x,t,\varphi) > 0$, $t > t_1$.

Now $M_i(.,t,\varphi) \equiv 0$ or $K(.,t,\varphi) \equiv 0$ or $P(.,t,\varphi) \equiv 0$, $t > t_1$.

Now suppose $M_i(.,t,\varphi) \equiv 0, t \geq t_1$ then substituting into the fifth equation of System(2.1) we get $M_s(x,t,\varphi) = 0$ or $K(x,t,\varphi) = 0$, $x \in \Omega$ $t > t_1$.

If $M_s = 0$, we have $\lambda_m(x) = 0$, for all $x \in \Omega$, which is contradictory.

If $K = 0$ we have $\lambda_h(x) = 0$, for all $x \in \Omega$, which is also contradictory.

Thus, $w(\varphi) = E_0$ for all $\varphi \in M_\partial$, and thus $\bigcup_{\varphi\in M_\partial} w(\varphi) = E_0$.

The same reasoning applies if either $M_i(.,t,\varphi) \equiv 0$, $K(.,t,\varphi) \equiv 0$ or $P(.,t,\varphi) \equiv 0$, $\forall t \geq 0$, to show that $\bigcup_{\varphi\in M_\partial} w(\varphi) = E_0$. ■

Theorem 4.4. *Assume (A1)-(A6) are satisfied. Let $Z(x,t,\varphi)$ be a solution of System (2.1), with $Z(.,0,\varphi) = \varphi \in \Omega_0$. If $R_0 > 1$, then there exists a real $k > 0$ such that,*

$$\liminf_{t\to+\infty} H_s(x,t,\varphi) \geq k, \liminf_{t\to+\infty} H_i(x,t,\varphi) \geq k, \liminf_{t\to+\infty} K(x,t,\varphi) \geq k,$$

$$\liminf_{t\to+\infty} M_s(x,t,\varphi) \geq k, \liminf_{t\to+\infty} M_i(x,t,\varphi) \geq k, \liminf_{t\to+\infty} P(x,t,\varphi) \geq k,$$

uniformly for all $x \in \overline{\Omega}$.

Proof. From lemma 4.2, we obtain that E_0 is an isolated and invariant set for φ in Ω_0 and that $w^S(E_0) \cap \Omega_0 = \varnothing$, where $w^S(E_0)$ denotes the stable subspace of (E_0) for φ.

From Lemma 4.3, we also note that any orbit that starts in M_∂ converges to E_0. Moreover there is no cycle from E_0 to E_0 in $\partial\Omega_0$.

Consider the following function $q : X^+ \to [0, +\infty[$ such that

$$q(\varphi) = min\{\min_{x\in\overline{\Omega}} \varphi_2(x), \min_{x\in\overline{\Omega}} \varphi_3(x), \min_{x\in\overline{\Omega}} \varphi_5(x), \min_{x\in\overline{\Omega}} \varphi_6(x)\},$$

we have

$$q^{-1}(]0, +\infty[) \subset \Omega_0.$$

Posing $M = \{ E_0\}$ we have :

- $\bigcup_{\varphi\in M_\partial} w(\varphi) = E_0 \subseteq M$.
- There is no limit cycle from E_0 to E_0 in M_∂.
- M is isolated in X^+.
- $\forall\varphi \in \Omega_0$ let $L = w(\varphi)$ it is clear that $L \nsubseteq M = E_0$.

Then by ([24] Theorem 3), there exists $\delta > 0$ such that $\min_{\phi\in w(\varphi)} q(\phi) > \delta, \forall\varphi \in \Omega_0$.

Hence $\liminf_{t\to+\infty} H_i(x,t,\varphi) \geq \delta$, $\liminf_{t\to+\infty} M_i(x,t,\varphi) \geq \delta$, $\liminf_{t\to+\infty} K(x,t,\varphi) \geq \delta$, $\liminf_{t\to+\infty} P(x,t,\varphi) \geq \delta$, $\forall x \in \overline{\Omega}$.

From Lemma 4.1 we know that there exists a $\rho > 0$ such that, $\liminf_{t\to+\infty} H_s(x,t,\varphi) \geq \rho$, $\liminf_{t\to+\infty} M_s(x,t,\varphi) \geq \rho$. take $k = \min\{\delta, \rho\}$ to conclude. ■

5. Homogeneous model

In this section, we shall study the case where all parameters in system (2.1) are strictly positive. The main objective is to establish the existence and global stability of a unique endemic equilibrium.

The assumptions (A1)-(A6) for system (2.1) become (B1)-(B6) below.

(B1): Ω is a bounded domain of $\mathbb{R}^n$, $n \in \mathbb{N}^*$.

(B2): $d_1, d_2, d_3, d_4, d_4, d_6, d_7$, λ_h, λ_m, μ_h, η, μ_m , μ_p, μ_k, α_1 et α_2 are strictly positive constants.

(B3): $d_1 = d_2$ and $d_4 = d_5$.

(B4): The functions f and g are continuous and twice derivable with respect to $P \in \mathbb{R}^+$ and $K \in \mathbb{R}^+$.

(B5): $f(0) = g(0) = 0$ and $f(P), g(K) > 0$, $\forall P, K > 0$.

(B6): $f'(P), g'(K) > 0$ and $f''(P), g''(K) \leqslant 0$, $\forall P, K \geq 0$.

For the convenience of the reader, we recall System(2.1) with space-independent parameters in (5.1).

$$\begin{cases} \frac{\partial H_s}{\partial t} &= d_1\Delta H_s + \lambda_h - H_S f(P) - \mu_h H_s \;\; x \in \Omega, \;\; t > 0, \\ \frac{\partial H_i}{\partial t} &= d_2\Delta H_i + H_S f(P) - (\mu_h + \eta + \sigma)H_i, \;\; x \in \Omega, \;\; t > 0, \\ \frac{\partial K}{\partial t} &= d_3\Delta K + \alpha_1 H_i - \mu_k K, \;\; x \in \Omega, \;\; t > 0, \\ \frac{\partial M_s}{\partial t} &= d_4\Delta M_s + \lambda_m - M_s g(K) - \mu M_s \;\; x \in \Omega, \;\; t > 0, \\ \frac{\partial M_i}{\partial t} &= d_5\Delta M_i + M_s g(K) - \mu_m M_i, \;\; x \in \Omega, \;\; t > 0, \\ \frac{\partial P}{\partial t} &= d_6\Delta P + \alpha_2 M_i - \mu_p P, \;\; x \in \Omega, \;\; t > 0, \\ \frac{\partial R}{\partial t} &= d_7\Delta R + \sigma H_i - \mu_h R, \;\; x \in \Omega, \;\; t > 0, \end{cases} \tag{5.1}$$

System (5.1) is appended with the following initial and boundary condition.

$$\frac{\partial H_s}{\partial n} = \frac{\partial H_i}{\partial n} = \frac{\partial K}{\partial n} = \frac{\partial M_s}{\partial n} = \frac{\partial M_i}{\partial n} = \frac{\partial P}{\partial n} = \frac{\partial R}{\partial n} = 0, \;\; x \in \partial\Omega, \;\; t > 0, \tag{5.2}$$

and the initial condition:

$$\begin{aligned} H_s(x,0) &= H_S^0(x) > 0, H_i(x,0) = H_i^0(x) \geq 0, K(x,0) = K^0(x) \geq 0, \;\; x \in \Omega, \\ M_s(x,0) &= M_S^0(x) > 0, M_i(x,0) = M_i^0(x) \geq 0, P(x,0) = P^0(x) \geq 0, \;\; x \in \Omega. \end{aligned} \tag{5.3}$$

In the rest of this section, when we talking about the System (5.1), we refer to (5.1), supplemented by the initial conditions in (5.3) and the boundary conditions in (5.3).

5.1. Basic reproduction ratio and stability of disease free equilibrium

At the disease-free equilibrium, we have $H_i = M_i = K = P = 0$. By substituting in the system(5.1) we obtain $H_s = \lambda_h/\mu_h$ and $M_s = \lambda_m/\mu_m$. It can therefore be deduced that

$$E_0 = (H_0, 0, 0, M_0, 0, 0) = (\frac{\lambda_h}{\mu_h}, 0, 0, \frac{\lambda_m}{\mu_m}, 0, 0)$$

is the only disease-free equilibrium in our system.

Here we use the method developed in [23], to determine the basic reproduction number R_0, defined as the spectral radius of the next generation matrix (FV^{-1}), where,

$$F = \begin{pmatrix} 0 & 0 & 0 & H_0 f'(0) \\ 0 & 0 & M_0 g'(0) & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix} \text{ and } V = \begin{pmatrix} \mu_h + \eta + \sigma & 0 & 0 & 0 \\ 0 & \mu & 0 & 0 \\ -\alpha_1 & 0 & \mu_k & 0 \\ 0 & -\alpha_2 & 0 & \mu_p \end{pmatrix},$$

Thus,

$$R_0 = \rho(FV^{-1}) = \sqrt{\frac{\alpha_1 \alpha_2 H_0 f'(0) M_0 g'(0)}{\mu_m \mu_k \mu_p (\mu_h + \eta + \sigma)}} = \sqrt{\frac{\alpha_1 H_0 f'(0)}{\mu_p (\mu_h + \eta + \sigma)}} \times \sqrt{\frac{\alpha_2 M_0 g'(0)}{\mu_m \mu_k}} = R_0^H \times R_0^M.$$

Theorem 5.1. *Suppose that (B1)-(B6) hold. If $R_0 < 1$ then the disease-free equilibrium $(H_0, 0, 0, M_0, 0, 0)$ is globally asymptotically stable.*

We have shown in Theorem 3.2 that if $R_0 < 1$ them,

$$\limsup_{t \to +\infty} (H_s(x,t), H_i(x,t), K(x,t), M_s(x,t), M_i(x,t), P(x,t)) = (H_0, 0, 0, M_0, 0, 0), \quad x \in \overline{\Omega}.$$

5.2. Existence and stability of the endemic equilibrium

Here we will show the existence and global stability of the unique endemic equilibrium by constructing an appropriate Lyapunov function.

Theorem 5.2. *Assume (B1)-(B6) are satisfied. If $R_0 > 1$, System (5.1) admits a unique endemic equilibrium $(H_s^*, M_s^*, K^*, H_i^*, M_i^*, P^*)$. Then this endemic equilibrium is globally asymptotically stable.*

Proof. We start by proving the existence. At the point of endemic equilibrium we have

$$\begin{cases} \lambda_h - H_S^* f(P^*) - \mu_h H_S^* &= 0, \\ H_S^* f(P^*) - (\mu_h + \eta + \sigma) H_i^* &= 0, \\ \alpha_1 H_i^* - \mu_k K^* &= 0, \\ \lambda_m - M_s^* g(K*) - \mu_m M_s^* &= 0, \\ M_s^* g(K^*) - \mu_m M_i^* &= 0, \\ \alpha_2 M_i^* - \mu_p P^* &= 0, \end{cases} \tag{5.4}$$

Therefore,

$$\begin{cases} H_s^* &= \dfrac{\lambda_h - (\mu_h + \eta + \sigma) H_i^*}{\mu_h}, \\ K^* &= \dfrac{\alpha_1}{\mu_k} H_i^*, \\ M_i^* &= \dfrac{\lambda_h g(\frac{\alpha_1}{\mu_k} H_i^*)}{\mu_m^2 + \mu_m g(\frac{\alpha_1}{\mu_k} H_i^*)}, \\ P^* &= \dfrac{\alpha_2}{\mu_p} M_i^*, \\ M_s^* &= \dfrac{\lambda_h - \mu_m M_i^*}{\mu_m}, \\ 0 &= H_S^* f(P^*) - (\mu_h + \eta + \sigma) H_i^*. \end{cases} \tag{5.5}$$

Replacing H_s^* et P^* in the last equation of (5.5) gives:

$$\left(\frac{\lambda_h-(\mu_h+\eta+\sigma)H_i^*}{\mu_h}\right)f\left(\frac{\alpha_2}{\mu_p}\frac{\lambda_h g(\frac{\alpha_1}{\mu_k}H_i^*)}{\mu_m^2+\mu_m g(\frac{\alpha_1}{\mu_k}H_i^*)}\right)-(\mu_h+\eta+\sigma)H_i^*=0.$$

We pose

$$h(H_i)=\left(\frac{\lambda_h-(\mu_h+\eta+\sigma)H_i}{\mu_h}\right)f\left(\frac{\alpha_2}{\mu_p}\frac{\lambda_h g(\frac{\alpha_1}{\mu_k}H_i)}{\mu_m^2+\mu_m g(\frac{\alpha_1}{\mu_k}H_i)}\right)-(\mu_h+\eta+\sigma)H_i.$$

We have $h(0)=0$ and $h\left(\frac{\lambda_h}{\mu_h}\right)<0$. Moreover

$$h'(0)=\frac{\lambda_h}{\mu_h}\left[\frac{\alpha_1\alpha_2\lambda_m\mu_m}{\mu_p\mu_k\mu_m^2}g'(0)f'(0)\right]-(\mu_h+\eta+\sigma)=(\mu_h+\eta+\sigma)[R_0^2-1]>0.$$

Therefore, the equation $h(H_i)=0$ admits a unique solution $H_i^*\in\left(0;\frac{\lambda_h}{\mu_h}\right)$ and thus the existence of our endemic equilibrium point.

Finally, we establish the global stability of endemic equilibrium point.

Let $\Phi(y)=y-1-lny, y>0$ and define the following Lyapunov candidate function.

$$W\equiv W(H_s,H_i,K,M_s,M_i,P)=\int_\Omega L(H_s,H_i,K,M_s,M_i,P)dx,$$

where,

$$\begin{aligned}L(H_s,H_i,K,M_s,M_i,P) &= \xi_1H_s^*\Phi(\frac{H_s}{H_s^*})+\xi_1H_i^*\Phi(\frac{H_i}{H_i^*})+\xi_2M_s^*\Phi(\frac{M_s}{M_s^*})\\ &+ \xi_2M_i^*\Phi(\frac{M_i}{M_i^*})+\xi_3K^*\Phi(\frac{K}{K^*})+\xi_4P^*\Phi(\frac{P}{P^*}),\end{aligned}\tag{5.6}$$

and

$$\xi_1=\mu_k\mu_pP^*K^*M_s^*g(K^*),\xi_2=\mu_k\mu_pP^*K^*H_s^*f(P^*),\xi_3=\mu_pP^*H_s^*f(P^*)M_s^*g(K^*),\xi_4=\mu_kK^*H_s^*f(P^*)M_s^*g(K^*).$$

The derivative of L along the solution trajectory of System (5.1) is calculated as given below.

$$\begin{aligned}\frac{dL}{dt} &= \xi_1\left(1-\frac{H_s^*}{H_s}\right)\frac{\partial H_s}{\partial t}+\xi_1\left(1-\frac{H_i^*}{H_i}\right)\frac{\partial H_i}{\partial t}+\xi_2\left(1-\frac{M_s^*}{M_s}\right)\frac{\partial M_s}{\partial t}\\ &+ \xi_2\left(1-\frac{M_i^*}{M_i}\right)\frac{\partial M_i}{\partial t}+\xi_3\left(1-\frac{K^*}{K}\right)\frac{\partial K}{\partial t}+\xi_4\left(1-\frac{P^*}{P}\right)\frac{\partial P}{\partial t}\\ &= \xi_1H_s^*f(P^*)\left[1-\frac{H_sf(P)}{H_s^*f(P^*)}-\frac{H_s^*}{H_s}+\frac{f(P)}{f(P^*)}\right]+\xi_1H_s^*f(P^*)\left[\frac{H_sf(P)}{H_s^*f(P^*)}-\frac{H_i}{H_i^*}-\frac{H_i^*H_sf(P)}{H_iH_s^*f(P^*)}+1\right]\\ &+ \xi_1H_s^*f(P^*)\left[1-\frac{M_sg(K)}{M_s^*fg(K^*)}-\frac{M_s^*}{M_s}+\frac{g(K)}{g(K^*)}\right]+\xi_1H_s^*f(P^*)\left[\frac{M_sg(K)}{M_s^*g(K^*)}-\frac{M_i}{M_i^*}-\frac{M_i^*M_sg(K)}{M_iM_s^*g(K^*)}+1\right]\\ &+ \xi_1H_s^*f(P^*)\left[\frac{H_i}{H_i^*}-\frac{K}{K^*}-\frac{KH_i}{K^*H_i^*}+1\right]+\xi_1H_s^*f(P^*)\left[\frac{M_i}{M_i^*}-\frac{P}{P^*}-\frac{P^*H_i}{PM_i^*}+1\right]\\ &+ \xi_1\left(1-\frac{H_s^*}{H_s}\right)(d_1\Delta H_s)+\xi_1\left(1-\frac{H_i^*}{H_i}\right)(d_2\Delta H_i)+\xi_2\left(1-\frac{M_s^*}{M_s}\right)(d_4\Delta M_s)\\ &+ \xi_2\left(1-\frac{M_i^*}{M_i}\right)(d_5\Delta M_i)+\xi_3\left(1-\frac{K^*}{K}\right)(d_3\Delta K)+\xi_4\left(1-\frac{P^*}{P}\right)(d_6\Delta P)\end{aligned}$$

After some algebraic simplifications, we obtain

$$\begin{aligned}\frac{dL}{dt} &= \xi_1H_s^*f(P^*)\left[6-\frac{H_s^*}{H_s}+\frac{f(P)}{f(P^*)}-\frac{H_i^*H_sf(P)}{H_iH_s^*f(P^*)}-\frac{M_s^*}{M_s}+\frac{g(K)}{g(K^*)}-\frac{M_i^*M_sg(K)}{M_iM_s^*g(K^*)}-\frac{K}{K^*}-\frac{KH_i}{K^*H_i^*}-\frac{P}{P^*}-\frac{P^*H_i}{PM_i^*}\right]\\ &+ \xi_1\left(1-\frac{H_s^*}{H_s}\right)(d_1\Delta H_s)+\xi_1\left(1-\frac{H_i^*}{H_i}\right)(d_2\Delta H_i)+\xi_2\left(1-\frac{M_s^*}{M_s}\right)(d_4\Delta M_s)\\ &+ \xi_2\left(1-\frac{M_i^*}{M_i}\right)(d_5\Delta M_i)+\xi_3\left(1-\frac{K^*}{K}\right)(d_3\Delta K)+\xi_4\left(1-\frac{P^*}{P}\right)(d_6\Delta P)\end{aligned}$$

Using the properties of the Φ function we have,

$$\begin{aligned}\frac{dL}{dt} &= \xi_1 H_s^* f(P^*)\left[\Phi\left(\frac{f(P)}{f(P^*)}\right)-\Phi\left(\frac{P}{P^*}\right)+\Phi\left(\frac{g(K)}{g(K^*)}\right)-\Phi\left(\frac{K}{K^*}\right)\right]\\ &- \xi_1 H_s^* f(P^*)\left[\Phi\left(\frac{H_s^*}{H_s}\right)+\Phi\left(\frac{H_i^* H_s f(P)}{H_i H_s^* f(P^*)}\right)+\Phi\left(\frac{M_s^*}{M_s}\right)+\Phi\left(\frac{M_i^* M_s g(K)}{M_i M_s^* g(K^*)}\right)+\Phi\left(\frac{K H_i}{K^* H_i^*}\right)+\Phi\left(\frac{P^* H_i}{P M_i^*}\right)\right]\\ &+ \xi_1\left(1-\frac{H_s^*}{H_s}\right)(d_1\Delta H_s)+\xi_1\left(1-\frac{H_i^*}{H_i}\right)(d_2\Delta H_i)+\xi_2\left(1-\frac{M_s^*}{M_s}\right)(d_4\Delta M_s)\\ &+ \xi_2\left(1-\frac{M_i^*}{M_i}\right)(d_5\Delta M_i)+\xi_3\left(1-\frac{K^*}{K}\right)(d_3\Delta K)+\xi_4\left(1-\frac{P^*}{P}\right)(d_6\Delta P).\end{aligned}$$

Using the Green formulae, and the homogeneous Neumann condition, we obtain

$$\int_\Omega \Delta H_s dx = \int_\Omega \Delta H_i dx = \int_\Omega \Delta K dx = 0 = \int_\Omega \Delta M_s dx = \int_\Omega \Delta M_i dx = \int_\Omega \Delta P dx = 0.$$

$$\int_\Omega (\Delta H_s)\frac{1}{H_s}dx = \int_\Omega \frac{|\nabla H_s|^2}{H_s^2}dx \geq 0, \int_\Omega (\Delta H_i)\frac{1}{H_i}dx = \int_\Omega \frac{|\nabla H_i|^2}{H_i^2}dx \geq 0,$$

$$\int_\Omega (\Delta K)\frac{1}{K}dx = \int_\Omega \frac{|\nabla K|^2}{K^2}dx \geq 0, \int_\Omega (\Delta M_s)\frac{1}{M_s}dx = \int_\Omega \frac{|\nabla M_s|^2}{M_s^2}dx \geq 0,$$

$$\int_\Omega (\Delta M_i)\frac{1}{M_i}dx = \int_\Omega \frac{|\nabla M_i|^2}{M_i^2}dx \geq 0, \int_\Omega (\Delta P)\frac{1}{P}dx = \int_\Omega \frac{|\nabla P|^2}{P^2}dx \geq 0.$$

By virtue of hypothesis (B4), (B5) and (B6), we have

$$\Phi\left(\frac{f(P)}{f(P^*)}\right)-\Phi\left(\frac{P}{P^*}\right)=\left(\frac{f(P)}{f(P^*)}-\frac{P}{P^*}\right)\left(1-\frac{f(P)}{f(P^*)}\right)\leq 0 \text{ and } \Phi\left(\frac{g(K)}{g(K^*)}\right)-\Phi\left(\frac{K}{K^*}\right)=\left(\frac{g(K)}{g(K^*)}-\frac{K}{K^*}\right)\left(1-\frac{g(K)}{g(K^*)}\right)\leq 0.$$

Thus,

$$\begin{aligned}\frac{dW}{dt} &= \int_\Omega \frac{\partial L(x,t)}{\partial t}dx\\ &\leq \int_\Omega \xi_1 H_s^* f(P^*)\left[\Phi\left(\frac{f(P)}{f(P^*)}\right)-\Phi\left(\frac{P}{P^*}\right)+\Phi\left(\frac{g(K)}{g(K^*)}\right)-\Phi\left(\frac{K}{K^*}\right)\right]\\ &- \xi_1 H_s^* f(P^*)\left[\Phi\left(\frac{H_s^*}{H_s}\right)+\Phi\left(\frac{H_i^* H_s f(P)}{H_i H_s^* f(P^*)}\right)+\Phi\left(\frac{M_s^*}{M_s}\right)+\Phi\left(\frac{M_i^* M_s g(K)}{M_i M_s^* g(K^*)}\right)+\Phi\left(\frac{K H_i}{K^* H_i^*}\right)+\Phi\left(\frac{P^* H_i}{P M_i^*}\right)\right]dx\\ &\leq 0.\end{aligned}$$

Thus, W is a strict Lyapunov function of the EE, and this concludes the proof. ■

6. Numerical simulations

In this section we will realize the numerical simulations to confirm our theoretical results using parameter values in Table 2. To simplify the work, we will work in dimension 1: $\Omega \subset \mathbb{R}$, and use the finite difference method to obtain discrete counterpart of the model. For parabolic partial differential equations with constant diffusive coefficients, such discrete method is well-known to guarantee the accuracy and convergence of numerical scheme.

To do this, for $\Omega = [0, H]$, we pose $x_{i+1} = x_i + \Delta x$ with $x_1 = 0$, $i = 1...m$, $\Delta x = H/m$.

For t in interval $[0, T_{Max}]$, we set $t_{i+1} = t_i + \Delta t$ with $t_1 = 0$, $i = 1...n$, $\Delta t = T_{Max}/n$.

Thus have the following approximations,

$$u(x_i, t_j) = u_j^i,\ u_t(x_i, t_j) = \frac{u_j^i - u_{j-1}^i}{\Delta t},\ u_{xx}(x_i, t_j) = \frac{u_j^{i+1} - 2u_j^i - u_{j-1}^{i-1}}{\Delta x}.$$

We fix the following initial conditions.

We choose the following initial values. For, $x \in [0, 10]$,

$$H_s^0(x) = 1000 \times \frac{1}{0.5\sqrt{2\pi}} e^{\frac{-(x-5)^2}{2\times 0.5^2}},\ H_i^0(x) = 500 \times \frac{1}{0.5\sqrt{2\pi}} e^{\frac{-(x-5)^2}{2\times 0.5^2}},\ K^0(x) = 0,$$

$$M_s^0(x) = 200 \times \frac{1}{0.4\sqrt{2\pi}} e^{\frac{-(x-5)^2}{2\times 0.4^2}},\ M_i^0(x) = 100 \times \frac{1}{0.4\sqrt{2\pi}} e^{\frac{-(x-5)^2}{2\times 0.4^2}},\ P^0(x) = 0.$$

In the following we consider

$$f(x, P) = \frac{\beta_1(x)P}{1 + aP} \text{ and } g(x, K) = \frac{\beta_2(x)K}{1 + bK}.$$

$\beta_i(.) \in C^2(\overline{\Omega})$, $i = 1, 2$ are strictly positive and bounded continuous functions on $\overline{\Omega}$ and $(a, b) = (10^{-6}, 10^{-5})$.

Table 2
Parameters ranges and related references.

Parameter	Values	Range	Source	Dimension
λ_h	8000	[6000, 1000]	Chiyaka et al. (2010) [25]	day^{-1}
λ_m	200	[150, 3000]	Chiyaka et al. (2010) [25]	day^{-1}
μ_h	0.014	[0, 0.5]	Chiyaka et al. (2010) [25]	day^{-1}
η	0.01	[0.0001, 0.3]	Feng et al. (2004) [26]	day^{-1}
σ	0.0075	[10^{-7}, 0.01]	Feng et al. (2004) [26]	day^{-1}
α_1	500	[300, 800]	Mangal et al. (2008) [27]	day^{-1}
α_2	0.08	[0.03, 0.1]	Mangal et al. (2008) [27]	day^{-1}
μ_k	2.52	[2, 10]	Mangal et al. (2008) [27]	day^{-1}
μ_p	1	[1, 5]	Mangal et al. (2008) [27]	day^{-1}
μ_m	0.001	[0.001, 0.04]	Mangal et al. (2008) [27]	day^{-1}

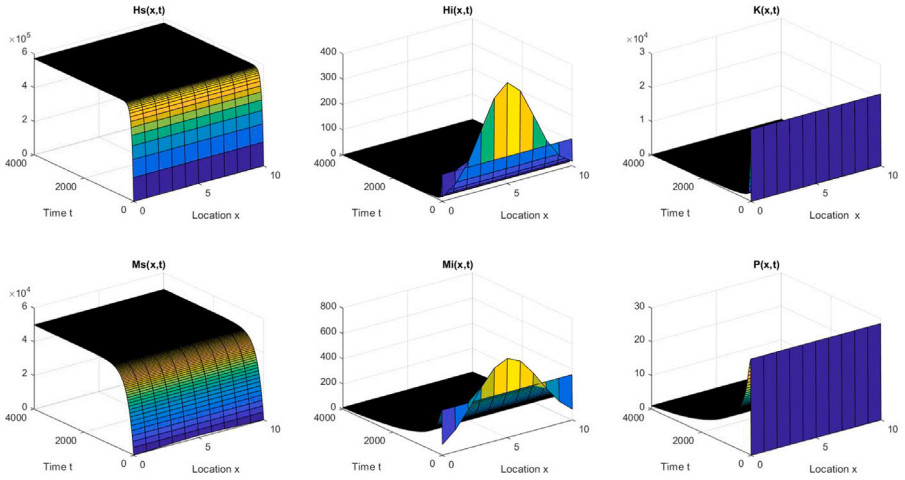

Fig. 1. Solutions of the spatially homogeneous model for $R_0 = 0.9019 < 1$. Here, $d_{i=1...6} = 1$, $\beta_1 = 2.26 \times 10^{-8}$, $\beta_2 = 10^{-8}$, $\sigma = 0.0075$.

6.1. The homogeneous case

Here we consider the homogeneous model: $\beta_i(x) = \beta_i > 0$, $i = 1, 2$. We can then calculate R_0 as in (5.1).

Then for $d_{i=1...6} = 1, \beta_1 = 2.26 \times 10^{-8}, \beta_2 = 10^{-8}$ we get $R_0 = 0.9019 < 1$. We notice from Theorem 5.1 that the disease-free equilibrium point $E_0 = (H_0, 0, 0, M_0, 0, 0) = (5.7143 \times 10^5, 0, 0, 5 \times 10^4, 0, 0)$ is globally asymptotically stable. Fig. 1 shows us that the densities of infected individuals (H_i); infected snails (M_i); miracidia (K) and cercariae (P) all converge to zero. On the other hand, the densities of humans and snails converge respectively to H_0 and M_0. For $d_{i=1...6} = 1, \beta_1 = 4 \times 10^{-8}, \beta_2 = 10^{-8}$ and $\sigma = 0$ we get $R_0 = 1.3746 > 1$. Then from Theorems 5.2, we show that the system admits a endemic equilibrium point $(H_s^*, M_s^*, K^*, H_i^*, M_i^*, P^*)$, which is globally symptomatically stable. Fig. 2 shows us that the different trajectories converge towards sadly positive constants.

6.2. The heterogeneous case

Here, we consider spatially heterogeneous model by choosing:

$\beta_1(x) = \beta_1'(1 + c_1 cos(2\pi x))$ with $0 \le c_1 \le 1$; $\beta_2(x) = \beta_2'(1 + c_2 cos(2\pi x))$ with $0 \le c_2 \le 1$, where $\beta_1' > 0$ and $\beta_2' > 0$ are strictly positive constants, $x \in [0; 10]$.

Note here that, c_1 and c_2 represent intensity of spatial heterogeneity.

We use the method developed in [23] to give an estimation of the basic reproduction number R_0.

For $(\beta_1', \beta_2') = (10^{-8}, 1.7 \times 10^{-8})$, $d_{i=1...6} = 1$, $\sigma = 0.0075$ and $c_1 = c_2 = 0.148$, we obtain $R_0 = 0.9521 < 1$. We notice from Theorem 3.2 that the disease-free equilibrium point $E_0 = (H_0, 0, 0, M_0, 0, 0) = (5.714 \times 10^5, 0, 0, 5 \times 10^4, 0, 0)$ is globally asymptotically stable. Fig. 3 shows us that the densities of infected individuals (H_i); infected snails (M_i); miracidia (K), cercariae (P) all converge to zero. While the densities of humans and snails converge respectively to H_0 and M_0. For $(\beta_1', \beta_2') = (2 \times 10^{-8}, 2 \times 10^{-8})$, $d_{i=1...6} = 1$, $\sigma = 0$, $c_1 = c_2 = 0.148$, we obtain $R_0 = 1.1711 > 1$. Then according to the Theorem 4.4, we know that the system is uniformly persistent. Fig. 4 shows us that the different trajectories converge to sadly positive constants. Finally, we investigate the effect of the spatial heterogeneity and control measures on the basic reproduction number R_0.

We start by evaluating the effect of population diffusion, on R_0. Using the method developed by Wendi Wang and Xia-Qiang Zho [23] in the spatially heterogeneous case, R_0 depends on the diffusion coefficients d_2 and d_3. Fig. 5 gives us an overview of the variation of R_0 as a function of the diffusion coefficients. We show that R_0 is a decreasing function of d_2 and d_3. Thus, diffusion of

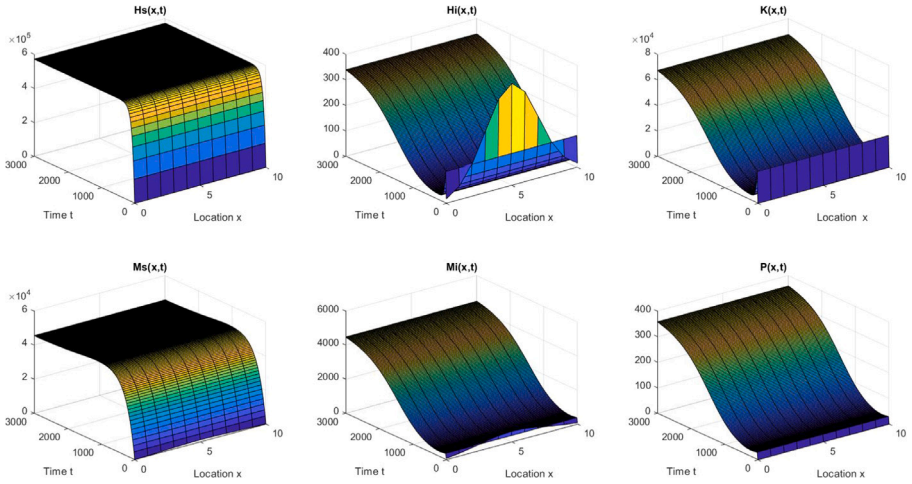

Fig. 2. Solutions of the spatially homogeneous model for $R_0 = 1.3746 > 1$. Here $d_{i=1\ldots6} = 1, \beta_1 = 4 \times 10^{-8}, \beta_2 = 10^{-8}$ and $\sigma = 0$.

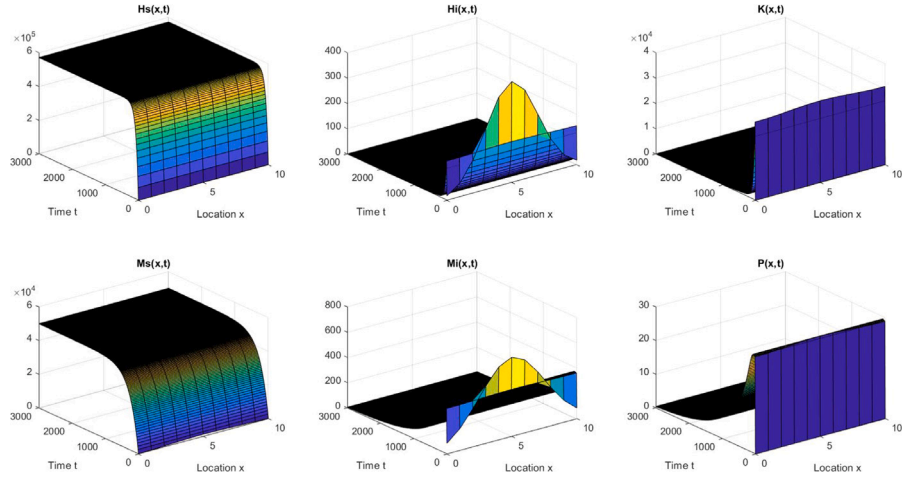

Fig. 3. Solutions of the spatially heterogeneous model for $R_0 = 0.9521 < 1$. Here, we choose: $(\beta_1', \beta_2') = (10^{-8}, 1.7 \times 10^{-8})$, $d_{i=1\ldots6} = 1$, $\sigma = 0.0075$ and $c_1 = c_2 = 0.148$.

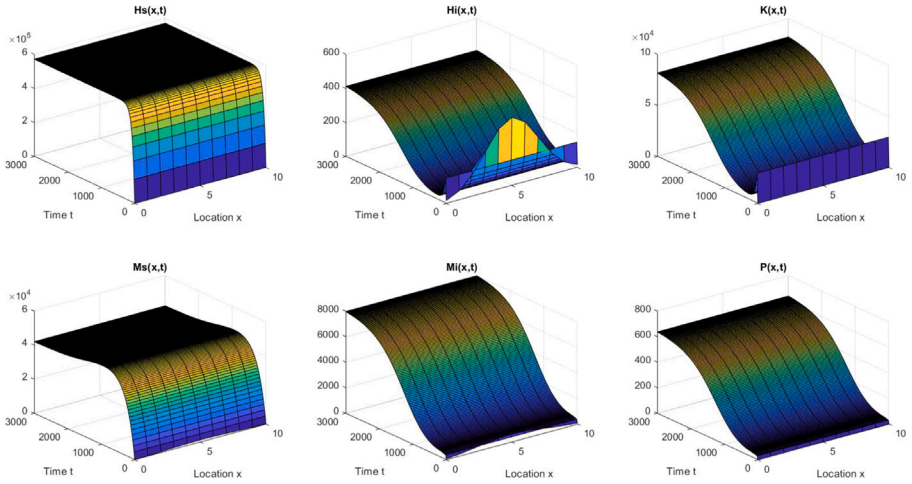

Fig. 4. Solutions of the spatially heterogeneous model for $R_0 = 1.1711 > 1$. Here, we choose: $(\beta_1', \beta_2') = (2 \times 10^{-8}, 2 \times 10^{-8})$, $d_{i=1\ldots6} = 1$, $\sigma = 0$, $c_1 = c_2 = 0.148$.

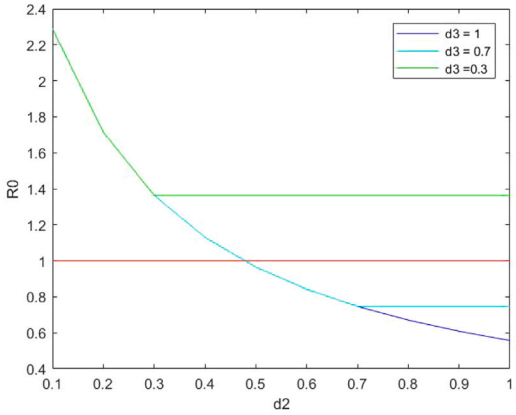

Fig. 5. Impact of d_2 on R_0 with $d_3 = 1$, $d_3 = 0.7$, $d_3 = 0.3$, $\beta_1' = 10^{-8}$, $\beta_2' = 10^{-8}$, $c_1 = c_2 = 0.148$ and $\sigma = 0$.

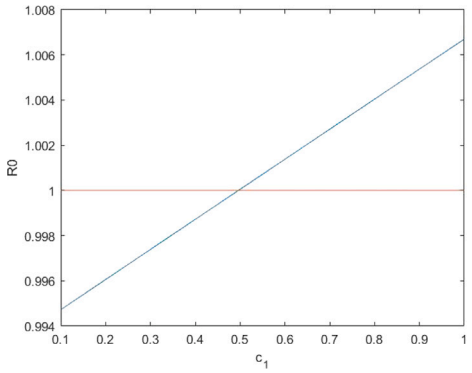

Fig. 6. Impact of c_1 on R_0 with $\beta_1' = 5 \times 10^{-8}$, $\beta_2' = 5 \times 10^{-8}$ and $c_2 = 0.148$.

population may reduce the risk of spreading the disease. Next, we evaluated the effect of the spatial heterogeneity on R_0, symbolized here by c_1 and c_2 by perfoming Fig. 6 and Fig. 7. These figures show that R_0 is increasing function of c_1 and c_2. Thus, the spatially heterogeneous infection can induce the persistence of disease.

We end with the impact of control measures (treatment and awareness) on the basic reproduction number R_0, characterized here by σ. We fix $(\beta_1', \beta_2') = (2 \times 10^{-8}, 4 \times 10^{-8})$, $d_{i=1\ldots6} = 1$ and $c_1 = c_2 = 0.148$. Fig. 8 shows us that R_0 is a decreasing function of σ. Thus, the more we increase the control measures, the more we reduce the risk of spreading the disease.

7. Conclusion

In this paper we have constructed and presented a reaction–diffusion model of schistosomiasis, to reflect the spatial movements of humans, snails, miraciduim and cercaria, which are part of the disease transmission cycle. The model uses general impact functions with spatial dependence to reflect the contacts between humans and cercariae, snails and miracidia. This is done in order to understand and explain all the processes involved in the transmission of the disease, in particular the phenomena of storage, water irrigation, and population migrations, which are crucial elements in the development of the disease [4,6,7].

To do this, we first studied the spatially heterogeneous model. The characterization of an epidemiological threshold (basic reproduction number) R_0 which is characterized as the spectral radius of the next generation operator. Mathematical results reveal that if $R_0 < 1$ the disease will die out, and disease will persist if $R_0 > 1$. The numerical simulations has allowed us to confirm our theoretical results. This also allowed us to show that population diffusion and treatment reduce the risk of disease spread, whereas spatial heterogeneity accentuates disease spread. Then, we studied the spatially homogeneous model. There, we determined the exact value of our biological threshold R_0. Then we determined and showed the existence and global stability of an endemic equilibrium for $R_0 > 1$ using a Lyapunov function. Numerical simulations have also allowed us to confirm the result.

In the next steps of our work, we are planning to introduce advection/transport phenomenon in the previous model. This will make our model more realistic as water flow may carry alone several individuals that influence the dynamics of the disease,

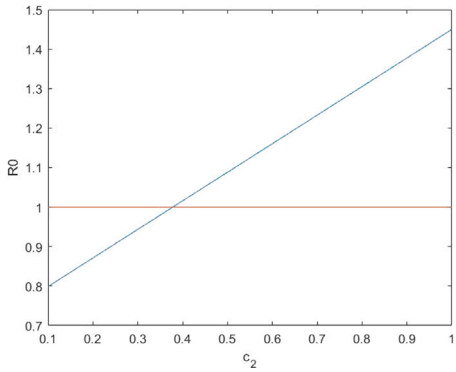

Fig. 7. Impact of c_2 on R_0 with $\beta_1' = 5 \times 10^{-8}$, $\beta_2' = 5 \times 10^{-8}$ and $c_1 = 0.148$.

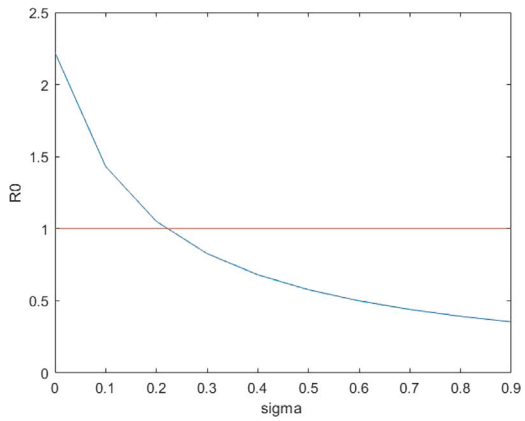

Fig. 8. Impact of control measure σ on R_0 with $\beta_1' = 2 \times 10^{-8}$, $\beta_2' = 4 \times 10^{-8}$ and $c_1 = c_2 = 0.148$.

notably: the intermediate molluscs, the cercaria and the miracidia. We are already working on building and analysing a non-standard numerical scheme of the previous model with space-dependent diffusive coefficients, and conduct some comparisons at the level of convergence with the analytical model.

CRediT authorship contribution statement

Franck Eric Thepi Nkuimeni: Formal analysis, Investigation, Software, Visualization, Writing – original draft, Writing – review & editing. **Berge Tsanou:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors have no competing interest to declare for their manuscript title : Schistosomiasis mathematical model in a spatially heterogeneous environment.

Data availability

No data was used for the research described in the article.

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Appendix

For more information on the codes and numerical methods used, please consult, https://github.com/Franck202101/-SchistosomiasisReactiondiffusion.git.

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