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Optimal Control *Aedes Aegypti* Populations by *Wolbachia*-based Strategies

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Abstract. *Wolbachia* is a bacterium that establishes symbiotic relationship to the most of the arthropods. Recently, it was discovered that *Aedes aegypti*, infected with *Wolbachia*, limits dengue virus replication. In this work, the linear feedback control strategy is proposed to indicate how the *Wolbachia*-infected mosquitoes should be introduced in the environment to reduce the non-*Wolbachia* mosquito population. The numerical simulations show that the proposed strategy reduces the population level of non-*Wolbachia* mosquitos, avoiding mosquito spread, and, consequently, it reduces the number of cases of vector-borne diseases.

Keywords. Optimal control, *Aedes aegypti*, *Wolbachia*, Mosquito Populations

1 Introdution

Mosquito *Aedes aegypti* is responsible for transmitting vector-borne diseases such as dengue, zika and chikungunya. Conventional strategies, such as chemicals and extermination of reproduction spots, are ineffective to control mosquito populations, and, consequently, to avoid epidemics of the above mentioned diseases. One alternative control strategy of mosquito population is infecting *Aedes aegypti* mosquitoes with *Wolbachia* which is a bacterium that can live inside the cells of most of the arthropods establishing a symbiotic relationship with them. Recently, it was discovered that *Aedes aegypti*, infected with the wMel strain of *Wolbachia*, limits dengue virus replication. The field releases of the *Wolbachia*-infected mosquitoes in Cairns, Australia, as a biocontrol strategy indicate that virus-blocking is likely to persist in Wolbachia-

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infected mosquitoes after their release and establishment in wild populations, suggesting that *Wolbachia* biocontrol may be a successful strategy for reducing dengue transmission in the field [1].

The mathematical model which determines the persistence of *Wolbachia*-infected mosquitoes by considering the competition between *Wolbachia*-infected and non-*Wolbachia* mosquitoes was proposed in [2]. The stability of the steady state with the persistence of *Wolbachia*-infected mosquitoes depends on values of the model coefficients and initial conditions. There are many cases when the steady state with the persistence of *Wolbachia*-infected mosquitoes is unstable.

In this work, the linear feedback control strategy is proposed to indicate how the *Wolbachia*-infected mosquitoes should be introduced in order to give stability for the steady state with the persistence of *Wolbachia*-infected mosquitoes.

2 Mathematical Model

The mosquito population model, proposed in [2], is described by the following system of differential equations:

$$
\begin{aligned}
\frac{dA_n}{dt} &= \frac{\rho_n F_n^2}{2(F_n + F_w)}\left(1 - \frac{A_n + A_w}{K}\right) - \mu_{na} A_n - \tau_n A_n \\
\frac{dF_n}{dt} &= \frac{\tau_n A_n}{2} - \mu_n F_n + \frac{(1-\alpha_w)\tau_w A_w}{2} \\
\frac{dA_w}{dt} &= \frac{\rho_w F_w}{2}\left(1 - \frac{A_n + A_w}{K}\right) - \mu_{wa} A_w - \tau_w A_w \\
\frac{dF_w}{dt} &= \frac{\alpha_w \tau_w A_w}{2} - \mu_w F_w
\end{aligned}
\qquad (1)
$$

where A_n and A_w are non-*Wolbachia* and *Wolbachia*-infected mosquito populations, respectively, F_n and F_w are female of non-*Wolbachia* and *Wolbachia*-infected mosquito populations, respectively. The parameter K is the carrying capacity, which is the capacity of the environment to sustain the aquatic mosquitoes. The populations can be adimensionalized with respect to this value. Other parameters of model (1) are described in Table 1, extracted from [2].

According to [2] the model (1) has four steady states:

$$
\begin{aligned}
P_1 &= (0,0,0,0) \\
P_2 &= \left(A_{n2}^*, F_{n2}^*, 0, 0\right) \\
P_3 &= (A_{n3}^*, F_{n3}^*, A_{w3}^*, F_{w3}^*,) \\
P_4 &= (A_{n4}^*, F_{n4}^*, A_{w4}^*, F_{w4}^*,)
\end{aligned}
$$

where $A_{n2}^* = 1 - \dfrac{4\mu_n(\mu_{na} + \tau_n)}{\rho_n \tau_n}$, $\quad F_{n2}^* = \dfrac{\tau_n A_{n2}^*}{2\mu_n}$, $F_{ni}^* = \dfrac{B_4 A_{ni}^* + B_5}{2\mu_n}$,

$$F_{ni}^{*} = B_2 B_3 - B_3 A_{ni}^{*}, \quad A_{wi}^{*} = B_2 - A_{ni}^{*}, \quad i = 3,4$$

Table 1: Parameter descriptions of the model (1) (extracted from [2])

Parameter	Description	Value
ρ_n	Non-*Wolbachia* reproductive rate	1.25
ρ_w	*Wolbachia* reproductive rate	2.1 ρ_n
μ_{na}	Non-*Wolbachia* aquatic death rate	1/7.78
μ_{wa}	*Wolbachia* aquatic death rate	1/7.78
τ_n	Non-*Wolbachia* maturation rate	1/6.67
τ_w	*Wolbachia* maturation rate	1/6.67
μ_n	Non-*Wolbachia* adult death rate	1/14
μ_w	*Wolbachia* adult death rate	1/7
α_w	Maternal transmission	0.8 – 0.9
K	Carrying capacity	1

where

$$A_{n2}^{*} = 1 - \frac{4\mu_n(\mu_{na} + \tau_n)}{\rho_n \tau_n}, \qquad F_{n2}^{*} = \frac{\tau_n A_{n2}^{*}}{2\mu_n},$$

$$F_{ni}^{*} = \frac{B_4 A_{ni}^{*} + B_5}{2\mu_n}, \quad F_{ni}^{*} = B_2 B_3 - B_3 A_{ni}^{*}, \quad A_{wi}^{*} = B_2 - A_{ni}^{*}, \quad i = 3,4$$

with A_{n3}^{*} and A_{n4}^{*} ($A_{n3}^{*} > A_{n4}^{*}$) given by the nonnegative roots of $C_1 A_n^{*2} + C_2 A_n^{*} + C_3 = 0$, where

$$C_1 = \left(\frac{1}{B_1} - \frac{B_4}{2\mu_n}\right)\frac{B_4}{2\mu_n} - \frac{B_3}{B_1}, \quad C_1 = \left(\frac{1}{B_1} - \frac{B_4}{2\mu_n}\right)\frac{B_5}{2\mu_n} + \frac{B_3 B_2}{B_1} - \frac{B_4 B_5}{\mu_n^2},$$

$$C_1 = -\frac{B_5^2}{4\mu_n^2},$$

where B_1, B_2, B_3, B_4, B_5 are defined in terms of the parameter values as

$$B_1 = \frac{2\rho_n \mu_w(\mu_{wa} + \tau_w)}{(\mu_{na} + \tau_n)\rho_w \tau_w \alpha_w}, \quad B_1 = 1 - \frac{4\mu_w(\mu_{wa} + \tau_w)}{\rho_w \tau_w \alpha_w}, \quad B_3 = \frac{\alpha_w \tau_w}{2\mu_w},$$

$$B_4 = \tau_n - (1 - \alpha_w)\tau_w, \quad B_5 = (1 - \alpha_w)\tau_w B_2.$$

The steady state $P_1 = (0,0,0,0)$ is unstable. The steady state $P_2 = \left(A_{n2}^{*}, F_{n2}^{*}, 0, 0\right)$ is stable for $\rho_n > \dfrac{4(\mu_{na} + \tau_n)\mu_n}{\tau_n}$. The *Wolbachia*-infected mosquito population goes to extinction in this case.

The stability of the steady states P_3 and P_4 depends on of the parameter α_w. For $\alpha_w < 0.816$ the steady states P_3 and P_4 are unstable, and the steady state P_2 is stable (Figure 1).

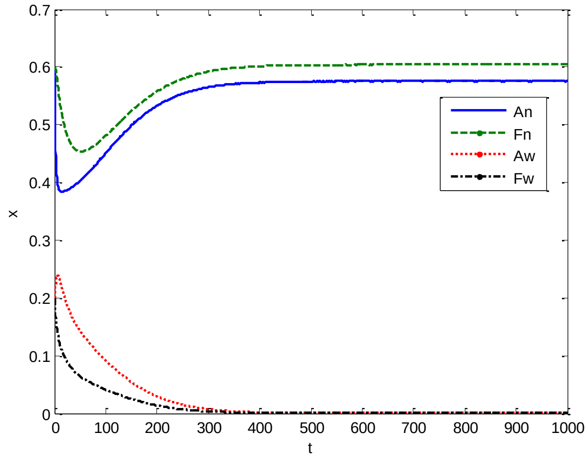

Figure 1: Numerical simulations show that the non-*Wolbachia* mosquito population persists for $\alpha_w = 0.8$ and initial conditions (0.6, 0.6, 0.2, 0.2)

For $0.816 < \alpha_W < 1$ the steady state P_3 is real, positive and unstable, and P_4 is real, positive and stable (Figure 2).

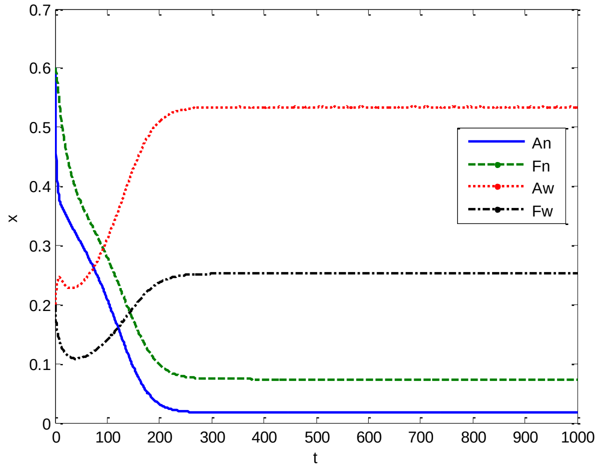

Figure 2: Numerical simulations for $\alpha_w = 0.9$ and initial conditions (0.6, 0.6, 0.2, 0.2)

Consequently, small changes in initial conditions and values of the parameter α_w can lead to extinction the *Wolbachia*-infected mosquito populationia. The aim of this work is to find a strategy of introduction of *Wolbachia*-infected mosquitoes which brings the system into the steady state P_4 for any values of initial conditions and parameter α_w. The linear optimal control of nonlinear systems is presented in the next chapter.

3 Optimal control problem

Let us *u* the control function that characterizes the daily introduction of *Wolbachia*-infected mosquitoes. The system (1) with control *u* has the following form:

$$\begin{aligned}
\frac{dA_n}{dt} &= \frac{\rho_n F_n^2}{2(F_n + F_w)}[1-(A_n + A_w)] - \mu_{na} A_n - \tau_n A_n \\
\frac{dF_n}{dt} &= \frac{\tau_n A_n}{2} - \mu_n F_n + \frac{(1-\alpha_w)\tau_w A_w}{2} \\
\frac{dA_w}{dt} &= \frac{\rho_w F_w}{2}[1-(A_n + A_w)] - \mu_{wa} A_w - \tau_w A_w \\
\frac{dF_w}{dt} &= \frac{\alpha_w \tau_w A_w}{2} - \mu_w F_w + u
\end{aligned} \tag{2}$$

Defining the following new variables

$$y = \begin{bmatrix} A_n - A_{n4}^* & F_n - F_{n4}^* & A_w - A_{w4}^* & F_w - F_{w4}^* \end{bmatrix}^T, \tag{3}$$

we get the following error system:

$$\dot{y} = Ay + H(y) + Bu \tag{4}$$

where the matrices *A* and *B* are

$$A = \begin{bmatrix} -a_2 & 0 & 0 & 0 \\ a_3 & -a_4 & a_5 & 0 \\ -b_1 F_{w4}^* & 0 & b_1 F_{w4}^* - b_2 & b_1(1 - A_{n4}^* - A_{w4}^*) \\ 0 & 0 & b_3 & -b_4 \end{bmatrix}, \quad B = \begin{bmatrix} 0 \\ 1 \\ 0 \end{bmatrix}, \tag{5}$$

the vector *H(z)* has a form: $H(y) = \begin{bmatrix} h_1 & 0 & h_3 & 0 \end{bmatrix}^T$

and $a_1 = \rho_n$, $a_2 = \tau_n + \mu_{na}$, $a_3 = \tau_n / 2$, $a_4 = \mu_n$, $a_5 = (1-\alpha_w)\tau_w / 2$, $b_1 = \rho_w / 2$, $b_2 = \tau_w + \mu_{wa}$, $b_3 = \alpha_w \tau_w / 2$, $b_4 = \mu_w$, $h_3 = -b_1 y_4 (y_1 + y_3)$

$$h_1 = \frac{a_1 (y_2 + F_{n4}^*)^2 (1 - A_{n4}^* - A_{w4}^* - y_1 - y_3)}{2(y_1 + y_2 + F_{n4}^* + F_{w4}^*)} - \frac{a_1 F_{n4}^{*2} (1 - A_{n4}^* - A_{w4}^*)}{2(F_{n4}^* + F_{w4}^*)} \tag{6}$$

The optimal control *u* can be determined applying the following theorem.

Theorem 3.1 [3]**.** *If there exist constant matrices Q, and R, positive definite, being Q* *symmetric, such as that the function*

$$L(z) = y^T Q y - h^T(y) P z - y^T P h(y), \tag{7}$$

is positive definite then the linear feedback control

$$u = -R^{-1} B^T P y \tag{8}$$

is optimal, in order to transfer the nonlinear system (4) from an initial to final state

$$y(\infty) = 0 \tag{9}$$

minimizing the functional

$$J = \int_0^\infty [L(y) + u^T R u] dt \tag{10}$$

where P *the symmetric, positive definite matrix, is the solution of the matrix algebraic Riccati equation*

$$PA + A^T P - PBR^{-1} B^T P + Q = 0 \tag{11}$$

In addition, with the feedback control (8), there exists a neighborhood $\Gamma_0 \subset \Gamma$, $\Gamma \subset \Re^n$, *of the origin such that if* $y_0 \in \Gamma_0$, *the solution* $y(t) = 0,\ t \ge 0$, *of the controlled system (4) is locally asymptotically stable, and* $J_{\min} = z_0^T P(0) z_0$. *Finally, if* $\Gamma = \Re^n$ *then the solution* $y(t) = 0,\ t \ge 0$, *of the controlled system (4) is globally asymptotically stable.*

From this theorem one can conclude that the error dynamical system (4) controlled by linear feedback control u is locally asymptotically stable, and hence, the system (3), controlled by u, tends to the desired steady state P_4.

4 Numerical simulations

We will stabilize the system (2) at the desired steady state $P_4 = (A_{n4}^*, F_{n4}^*, A_{w4}^*, F_{w4}^*,)$. For $\alpha_w = 0.8$ the desired steady state is $P_4 = (0.0366,\ 0.1345,\ 0.4580,\ 0.1923)$. Choosing

$$Q = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 10 & 0 \\ 0 & 0 & 0 & 10 \end{bmatrix}, \quad R = [1] \text{ we obtain } P = \begin{bmatrix} 112.9500 & 0.9306 & -16.3777 & -3.7706 \\ 0.9306 & 6.9962 & 0.1237 & 0.0234 \\ -16.3777 & 0.1237 & 7.8359 & 1.3593 \\ -3.7706 & 0.0234 & 1.3593 & 3.2957 \end{bmatrix}$$

from the solution of the Riccati equation (11) using the MATLAB command LQR.

In this case the optimal strategy has the following form:

$$u = -3.7706 y_1 + 0.0234 y_2 + 1.3593 y_3 + 3.2957 y_4 \tag{12}$$

The optimal control (12) is designed to drive the trajectory of the system (2) to desired steady state P_4, as shown in Figure 3.

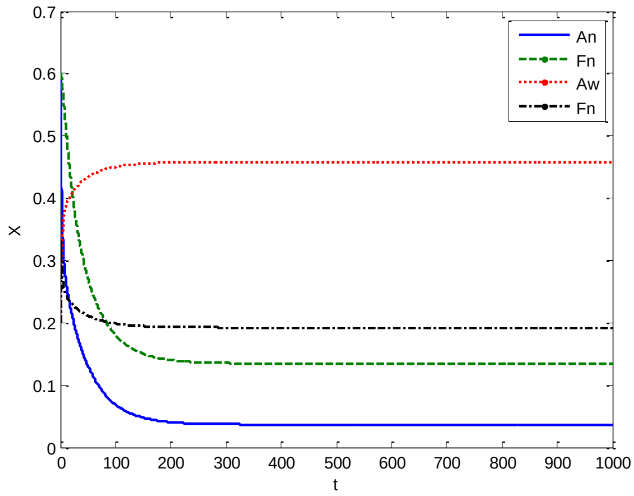

Figure 3: Dynamics of the controlled system for $\alpha_w = 0.8$ and initial conditions (0.6, 0.6, 0.2, 0.2)

The proposed strategies (12) reduce the population level of A_n and F_n, avoiding mosquito spread, and, consequently, it reduces the number of cases of dengue, zika and chikungunya.

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