Optimal Control of Arboviral Diseases

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ABSTRACT. In this paper, we derive and analyse a model for the control of arboviral diseases which takes into account an imperfect vaccine combined with some other mechanisms of control already studied in the literature. We use five time dependent controls, to assess the impact of vaccination combined with treatment, individual protection and vector control strategies such as killing adult vectors, reduction of eggs and larvae. By using optimal control theory, we establish optimal conditions under which the disease can be eradicated and we examine the impact of a possible combined control tools on the disease transmission. The Pontryagin's maximum principle is used to characterize the optimal control. Numerical simulationsshow that, vaccination combined with other control mechanisms, would reduce the spread of the disease appreciably.

RÉSUMÉ. Dans cet article, nous dérivons et analysons un modèle, pour le contrôle des arboviroses, qui prend en compte un vaccin imparfait combiné avec d'autres mécanismes de contrôle déjà étudiés dans la littérature. Nous utilisons cinq contrôles dépendant du temps, pour évaluer l'impact de la vaccination combiné avec le traitement, la protection individuelle et les stratégies de lutte anti-vectoriel telles que l'utilisation des adulticides et des larvicides. En utilisant la théorie du contrôle optimal, nous établissons des conditions optimales dans lesquelles la maladie peut être éradiquée et nous examinons l'impact d'une éventuelle combinaison de contrôle sur la transmission de la maladie. Le principe du maximum de Pontryagin est utilisé pour caractériser le contrôle optimal. Des simulations numériques montrent que la vaccination combinée avec d'autres mécanismes de contrôle, permettrait de réduire de façon considérable la propagation de la maladie.

KEYWORDS : Arboviral diseases; Optimal control; Pontryagin's Maximum Principle.

MOTS-CLÉS : Arboviroses, Contrôle optimal, Maximum de Pontryagin.

1. Introduction

Arboviral diseases are affections transmitted by hematophagous arthropods. There are currently 534 viruses registered in the International Catalog of Arboviruses and 25% of them have caused documented illness in human populations [6, 11]. Examples of those kinds of diseases are Dengue, Yellow fever, Saint Louis fever, Encephalitis, West Nile fever and Chikungunya. A wide range of arboviral diseases are transmitted by mosquito bites and constitute a public health emergency of international concern. For example, Dengue, caused by any of four closely-related virus serotypes (DEN-1-4) of the genus Flavivirus, causes 50–100 million infections worldwide every year, and the majority of patients worldwide are children aged 9 to 16 years [19, 22].

For all the diseases mentioned above, only yellow fever has a licensed vaccine. Nevertheless, considerable efforts are made to obtain vaccines for other diseases. In the case of dengue, for example, tests carried out in Asia and Latin America, have shown that the future dengue vaccine will have a efficacy between 30.2% and 77.7%, and this, depending on the serotype [18, 21]. Also, the future dengue vaccine will have an overall efficacy of 60.8% against all forms of the disease in children and adolescents aged 9-16 years who received three doses of the vaccine[20].

As the future vaccines (e.g., dengue vaccine) will be imperfect, it is therefore necessary to combine such vaccines with some control mechanisms (individual protection, treatment, chemical control) [1, 2, 15], to find the best sufficient combination, which permit to decrease the expansion of these kind of diseases in human communities.

A number of studies have been conducted to study host-vector models for arboviral diseases transmission. Some of these works have been conducted to explore optimal control theory for arboviral disease models (see [3, 4, 7, 14, 17]).

None of the above mentioned models takes into account the combination of optimal control mechanisms such as vaccination, individual protection, treatment and vector control strategies. In our effort, we investigate such optimal strategies for vaccination combined with individual protection, treatment and two vector controls (adulticiding–killing of adult vectors, and larviciding–killing eggs and larvae), using two systems of ODEs which consist of a complete stage structured model Eggs-Larvae-Pupae for the vectors, and a SEI/SEIR type model for the vector/host population. This provides a new different mathematical perspective to the subject.

The rest of the paper is organized as follows. In Section 2 we present the optimal control problem and its mathematical analysis. Section 3 is devoted to numerical simulations. A conclusion round up the paper.

2. A Model for Optimal Control

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 addition of controls used in [14], we add vaccination and the control of adult vectors as control variables to reduce or even eradicate the disease. So we introduce five time dependent controls:

1) The first control $0 \leq u_1(t) \leq 1$ denotes the percentage of susceptible individuals that one decides to vaccinate at time t. A parameter ω associated to the control $u_1(t)$ represents the waning immunity process [17].

2) The second control $0 \leq u_2(t) \leq 1$ represents efforts made to protect human from mosquito bites. It mainly consists to the use of mosquito nets or wearing appropriate clothes [14]. Thus we modify the infection term as follows:

$$\lambda_h^c = (1 - \alpha_1 u_2(t))\lambda_h, \quad , \lambda_v^c = (1 - \alpha_1 u_2(t))\lambda_v \tag{1}$$

where α_1 measures the effectiveness of the prevention measurements against mosquito bites.

3) The third control $0 \leq u_3(t) \leq 1$ 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 [14]. Thus we modify the recovery rate such that $\sigma_h^c := \sigma_h + \alpha_2 u_3$. α_2 is the effectiveness of the anti-arboviral diseases drugs with $\alpha_2 = 0.3$ [14]. Note that this control also permit to reduce the disease-induced death.

4) The fourth control $0 \leq u_4(t) \leq 1$ represents mosquitoes adulticiding effort with killing efficacy c_m. Thus the mosquito natural mortality rate becomes $\mu_v^c = \mu_v + c_m u_4(t)$.

5) The fifth control $0 \leq u_5(t) \leq 1$ represents the effect of interventions used for the vector control. It mainly consists in the reduction of breeding sites with chemical application methods, for instance using larvicides like BTI (*Bacillus Thuringensis Israelensis*) which is a biological larvicide, or by introducing larvivore fish. This control focuses on the reduction of the number of larvae, and thus eggs, of any natural or artificial water-filled container [14]. Thus the eggs and Larvae natural mortality rate become $\mu_E^c = \mu_E + \eta_1 u_5(t)$ and $\mu_L^c = \mu_L + \eta_2 u_5(t)$ where η_1, η_2, represent the chemical eggs and larvae mortality rate, respectively [14].

Note that $0 \leq u_i \leq 1$, for $i = 1, \ldots, 5$, means that when the control is zero there is no any effort invested (i.e. no control) and when it is one, the maximum control effort is invested.

Therefore, our optimal control model of arboviral diseases reads as

$$\begin{cases} \dot{S}_h &= \Lambda_h - \left[(1 - \alpha_1 u_2(t))\lambda_h + \mu_h + u_1(t)\right] S_h + \omega u_1(t) R_h \\ \dot{E}_h &= (1 - \alpha_1 u_2(t))\lambda_h S_h - (\mu_h + \gamma_h) E_h \\ \dot{I}_h &= \gamma_h E_h - \left[\mu_h + (1 - \alpha_2 u_3(t))\delta + \sigma + \alpha_2 u_3(t)\right] I_h \\ \dot{R}_h &= (\sigma + \alpha_2 u_3(t)) I_h + u_1 S_h - (\mu_h + \omega u_1) R_h \\ \dot{S}_v &= \theta P - (1 - \alpha_1 u_2(t))\lambda_v S_v - (\mu_v + c_m u_4(t)) S_v \\ \dot{E}_v &= (1 - \alpha_1 u_2(t))\lambda_v S_v - (\mu_v + \gamma_v + c_m u_4(t)) E_v \\ \dot{I}_v &= \gamma_v E_v - (\mu_v + c_m u_4(t)) I_v \\ \dot{E} &= \mu_b \left(1 - \frac{E}{\Gamma_E}\right)(S_v + E_v + I_v) - (s + \mu_E + \eta_1 u_5(t)) E \\ \dot{L} &= sE \left(1 - \frac{L}{\Gamma_L}\right) - (l + \mu_L + \eta_2 u_5(t)) L \\ \dot{P} &= lL - (\theta + \mu_P) P \end{cases} \tag{2}$$

with initial conditions given at $t = 0$.

The states variables and parameters of model (2) are described in Table 1 and 2.

For the non-autonomous system (2), the rate of change of the total populations of humans and adults vectors is given, respectively, by

$$\begin{cases} \dot{N}_h &= \Lambda_h - \mu_h N_h - (1 - \alpha_2 u_3(t))\delta I_h \\ \dot{N}_v &= \theta P - (\mu_v + c_m u_4(t)) N_v \end{cases} \tag{3}$$

For bounded Lebesgue measurable controls and non-negative initial conditions, non-negative bounded solutions to the state system exist [12].

Table 1: The state variables of model (2).

	Humans		Aquatic Vectors		Adult Vectors
S_h:	Susceptible	E:	Eggs	S_v:	Susceptible
E_h:	Infected in latent stage	L:	Larvae	E_v	Infected in latent stage
I_h:	Infectious	P:	Pupae	I_v	Infectious
R_h:	Resistant (immune)				

Table 2: Description and baseline values/range of parameters of model 2. The baseline values refer to dengue fever transmission.

Parameter	Description	Baseline value/range	Sources
Λ_h	Recruitment rate of humans	$2.5\ day^{-1}$	[10]
μ_h	Natural mortality rate in humans	$\frac{1}{(67\times365)}\ day^{-1}$	[10]
a	Average number of bites	$1\ day^{-1}$	[3, 10]
β_{hv}	Probability of transmission of infection from an infected vector to a susceptible human	$0.1, 0.75\ day^{-1}$	[3, 10]
γ_h	Progression rate from E_h to I_h	$\left[\frac{1}{15}, \frac{1}{3}\right]\ day^{-1}$	[8]
δ	Disease–induced death rate	$10^{-3}\ day^{-1}$	[10]
σ	Recovery rate for humans	$0.1428\ day^{-1}$	[3, 10]
η_h,η_v	Modifications parameter	$[0, 1)$	[10]
μ_v	Natural mortality rate of vectors	$\left[\frac{1}{30}, \frac{1}{14}\right]\ day^{-1}$	[3, 10]
γ_v	Progression rate from E_v to I_v	$\left[\frac{1}{21}, \frac{1}{2}\right]\ day^{-1}$	[8]
β_{vh}	Probability of transmission of infection from an infected human to a susceptible vector	$0.1, 0.75\ day^{-1}$	[3, 10]
θ	Maturation rate from pupae to adult	$0.08\ day^{-1}$	[8, 14]
μ_b	Number of eggs at each deposit	$6\ day^{-1}$	[8]
Γ_E	Carrying capacity for eggs	$10^3, 10^6$	[3]
Γ_L	Carrying capacity for larvae	$5\times10^2, 5\times10^5$	[3]
μ_E	Eggs death rate	0.2 or 0.4	[14]
μ_L	Larvae death rate	0.2 or 0.4	[14]
μ_P	Pupae death rate	0.4	Assumed
s	Transfer rate from eggs to larvae	$0.7\ day^{-1}$	[14]
l	Transfer rate from larvae to pupae	$0.5\ day^{-1}$	[13]

The objective of control is to minimize: the number of symptomatic humans infected with arboviruses (that is, to reduce sub-population I_h), the number of vector (N_v) and the number of eggs and larvae (that is, to reduce sub-population E and L, respectively), while keeping the costs of the control as low as possible.

To achieve this objective we must incorporate the relative costs associated with each policy (control) or combination of policies directed towards controlling the spread of arboviral diseases. We define the objective function as

$$J(u_1,u_2,u_3,u_4,u_5)=\int_0^{t_f}\left[D_1I_h(t)+D_2N_v(t)+D_3E(t)+D_4L(t)+\sum_{i=1}^{5}B_iu_i^2(t)\right]dt \tag{4}$$

and the control set

$$\Delta=\{(u_1,u_2,u_3,u_4,u_5)|u_i(t)\text{ is Lebesgue measurable on }[0,t_f],\ 0\le u_i(t)\le 1, i=1,\dots,5\}.$$

The first fourth terms in the integrand J represent benefit of I_h, N_v, E and L populations, describing the comparative importance of the terms in the functional. A high value of D_1 for example, means that it is more important to reduce the burden of disease as reduce the costs related to all control strategies [5]. Positive constants B_i, $i=1,\dots,5$ are weight for vaccination, individual protection (human), treatment and vector control effort respectively, which regularize the optimal control. In line with the authors of some studies on the optimal control (see [7, 14, 17]), we choose a linear function for the cost on infection, D_1I_h, D_2N_v, D_3E, D_4L, and quadratic forms for the cost on the controls $B_1u_1^2$, $B_2u_2^2$, $B_3u_3^2$, $B_4u_4^2$, and $B_5u_5^2$. This choice can be justified by the following arguments:

1) An epidemiological control can be likened to an expenditure of energy, by bringing to the applications of physics in control theory;

2) In a certain sense, minimize u_i is like minimize u_i^2, because $u_i\ge 0$, $i=1,\dots,5$.

3) Among the nonlinear representation of intervention costs, the quadratic approximation is the simplest and most widely used, contrary to the linear controls that usually lead to the bang-bang controls.

We solve the problem using optimal control theory.

Theorem 1. *Let $X=(S_h,E_h,I_h,R_h,S_v,E_v,I_v,E,L,P)$. The following set*

$$\Omega=\left\{X\in\mathbf{R}^{10}:N_h\le\frac{\Lambda_h}{\mu_h};E\le\Gamma_E;L\le\Gamma_L;P\le\frac{l\Gamma_L}{k_7};N_v\le\frac{\theta l\Gamma_L}{k_7k_8}\right\}$$

is positively invariant under system (2).

Proof. On the one hand, one can easily see that it is possible to get,

$$\begin{cases}\dot{S}_h & \ge-(\lambda_h+\mu_h)S_h,\ \dot{E}_h\ge-(\mu_h+\gamma_h)E_h,\ \dot{I}_h\ge-(\mu_h+\delta+\sigma)I_h,\ \dot{R}_h\ge-\mu_hR_h\\ \dot{E} & \ge-(\frac{\mu_b}{K_E}+s+\mu_E+\eta_1)E,\ \dot{L}\ge-(\frac{s}{K_L}+l+\mu_L+\eta_2)L,\ \dot{P}\ge-(\theta+\mu_P+\eta_3)P\\ \dot{S}_v & \ge-(\lambda_v+\mu_v)S_v,\ \dot{E}_v\ge-(\mu_v+\gamma_v)E_v,\ \dot{I}_v\ge-\mu_vI_v,\end{cases} \tag{5}$$

for $(S_h(0),E_h(0),I_h(0),R_h(0),E(0),A(0),P(0),S_v(0),E_v(0),I_v(0))\ge 0$. Thus, solutions with initial value in Ω remain nonnegative for all $t\ge 0$. On the other hand, we have

$$\begin{cases} \dot{N}_h & \leq \Lambda_h - \mu_h N_h \\ \dot{N}_v & \leq \theta P - \mu_v N_v \\ \dot{E} & \leq \mu_b \left(1 - \dfrac{E}{K_E}\right)(S_v + E_v + I_v) - (s + \mu_E)E \\ \dot{L} & \leq sE \left(1 - \dfrac{L}{K_L}\right) - (l + \mu_L)L \\ \dot{P} & \leq lL - (\theta + \mu_P)P \end{cases} \tag{6}$$

The right hand side of the inequalities correspond to the transmission model without control, and it is easy to show that solutions remain in Ω. Then using Gronwall's inequality, we deduce that solutions of (2) are bounded. □

2.1. Existence of an optimal control

The existence of an optimal control can be obtained by using a result of Fleming and Rishel [9].

Theorem 2. *Consider the control problem with system* (2)*.*
There exists $u^\star = (u_1^\star, u_2^\star, u_3^\star, u_4^\star, u_5^\star)$ *such that*

$$\min_{(u_1,u_2,u_3,u_4,u_5)\in\Delta} J(u_1, u_2, u_3, u_4, u_5) = J(u_1^\star, u_2^\star, u_3^\star, u_4^\star, u_5^\star)$$

Proof. To use an existence result, Theorem III.4.1 from [9], we must check if the following properties are satisfied:

1) the set of controls and corresponding state variables is non empty;

2) the control set Δ is convex and closed;

3) the right hand side of the state system is bounded by a linear function in the state and control;

4) the integrand of the objective functional is convex;

5) there exist constants $c_1 > 0$, $c_2 > 0$, and $\beta > 1$ such that the integrand of the objective functional is bounded below by $c_1 \left(\sum_{i=1}^{5} |u_i|^2\right)^{\frac{\beta}{2}} - c_2$.

In order to verify these properties, we use a result from Lukes [12] to give the existence of solutions for the state system (2) with bounded coefficients, which gives condition 1. Since by definition, the control set Δ is bounded , then condition 2 is satisfied. The right hand side of the state system (2) satisfies condition 3 since the state solutions are bounded. The integrand of our objective functional is clearly convex on Δ, which gives condition 4. There are $c_1 > 0, c_2 > 0$ and $\beta > 1$ satisfying $D_1 I_h + D_2 N_v + D_3 E + D_4 L + \sum_{i=1}^{5} B_i u_i^2 \geq c_1 \left(\sum_{i=1}^{5} |u_i|^2\right)^{\frac{\beta}{2}} - c_2$, because the states variables are bounded. Thus condition 5 is satisfied. We conclude that there exists an optimal control $u^* = (u_1^\star, u_2^\star, u_3^\star, u_4^\star, u_5^\star)$ that minimizes the objective functional $J(u_1, u_2, u_3, u_4, u_5)$. □

2.2. Characterization of an optimal control

The necessary conditions that an optimal control must satisfy come from the Pontryagin's Maximum Principle (PMP) [16]. This principle converts (2)-(4) into a problem of minimizing point wise a Hamiltonian $\mathbb{H}$, with respect to $(u_1, u_2, u_3, u_4, u_5)$:

$$\begin{aligned}
\mathbb{H} &= D_1 I_h + D_2 N_v + D_3 E + D_4 L + \sum_{i=1}^{5} B_i u_i^2 \\
&+ \lambda_{S_h} \left\{ \Lambda_h - \left[(1-\alpha_1 u_2)\lambda_h + \mu_h + u_1 \right] S_h + \omega u_1 R_h \right\} \\
&+ \lambda_{E_h} \left\{ \left[1-\alpha_1 u_2 \right] \lambda_h S_h - (\mu_h + \gamma_h) E_h \right\} \\
&+ \lambda_{I_h} \left\{ \gamma_h E_h - (\mu_h + (1-\alpha_2 u_3)\delta + \sigma + \alpha_2 u_3) I_h \right\} \\
&+ \lambda_{R_h} \left\{ (\sigma + \alpha_2 u_3) I_h + u_1 S_h - (\mu_h + \omega u_1) R_h \right\} \\
&+ \lambda_{S_v} \left\{ \theta P - \left[1-\alpha_1 u_2 \right] \lambda_v S_v - (\mu_v + c_m u_4) S_v \right\} \\
&+ \lambda_{E_v} \left\{ (1-\alpha_1 u_2)\, \lambda_v S_v - (\mu_v + \gamma_v + c_m u_4) E_v \right\} + \lambda_{I_v} \left\{ \gamma_v E_v - (\mu_v + c_m u_4) I_v \right\} \\
&+ \lambda_E \left\{ \mu_b \left(1 - \frac{E}{\Gamma_E} \right) (S_v + E_v + I_v) - (s + \mu_E + \eta_1 u_5) E \right\} \\
&+ \lambda_L \left\{ sE \left(1 - \frac{L}{\Gamma_L} \right) - (l + \mu_L + \eta_2 u_5) L \right\} \\
&+ \lambda_P \left\{ lL - (\theta + \mu_P) P \right\}
\end{aligned} \tag{7}$$

where the λ_i, $i = S_h, E_h, I_h, R_h, S_v, E_v, I_v, E, L, P$ are the adjoint variables or co-state variables. Applying Pontryagin's Maximum Principle [16], we obtain the following result.

Theorem 3. *Given an optimal control* $u^\star = (u_1^\star, u_2^\star, u_3^\star, u_4^\star, u_5^\star)$ *and solutions* $(S_h^\star, E_h^\star, I_h^\star, R_h^\star, S_v^\star, E_v^\star, I_v^\star, E^\star, A^\star, P^\star)$ *of the corresponding state system* (2)*, there exist adjoint variables* $\Pi = (\lambda_{S_h}, \lambda_{E_h}, \lambda_{I_h}, \lambda_{R_h}, \lambda_{S_v}, \lambda_{E_v}, \lambda_{I_v}, \lambda_E, \lambda_L, \lambda_P)$ *satisfying,*

$$\begin{aligned}
\frac{d\lambda_{S_h}}{dt} &= \mu_h \lambda_{S_h} + u_1(\lambda_{S_h} - \lambda_{R_h}) + (1-\alpha_1 u_2)\lambda_h \left(1 - \frac{S_h}{N_h} \right) (\lambda_{S_h} - \lambda_{E_h}) \\
&\quad + (1-\alpha_1 u_2) \frac{S_v \lambda_v}{N_h} (\lambda_{E_v} - \lambda_{S_v})
\end{aligned} \tag{8}$$

$$\begin{aligned}
\frac{d\lambda_{E_h}}{dt} &= \mu_h \lambda_{E_h} + \gamma_h (\lambda_{E_h} - \lambda_{I_h}) + (1-\alpha_1 u_2) \frac{S_h \lambda_h}{N_h} (\lambda_{E_h} - \lambda_{S_h}) \\
&\quad + (1-\alpha_1 u_2) \frac{S_v}{N_h} (a\beta_{vh}\eta_h - \lambda_v) (\lambda_{S_v} - \lambda_{E_v})
\end{aligned} \tag{9}$$

$$\begin{aligned}
\frac{d\lambda_{I_h}}{dt} &= -D_1 + \left[\mu_h + (1-\alpha_2 u_3)\delta \right] \lambda_{I_h} + (\sigma + \alpha_2 u_3)(\lambda_{I_h} - \lambda_{R_h}) \\
&\quad + (1-\alpha_1 u_2) \frac{S_h \lambda_h}{N_h} (\lambda_{E_h} - \lambda_{S_h}) + (1-\alpha_1 u_2) \frac{S_v}{N_h} (a\beta_{vh} - \lambda_v) (\lambda_{S_v} - \lambda_{E_v})
\end{aligned} \tag{10}$$

$$\frac{d\lambda_{R_h}}{dt} = \mu_h\lambda_{R_h} + \omega u_1(\lambda_{R_h} - \lambda_{S_h}) + (1-\alpha_1 u_2)\frac{S_h\lambda_h}{N_h}(\lambda_{E_h} - \lambda_{S_h}) + (1-\alpha_1 u_2)\frac{S_v\lambda_v}{N_h}(\lambda_{E_v} - \lambda_{S_v}) \tag{11}$$

$$\frac{d\lambda_{S_v}}{dt} = -D_2 + (\mu_v + c_m u_4)\lambda_{S_v} + (1-\alpha_1 u_2)\lambda_v(\lambda_{S_v} - \lambda_{E_v}) - \mu_b\left(1 - \frac{E}{\Gamma_E}\right)\lambda_E \tag{12}$$

$$\frac{d\lambda_{E_v}}{dt} = -D_2 + (\mu_v + c_m u_4)\lambda_{E_v} + \gamma_v(\lambda_{E_v} - \lambda_{I_v}) + a\eta_v\beta_{hv}(1-\alpha_1 u_2)(\lambda_{S_h} - \lambda_{E_h})\frac{S_h}{N_h} - \mu_b\left(1 - \frac{E}{\Gamma_E}\right)\lambda_E \tag{13}$$

$$\frac{d\lambda_{I_v}}{dt} = -D_2 + (\mu_v + c_m u_4)\lambda_{I_v} + a\beta_{hv}(1-\alpha_1 u_2)\frac{S_h}{N_h}(\lambda_{S_h} - \lambda_{E_h}) - \mu_b\left(1 - \frac{E}{\Gamma_E}\right)\lambda_E \tag{14}$$

$$\frac{d\lambda_E}{dt} = -D_3 + \left[\frac{\mu_b}{\Gamma_E}N_v + s + \mu_E + \eta_1 u_5\right]\lambda_E - s\left(1 - \frac{L}{\Gamma_L}\right)\lambda_L \tag{15}$$

$$\frac{d\lambda_L}{dt} = -D_4 - l\lambda_P + \left[\frac{s}{\Gamma_L}E + \mu_L + l + \eta_2 u_5\right]\lambda_L \tag{16}$$

$$\frac{d\lambda_P}{dt} = (\mu_P + \theta)\lambda_P - \theta\lambda_{S_v} \tag{17}$$

and the transversality conditions

$$\lambda_i^*(t_f) = 0, \qquad i = 1, \ldots 10. \tag{18}$$

Furthermore,

$$\begin{aligned}
u_1^\star &= \min\left\{1, \max\left(0, \frac{(S_h - \omega R_h)(\lambda_{S_h} - \lambda_{R_h})}{2B_1}\right)\right\},\\
u_2^\star &= \min\left\{1, \max\left(0, \frac{\alpha_1\left[\lambda_h S_h(\lambda_{E_h} - \lambda_{S_h}) + \lambda_v S_v(\lambda_{E_v} - \lambda_{S_v})\right]}{2B_2}\right)\right\},\\
u_3^\star &= \min\left\{1, \max\left(0, \frac{\alpha_2\left[(1-\delta)\lambda_{I_h} - \lambda_{R_h}\right]I_h}{2B_3}\right)\right\},\\
u_4^\star &= \min\left\{1, \max\left(0, \frac{c_m\left[S_v\lambda_{S_v} + E_v\lambda_{E_v} + I_v\lambda_{I_v}\right]}{2B_4}\right)\right\},\\
u_5^\star &= \min\left\{1, \max\left(0, \frac{\eta_1 E\lambda_E + \eta_2 L\lambda_L}{2B_5}\right)\right\}.
\end{aligned} \tag{19}$$

Proof. The differential equations governing the adjoint variables are obtained by differentiation of the Hamiltonian function, evaluated at the optimal control. Then the adjoint system can be written as

$$\frac{d\lambda_{S_h}}{dt} = -\frac{\partial \mathbb{H}}{\partial S_h}, \ \frac{d\lambda_{E_h}}{dt} = -\frac{\partial \mathbb{H}}{\partial E_h}, \ \frac{d\lambda_{I_h}}{dt} = -\frac{\partial \mathbb{H}}{\partial I_h}, \ \frac{d\lambda_{R_h}}{dt} = -\frac{\partial \mathbb{H}}{\partial R_h}, \ \frac{d\lambda_{S_v}}{dt} = -\frac{\partial \mathbb{H}}{\partial S_v}$$
$$\frac{d\lambda_{E_v}}{dt} = -\frac{\partial \mathbb{H}}{\partial E_v}, , \ \frac{d\lambda_{I_v}}{dt} = -\frac{\partial \mathbb{H}}{\partial I_v}, \ \frac{d\lambda_E}{dt} = -\frac{\partial \mathbb{H}}{\partial E}, \ \frac{d\lambda_L}{dt} = -\frac{\partial \mathbb{H}}{\partial L}, \ \frac{d\lambda_P}{dt} = -\frac{\partial \mathbb{H}}{\partial P},$$

with zero final time conditions (transversality).

To get the characterization of the optimal control given by (19), we follow [14, 17] and solve the equations on the interior of the control set,

$$\frac{\partial \mathbb{H}}{\partial u_i} = 0, \ i = 1, \ldots, 5.$$

Using the bounds on the controls, we obtain the desired characterization. This ends the proof. □

3. Numerical simulations and discussion

The simulations were carried out using the values of Table 3. We use an iterative scheme to solve the optimality system.

The optimality system for our problem is derived (see Appendix) and numerically solved by using the so called forward–backward sweep method (FBSM).The process begin with an initial guess on the control variable. Then, the state equations are solved simultaneously forward in time, and next the adjoint equations (8)– (17) are simultaneously solved backward in time. The control is updated by inserting the new values of states and adjoints into its characterization, and the process is repeated until convergence occurs (see e.g. [5, 14]).

The values chosen for the weights in the objective functional J (see Eq. (4)) are given in Table 4. Table 5 gives the initial conditions of state variables. We simulated the system (2) in a period of twenty days ($t_f = 20$).

Table 3: Value of parameters used in numerical simulations.

Parameter	Value	Parameter	Value	Parameter	Value	Parameter	Value
μ_v	$\frac{1}{30}$	l	0.5	α_2	0.5	γ_h	$\frac{1}{14}$
a	1	μ_E	0.2	μ_h	$\frac{1}{67*365}$	γ_v	$\frac{1}{21}$
Λ_h	2.5	μ_b	6	θ	0.08	μ_P	0.4
β_{hv}	0.75			σ	0.1428	η_v	0.35
β_{vh}	0.75	ω	0.05	μ_L	0.4	δ	10^{-3}
Γ_E	10000	s	0.7	η_1	0.001	η_2	0.3
Γ_L	5000	η_h	0.35	c_m	0.2	α_1	0.5

3.1. Vaccination combined with individual protection, adulticide and larvicide

With this strategy, only the combination of the control u_1 on vaccination, the control u_2 on individual protection, the control u_4 on adulticide and the control u_5 on larvicide, is used to minimise the objective function J (4), while the other control u_3 are set to zero.

Table 4: Numerical values for the cost functional parameters.

Parameters	Value	Source	Parameters	Value	Source
D_1:	10,000	[14]	B_1	10	Assumed
D_2:	10,000	[14]	B_2:	10	[14]
D_3:	5000	Assumed	B_3:	10	[14]
D_4:	1	[14]	B_4:	10	Assumed
			B_5	10	[14]

Table 5: Initial conditions.

Human states	Initial value	Adult Vector states	Initial value	Aquatic states	Initial value
S_{h_0}:	700	S_{v_0}	3000	E_0	10000
E_{h_0}:	220	E_{v_0}	400	L_0	5000
I_{h_0}:	100	I_{v_0}	120	P_0	3000
R_{h_0}:	60				

On figure 1, we observed that the control strategy resulted in a decrease in the number of infected humans (I_h) while an increase is observed in the number of infected humans (I_h) in strategy without control. The use of this combination have a great impact on the decreasing total vector population (N_v), as well as aquatic vector populations (E and L).

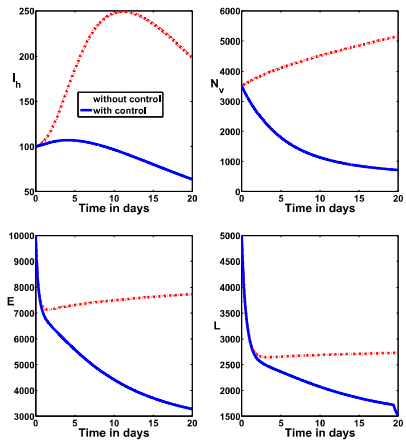

Figure 1: Simulation results of optimal control model (2) showing the effect of using optimal vaccination combined with individual protection, adulticide and larvicide ($u_1 \neq 0$, $u_2 \neq 0$, $u_4 \neq 0$, $u_5 \neq 0$).

3.2. The combination of all the five controls

In this strategy, the combination of all the five controls is applied. On figure 2, we observed that combining all the five controls gives a better result in a decrease in the

number of infected humans (I_h), as well as, the total number of vector population (N_v), and the aquatic vector populations (E and L).

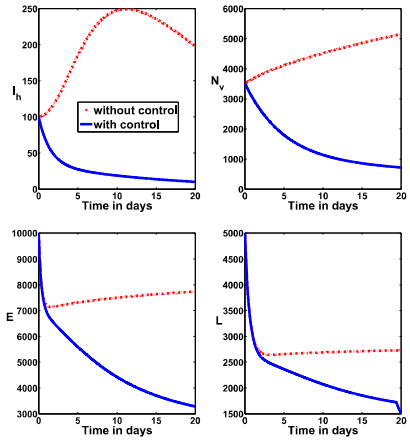

Figure 2: Simulation results of optimal control model (2) showing the effect of using the combination of all the five controls ($u_i \neq 0, i = 1, \ldots, 5$).

4. Conclusion

In this paper, we derived and analysed a model for the control of arboviral diseases with non linear form of infection and complete stage structured model for vectors, and which takes into account a vaccination with waning immunity, treatment, individual protection and vector control strategies (adult vectors, eggs and larvae reduction strategies).

We performed optimal control analysis of the model. In this light, we addressed the optimal control by deriving and analysing the conditions for optimal eradication of the disease and in a situation where eradication is impossible or of less benefit compared with the cost of intervention, we also derived and analysed the necessary conditions for optimal control of the disease.

From the numerical results, we concluded that the optimal strategy to effectively control arboviral diseases is the combination of vaccination, individual protection, (with or without treatment), and other mechanisms of vector control (by chemical intervention). However this conclusion must be taken with caution because of the uncertainties around the parameter values and to the budget/resource limitation.

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