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Stability Analysis of a Model with Integrated Control for Population Growth of the *Aedes Aegypti* Mosquito

Ana M. Pulecio[1,*], *Anibal Muñoz*[2] *and Gerard Olivar*[3]

[1] Basic Sciences Department, University CESMAG, Pasto, Colombia.
[2] Faculty of Education, University of the Quindío, Armenia, Colombia.
[3] Mathematics Department, National University of Colombia, Manizales, Colombia.

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Abstract: We present a system of ordinary nonlinear differential equations describing the population growth dynamics of the *Aedes aegypti* mosquito, the main transmitter of the dengue virus in Colombia. This model incorporates the three types of known control for mosquito eradication: mechanical, biological and chemical, focusing on biological control through the use of the *Wolbachia* bacterium, which is the new hope for the control of the diseases transmitted by this mosquito. A local stability analysis of the model is performed on the three equilibrium points that are found, determining the conditions under which those points become stable or unstable. Finally, we present numerical simulations implemented in Matlab, where the numerical results are obtained using hypothetical values of the parameters obtained from the literature.

Keywords: *Aedes aegypti*; integrated control; *Wolbachia*; stability.

1 Introduction

Aedes aegypti is a mosquito that mainly lives close to human populations. It flies only short distances and requires blood (primarily human), to reproduce [1], [7].

During their lifetime the mosquitoes go through two stages: immature and mature. In the immature phase, the mosquito is aquatic and undergoes a metamorphosis from egg to an adult. It feeds mainly on residues in the water where they were laid by the female. Adult mosquitoes are airborne and while the males feed on plant nectar, the females feed on blood. [4].

By feeding on blood, in order to mature and deposit her eggs, the female mosquito promotes the transmission of viruses and pathogens that cause various diseases including Dengue fever. For this reason global campaigns have been founded to eradicate the mosquito. So far, the struggle has been unsuccessful because although some countries have achieved temporary the extinction, the mosquito soon returns due to the infestation of neighbouring countries [2], [7].

There are three main mechanisms to control the propagation of mosquitoes, namely: mechanical control, focused on preventing the reproduction of the mosquito using traps, destroying breeding grounds, etc.; chemical control based on insecticides or larvicides; and biological control that makes use of other living organisms such as the *Wolbachia* bacterium which reduces the life span of the mosquito and also, in the case of dengue, almost eliminates the probability of transmitting the virus to humans [5], [7], [8].

The present article demonstrates a mathematical model that describes the population growth of the female mosquito in the adult phase. The model incorporates all three control mechanisms for the mosquito. A stability analysis is performed and we show how the population growth dynamics change in response to a program of biological control via the introduction of the *Wolbachia* bacterium into the population. In this way, the model will serve as a tool for the those who wish to determine the way in which mechanical, chemical and biological controls should be applied to diminish the breeding of mosquitoes and, therefore, the propagation of diseases like dengue that are transmitted by them.

* Corresponding author e-mail: ampuleciom@unal.edu.co

2 The Model

The following hypotheses are considered in the creation of the model:

–The population of interest is that of the adult female *Aedes aegypti* mosquitoes.
–There are two populations of adult female mosquitoes: those that are infected by the *Wolbachia* bacterium and those that are not.
–The death rate of an adult mosquito infected with the bacterium is greater than the death rate of an uninfected mosquito.
–Three controls on the mosquito population are used: traps that prevent the eggs from reaching adulthood (mechanical control); in the immature state a proportion of the eggs are infected by the *Wolbachia* bacterium, which genetically manipulates the mosquito and is transmitted vertically (biological control); a proportion of adult mosquitoes die from the use of insecticides (chemical control).

Taking these hypotheses into account, let us consider b, the total number of adult female mosquitoes that are *not* infected with the bacterium at time t; and B, the total number of adult female mosquitoes that *are* infected with the bacterium in a time t. We also consider the parameters in Table 1. In this analysis we use the week as the period of time because it is short enough that a single female mosquito will lay eggs at most once during the period.

Table 1: Parameters of the model

Parameter	Description
ξ	Rate of development of a mosquito from the immature phase to the adult phase
f	Proportion of immature mosquitoes that develop into adult females
ϕ	The probability that an adult female mosquito will lay eggs in the week
δ	The average number of eggs laid at a time by an adult female mosquito
π	The natural death rate of immature mosquitoes
κ	The maximum number of mosquitoes that the environment can support
ε	The natural death rate of the mosquito without *Wolbachia*
ν	The death rate of mosquitoes infected by *Wolbachia*
u_1	The proportion of immature mosquito deaths caused by traps
u_2	The proportion of immature mosquito deaths caused by insecticides
u_3	The proportion of eggs infected by the *Wolbachia* bacterium through micro-injection

If we consider the variation of b with over time, we recognise that this population grows continuously as a result of the development of immature mosquitoes. It also decreases as a result of the natural death of mosquitoes or the use of insecticides. Therefore, in terms of the parameters shown in Table 1, we see that the expression $(1-u_3)\frac{\xi f\phi\delta}{\pi+u_1}$ represents, for each adult female that lays eggs in the week, the average number of eggs that survive to adulthood without being infected by the *Wolbachia* bacterium. Furthermore, the expression $1-\frac{b+B}{\kappa}$ represents the probability that a mosquito that develops to the mature phase finds space available in the environment. From these, we have the number of mosquitoes that enter the population of adult females without being infected by the bacterium is given by $(1-u_3)\frac{\xi f\phi\delta}{\pi+u_1}\left(1-\frac{b+B}{\kappa}\right)b$. Similarly, the number of female mosquitoes in this state that die in each instant is given by $(\varepsilon+u_2)b$. Thus we have that:

$$\frac{db}{dt}=(1-u_3)\frac{\xi f\phi\delta}{\pi+u_1}\left(1-\frac{b+B}{\kappa}\right)b-(\varepsilon+u_2)b.$$

Now, the mosquitoes that enter the population of adult females infected by the *Wolbachia* bacterium are those that develop from eggs that have been laid by an infected female mosquito (because the bacterium is transmitted vertically) and those that develop from eggs that have been laid by uninfected females but are infected through micro-injection Therefore the change in this population is given by:

$$\frac{dB}{dt}=\frac{\xi f\phi\delta}{\pi+u_1}\left(1-\frac{b+B}{\kappa}\right)B+\frac{u_3\xi f\phi\delta}{\pi+u_1}\left(1-\frac{b+B}{\kappa}\right)b \\ -(\nu+u_2)B.$$

Thus the system of ordinary non-linear equations representing the growth dynamic of the population of adult female mosquitoes both with and without *Wolbachia* infection is given by:

$$\begin{aligned}\frac{db}{dt}&=(1-u_3)\frac{\xi f\phi\delta}{\pi+u_1}\left(1-\frac{b+B}{\kappa}\right)b-(\varepsilon+u_2)b \qquad (1)\\ \frac{dB}{dt}&=\frac{\xi f\phi\delta}{\pi+u_1}\left(1-\frac{b+B}{\kappa}\right)(B+u_3b)-(\nu+u_2)B.\end{aligned}$$

3 Points of Equilibrium

Setting the right hand side of the system's differential equations to zero, we find that the model has three points of equilibrium:

$$P_1=(0,0),\quad P_2=\left(0,k\left(\frac{H-1}{H}\right)\right)\quad \text{and}\quad P_3=(b_1,B_1)$$

where

$$b_1 = k\frac{h-1}{h}\left(1-\frac{u_3(\varepsilon+u_2)}{(\nu-\varepsilon)(1-u_3)}\right),$$

$$B_1 = \frac{h-1}{h}\frac{u_3k(\varepsilon+u_2)}{(\nu-\varepsilon)(1-u_3)},$$

with

$$H = \frac{\xi f\phi\delta}{(\nu+u_2)(\pi+u_1)} \quad \text{and} \quad h = \frac{(1-u_3)\xi f\phi\delta}{(\pi+u_1)(\varepsilon+u_2)},$$

which represent the thresholds of the growth of the populations of adult female mosquitoes with and without *Wolbachia* infection respectively.

We can further see that, when $u_3 = 0$, the third point of equilibrium can be written as:

$$P_3 = \left(k\frac{h-1}{h}, 0\right)$$

4 Stability Analysis

Theorem 1. *The local stability of the system can be summarised as:*

1. *If $h \neq H$, $h < 1$ and $H < 1$, P_1 is asymptotically stable, and the points P_2 and P_3 are unstable.*
2. *If $h = H$ and $h < 1$, P_1 is asymptotically stable and the points P_2 y P_3 are not hyperbolic.*
3. *If $h = H = 1$, none of the three points of equilibrium are hyperbolic.*
4. *If $h = 1$ and $H \neq 1$, P_1 and P_3 are not hyperbolic, but P_2 is asymptotically stable when $H > 1$ and unstable when $H < 1$.*
5. *If $H = 1$ and $h \neq 1$, P_1 y P_2 are not hyperbolic, but P_3 is asymptotically stable when $h > 1$ and unstable when $h < 1$.*
6. *If $h < H$, $h \neq 1$ y $H > 1$, P_2 is asymptotically stable and the points P_1 and P_3 are unstable.*
7. *If $h > H$, $h > 1$ y $H \neq 1$, P_3 is asymptotically stable and the points P_1 and P_2 are unstable.*
8. *If $h = H$, $h > 1$, P_1 is unstable and the points P_2 y P_3 are not hyperbolic.*

Proof. We can see that the Jacobian matrix associated with the linearised system about P_1 is given by:

$$J(P_1) = \begin{pmatrix} (\varepsilon+u_2)(h-1) & 0 \\ (\nu+u_2)u_3H & (\nu+u_2)(H-1) \end{pmatrix}$$

and so it's characteristic equation is

$$(\lambda-(\varepsilon+u_2)(h-1))(\lambda-(\nu+u_2)(H-1)) = 0. \quad (2)$$

For the linearisation about the point P_2, we have the matrix:

$$J(P_2) = \begin{pmatrix} (\varepsilon+u_2)\left(\frac{h-H}{H}\right) & 0 \\ (\nu+u_2)(u_3-(H-1)) & (\nu+u_2)(1-H) \end{pmatrix}$$

and the characteristic equation of this system is

$$(\lambda-\lambda_1)(\lambda-\lambda_2) = 0. \quad (3)$$

where

$$\lambda_1 = (\varepsilon+u_2)\left(\frac{h-H}{H}\right) \quad \text{and} \quad \lambda_2 = (\nu+u_2)(1-H).$$

Finally, the matrix for the linearised system around P_3 is:

$$J(P_3) = \begin{pmatrix} a_{11} & a_{12} \\ a_{21} & a_{22} \end{pmatrix}$$

where

$$a_{11} = (\varepsilon+u_2)\left[(h-1)\left(\frac{u_3(\varepsilon+u_2)}{(\nu-\varepsilon)(1-u_3)}-1\right)\right]$$

$$a_{12} = -(\varepsilon+u_2)(h-1)\left[1-\frac{u_3(\varepsilon+u_2)}{(\nu-\varepsilon)(1-u_3)}\right]$$

$$a_{21} = -u_3(\nu+u_2)\frac{H}{h}\left[(h-1)\left(\frac{\nu+u_2}{\nu-\varepsilon}\right)-1\right]$$

$$a_{22} = (\nu+u_2)\left[\frac{H}{h}\left(1-\frac{u_3(h-1)(\nu+u_2)}{\nu-\varepsilon}\right)-1\right]$$

and it's characteristic equation is:

$$\lambda^2 + \frac{\nu+u_2}{h}[H(h-1)+(h-H)]\lambda + \quad (4)$$
$$+(\varepsilon+u_2)(h-1)(\nu-\varepsilon)\left(1-\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h}\right) = 0.$$

Thus we have:

1. If $h < 1$, $H < 1$, by equation (2) the eigenvalues of $J(P_1)$ are real and negative, from which the equilibrium point P_1 is asymptotically stable at the local level.
If we consider further that $H \neq h$, from equation (3) we can see that there are no null eigenvalues and that, because $1-H > 0$, there exists an eigenvalue that is real and positive. This leads us to conclude that P_2 is an unstable point of equilibrium.
Finally, under this hypothesis, we have that $h < H < 1$ or $H < h < 1$. If $H < h < 1$ and $h \neq \frac{2H}{H+1}$, then $H(h-1)+(h-H) \neq 0$ and $\frac{H}{h} < 1$. That is to say that

$\frac{\varepsilon+u_2}{(\nu+u_2)(1-u_3)} < 1$ and, applying algebraic operations to this equation, we arrive at $\frac{u_3(\nu+u_2)}{\nu-\varepsilon} < 1$. From this we get:

$$(\varepsilon+u_2)(h-1)(\nu-\varepsilon)\left(1-\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h}\right) < 0,$$

from which we conclude, by the Routh-Hurwitz criterion, that equation (4) has at least one root with a positive real part and so P_3 is unstable. Similarly, when $H < h < 1$ y $h = \frac{2H}{H+1}$, the roots of equation (4) are real and of opposite signs which implies that P_3 is an unstable point of equilibrium. On the other hand, if si $h < H < 1$, then $H(h-1)+(h-H) < 0$ and $(\varepsilon+u_2)(h-1)(\nu-\varepsilon)\left(1-\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h}\right) \neq 0$, and by the Routh-Hurwitz criterion, equation (4) has at least one root with a positive real part which implies that the point P_3 is unstable.

2.Analogously, if we have that $h = H$, $h < 1$, the point of equilibrium P_1 is asymptotically stable at **the local level**. However, when $h = H$, equation (3) has an eigenvector of **zero**, which implies that P_2 is not a hyperbolic point. Similarly, $\frac{H}{h} = 1$ gives us $\frac{u_3(\nu+u_2)}{\nu-\varepsilon} = 1$ and, from equation (4), we have that the matrix $J(P_3)$ has a zero eigenvalue; and so P_3 is not hyperbolic either.

3.We observe that when $h = 1$ and $H = 1$, we find a zero eigenvalue in each of the three characteristic equations and therefore none of the three points of equilibrium are hyperbolic.

4.Analogously to the previous case, when $h = 1$, the characteristic equations for P_1 and P_3 give eigenvalues of zero, and these points are therefore not hyperbolic. However, when $H < 1$ in equation (3) we get a positive real eigenvalue and another non-zero. Thus the point P_2 is unstable. In the case that $H > 1$, from equation (2) we get negative real eigenvalues which means that the point P_2 is asymptotically stable.

5.If $H = 1$, the characteristic equations for P_1 and P_2 we get eigenvalues of zero which implies that neither point is hyperbolic. When $h > 1$, $H(h-1)+(h-H) > 0$ and $\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h} < 1$, and so all the coefficients in the characteristic equation for P_3 are positive. Thus, by the Routh-Hurwitz criterion, the eigenvalues of $J(P_3)$ have a negative real part and P_3 is asymptotically stable. However, when $h < 1$, $H(h-1)+(h-H) < 0$ and $(\varepsilon+u_2)(h-1)(\nu-\varepsilon)\left(1-\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h}\right) \neq 0$, and by the Routh-Hurwitz criterion there exists an eigenvalue with a positive real part and thus P_3 is unstable.

6.If $H > 1$, we can see that from equation (2) we obtain an positive real eigenvalue and, as $h \neq 1$, there are no zero eigenvalues. Therefore, the point of equilibrium P_1 is unstable. If we also have that $h < H$, equation (3) gives us negative real eigenvalues from which we conclude that P_2 is asymptotically stable at the local level.

On the other hand, if $h \neq 1$, we must have either $h < 1$ or $h > 1$. But if $h < 1$ and $h < H$, we have that $H(h-1)+(h-H) < 0$ and $(\varepsilon+u_2)(h-1)(\nu-\varepsilon)\left(1-\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h}\right) \neq 0$, and therefore, by the Routh-Hurwitz criterion, equation (4) has at least one root with a positive real part which means that P_3 is unstable. Similarly, if $h > 1$ y $h < H$, then $(\varepsilon+u_2)(h-1)(\nu-\varepsilon)\left(1-\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h}\right) < 0$, which leads us to the same conclusion.

7.If $h > 1$, equation (2) gives us a positive real eigenvalue and, since $H \neq 1$, there are no zero eigenvalues which implies that the equilibrium point P_1 is unstable. If, in addition, $h > H$, equation (3) has no zero roots and also we get a positive real eigenvalue, so P_2 is unstable.

We also observe that under these hypotheses, $\frac{\nu+u_2}{h}[H(h-1)+(h-H)] > 0$ and $(\varepsilon+u_2)(h-1)(\nu-\varepsilon)\left(1-\frac{u_3(\nu+u_2)}{\nu-\varepsilon}\frac{H}{h}\right) > 0$, which, by the Routh-Hurwitz criterion, guarantees that equation (4) gives eigenvalues having a negative real part. Thus the point P_3 is asymptotically stable a the local level.

8.If $h = H$ and $h > 1$, from equation (2) we get $J(P_1)$ has two positive real eigenvalues and therefore P_1 is unstable. However, from equations (3) and (4) we have zero eigenvalues which implies that the equilibrium points P_2 and P_3 and not hyperbolic.

5 Numeric Results

For the numerical results, hypothetical values have been considered for each of the parameters in the model. In Tables 2 and 3 we can see the values that have been given to these parameters for the different scenarios and also the values of the thresholds h and H.

The simulations corroborate the analytic results. However, of special interest are the cases in which the local stability analysis doesn't determine the asymptotic values of the system, as is the case where $h = H = 1$. In this case, according to Figure 3 which uses the conditions given in Scenario 3 of Table 2, the stable solution is the point P_1. This result is also obtained when $h = 1$ and $H < 1$ under the conditions given in scenario 5 of Table 2, or when $H = 1$ and $h < 1$ under the conditions given in scenario 7 of Table 3. These results can be seen Figures 5 and 7, respectively. On the other hand, when $h = H > 1$,

Table 2: Values of the parameters in scenario 1-5

Parameter	Sce. 1	Sce. 2	Sce. 3	Sce. 4	Sce. 5
ξ	0.5	0.4	0.5	0.5	0.5
f	0.4	0.4	0.4	0.4	0.4
ϕ	0.5	0.4	0.5	0.5	0.5
δ	10	10	10	10	10
π	0.2	0.2	0.2	0.2	0.2
k	10000	10000	10000	10000	10000
ε	0.1428	0.1428	0.1	0.1	0.1
ν	0.4	0.21	0.2	0.16	0.21
u_1	0.8	0.9	0.8	0.8	0.8
u_2	0.8	0.462	0.8	0.8	0.8
u_3	0.8	0.1	0.1	0.1	0.1
h	0.2121	0.8658	1	1	1
H	0.8333	0.8658	1	1.0417	0.9901

Table 3: Values of the parameters in scenario 6-10

Parameter	Sce. 6	Sce. 7	Sce. 8	Sce. 9	Sce. 10
ξ	0.5	0.5	0.8	0.6	0.6
f	0.4	0.4	0.7	0.4	0.4
ϕ	0.5	0.5	0.9	0.5	0.5
δ	10	10	10	10	10
π	0.2	0.2	0.143	0.2	0.2
k	10000	10000	10000	10000	10000
ε	0.09	0.1428	0.1428	0.1	0.1428
ν	0.2	0.2	0.28	0.21	0.21
u_1	0.8	0.8	0.4	0.8	0.8
u_2	0.8	0.8	0.3	0.8	0.462
u_3	0.1	0.1	0.4	0.1	0.1
h	1,0112	0.9546	12.5769	1.2	1.7857
H	1	1	16.0031	1.1881	1.7857

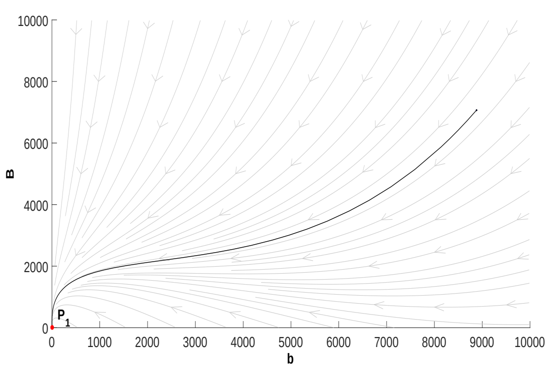

Fig. 1: Scenario 1.

according to Figure 10 which uses the conditions given in scenario 10 of Table 3, the stable solution is the equilibrium P_2.

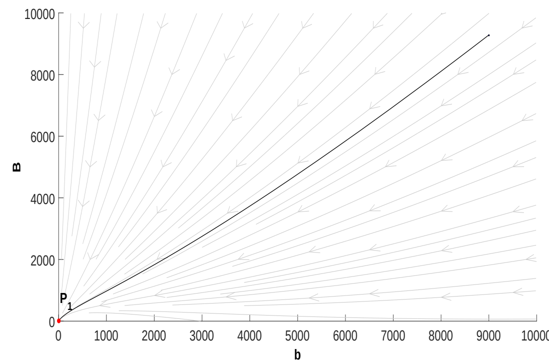

Fig. 2: Scenario 2.

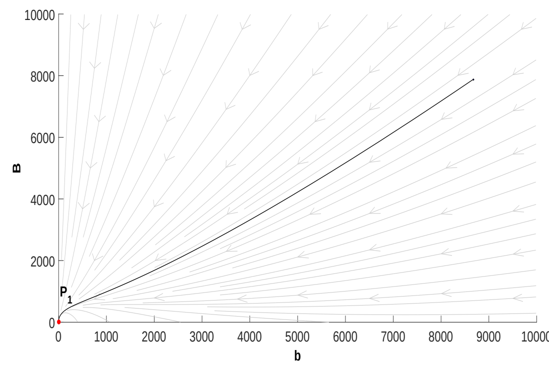

Fig. 3: Scenario 3.

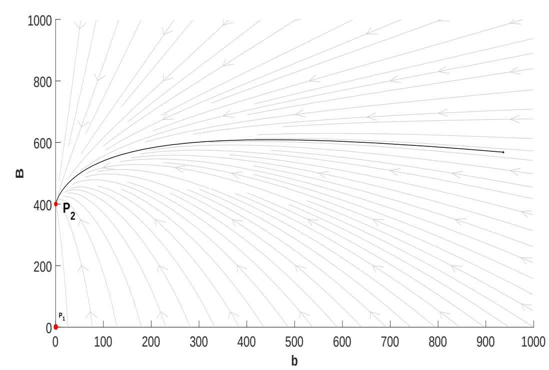

Fig. 4: Scenario 4.

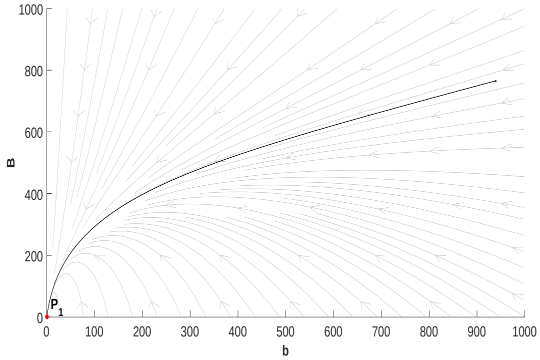

Fig. 5: Scenario 5.

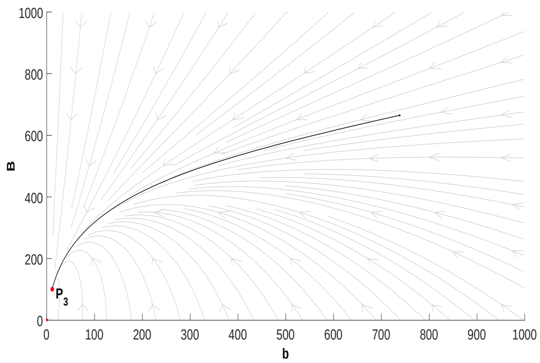

Fig. 6: Scenario 6.

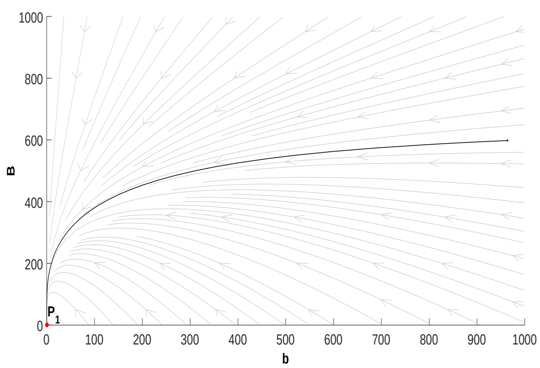

Fig. 7: Scenario 7.

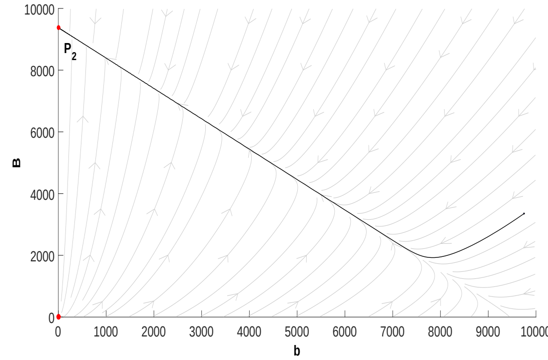

Fig. 8: Scenario 8.

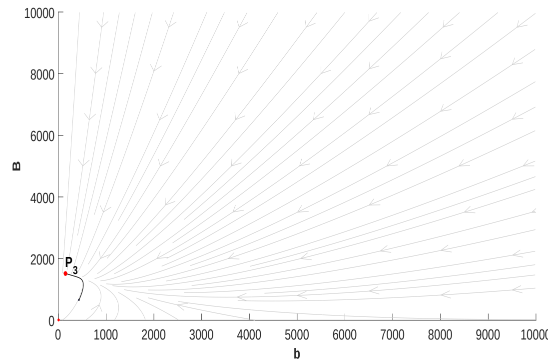

Fig. 9: Scenario 9.

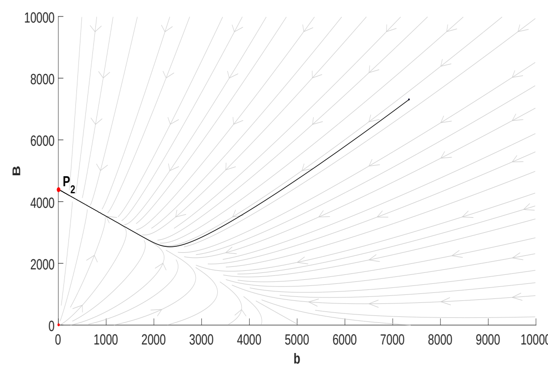

Fig. 10: Scenario 10.

6 Conclusions

In the proposed model, as in all mathematical models based on ordinary differential equations that describe population growth, the so-called Growth Threshold was determined. This, like the Basic Reproduction Number described in [9], determines the number of new individuals of a species that are generated during the lifetime of one of them, and which are capable reproducing when introduced into a free environment of that species.

For this model two growth thresholds have been found, since adult female mosquitoes are classified into two groups: those that are carriers of the *Wolbachia* bacterium and those that aren't. Thus H represents the number of infected adult female mosquitoes that can be generated by a single mosquito with these characteristics during its life span. Similarly, h represents the number of adult female mosquitoes without the bacterium that can be generated by a single mosquito during its lifetime.

The stability analysis of the system, determined that there are three equilibrium points. Biologically, the point of equilibrium P_1 represents the free equilibrium of the two populations, i.e. where neither of the two groups of adult female mosquitoes exist. The equilibrium point P_2 represents the situation where all adult female mosquito population are carriers, while non-carriers disappear from the environment. On the other hand, the equilibrium P_3 is the point at which the two groups of adult female mosquitoes coexist. In this case it is necessary that the control u_3 be practised permanently, otherwise, the adult female mosquito population without *Wolbachia* continues and those who are infected with the bacterium disappear.

Analytically we have established that when $h < H$ and $H > 1$, under initial conditions close to P_2, the population of adult female mosquitoes with the *Wolbachia* bacterium will persist in the environment and the other population will be extinguished, as demonstrated by conditions 4 and 6 of Theorem 1. This also seems to be the result in the case where $h = H$ as shown in Figure 10, but the local stability analysis does not prove this. When $H < h$ and $h > 1$, under initial conditions close to point P_3, the two groups of mosquitoes will coexist in the medium (provided that $u_3 \neq 0$), as demonstrated by conditions 5 and 7 of Theorem 1. Finally, when both thresholds are less than one, under initial conditions close to P_1, both populations will disappear, as demonstrated by conditions 1 and 2 of Theorem 1. This condition seems to persist when the thresholds are equal to one, as shown in Figure 3, and also when $h = 1$ and $H < 1$ as shown in Figure 5, or in the case where $H = 1$ and $H < 1$ as shown in Figure 7.

7 Materials and Methods

The numerical solutions of the proposed model were derived using the software Matlab 2015a and its ODE45 function. This function is based on the Runge-Kutta method, which is defined in [6] and is useful for solving ordinary differential equations with initial conditions.

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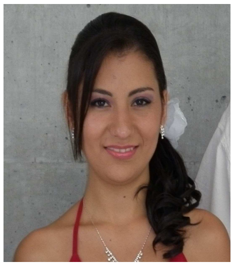

Ana María Pulecio Montoya received the title of Mathematician from the National University of Colombia in 2011. She received the title of Magister in Sciences - Applied Mathematics from the National University of Colombia in 2013. At present, she is PhD student of Automatic engineering in the National University of Colombia. Her subjects of interest are in Mathematical Epidemiology and Applied Mathematics.

Anibal Muñoz Loaiza, Specialization in Biomathematics, University of Quindo, Colombia; Dr. in Mathematical Sciences, FCFM-BUAP, Mexico; Researcher at the Faculty of Education, Universidad del Quindo, Colombia and director of the Mathematical Modeling in Epidemiology Group (GMME). 45 articles in different journal, numerous presentations as speaker and lecturer in events in different countries. At present, he is developing a postdoctoral project on Mathematical Modeling with new technologies and inclusion of limiting factors to control vectors of arbovirosis, in the Federal Center of Technological Education of Minas Gerais, Department of Physics and Mathematics (DFM), Brazil. With Dr. Rodrigo Toms Nogueira Cardoso and his doctoral students.

Gerard Olivar received the title of Mathematician from the University of Barcelona (Barcelona, Spain) in 1987 and the Doctor of Sciences - Mathematics by the Universitat Politcnica de Catalunya (Barcelona, Spain) in 1997 (Cum Laude). From 1987 to 2005 he was assigned to the Department of Applied Mathematics IV at the Universitat Politcnica de Catalunya, where he was Professor. Since 2005 he has been linked to the National University of Colombia, where he currently works as a Full Professor. His subjects of interest are in Mathematical Engineering and Applied Mathematics. Specifically, in applications to science and engineering modeling and simulation, nonlinear dynamics and complex systems. Since 2011, he has held the Presidency of the Colombian Section of the Society for Industrial and Applied Mathematics (SIAM).