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OPTIMAL CONTROL OF *Aedes aegypti* MOSQUITOES BY STERILE INSECT TECHNIQUE, INSECTICIDE AND LARVICIDE

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Abstract. *The present work presents a model to describe the dynamics of an Aedes aegypti mosquitoes population when sterile individuals are introduced as a biological control, in addition to the usual application of insecticide and larvicide. In order to analyze the minimal* *effort to reduce the number of female mosquitoes, which are responsible for the spread of diseases like dengue, chikungunya and zika, an optimal control strategy is derived. To derive such strategy, we take into account the cost of insecticide and the larvicide application, and the production and delivery costs of sterile mosquitoes. The optimal control is obtained by applying the Pontryagin's maximum principle.*

Keywords: *Optimal Control, Mathematical Modelling, Pontryagin's Maximum Principle, Aedes aegypti*

1 INTRODUCTION

Containing a vector related to the spread of diseases is an effort that engages individuals, government and researchers. When it comes to controlling the *Aedes aegypti* population, an special interest is in place, since these mosquitoes are known to be the main transmitters of diseases like Dengue, Chukungunya and Zika (Tauil, 2002, Thomé, 2007, chikungunya). Indeed, the referred diseases are a major source of concern for public health policy makers in Brazil.

Aedes aegypti mosquitoes are regarded as urban and generally feed at certain times of the day. Disease transmission occurs when an infected adult female bites an individual. After mating, the females release their eggs in different locations, thus ensuring the birth of new mosquitoes. Once a female has sucked the blood from an infected individual, this may transmit the virus to susceptible individuals. More information about mosquito behavior and its relationship to the spread of Dengue can be found in the work of Thomé et al. (2010).

Given the importance of the *Aedes aegypti* dynamics in the proliferation of Dengue, Chikungunya and Zika, the model proposed here takes into account the iterations among the population of mosquitoes, divided in males, fertilized and unfertilized females. It also considers the distribution of population in its two main phases: the aquatic phase (eggs, larvae and pupae) and the mature phase. The model mainly considers different mechanisms of control to prevent the proliferation of mosquitoes, based on what is commonly used today, such as larvicides and insecticides. Thus, the mortality of larvae and pupae is induced, as well as that of adult mosquitoes. Finally, we also consider the control of mosquitoes by the release of sterile male insects in the natural environment. The mating of the inserted mosquitoes result in non-viable eggs, which helps the control of the mosquito population (Knipling, 1955, Bartlet, 1990).

A sterilization technique to be considered in out model is known as RIDL© (release of insects carrying a dominant lethal). This technique constitutes a conditional sterilization, which considers the automatic separation of genres and so removes the need for radiation, and hence does not affect the environment (Wise Valdez et al, 2011).

To derive control strategies that are effective, particularly in view of the scarcity of government resources, one needs to keep in mind a clear assessment of operating costs and evaluate which combination of control mechanisms leads to eradication or effectively low levels of mosquito population with the lowest possible cost. It is worth noticing that it is desirable to keep the mosquito population to an acceptable level so as not to cause ecological imbalances. With the decrease of the mosquito population, the number of infected individuals (in human population) is also expected to decrease considerably. All ain all, the application of optimal control theory plays a fundamental role in minimizing the dynamic costs related to keeping the mosquito population within acceptable levels in a prescribed planning period.

2 THE MATHEMATICAL MODEL

The proposed model of the dynamics of *Aedes aegypti* mosquitoes considers that its life cycle is divided into aquatic phase and winged phase or adulthood. We employ the following notation:

$A(t)$ is the population of mosquitoes in the aquatic phase (egg, larvae, pupae);
$I(t)$ is the population of immature female mosquitoes, or prior to mating;
$F(t)$ is the mosquito population fertilized females after mating;
$U(t)$ is the population of non-fertilized female mosquitoes after mating;
$M(t)$ is the population of natural male mosquitoes;
$S(t)$ is the population of sterile male mosquitoes through technical RIDL©.

Figure 1 shows the population dynamic. Note that the *per capita* mortality rates are given by $\mu' s$ for each compartment considered in the model. The oviposition rate of fertilized females F increases its population, regulated by the effective capacity (breeding available). The *per capita* rate of oviposition is given by $\phi(1 - \frac{A}{C})$ where ϕ is the intrinsic oviposition rate and C the environment capacity.

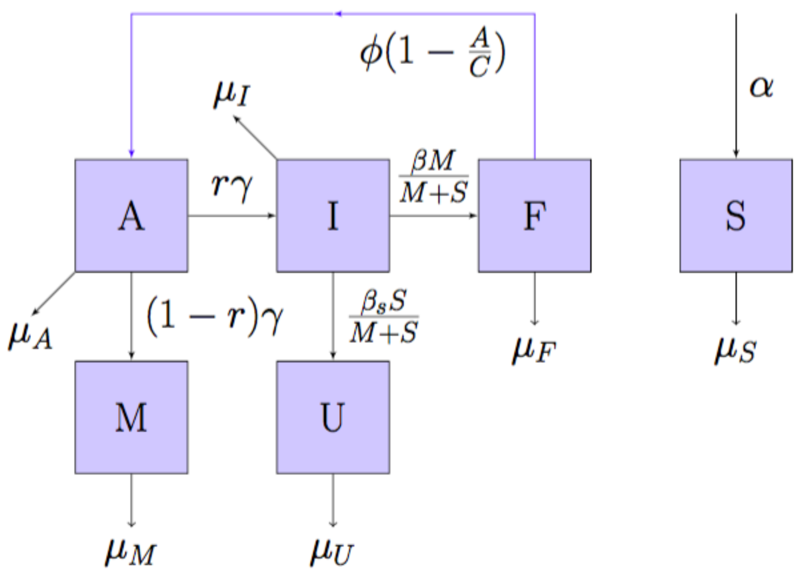

Figure 1: Population Dynamic.

Mosquitoes transition from the aquatic phase A to the winged stage according to a *per capita* rate γ. The probability that the released insect is female r, and that of male release is, therefore, $(1 - r)$.

Immature females I become fertilized F or non-fertilized U females, depending on the male they copulate with. Fertilized females are the ones that copulate with natural males M, whereas non-ferlitized females are the ones that mate with sterile males S. We assume that the probability of an encounter between immature female and natural male is $\frac{M}{M+S}$, and that of an encounter between immature female and sterile male is $\frac{pS}{M+S}$, where p; $0 \leq p \leq 1$ is the ratio with which the sterile male are suitably introduced into the environment. The *per capita* rate of fertilization by natural males is given by $\frac{\beta M}{M+S}$, whereβ is the mating rate of natural males, whereas the *per capita* rate of fertilization by sterile males is given by $\frac{\beta_s M}{M+S}$, where $\beta_s = p\,\beta$ is the mating rate of sterile males.

2.1 The Uncontrolled Model

If we consider that the sterile mosquitoes are introduced at a constant rate α, we have the following state dynamic system (Esteva & Yang, 2005):

$$\begin{cases} \frac{dA}{dt} = \phi(1-\frac{A}{C})F - (\gamma+\mu_A)A \\ \frac{dI}{dt} = r\gamma A - \frac{\beta M I}{M+S} - \frac{\beta_s S I}{M+S} - \mu_I I \\ \frac{dF}{dt} = \frac{\beta M I}{M+S} - \mu_F F \\ \frac{dU}{dt} = \frac{\beta_s S I}{M+S} - \mu_U U \\ \frac{dM}{dt} = (1-r)\gamma A - \mu_M M \\ \frac{dS}{dt} = \alpha - \mu_S S \end{cases} \tag{1}$$

The trivial and non-trivial equilibrium points, as well as the stability of the model were studied in detail by Esteva & Yang (2005) and Thomé et al. (2010). Based on these studies we have the following initial conditions for the state system:

$$\begin{cases} A_0 = \frac{(R-1)C}{R} \\ I_0 = \frac{r\gamma A_0 (M_0 + \frac{\alpha}{\mu_S})}{(\mu_I+\beta)M_0 + (\mu_I+\beta_s)\frac{\alpha}{\mu_S}} \\ F_0 = \frac{(\gamma+\mu_A)CA_0}{\phi(C-A_0)} \\ M_0 = \frac{(1-r)\gamma A_0}{\mu_M} \\ U_0 = \frac{\alpha\beta_s I_0}{\mu_U(\mu_S M_0 + \alpha)} \\ S_0 = \frac{\alpha}{\mu_S} \end{cases} \tag{2}$$

where $R = \frac{\phi r \gamma \beta}{(\gamma+\mu_A)(\beta+\mu_I)\mu_F}$. Note that $R \geq 1$ once $A_0 \geq 0$.

3 THE OPTIMAL CONTROL PROBLEM

As previously mentioned, the purpose of this study is to minimize the costs involved with the control of the mosquito population by applying larvicides, insecticides, introducing sterile male mosquitoes in the environment. With this goal, the following control variables are introduced to the problem:

- $u_1 \geq 0$, represents the investment in insecticides;
- $u_2 \geq 0$ represents the investment sterile male mosquitoes ;
- $u_3 \geq 0$ represents the investment in larvicides.

Control variable u_1 expresses the amount of insecticide that will be released at each time up to the planning period T; the control variable u_2 the amount of sterile mosquitoes to be introduced in nature, while the control variable u_3 determines the amount of larvicide to be released. Note that u_2 thereby increases the population of sterile mosquitoes $S(t)$. We also define the following functional:

$$J[u_1, u_2, u_3] = \frac{1}{2}\int_0^T (c_1 u_1^2 + c_2 u_2^2 + c_3 u_3^2 + c_4 F^2)\, dt. \tag{3}$$

For greater efficiency, one should be concerned with minimizing the population of fertilized female mosquitoes, given that it is this population that is responsible for the spread of the virus. The insecticide released according to u_1 directly reduces the fertilized female population, while the release of sterile males according to u_2 affects this population indirectly, by preventing fertilization. In the above function in Eq. (3), c_1 represents the cost of insecticide, c_2 denotes the production and release cost of sterile mosquitoes, c_3 the cost with the larvicide, c_4 is the social cost associated to the population F, which cause the spread of diseases. Each coefficient thus establishes a relative importance to each contributing factor in the total cost of disease control.

3.1 The Controlled Model

Let us define a new state system with the introduction of the optimal control variables:

$$\begin{cases} \frac{dA}{dt} = \phi(1 - \frac{A}{C})F - (\gamma + \mu_A + u_3)A \\ \frac{dI}{dt} = r\gamma A - \frac{\beta M I}{M+S} - \frac{\beta_s S I}{M+S} - (\mu_I + u_1)I \\ \frac{dF}{dt} = \frac{\beta M I}{M+S} - (\mu_F + u_1)F \\ \frac{dU}{dt} = \frac{\beta_s S I}{M+S} - (\mu_U + u_1)U \\ \frac{dM}{dt} = (1-r)\gamma A - (\mu_M + u_1)M \\ \frac{dS}{dt} = u_2 - (\mu_S + u_1)S \end{cases} \tag{4}$$

The rate of introduction of sterile mosquitoes α has been replaced by the control parameter u_2, aiming to introduce this population efficiently. Note that the equation describing the aquatic phase A is not affected by control u_1, since insecticides only have effect on the winged stage of the mosquito.

The system is subject to initial conditions derived from Eq. (2), with $\alpha = 0$. Thus we have:

$$\begin{cases} A_0 = \frac{(R-1)C}{R} \\ I_0 = \frac{r\gamma A_0}{\mu_I+\beta} \\ F_0 = \frac{(\gamma+\mu_A)CA_0}{\phi(C-A_0)} \\ M_0 = \frac{(1-r)\gamma A_0}{\mu_M} \\ U_0 = 0 \\ S_0 = 0 \end{cases} \tag{5}$$

Based on the previous equations we define the Control Problem:

The Control Problem:

$$\begin{aligned} &\text{Minimize J },\\ &\quad \text{subject to (4) and (5).} \end{aligned} \tag{6}$$

where J is defined in (3).

3.2 The Solution of the Controlled Model

To solve the problem formulated in (6), we make use of Pontryagin's Maximum Principle (Fleming & Rishel, 1975). This principle establishes a set of necessary optimality conditions in terms of the system's Hamiltonian, defined as:

$$H = \begin{cases} \frac{1}{2}[c_1u_1^2 + c_2u_2^2 + c_3u_3^2 + c_4F^2] + w_1[\phi(1 - \frac{A}{C}F - (\gamma + \mu_A + u_3)A] + \\ \quad +w_2[r\gamma A - \frac{\beta MI}{M+S} - \frac{\beta_s SI}{M+S} - (\mu_I + u_1)I] + w_3[\frac{\beta MI}{M+S} - (\mu_F + u_1)F] + \\ \quad +w_4[\frac{\beta_s SI}{M+S} - (\mu_U + u_1)U] + w_5[(1-r)\gamma A - (\mu_M + u_1)M] + \\ \quad +w_6u_2 - (\mu_S + u_1)S] + v_1u_1 + v_2u_2 + v_3u_3, \end{cases} \tag{7}$$

where $w_i's$ are additional functions called adjoint variables or co-state variables. The variables v_1, v_2 and v_3 are penalty multipliers or slack variables introduced to make sure that $u_1 \geq 0$, $u_2 \geq 0$ and $u_3 \geq 0$. To ensure that the optimal control variables $u_1^\star$, $u_2^\star$ and $u_3^\star$ are indeed constrained to non-negative values we make $v_1u_1^\star = v_2u_2^\star = v_3u_3^\star = 0$. Optimal control theory yields that, for every time $t \geq 0$, the optimal control variables should maximize the Hamiltonian over all feasible values. That implies the following necessary optimality condition:

$$\frac{\partial H}{\partial u_1^\star} = \frac{\partial H}{\partial u_2^\star} = \frac{\partial H}{\partial u_3^\star} = 0.$$

Then, the optimal control problem is characterized by:

$$\begin{cases} u_1^\star = max\{0, \frac{w_2 I + w_3 F + w_4 U + w_5 M + w_6 S}{c_1}\} \\ u_2^\star = max\{0, -\frac{w_6}{c_2}\}, \\ u_3^\star = max\{0, \frac{w_1 A}{c_3}\}. \end{cases} \tag{8}$$

Co-state variables have to satisfy the maximum principle: $\frac{\partial w}{\partial t} = -\frac{\partial H}{\partial x}$, thus generating the adjoint system:

$$\begin{cases} \frac{dw_1}{dt} = (\phi\frac{F}{C} + \gamma + \mu_A + u_3)w_1 - r\gamma w_2 - (1-r)\gamma w_5 \\ \frac{dw_2}{dt} = (\frac{\beta M}{M+S} - \frac{\beta_s S}{M+S} + \mu_I + u_1)w_2 - \frac{\beta M}{M+S}w_3 - \frac{\beta_s S}{M+S}w_4 \\ \frac{dw_3}{dt} = -c_4 F - \phi(1-\frac{A}{C})w_1 + (\mu_F + u_1)w_3 \\ \frac{dw_4}{dt} = (\mu_U + u_1)w_4 \\ \frac{dw_5}{dt} = [(\beta - \beta_s)w_2 - \beta w_3 - \beta_s w_4]\frac{SI}{(M+S)^2} + (\mu_M + u_1)w_5 \\ \frac{dw_6}{dt} = -[(\beta - \beta_s)w_2 - \beta w_3 - \beta_s w_4](\frac{MI}{(M+S)^2}) + (\mu_S + u_1)w_6 \end{cases} \tag{9}$$

The so-called Transversality Conditions (Fleming & Rishel, 1975) are the final conditions of the adjoint system:

$$w_i(T) = 0; \quad i = 1, \ldots, 6. \tag{10}$$

We can thus define the optimality problem:

Optimality Problem: The optimality problem is formed by the state system (4), the adjoint system (9), the optimal control variables (8), the initial conditions of the system (5) and the transversality conditions (10).

4 NUMERICAL SOLUTION

As the optimal control variables in (8) depend on the co-state variables in the optimal trajectory, they cannot be found analytically. That is because the optimal trajectory is not known a priori. Hence, one has to resort to numerical methods to solve the optimality equations. In the proposed experiments, we make use of an specialized gradient algorithm (Kirk, 1970) to solve Problem (6) to optimality. The solution of the differential equations in the Optimality Problem above was found by means of the finite difference method. We considered a planning period of 365 days.

In solving the problem we seek to optimal controls that simultaneously solve the initial value problem described by the state system and the final value problem described by the adjoint system. In this work, the trajectories of optimal controls are iteratively obtained by employing an classical specialist gradient algorithm (Kirk, 1970).

4.1 EXPERIMENTS

For the epidemiological and demo-graphic parameters in all simulations, we use the values given in Table 1.

To validate the model, we present an example with $c_1 = 1,\ c_2 = 10;\ c_3 = 100;\ c_4 = 1$ in Eq. (3). These parameters may be interpreted as weights: the higher the weight, the more expensive the control.

Our aim is to understand the effect of the use of each of the three proposed control mechanisms. Note that there seems to be a conflict between two control mechanisms, namely, insecticide application and the release of sterilized male mosquitoes, for the insecticide certainly exterminates the sterilized mosquitoes. On the other hand, the larvicide combines well with both of the other control mechanisms.

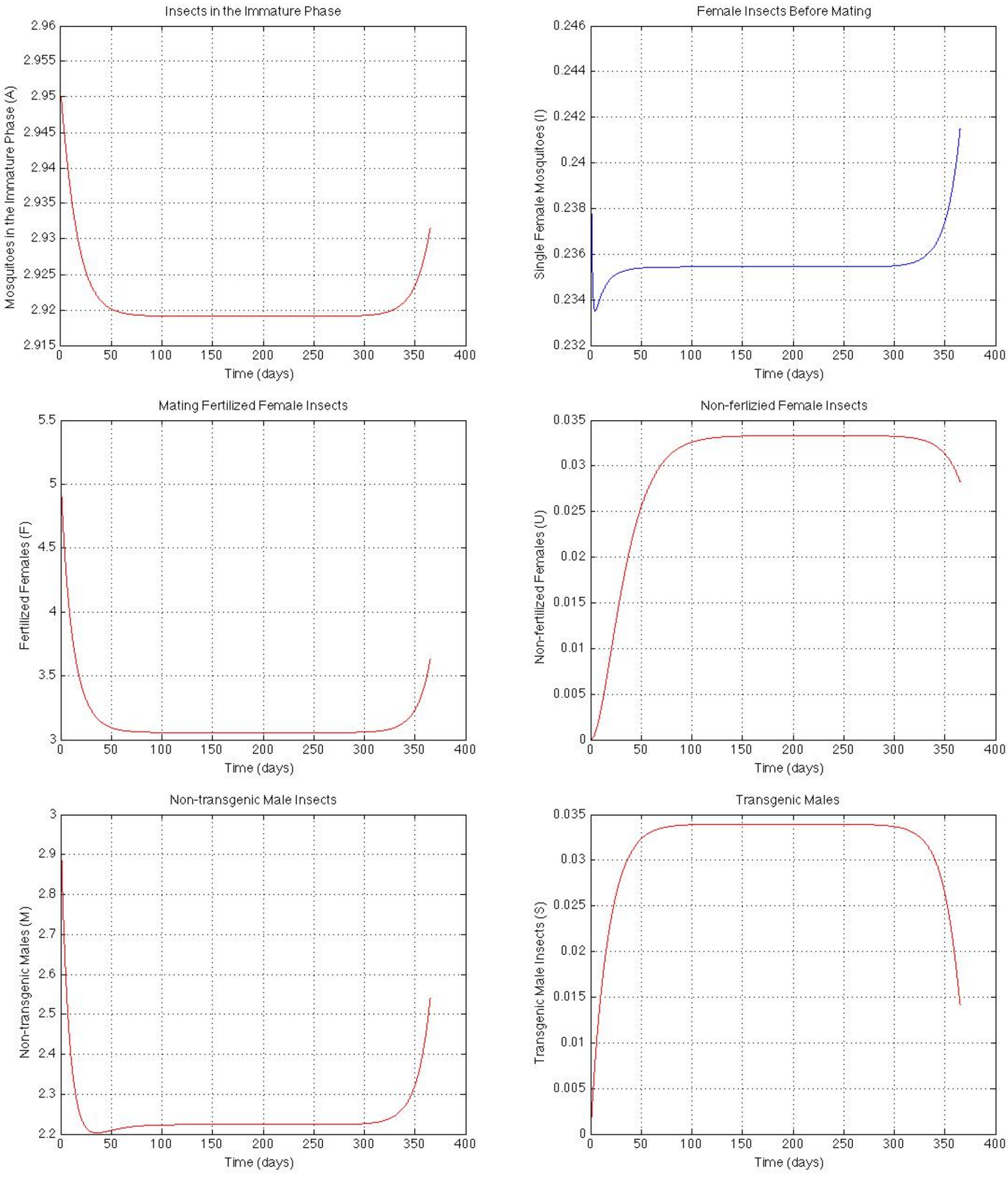

Figure 2: Numerical Experiments - StateVariables.

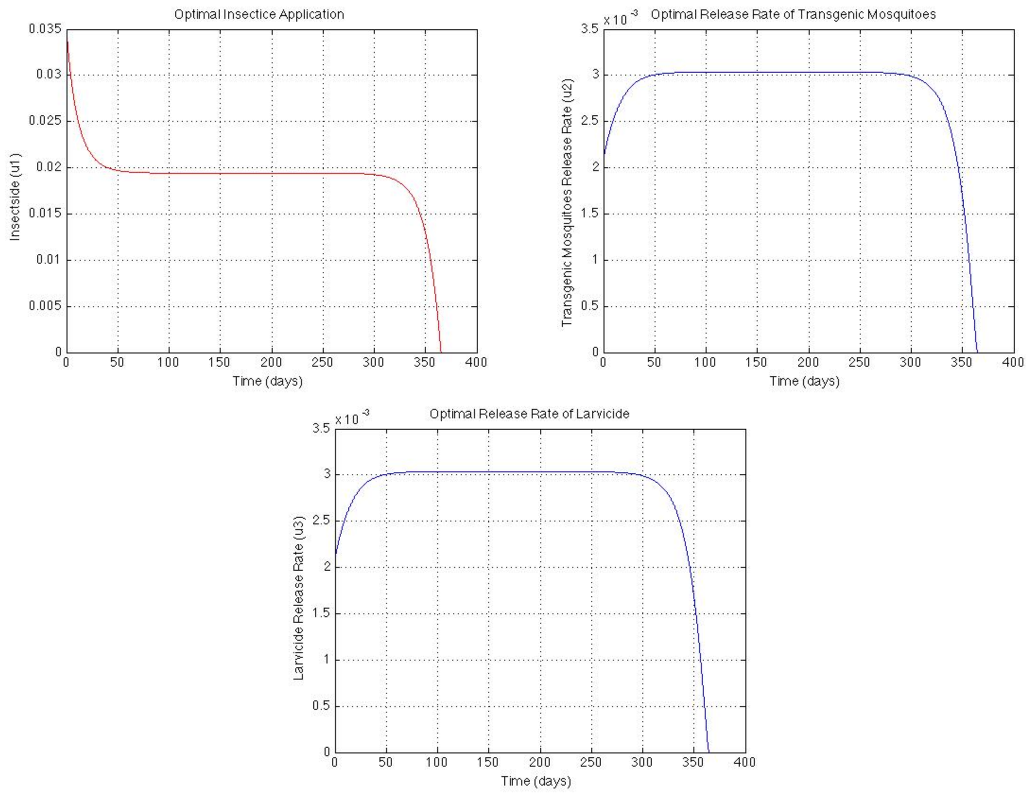

Figure 3: Numerical Experiments - Optimal Variables $u_1,\ u_2,\ u_3$.

Figure 3 shows the optimal control variables $u_1^*,\ u_2^*,\ u_3^*$ over time, while Figure 2 depicts the optimal trajectory of the other variables over time. Observe that we start with a high dosage of insecticide to immediately reduce the population of mosquitoes in the winged phase. This quantity is then reduced over time until it becomes constant after the second month. As the insecticide is reduced, the larvicide and the sterile males are introduced, their levels increasing to a constant level that is reached in the second month and kept constant thereafter. Figure 2 demonstrates that the controls combined to stabilize the populations of fertilized females and mosquitoes in the aquatic phase within low levels at all times.

5 CONCLUDING REMARKS

This paper addresses a population dynamics model of the spread of *Aedes aegypti* mosquitoes, with the introduction of optimal control variables to represent the effects of insecticides, larvicides and the introduction of sterile males mosquitoes in the environment. These mechanisms are employed to control the population of female mosquitoes, known to be the vector of diseases like Dengue, Chikungunya and Zika.

We know that that the use of sterile mosquitoes conflicts with the use of insecticide, since the latter exterminates both natural and artificially introduced mosquitoes. In addition, as every control mechanism has its cost, we seek for an optimal combination of control mechanisms in such a way as to keep the mosquito population at low levels while also minimizing the cost of the prescribed controls.

Table 1: Parameters Values for the Optimality System (Thomé et al., 2010).

Parameter	Nomenclature	Value
Intrinsic oviposition rate	ϕ	$6.353\ days^{-1}$
Mortality rate for mosquitoes in aquatic phase	μ_A	$0.0583\ days^{-1}$
Mortality rate for immature female mosquitoes	μ_I	$0.0337\ days^{-1}$
Mortality rate for fertilized female mosquitoes	μ_F	$0.0337\ days^{-1}$
Mortality rate for non-fertilized female mosquitoes	μ_U	$0.0583\ days^{-1}$
Mortality rate for natural male mosquitoes	μ_M	$0.06\ days^{-1}$
Mortality rate for sterile male mosquitoes	μ_S	$0.07\ days^{-1}$
Transport rate from aquatic phase to winged stage	α	$0.121\ days^{-1}$
Birth of female ratio	r	0.5
Mating rate of natural males mosquitoes	β	$0.7\ days^{-1}$
Mating rate of sterile males mosquitoes	β_S	$0.5\ days^{-1}$
Capacity of the medium	C	$3\ days^{-1}$
Time	T	$365\ days$

We use Pontryagin's optimal principle to derive the optimal control strategy for a prescribed planning period, and experiments suggested that a high insecticide dosage should be applied at the starting time and decreased at a rather steep rate for a short period. In contrast, larvicide and sterilized males should be released in increasing rates up to a stabilizing point, thereby being kept constant up to the end of the planning period.

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REFERENCES

Ascher, U. M, Mattheij, R. M. M., Russell, R. D., 1995. *Numerical solution of boundary value problem for ordinary differential equations*. SIAM.

Bartlett, A. C., 1990. *Insect sterility, insect genetics and insect control.* In Handbook of Pest Management in Agriculture. Vol. II. Ed. CRC Press, Boca Raton, FL, pp. 279-287.

Bradley, D. J., May, R. M., 1978. Consequences of helminth aggregation for dynamics of schistosomiasis. *Trans. R. Soc. trop. Med. Hyg.*, vol. 72, n. 3, pp 262-273.

Esteva, L., Yang, H. M., 2005. Mathematical Model to Asses the Control of *Aedes aegypti* Mosquitoes by the Sterile Insect Technique. *Mathematical Bioscience*, vol. 198, pp. 132-147.

Fleming, W., Rishel, R., 1975. *Deterministic and stochastic optimal control*. Springer-Verlag, New York.

Kirk, D., 1970. *Optimal control theory: An introduction*. Prentice-Hall.

Knipling, E. F., 1997. Possibilities of insect control or eradication through the use of sexually sterile males. *J. Econ. Entomol.* vol. 48, pp. 459-462.

Leitão, A., 2001. Cálculo variacional e controle ótimo. 23^0 *Colóquio Brasileiro de Matemática*. IMPA, Rio de Janeiro.

Thomé, R. C. A., 2007. *Controle Ótimo Aplicado na Estratégia de Combate ao Aedes aegypti Utilizando Inseticida e Mosquitos Estéreis*, D, Sc. Thesis, UNICAMP, Campinas/SP.

Thomé, R. C. A., Yang, H. M., Esteva, L., 2010. Optimal control of *Aedes aegypti* mosquitoes by the sterile insect technique and insecticide. *Mathematical Bioscience*, vol. 223, pp. 12-23.

Tauil, P. L., 2002. Aspectos críticos do controle do dengue no Brasil. *Cad. Saúde Pública*. vol.18, pp. 867-871.

Wise de Valdez, M. R., Nimmo, D., Betz, J., Gong, H. P., James, A. A., Alphey, L. & Black IV, C., 2011. Genetic elimination of dengue vector mosquitoes. *Proceedings of the National Academy of Sciences of the United States of America*. vol. 18, n. 12, pp 4772–4775.