Optimal Control Strategy for a Discrete Chikungunya Model

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Abstract: ***Throught history, anthropod-borne-viruses including Malaria, Dengue, Yellow fever or, more recently chikungunya, have existed, they maitain themselves in nature by going through a cycle between a host. Preliminary diagnosis of arbovirus infection is usually based on clinical presentations of symptoms, places and dates of travel, activities and epidemiological history of location where infection occured. Vector control measures, especially mosquito control are essential to reducing the transmission of disease by anthropod-borne-virus (arboviruses). In this paper, we give an optimal control strategy based on biological observations in the case of tropical disease: chikungunya virus, transmitted by mosquitos of Aedes genus. Until no effective treatment have been yet discovered, two main efforts to limit chikungunya infections are introduced in this study and for which optimal control theory is applied, using numerical simulations to prove the effectiveness of the approach.***

Keywords: optimal control, chikungunya, discrete time, numerical simulations.

1. Introduction

Since the beginning of time, vector-borne diseases have been the scourge of man and animals. Historically, these are the diseases that caused the great plagues such as the `Black Death' in Europe in the 14th Century and the epidemics of yellow fever that plagued the development of the New World. Others, such as Nagana, contributed to the lack of development in Africa for many years. The maintenance and resurgence of vector-borne diseases is related to ecological changes that favor increased vector densities or vector--host interactions, among other factors [13].

The 1970s was a time in which there were major changes to public health policy. Global trends, combined with changes in animal husbandry, urbanisation, modern transportation and globalisation, so it have resulted in a global re-emergence of epidemic vector-borne diseases affecting both humans and animals over the past 30 years.

It was in 1877 when Sir Patrick Manson first demonstrated that a parasite of humans, Wuchereria bancrofti, was transmitted among humans by a mosquito, Culex pipiens fatigans (Cx. pipiens quinquefasciatus). In 1893, Texas cattle fever was shown to be transmitted by the hard tick Boophilus annulatus, and in 1898, malaria was shown to be transmitted by anopheline mosquitoes. Since that time, many important disease pathogens of humans and animals have been shown to depend on blood-sucking arthropods to complete their transmission cycles.

Chikungunya virus is one of those arthropod borne virus, The mosquito responsible of this epidemic is the Aedes aegypti [1]. This mosquito is most known for being the main vector of the dengue fever [11], and chikungunya is the most rapidly spreading mosquito-borne viral disease in the world. the virus was first isolated in Tanzania, Africa in 1953 and has sporadically caused human epidemics in South-east Asia, southern India. it is a zoonotic virus with a life cycle that principally involves primates and the Aedes mosquitoes. The virus is transmitted from human to human by the bites of infected female mosquitoes. Most commonly, the mosquitoes involved are Aedes aegypti and Aedes albopictus, two species which can also transmit other mosquito-borne viruses, including dengue. These mosquitoes can be found biting throughout daylight hours, though there may be peaks of activity in the early morning and late afternoon. Both species are found biting outdoors. Humans that are infected may develop relatively high viremias and fever that can elevate up to 104 degrees Fahrenheit. Chikungunya has spread across the globe in recent years and remains a viral disease with no anti-viral medication available. The clinical picture is characterized by a sudden onset of fever, rash and severe pain in the joints. The name Chikungunya comes from the Swahili language for stooped walk, reflecting the physique of a person suffering from the disease.

Indeed, in the last 50 years, the incidence of Chikungunya virus has increased with increasing geographic expansion to new countries, and in the last decades, from urban to rural settings. Moreover, approximately one billion people live in dengue endemic countries and annually, an estimated 50 million dengue infections occur, and that's why chikungunya appears also to be one of the most important vector-borne disease [1].

The Chikungunya virus is characterized by an abrupt onset of fever frequently accompanied by joint pain. Other common signs and symptoms include muscle pain, headache, nausea, fatigue and rash. The joint pain is often very debilitating, but usually lasts for a few days or may be prolonged to weeks.

Most patients recover fully, but in some cases joint pain may persist for several months, or even years. Occasional cases of eye, neurological and heart complications have been reported, as well as gastrointestinal complaints. Serious complications are not common, but in older people, the disease can contribute to the cause of death. Often symptoms in infected individuals are mild and the infection may go unrecognized, or be misdiagnosed in areas where dengue occurs. After the bite of an infected mosquito, onset of illness occurs usually between four and eight days but can range from two to 12 days.

Unfortunately, this disease has neither specific treatment nor vaccine that is why reducing chikungunya virus transmission depends mainly on control of the mosquito vectors. Actions focus on individual protection against mosquito bites, symptomatic treatment of patients and mosquito proliferation control. For instance, the number of breeding sites are reduced by eliminating container habitats that are favorable oviposition sites and that permit the development of aquatic stages. Indeed, the Aedes albopictus female lays its eggs in wet places adjacent to the surface of water in all sorts of receptacles: vases, rainwater barrels, used tyres, etc. Moreover, as winter approaches, eggs may enter a diapause, that is to say the progression from egg to adult is interrupted by a period of dormancy [12]. In this stage, eggs are resistant to cold climates and droughts, and can wait until next spring to hatch. This diapause may explain the adaptation of the mosquito to temperate climate.

In this paper, using models described in [1] for the mosquito population dynamics and the transmission virus, we formulate the associated control model in order to derive optimal treatment strategy with minimal implementation cost. Controls used here are based on two main actions applied in the recent epidemics.

The paper is organized as follows. In section 2, we present the compartmental model used in [1] in discrete time, to describe the Aedes albopictus population dynamics and the chikungunya virus transmission to the human population. In section 3, we formulate an optimal control problem, the we derive the optimality system which characterizes the optimal control using Pontryagin's Maximum Principle [14]. In section 4 numerical results illustrate our theoretical results. The conclusion is presented in a final section.

2. Model Formulation

As Chikungunya is vector-borne disease that is spread by mosquitoes to human population, we propose a discrete two models to describe the population dynamics of the Aedes albopictus mosquito population and the transmission of the virus to human population. The vector population is described by a stage-structured model based on the biological life cycle. It consists in four main stages described by the following compartment: egg (E), larvae and pupae (L) which are biologically very closed stages, and the adult stage (A) which contains only females because they are responsible for the transmission [1]. we define parameters used to describe the mosquitoe model:

- d, d_L, d_m is the percapita mortality rate of eggs, larvae and adults respectively.
- K_E is the carrying capacity related to the amount of available nutrients and space.
- b is the intrinsic oviposition rate.
- s is the percapita transfer rate of egg population to become larve ;
- s_L is percapita transfer rate of larve population to beome mosquito female.
- K_L the carrying capacity, added to the transfer s, due to the intra-specific competition with young larvae.

We present the dynamics of mosquito population in discrete time as follows:

$$\begin{cases} E_{k+1} = bA_k\left(1-\dfrac{E_k}{K_E}\right)-(s+d)E_k \\ L_{k+1} = sE_k\left(1-\dfrac{L_k}{K_L}\right)-(s_L+d_L)L_k \\ A_{k+1} = s_L L_k - d_m + d_L A_k \end{cases} \tag{1}$$

As given in [1], this system is defined on the bounded subset of $\mathbb{R}^3$

$$\Gamma = \left\{ (E_k, L_k, A_k) \backslash \quad \begin{matrix} 0 \le E_k \le K_E \\ 0 \le L_k \le K_l \\ 0 \le A_k \le \dfrac{s_L}{d_m} K_L \end{matrix} \right\}$$

We use SI and SIR models to describe the infection for the mosquito population considering susceptible $\left(\overline{S}_{m,k}\right)$ and infectious $\left(\overline{I}_{m,k}\right)$ because an infected vector remains infective until its death and the ordinary differential equations describing the numbers of susceptible $\left(\overline{S}_{H,k}\right)$, infective $\left(\overline{I}_{H,k}\right)$ and recovered $\left(\overline{R}_{H,k}\right)$ individuals during an epidemic. The total size of the mosquitoes population is $A_k = \overline{S}_{m,k} + \overline{I}_{m,k}$ where A_k is defined above in the system (1). The chikungunya infection occurs when susceptible mosquitoes $\left(\overline{S}_{m,k}\right)$ are infected during the blood meal from infectious humans $\left(\overline{I}_{H,k}\right)$. The chikungunya infection among humans occurs when susceptible individuals $\left(\overline{S}_{H,k}\right)$ are bitten by infectious mosquitoes $\left(\overline{I}_{m,k}\right)$ during the blood meal.

We consider N_H the total number of human population which is constant. So that we have $N_H = \overline{S}_{H,k} + \overline{I}_{H,k} + \overline{R}_{H,k}$.

Introducing proportions $S_{H,k} = \dfrac{\overline{S}_{H,k}}{N_H}$, $I_{H,k} = \dfrac{\overline{I}_{H,k}}{N_H}$, $R_{H,k} = \dfrac{\overline{R}_{H,k}}{N_H}$, $S_{m,k} = \dfrac{\overline{S}_{m,k}}{A}$, $I_{m,k} = \dfrac{\overline{I}_{m,k}}{A}$ and the derivative $\dfrac{dS_{H,k}}{dt} = \dfrac{d\overline{S}_{H,k}}{dt}\dfrac{1}{N_H}$, $\dfrac{dI_{H,k}}{dt} = \dfrac{d\overline{I}_{H,k}}{dt}\dfrac{1}{N_H}$ and $\dfrac{dI_{m,k}}{dt} = \left(\dfrac{1}{A_k^2}\right)\left(\left(\dfrac{d\overline{I}_{m,k}}{dt}\right)A - \overline{I}_{m,k}\left(\dfrac{dA_k}{dt}\right)\right)$, we obtain the dynamics of the two models which are governed by the following system of differential equations in discrete time subject to non-negative initial conditions

$$\begin{cases} E_{k+1} = bA_k\left(1-\dfrac{E_k}{K_E}\right)-(s+d)E_k \\ L_{k+1} = sE_k\left(1-\dfrac{L_k}{K_L}\right)-(s_L+d_L)L_k \\ A_{k+1} = s_L L_k - d_m A_k \\ S_{H,k+1} = -\left(b_H+\beta_H I_{m,k}\right)S_{H,k}+b_H \\ I_{H,k+1} = \beta_H I_{m,k}\beta_H S_{H,k}-(\gamma+b_H)I_{H,k} \\ I_{m,k+1} = -s_L\dfrac{L_k}{A_k}I_{m,k}+\beta_m I_{H,k}\left(1-I_{m,k}\right) \end{cases} \quad (2)$$

The first control $u_{1,k}$ 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. This control focuses on the reduction of the number of larvae, and thus eggs, of any natural or artificial water-filled container. Moreover, in France, one other type of intervention is the use of traps. This consists in using simple black buckets (black colour is recognized as being attractive), with a capacity of one liter of water, three-quarters full with tannic water (water macerated for 3 days with dead branches and leaves). This traps contain laying sites (little plates of square extruded polystyrene placed on the surface of the water). Finally tablets of bio-insecticide (Dimilin) are introduced in the traps in order to neutralise the potential development of larvae.

The second control $u_{2,k}$ represents efforts made for prevention on a time interval $[0,T]$, It mainly consists in reducing the number of vector-host contacts due to the use of repulsive against adult mosquitoes and protection with mosquito nets or wearing appropriate clothing. Indeed Aedes albopictus has a peak of activity during fresh temperatures, early in the morning and late in the afternoon.

Therefore, our transmission and optimal control model of chikungunya disease in discrete time reads as

$$\begin{cases} E_{k+1} = bA_k\left(1-\dfrac{E_k}{K_E}\right)-(s+d)E_k-\left(s+d+\varepsilon u_{1,k}\right)E_k \\ L_{k+1} = sE_k\left(1-\dfrac{L_k}{K_L}\right)-(s_L+d_L)L_k-(s_L+d_L)L_k-d_c u_{1,k}L_k \\ A_{k+1} = s_L L_k - d_m A_k \\ S_{H,k+1} = -\left(b_H+\beta_H I_{m,k}\right)S_{H,k}+b_H \\ I_{H,k+1} = \beta_H I_{m,k}\beta_H S_{H,k}-(\gamma+b_H)I_{H,k} \\ I_{m,k+1} = -s_L\dfrac{L_k}{A_k}I_{m,k}+\beta_m I_{H,k}\left(1-I_{m,k}\right) \end{cases} \quad (3)$$

with $E_k(0)\geq 0$, $L_k(0)\geq 0$, $A_k(0)\geq 0$, $S_{H,k}(0)\geq 0$, $I_{H,k}(0)\geq 0$, and $I_{m,k}(0)\geq 0$ are given.

3. Optimal Control Problem

In this work, we use the optimal control theory to analyse the behavior of the model (3) attempting to minimize the number of both infected mosquitos and humans, to reduce the number of eggs and larveas, and also the controls used in this optimal strategy. We define the objective functional as follows:

$$J(u_{1,k},u_{2,k}) = A_{1,T}I_{H,T}+A_{2,T}I_{m,T}+A_{3,T}E_T+A_{4,T}L_T+ \sum_{k=0}^{T-1}\left(A_{1,k}I_{H,k}+A_{2,k}I_{m,k}+A_{3,k}E_k+A_{4,k}L_k+\frac{B_{1,k}}{2}u_{1,k}^2+\frac{B_{2,k}}{2}u_{2,k}^2\right) \quad (4)$$

where $A_{1,k}>0$, $A_{2,k}>0$, $A_{3,k}>0$, $A_{4,k}>0$, $B_{1,k}>0$, $B_{2,k}>0$ are the cost coefficients, they are selected to weight the relative importance of $I_{H,k}$, $I_{m,k}$, E_k, L_k, $u_{1,k}$, $u_{2,k}$ at step k,T is the final time, we are minimizing the number of infected humans, infected insects.

$$J\left(u_{1,k}^*,u_{2,k}^*\right)=min\left\{J\left(u_{1,k},u_{2,k}\right):u_{1,k},u_{2,k}\in U\right\} \quad (5)$$

Where U is the set of admissible controls defined by

$$U=\left\{u_{1,k},u_{2,k}: a_1\leq u_{1,k}\leq b_1,\ a_2\leq u_{2,k}\leq b_2,\ u \text{ is measurable } k=0,1,\dots,T-1\right\}$$

Pontryagin's Maximum Principal in discrete time converts (3), (4) and (5) into a problem of minimizing a Hamiltonian, defined by

$$H = A_{1,k}I_{H,k}+A_{2,T}I_{m,k}+A_{3,k}E_k+A_{4,k}L_k +\frac{B_{1,k}}{2}u_{1,k}^2+\frac{B_{2,k}}{2}u_{2,k}^2\sum_{j=1}^{6}\lambda_{j,k+1}f_{j,k+1} \quad (6)$$

where $f_{j,k+1}$ is the right side of the differential equation of the j^{th} state variable.

By applying the Pontryagin's maximum principle in discrete time [14].

Given an optimal control $u_{1,k}^*$, $u_{2,k}^*$, and solutions E_k^*, L_k^*, A_k^*, $S_{H,k}^*$, $I_{H,k}^*$ and $I_{m,k}^*$ of the corresponding state system, there exists an adjoint vector $\lambda=\left[\lambda_{1,k},\lambda_{2,k},\lambda_{3,k},\lambda_{4,k},\lambda_{5,k},\lambda_{6,k}\right]$ satisfying

$$\lambda_{1,k} = A_{3,k} + \lambda_{1,k+1}\left(-\frac{bA_k}{K_E} - \left(s + d + \varepsilon u_{1,k}\right)\right) + \lambda_{2,k+1}\left(s - \frac{sL_k}{K_L}\right)$$

$$\lambda_{2,k} = A_{4,k} + \lambda_{2,k+1}\left(-\frac{sE_k}{K_L} - \left(s_L + d_L + d_c u_{1,k}\right)\right) + \lambda_{3,k+1}s_L + \lambda_{6,k+1}s_L\left(-\frac{sI_{m,k}}{A_k}\right)$$

$$\lambda_{3,k} = \lambda_{1,k+1}\left(b - \frac{bE_k}{K_E}\right) - \lambda_{3,k+1}d_m$$

$$\lambda_{4,k} = -\lambda_{4,k+1}b_H - \beta_H\left(1 - u_{2,k}\right) + I_{m,k}\left(\lambda_{5,k+1} - \lambda_{4,k+1}\right)$$

$$\lambda_{5,k} = -\lambda_{5,k+1}\left(\gamma + b_H\right) + \lambda_{6,k+1}\beta_m\left(1 - u_{2,k}\right)\left(1 - I_{m,k}\right) + A_{1,k}$$

$$\lambda_{6,k} = \beta_H\left(1 - u_{2,k}\right)S_{H,k}\left(\lambda_{5,k+1} - \lambda_{4,k+1}\right) + \lambda_{6,k+1}\left(\frac{sL_k}{K_L} - \beta_m I_{H,k}\left(1 - u_{2,k}\right)\right) + A_{2,k}$$

Theorem 1 with the transversality conditions

$\lambda_{3,T} = \lambda_{4,T} = 0,\ \lambda_{1,T} = A_{3,T},\ \lambda_{2,T} = A_{4,T},\ \lambda_{5,T} = A_{1,T},\ \lambda_{6,T} = A_{2,T}$

Futhermore, the optimal control $\left(u_{1,k}^*,\ u_{2,k}^*\right)$ is given by

$$u_{1,k}^* = \max\left(a_1,\ \min\left(b_1,\ \frac{\left(\lambda_{1,k+1}\varepsilon E_k + \lambda_{2,k+1}d_c L_k\right)}{B_{1,k}}\right)\right) \quad (7)$$

$$u_{2,k}^* = \max\left(a_2,\ \min\left(b_2,\ \frac{I_{m,k}\left(\lambda_{5,k+1} - \lambda_{4,k+1}\right)\beta_H S_{H,k} + \lambda_{6,k+1}\beta_m I_{H,k}\left(1 - I_{m,k}\right)}{B_{2,k}}\right)\right) \quad (8)$$

Proof For $k = 0,\ 1,\ \cdots,\ T-1$ The adjoint equations and transversality conditions can ben obtained by using Pontryagin's Maximum Principle in discrete time such that

$$\begin{cases} \lambda_{1,k} = \dfrac{\partial H_k}{\partial E_k}, & \lambda_{1,T} = A_{3,T} \\ \lambda_{2,k} = \dfrac{\partial H_k}{\partial L_k}, & \lambda_{2,T} = A_{4,T} \\ \lambda_{3,k} = \dfrac{\partial H_k}{\partial A_k}, & \lambda_{3,T} = 0 \\ \lambda_{4,k} = \dfrac{\partial H_k}{\partial S_{H,k}}, & \lambda_{4,T} = 0 \\ \lambda_{5,k} = \dfrac{\partial H_k}{\partial S_{H,k}}, & \lambda_{5,T} = A_{1,T} \\ \lambda_{6,k} = \dfrac{\partial H_k}{\partial E_k}, & \lambda_{6,T} = A_{2,T} \end{cases}$$

The optimal control $\left(u_{1,k}^*,\ u_{2,k}^*\right)$ can be solve from the optimality condition,

$$\frac{\partial H_k}{\partial u_{1,k}} = 0,\quad \frac{\partial H_k}{\partial u_{2,k}} = 0$$

that is

$$\frac{\partial H_k}{\partial u_{1,k}} = -\lambda_{1,k+1}\varepsilon E_k - \lambda_{2,k+1}d_c L_k + B_{1,k}u_{1,k} = 0$$

$$\frac{\partial H_k}{\partial u_{2,k}} = I_{m,k}\left(\lambda_{4,k+1} - \lambda_{5,k+1}\right)\beta_H S_{H,k} - \lambda_{6,k+1}\beta_m I_{H,k}\left(1 - I_{m,k}\right) + B_{2,k}u_{2,k} = 0$$

By the bounds in the control U , it is easy to obtain $\left(u_{1,k}^*,\ u_{2,k}^*\right)$ in the form of (7)

4. Numerical Simulations

Solving numerically the optimality system we obtain results that we present in this section. We note that there were initial conditions for the state variables and terminal conditions for the adjoints. That is, the optimality system is a two-point boundary value problem, with separated boundary conditions at times step $k = 0$ and $k = T$. We solve the optimality system by an iterative method with forward solving of the state system followed by backward solving of the adjoint system. We start with an initial guess for the control at the first iteration and then before the next iteration, we update the control by using the characterization given above. We continue until convergence of successive iterates is achieved.
The initial conditions and parameters of the system (2) are taken from [1] and are presented in Table1, so the optimality system is solved forward in time with initial conditions $Z(0) = (1000,\ 500,\ 400,\ 0.09,\ 0.01,\ 0.02)$ while the adjoint (or costate) system (14) is solved backward in time with terminal conditions $(T) = (0,\ 0,\ 0,\ 0,\ 0,\ 0)$, where $T = 50$ days.

In the objective functional, the weight constant values are chosen as follows:

$$A1 = A2 = 10000,\ A3 = 0,\ A3 = 1,\ B1 = B2 = 10,$$

In Table1 we present values of parameters in the chikungunya model. Most of the values were obtained from entomologists and given for instance in [1]

Parameter	description	Value
b	per capita oviposition rate	1 or 6
K_E	carrying capacity for eggs	1000
ε	chemical eggs mortality rate	0.001
K_L	carrying capacity for larvae	500
s	transfer rate from eggs to larvae	0.7
s_L	transfer rate from larvae to mosquitoes	0.5
d	eggs death rate	0.2 or 0.4
d_L	larvae natural mortality rate	0.2 or 0.4
d_c	chemical larvae mortality rate	0.3
d_m	adult mosquitoes mortality rate	0.25 or 0.5
b_H	human birth rate	0.0000457
β_H	effective contact rate human - vector	0.2 or 0.75
β_m	effective contact rate vector -human	0.1 or 0.5
γ_H	natural recovery rate	0.1428

5. Figures

The graphs below present optimal solutions, together with non optimal solutions corresponding to no control functions for comparaison, in order to show the effectiveness of the optimal strategy. Figure1 gives an example of the evolution of the eggs without the application of the control and with the use of control. We notice that we have difference in presence of control the number of eggs than without using it.

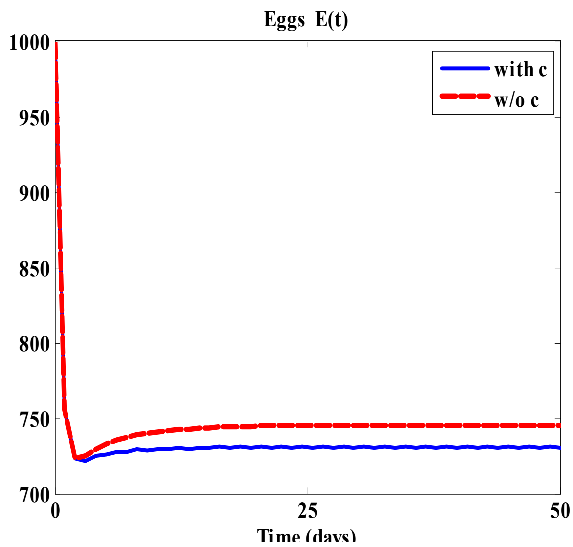

Figure1: The evolution of eggs with and without control

Figure 2 also shows the effect of the control on the number of larvaes during the period of 50 days by comparing the two functions with and without control.

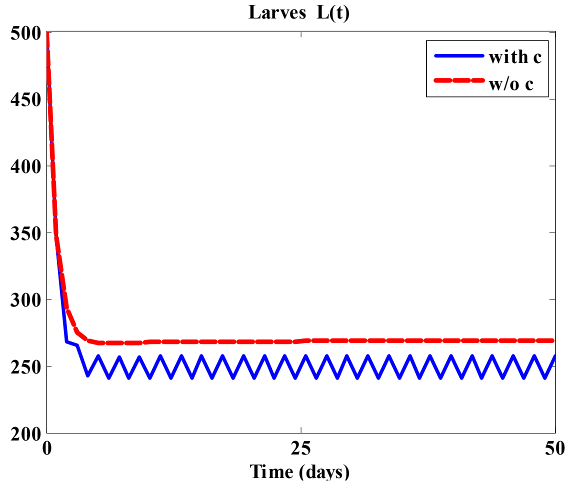

Figure 2: The evolution of Larves with and without control

We investigate in Figure3 effects of the efforts made to reduce the number of vector-host especially adult mosquitoes, so that from the second day of the optimal strategy, the difference between case with control and that without control is evident.

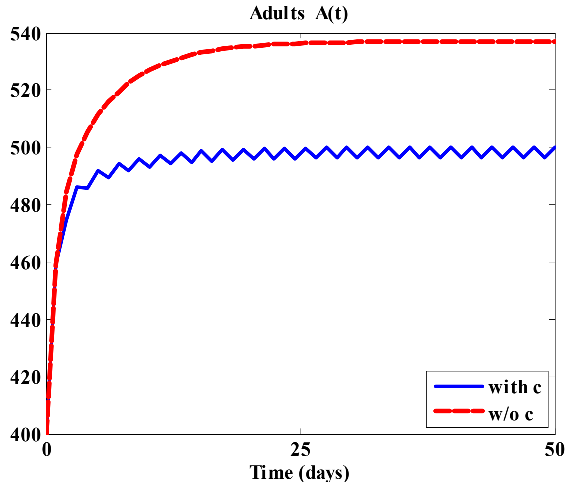

Figure 3: The evolution of adult mosquitoes with and without control

By performing numerical simulations with values of parameter used in the model, we investigate effects of the control, governing the dynamics of the mosquito stage population and the proportion of individuals in each class. Having as hole aim to reduce the number of infected humans, we introduce numerically values of control to attempt this objectif. In .gure4, the graph allow us to deduce the effectiveness of the control strategy to eradicate defnitevely the disease in human population. so that from the 4th day the number of human infected population begin to decrease rapidly.

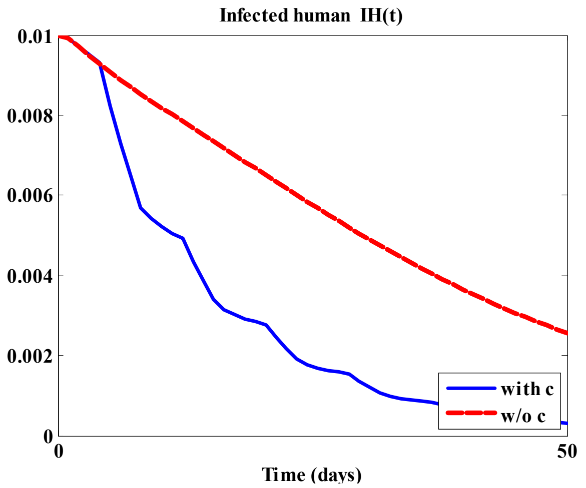

Figure 4: The evolution of infected humans with and without control.

Because of the nature of the chikungunya disease and the way it spreads between humans and mosquitoes, we have to show also numerically the importance of that dependence by reducing the number of the vector. The graph in Figure5 show the positif impact of the optimal measure to eradicate the Chikungunya disease by presenting the evolution of infected mosquitoes with and without control.

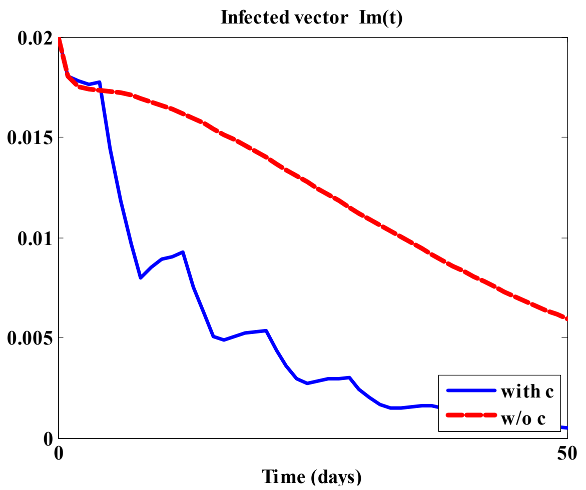

Figure 5: The evolution of infected vector with and without control.

6. Conclusion

Time dependent intervention strategies have been implemented, in the present work, to limit the bad effects of vector-borne disease \ss on a finite time interval. All interventions or strategies are important to consider in order to reduce the Chikungunya disease, but may not be efficient while taking on vision human and mosquitoes mobilization. By the way of prevention efforts and for instance, after each rainfall, it is advisable to check around the houses regularly and systematically empty or clean all the water receptacles where mosquitoes could lay eggs. By the same way to reduce the Chikungunya disease, In this paper, two main strategies have been implemented, we attempt to reduce the numer of infected human and mosquitoes, the number of eggs, larves and adults insects, and the cost of the optimal strategy. This aim was proved numerically which show the effectiveness of the optimal approach.

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