A mathematical model for malaria involving differential susceptibility, exposedness and infectivity of human host

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Abstract

The main purpose of this paper is to formulate a deterministic mathematical model for the transmission of malaria which considers two host types in the human population. The one type is called "child" comprising to all humans who have never acquired immunity against the malaria and the other one "adult". Children are divided into susceptible, exposed and infectious and adults are divided into susceptible, exposed, infectious and semi-immune. We obtain explicit formula for the reproductive number, R_0 in function of the weight of the transmission *adult-mosquito-adult*, R_{0a}, and the weight of the transmission *child-mosquito-child*, R_{0e}. Then we study the existence of endemic equilibria by using bifurcation analysis. We give a simple criterion for forward and backward bifurcation when R_0 crosses one. We explore the possibility of a control of the malaria through a specific sub-group as children or adults or mosquitoes. We also provide numerical examples.

Keywords: Malaria; Reproductive number, Type-reproduction number, Bifurcation analysis.

1 Introduction

Malaria is a mosquito-borne infection caused by protozoa of the genus plasmodium. Four species of the parasite, namely: P. falciparum, P. vivax, P. ovale and P. malariae infect humans. P. falciparum causes the most serious illness and is the most widespread in the tropics. It is estimated that about 1.5–3 million people, mostly children, die of malaria every year [41]. The parasites are transmitted indirectly from human to human by the bite of infected female mosquitos of the genus Anopheles. The biology of the four species of plasmodium is generally similar and consists of two distinct phases: *sexual* at the mosquito host and *asexual* at the human host. The asexual phase consists of at least three forms: sporozoites, merozoites, and trophozoites. After the bite by an infectious mosquito, the sporozoite (parasite) enter the victims blood stream and invade a variety of liver cells.

Here, they give rise to the merozoite form after replication. The merozoites invade red blood cells and they become the trophozoite form. Some merozoites differentiate into the sexual forms of the parasite, either male or female, called gametocytes. Gametocytes are transmitted to a mosquito during the blood meal of an infected person. In summary, gametocytes thus play a key role in malaria transmission from human to mosquito and the sporozoites from mosquito to human.

Starting by the Ross's model [38], mathematical modeling of malaria has known many refinements. In 1957, Macdonald [27] reformulated the Ross's model; the addition of acquired immunity by Dietz et *al.* [13] has been the most outstanding. Further, other extensions has been made: on acquired immunity in malaria which has been conducted in [3] and [6], on environmental effects in [26, 43] and [44], on the spread of resistance to antimalarial drug in [5, 22] and [33], or on the coevolution of immunity in [23]. Ngwa and Shu [32] and Ngwa [31] proposed a model involving the growing of both population (humans and mosquitoes). Chitnis et *al.* [10, 9] included human immigration.

These models do not make distinction between the susceptibility, the exposedness and the infectivity of human host. However, the susceptibility of human host is depending on whether host has lost his immunity (and is then becoming susceptible) or has not yet acquired it. immunity; in the same way, the infectivity is differentiated following the host type. Indeed, acquired immunity is developed after repeated infections generally after many years of chronic infection. It is never complete and after interruption of exposure, human can lose his immunity and becomes susceptible (see [3, 6, 4]). But by immunology memory, lost immunity can be rapidly restored when human begin to be re-exposed against to infection. Humans who have acquired their immunity can tolerate parasites without developing symptoms. They may become asymptomatic carriers of parasites in the form of gametocyte but their infectivity of gametocytes to mosquitoes is very low following the known principle *transmission-blocking immunity* (cf. [11, 20, 36]). New born (of a mother immune) are protected due to maternal antibodies in the first 3-6 months of life. After these first months they are vulnerable to clinical malaria episodes until they have built their own immunity [19] and [39].

In order to differentiate the susceptibility, the exposedness and the infectivity of human host, we develop in this paper a deterministic mathematical model for the transmission of malaria which considers two host types in the human population. The one type host is considered vulnerable because he can suffer and/or die of malaria and the second host type cannot[1] die of malaria but can only suffer. We assume that all humans who have never acquired immunity against the malaria are considered vulnerable and the other ones are assumed not vulnerable. Next, we call "child" any human considered as vulnerable and "adult" any human considered as not vulnerable and denote by, e, and, a, respectively the children and adults index. In endemic area, the real children[2] under 5 years of age are in majority the most vulnerable of malaria [28, 39, 19, 41, 34] and [8] because they have not acquired their own immunity. Humans old in age (real adults) in a non-endemic area such as the East African highlands and many parts of South America and Asia are considered as some children according to our definition. Indeed, it has been shown that real children and real adults have the same risk of malarial disease and infection depending on their first infections [7] and [1]. That is what motivates us to disregard the age of the individual but rather the immunity of the individual to structure the population. We model children group with a Susceptible-Exposed-

[1]Although this host type can die of malaria, the death rate is very weak so that we can neglect it in order to simplify the model.

[2]The real children within the meaning of the word.

Infectious-Susceptible ($S_eE_eI_eS_e$) model type until some children become adults and remains for life and will follow the Susceptible-Exposed-Infectious-Recovered-Susceptible ($S_aE_aI_aR_aS_a$) model type. We model mosquito population with Susceptible-Exposed-Infectious ($S_vE_vI_v$) model type. Our goal is to develop a model in order to prevent malaria in areas of low, intermediary and high transmission. This allows us to discuss on the effort required to control malaria through a specific subgroup as the children group, adults group or mosquitoes group following the area studied and the reservoir of infection for each sub-group.

The paper is organized as follows: In Section 2 we briefly outline the derivation of the model and investigate the existence and stability of steady-state solution in Section 3. In Section 4, we present some conditions required to control the malaria. Numerical simulations and some concluding remarks will follow respectively in Section 5 and 6.

2 Malaria model

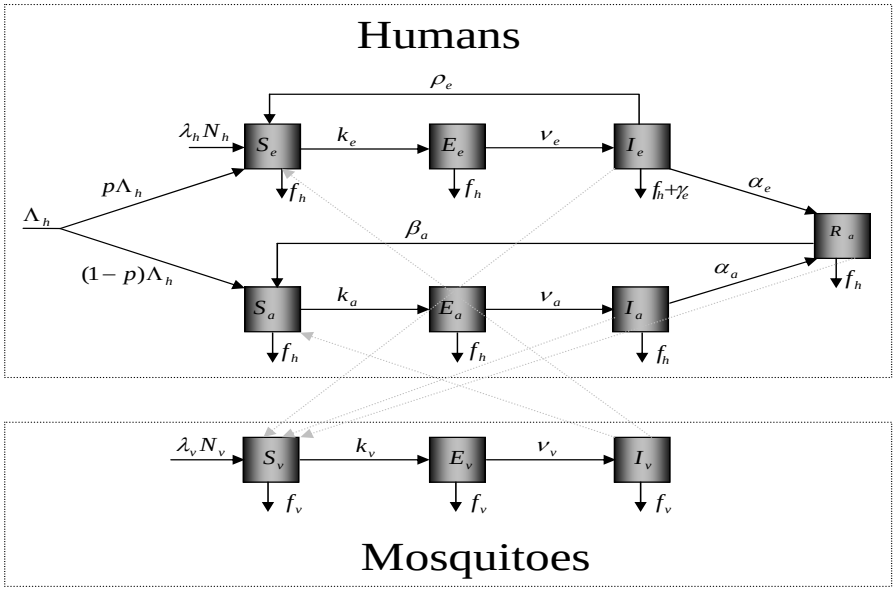

Figure 1: *A schematic of the mathematical model for malaria transmission involving the human host susceptibility, exposedness and infectivity with variable children, adults and mosquito populations.*

In order to derive our model, we divide the human population into seven subclasses (see figure 1): susceptible children S_e, susceptible adults S_a, exposed children E_e, exposed adults E_a, infectious children I_e, infectious adults I_a and immune[3] adults R_a. Hence the total size of the population at any time t is denoted by $N_h(t) = S_e(t) + S_a(t) + E_e(t) + E_a(t) + I_e(t) + I_a(t) + R_a(t)$.
We divide the mosquito population into three subclasses: susceptible, S_v; exposed, E_v; and infectious, I_v. Hence the total size of the mosquito population at any time t is denoted by $N_v(t) = S_v(t) + E_v(t) + I_v(t)$.

[3]Immune is also call semi-immune because they are asymptotic carriers of parasites and are slightly infectious.

We begin to make the following assumptions:
(**H1**) We assume that both humans and mosquitoes are born susceptible.
(**H2**) We also suppose an immigration of children into children susceptible class at rate $p \cdot \Lambda_h$ and an immigration adults into adults susceptible class at rate $(1-p) \cdot \Lambda_h$ where $p \in [0,1]$ is the probability for an immigrant to be a child, $(1-p)$ is the probability for an immigrant to be a children and Λ_h is the constant immigration rate of humans at any time t.
(**H3**) In order to simplify the model, we neglect as in Chitnis [10] immigration of exposed, infectious and semi-immune humans.

Children enter the susceptible class, S_e, either through birth at a per capita birth rate λ_h or through immigration at a constant rate $p \cdot \Lambda_h$ or by migration of an infectious child at rate ρ_e. Adults enter the susceptible class, S_a, either through immigration at rate $(1-p) \cdot \Lambda_h$ or by migration of adults in class R_a at rate β_a. Mosquitoes enter the susceptible class, S_v by birth at a per capita birth rate of mosquitoes λ_v.

When an infectious mosquito (in class I_v) bites a susceptible child (resp. adult), the parasite enters the child (resp. adult) body with some probability c_{ve} (resp. c_{va}) and the child (resp. adult) will move to the exposed class, E_e, (resp. E_a). After a given time the child (resp. adult) moves from the exposed class into the infectious class, I_e, (resp. I_a) at a rate ν_e (resp. ν_a). Infectious children can go back to the susceptible class, S_e, at a rate ρ_e if they have not yet acquired their immunity or move to the immune class, R_a, at a rate α_e after many years of chronic infection. By immunology memory, immunity of infectious adults in class I_a might be rapidly restored when they begin to be re-exposed at infection. Consequently, we assume that infectious adults move to the immune class, R_a, at a rate α_a before becoming susceptible. Immune individuals in class R_a, can lose their immunity if they have not a continuous exposure to the parasite and go back to the susceptible class, S_a. Children leave the population through a density-dependent per capita natural death rate f_h and through a per capita disease-induced death rate γ_e. But adults leave the population only through a per capita density-dependent natural death rate f_h.

When a susceptible mosquito bites an infectious child (resp. adult, resp. immune) the parasite enters the mosquito with some probability c_{ev} (resp. c_{av}, resp. $\widetilde{c}_{av}$)[4] and the mosquito moves from the susceptible to the exposed class E_v. The exposed mosquito becomes infectious and enters the class I_v after a given time and remains infectious for life. Mosquitoes leave the population through a per capita density-dependent natural death rate f_v.

Let μ_h (resp. μ_v) be the density independent part of the death rate for humans (resp. mosquitoes) and μ_{2h} (resp. μ_{2v}) be the density dependent part of the death rate for humans (resp. mosquitoes). As in [32] and [10], we assume $f_h(N_h) = \mu_h + \mu_{2h} N_h$ and $f_v(N_v) = \mu_v + \mu_{2v} N_v$.

Let n_e, (resp. n_a) be the average number of bites given to children (resp. adults) by one mosquito per unit time.

The probabilities c_{ve}, c_{va}, c_{ev}, c_{av} and $\tilde{c}_{av}$ are assumed belong to the interval]0,1[, the parameters λ_h, λ_v, ν_e, ν_a, ν_v, α_e α_a, ρ_e, β_a, μ_v, μ_{2v}, μ_h, μ_{2h}, n_e, n_a, and Λ_h are assumed to be positive except for the disease-induced death rate, γ_e, which is assumed to be nonnegative.

Using the standard incidence as in the model of Ngwa and shu and Ross-Macdonald, define respectively the infection incidence from mosquitoes to adults, k_a, from mosquitoes to children, k_e,

[4]The probability of transmission of the infection from infectious adults is much lower than the one from infectious children ($c_{ev} \geq c_{av}$) and the probability of infection transmission from recovered humans is much lower than the one from infectious adults ($c_{av} \geq \widetilde{c}_{av}$) (cf. [11, 20, 36]).

from adults and children to mosquitoes, k_v, at any time t as follows

$$k_a = c_{va} n_a \frac{I_v}{N_h}, \quad k_e = c_{ve} n_e \frac{I_v}{N_h}, \quad k_v = c_{av} n_a \frac{I_a}{N_h} + c_{ev} n_e \frac{I_e}{N_h} + \tilde{c}_{av} n_a \frac{R_a}{N_h}. \tag{1}$$

Now, we write the model describing the spread of malaria in the form:

$$\begin{aligned}
\frac{dS_e}{dt} &= p\Lambda_h + \lambda_h N_h + \rho_e I_e - f_h(N_h) S_e - k_e(t) S_e, && \text{(2a)}\\
\frac{dS_a}{dt} &= (1-p)\Lambda_h + \beta_a R_a - f_h(N_h) S_a - k_a(t) S_a, && \text{(2b)}\\
\frac{dE_e}{dt} &= k_e(t) S_e - (\nu_e + f_h(N_h)) E_e, && \text{(2c)}\\
\frac{dE_a}{dt} &= k_a(t) S_a - (\nu_a + f_h(N_h)) E_a, && \text{(2d)}\\
\frac{dI_e}{dt} &= \nu_e E_e - (\alpha_e + \gamma_e + \rho_e + f_h(N_h)) I_e, && \text{(2e)}\\
\frac{dI_a}{dt} &= \nu_a E_a - (\alpha_a + f_h(N_h)) I_a, && \text{(2f)}\\
\frac{dR_a}{dt} &= \alpha_e I_e + \alpha_a I_a - (\beta_a + f_h(N_h)) R_a, && \text{(2g)}\\
\frac{dS_v}{dt} &= \lambda_v N_v - f_v(N_v) S_v - k_v(t) S_v, && \text{(2h)}\\
\frac{dE_v}{dt} &= k_v(t) S_v - (\nu_v + f_v(N_v)) E_v, && \text{(2i)}\\
\frac{dI_v}{dt} &= \nu_v E_v - f_v(N_v) I_v. && \text{(2j)}
\end{aligned}$$

By adding up the equations (2a)-(2g) (resp. (2h)-(2k)) we obtain the equation for human (resp. mosquitoes) total population:

$$\begin{aligned}
\frac{dN_h}{dt} &= \Lambda_h + \lambda_h N_h - f_h(N_h) N_h - \gamma_e I_e, && \text{(3a)}\\
\frac{dN_v}{dt} &= \lambda_v N_v - f_v(N_v) N_v. && \text{(3b)}
\end{aligned}$$

To analyze this model, we make the change of variables:

$$\begin{aligned}
&s_e = \frac{S_e}{N_h}, \quad s_a = \frac{S_a}{N_h}, \quad e_e = \frac{E_e}{N_h}, \quad e_a = \frac{E_a}{N_h}, \quad i_e = \frac{I_e}{N_h}, \quad i_a = \frac{I_a}{N_h}, \quad r_a = \frac{R_a}{N_h},\\
&s_v = \frac{S_v}{N_v}, \quad e_v = \frac{E_v}{N_v}, \quad i_v = \frac{I_v}{N_v},
\end{aligned} \tag{4}$$

so that

$$(s_e + s_a) + (e_e + e_a) + (i_e + i_a) + r_a = 1, \quad s_v + e_v + i_v = 1. \tag{5}$$

Using precedences, the infection rates (1) become

$$k_a = c_{va} n_a i_v \cdot \frac{N_v}{N_h}, \quad k_e = c_{ve} n_e i_v \cdot \frac{N_v}{N_h}, \quad k_v = c_{av} n_a i_a + c_{ev} n_e i_e + \tilde{c}_{av} n_a r_a. \tag{6}$$

If we introduce the following variables

$$\begin{aligned} M_1 &= \frac{\Lambda_h}{N_h}p + \lambda_h, \quad M_2 = \frac{\Lambda_h}{N_h} + \lambda_h, \quad M_3 = \frac{\Lambda_h}{N_h} + \nu_e + \lambda_h, \\ M_4 &= \frac{\Lambda_h}{N_h} + \nu_a + \lambda_h, \quad M_5 = \frac{\Lambda_h}{N_h} + \lambda_h + \alpha_e + \gamma_e + \rho_e, \\ M_6 &= \frac{\Lambda_h}{N_h} + \lambda_h + \alpha_a, \quad M_7 = \frac{\Lambda_h}{N_h} + \lambda_h + \beta_a, \quad M_8 = \nu_v + \lambda_v, \end{aligned} \tag{7}$$

then system (2)-(3) re-writes:

$$\frac{ds_e}{dt} = M_1(t) - M_2(t)s_e + \rho_e i_e + \gamma_e i_e s_e - k_e(t)s_e, \tag{8a}$$

$$\frac{de_e}{dt} = k_e(t)s_e + \gamma_e i_e e_e - M_3(t)e_e, \tag{8b}$$

$$\frac{de_a}{dt} = k_a(t)\cdot(1 - s_e - (e_e + e_a) - (i_e + i_a) - r_a) + \gamma_e i_e e_a - M_4(t)e_a, \tag{8c}$$

$$\frac{di_e}{dt} = \nu_e e_e + \gamma_e i_e^2 - M_5(t)i_e, \tag{8d}$$

$$\frac{di_a}{dt} = \nu_a e_a + \gamma_e i_e i_a - M_6(t)i_a, \tag{8e}$$

$$\frac{dr_a}{dt} = \alpha_e i_e + \alpha_a i_a + \gamma_e i_e r_a - M_7(t)r_a, \tag{8f}$$

$$\frac{de_v}{dt} = k_v(t)\cdot(1 - e_v - i_v) - M_8 e_v, \tag{8g}$$

$$\frac{di_v}{dt} = \nu_v e_v - \lambda_v i_v, \tag{8h}$$

$$\frac{dN_h}{dt} = \Lambda_h + \lambda_h N_h - f_h(N_h)N_h - \gamma_e i_e N_h, \tag{8i}$$

$$\frac{dN_v}{dt} = \lambda_v N_v - f_v(N_v)N_v. \tag{8j}$$

We assume that the initial conditions lie in Ω defined by $\Omega = \Omega_1 \times \Omega_2$ where

$$\Omega_1 = \{(s_e, e_e, e_a, i_e, i_a, r_a, e_v, i_v) \in [0,1]^8 / 0 \leq e_v + i_v \leq 1; 0 \leq s_e + e_e + e_a + i_e + i_a + r_a \leq 1\}, \tag{9}$$

and for $\lambda_v > \mu_v$,

$$\Omega_2 = \left\{ (N_h, N_v) \in \mathbb{R}^2 / 0 < N_h \leq \frac{\lambda_h - \mu_h + \sqrt{(\lambda_h - \mu_h)^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}; 0 < N_v \leq \frac{\lambda_v - \mu_v}{\mu_{2v}} \right\}. \tag{10}$$

We denote points in Ω by $x = (s_e, e_e, e_a, i_e, i_a, r_a, e_v, i_v, N_h, N_v)^t$. Then we re-write system (8) in the compact form

$$\frac{dx_i}{dt} = f_i(x), \quad i = 1, \ldots, 10, \tag{11}$$

and we readily obtain the following result which will guaranty the global well-posedness of malaria model (8):

Theorem 1. *If the density-dependent mosquito birth rate λ_v is greater than the density-independent mosquito death rate μ_v, for any initial condition in Ω, system (8) has a unique globally defined solution which remains in Ω for all time $t \geq 0$.*

Proof. Local existence of solution follows from the regularity of function $f = (f_1, \ldots, f_{10})$ which is of the class C^1 in Ω. It remains to show the positivity and boundedness of solutions. We first show that Ω_1 is forward-invariant for all $(N_h, N_v) \in \Omega_2$. It is easy to see that if $x_i = 0$, then $x_i' = dx_i/dt = f_i(x) \geq 0$, $i = 1, \ldots, 8$. It follows that if $e_v + i_v = 0$ then $e_v' + i_v' \geq 0$, if $s_e + e_e + e_a + i_e + i_a + r_a = 0$ then $s_e' + e_e' + e_a' + i_e' + i_a' + r_a' \geq 0$. Moreover, if $e_v + i_v = 1$ then $e_v' + i_v' = -\lambda_v < 0$, if $s_e + e_e + e_a + i_e + i_a + r_a = 1$ then $s_e' + e_e' + e_a' + i_e' + i_a' + r_a' = \frac{\Lambda_h}{N_h}(p-1) - \beta_a r_a < 0$ because $p \in [0, 1]$.
Next, we show that Ω_2 is forward-invariant for all $(s_e, e_e, e_a, i_e, i_a, r_a, e_v, i_v) \in \Omega_1$. For some $m_h, m_v > 0$ small enough, if $N_h = m_h$, then $N_h' > 0$ because $N_h' = \Lambda_h + \lambda_h m_h - \mu_h m_h - \mu_{2h} m_h^2 - \gamma_e i_e m_h \to \Lambda_h > 0$ as $m_h \to 0$; if $N_v = m_v$, then $N_v' = m_v(\lambda_v - \mu_v - \mu_{2v} m_v) > 0$ if only $\lambda_v > \mu_v + \mu_{2v} m_v$. It follows that for $m_v \to 0$, $N_v' > 0$ because we have assumed that $\lambda_v > \mu_v$. It is easy to see that $\limsup_{t\to\infty} N_v(t) \leq (\lambda_v - \mu_v)/\mu_{2v}$ and
$\limsup_{t\to\infty} N_h(t) \leq (\lambda_h - \mu_h + \sqrt{(\lambda_h - \mu_h)^2 + 4\mu_{2h}\Lambda_h})/\mu_{2h}$. We conclude that the solutions of malaria model exist globally in Ω. □

3 Existence and stability of steady-state solution

In this section, we analyze the existence and stability of equilibria including disease free equilibrium as well as endemic equilibria. We recall that equilibria for system (8) are defined as the zeros in Ω of the vector valued function $f = (f_1, \ldots, f_{10})$.

3.1 Disease-free equilibrium point and reproductive number

3.1.1 Disease-free equilibrium point

The equilibria solutions for which there is no disease are generally called disease-free equilibrium point (DFE). A disease will not exist within the three populations if the following classes e_e, e_a, i_e, i_a, r_a, e_v, i_v are all zero. Let x_{dfe} (resp. X_{dfe}) be the disease free equilibrium with the proportion (resp. original) variables for malaria model (8) (resp. (2)). The following theorem shows that x_{dfe} (resp. X_{dfe}) exists and is unique. Like models (2) and (8) are equivalent x_{dfe} and X_{dfe} are also.

Theorem 2. *The malaria model* (2) *or* (8) *has a unique equilibrium point with no disease in the population on Ω where*

$$x_{dfe} = (s_e^*, 0, 0, 0, 0, 0, 0, 0, N_h^*, N_v^*) \tag{12a}$$

$$X_{dfe} = (S_e^*, 0, 0, S_a^*, 0, 0, 0, S_v^*, 0, 0) \tag{12b}$$

and

$$N_h^* = \frac{\lambda_h - \mu_h + \sqrt{(\lambda_h - \mu_h)^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}, \quad N_v^* = \frac{\lambda_v - \mu_v}{\mu_{2v}}, \tag{13a}$$

$$s_e^* = \frac{\frac{\Lambda_h}{N_h^*}p + \lambda_h}{\frac{\Lambda_h}{N_h^*} + \lambda_h}, \quad s_a^* = 1 - s_e^*, \tag{13b}$$

$$S_e^* = s_e^* N_h^*, \quad S_a^* = s_a^* N_h^*, \tag{13c}$$

$$S_v^* = s_v^* N_v^* = 1 \cdot N_v^*. \tag{13d}$$

The proof is given in Appendix **A.1**.
Next, at the DFE we simplify the writings as follows. We denoted

$$M_i^* = M_i(N_h^*), i = 1, \ldots, 8, \quad f_h^* = f_h(N_h^*), \quad f_v^* = f_v(N_v^*) \quad \text{from} \quad (14).$$

Note also that $f_h^* = \frac{\Lambda_h}{N_h^*} + \lambda_h$ from (8i) and $f_v^* = \lambda_v$ from (8j) at the DFE. It follows

$$\begin{array}{l} M_3^* = f_h^* + \nu_e, \quad M_4^* = f_h^* + \nu_a, \quad M_5^* = f_h^* + \alpha_e + \gamma_e + \rho_e, \\ M_6^* = f_h^* + \alpha_a, \quad M_7^* = f_h^* + \beta_a, \quad M_8^* = M_8 = \nu_v + \lambda_v. \end{array} \tag{14}$$

3.1.2 Reproductive number R_0

A key concept in epidemiology is the basic reproductive number, commonly denoted by R_0. Usually, R_0 is defined as the expected number of secondary individuals produced, in a completely susceptible population, by a typical infected individual during its entire period of infectiousness. In the case of malaria where the disease is transmitted between two hosts types (humans and mosquitos), the interpretation of 'secondary individuals' has lead some authors to define R_0 as the number of *humans* infected by single infected *humans* during his entire infectious period (cf. [27, 32, 2]); that is a definition originally used for malaria. Others Authors define R_0 using the next-generation matrix approach [2, 10, 9] described in [12, 42]. This approach defined R_0 as the number of individuals (*humans or mosquitoes*) infected by a single infected individual (*humans or mosquitoes*) during his entire infectious period, in a population (*humans and mosquitoes*) which is entirely susceptible. The difference is that the first definition approximates the total number of infections within a human class given by one infective human belonging to this class whereas the second one gives the *mean* number of new infections per infective in any class per generation where a generation refers to the infection. We will see in Section 4 that these two definitions depend on the goal we want to reach.

To derive the reproductive number for our model, we use the next generation approach. We have three host types indexed by e for children, a for adults and v for mosquitoes. The next-generation matrix K is :

$$K = \begin{pmatrix} K_{ee} & K_{ea} & K_{ev} \\ K_{ae} & K_{aa} & K_{av} \\ K_{ve} & K_{va} & K_{vv} \end{pmatrix},$$

where each element K_{rs} represents the expected number of secondary cases in host, indexed by s, produced by a typical primary case in host, indexed by r in a completely susceptible population. We assume that there are no infections transmission between children, between adults, between adults and children, only transmission from children to mosquitoes, from mosquitoes to children,

from adults to mosquitoes, from mosquitoes to adults, therefore $K_{ee} = K_{aa} = K_{vv} = K_{ae} = K_{ea}$. As a consequence, K simplifies to

$$K = \begin{pmatrix} 0 & 0 & K_{ev} \\ 0 & 0 & K_{av} \\ K_{ve} & K_{va} & 0 \end{pmatrix}. \tag{15}$$

Like K_{rs} has the concept of reproductive number, it can be easily derived as *the product of the survival probability until the infectious state, the contact number per unit time, the probability of transmission per contact and the mean duration of the infectious lifetime* see [18].

We derive heuristically the elements $K_{ev}, K_{av}, K_{ve}, K_{va}$ of K. We recall that the disease-free equilibrium (DFE) corresponds to steady state solutions where there is no disease within the three host types; this means that the populations are entirely susceptible. The infectious class corresponds to variables I_e, I_a, R_a, I_v and the infected class are the variables E_e, E_a, E_v. When a disease is newly introduced in a population by one infected individual, the next generation approach defines R_0 as the *average* number of secondary cases produced by that infected during his entire infectious period. In the case of our model, a new infected can be introduced either in the susceptible children or susceptible adults or susceptible mosquitoes.

• First, we introduce a single newly infected child in population at the DFE state (ie. all adults and mosquitoes are assumed to be susceptible). Note that this child can infect a mosquito if he survives in the class E_e and enters respectively in the infectious classes I_e and R_a. Let K_{ev}, be the expected number of mosquitoes that this child will infect. This child comes out of the class E_e with a survival probability, $\nu_e/(f_h^* + \nu_e)$, and enters the class, I_e, where he/her could infect a susceptible mosquito if there are infectious contact with a probability c_{ev} and a contact number, $n_e \frac{S_v^*}{N_h^*}$, with a mean duration of the infectious lifetime, $1/(f_h^* + \alpha_e + \gamma_e + \rho_e)$, in that class. This child might become adult in entering the class R_a with a probability $\nu_e/(f_h^* + \nu_e) \cdot \alpha_a/(f_h^* + \alpha_e + \gamma_e + \rho_e)$; where he could still infect a susceptible mosquito if there are infectious contact with a probability c_{av} and a contact number, $n_a \frac{S_v^*}{N_h^*}$, with a lifetime, $1/(f_h^* + \beta_a)$, in that class. Consequently, we can write K_{ev} as the sum of expected number of mosquitoes infected by the class I_e denoted, $K_{ev}^{I_e}$ and by the class R_a denoted $K_{ev}^{R_a}$, ie.

$$K_{ev} = K_{ev}^{I_e} + K_{ev}^{R_a}, \quad \text{where} \tag{16a}$$

$$K_{ev}^{I_e} = \frac{\nu_e}{f_h^* + \nu_e} \cdot n_e \frac{S_v^*}{N_h^*} \cdot c_{ev} \cdot \frac{1}{f_h^* + \alpha_e + \gamma_e + \rho_e}, \tag{16b}$$

$$K_{ev}^{R_a} = \frac{\nu_e}{f_h^* + \nu_e} \frac{\alpha_e}{f_h^* + \alpha_e + \gamma_e + \rho_e} \cdot n_a \frac{S_v^*}{N_h^*} \cdot \widetilde{c}_{av} \cdot \frac{1}{f_h^* + \beta_a}. \tag{16c}$$

• Now, we introduce a single newly infected adult in the population at the DFE state (ie. all children and mosquitoes are assumed susceptible). Let K_{av}, be the expected number of mosquitoes for which this child will infect. Using the same reasoning as previous , we can write K_{av} as the sum of expected number of mosquitoes infected by the class I_e denoted, $K_{av}^{I_a}$ and by the class R_a

denoted $K_{av}^{R_a}$, ie.

$$K_{av} = K_{av}^{I_a} + K_{av}^{R_a}, \quad \text{where} \tag{17a}$$

$$K_{av}^{I_a} = \frac{\nu_a}{f_h^* + \nu_a} \cdot n_a \frac{S_v^*}{N_h^*} \cdot c_{av} \cdot \frac{1}{f_h^* + \alpha_a}, \tag{17b}$$

$$K_{av}^{R_a} = \frac{\nu_a}{f_h^* + \nu_a} \frac{\alpha_a}{f_h^* + \alpha_a} \cdot n_a \frac{S_v^*}{N_h^*} \cdot \widetilde{c}_{av} \cdot \frac{1}{f_h^* + \beta_a}. \tag{17c}$$

• Next, we consider adults and children entirely susceptible near the DFE and introduce a single newly infected mosquito in the mosquito population. Let K_{ve}, (resp. K_{va}) be the expected number of susceptible children (resp. adults) for which this mosquito will infect.

This mosquito comes out of the class E_v with a survival probability, $\nu_v/(f_v^* + \nu_v)$, and enters the class, I_v, where it could infect a susceptible children (resp. adult) if there are infectious contact with a probability c_{ve}(resp. c_{va}) and a contact number, $n_e \frac{S_e^*}{N_h^*}$ (resp. $n_a \frac{S_a^*}{N_h^*}$), with a mean duration of the infectious lifetime, $1/f_v^*$, in that class I_v. We define :

$$K_{ve} = \frac{\nu_v}{f_v^* + \nu_v} \cdot n_e \frac{S_e^*}{N_h^*} \cdot c_{ve} \cdot \frac{1}{f_v^*}, \tag{18a}$$

$$K_{va} = \frac{\nu_v}{f_v^* + \nu_v} \cdot n_a \frac{S_a^*}{N_h^*} \cdot c_{va} \cdot \frac{1}{f_v^*}. \tag{18b}$$

The value of R_0 is mathematically defined as the spectral radius of K (see [12]). Therefore we can state the following proposition:

Proposition 2.1. *The reproductive number for malaria model* (2) *is explicitly given by the formula* (19) *where* K_{ve}, K_{va}, K_{ev} *and* K_{av} *are respectively defined in* (18a), (18b),(16) *and* (17) *:*

$$R_0 = \sqrt{K_{ve} \cdot K_{ev} + K_{va} \cdot K_{av}}. \tag{19}$$

Consider a human population at the DFE without adults. This means that all susceptible adults are protected by a vaccine or other control measures type. This also corresponds to an area where there are no adult at the DFE. Therefore $S_a^* = 0$ and $S_e^* = N_h^*$ *ie.* $s_e^* = 1$ allowing to take $K_{va} = 0$ in Equation (18b). It follows that $R_0 = \sqrt{K_{ve}^1 \cdot K_{ev}}$ where we denoted $K_{ve}^1 = K_{ve}$ when $s_e^* = 1$.
Now, consider a human population at the DFE without children. $S_e^* = 0$, allowing to take $K_{ve} = 0$ in Equation (18a). It follows $R_0 = \sqrt{K_{va}^1 \cdot K_{av}}$ and $K_{va}^1 = K_{va}$ when $s_a^* = 1$.

We can define a reproductive number for an infection due to transmission *adult-mosquito-adult* denoted R_{0a}^1, and for an infection due to transmission *child-mosquito-child* denoted R_{0e}^1 so that R_{0e}^1 approaches the average number of children or mosquitoes infected by a single infected child or mosquito during his entire infectious period in a population (children and mosquitoes) which is entirely susceptible assuming there are no adult in the population at the DFE; and R_{0a}^1, approaches the average number of adults or mosquitoes infected by a single infected adult or mosquito during his entire infectious period, in a population (adults and mosquitoes) which is entirely susceptible assuming there are no children in the population at the DFE. It is clear that $R_{0e}^1 = \sqrt{K_{ve}^1 \cdot K_{ev}}$ and $R_{0a}^1 = \sqrt{K_{va}^1 \cdot K_{av}}$.

If we denote $R_{0a} = s_a^* R_{0a}^1$ and $R_{0e} = s_e^* R_{0e}^1$, we can interpreted R_{0a}, as the weight of the transmission *adult-mosquito-adult* dues to the the susceptibility of adults and R_{0e}, as the weight for the transmission *child-mosquito-child* dues to the the susceptibility of adults.

Therefore, using (19), we can rewrite R_0 in function of both weights of transmission R_{0e} and R_{0a} as follows:

$$R_0 = \sqrt{R_{0e}^2 + R_{0a}^2} \tag{20}$$

The local stability of the disease-free equilibrium, X_{dfe}, is governed by the reproductive number R_0. Using standard methods, we can show that the basic reproductive number R_0 defined above acts as a threshold for the stability of the disease-free equilibrium X_{dfe}; if $R_0 < 1$ then the DFE is locally asymptotically stable. This means that introduction of a small number of individuals near the disease free state does not lead a epidemic. Whereas it is unstable if $R_0 > 1$.

In the following subsection, we simplify the writing of R_{0a}^2 and R_{0e}^2 by writing it in terms of M_i^*, $i = 1 \dots 8$ as follows:

$$R_{0a}^2 = \underbrace{\frac{\nu_v}{M_8^*} \cdot n_a s_a^* \cdot c_{va} \cdot \frac{1}{\lambda_v}}_{K_{va}} \times \underbrace{\frac{\nu_a}{M_4^*} \cdot \frac{1}{M_6^*} \cdot \frac{N_v^*}{N_h^*} \cdot \left(n_a c_{av} + n_a \widetilde{c}_{av} \alpha_a \frac{1}{M_7^*} \right)}_{K_{av}}, \tag{21a}$$

$$R_{0e}^2 = \underbrace{\frac{\nu_v}{M_8^*} \cdot n_e s_e^* \cdot c_{ve} \cdot \frac{1}{\lambda_v}}_{K_{ve}} \times \underbrace{\frac{\nu_e}{M_3^*} \cdot \frac{1}{M_5^*} \cdot \frac{N_v^*}{N_h^*} \cdot \left(n_e c_{ev} + n_a \widetilde{c}_{av} \alpha_e \frac{1}{M_7^*} \right)}_{K_{ev}}. \tag{21b}$$

3.2 Bifurcation analysis for R_0 near one

An endemic equilibrium point is stationary solution of the evolution system (8) where the component are positive. In this case, the disease persists in the population. It is difficult to find an explicit formula of the endemic equilibrium point because the system of equations (8) is complex. Consequently, we give a simple criterion for existence and stability of super and sub-threshold endemic equilibria for R_0 near one. Before stating these results, we first rewrite the equilibrium equations for model (8) in two dimensions. We recall that the stationary solution is obtained by solving $f(\bar{x}) = 0$ where $f = (f_1 \dots f_{10})$ from Equation (11).

Lemma 2.1. *The stationary system (8) can be reduced to two dimensions in the form :*

$$F(\bar{u}) = 0, \quad \bar{u} = (\bar{i}_a, \bar{i}_e) \in U_a \times U_e \subset \mathbf{R}^2, \tag{22}$$

where $F \in \mathcal{C}^m(U_a \times U_e, \mathbf{R}^2)$, $m \geq 2$, $U_a =]-\delta_a, \delta_a[$ *and* $U_e =]-\delta_e, \delta_e[$ *with* $\delta_e, \delta_a \in]0, 1[$.
Moreover by setting $U_a^+ =]0, \delta_a[$ *and* $U_e^+ =]0, \delta_e[$, *to each solution of Equation* $F(\bar{u}) = 0$ *belonging to the set* $U_a^+ \times U_e^+$ *correspond to a unique solution of initial stationary problem* $f(\bar{x}(\bar{u})) = 0$ *where* $\bar{x}(\bar{u}) \in \Omega$.

F is explicitly given by Equation (39) and all the details of Lemma 2.1 are proved in Appendix **A.2**. Next, we denote by $U = U_a \times U_e$. Now in order to carry out a bifurcation analysis, we re-write (22) in the form

$$F(\bar{u}, \lambda) \equiv 0, \tag{23}$$

where λ is a bifurcation parameter introduced. The latest having the following properties
(**A1**: $\lambda \in V \subset \mathbb{R}$ where V is a neighborhood of $\lambda = 0$.
(**A2**): $R_0 > 1 \Longleftrightarrow \lambda > 0$ and $R_0 = 1$ for $\lambda = 0$.

(**A3**): $F(0,\lambda)=0$ for all $\lambda \in V$.
(**A4**): $D_{\bar{u}}F(\bar{u},\lambda)$, $D^2_{\bar{u}}F(\bar{u},\lambda) \in \mathcal{C}^2(U\times V)$.

From Theorem 2., there exists a unique DFE; hence the point $\bar{u}=0$ corresponds to x_{dfe}. Let (u_{dfe},λ) be the disease-free equilibrium for Equation (23) where $u_{dfe}(i_a,i_e)=(0,0)$. Assumption (**A3**) implies that u_{dfe} remains a disease-free equilibrium for all values of λ. Next, we denote by $A(\lambda)$ the quantity $D_{\bar{u}}F(u_{dfe},\lambda)$. We can then derive the following properties for the function $F(\bar{u},\lambda)$:

Lemma 2.2. *For each $\lambda \in V$, matrix $A(\lambda)$ has two simple eigenvalues $\sigma_1(\lambda)$ and $\sigma_2(\lambda)$ such that $\sigma_1(0)=0$; $\sigma_2(0)<0$ and $\sigma_1(\lambda)\neq 0$ if $\lambda \neq 0$.*

The above lemma is proved in Appendix **A.3**. Let v and v^{**} be the *positive* right and left eigenvectors of $A(0)$ corresponding to the null eigenvalue, $\sigma_1(0)$ normalized by $v^T v = v^{**}v = 1$. If we set $h = v^{**}D^2_{\bar{u}}F(u_{dfe},0)\langle v,v\rangle$, we can state this following result:

Theorem 3. *If $h\neq 0$ then, there exists a neighborhood $\mathcal{U}\subset U$ of $\bar{u}=0$ and a neighborhood $\mathcal{V}\subset V$ of $\lambda=0$ such that $\forall \lambda\in\mathcal{V}$, the equilibrium equation (23) has a solution $\bar{u}(\lambda)\in\mathcal{U}\setminus\{0\}$. Moreover, the solution $\bar{u}(\lambda)$ is strictly positive if and only the product $h\sigma_1(\lambda)$ is strictly negative.*

The proof of this result directly follows from a general bifurcation result stated for instance in [14, Appendix 2]. We can now investigate the direction of the bifurcating solution $\bar{u}(\lambda)$.

Corollary 3.1. *Let*

$$\eta_c = \frac{c_{ve}n_e\nu_v\nu_e s_e^* M_4^* M_6^*}{\nu_a\lambda_v M_3^* M_5^* M_8^*}\frac{N_v^*}{N_h^*}. \tag{24}$$

There exists $\eta\in]0,\eta_c[$ such that

1. *If $h<0$, then there exists an endemic equilibria $\bar{x}\in\Omega$ near the disease-free equilibrium, x_{dfe} for $1<R_0^2<1+\eta$.*
2. *If $h>0$, then there exists an endemic equilibria $\bar{x}\in\Omega$ near the disease-free equilibrium, x_{dfe} for $1-\eta<R_0^2<1$.*

The proof of the above corollary can be found in Appendix **A.5**. The threshold parameter expression h is explicitly derived in Appendix **A.4** and follows from heavy computations.

To give a biologically meaningful interpretation of the above result, note that when $h<0$, making R_0 slightly greater than 1 by a small changes in parameters gives rise to a positive branch of equilibrium. But if we decrease R_0 slightly less than 1 there is no endemic steady state. This bifurcation type is often called a supercritical or forward bifurcation. Now, when $h>0$, we obtain a positive branch of equilibrium when R_0 is slightly less than one. This bifurcation type is also called a backward bifurcation or a subcritical bifurcation. To summarize, if we use directly the quantity R_0 to control the malaria, we must lower R_0 below 1 to prevent it when $h<0$. But when $h>0$, R_0 should be less that a quantity, denoted by R_c to prevent the malaria. From Corollary 4.1, we can expect $R_c^2\leq 1-\eta$ for all $\eta\in[0,\eta_c]$. We recall that in most epidemic models investigated, the bifurcation tends to be forward at $R_0=1$. Recently some authors have found epidemic models leading to the subcritical (backward) bifurcation at $R_0=1$ and stressed its important consequences for the control of infectious disease, cf. [14, 15, 17, 25, 24, 29, 9, 42]. Indeed, for a given parameter set, multiple stable states could exist even if $R_0<1$. For small changes in the values of these parameters, major changes in equilibrium behavior can occur.

4 Effort required to control malaria

For a disease which is transmitted at least between two host types such as the malaria, Roberts and Heesterbeek, in [16, 37], showed that R_0 defined as an *average* (via the next generation approach) would be a bad indicator when the required control effort is aimed to a specific host type. They suggested an appropriate reproductive number where they introduce the "type-reproduction number T" for each host type. It is interpreted in [16] as " the expected number of cases in individuals of type 1, caused by one infected individual of type 1 in a completely susceptible population, either directly or indirectly". The previous models for malaria transmission consider two host types: human and mosquito. It is clear that the original definition of the reproductive number for malaria coincides with the type reproduction number T_1 if we consider the human population as type host 1. Our model consider three host types: adults, children and mosquitoes. If we use directly the quantity R_0 to control the malaria, the previous section shows that we must lowers R_0 less than 1 (resp. R_c) to prevent the malaria when $h < 0$ (resp. $h > 0$). In each condition required, we need to target the control simultaneously at all the sub-groups to reduce R_0 below 1 or R_c. Given that it is very difficult and expensive to aim a control to all sub-groups to eliminate the malaria, we ask the following question: can we prevent malaria through a specific subgroup as adults or children or mosquitoes?

Using the method developed by Roberts and Heesterbeek [16, 37], we evaluate the type-reproductive number T_e, T_a, T_v, respectively for each host type: child, adult and mosquito. We begin to denote by $\rho(Q)$ the spectral radius of a matrix Q, the prime denotes the transpose of a vector and I the 3×3 identity matrix.

By definition, cf. [37], for all $l = a, e, v$, $T_l = E_l^{'}(K(I - (I - P_l)K)^{-1}E_l$,
where

$$P_e = \begin{pmatrix} 1 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}, P_a = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 0 \end{pmatrix}, P_v = \begin{pmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 1 \end{pmatrix},$$

$$E_e = \begin{pmatrix} 1 & 0 & 0 \end{pmatrix}, E_a = \begin{pmatrix} 0 & 1 & 0 \end{pmatrix}, E_v = \begin{pmatrix} 0 & 0 & 1 \end{pmatrix},$$

and K is the next-generation matrix defined in Equation (15). the authors show in [16, 37] that T_l is well defined if the host types $k \neq l$ (*ie.* other than host type l) cannot support by themselves an epidemic. Mathematically, it is shown that T_l is well defined if $\rho((I - P_l)K) < 1$. Indeed, if T_l is well defined, reduce T_l below 1 is sufficient to reduce R_0 below 1, by only targeting a control to the specific host l.

Their assumption is valid when the model cannot exhibit a backward bifurcation *i.e* $h < 0$. But when $h > 0$, we replace the criterion $\rho((I - P_l)K) < 1$ by $\rho((I - P_l)K) < R_c < 1$. Using the above definition, the expressions of T_e, T_a and T_v are obtained as follow

$$T_e = \frac{R_{0e}^2}{1 - R_{0a}^2} \quad \text{and } \rho((I - P_e)K) = R_{0a}, \tag{25a}$$

$$T_a = \frac{R_{0a}^2}{1 - R_{0e}^2} \quad \text{and } \rho((I - P_a)K) = R_{0e}, \tag{25b}$$

$$T_v = R_0^2 \quad \text{and } \rho((I - P_v)K) = 0. \tag{25c}$$

Assume $h > 0$. The same reasoning can be applied when $h < 0$ by setting $R_c = 1$.
It is clear that T_e is well defined if $R_{0a} < R_c$. T_a is also well defined if only $R_{0e} < R_c$. As $\rho((I -$

$P_v)K) = 0 < 1$, T_v is always well defined without condition upon the adults or children. We may summarize the results as follows:

(i) In area where $R_{0e} < R_c$ and $R_{0a} < R_c$ such as $1 < R_0 < R_c\sqrt{2}$ or $1 < T_v < 2R_c^2$, it suffices to target a control to one of the three host types to eliminate the malaria.

(ii) In area where $R_{0e} < R_c$ and $R_{0a} > R_c$, it is sufficient to target a control to adult or mosquito host types to eliminate the malaria.

(iii) In area where $R_{0a} < R_c$ and $R_{0e} > R_c$, it suffices to target a control to child or mosquito host types to eliminate the malaria.

(iv) In area where $R_{0e} > R_c$ and $R_{0a} > R_c$, we need to target a control to mosquito or simultaneously to adult and child host types.

Assuming that the malaria control program is aimed to reduce the number of susceptible in a given host type l, $l = a, e, v$ following one of the conditions (**i-iv**). Recall that the next generation matrix coefficients, denoted by K_{jl}, represent the expected number of individuals of host type l which would be infected by a single infectious host type j. Assuming that the above controls act linearly on K_{jl}, one can linearly reduce the number of susceptible host type l with $l, j = a, e, v$. A proportion $s_l > 1 - R_c^2/T_l$ of susceptible host type l need to be protected (by the control) to eliminate over time the malaria in the three populations (cf. [16, 37] when $R_c = 1$). For the adults or children, this control strategy is feasible by using insecticide-treated bed nets or intermittent prophylactic treatment or a vaccine. Concerning the mosquitoes, the vector control measures such as indoor residual spraying with insecticides is possible.

In area where the condition (**i**) is satisfied, it suffices to protect permanently a proportion of adult greater than $1 - R_c^2/T_a$ or a proportion of children greater than $1 - R_c^2/T_e$, or eliminate a fraction of mosquitoes greater than $1 - R_c^2/T_v$ but smaller than 0.5.
In area where the condition (**ii**) is satisfied, it suffices to protect permanently a proportion of adults greater than $1 - R_c^2/T_a$ or eliminate a fraction of mosquitoes greater than $1 - R_c^2/T_v$.
In area where the condition (**iii**) is satisfied, it suffices to protect permanently a proportion of children greater than $1 - R_c^2/T_e$ or eliminate a fraction of mosquitoes greater than $1 - R_c^2/T_v$.
In area where the condition (**iv**) is satisfied, it suffices to eliminate permanently a proportion of mosquitoes greater than $1 - R_c^2/T_v$ at birth to eradicate the malaria or protect simultaneously the children and the adults.

Now, we will explore the natural fulfilment of conditions (**ii**) and (**iii**) depending on the study area. We need to recall some results: note from Equation (41) that $R_{0e} = s_e^* R_{0e}^1$ and $R_{0a} = s_a^* R_{0a}^1$ where $s_e^* = (\frac{\Lambda_h}{N_h^*}p + \lambda_h)/(\frac{\Lambda_h}{N_h^*} + \lambda_h)$, $\quad s_a^* = (\frac{\Lambda_h}{N_h^*}(1-p))/(\frac{\Lambda_h}{N_h^*} + \lambda_h)$ and $s_e^* + s_a^* = 1$.

• **Natural fulfilment of the condition (ii).**
Consider an area where the per capita birth rate of human, λ_h, is very low so that it can be neglected. Only the immigration of people supports the human population. Mathematically if $\lambda_h \longrightarrow 0$, then $s_e^* \longrightarrow p$ and $s_a^* \longrightarrow 1 - p$. It follows that if most of immigrants travel over a long distance by leaving an endemic area and go to an non-endemic area, then $p \longrightarrow 0$ leading to $R_{0e} < 1$. We then must target the control to the adults to prevent the disease. Hence, if a vaccine were available, it suffices to vaccinate any susceptible immigrant.

• **Natural fulfilment of the condition (iii)**

Example 1: R_{0a} might be naturally below 1 following the principle known as *transmission-blocking immunity* (cf. [11, 20, 36], which consider that immunity reduces the transmission of parasite from adult to the mosquito. Hence the probability of transmission from semi-immune to mosquito is neglected, $\widetilde{c}_{av} \sim 0$ allowing to take $K_{ev}^{R_a} = K_{av}^{R_a} \sim 0$. Also the probability of transmission from a infectious adult to mosquito c_{av} may be become smaller due to the fact that the adults already acquired an immune memory.

Example 2: Suppose that most of immigrants travel over a long distance. Assuming they leave an area where there is no malaria (as a part of Europe) and go to an endemic area, then $p \longrightarrow 1$. Consequently $R_{0a} \longrightarrow 0 < 1$.

Example 3: Assume that the constant immigration rate Λ_h is very low, $s_e^* \longrightarrow 1$ and $s_a^* \longrightarrow 0$ and $R_{0a} < 1$.

Example 4: If the per capita birth rate of human, λ_h, is very large such that $\lambda_h \gg \mu_h + 4\mu_{2h}\Lambda_h$ then $N_h^*/\Lambda_h \longrightarrow 0$ and $s_a^* \longrightarrow 0$ while $s_e^* \longrightarrow 1$. It follows that $R_{0a} < 1$.

These results will be discussed in the last Section.

5 Simulations

In this section, we first give a simple example to prove that our model can exhibit a backward bifurcation following the criterion derived in Section 3. Furthermore, we explore the behavior of the malaria model (8).

To illustrate the bifurcation analysis, we have chosen realistic parameter values compatible with malaria, and such that R_0 is close to 1. Specifically, with the set of parameters in Table 3 (area 1) except Λ_h, p and n_e. The simulations were conducted using Maple. In order to evaluate the criterion described in Corollary 4.1, we consider two cases: in each case, we set the parameters Λ_h and p, and consider $\lambda = n_e - n_{R_0}$ the bifurcation parameter. We denoted by n_{R_0} the value of the parameter n_e for which $R_0 = 1$.

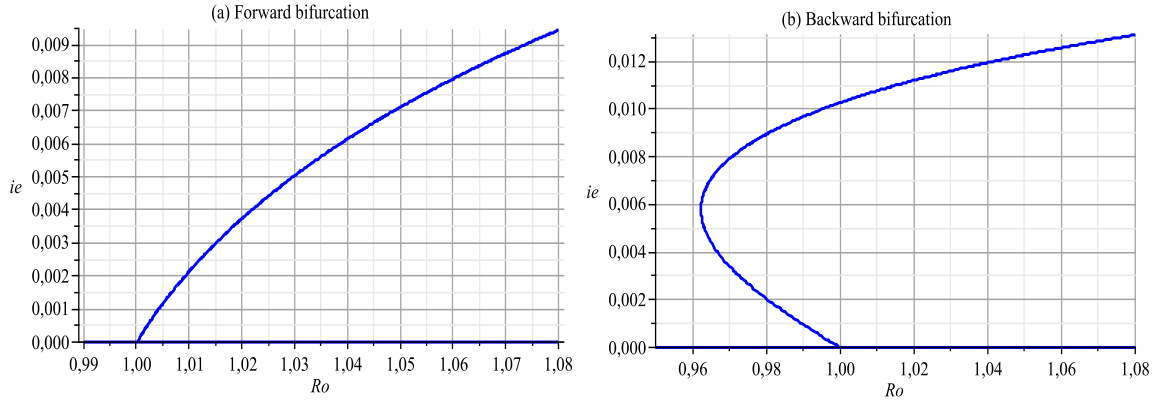

Figure 2: *Bifurcation diagram for model (8) showing the endemic equilibrium values for the proportion of infectious, i_e. We used the parameters in Table 3 (area 1) except $\Lambda_h = 0.06, p = 0.5$ for a forward bifurcation and $\Lambda_h = 0.01, p = 0.30$ for a backward ones. The simulations were conducted using Maple's implicitplot.*

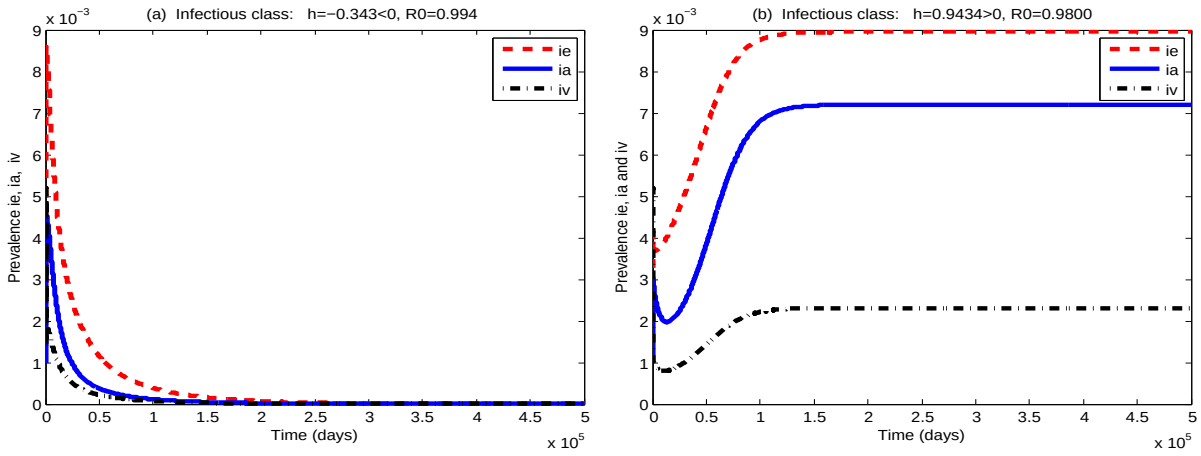

Figure 3: *Initial conditions:* $s_e = 0.5838, e_e = 0.0000, e_a = 0.0000, i_e = 0.0025, i_a = 0.0001, r_a = 0.0916, e_v = 0.01, i_v = 0.005, N_h = 500, N_v = 12000$. *The system approaches the endemic equilibrium point given in Table 2 for the figure (b). The simulations were conducted using MATLAB's ode45.*

$\Lambda_h = 0.01, p = 0.30$; for various values of n_e between 0.150 and 0.190, R_0 varies between 0.96 and 1.10 such that h remains strictly positive *i.e.* $h \in [0.909, 0.946]$. The set of parameter values describe a backward bifurcation see Figure (2b). We note in Figure (2b) that when (for example) we set $n_e = 0.15473$ so that $R_0 = 0.9800$ and $h = 0.9434 > 0$, we obtain two equilibrium values: One stable $\bar{i}_e = 0.009$ and other unstable $\bar{i}_e = 0.004$. For a given initial condition, Figure (3b) shows that the system converges toward the stable equilibrium $\bar{i}_e = 0.009$. Table 1 summarizes the equilibrium values calculated for all the variables.

$\Lambda_h = 0.06, p = 0.5$; for various values of n_e between 0.234 and 0.278, R_0 varies between 0.989 and 1.099 such that h remains strictly negative *i.e.* $h \in [-0.346, -0.289]$. The set of parameter values describe a forward bifurcation see the figure (2a). The dynamic of the system is given in Figure (3a) for $n_e = 0.236$, giving $R_0 = 0.9947 < 1, h = -0.3430 < 0$. We see the extinction of the disease over the time.

To explore the malaria model (8), first we use the set of parameters in Table 3. (area 2) which corresponds to a stable area of transmission (for example in parts of Africa). Figure 4 (left) illustrates the behavior of the malaria System (8) showing that the endemic steady state solution is unique and is locally asymptotically stable. In this area, $R_{0e}, R_{0a} > 1$. If we want to eliminate malaria, we must target a control simultaneously on the children and adults or on the mosquitoes which is very difficult because $T_v = 6.4719$ and we must eliminate continuously 84.55% of susceptible mosquitoes at birth $(1 - 1/T_v = 0.8455)$. Now, we use the set of parameters in table 3. (area 1) with $\Lambda_h = 0.033, n_e = 0.24, n_a = 0.35$ which correspond to a low area of transmission see figure 4 (right). Here, we have $R_{0e}, R_{0a} < 1$ but $R_0 > 1$. In this area, malaria can be eliminate through a specific host type. It suffices to protect either a proportion of children greater than 0.465 or adults greater than 0.835, or eliminate a proportion of mosquitoes greater than 0.297. That will depend on the feasibility.

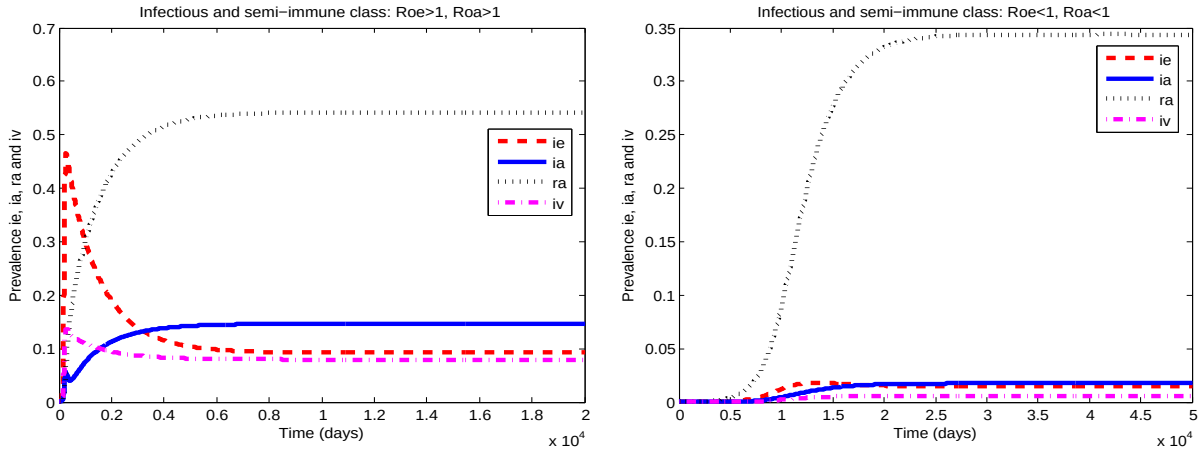

Figure 4: *A numerical simulation of the malaria model (8). The left figure is plotted with parameter values defined in Table 3 (area 2) giving* $R_{0e} = 2.071 > 1, R_{0a} = 1.477 > 1, R_0 = 2.544$. *The right figure is obtained with parameter values defined in Table 3 (area 1) except* $\Lambda_h = 0.033, n_e = 0.24, n_a = 0.35$ *giving* $R_{0e} = 0.957 < 1, R_{0a} = 0.712 < 1, R_0 = 1.193 > 1, T_e = 1.869, T_a = 6.076, T_v = 1.424$. *Initial conditions:* $s_e = 0.9$, $e_e = 0.0$, $e_a = 0.0$, $i_e = 0.0$, $i_e = 0.0$, $r_a = 0.0$, $e_v = 0.0$, $i_v = 0.001$, $N_h = 500$, $N_v = 800$.

$\bar{s}_e$	$\bar{s}_a$	$\bar{e}_e$	$\bar{e}_a$	$\bar{i}_e$	$\bar{i}_a$	$\bar{r}_a$	$\bar{N}_h$
0.5253	0.2859	0.0012	8.1094e-004	0.009	0.0072	0.1706	395.0297

$\bar{s}_v$	$\bar{e}_v$	$\bar{i}_v$	$\bar{N}_v$
0.9990	0.0033	0.0023	12125

Table 1: *Equilibrium values for the parameters in table 3 (area 1) except* $\Lambda_h = 0.01, n_e = 0.154$ *and* $p = 0.30$ *giving* $R_0 = 0.9800 < 1$.

6 Concluding Remarks

We formulated a compartmental model for malaria transmission involving the human host susceptibility, exposedness and infectivity with variable children, adults and mosquito populations. The human population is split into seven classes: susceptible, exposed, infectious and semi-immune where the susceptible humans are divided into two groups based on their susceptibilities; the exposed ones are divided into two groups according to their incubating period, the infectious ones are divided into two groups according to their infectivities. We divided the mosquito population into three classes: susceptible, exposed and infectious. We defined a domain where the malaria model has a unique globally defined solution which remains in this domain for all nonnegative time. We obtain explicit formula for the reproductive number, R_0, derived from the local stability of the disease-free equilibrium point, x_{dfe}. We defined the weight of the transmission *adult-mosquito-adult*, R_{0a}, and the weight of the transmission *child-mosquito-child*, R_{0e}, due to transmission *child-mosquito-child*. Then the reproductive number for the entire population is a square root of the sum of the square of these weights for the two interaction types.

We gave a simple criterion for existence of super and sub-threshold endemic equilibria for R_0

near one depending on a parameter h. For the forward bifurcation *i.e.* $h < 0$, there are super-threshold endemic equilibria near the disease-free equilibrium point, x_{dfe}. Further, for a backward bifurcation *i.e.* $h > 0$, there are sub-threshold endemic equilibria near, x_{dfe}. We did not provide stability results on these equilibria.

We investigated the possibility of a control of malaria through one of the three host type (adults or children or mosquitoes). We formulated the reproductive number specific to each host type. Our model suggests that, in an area of low or intermediary transmission, it suffices to target a control to one of specific host type to eliminate malaria. In an area of high transmission for which, most of immigrants come from an area where there is no malaria, malaria can be eliminated through the children. In the same way, in an endemic area where the constant immigration rate Λ_h is very low or the per capita birth rate of human, λ_h, is very large, malaria can be always controlled through the children. Sometimes epidemics occur in unstable malaria areas where the transmission differs greatly from year to year. In these areas, if λ_h is very low, malaria can be eliminated by using vaccines or by protecting any susceptible immigrant adult or child entering in these areas. On the basis of our analysis, we conclude that if a vaccine or a simple preventive action were available, we must research the specific host type to target the control in order to eliminate the malaria. In area where we cannot target a control towards either child or adult host types to control malaria, our model shows that, we can always target a control to mosquitoes to eliminate the malaria. It is a well known result. But elimination of mosquitoes does not appear to be feasible in an endemic area where the density of mosquitoes is very large. Even if these measures are feasible it is very difficult and costly. But in an area with a relatively low intensity of transmission, the malaria can be eradicated with success through the control of mosquitoes density. The typical example is in Europe where the large-scale application of vector control measures such as indoor residual spraying with insecticides has strongly lowered the transmission of malaria.

Since, the most vulnerable relate mostly to children, we must begin the control through the children. This contributes to reduce the morbidity and the mortality. Furthermore, as the fulfilment of the condition **(iii)** is frequently obtained, this control could also contribute to eliminate the malaria over the time.

From the simulations with realistic parameter sets, we know that a backward bifurcation of endemic steady states is possible for the malaria model (2). Hence, lower R_0 below 1 is not always sufficient to eliminate the malaria. Also, even if the malaria has been eliminated in a given area, a small disturbance as the ecological changes could re-establish malaria in the three populations (mosquitoes, children and adults). We must reduce R_0 so that it enters the domain where the point x_{dfe} is globally asymptotically stable.

As we have an explicit formula of h, in a next paper, we will investigate the non-fulfilment of the criterion $h > 0$ giving the backward bifurcation. We will analyze the sensibility of both weight of transmission R_{0e}, R_{0a}. We will formulate a optimal control problem in order to investigate the selection of a strategy of feasible control (technically and in costly) following the studying area. We will take into account of semi-immune immigration that could transport an infection from malaria to non-malarial area. We will model the immune rate, α_e, and the recovery rate ρ_e of children depending on the force of infection, k_e. We will also consider the lost of immunity rate, β_a, depending on the force of infection, k_a.

A Proofs

A.1 Proof of Theorem 2

Let x_{dfe} be the disease free equilibrium with the fraction variables for model (8). It is easy to verify that x_{dfe} is a solution of the equilibrium system of equations $f_i = 0, i = 1 \dots 10$ for the model (8) in Ω, so x_{dfe} is an equilibrium point. Reciprocally we know that there is no disease in the human (resp. mosquito) population if only $e_e = e_a = i_e = i_a = r_a = 0$ (resp. $e_v = i_v = 0.$). If we substitute these zero values of terms e_e, e_a, i_e, i_a, r_a, e_v, i_v into the equilibrium equations, we find that the only equilibrium point for s_e in Ω_1 from (8a) is s_e^*; the only equilibrium point for N_h in Ω_2 from (8i) is N_h^*; and the only equilibrium point for N_v in Ω_2 from (8j) is N_v^*. Then the only equilibrium point on Ω is x_{dfe}.

Let X_{dfe} be the disease free equilibrium with the original variables for model (2). By substituting x_{dfe} in (4) after having used (5) to show that $s_a^* = 1 - s_e^*$ and $s_v^* = 1$, we find:
$X_{dfe}(S_e, E_e, I_e, S_a, E_a, I_a, R_a, S_v, E_v, I_v) = (S_e^*, 0, 0, S_a^*, 0, 0, 0, S_v^*, 0, 0)$, where
$S_e^* = s_e^* N_h^*$, $S_a^* = s_a^* N_h^*$ and $S_v^* = N_v^*$.

A.2 Proof of Lemma 2.1

We first rewrite the stationary system of equations in two dimensions.
Let $\bar{x} = (\bar{s}_e, \bar{e}_e, \bar{e}_a, \bar{i}_e, \bar{i}_a, \bar{r}_a, \bar{e}_v, \bar{i}_v, \bar{N}_h, \bar{N}_v) \in \Omega$ the stationary solution of model (8) *ie.* $f(\bar{x}) = d\bar{x}/dt = 0$.
Let $\bar{M}_i, i = 1, \dots 8$, the endemic values associated of variables defined in (14). Using (8f), we solve $\bar{r}_a$ in term of $\bar{i}_e$ and $\bar{i}_a$

$$\bar{r}_a = \frac{\alpha_e \bar{i}_e}{\bar{M}_7 - \gamma_e \bar{i}_e} + \frac{\alpha_a \bar{i}_a}{\bar{M}_7 - \gamma_e \bar{i}_e}. \tag{26}$$

From (8d), we solve $\bar{e}_e$ in term of $\bar{i}_e$

$$\bar{e}_e = \frac{\bar{M}_5 - \gamma_e \bar{i}_e}{\nu_e} \cdot \bar{i}_e. \tag{27}$$

Solving for $\bar{e}_a$ in (8e) in term of $\bar{i}_e$ and $\bar{i}_a$, we find

$$\bar{e}_a = \frac{\bar{M}_6 - \gamma_e \bar{i}_e}{\nu_a} \cdot \bar{i}_a. \tag{28}$$

By adding (8a) and (8b) we solve $\bar{s}_e$ in term of i_e

$$\bar{s}_e = \frac{\nu_e \bar{M}_1 + \rho_e \nu_e \bar{i}_e + (\gamma_e \bar{i}_e - \bar{M}_3)(\bar{M}_5 - \gamma_e \bar{i}_e)\bar{i}_e}{\nu_e(\bar{M}_2 - \gamma_e \bar{i}_e)}. \tag{29}$$

Using (8j), we solve explicitly the positive equilibrium for the total mosquito population as

$$\bar{N}_v = \frac{\lambda_v - \mu_v}{\mu_{2v}}. \tag{30}$$

We write the positive equilibrium for the total human population, $\bar{N}_h$, in terms of $\bar{i}_e$ from (8i) as

$$\bar{N}_h = \frac{\lambda_h - \mu_h - \gamma_e \bar{i}_e + \sqrt{(\lambda_h - \mu_h - \gamma_e \bar{i}_e)^2 + 4\mu_{2h}\Lambda_h}}{2\mu_{2h}}. \tag{31}$$

Solving from (8h) in terms of $\bar{e}_v$ we find:

$$\bar{i}_v = \frac{\nu_v}{\lambda_v} \bar{e}_v. \tag{32}$$

In order to solve $\bar{e}_v$ in term of $\bar{i}_e$, we begin to solve $\bar{k}_e$ in term of $\bar{i}_e$ by using (8b) and (27),

$$\bar{k}_e = \frac{(\bar{M}_3 - \gamma_e \bar{i}_e)(\bar{M}_5 - \gamma_e \bar{i}_e)\bar{i}_e}{\nu_e \bar{s}_e}. \tag{33}$$

If we substitute the expression of $\bar{i}_v$ from (32) into the expression of $\bar{k}_e$ from (6) and identifying with the expression of $\bar{k}_e$ given in (33), we solve $\bar{e}_v$ in term of $\bar{i}_e$ as

$$\bar{e}_v = \frac{(\bar{M}_3 - \gamma_e\bar{i}_e)(\bar{M}_5 - \gamma_e\bar{i}_e)\bar{i}_e}{\nu_e\epsilon\bar{s}_e} \tag{34}$$

where

$$\epsilon(\bar{i}_e) = c_{ve}n_e\frac{\nu_v}{\lambda_v}\frac{\bar{N}_v}{\bar{N}_h}. \tag{35}$$

Consequently we rewrite (32) in term of $\bar{i}_e$ as follows

$$\bar{i}_v = \frac{(\bar{M}_3 - \gamma_e\bar{i}_e)(\bar{M}_5 - \gamma_e\bar{i}_e)\bar{i}_e}{\nu_e\epsilon\bar{s}_e}\frac{\nu_v}{\lambda_v}. \tag{36}$$

The equilibrium inoculation rates defined in (1) rewrites in term of $\bar{i}_e$ and $\bar{i}_a$ as follows:

$$\begin{aligned}
\bar{k}_e(\bar{i}_e) &= \epsilon(\bar{i}_e)\cdot\bar{e}_v(\bar{i}_e), && (37a)\\
\bar{k}_a(\bar{i}_e) &= \frac{c_{va}n_a}{c_{ve}n_e}\cdot\bar{k}_e(\bar{i}_e), && (37b)\\
\bar{k}_v(\bar{i}_a,\bar{i}_e) &= \left(c_{av}n_a + \widetilde{c}_{av}n_a\alpha_a\frac{1}{\bar{M}_7-\gamma_e\bar{i}_e}\right)\bar{i}_a + \left(c_{ev}n_e + \widetilde{c}_{av}n_a\alpha_e\frac{1}{\bar{M}_7-\gamma_e\bar{i}_e}\right)\bar{i}_e. && (37c)
\end{aligned}$$

Finally, we substitute the terms $\bar{s}_e(\bar{i}_e)$, $\bar{e}_e(\bar{i}_e)$, $\bar{r}_a(\bar{i}_a,\bar{i}_e)$, $\bar{i}_v(\bar{i}_e)$, $\bar{N}_h(\bar{i}_e)$ into the equilibrium equations (8c) and (8g) which only on $\bar{i}_a$ and $\bar{i}_e$. Therefore

$$\begin{aligned}
&\bar{k}_a(\bar{i}_e)\cdot(1-\bar{s}_e(\bar{i}_e)-\bar{e}_e(\bar{i}_e)-\bar{e}_a(\bar{i}_a,\bar{i}_e)-\bar{i}_e-\bar{i}_a-\bar{r}_a(\bar{i}_a,\bar{i}_e))+(\gamma_e\bar{i}_e-\bar{M}_4)\cdot\bar{e}_a(\bar{i}_a,\bar{i}_e)=0\\
&\bar{k}_v(\bar{i}_a,\bar{i}_e)\cdot\left(1-\frac{\bar{M}_8}{\lambda_v}\cdot\bar{e}_v(\bar{i}_e)\right)-\bar{M}_8\cdot\bar{e}_v(\bar{i}_e)=0.
\end{aligned} \tag{38}$$

Let

$$\begin{aligned}
F_1(\bar{i}_a,\bar{i}_e) &= \bar{k}_a(\bar{i}_e)\cdot(1-\bar{s}_e(\bar{i}_e)-\bar{e}_e(\bar{i}_e)-\bar{e}_a(\bar{i}_a,\bar{i}_e)-\bar{i}_e-\bar{i}_a-\bar{r}_a(\bar{i}_a,\bar{i}_e))\\
&\quad+(\gamma_e\bar{i}_e-\bar{M}_4)\cdot\bar{e}_a(\bar{i}_a,\bar{i}_e)\\
F_2(\bar{i}_a,\bar{i}_e) &= \bar{k}_v(\bar{i}_a,\bar{i}_e)\cdot\left(1-\frac{\bar{M}_8}{\lambda_v}\cdot\bar{e}_v(\bar{i}_e)\right)-\bar{M}_8\cdot\bar{e}_v(\bar{i}_e).
\end{aligned} \tag{39}$$

By setting $F(\bar{i}_a,\bar{i}_e) = (F_1(\bar{i}_a,\bar{i}_e), F_2(\bar{i}_a,\bar{i}_e))$, the equilibrium system of equations for model (8) becomes $F(\bar{u}) = 0$ where $\bar{u} = (\bar{i}_a,\bar{i}_e) \in \mathbf{R}^2$.

Next, we show that there exists a neighborhood $U \subset \mathbf{R}^2$ of $\bar{u} = (0,0)$ such that F at least $\mathcal{C}^2(U,\mathbf{R}^2)$, with respect to $\bar{u} = (\bar{i}_a,\bar{i}_e)$.

Let us assume i_e (resp. i_a) is bounded in the interval $U_e =]-\delta_e,\delta_e[$ (resp. $U_a =]-\delta_a,\delta_a[$) with $\delta_e,\delta_a \in]0,1[$. Then, $\bar{N}_h(\bar{i}_e) > 0$ from (31) and it follows that $1/\bar{N}_h(\bar{i}_e), \bar{M}_i(\bar{i}_e) \in \mathcal{C}^m(U_a\times U_e,\mathbf{R})$, $m \geq 2$, $i = 1\ldots 7$. Also, from (27) and (28), it is easy to see that $\bar{e}_e(\bar{i}_e) \in \mathcal{C}^m(U_a\times U_e,\mathbf{R})$, $m \geq 2$. Note that $\bar{M}_i - \gamma_e i_e > 0$, $i = 2\ldots 7$.
Indeed, $\Lambda_h+\lambda_h\bar{N}_h-f_h(\bar{N}_h)\bar{N}_h-\gamma_e\bar{i}_e\bar{N}_h = 0$ from Equation (8i). As $\bar{N}_h(\bar{i}_e) > 0$, it follows $\Lambda_h/\bar{N}_h+\lambda_h-\gamma_e\bar{i}_e = f_h(\bar{N}_h)$ ie. $\bar{M}_2 - \gamma_e\bar{i}_e = f_h(\bar{N}_h) = \mu_h + \mu_{2h}\bar{N}_h > 0$. We readily obtain the following results:

$$\begin{aligned}
\bar{M}_3-\gamma_e\bar{i}_e &= f_h(\bar{N}_h)+\nu_e > 0, && (40a)\\
\bar{M}_4-\gamma_e\bar{i}_e &= f_h(\bar{N}_h)+\nu_a > 0,, && (40b)\\
\bar{M}_5-\gamma_e\bar{i}_e &= f_h(\bar{N}_h)+\alpha_e+\gamma_e+\rho_e > 0, && (40c)\\
\bar{M}_6-\gamma_e\bar{i}_e &= f_h(\bar{N}_h)+\alpha_a > 0, && (40d)\\
\bar{M}_5-\gamma_e\bar{i}_e &= f_h(\bar{N}_h)+\beta_a > 0. && (40e)
\end{aligned}$$

We can conclude respectively from (26), (27), (28),(29), (32), (33), (34), (35), (36), (37a), (37b), (37c), that $\bar{r}_a(\bar{i}_a,\bar{i}_e)$, $\bar{e}_e(\bar{i}_a,\bar{i}_e)$, $\bar{e}_a(\bar{i}_a,\bar{i}_e)$, $\bar{s}_e(\bar{i}_a,\bar{i}_e)$, $\bar{e}_v(\bar{i}_a,\bar{i}_e)$, $\bar{k}_e(\bar{i}_a,\bar{i}_e)$, $\bar{k}_a(\bar{i}_a,\bar{i}_e)$, $\bar{k}_v(\bar{i}_a,\bar{i}_e)$ belong to $\mathcal{C}^m(U_a\times U_e,\mathbf{R})$, $m\geq 2$. Thus each function $F_i\in\mathcal{C}^m(U_a\times U_e,\mathbf{R})$, $m\geq 2$, $i=1,2$, so that $F=(F_1,F_2)\in\mathcal{C}^m(U_a\times U_e,\mathbf{R}^2)$, $m\geq 2$. If U is defined by $U_a\times U_e\subset\mathbf{R}^2$, it is clear that U is a neighborhood of $\bar{u}=(0,0)$.

Let us denote by $U_e^+=]0,\delta_e[$, $U_a^+=]0,\delta_a[$ and $U^+=U_a^+\times U_e^+$. Since $\bar{M}_i-\gamma_e i_e>0$, $i=2\dots 7$, it is easy to verify that for all $\bar{u}=(\bar{i}_a,\bar{i}_e)\in U^+$, there exists $\bar{x}(\bar{i}_a,\bar{i}_e)=(\bar{s}_e,\bar{e}_e,\bar{e}_a,\bar{i}_e,\bar{i}_a,\bar{r}_a,\bar{e}_v,\bar{i}_v,\bar{N}_h,\bar{N}_v)\in\Omega$. This concludes the proof Lemma 2.1.

A.3 Proof of Lemma 2.2

From Lemma 2.1, $F(\bar{u},\lambda)$ is continuously differentiable at least twice with respect to $\bar{u}$ on U. Therefore we can compute $D_{\bar{u}}F(u_{dfe},\lambda)$.

$$D_{\bar{u}}F(u_{dfe},\lambda)=\begin{pmatrix} -\dfrac{M_4^*M_6^*}{\nu_a} & \dfrac{c_{va}n_a}{c_{ve}n_e}\dfrac{s_a^*M_3^*M_5^*}{\nu_e s_e^*} \\ \\ n_a c_{av}+n_a\widetilde{c}_{av}.\alpha_a\dfrac{1}{M_7^*} & \dfrac{\lambda_v M_3^*M_5^*M_8^*}{c_{ve}n_e\nu_v\nu_e s_e^*}\dfrac{N_h^*}{N_v^*}\cdot(1-R_{0e}^2)\end{pmatrix}, \tag{41}$$

We denote $A(\lambda)=D_uF(u_{dfe},\lambda)$ and let us evaluate the determinant and the trace of the stability matrix, $A(\lambda)$. We find

$$\det A(\lambda) = \frac{\lambda_v M_3^*M_4^*M_5^*M_6^*M_8^*}{c_{ve}n_e\nu_v\nu_e\nu_a s_e^*}\frac{N_h^*}{N_v^*}\cdot(1-R_0^2), \tag{42a}$$

$$\mathrm{Tr}A(\lambda) = -\left(\frac{M_4^*M_6^*}{\nu_a}+\frac{\lambda_v M_3^*M_5^*M_8^*}{c_{ve}n_e\nu_v\nu_e s_e^*}\frac{N_h^*}{N_v^*}\cdot(1-R_{0e}^2)\right). \tag{42b}$$

The matrix, $A(\lambda)$, has 2 eigenvalues for all λ. Let $\sigma_1(\lambda)$ and $\sigma_2(\lambda)$ be these eigenvalues defined below.

$$\sigma_1(\lambda)=\frac{\mathrm{Tr}A(\lambda)+\sqrt{(\mathrm{Tr}A(\lambda))^2-4\det A(\lambda)}}{2}, \tag{43a}$$

$$\sigma_2(\lambda)=\frac{\mathrm{Tr}A(\lambda)-\sqrt{(\mathrm{Tr}A(\lambda))^2-4\det A(\lambda)}}{2}. \tag{43b}$$

$\lambda=0\Longleftrightarrow R_0=1\Longleftrightarrow R_{0a}=1-R_{0e}\geq 0$, it follows that $\det A(0)=0$ and $\mathrm{Tr}A(0)<0$. As an immediate consequence $\sigma_2(0)=\mathrm{Tr}A(0)<0$ and $\sigma_1(0)=0$. We conclude that $D_{\bar{u}}F(u_{dfe},0)$ has a simple zero eigenvalue. As the equilibria are strictly positive, from Lemma 2.1, each equilibrium corresponds to a unique solution of initial stationary problem $f(\bar{x}(\bar{u}))=0$ where $\bar{x}(\bar{u})\in\Omega$. We conclude the proof of the corollary.

A.4 Proof of proposition 3.1

To compute $h:=v^{**}D_{\bar{u}}^2F(u_{dfe},0)\langle v,v\rangle$, we first evaluate the right v and left v^{**} eigenvectors of $A(0)$ checking $v^Tv=v^{**}v=1$.
$x_0=(x_1,x_2)^T$ respectively $x_0^{**}=(x_1^{**},x_2^{**})$ is the right respectively left eigenvectors of $A(0)$ where

$$x_1=k_{va}\cdot\frac{\nu_a}{M_4^*M_6^*},\quad x_2=k_{ve}\cdot\frac{\nu_e}{M_3^*M_5^*},\quad x_1^{**}=k_{av},\quad x_2^{**}=\frac{N_v^*}{N_h^*}.$$

Let

$$v_1 = \frac{x_1}{\sqrt{x_1^2+x_2^2}},\quad v_2=\frac{x_2}{\sqrt{x_1^2+x_2^2}} \tag{44a}$$

$$v_1^{**} = \frac{\sqrt{x_1^2+x_2^2}}{x_1^{**}x_1+x_2^{**}x_2}\cdot x_1^{**},\quad v_2^{**}=\frac{\sqrt{x_1^2+x_2^2}}{x_1^{**}x_1+x_2^{**}x_2}\cdot x_2^{**}, \tag{44b}$$

then $v := (v_1, v_2)^T$ respectively $v^{**} := (v_1^{**}, v_2^{**})$ is also the right respectively left eigenvectors of $A(0)$ checking $v^T v = v^{**} v = 1$.

It remains to compute $D_{\tilde{u}}^2 F(u_{dfe}, \lambda)$. Calculations show that $\dfrac{\partial^2 F_1}{\partial i_a^2}(u_{dfe}, \lambda) = \dfrac{\partial^2 F_2}{\partial i_a^2}(u_{dfe}, \lambda) = 0$ and

$$\frac{\partial^2 F_1}{\partial i_a \partial i_e}(u_{dfe}, \lambda) = \frac{\partial^2 F_1}{\partial i_e \partial i_a}(u_{dfe}, \lambda) = -\frac{c_{va} n_a}{c_{ve} n_e} \cdot \frac{M_3^* M_5^*}{\nu_e s_e^*} \left(\frac{M_6^*}{\nu_a} + \frac{\alpha_a}{M_7^*} + 1 \right) - \frac{\gamma_e}{\nu_a}(\xi - 1)(M_6^* + M_4^*),$$

$$\frac{\partial^2 F_2}{\partial i_a \partial i_e}(u_{dfe}, \lambda) = \frac{\partial^2 F_2}{\partial i_e \partial i_a}(u_{dfe}, \lambda) = -\frac{\gamma_e}{M^{*2}_7}(\xi - 1) \cdot \widetilde{c}_{av} n_a \alpha_a - \frac{M_3^* M_5^* M_8^*}{\epsilon^* s_e^* \nu_e} \cdot \frac{G_a}{\lambda_v},$$

$$\frac{\partial^2 F_1}{\partial i_e^2}(u_{dfe}, \lambda) = -2 \cdot \frac{c_{va} n_a}{c_{ve} n_e} \cdot \frac{M_3^* M_5^*}{\nu_e s_e^*} \left(\frac{s_e^{(e)}}{s_e^*} + \frac{M_5^*}{\nu_e} + \frac{\alpha_e}{M_7^*} + 1 + (1 - s_e^*)\gamma_e \left(\frac{1}{M_3^*} + \frac{1}{M_5^*} \right) \right),$$

$$\frac{\partial^2 F_2}{\partial i_e^2}(u_{dfe}, \lambda) = -2 \cdot \frac{\gamma_e}{M^{*2}_7}(\xi - 1) \cdot \widetilde{c}_{av} n_a \alpha_e - 2 \cdot \frac{M_3^* M_5^* M_8^*}{\epsilon^* s_e^* \nu_e} \left(\frac{G_e}{\lambda_v} - \frac{\gamma_e \xi N_h^*}{\Lambda_h} - \frac{s_e^{(e)}}{s_e^*} - \frac{\gamma_e}{M_3^*} - \frac{\gamma_e}{M_5^*} \right),$$

where

$$\begin{aligned} &\xi = \frac{2\Lambda_h}{N_h^* \sqrt{(\lambda_h - \mu_h)^2 + 4\mu_{2h}\Lambda_h}}, \quad s_e^{(e)} = \frac{1}{\nu_e M_2^*}(\gamma_e \nu_e \xi + \nu_e \rho_e - M_3^* M_5^* - \gamma_e \nu_e s_e^*(\xi - 1)), \\ &G_e = c_{ev} n_e + \widetilde{c}_{av} n_a \alpha_e \frac{1}{M_7^*}, \quad G_a = c_{av} n_a + \widetilde{c}_{av} n_a \alpha_a \frac{1}{M_7^*}, \quad \epsilon^* = c_{ve} n_e \frac{\nu_v}{\lambda_v} \frac{N_v^*}{N_h^*}. \end{aligned} \tag{45}$$

Finally when λ close to 0,

$$h = v_2 \left(2\frac{\partial^2 F_1}{\partial i_a \partial i_e}(u_{dfe}, 0) v_1^{**} v_1 + \frac{\partial^2 F_1}{\partial i_e^2}(u_{dfe}, 0) v_1^{**} v_2 + 2\frac{\partial^2 F_2}{\partial i_a \partial i_e}(u_{dfe}, 0) v_2^{**} v_1 + \frac{\partial^2 F_2}{\partial i_e^2}(u_{dfe}, 0) v_2^{**} v_2 \right).$$

We rewrite h in the form $h = v_2(v_1^{**} A + v_2^{**} B)$ where

$$A = 2\frac{\partial^2 F_1}{\partial i_a \partial i_e}(u_{dfe}, 0) v_1 + \frac{\partial^2 F_1}{\partial i_e^2}(u_{dfe}, 0) v_2 \text{ and } B = 2\frac{\partial^2 F_2}{\partial i_a \partial i_e}(u_{dfe}, 0) v_1 + \frac{\partial^2 F_2}{\partial i_e^2}(u_{dfe}, 0) v_2.$$

Some algebraic manipulations produce

$$\begin{aligned} A = &-2v_1 \cdot \left\{ \frac{c_{va} n_a}{c_{ve} n_e} \cdot \frac{M_3^* M_5^*}{\nu_e s_e^*} \left(\frac{M_6^*}{\nu_a} + \frac{\alpha_a}{M_7^*} + 1 \right) + \frac{\gamma_e}{\nu_a}(\xi - 1)(M_6^* + M_4^*) \right\} \\ &-2v_2 \cdot \frac{c_{va} n_a}{c_{ve} n_e} \cdot \frac{M_3^* M_5^*}{\nu_e s_e^*} \left\{ \frac{s_e^{(e)}}{s_e^*} + \frac{M_5^*}{\nu_e} + \frac{\alpha_e}{M_7^*} + 1 + s_a^* \gamma_e \left(\frac{1}{M_3^*} + \frac{1}{M_5^*} \right) \right\}, \end{aligned} \tag{46}$$

$$\begin{aligned} B = &-2v_1 \left(\frac{\gamma_e}{M_7^{*2}}(\xi - 1)\widetilde{c}_{av} n_a \alpha_a + \frac{M_3^* M_5^* M_8^*}{\epsilon^* s_e^* \nu_e} \cdot \frac{G_a}{\lambda_v} \right) \\ &-2v_2 \left\{ \frac{\gamma_e}{M_7^{*2}}(\xi - 1)\widetilde{c}_{av} n_a \alpha_e + \frac{M_3^* M_5^* M_8^*}{\epsilon^* s_e^* \nu_e} \left(\frac{G_e}{\lambda_v} - \frac{\gamma_e \xi N_h^*}{\Lambda_h} - \frac{s_e^{(e)}}{s_e^*} - \frac{\gamma_e}{M_3^*} - \frac{\gamma_e}{M_5^*} \right) \right\}, \end{aligned} \tag{47}$$

and $\xi, s_e^{(e)}, G_e, G_a$ and ϵ^* are defined in Equation (45).

A.5 Proof of Corollary 3.1

We first recall the results obtained in Appendix **A.5**. The eigenvalues read
$\sigma_1(\lambda) = \mathrm{Tr}A(\lambda) + \sqrt{(\mathrm{Tr}A(\lambda))^2 - 4\det A(\lambda)}/2$, and $\sigma_2(\lambda) = \mathrm{Tr}A(\lambda) - \sqrt{(\mathrm{Tr}A(\lambda))^2 - 4\det A(\lambda)}/2$, where

$$\det A(\lambda) = \frac{\lambda_v M_3^* M_4^* M_5^* M_6^* M_8^*}{c_{ve} n_e \nu_v \nu_e \nu_a s_e^*} \frac{N_h^*}{N_v^*} \cdot (1 - R_0^2) \quad \text{and}$$

$$\mathrm{Tr}A(\lambda) = -\left(\frac{M_4^* M_6^*}{\nu_a} + \frac{\lambda_v M_3^* M_5^* M_8^*}{c_{ve} n_e \nu_v \nu_e s_e^*} \frac{N_h^*}{N_v^*} \cdot (1 - R_{0e}^2) \right).$$

From Theorem 3., the bifurcating solution exists for $\lambda \in \mathcal{V}$. Note that for all $\lambda \in \mathcal{V}$ and according to Assumption **(A1)**, we can always find a small η, strictly positive such that R_0^2 belongs to the interval $]1-\eta, 1+\eta[$. As we are seeking strictly positive solutions, we have to find parameter values for which the product $\sigma_1(\lambda)h$ is strictly negative.

Let us first assume $h > 0$, then $\mathrm{sign}(h\sigma_1(\lambda)) = \mathrm{sign}(\sigma_1(\lambda))$. Note that $\mathrm{Tr}A(\lambda) < 0$ is a necessary condition to have $\sigma_1(\lambda) < 0$. As $R_0^2 = R_{0e}^2 + R_{0a}^2 \in]1-\eta, 1+\eta[$, then $R_{0e}^2 < 1 + \eta$.

$$\text{Note that} \quad \mathrm{Tr}A(\lambda) = -\frac{\lambda_v M_3^* M_5^* M_8^*}{c_{ve} n_e \nu_v \nu_e s_e^*} \frac{N_h^*}{N_v^*} (\eta_c + 1 - R_{0e}^2) \quad \text{where} \quad \eta_c = \frac{c_{ve} n_e \nu_v \nu_e s_e^* M_4^* M_6^*}{\nu_a \lambda_v M_3^* M_5^* M_8^*} \frac{N_v^*}{N_h^*}.$$

It is clear that for all $\eta \in]0, \eta_c[$, then $\mathrm{Tr}A(\lambda) < 0$. As an immediate consequence, $\sigma_1(\lambda) < 0 \iff 1 - \eta < R_0^2 < 1$. We conclude that there exists an endemic equilibria $\bar{u}(\lambda)$ strictly positive near the disease-free equilibrium, u_{dfe} for $1 - \eta < R_0^2 < 1$.

Let us now assume $h < 0$, then $\mathrm{sign}(h\sigma_1(\lambda)) = -\mathrm{sign}(\sigma_1(\lambda))$. As $\mathrm{Tr}A(\lambda) < 0$ for all $\eta \in]0, \eta_c[$, it is easy to check that $\sigma_1(\lambda) > 0 \iff 1 < R_0^2 < 1 + \eta$. It follows $\sigma_1(\lambda) > 0$ and $\sigma_2(\lambda) < 0$. Finally, if $h < 0$, then there exists an endemic equilibria $\bar{u}(\lambda)$ strictly positive near the disease-free equilibrium, u_{dfe} for $1 < R_0^2 < 1 + \eta$.

A.6 Parameter values

Parameters	Area 1	Area 2	Range
1.Λ_h	$\cdots$	0.033	0.0027–0.27
2.λ_h	1.1×10^{-4}	1.1×10^{-4}	$2.7 \times 10^{-5} - 1.4 \times 10^{-4}$
3.λ_v	0.13	0.13	0.020–0.27
4.c_{ve}	0.021	0.07	0.01–0.27
5.c_{va}	0.012	0.022	0.01–0.27
6.c_{ev}	0.11	0.45	0.072–0.64
7.c_{av}	0.08	0.35	0.072–0.64
8.$\tilde{c}_{av}$	0.008	0.002	0.0072–0.64
9.ν_e	0.10	0.10	0.067–0.20
10.ν_a	0.09	0.09	0.067–0.20
11.ν_v	0.091	0.083	0.029–0.33
12.α_a	0.01	0.01	0.0014–0.017
13.α_e	0.005	0.001	0.0014–0.017
14.γ_e	9.0×10^{-5}	1.8×10^{-5}	$0 - 4.1 \times 10^{-4}$
15.ρ_e	0.0083	0.033	0.0033–0.0714
16.β_a	5.5×10^{-4}	2.7×10^{-3}	$1.1 \times 10^{-2} - 5.5 \times 10^{-5}$
17.μ_h	1.6×10^{-5}	1.6×10^{-5}	$1.0 \times 10^{-6} - 1.0 \times 10^{-3}$
18.μ_{2h}	3.0×10^{-7}	3.0×10^{-7}	$1.0 \times 10^{-8} - 1.0 \times 10^{-6}$
19.μ_v	0.033	0.033	0.0010–0.10
20.μ_{2v}	8.0×10^{-6}	8.0×10^{-6}	$1.0 \times 10^{-6} - 1.0 \times 10^{-3}$
21.n_e	$\cdots$	0.30	0.13–0.47
22.n_a	0.30	0.40	0.13–0.47
23.p	$\cdots$	0.30	0.0–1.0

Table 2: *Baseline values and ranges found in the literature for the model's parameters which the most is derived from [10, 32, 43] and [44] data. The dimensionless parameters are* p, c_{ve}, c_{va}, c_{ev}, c_{av} *and* $\tilde{c}_{av}$. *Moreover* λ_h, λ_v, ν_e, ν_v α_e α_a, γ_e, ρ_e, β_a, μ_v, μ_h, n_e *and* n_a *have as dimension* $days^{-1}$, Λ_h *and* μ_{2h} *have as dimension* $humans^{-1}\times days^{-1}$ *and finally* μ_{2v} *is in* $mosquitoes^{-1}\times days^{-1}$. *We supposed that* $n_a \geq n_e$ *because the most vulnerable are tendency to protect her body (for exemple In [35], Port et* al. *showed that real children are less exposed than adults to mosquito bites).*

Appendix C : Acknowledgement

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