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**OPTIMAL CONTROL OF MALARIA TRANSMISSION
DYNAMICS COMBINING SOME USUAL STRATEGIES
AND AN IMPERFECT VACCINE**

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Abstract

This work is an extension of a previous publication. An optimal control theory is applied to a model of malaria transmission dynamics to investigate the control strategies for eliminating malaria using time dependent controls. Four main efforts are considered including the treatment of infected humans, the individual protection, vectors control strategies such as killing adult anopheles and both aquatic stages and the implementation of an imperfect vaccine which has already been tried in certain areas. The characterization of the optimal control is carried out via the Pontryagin's Maximum Principle which shows the necessary conditions for controlling malaria. Numerical simulations of the model show that restricted and proper use of control measures might considerably decrease the size of mosquito population and the number of infected among the human population accordingly.

Keywords: mathematical modeling, malaria dynamics, optimal control, usual strategies, vaccination, Pontryagin's Maximum Principle.

2010 Mathematics Subject Classification: 65L12, 65M20, 65N40.

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1. INTRODUCTION

Malaria is a reemerging vector-borne disease which became one of the top ten diseases that challenge most low incomes countries. It is very devastating and provokes tens of thousands of deaths all over the world. Nearly, 90% of malaria cases occur in Sub-Saharan Africa of whom 83% are children under 5 [24, 43]. Although governments and scientists work together for hundreds of years to overcome malaria spreading and its outcomes on economy; it keeps increasing making lot of deaths and morbidities around the world. And the burden is especially huge in Sub-Saharan Africa, Asia and Latin America [20, 42]. The use of mathematical models plays an important role in controlling mosquito population increasing and accordingly mosquito-borne diseases. In the existing literatures, many mathematical models exist describing diseases transmission dynamics and applying some of the control strategies in order to eradicate them [32, 41]. Numerous mathematical and statistical modeling works have been carried out to gain insights into the transmission dynamics of several diseases, dating back to the pioneering work of Daniel Bernoulli (1766) [7, 34, 35]. Lambert, in 1772, followed up the work of Bernoulli extending the model by incorporating age-dependent parameters. Laplace has also worked on the same concept [9, 10, 14]. However, this line of research has not been developed systematically until the benchmark paper of Ross in 1911, which actually establishes modern mathematical epidemiology [13, 15, 16, 30, 38]. In his work, Ross addressed the modeling approach using a set of equations to gain insights into the transmission dynamics of malaria [1, 8, 20, 22].

In the case of malaria, since hundreds of years, following up the pioneering work of Sir Ronald Ross, a vast number of approaches have been proposed looking at the problem from different perspectives [1, 5, 11, 12]. All these works aim first at deeply explaining the transmission dynamics and secondly at controlling the disease propagation. See for instance works of Chiyaka *et al.* [14], Chitnis *et al.* [13], McQueen and McKenzie [10, 20], Ngwa and Shu [30], to list a few. Furthermore, many others mathematical studies have been recently proposed by Zongo *et al.* [17], Traoré *et al.* [42], Koutou *et al.* [24] that incorporate a number of new insights into the transmission dynamics of malaria. Thereby, many aspects of the disease have been investigated such as heterogeneity within human population, seasonality that accounts for climate changes and environmental effects, impact of the immature stages and the gonotrophic cycle, latency due to the incubation period, role of partially immune individuals in the disease persistence, evolution of immunity, resistance to drugs, attempts to develop effective vaccine and new drugs [23, 27, 39].

One of the purposes of modeling epidemics is to provide a rational basis for policies designed to control the spread of a disease. The inclusion of practical

optimal strategies in models allows for the assessment of the intervention of public health authorities [19, 25, 39]. Optimal control is a powerful mathematical tool in decision making that involves employing appropriate strategies to eradicate epidemics from the population. The decisions include determining the proportion of the population that should be treated as time evolves in a given epidemic to minimize both the number of infections in the population and the implementation cost [21, 27, 30]. In areas in where malaria and many other communicable diseases have been eradicated, that victory has largely been achieved because of local control of mosquito population. Otherwise, many other control strategies are used a lot, among which intermittent preventive treatment in pregnant women and infants that are the most vulnerable to malaria, indoor and outdoor spray of insecticide, the use of insecticide treated bed-nets, etc. Actually, the control efforts of the disease focus more on mosquito population eradication, new drugs and effective vaccine development [13, 15, 28]. Even though, malaria vaccine is still considered as imperfect, a first try has been implemented in Ghana, Kenya and Malawi, [37, 43]. Since then, there is great hope about controlling malaria to the point where it would not be no longer a public health problem. However, drug resistance, insecticide resistance, inefficiency to store drugs and the poverty of the target populations are just some of the major barriers to providing effective treatment in endemic areas [36, 37].

Indeed, mathematical control theories are basic principles that underlie the analysis and design the control systems. A lot of epidemiological models have used control theories among which we count works of Moulay *et al.* [29, 40] that deals with Chikungunya disease, Omondi *et al.* [31] studying HIV disease dynamics in Kenya, Hugo *et al.* [21, 33, 38] who propose an optimal control model to tackle the Newcastle disease that was devastating both chicken and human population in Tanzania etc. This theory is used to influence the objects behavior so as to achieve a desired goal [21] and determine whether the disease persists or extincts naturally. The main purpose of this work is to extend the study proposed in [24, 40] by incorporating both some usual strategies and an imperfect vaccine to investigate how they influence the dynamic behavior of malaria within an endemic area. We then use four main control strategies such as treatment, larva destruction and prevention that includes the use of an imperfect malaria vaccine and self-protection to mosquito bites.

We organize the rest of the paper as follows. In Section 2, we briefly recall some main results of our baseline model. In Section 3, we formulate the control problem. Section 4 is devoted to the application of optimal control theory. First, we investigate the existence of an optimal control, then we derive the optimality system which characterizes the optimal control using Pontryagin's Maximum Principle. Some simulations results have been illustrated in Section 5 to show the impact of the control strategies on the disease burden. Finally, in Section 6

we take stock of the work done in the paper and we also propose some recommendations to tackle the devastating effects of malaria in developing countries.

2. THE BASIC MODEL OF MALARIA TRANSMISSION DYNAMICS

In [24], we proposed two models to describe the growth dynamic of anopheles mosquito population and the transmission of parasites to human population. For the reader convenience, we briefly recall the main results of the baseline model [24, 28].

(I) The global dynamics of vector population is formulated following up a stage structured model based on the mosquito life cycle described in the biological literature. Indeed, mosquitoes undergo complete metamorphosis going through four distinct life-history stages of development. It begins with eggs (E) which hatch into larvae (L) under suitable conditions within one or two weeks. Larvae molt four times totally as they grow and after the fourth molt, they are called pupae (P). Pupae live near the surface of water and the skin splits after a couple of days, from a pupae an adult mosquito emerges [24, 42]. Female mosquitoes that are mainly involved in the disease transmission are denoted by (A). The parameters d_E , d_L , d_P , f_m denote the natural death rate of eggs, larvae, pupae and females, respectively. The net oviposition rate per female insect is b and is proportional to their density. It is also assumed that the growth dynamic of each of those compartment depends on the availability of nutrients, oviposition habitats, space etc. that is called carrying capacity. So, the new numbers of eggs, larva and pupa are $bA(t)(1 - E(t)/K_E)$, $s_E E(t)(1 - L(t)/K_L)$ and $s_L L(t)(1 - P(t)/K_P)$ respectively. The mosquito growth dynamic model is described by the diagram of Figure 1.

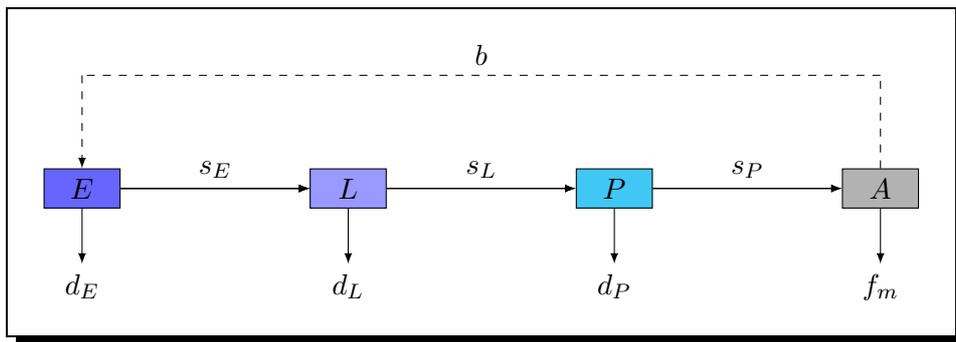


Figure 1. An age-structured compartmental model for vector population growth dynamics.

Making the input-output balance in each evolution stage through the flow chart in Figure 1, yields the following system of ordinary differential equations

$$(1) \quad \begin{cases} E'(t) = bA(t) \left(1 - \frac{E(t)}{K_E}\right) - (s_E + d_E)E(t) \\ L'(t) = s_E E(t) \left(1 - \frac{L(t)}{K_L}\right) - (s_L + d_L)L(t) \\ P'(t) = s_L L(t) \left(1 - \frac{P(t)}{K_P}\right) - (s_P + d_P)P(t) \\ A'(t) = s_P P(t) - f_m A(t). \end{cases}$$

It has been shown [24] that system (1) is mathematically and biologically well posed in

$$\Delta = \left\{ (x, y, z, w) \in \mathbb{R}^4 \mid 0 \leq x \leq K_E, 0 \leq y \leq K_L, 0 \leq z \leq K_P, 0 \leq w \leq \frac{s_P}{f_m} K_P \right\}.$$

Let us consider the following threshold parameter given by equation (2) and commonly called mosquito reproduction number. It is obtained in an obvious manner by making an input-output balance of model (1)

$$(2) \quad r = \left(\frac{b}{s_E + d_E} \right) \left(\frac{s_E}{s_L + d_L} \right) \left(\frac{s_L}{s_P + d_P} \right) \left(\frac{s_P}{f_m} \right).$$

Indeed, the mosquito population growth dynamic is fully governed by the mosquito so-called mosquito reproduction number. It has been highlighted in several models dealing with mosquito growth dynamic and vector-borne diseases. Mathematical studies have proven that this threshold parameter is highly involved in the transmission dynamics of arboviral diseases such as dengue fever, malaria chikunguya [24, 30, 40].

Theorem 2.1 [24, 29].

- (i) *The equilibrium $X_0^* = (0, 0, 0, 0)$ is globally asymptotically stable if and only if $r < 1$.*
- (ii) *If $r > 1$, there is a unique nontrivial equilibrium point which is globally asymptotically stable and is given by*

$$(3) \quad X^* = \left(1 - \frac{1}{r} \right) \left(\frac{K_E}{\chi_E}, \frac{K_L}{\chi_L}, \frac{K_P}{\chi_P}, \frac{s_P K_P}{f_m \chi_P} \right) = (E^*, L^*, P^*, A^*)$$

where

$$\begin{aligned}\chi_E &= \left(1 - \frac{1}{r}\right) + \frac{f_m(s_E + d_E)\chi_P}{bs_P K_P}, \\ \chi_L &= \left(1 - \frac{1}{r}\right) \left(1 + \frac{(s_L + d_L)K_L}{s_E K_E}\right) + \frac{(s_E + d_E)(s_L + d_L)K_L \chi_P}{bs_E s_P K_P}, \\ \chi_P &= 1 + \frac{s_E K_E K_P (s_P + d_P) + (s_L + d_L)(s_P + d_P)K_L K_P}{s_E s_L K_E K_L}.\end{aligned}$$

The above results show that, a vector control strategy that brings and maintains the threshold quantity r , to a value less than unity will lead to an effective control of mosquitoes population growth from the community. In other words, the requirement $r \leq 1$ is necessary and sufficient for the effective control of mosquitoes population growth.

(II) The second model concerns the disease transmission to the human and mosquito hosts. In this model, human hosts follow an SEIRS-like pattern and vector hosts follow the SEI pattern due to their short life cycle. The compartments S , E , I and R represent respectively the susceptible, the exposed, the infectious and the recovered individuals during an epidemic. However, the human population is split into two types. The first type, called non-immune is divided into three sub-classes and the second type called semi-immune is divided in four classes.

The following Tables 1–6 give a description of all these classes.

Notation	Description
S_e	class of non-immune susceptible.
S_a	class of semi-immune susceptible.
E_e	class of non-immune latent.
E_a	class of semi-immune latent.
I_e	class of non-immune infectious.
I_a	class of semi-immune infectious.
R_a	class of immune semi-immune.

Table 1. Parameters for human hosts.

Notation	Description
S_m	class of susceptible mosquitoes.
E_m	class of latent mosquitoes.
I_m	class of infectious mosquitoes.

Table 2. Parameters for vectors hosts.

Parameters	Biological description
Λ_h	constant recruitment rate of human (it also includes births).
p	probability for a new recruit to be non-immune.
$1 - p$	probability for a new recruit to be semi-immune.

Table 3. Parameters common to non-immune and semi-immune

Parameters	Biological description
ν_a	rate of passage from latent semi-immune to infectious
α_a	rate of passage from infectious semi-immune to immune.
β_a	rate of loss of immune immunity

Table 4. Parameters for semi-immune hosts.

Parameters	Biological description
n_a	average number of bites per mosquito per unit of time
c_{me}	probability that an infectious mosquito bite on a susceptible non-immune transfers the infection to the non-immune
c_{ma}	probability that an infectious mosquito bite on a susceptible semi-immune transfers the infection to the semi-immune.
c_{em}	probability that a bite from a susceptible mosquito on an infectious non-immune transfers the infection to the mosquito
c_{am}	probability that a bite from a susceptible mosquito on an infectious semi-immune transfers the infection to the mosquito
\tilde{c}_{am}	probability that a bite from a susceptible mosquito on an infectious immune transfers the infection to the mosquito

Table 5. Contact parameters between non-immune, semi-immune and mosquito

Parameters	Biological description
ν_e	rate of passage from latent non-immune to infectious
α_e	rate of passage from infectious non-immune to immune
γ_e	mortality rate due to malaria on non-immune
γ_a	mortality rate due to malaria on semi-immune

Table 6. Parameters for the non-immune hosts.

The total human population at each instant t is given by:

$$(4) \quad N_h(t) = S_e(t) + E_e(t) + I_e(t) + S_a(t) + E_a(t) + I_a(t) + R_a(t).$$

And the total vector population at each instant t is given by:

$$(5) \quad A(t) = S_m(t) + E_m(t) + I_m(t),$$

where $A(t)$ is previously defined.

Malaria occurs when susceptible mosquitoes S_m are infected during the blood meal with the infected humans from the classes I_e , I_a and R_a , respectively. The per capita incidence rate among mosquitoes is given by $k_m = c_{am}n_a I_a/N_h + c_{em}n_a I_e/N_h + \tilde{c}_{am}n_a R_a/N_h$ and it depends on the fraction of infected humans I_a/N_h , I_e/N_h and R_a/N_h where n_a is the average number of bites per mosquito per unit of time, and c_{em} , c_{am} and \tilde{c}_{am} are probabilities that a bite from a susceptible mosquito on an infectious non-immune, an infectious semi-immune and a partially immune individual transfers the infection to the mosquito, respectively.

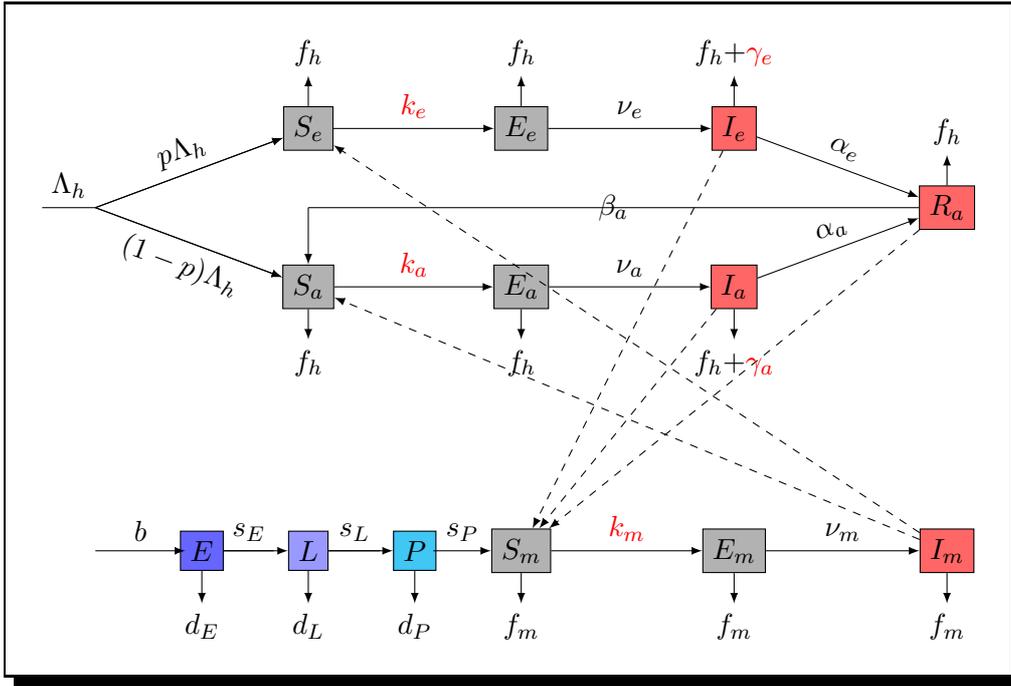


Figure 2. A schematic of the mathematical model for malaria transmission involving the human host susceptibility, exposedness and infectivity with variable non-immune, semi-immune and mosquitoes population. The dashed arrows indicate the direction of the infection and the solid arrows represent the transition from one class to another.

However, malaria infection among humans may occur when susceptible individuals S_e or S_a get into contact with infected mosquitoes during the blood meal.

The per capita incidence rates among susceptible humans are $k_e = c_{me}n_a I_m/N_h$ and $k_a = c_{ma}n_a I_m/N_h$ respectively for non-immune and semi-immune humans and both of them depends on the fraction of infected mosquitoes I_m/N_h , where c_{me} and c_{ma} are the probabilities that an infectious mosquito bite on a susceptible non-immune and susceptible semi-immune humans transfers the infection to them, respectively.

Then, through the flow chart in Figure 2 which describes the overall dynamics of the spread of malaria, yields the following system

$$(6) \quad \left\{ \begin{array}{l} \left\{ \begin{array}{l} E'(t) = bA(t) \left(1 - \frac{E(t)}{K_E}\right) - (s_E + d_E)E(t) \\ L'(t) = s_E E(t) \left(1 - \frac{L(t)}{K_L}\right) - (s_L + d_L)L(t) \\ P'(t) = s_L L(t) \left(1 - \frac{P(t)}{K_P}\right) - (s_P + d_P)P(t) \end{array} \right. \quad (S1) \\ \\ \left\{ \begin{array}{l} S'_e(t) = p\Lambda_h - (f_h + k_e)S_e(t) \\ E'_e(t) = k_e S_e(t) - (f_h + \nu_e)E_e(t) \\ I'_e(t) = \nu_e E_e(t) - (f_h + \gamma_e + \alpha_e)I_e(t) \end{array} \right. \\ \\ \left\{ \begin{array}{l} S'_a(t) = (1-p)\Lambda_h + \beta_a R_a(t) - (f_h + k_a)S_a(t) \\ E'_a(t) = k_a S_a(t) - (f_h + \nu_a)E_a(t) \\ I'_a(t) = \nu_a E_a(t) - (f_h + \gamma_a + \alpha_a)I_a(t) \\ R'_a(t) = \alpha_e I_e(t) + \alpha_a I_a(t) - (f_h + \beta_a)R_a(t) \end{array} \right. \quad (S2) \\ \\ \left\{ \begin{array}{l} S'_m(t) = s_P P(t) - (f_m + k_m)S_m(t) \\ E'_m(t) = k_m S_m(t) - (f_m + \nu_m)E_m(t) \\ I'_m(t) = \nu_m E_m(t) - f_m I_m(t). \end{array} \right. \end{array} \right.$$

In system (6), the subsystem (S1) represents the vectors population growth global dynamics and subsystem (S2) represents the disease transmission. Indeed, (S1) is coupled with (S2) through the variable $P(t)$. However, to analyze system (6) in a decoupled form, we can use the principle of limiting system, [23, 24].

From equation (5), we obtain that

$$(7) \quad S_m(t) = A(t) - E_m(t) - I_m(t).$$

And then, substituting $S_m(t)$ given by (7) into (6), we have

$$(8) \quad \left\{ \begin{array}{l} \left\{ \begin{array}{l} E'(t) = bA(t) \left(1 - \frac{E(t)}{K_E} \right) - (s_E + d_E)E(t) \\ L'(t) = s_E E(t) \left(1 - \frac{L(t)}{K_L} \right) - (s_L + d_L)L(t) \\ P'(t) = s_L L(t) \left(1 - \frac{P(t)}{K_P} \right) - (s_P + d_P)P(t) \\ A'(t) = s_P P(t) - f_m A(t) \end{array} \right. \quad (S1) \\ \left\{ \begin{array}{l} S'_e(t) = p\Lambda_h - (f_h + k_e)S_e(t) \\ E'_e(t) = k_e S_e(t) - (f_h + \nu_e)E_e(t) \\ I'_e(t) = \nu_e E_e(t) - (f_h + \gamma_e + \alpha_e)I_e(t) \\ S'_a(t) = (1-p)\Lambda_h + \beta_a R_a(t) - (f_h + k_a)S_a(t) \\ E'_a(t) = k_a S_a(t) - (f_h + \nu_a)E_a(t) \\ I'_a(t) = \nu_a E_a(t) - (f_h + \gamma_a + \alpha_a)I_a(t) \\ R'_a(t) = \alpha_e I_e(t) + \alpha_a I_a(t) - (f_h + \beta_a)R_a(t) \end{array} \right. \quad (S2) \\ \left\{ \begin{array}{l} E'_m(t) = k_m(A(t) - E_m(t) - I_m(t)) - (f_m + \nu_m)E_m(t) \\ I'_m(t) = \nu_m E_m(t) - f_m I_m(t). \end{array} \right. \end{array} \right.$$

It is easy to see that system (8) leads to the following limit system [23, 30]

$$(9) \quad \left\{ \begin{array}{l} \left\{ \begin{array}{l} S'_e(t) = p\Lambda_h - (f_h + k_e)S_e(t) \\ E'_e(t) = k_e S_e(t) - (f_h + \nu_e)E_e(t) \\ I'_e(t) = \nu_e E_e(t) - (f_h + \gamma_e + \alpha_e)I_e(t) \\ S'_a(t) = (1-p)\Lambda_h + \beta_a R_a(t) - (f_h + k_a)S_a(t) \\ E'_a(t) = k_a S_a(t) - (f_h + \nu_a)E_a(t) \\ I_a(t) = \nu_a E_a(t) - (f_h + \gamma_a + \alpha_a)I_a(t) \\ R'_a(t) = \alpha_e I_e(t) + \alpha_a I_a(t) - (f_h + \beta_a)R_a(t) \end{array} \right. \\ \left\{ \begin{array}{l} E'_m(t) = k_m(A^* - E_m(t) - I_m(t)) - (f_m + \nu_m)E_m(t) \\ I'_m(t) = \nu_m E_m(t) - f_m I_m(t). \end{array} \right. \end{array} \right.$$

System (9) is well defined in the domain $\Omega_{h,m} = \Omega_h \times \Omega_m \subset \mathbb{R}_+^9$ where

$$\Omega_h = \left\{ (S_e, E_e, I_e, S_a, E_a, I_a, R_a) \mid 0 \leq N_h \leq \frac{\Lambda_h}{f_h} \right\}$$

and

$$\Omega_m = \left\{ (E_m, I_m) \mid 0 \leq E_m + I_m \leq \frac{s_P}{f_m} K_P \right\}.$$

The disease-free equilibrium and the endemic equilibrium of the limit system (9) have been determined. Besides, using the next generation operator method the basic reproduction number has also been calculated and the stability results given (see [24]). Moreover, for $r > 1$ a functional relation has been established between the mosquito reproduction number and the common basic reproduction number as follows

$$\mathcal{R}_0 = \sqrt{\kappa \left(1 - \frac{1}{r} \right)},$$

where κ is a given value that depends on the model parameters.

Lemma 2.1 [16, 24]. *Let consider the following threshold parameter $r_0 = \frac{\kappa}{\kappa-1}$, $\kappa \neq 1$.*

- (i) $\mathcal{R}_0 < 1$ is equivalent to $1 < r < r_0$.
- (ii) $\mathcal{R}_0 > 1$ is equivalent to $r > r_0$.

Let $(0, 0, 0, 0, S_e^*, 0, 0, S_a^*, 0, 0, 0, 0, 0)$ and $(E^*, L^*, P^*, A^*, S_e^*, 0, 0, S_a^*, 0, 0, 0, 0, 0)$ the disease-free equilibrium and $(E^*, L^*, P^*, A^*, S_e^{**}, E^{**}, I_e^{**}, S_a^{**}, E_a^{**}, I_a^{**}, R_a^{**}, E_m^{**}, I_m^{**})$ the endemic equilibrium of system (8). Their global stability results are given in the following theorem

Theorem 2.2 [24, 26, 40].

- (i) *If $r \leq 1$, then the disease-free equilibrium $(0, 0, 0, 0, S_e^*, 0, 0, S_a^*, 0, 0, 0, 0, 0)$ of system (8) is globally asymptotically stable.*
- (ii) *If $1 < r < r_0$, then the disease-free equilibrium point $(E^*, L^*, P^*, A^*, S_e^*, 0, 0, S_a^*, 0, 0, 0, 0, 0)$ of system (8) is globally asymptotically stable.*
- (iii) *If $r > r_0$, then the endemic equilibrium $(E^*, L^*, P^*, A^*, S_e^{**}, E^{**}, I_e^{**}, S_a^{**}, E_a^{**}, I_a^{**}, R_a^{**}, E_m^{**}, I_m^{**})$ of system (8) is globally asymptotically stable.*

Proof. The key idea to prove this theorem is to use the theory of internally chain transitive sets, [24, 26, 28, 40]. ■

3. DERIVATION OF THE MATHEMATICAL MODEL OF CONTROL

In this section, we formulate a model that minimizes malaria infection in the human population. Indeed, there are several possible interventions in order to reduce or limit the proliferation of mosquitoes and the explosion of the number of infected humans and mosquitoes. In the existing literatures, several approaches have been proposed to fight against mosquito population increasing and

the spread of malaria. But all those approaches are mainly depending on: environmental management which consists of environmental modification, manipulation of breeding sites, and changes in human habitations and behaviors; biological control which is a new insight in malaria control strategies and it consists in the introduction of biological enemies of the vector and chemical control which relies on the use of chemical products for instance anti-malarial distribution, the use of insecticide treated nets, the use of biological larvicide or adulticide that also ensure that the breeding sites are minimized and some other new policies as malaria vaccine implementation [2, 3].

The purpose of introducing the control functions $u_i(t)$, $i = 1, 2, 3, 4$ in the model is to find the optimal level of the intervention strategy preferred to reduce the spread and the cost of implementation of the disease control. It is important to note that controls are fully effective when $u_i(t) = 1$ and not effective when $u_i(t) = 0$ with $i = 1, 2, 3, 4$.

- The forces of infection k_e , k_a and k_m corresponding to human population and mosquito population are respectively reduced by the factor $(1 - u_1(t))$, where $u_1(t)$ measures the level of successful exposure prevention efforts. It represents the use of alternative prevention measures to minimize or eliminate the mosquito-human contacts. Such measures include the use of insect repellents, wearing protective coats and long sleeves [24, 40].
- The second control $u_2(t)$ represents efforts made for treatment. It mainly consists in isolating infected patients in hospitals, installing an anti-mosquito electric diffuser in the hospital room or symptomatic treatments [24, 37].
- The third control $u_3(t)$ represents the effects of interventions used for the vector control. This control management mainly consists in the reduction of breeding sites with chemical application methods, for instance using larvicides and adulticides. The goal of this control is to reduce eggs, larvae and pupae but it is more focused on larvae and pupae reduction because of eggs resistance [14, 28].
- The fourth control $u_4(t)$ denotes the percentage of susceptible individuals that decide to vaccinate at time t . Vaccination plays an essential role in eliminating infectious diseases and used as an effective method to eliminate the infection by reducing the strength of the susceptible groups. However, malaria vaccine is not yet perfect but it is necessary to combine it with some other mechanisms to find the best combination which permits to decrease the spread of malaria [4, 6].

In this study, we assume that malaria vaccine is exclusively aimed to newborns and those who have never contracted the disease. Indeed, this segment of the population is more vulnerable and the vaccine just keeps them out of serious illness. Thus, after getting vaccinated a non-immune individual acquires a certain immunity and then joins the partially immune individual class. In this

situation, although partially immune individuals still remain slightly infectious to mosquitoes, we make the assumption that they do not lose their immunity. Then, our control model of malaria transmission is given by

$$(10) \quad \left\{ \begin{array}{l} \left\{ \begin{array}{l} E'(t) = bA(t) \left(1 - \frac{E(t)}{K_E}\right) - (s_E + d_E)E(t) - \epsilon u_3(t)E(t) \\ L'(t) = s_E E(t) \left(1 - \frac{L(t)}{K_L}\right) - (s_L + d_L)L(t) - d_1 u_3(t)L(t) \\ P'(t) = s_L L(t) \left(1 - \frac{P(t)}{K_P}\right) - (s_P + d_P)P(t) - d_2 u_3(t)P(t) \\ A'(t) = s_P P(t) - f_m A(t) \end{array} \right. \\ \left\{ \begin{array}{l} \left\{ \begin{array}{l} S'_e(t) = p\Lambda_h - (f_h + k_e(1 - u_1(t)))S_e(t) - \omega u_4(t)S_e(t) \\ E'_e(t) = k_e(1 - u_1(t))S_e(t) - (f_h + \nu_e)E_e(t) \\ I'_e(t) = \nu_e E_e(t) - (f_h + \gamma_e + \alpha_e)I_e(t) - \rho_e u_2(t)I_e(t) \end{array} \right. \\ \left\{ \begin{array}{l} S'_a(t) = (1 - p)\Lambda_h - (f_h + k_a(1 - u_1(t)))S_a(t) \\ E'_a(t) = k_a(1 - u_1(t))S_a(t) - (f_h + \nu_a)E_a(t) \\ I'_a(t) = \nu_a E_a(t) - (f_h + \gamma_a + \alpha_a)I_a(t) - \rho_a u_2(t)I_a(t) \\ R'_a(t) = (\alpha_e + \rho_e u_2(t))I_e(t) + (\alpha_a + \rho_a u_2(t))I_a(t) + \omega u_4(t)S_e(t) - f_h R_a(t) \end{array} \right. \\ \left\{ \begin{array}{l} E'_m(t) = k_m(1 - u_1(t))(A - I_m) - (f_m + \nu_m + k_m(1 - u_1(t)))E_m(t) \\ I'_m(t) = \nu_m E_m(t) - f_m I_m(t). \end{array} \right. \end{array} \right.$$

Since, $u_2(t)$ corresponds to the treatment of infected individuals, the quantities $\rho_e u_2(t)$ and $\rho_a u_2(t)$ are the per capita recovery rates of non-immune and semi-immune infected people that move to the partially immune individual compartment due to the treatments, respectively. In the same line, $u_3(t)$ corresponds to the reduction of the mosquito proliferation effort, then $\epsilon u_3(t)$, $d_1 u_3(t)$ and $d_2 u_3(t)$ represent the per capita mortality rates of eggs, larva and pupa induced by chemical interventions, respectively. And $\omega u_4(t)$ corresponds to the per capita recovery rate induced by malaria vaccine.

4. APPLICATION OF OPTIMAL CONTROL THEORY

4.1. Optimal problem presentation

In this section, we investigate the optimal level of efforts that would be required to control malaria prevalence among the population at a minimum cost. Using bounded Lebesgue measurable control, the objective functional to be minimized

is given by

$$(11) \quad \mathcal{J} = \int_0^{t_f} \left(A_1 E + A_2 L + A_3 P + A_4 A + A_5 S_e + A_6 I_e + A_7 I_a + \frac{1}{2} \sum_{i=1}^4 B_i u_i^2 \right) dt$$

subject to the state system given in system (10).

According to the available means, we aim to minimize both the number aquatic stages and the mature mosquito population (E, L, P, A), the non-immune susceptible individuals, the non-immune and the semi-immune infectious (S_e, I_e, I_a) and the cost of implementing the control by use of possible minimum variables $u_i, i = 1, 2, 3, 4$.

From the objective functional (11) given above, the social costs related to the resources needed to prevent mosquito-human contacts is $\frac{1}{2}B_1u_1^2$, the treatment of infectious is $\frac{1}{2}B_2u_2^2$, spraying of larvicide operations in order to reduce the breeding sites is $\frac{1}{2}B_3u_3^2$ and the coverage vaccination is $\frac{1}{2}B_4u_4^2$. The quantities A_i for $i = 1, 2, 3, 4$ represent the cost associated with reducing the aquatic stages and adult mosquitoes, respectively while A_i for $i = 5, 6, 7$ represent the cost needed to treat both types of infectious individuals and to vaccinate the non-immune susceptible individuals, respectively. The quantity t_f is the time period of intervention. The quantities $B_i, i = 1, 2, 3, 4$ represent the weight constants for personal protection from mosquito bites, disease treatment, spraying of larvicide operations and applying vaccination to non-immune susceptible individuals, respectively. According to the costs associated with A_1E, A_2L, A_3P and A_4A are linear while the cost control functions $\frac{1}{2}B_1u_1^2, \frac{1}{2}B_2u_2^2, \frac{1}{2}B_3u_3^2$ and $\frac{1}{2}B_4u_4^2$ should be non-linear and we consider quadratic form. This choice can be justified as follows: firstly an epidemiological control can be considered as an expenditure of energy, by bringing to the application of physics in control theory; secondly because of positivity condition on each control $u_i, i = 1, \dots, 4$, minimize u_i is like minimize u_i^2 . Moreover, the quadratic approximation is the simplest and the most widely used.

We seek to minimize the objective functional over the given time interval $[0, t_f]$. And the purpose of the optimal control is to find out some optimal control functions $(u_1^*, u_2^*, u_3^*, u_4^*)$ such that

$$(12) \quad \mathcal{J}(u_1^*, u_2^*, u_3^*, u_4^*) = \min_U \mathcal{J}(u_1, u_2, u_3, u_4)$$

where

$$(13) \quad U = \{u_1, u_2, u_3, u_4 | 0 \leq u_i(t) \leq 1, i = 1, 2, 3\}$$

is the control set and is Lebesgue measurable. Pontryagin's Maximum Principle is used to solve this optimal control problem and the derivation of the necessary conditions. First, we prove the existence of an optimal control for system (10) and then derive the optimality system.

4.2. Existence and well-posedness of control problem

Firstly, we find the Lagrangian and Hamiltonian for the optimal control problems (11) and (10). The Lagrangian \mathbb{L} , is given by the following function:

$$(14) \quad \mathbb{L} = A_1E + A_2L + A_3P + A_4A + A_5S_e + A_6I_e + A_7I_a + \frac{1}{2} \sum_{i=1}^4 B_i u_i^2.$$

We are looking for the Lagrangian minimum value. In order to achieve this, we consider the Hamiltonian \mathbb{H} , for the control problem as follows:

$$\begin{aligned} \mathbb{H} = & A_1E + A_2L + A_3P + A_4A + A_5S_e + A_6I_e + A_7I_a + \frac{1}{2} \sum_{i=1}^4 B_i u_i^2 \\ & + \lambda_1 \left[bA(t) \left(1 - \frac{E(t)}{K_E} \right) - (s_E + d_E)E(t) - \epsilon u_3(t)E(t) \right] \\ & + \lambda_2 \left[s_E E(t) \left(1 - \frac{L(t)}{K_L} \right) - (s_L + d_L)L(t) - d_1 u_3(t)L(t) \right] \\ & + \lambda_3 \left[s_L L(t) \left(1 - \frac{P(t)}{K_P} \right) - (s_P + d_P)P(t) - d_2 u_3(t)P(t) \right] \\ & + \lambda_4 [s_P P(t) - f_m A(t)] \\ & + \lambda_5 [p\Lambda_h - (f_h + k_e(1 - u_1(t)))S_e(t) - \omega u_4(t)S_e(t)] \\ & + \lambda_6 [k_e(1 - u_1(t))S_e(t) - (f_h + \nu_e)E_e(t)] \\ & + \lambda_7 [\nu_e E_e(t) - (f_h + \gamma_e + \alpha_e)I_e(t) - \rho_e u_2(t)I_e(t)] \\ & + \lambda_8 [(1 - p)\Lambda_h - (f_h + k_a(1 - u_1(t)))S_a(t)] \\ & + \lambda_9 [k_a(1 - u_1(t))S_a(t) - (f_h + \nu_a)E_a(t)] \\ & + \lambda_{10} [\nu_a E_a(t) - (f_h + \gamma_a + \alpha_a)I_a(t) - \rho_a u_2(t)I_a(t)] \\ & + \lambda_{11} [(\alpha_e + \rho_e u_2(t))I_e(t) + (\alpha_a + \rho_a u_2(t))I_a(t) + \omega u_4(t)S_e(t) - f_h R_a(t)] \\ & + \lambda_{12} [k_m(1 - u_1(t))(A - I_m) - (f_m + \nu_m + k_m(1 - u_1(t)))E_m(t)] \\ & + \lambda_{13} [\nu_m E_m(t) - f_m I_m(t)]. \end{aligned}$$

Theorem 4.1 [32, 37]. *There exists an optimal control $(u_1^*, u_2^*, u_3^*, u_4^*) \in U$ satisfying (12) subject to the control system (10) together with the initial conditions.*

Proof. Thanks to Fleming and Rishel [18] we prove the existence of the optimal control. It is obvious to see that model (10) is bounded by considering a super-solution of the system of equations (10); and the state variables are non-negative. Furthermore, in this minimizing problem, the control set U is convex and closed by definition. The optimal system is bounded which determines the compactness needed for the existence of the optimal control. The Lagrangian \mathbb{L} is clearly convex on the convex set U . Moreover, there exists some constants $c_1 > 0$, $c_2 > 0$ and $\beta > 1$ such as the integrand of the objective function is bounded below by the following quantity $c_1 \left(\sum_{i=1}^4 |u_i|^2 \right)^{\frac{\beta}{2}} - c_2$ with regards to the boundedness of the state variables of model (10). Therefore, $\mathcal{J}(u_1, u_2, u_3, u_4) \geq c_1 \left(\sum_{i=1}^4 |u_i|^2 \right)^{\frac{\beta}{2}} - c_2$. This completes the proof. ■

4.3. Optimality of the system

As we have previously mentioned, the characterization of the optimal solution is obtained by employing Pontryagin's Maximum Principle [25, 32] to the control system's Hamiltonian such that if (x, u) is an optimal solution of the optimal control problem, then there exists a non-trivial vector $\lambda = (\lambda_1, \dots, \lambda_n)$ satisfying the following conditions

$$(15) \quad \frac{dx}{dt} = \frac{\partial \mathbb{H}(t, x, u, \lambda)}{\partial \lambda}, \quad 0 = \frac{\partial \mathbb{H}(t, x, u, \lambda)}{\partial u}, \quad \frac{d\lambda}{dt} = -\frac{\partial \mathbb{H}(t, x, u, \lambda)}{\partial x}.$$

Now, we derive the necessary conditions to the Hamiltonian \mathbb{H} that optimal control functions and corresponding states must satisfy.

Theorem 4.2 [28, 32]. *Given an optimal control $(u_1^*, u_2^*, u_3^*, u_4^*) \in U$ and corresponding states $E^*, L^*, P^*, A^*, S_e^*, E_e^*, I_e^*, S_a^*, E_a^*, I_a^*, R_a^*, E_m^*$ and I_m^* then there exists adjoint functions λ_i for $i = 1, \dots, 13$ satisfying*

$$\begin{aligned} \lambda_1' &= -A_1 + \lambda_1 \left(\frac{bA}{K_E} + s_E + d_E + \epsilon u_3 \right) - \lambda_2 s_E \left(1 - \frac{L}{K_L} \right) \\ \lambda_2' &= -A_2 + \lambda_2 \left(\frac{s_E E}{K_L} + s_L + d_L + d_1 u_3 \right) - \lambda_3 s_L \left(1 - \frac{P}{K_P} \right) \\ \lambda_3' &= -A_3 + \lambda_3 \left(\frac{s_L L}{K_P} + s_P + d_P + d_2 u_3 \right) - \lambda_4 s_P \\ \lambda_4' &= -A_4 + \lambda_4 f_m - \lambda_{12} k_m (1 - u_1) - \lambda_1 b \left(1 - \frac{E}{K_E} \right) \end{aligned}$$

$$\begin{aligned}
\lambda'_5 &= -A_5 + \lambda_5(f_h + \omega u_4) - \lambda_{11}\omega u_4 + (\lambda_5 - \lambda_6)(1 - u_1)\frac{c_{me}n_a I_m}{N_h} \\
&+ (\lambda_6 - \lambda_5)(1 - u_1)\frac{c_{me}n_a I_m S_e}{N_h^2} + (\lambda_9 - \lambda_8)(1 - u_1)\frac{c_{ma}n_a I_m S_a}{N_h^2} \\
&+ \lambda_{12}(1 - u_1)(A - E_m - I_m)\frac{c_{em}n_a I_e + c_{am}n_a I_a + \tilde{c}_{am}n_a R_a}{N_h^2} \\
\lambda'_6 &= (\lambda_6 - \lambda_5)(1 - u_1)\frac{c_{me}n_a I_m S_e}{N_h^2} + \lambda_6 f_m + (\lambda_6 - \lambda_7)\nu_e \\
&+ (\lambda_9 - \lambda_8)(1 - u_1)\frac{c_{ma}n_a I_m S_a}{N_h^2} \\
&+ \lambda_{12}(1 - u_1)(A - E_m - I_m)\frac{c_{em}n_a I_e + c_{am}n_a I_a + \tilde{c}_{am}n_a R_a}{N_h^2} \\
\lambda'_7 &= -A_6 + (\lambda_6 - \lambda_5)(1 - u_1)\frac{c_{me}n_a I_m S_e}{N_h^2} + (\lambda_9 - \lambda_8)(1 - u_1)\frac{c_{ma}n_a I_m S_a}{N_h^2} \\
&+ (\lambda_7 - \lambda_{11})(\alpha_e + \rho_e u_2) + \lambda_7(f_h + \gamma_e) \\
&+ \lambda_{12}(1 - u_1)(A - E_m - I_m)\frac{c_{am}n_a I_a + \tilde{c}_{am}n_a R_a - c_{em}n_a(N_h - I_e)}{N_h^2} \\
\lambda'_8 &= (\lambda_6 - \lambda_5)(1 - u_1)\frac{c_{me}n_a I_m S_e}{N_h^2} + (\lambda_8 - \lambda_9)(1 - u_1)\frac{c_{ma}n_a I_m}{N_h} + \lambda_8 f_h \\
&+ (\lambda_9 - \lambda_8)(1 - u_1)\frac{c_{ma}n_a I_m S_a}{N_h^2} \\
&+ \lambda_{12}(1 - u_1)(A - E_m - I_m)\frac{c_{em}n_a I_e + c_{am}n_a I_a + \tilde{c}_{am}n_a R_a}{N_h^2} \\
\lambda'_9 &= (\lambda_6 - \lambda_5)(1 - u_1)\frac{c_{me}n_a I_m S_e}{N_h^2} \\
&+ (\lambda_9 - \lambda_8)(1 - u_1)\frac{c_{ma}n_a I_m S_a}{N_h^2} + \lambda_9 f_h + (\lambda_9 - \lambda_{10})\nu_a \\
&+ \lambda_{12}(1 - u_1)(A - E_m - I_m)\frac{c_{em}n_a I_e + c_{am}n_a I_a + \tilde{c}_{am}n_a R_a}{N_h^2} \\
\lambda'_{10} &= -A_7 + (\lambda_6 - \lambda_5)(1 - u_1)\frac{c_{me}n_a I_m S_e}{N_h^2} + (\lambda_9 - \lambda_8)(1 - u_1)\frac{c_{ma}n_a I_m S_a}{N_h^2} \\
&+ (\lambda_{10} - \lambda_{11})(\alpha_a + \rho_a u_2) + \lambda_{10}(f_h + \gamma_a) \\
&+ \lambda_{12}(1 - u_1)(A - E_m - I_m)\frac{c_{am}n_a I_a + \tilde{c}_{am}n_a R_a - c_{em}n_a I_e(N_h - I_a)}{N_h^2}
\end{aligned}$$

$$\begin{aligned}
\lambda'_{11} &= (\lambda_6 - \lambda_5)(1 - u_1) \frac{c_{me} n_a I_m S_e}{N_h^2} + (\lambda_9 - \lambda_8)(1 - u_1) \frac{c_{ma} n_a I_m S_a}{N_h^2} + \lambda_{11} f_h \\
&\quad + \lambda_{12}(1 - u_1)(A - E_m - I_m) \frac{c_{em} n_a I_e + c_{am} n_a I_a - \tilde{c}_{am} n_a (N_h - R_a)}{N_h^2} \\
\lambda'_{12} &= \lambda_{12} f_m + (\lambda_{12} - \lambda_{13}) \nu_m + \lambda_{12}(1 - u_1) \frac{c_{em} n_a I_e + c_{am} n_a I_a + \tilde{c}_{am} n_a R_a}{N_h} \\
\lambda'_{13} &= \lambda_{13} f_m + \lambda_{12}(1 - u_1) \frac{c_{em} n_a I_e + c_{am} n_a I_a + \tilde{c}_{am} n_a R_a}{N_h} \\
&\quad + (\lambda_5 - \lambda_6)(1 - u_1) \frac{c_{me} n_a S_e}{N_h} + (\lambda_8 - \lambda_9)(1 - u_1) \frac{c_{ma} n_a S_a}{N_h}
\end{aligned}$$

called system of transversality with the boundary conditions $\lambda_i(t_f) = 0$, $i = 1, \dots, 13$.

Moreover, the optimal control components u_i^* , $i = 1, \dots, 4$ are given by

$$\begin{aligned}
u_1^* &= \max \left\{ \min \left\{ \frac{(\lambda_6 - \lambda_5)k_e S_e^* + (\lambda_9 - \lambda_8)k_a S_a^* + \lambda_{12}k_m(A^* - E_m^* - I_m^*)}{B_1}, u_1^{\max} \right\}, 0 \right\} \\
u_2^* &= \max \left\{ \min \left\{ \frac{(\lambda_{11} - \lambda_7)\rho_e I_e^* + (\lambda_{11} - \lambda_{10})\rho_a I_a^*}{B_2}, u_2^{\max} \right\}, 0 \right\} \\
u_3^* &= \max \left\{ \min \left\{ \frac{\lambda_1 \epsilon E^* + \lambda_2 d_1 L^* + \lambda_3 d_2 P^*}{B_3}, u_3^{\max} \right\}, 0 \right\} \\
u_4^* &= \max \left\{ \min \left\{ \frac{(\lambda_5 - \lambda_{11})\omega S_e^*}{B_4}, u_4^{\max} \right\}, 0 \right\}.
\end{aligned}$$

Proof. Indeed, from Pontryagin's Maximum Principle we have

$$\begin{aligned}
\lambda'_1 &= -\frac{\partial \mathbb{H}}{\partial E}, & \lambda'_2 &= -\frac{\partial \mathbb{H}}{\partial L}, & \lambda'_3 &= -\frac{\partial \mathbb{H}}{\partial P}, & \lambda'_4 &= -\frac{\partial \mathbb{H}}{\partial A} \\
\lambda'_5 &= -\frac{\partial \mathbb{H}}{\partial S_e}, & \lambda'_6 &= -\frac{\partial \mathbb{H}}{\partial E_e}, & \lambda'_7 &= -\frac{\partial \mathbb{H}}{\partial I_e}, \\
\lambda'_8 &= -\frac{\partial \mathbb{H}}{\partial S_a}, & \lambda'_9 &= -\frac{\partial \mathbb{H}}{\partial E_a}, & \lambda'_{10} &= -\frac{\partial \mathbb{H}}{\partial I_a}, & \lambda'_{11} &= -\frac{\partial \mathbb{H}}{\partial R_a} \\
\lambda'_{12} &= -\frac{\partial \mathbb{H}}{\partial E_m}, & \lambda'_{13} &= -\frac{\partial \mathbb{H}}{\partial I_m}.
\end{aligned}$$

In characterizing each control, we consider three cases concerning the control bounds. And we show this in detail for the characterization of the first control u_1^* .

1. Firstly, on the set $\{t|0 < u_1^*(t) < u_1^{\max}\}$, we have

$$0 = \left. \frac{\partial \mathbb{H}}{\partial u_1} \right|_{u_1^*} = B_1 u_1^* + (\lambda_5 - \lambda_6) k_e S_e^* + (\lambda_8 - \lambda_9) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*).$$

Solving the above equation for u_1^* yields

$$u_1^* = \frac{(\lambda_5 - \lambda_6) k_e S_e^* + (\lambda_8 - \lambda_9) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*)}{-B_1}.$$

2. Secondly, on the set $\{t|u_1^*(t) = 0\}$, we have

$$0 \leq \left. \frac{\partial \mathbb{H}}{\partial u_1} \right|_{u_1^*} = B_1 u_1^* + (\lambda_6 - \lambda_5) k_e S_e^* + (\lambda_9 - \lambda_8) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*).$$

Since $-B_1 < 0$, it then follows that

$$0 \geq \frac{(\lambda_5 - \lambda_6) k_e S_e^* + (\lambda_8 - \lambda_9) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*)}{-B_1},$$

and thus

$$u_1^* = \max \left(\frac{(\lambda_5 - \lambda_6) k_e S_e^* + (\lambda_8 - \lambda_9) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*)}{-B_1}, 0 \right)$$

holds on this set.

3. Finally, on the set $\{t|u_1^*(t) = u_1^{\max}\}$, we have

$$0 \geq \left. \frac{\partial \mathbb{H}}{\partial u_1} \right|_{u_1^{\max}} = B_1 u_1^{\max} + (\lambda_6 - \lambda_5) k_e S_e^* + (\lambda_9 - \lambda_8) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*),$$

or equivalently

$$-B_1 u_1^{\max} \geq (\lambda_6 - \lambda_5) k_e S_e^* + (\lambda_9 - \lambda_8) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*).$$

And dividing both sides by the negative quantity $-B_1$, it yields

$$u_1^{\max} \leq \frac{(\lambda_5 - \lambda_6) k_e S_e^* + (\lambda_8 - \lambda_9) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*)}{-B_1}.$$

Therefore,

$$u_1^* = \min \left(\frac{(\lambda_6 - \lambda_5) k_e S_e^* + (\lambda_9 - \lambda_8) k_a S_a^* + \lambda_{12} k_m (A^* - E_m^* - I_m^*)}{B_1}, u_1^{\max} \right).$$

After examining these three cases, we characterize the optimal control as

$$u_1^* = \max \left(\min \left(\frac{(\lambda_5 - \lambda_6) k_e S_e^* + (\lambda_8 - \lambda_9) k_a S_a^* - \lambda_{12} k_m (A^* - E_m^* - I_m^*)}{B_1}, u_1^{\max} \right), 0 \right).$$

Similarly by going through the three-step arguments the remaining optimal controls u_2^* , u_3^* , u_4^* can also be obtained explicitly.

Furthermore, it is obvious to see that

$$\frac{\partial^2 \mathbb{H}}{\partial u_1^2} = B_1 > 0, \quad \frac{\partial^2 \mathbb{H}}{\partial u_2^2} = B_2 > 0, \quad \frac{\partial^2 \mathbb{H}}{\partial u_3^2} = B_3 > 0, \quad \frac{\partial^2 \mathbb{H}}{\partial u_4^2} = B_4 > 0,$$

indicating that the optimal controls minimize the Hamiltonian. ■

5. NUMERICAL SIMULATIONS

In this section, we present some numerical simulation to illustrate the results obtained in the earlier sections. The parameter values of the disease used to illustrate our theoretical results are from an area of intense transmission. Our main purpose is to show the impact of the different control strategies used together on both the anopheles mosquito population and the number of infected humans within an endemic area. For the readers convenience, they should remember that each of the individuals without control is marked by blue lines. The individuals with control are marked by red lines. For the illustration purposes, we use the parameters values given in Table 7 and the weight constant values in the objective functional are $A_1 = 10, A_2 = 10, A_3 = 10, A_4 = 10, A_5 = 10, A_6 = 10, A_7 = 10, B_1 = 1, B_2 = 1, B_3 = 1$ and $B_4 = 1$.

Figure 3 represents the population of eggs, larva, pupa and adults mosquitoes respectively in two systems, system (8) without control and system (10) with control.

In Figure 4, we illustrate the dynamic of susceptible non-immune humans, partially immune individuals, infectious non-immune and infectious semi-immune individuals with and without control strategies. Furthermore, the different control profiles are illustrated in Figure 5.

From Figure 3 and Figure 4, one can notice that using the different control measures both together leads to the reduction of mosquito population and the number of vulnerable and infected humans within an endemic area.

6. DISCUSSIONS AND CONCLUSION

Based on the susceptibility, the exposure and infectivity of human hosts, Ducrôt *et al.* [17], Koutou *et al.* [24] and Traoré *et al.* [40] have developed two-species malaria model formulated by considering two types of hosts in the human population: non-immune individuals and semi-immune individuals. This paper has

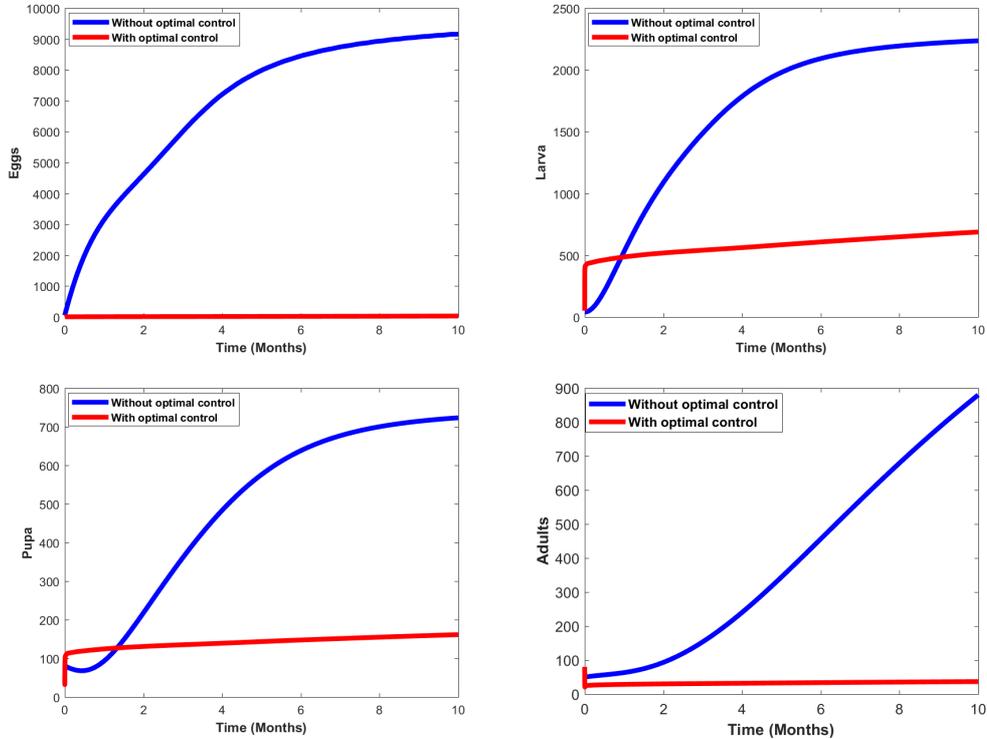


Figure 3. Dynamics behaviors of eggs, larva, pupa and adults mosquitoes, respectively with and without control when $r > r_0$.

extended some previous works [17, 37] and more precisely the study proposed in [24] by considering an optimal control problem of malaria transmission dynamics. Time-dependent intervention strategies have been implemented to reduce the disease transmission over a limited time interval through four types of control. The first three controls account for treatment of infected humans, personal protection and vector control strategies. Indeed, malaria vaccine is undergoing experimentation and has already been implemented in some countries such as Ghana, Kenya, Malawi, to name a few. In the light of that, we have then introduced a fourth control that represents the implementation of an imperfect vaccine. Furthermore, the non-immunes are more vulnerable to malaria than the semi-immunes because they have never acquired immunity against the disease; while the semi-immune individuals have at least once acquired immunity in their life. Hence the reason why, the control $u_4(t)$ targets non-immune individuals who represent children under 5, pregnant women, and people traveling from a non-malaria area to an endemic area.

In addition, the mathematical analysis of the control model has been car-

Parameters	Values	Reference	Dimension
p	0.8	estimated	dimensionless
c_{me}	0.03	[17, 24]	dimensionless
c_{em}	0.45	[17, 24]	dimensionless
c_{ma}	0.022	[17, 24]	dimensionless
c_{am}	0.35	[17, 24]	dimensionless
\tilde{c}_{am}	0.002	[17, 24]	dimensionless
ν_e	0.10	[17, 24]	/month
ν_a	0.09	[17, 24]	/month
ν_m	0.083	[17, 24]	/month
α_e	0.001	[17, 24]	/month
α_a	0.01	[17, 24]	/month
γ_e	0.000018	[17, 24]	/month
γ_a	0.00003	[17, 24]	/month
β_a	0.0027	[17, 24]	/month
ρ_e	0.3	[17, 24]	/month
ρ_a	0.09	[17, 24]	/month
Λ_h	85	estimated	humans/week
f_h	0.00063	[17, 24]	/human/month
f_m	0.1	[17, 24]	/mosquito/days
n_a	0.5	[17, 24]	human/days
K_E	10000	estimated	space
K_L	5000	estimated	space
K_P	4000	estimated	space
b	10.7	[17, 24, 29]	/days
s_E	0.4	[17, 24, 29]	dimensionless
d_E	0.36	[17, 24, 29]	dimensionless
S_L	0.5	[17, 24, 29]	dimensionless
d_L	0.34	[17, 24, 29]	dimensionless
s_P	0.3	[17, 24, 29]	dimensionless
d_P	0.17	[17, 24, 29]	dimensionless
f_m	0.15	[17, 24, 29]	dimensionless

Table 7. Humans and vectors parameter's values for malaria model.

ried out. Using Pontryagin's Maximal Principle [6, 21], we have established the necessary conditions for the existence of optimal control. Indeed, the main prevention measures recommended by the World Health Organization are the use of adult mosquito repulsive, appropriate clothing or treated mosquito nets. And, the means of treatment are essentially the use of drugs such as Aryl aminoalcohol compounds, Antifolate compounds and Artemisinin compounds [43]. However, we are more and more witnessing a genetic mutation in anopheles that gives re-

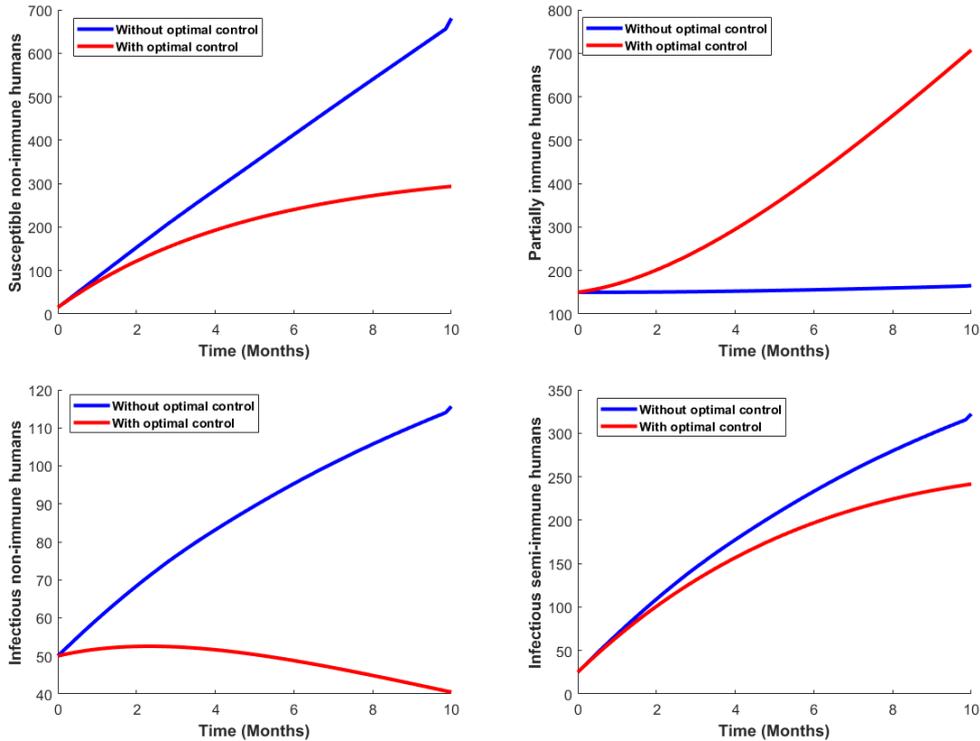


Figure 4. Dynamics behaviors of susceptible humans, partially immune humans, infectious non-immune and semi-immune humans respectively with and without control when $r > r_0$.

sistance to anopheles as well as plasmodium [4, 23, 25]. Therefore, finding other more effective means such as a vaccine is necessary. Moreover, our numerical simulation results show that the reduction or even the eradication of malaria can be achieved by combining prevention and treatment measures. In this case, massive destruction of the aquatic stages of the vector would reduce the number of adult mosquitoes and malaria accordingly (see Figure 3). Besides, a large vaccination campaign targeting the most vulnerable combined with some previous control strategies would reduce the number of vulnerable people, the number of infectious individuals (see Figure 4(a), (c), (d)) and increase the number of partially-immune individuals who are less vulnerable to malaria (see Figure 4(b)). In this regard, we can conclude by saying that even if the malaria vaccine is not yet perfect, combining it with some of the usual malaria control mechanisms would significantly reduce the disease prevalence [2, 6, 39]. Furthermore, major awareness campaigns are also necessary because all these strategies mentioned above would not have a positive impact unless the targeted populations are mobilized for this aim. Thus, this study suggests that, in addition to existing mitigation

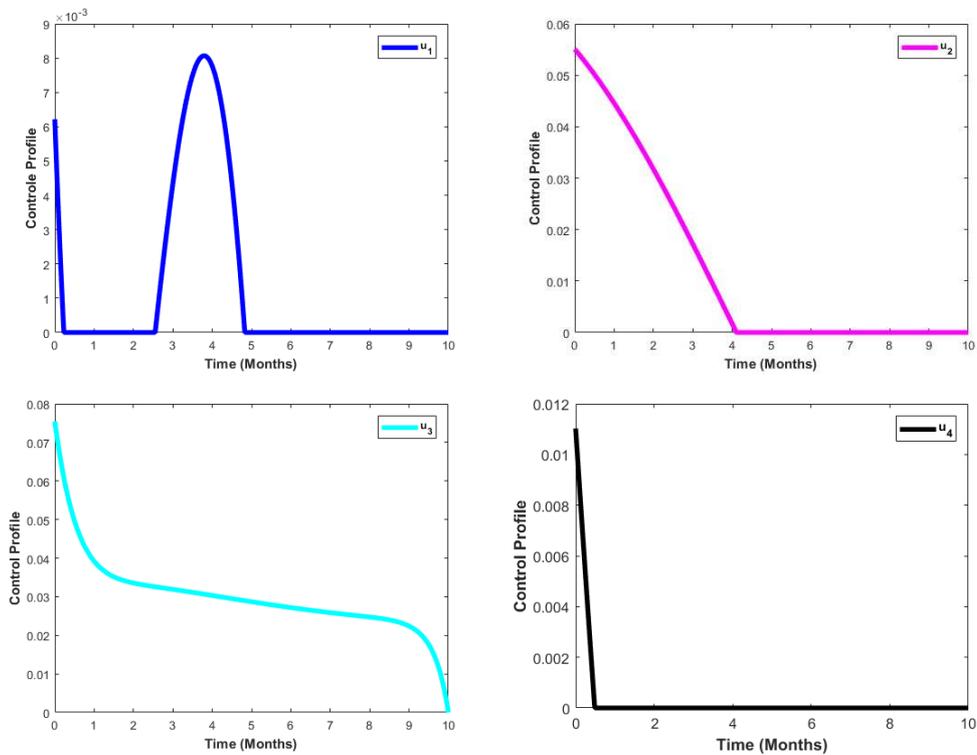


Figure 5. Representation of the different control functions.

strategies, vaccination, if available, would be a critical element of any response plan of malaria eradication [11, 14, 40].

REFERENCES

- [1] H. Abboubakar, J.C. Kamgang, L. N. Nkamba and D. Tieudjo, *Bifurcation thresholds and optimal control in transmission dynamics of arboviral diseases*, J. Math. Biol. **76** (2018) 379–427. doi:10.1007/s00285-017-1146-1
- [2] D. Aldila, T. Gotz and E. Soewono, *An optimal control problem arising from a dengue disease transmission model*, Math. Biosci. **242** (2013) 9–13. doi:10.1016/j.mbs.2012.11.014
- [3] J.K. Asamoah, F.T. Oduro, E. Bonyah and B. Seidu, *Modelling of rabies transmission dynamics using optimal control analysis*, J. Appl. Math., Vol. **2017**, Article ID 2451237, 23 pages. doi:10.1155/2017/2451237
- [4] Z. Bai and Y. Zhou, *Global dynamics of an SEIRS epidemic model with periodic vaccination and seasonal contact rate*, Nonlinear Anal. Real World Appl. **13** (2012)

1060–1068.

doi:10.1016/j.nonrwa.2011.02.008

- [5] E.A. Bakare and O.E. Abolarin, *Optimal control of malaria transmission dynamics with seasonality in rainfall*, Int. J. Pure Appl. Math. **119** (2018) 519–539.
- [6] F.G. Ball, E.S. Knock and P.D. O’Neil, *Control of emerging infectious diseases using responsive imperfect vaccination and isolation*, Math. Biosci. **216** (2008) 100–113.
doi:10.1016/j.mbs.2008.08.008
- [7] N.G. Becker and K. Dietz, *The effect of household distribution on transmission and highly infectious diseases*, Math. Biosci. **127** (1995) 207–219.
- [8] T. Berge, J. M.-S. Lubuma, G.M. Moremedi, N. Morris and R. Kondera-Shava, *A simple mathematical model for Ebola in Africa*, J. Biol. Dyn. **11** (2017) 42–74.
doi:10.1080/17513758.2016.1229817
- [9] D. Bernoulli, *Essai d’une nouvelle analyse de la mortalité causée par la petite vérole*, Mém. Math. Phys. Acad. Roy. Sci. Paris **1** (1766) 1–45.
- [10] J.C. Blackwood and L.M. Childs, *An introduction to compartmental modeling for the budding infectious disease modeler*, Lett. Biomath. **5** (2018) 195–221.
doi:10.1080/23737867.2018.1509026
- [11] K. Blayneh, Y. Cao and Hee-Dae Kwo, *Optimal control of vector-borne diseases: treatment and prevention*, Discrete Cont. Dyn. B **11** (2009) 1–31.
- [12] F. Brauer, *Mathematical epidemiology: Past, present, and future*, Infectious Diseases Modelling, **2** (2017) 113–127.
- [13] N. Chitnis, J.M. Hyman and J.M. Cushing, *Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model*, Bull. Math. Biol. **70** (2008) 1272–1296.
doi:10.1007/s11538-008-9299-0
- [14] C. Chiyaka, J. M. Tchenche, W. Garira and S. Dube, *A mathematical analysis of the effects of control strategies on the transmission dynamics of malaria*, Applied Math. Comput. **195** (2008) 641–662.
doi:10.1016/j.amc.2007.05.016
- [15] K. Cook, Van den Driessche and P.X. Zou, *Interaction of maturation delay and nonlinear birth in population and epidemic models*, J. Math. Biol. **39** (1999) 332–352.
doi:10.1007/s002850050194
- [16] O. Diekmann, J.A.P. Heesterbeek and J.A.J. Metz, *On the definition and the computation of the basic reproduction ratio \mathcal{R}_0 in models for infectious diseases in heterogeneous populations*, J. Math. Biol. **28** (1990) 365–382.
doi:10.1007/bf00178324
- [17] A. Ducrôt, S. Sirima, B. Somé and P. Zongo, *A mathematical model for malaria involving differential susceptibility, exposedness and infectivity of human host*, J. Biol. Dyn. **3** (2009) 574–598.
doi:10.1080/17513750902829393

- [18] W.H. Fleming and R.W. Rishel, *Deterministic and Stochastic Optimal Control* (Springer-Verlag, New York, 2005).
- [19] H. Gaff and E. Schaefer, *Optimal control applied to vaccination and treatment strategies for various epidemiological models*, *Math. Biosci. Eng.* **6** (2009) 469–492.
- [20] H.W. Hethcote, *The mathematics of infectious diseases*, *SIAM review* **42** (2000) 599–693.
- [21] A. Hugo, O.D. Makinde, S. Kumar and F.F. Chibwana, *Optimal control and cost effectiveness analysis for Newcastle disease eco-epidemiological model in Tanzania*, *J. Biol. Dyn.* **11** (2017) 190–209.
doi:10.1080/17513758.2016.1258093
- [22] W.O. Kermack and A.G. McKendrick, *A contribution to the mathematical theory of epidemics*, *Proceeding of the Royal Society of London A* **115** (1927) 700–721.
- [23] O. Koutou, B. Traoré and B. Sangaré, *Mathematical model of malaria transmission dynamics with distributed delay and a wide class of nonlinear incidence rates*, *Cogent Math. Stat.* **5** (2019) 1–25.
doi:10.1080/25742558.2018.1564531
- [24] O. Koutou, B. Traoré and B. Sangaré, *Mathematical modeling of malaria transmission global dynamics: taking into account the immature stages of the vectors*, *Adv. Differ. Equ.* **2018** (2018) 1–34.
doi:10.1186/s13662-018-1671-2
- [25] A.A. Lasharia and G. Zaman, *Optimal control of a vector borne disease with horizontal transmission*, *Nonlinear Anal., Real World Appl.* **13** (2012) 203–212.
doi:10.1016/j.nonrwa.2011.07.026
- [26] Y. Lou and X.-Q. Zhao, *Modelling malaria control by introduction of larvivorous fish*, *Bull. Math. Biol.* **73** (2011) 2384–2407.
doi:10.1007/s11538-011-9628-6
- [27] A.M. Lutambi, M.A. Penny, T. Smith and N. Chitnis, *Mathematical modelling of mosquito dispersal in a heterogeneous environment*, *Math. Biosci.* **241** (2013) 198–216.
doi:10.1016/j.mbs.2012.11.013
- [28] D. Moulay, M.A. Aziz-Alaoui and Hee-Dae Kwon, *Optimal control of chikungunya disease: larvae reduction, treatment and prevention*, *Math. Biosci. Eng.* **9** (2012) 369–392.
- [29] D. Moulay, M.A. Aziz-Alaoui and M. Cadivel, *The chikungunya disease: modeling, vector and transmission global dynamics*, *Math. Biosci.* **229** (2011) 50–63.
doi:10.1016/j.mbs.2010.10.008
- [30] G.A. Ngwa, *On the population dynamics of the malaria vector*, *Bul. Math. Biol.* **68** (2006) 2161–2189.
doi:10.1007/s11538-006-9104-x

- [31] E.O. Omondi, R.W. Mbogo and L.S. Luboobi, *Mathematical modelling of the impact of testing, treatment and control of HIV transmission in Kenya*, Cogent Math. Stat. **5** (2018) 1–16.
doi:10.1080/25742558.2018.1475590
- [32] E.O. Omondi, T.O. Orwa and F. Nyabadza, *Application of optimal control to the onchocerciasis transmission model with treatment*, Math. Biosci. **297** (2018) 43–57.
doi:10.1016/j.mbs.2017.11.009
- [33] H. Ouedraogo, W. Ouedraogo and B. Sangaré, *Bifurcation and stability analysis in complex cross-diffusion mathematical model of phytoplankton-fish dynamics*, J. Part. Diff. Eq. **32** (2019) 207–228.
doi:10.11145/j.biomath.2019.11.237
- [34] H. Ouedraogo, W. Ouedraogo and B. Sangaré, *A mathematical model with a trophic chain predation based on the ODEs to describe fish and plankton dynamics*, An. Univ. Craiova Ser. Mat. Inform. **46** (2019) 164–177.
- [35] H. Ouedraogo, W. Ouedraogo and B. Sangaré, *A self-Diffusion Mathematical Model to Describe the Toxin Effect on the Zooplankton Dynamics*, Nonlinear Dyn. Syst. Theory **18** (2018) 392–408.
- [36] M. Ozair, A.A. Lashari, I.H. Jung and K.O. Okusun, *Stability analysis and optimal control of a vector-borne disease with nonlinear incidence*, Discrete Dyn. Nat. Soc. **2012**, Article ID 595487, 21 pages
- [37] H.S. Rodrigues, M.T.T. Monteiro and D.F.M. Torres, *Vaccination models and optimal control strategies to dengue*, Math. Biosci. **247** (2014) 1–12.
- [38] A. Savadogo, H. Ouedraogo, B. Sangaré and W. Ouedraogo, *Mathematical analysis of a fish-plankton eco-epidemiological system*, Nonlinear Stud. **27** (2020) 237–258.
- [39] B. Traoré, O. Koutou and B. Sangaré, *A mathematical model of malaria transmission dynamics with general incidence function and maturation delay in a periodic environment*, Lett. Biomath. **7** (2020) 37–54.
- [40] B. Traoré, O. Koutou and B. Sangaré, *A global mathematical model of malaria transmission dynamics with structured mosquito population and temperature variations*, Nonlinear Anal. Real World Appl. **53** (2020) 1–33.
doi:10.1016/j.nonrwa.2019.103081
- [41] B. Traoré, O. Koutou and B. Sangaré, *Global dynamics of a seasonal mathematical model of schistosomiasis transmission with general incidence function*, J. Biol. Syst. **27** (2019) 1–31.
doi:10.1142/s0218339019500025
- [42] B. Traoré, B. Sangaré and S. Traoré, *Mathematical model of mosquito populations dynamics with logistic growth in a periodic environment*, An. Univ. Craiova, Ser. Mat. Inf. **45** (2018) 86–102.
- [43] World Health Organisation (WHO), *Global malaria programme*, World malaria report, 2018.

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