A Reaction-Diffusion Model for Controlling the *Aedes aegypti* with *Wolbachia*

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Abstract

We formulated and derived a stability analysis for a mathematical model of reaction-diffusion which describes the population dynamics of the mosquito *Aedes aegypti* when this is controlled by the *Wolbachia* bacterium. The model was simulated using both hypotetical and secondary source data. A Turing pattern study shows that for this particular model there is no spatial influence on the stability. Finally the model was simulated using parameters from secondary sources and hypothetical assumptions.

Keywords: *Aedes aegypti*, Dengue, *Wolbachia*, Reaction-Diffusion Model, Stability

1 Introduction

Infectious diseases are a public health problem of global scale, due to the fact that they constitute the main mortality cause. Even though there are vaccines and medicines to prevent and attack infectious diseases the most important action against it is prevention.

An *Aedes aegyptis* control implies the efficient use of limited resources to act against the vector in high risk of dengue epidemics; it is crucial that any campaign against mosquitoes include: chemical, physical and biological ways that require the citizen participation [4].

In biological control, other species are used, which take the role of predator in different stages of the mosquito life cycle *Aedes aegypti*; some of these species used are: nematodes, protozoa, fish and bacteria as: *Wolbachia.* This control was implemented due to the resistant mosquitoes appearance to pesticides and to high fauna and flora toxicity in areas where products were implemented.

The species of the genere *Wolbachia* are rickettsias, that is, they are coccoid gram-negative bacteria (arthropods intracellular parasite). *Wolbachia* does not cause pathologies in vertebrates, but it induces alterations in the reproductive cycles of its hosts [11], [9].

The infection caused by *Wolbachia* is the most dispersed among animals; the capacity of this bacterium to handle the reproduction of its hosts, place it in organisms biology center, affecting in process as the gender determination, the cell cycle; the species information and extinction and arthropods behavior; and among them can be taking into account several plagues and sicknesses vectors; characteristics as the *Wolbachia* vertical heritance, the spread speed in the populations that it affects; the capacity of blocking the pathogenic activity of several microorganism or to make shorter its hosts life cycle, represent the potential instrument that it is for controlling nematode and insect population that are harmful for society [12].

Many mathematical models have been created and analyzed, most of them use partial differential equations system focused on study: Special formation of patterns in epidemic models [13],[19]; Turing and Hopf unsteadiness in pray-predator system [15]; Crossed dissemination [19]; Turing and Hopf bifurcation analysis [16].

This paper is organized as follows. In Section 2 we describe the reaction-diffusion model, then we analized the stability of the model in the absence

of diffusion. In section 3 we show a mathematical analysis of the reaction-diffusion model to determine the stability of Turing. Finally, discussion and conclusions are given in Section 4.

2 The model

The assumptions of this model are: *A. aegypti* mosquitoes logistic growth of those that possess the dengue virus which are not infected with *Wolbachia*; logistic growth of *A. aegypti* dengue virus carrier infected by the bacterium; *A. aegyptis* infection caused by *Wolbachia*. Vector *A. aegyptis* life time shortening average. *A. aegyptis* reproductive incompatibility through the infection caused by *Wolbachia*. Vertical transmission of the infection produced by *Wolbachia* to mosquitos descendant and its mortality generated by the germs contagion.

The quantities used in the model are: $u(x, y, t)$: Average number of mosquitoes carrying dengue virus which are not infected with *Wolbachia*, $v(x, y, t)$: Average number of mosquitoes carrying dengue virus and infected with *Wolbachia* at time t, in a two dimensional space point (x, y), respectively. Additionally: α: increasing rate of dengue-carrying mosquitoes which are not infected by the bacterium *Wolbachia*, k_u: carrying capacity of dengue-carrying mosquitoes which are not infected with *Wolbachia*, $\alpha u \left(1 - \frac{u}{k_u}\right)$: logistic growth of dengue-carrying mosquitoes which are not infected with *Wolbachia*, σ: infection rate of wolbachia, ρ: increasing rate of dengue-carrying mosquitoes infected with *Wolbachia*, k_v:carrying capacity dengue-carrying mosquitoes infected with *Wolbachia*, $\rho v \left(1 - \frac{v}{k_v}\right)$: logistic growth dengue-carrying mosquitoes infected with *Wolbachia*, π: mosquito mortality rate caused by the infection transmitted by Wolbachia, ϕ_u , ϕ_v: Constant spread coefficients of dengue possessor mosquitoes either infected or not infected by *Wolbachia*, $\phi_u \nabla^2 u$, $\phi_v \nabla^2 v$: Diffusive terms of dengue carrier mosquitoes infected or not infected by the germ *Wolbachia* and Laplacian operator in 2 dimensions (x, y), where $\nabla^2(\cdot) = \frac{\partial^2}{\partial x^2} + \frac{\partial^2}{\partial y^2}$. The reaction-diffusion model is:

$$\frac{\partial u(x, y, t)}{\partial t} = \alpha u \left(1 - \frac{u}{k_u}\right) - \sigma u + \phi_u \nabla^2 u, \tag{1}$$

$$\frac{\partial v(x, y, t)}{\partial t} = \rho v \left(1 - \frac{v}{k_v}\right) + \sigma u - \pi v + \phi_v \nabla^2 v, \tag{2}$$

with initial conditions: $u(x, y, 0) > 0$; $v(x, y, 0) > 0$ and boundary conditions: $\frac{\partial u}{\partial \eta} = \frac{\partial v}{\partial \eta} = 0$, $(x, y) \in \partial\Omega$. where η is normal unitary vector of boundary $\partial\Omega$ of the region reaction-diffusion Ω.

2.1   Model without diffusion

It is determined by the following non-lineal ordinary differential equations system:

$$\frac{du}{dt} = \omega u \left(1 - \frac{u}{k_1} \right) \equiv f(u, v), \tag{3}$$

$$\frac{dv}{dt} = \xi v \left(1 - \frac{v}{k_2} \right) + \sigma u \equiv g(u, v), \tag{4}$$

where $\omega = \alpha - \sigma > 0$, $k_1 = \frac{k_u \omega}{\alpha} > 0$, $\xi = \rho - \pi > 0$ and $k_2 = \frac{k_v \xi}{\rho} > 0$. For the unsteadiness analysis of the no diffusion, we determine the unchanging results of the combination (3)-(4), doing $\frac{du}{dt} = 0$, $\frac{dv}{dt} = 0$ and solving the non-lineal algebraic structure for u, v, we get the stable solution $E_0 = (0,0)$ in absence of the mosquitoes infected and non infected by the bacterium *Wolbachia*; $E_1 = (0, k_2)$ in absence of mosquito infected and non infected and presence of mosquitoes affected by the germ, $E_3 = (k_1, v_1)$ and $E_4 = (k_1, v_2)$ in co-existence of mosquitoes infected and non infected with *Wolbachia*, where v_1 is the positive real root of the equation:

$$v^2 - k_2 v - \frac{\sigma k_2}{\xi} k_1 = 0, \tag{5}$$

That is $v_1 = \frac{1}{2} \left(k_2 + \sqrt{\psi} \right)$ where, $\psi = k_2^2 + 4\frac{\sigma k_1 k_2}{\xi}$.

Computing partial derivaties f and g concerning a u, v we obtain Jacobis matrix in the generic equilibrium point $E = (u^*, v^*)$:

$$J(E) = \begin{pmatrix} \omega - \frac{2\omega}{k_1} u^* & 0 \\ \sigma & \xi - \frac{2\xi}{k_2} v^* \end{pmatrix}$$

For $E_0 = (0,0)$, Jacobis matrix is triangular and it has proper values $\lambda_1 = \omega$, $\lambda_2 = \xi$. Therefore, the stable solution $E_0 = (0,0)$ es inestable, cuando $\omega > 0$ or $\xi > 0$ or in similar way $\alpha > \sigma$ o $\rho > \pi$.

Theorem 2.1 *The unchanging result E_0 of the combination (3)-(4) that belongs to the absence of population is unstable when $\omega > 0$ o $\xi > 0$.*

For the case $E_1 = (0, k_2)$, the proper values are $\lambda_1 = \omega$ and $\lambda_2 = -\xi$, what implies that the stable solution $E_1 = (0, k_2)$ is unsteady.

Theorem 2.2 *With the absence of dengue carrier infected and non infected mosquitoes with the germ Wolbachia, the stable result $E_1 = (0, k_2)$ of the equation (3)-(4) is unsteady when $\omega > 0$.*

In the case of $E_3 = (k_1, v_1)$, Jacobi's matrix is

$$J(k_1, v_1) = \begin{pmatrix} -\omega & 0 \\ \sigma & \xi - \frac{2\xi}{k_2}v_1^* \end{pmatrix}$$

and the trace and the determinant are:

$$tr J(k_1, v_1^*) = -\omega + \xi - \frac{2\xi}{k_2}v_1^* = -\omega - \xi\left(1 - \frac{2}{k_2}v_1^*\right) < 0, \qquad (6)$$

$$\det J(k_1, v_1^*) = -\omega\xi\left(1 - \frac{2}{k_2}v_1^*\right) > 0, \qquad (7)$$

where $v_1^* > \frac{k_2}{2}$. then, the steady solution $E_3 = (k_1, v_1^*)$ is a stable node.

Theorem 2.3 *With the non and the infected dengue carrier mosquitoes co-existence, the equilibrium point is $E_3 = (k_1, v_1^*)$ of the equation (3)-(4) is a steady node when the $tr J(k_1, v_1^*) < 0$ and the $\det J(k_1, v_1^*) > 0$ if $v_1^* > \frac{k_2}{2}$.*

The unchanging solution $E_4 = (k_1, v_2^*)$ is not analyzed since $v_2^* < 0$.

3 Diffusion Model

For determining Turing's unsteadiness, we consider the unchangeable solution of stable co-existence $E_3 = (k_1, v_1^*)$. To line up the scheme with spread formed by the equations (1)-(2) we shall considerate a perturbation of E_3 around the space and time:

$$u(x, y, t) = k_1^* + p(x, y, t) \quad , \quad v(x, y, t) = v_1^* + q(x, y, t) \qquad (8)$$

where, $|p(x, y, t)| \le k_1$ and $|q(x, y, t)| \le v_1^*$. We start to consider results of the form:

$$p(x, y, t) = \alpha_1 e^{(k_x x + k_y y)i + \mu t} \quad , \quad q(x, y, t) = \alpha_2 e^{(k_x x + k_y y)i + \mu t} \qquad (9)$$

A possible result is of the type:

$$p(x, y, t) = \alpha_1 e^{\mu t} \cos k_x x \cos k_y y \quad , \quad q(x, y, t) = \alpha_2 e^{\mu t} \cos k_x x \cos k_y y \qquad (10)$$

where, μ: is the growth rate of the perturbation in a time t, α_1, α_2: are the amplitude correspondents and son las correspondientes amplitudes y k_x, k_y: are the numbers of perturbation spatial wave.

These deflections make possible the system line up (1)-(2), getting the lineal

$$\frac{\partial p}{\partial t} = f_u(E_3)p + f_v(E_3)q + \phi_u\nabla^2 p, \qquad (11)$$

$$\frac{\partial q}{\partial t} = g_u(E_3)p + g_v(E_3)q + \phi_v\nabla^2 q, \qquad (12)$$

Replacing the derivates of the functions p and q concerning to x, y and t in the equations (11) and (12), we obtain the next system:

$$\alpha_1[\mu - f_u(E_3) + \phi_u k^2] - \alpha_2 f_v(E_3) = 0 \qquad (13)$$
$$-\alpha_1 g_u(E_3) + \alpha_2[\mu - g_v(E_3) + \phi_u k^2] = 0 \qquad (14)$$

where, $k^2 = k_x^2 + k_y^2$.

A solution to this system, is the $\alpha_1 = 0$, $\alpha_2 = 0$ trivial for all t and a non trivial solution can only exist if the determinant of the coefficient scheme (13) and (14) is zero:

$$\det \begin{pmatrix} \mu - f_u(E_3) + \phi_u k^2 & -f_v(E_3) \\ -g_u(E_3) & \mu - g_v(E_3) + \phi_v k^2 \end{pmatrix} = 0$$

As a result, the next characteristic equation:

$$(\mu - f_u(E_3) + \phi_u k^2)(\mu - g_v(E_3) + \phi_v k^2) - f_v(E_3)g_u(E_3) = 0$$

Simplifying, the quadrati equation is follows:

$$\mu^2 + B(k^2)\mu + C(k^2) = 0$$

where,

$$B(k^2) = tr J(E_3) - k^2(\phi_u + \phi_v)$$

$$C(k^2) = \phi_u \phi_v k^4 - (\phi_u g_v(E_3) + \phi_v f_u(E_3))k^2 + \det J(E_3)$$

4   Results and Conclusions

Using hypothetical values for the parameters, simulations in MAPLE are made, carrying out the no diffusion model represented by the combination (3)-(4). In the Figure 1, we can observe that the mosquito populations non affected and affected ones by *Wolbachia*, stabilize quickly in the time.

We found an equilibrium point which is local and asymptotically stable; in other words, the populations $u(t)$, $v(t)$ are reaching this equilibrium point at the same time that time elapses.
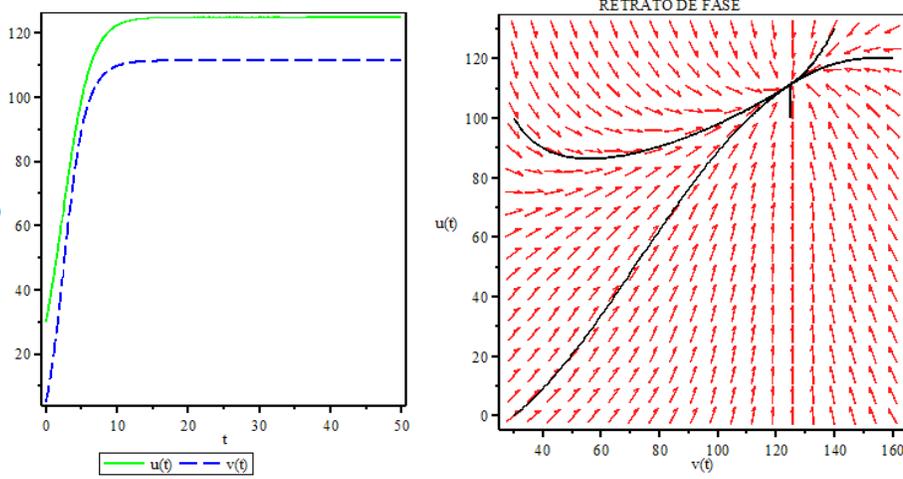
Figure 1: Behavior and phase portrait of mosquitoes population non infected $u(t)$ and infected $v(t)$ with the germ *Wolbachia* with $\alpha = 0.8$, $\sigma = 0.3$, $\rho = 0.4$, $k_u = 200$, $k_v = 70$ and $\pi = 0.1$.

For the diffusion model, sufficient and necessary inequalities for a Turin regime or unsteadiness are:

i. $f_u(E_3) + g_v(E_3) < 0$

ii. $f_u(E_3)g_v(E_3) - f_v(E_3)g_u(E_3) > 0$

iii. $\phi_v f_u(E_3) + \phi_u g_v(E_3) > 0$

iv. $(\phi_v f_u(E_3) + \phi_u g_v(E_3))^2 - 4\phi_u\phi_v(f_u(E_3)g_v(E_3) - f_v(E_3)g_u(E_3)) > 0$

So the signs of f_u and g_v in i) and iii) must be opposite, since the coefficient values are positive; for the second condition, $f_v g_u < 0$, indicating the opposition of sign between they both. So, Jacobians matrix, evaluated in the stable equilibrium point must have one of the next forms:

$$\begin{pmatrix} + & + \\ - & - \end{pmatrix} \ , \ \begin{pmatrix} + & - \\ + & - \end{pmatrix} \ , \ \begin{pmatrix} - & + \\ - & + \end{pmatrix} \ , \ \begin{pmatrix} - & - \\ + & + \end{pmatrix} \qquad (15)$$

and it is seen that the combination $(3),(4)$ is disengaged in a way, saying that the differential equation (3) does not depend on the variable v, and it allows that Jacobian matrix in the equilibrium $E_3 = (k_1, v_1^*)$ in of the next way

$$\begin{pmatrix} - & 0 \\ + & - \end{pmatrix} \qquad (16)$$

which does not belong to any of the matrixes (15), what let us to conclude that the reaction-diffusion system that model the dynamic does not present Turings patterns; the diffusion does not destabilize the structure, and in this case the inequalities are:

  i. $f_u(E_3) + g_v(E_3) < 0$

  ii. $f_u(E_3)g_v(E_3) > 0$

  iii. $\phi_v f_u(E_3) + \phi_u g_v(E_3) > 0$

  iv. $(\phi_v f_u(E_3) + \phi_u g_v(E_3))^2 - 4\phi_u \phi_v f_u(E_3)g_v(E_3) > 0$

Using hypothetical values for the parameters, simulations in MATLAB are developed for the diffused structure
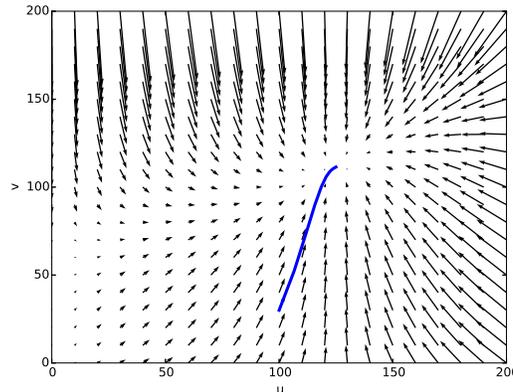

Figure 2: : Phase portrait of the diffusion model with $u(0) = 100$, $v(0) = 30$, $\alpha = 0.8$, $\sigma = 0.3$, $\rho = 0.4$, $k_u = 200$, $k_v = 70$ and $\pi = 0.1$.

In the Figura 2, there are directions per each trajectory, which go towards the same equilibrium point; that the difussed system continues to be steady.

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