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Dengue disease, basic reproduction number and control

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Dengue is one of the major international public health concerns. Although progress is underway, developing a vaccine against the disease is challenging. Thus, the main approach to fight the disease is vector control. A model for the transmission of dengue disease is presented. It consists of eight mutually exclusive compartments representing the human and vector dynamics. It also includes a control parameter (insecticide) in order to fight the mosquito. The model presents three possible equilibria: two disease-free equilibria (DFE) and another endemic equilibrium. It has been proved that a DFE is locally asymptotically stable, whenever a certain epidemiological threshold, known as the *basic reproduction number*, is less than one. We show that if we apply a minimum level of insecticide, it is possible to maintain the basic reproduction number below unity. A case study, using data of the outbreak that occurred in 2009 in Cape Verde, is presented.

Keywords: dengue; basic reproduction number; stability; Cape Verde; control

2010 Mathematics Subject Classifications: 92B05; 93C95; 93D20

1. Introduction

The first recognized dengue epidemic occurred almost simultaneously in Asia, Africa and North America in the 1780s, shortly after the identification and naming of the disease in 1779. It has spread especially in the tropical and subtropical regions around the world, and nowadays is a disease widely found in urban and semi-urban areas.

According to the World Health Organization, 50–100 million dengue infections occur yearly, including 500,000 dengue haemorrhagic fever (DHF) cases and 22,000 deaths, mostly among children [29]. Growing awareness of global climate change has stimulated several assessments of its likely effects on vector-borne disease as well as on health outcomes. Some of these studies have indicated that countries with a mild climate, such as in the Mediterranean, are at risk due to future climate conditions that may be favourable to this kind of disease [14]. This risk may be aggravated further due to the volume of international tourism and trade that this region experiences [21,24]. Travellers play an essential role in the global epidemiology. They act as viraemic travellers, carrying the disease into areas with mosquitoes that can transmit the infection. This is particularly

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true with respect to the reality in the archipelago of Cape Verde, where it is believed that the insects responsible for the outbreak that occurred in 2009 came from Brazil, transported by means of the frequent air transport [2].

There are two forms of dengue: dengue fever and DHF. The first one is characterized by a sudden fever without respiratory symptoms, accompanied by intense headaches and lasts between 3 and 7 days. The second has the previous symptoms but additionally also nausea, vomiting and fainting due to low blood pressure and can lead to death in 2 or 3 days [8].

There are four distinct, but closely related, viruses that cause dengue. Recovery from infection by one virus provides lifelong immunity against that virus but confers only partial and transient protection against subsequent infection by the other three viruses. There is good evidence that sequential infection increases the risk of developing DHF. Activities, such as triage and management, are critical in determining the clinical outcome of dengue. A rapid and efficient front-line response not only reduces the number of unnecessary hospital admissions but also saves lives.

There is no vaccine to protect against dengue. With four closely related viruses that can cause the disease, a vaccine would be needed to immunize against all four types to be effective. There is limited understanding of how the disease typically behaves and how the virus interacts with the immune system. Another challenge is that some studies show that some secondary dengue infection can lead to DHF, and theoretically a vaccine could be a potential cause of severe disease if a solid immunity is not established against the four serotypes. Research to develop a vaccine is ongoing and the incentives to study the mechanism of protective immunity are gaining more support, now that the number of outbreaks around the world is increasing [27].

The spread of dengue is attributed to expanding geographic distribution of the four dengue viruses and their mosquito vectors, the most important of which is the predominantly urban species *Aedes aegypti*; some notes about it are presented in Section 2. A mathematical model of the interaction between human and mosquito populations is presented in Section 3. Section 4 is concerned with the basic reproduction number, the equilibria of the epidemiological model and their stability. In Section 5, previous results are applied to a case study. Finally, concluding notes are given in Section 6.

2. Biological notes on *Aedes aegypti*

The mosquito *Aedes aegypti* is a tropical and subtropical specie widely distributed around the world, mostly between latitudes 35°N and 35°S, which corresponds, approximately, to a winter isotherm of 10 °C [4]. The life cycle of a mosquito has four distinct stages: egg, larva, pupa and adult. In the case of *A. aegypti*, the first three stages take place in or near water while air is the medium for the adult stage [18]. The eggs of *A. aegypti* can resist desiccation and low temperatures for up to 1 year. Although the hatching of mature eggs may occur spontaneously at any time, this is greatly stimulated by flooding. The larva moults four times in a period of a few days which culminates in the pupal stage. The pupal stage lasts from 1 day to a few weeks, depending on the temperature. At the end of this stage, the adult emerges from the pupal skin [7]. Studies suggest that most female mosquitoes may spend their lifetime in or around the houses where they emerge as adults. This means that people, rather than mosquitoes, rapidly move the virus within and between communities.

The adult stage of the mosquito is considered to last an average of 11 days in the urban environment. Dengue is spread only by adult females that require a blood meal for the development of eggs; male mosquitoes feed on nectar and other sources of sugar. In this process, the female acquires the virus while feeding on the blood of an infected person. After virus incubation for 8–10 days, an infected mosquito is capable, during probing and blood feeding, of transmitting

the virus for the rest of its life. *Aedes aegypti* is one of the most efficient vectors for arboviruses because it is highly anthropophilic, frequently bites several times before complete oogenesis and thrives in close proximity to humans [27].

It is very difficult to control or eliminate the *A. aegypti* mosquito because it adapts to the environment and becomes resistant to natural phenomena, e.g. droughts, or human interventions and control measures. Vector control is a key for combating mosquito-borne diseases and the major tool available for tackling the transmission of dengue, a disease for which there is no vaccine nor prophylaxis. There are two main methods for primary prevention: larval control and adult mosquito control, depending on the intended target [16]. In urban areas *Aedes* mosquitoes breed on water collections in artificial containers such as cans, plastic cups, used tires, broken bottles, flower pots, etc. Proper solid waste disposal and improved water storage practices, including covering containers to prevent access by egg-laying female mosquitoes, are methods that are encouraged through community-based programmes [6]. Active monitoring and surveillance of the natural mosquito population should accompany control efforts to determine programme effectiveness.

3. The mathematical model

The mathematical model is based on [10,11]. The novelty in this paper is the presence of the control parameter related to adult mosquito insecticide.

The notation used in our mathematical model includes four epidemiological states for humans:

$S_h(t)$	susceptible (individuals who can contract the disease)
$E_h(t)$	exposed (individuals who have been infected by the parasite but are not yet able to transmit to others)
$I_h(t)$	infected (individuals capable of transmitting the disease to others)
$R_h(t)$	resistant (individuals who have acquired immunity)

It is assumed that the total human population (N_h) is constant, so, $N_h = S_h + E_h + I_h + R_h$. There are also four other state variables related to the female mosquitoes (the male mosquitoes are not considered in this study because they do not bite humans and consequently they do not influence the dynamics of the disease):

$A_m(t)$	aquatic phase (that includes the egg, larva and pupa stages)
$S_m(t)$	susceptible (mosquitoes that are able to contract the disease)
$E_m(t)$	exposed (mosquitoes that are infected but are not yet able to transmit to humans)
$I_m(t)$	infected (mosquitoes capable of transmitting the disease to humans)

In order to analyse the effects of campaigns to fight the mosquito, there is also a control variable:

$c(t)$	level of insecticide campaigns

Some assumptions in this model:

- the total human population (N_h) is constant;
- there is no immigration of infected individuals into the human population;
- the population is homogeneous, which means that every individual of a compartment is homogenously mixed with the other individuals;
- the coefficient of transmission of the disease is fixed and does not vary seasonally;
- both human and mosquitoes are assumed to be born susceptible; there is no natural protection;
- for the mosquito there is no resistant phase, due to its short lifetime.

The parameters of the model are:

N_{h}	total population
B	average daily biting (per day)
β_{mh}	transmission probability from I_{m} (per bite)
β_{hm}	transmission probability from I_{h} (per bite)
$1/\mu_{\mathrm{h}}$	average lifespan of humans (in days)
$1/\eta_{\mathrm{h}}$	mean viraemic period (in days)
$1/\mu_{\mathrm{m}}$	average lifespan of adult mosquitoes (in days)
μ_b	number of eggs at each deposit per capita (per day)
μ_{A}	natural mortality of larvae (per day)
η_{A}	maturation rate from larvae to adult (per day)
$1/\eta_{\mathrm{m}}$	extrinsic incubation period (in days)
$1/\nu_{\mathrm{h}}$	intrinsic incubation period (in days)
m	female mosquitoes per human
k	number of larvae per human
K	maximal capacity of larvae

The dengue epidemic can be modelled by the following nonlinear time-varying state equations: human population

$$\begin{aligned}
\frac{\mathrm{d}S_{\mathrm{h}}}{\mathrm{d}t}(t) &= \mu_{\mathrm{h}}N_{\mathrm{h}} - \left(B\beta_{\mathrm{mh}}\frac{I_{\mathrm{m}}}{N_{\mathrm{h}}} + \mu_{\mathrm{h}}\right)S_{\mathrm{h}} \\
\frac{\mathrm{d}E_{\mathrm{h}}}{\mathrm{d}t}(t) &= B\beta_{\mathrm{mh}}\frac{I_{\mathrm{m}}}{N_{\mathrm{h}}}S_{\mathrm{h}} - (\nu_{\mathrm{h}} + \mu_{\mathrm{h}})E_{\mathrm{h}} \\
\frac{\mathrm{d}I_{\mathrm{h}}}{\mathrm{d}t}(t) &= \nu_{\mathrm{h}}E_{\mathrm{h}} - (\eta_{\mathrm{h}} + \mu_{\mathrm{h}})I_{\mathrm{h}} \\
\frac{\mathrm{d}R_{\mathrm{h}}}{\mathrm{d}t}(t) &= \eta_{\mathrm{h}}I_{\mathrm{h}} - \mu_{\mathrm{h}}R_{\mathrm{h}}
\end{aligned} \tag{1}$$

and vector population

$$\begin{aligned}
\frac{\mathrm{d}A_{\mathrm{m}}}{\mathrm{d}t}(t) &= \mu_b\left(1 - \frac{A_{\mathrm{m}}}{K}\right)(S_{\mathrm{m}} + E_{\mathrm{m}} + I_{\mathrm{m}}) - (\eta_A + \mu_A)A_{\mathrm{m}} \\
\frac{\mathrm{d}S_{\mathrm{m}}}{\mathrm{d}t}(t) &= -\left(B\beta_{\mathrm{hm}}\frac{I_{\mathrm{h}}}{N_{\mathrm{h}}} + \mu_{\mathrm{m}}\right)S_{\mathrm{m}} + \eta_A A_{\mathrm{m}} - cS_{\mathrm{m}} \\
\frac{\mathrm{d}E_{\mathrm{m}}}{\mathrm{d}t}(t) &= B\beta_{\mathrm{hm}}\frac{I_{\mathrm{h}}}{N_{\mathrm{h}}}S_{\mathrm{m}} - (\mu_{\mathrm{m}} + \eta_{\mathrm{m}})E_{\mathrm{m}} - cE_{\mathrm{m}} \\
\frac{\mathrm{d}I_{\mathrm{m}}}{\mathrm{d}t}(t) &= \eta_{\mathrm{m}}E_{\mathrm{m}} - \mu_{\mathrm{m}}I_{\mathrm{m}} - cI_{\mathrm{m}}
\end{aligned} \tag{2}$$

with the initial conditions

$$\begin{aligned}
&S_{\mathrm{h}}(0) = S_{h0},\ E_{\mathrm{h}}(0) = E_{h0},\ I_{\mathrm{h}}(0) = I_{h0},\ R_{\mathrm{h}}(0) = R_{h0}, \\
&A_{\mathrm{m}}(0) = A_{m0},\ S_{\mathrm{m}}(0) = S_{m0},\ E_{\mathrm{m}}(0) = E_{m0},\ I_{\mathrm{m}}(0) = I_{m0}.
\end{aligned} \tag{3}$$

Notice that the equation related to the aquatic phase does not have the control variable c, because the adulticide does not produce effects in this stage of the life of the mosquito. To combat the larval phase, it would be necessary to use larvicide. This treatment should be long-lasting and

have World Health Organization clearance for use in drinking water. As we want to study only a short period of time, this type of treatment has not been considered here.

With the condition $S_\mathrm{h} + E_\mathrm{h} + I_\mathrm{h} + R_\mathrm{h} = N_\mathrm{h}$, one can, in the example given, use $R_\mathrm{h} = N_\mathrm{h} - S_\mathrm{h} - E_\mathrm{h} - I_\mathrm{h}$ and consider an equivalent system for human population without considering the R_h differential equation.

4. Basic reproduction number, equilibrium points and stability

Let the set

$$\Omega = \{(S_\mathrm{h}, E_\mathrm{h}, I_\mathrm{h}, A_\mathrm{m}, S_\mathrm{m}, E_\mathrm{m}, I_\mathrm{m}) \in \mathbb{R}^7_+ : S_\mathrm{h} + E_\mathrm{h} + I_\mathrm{h} \leq N_\mathrm{h}, A_\mathrm{m} \leq kN_\mathrm{h}, S_\mathrm{m} + E_\mathrm{m} + I_\mathrm{m} \leq mN_\mathrm{h}\}$$

be the region of biological interest, that is positively invariant under the flow induced by the differential system (1)–(2) (see Appendix 1).

THEOREM 1 *Let Ω be defined as above. Consider also*

$$\mathcal{M} = -(c(\eta_A + \mu_A) + \mu_A\mu_\mathrm{m} + \eta_A(-\mu_b + \mu_\mathrm{m})).$$

System (1)–(2) admits at most two DFE points:

- *if $\mathcal{M} \leq 0$, there is a DFE, called trivial equilibrium, $E_1^* = (N_\mathrm{h}, 0, 0, 0, 0, 0, 0)$;*
- *if $\mathcal{M} > 0$, there is a biologically realistic DFE (BRDFE), $E_2^* = (N_\mathrm{h}, 0, 0, kN_\mathrm{h}\mathcal{M}/(\eta_A\mu_b), kN_\mathrm{h}\mathcal{M}/(\mu_b\mu_\mathrm{m}), 0, 0)$.*

Proof See Appendix 2. ■

Remark 1 The condition $\mathcal{M} > 0$ is equivalent, by algebraic manipulation, to the condition $(\eta_A + \mu_A)(\mu_\mathrm{m} + c)/(\mu_b\eta_A) < 1$, where the left-hand side corresponds to the basic offspring number for mosquitoes. Thus, if $M \leq 0$, then the mosquito population will collapse and the only equilibrium for the whole system is the trivial equilibrium. If $M > 0$, then the mosquito population is sustainable.

It is necessary to determine the *basic reproduction number* of the disease, $\mathcal{R}_0$. This number is very important from the epidemiologistic point of view. It represents the expected number of secondary cases produced in a completed susceptible population, by a typical infected individual during its entire period of infectiousness [12,13]. Following [9], we prove the following theorem.

THEOREM 2 *If $\mathcal{M} > 0$, then the square of the basic reproduction number associated to Equations (1) and (2) is*

$$\mathcal{R}_0^2 = \frac{B^2 S_h S_m \beta_\mathrm{hm}\beta_\mathrm{mh}\eta_\mathrm{m}\nu_\mathrm{h}}{N_\mathrm{h}^2(\eta_\mathrm{h} + \mu_\mathrm{h})(c + \mu_\mathrm{m})(c + \eta_\mathrm{m} + \mu_\mathrm{m})(\mu_\mathrm{h} + \nu_\mathrm{h})}.$$

The equilibrium point BRDFE is locally asymptotically stable if $\mathcal{R}_0 < 1$ and unstable if $\mathcal{R}_0 > 1$.

Proof See Appendix 3. ■

Remark 2 In our model, we have two different populations (human and vector), so the expected basic reproduction number reflects the infection human–vector and also vector–human, that is, $\mathcal{R}_0^2 = R_{\mathrm{hm}} \times R_{\mathrm{mh}}$ with $R_{\mathrm{hm}} = (BS_{\mathrm{m}}\beta_{\mathrm{hm}}\nu_{\mathrm{h}})/(N_h(\eta_{\mathrm{h}} + \mu_{\mathrm{h}})(\mu_{\mathrm{h}} + \nu_{\mathrm{h}}))$ and $R_{\mathrm{mh}} = (BS_{\mathrm{h}}\beta_{\mathrm{mh}}\eta_{\mathrm{m}})/(N_{\mathrm{h}}(c + \mu_{\mathrm{m}})(c + \eta_{\mathrm{m}} + \mu_{\mathrm{m}}))$. The term $B\beta_{\mathrm{hm}}(S_{\mathrm{m}}/N_{\mathrm{h}})$ represents the product between the transmission probability of the disease from humans to vectors and the number of susceptible mosquitoes per human, $1/(\eta_{\mathrm{h}} + \mu_{\mathrm{h}})$ is related to the human's viraemic period and $\eta_{\mathrm{m}}/(c + \eta_{\mathrm{m}} + \mu_{\mathrm{m}})$ represents the proportion of mosquitoes that survive the incubation period. Analogously, the term $B\beta_{\mathrm{mh}}(S_{\mathrm{h}}/N_{\mathrm{h}})$ is related to the transmission probability of the disease between mosquitoes and human, in a susceptible population; $1/(c + \mu_{\mathrm{m}})$ represents the lifespan of an adult mosquito and $\nu_{\mathrm{h}}/(\mu_{\mathrm{h}} + \nu_{\mathrm{h}})$ is the proportion of humans who survive the incubation period.

When $\mathcal{R}_0 < 1$, each infected individual produces, on average, less than one new infected individual, and therefore it is predictable that the infection will be cleared from the population. If $\mathcal{R}_0 > 1$, the disease is able to invade the susceptible population.

THEOREM 3 *If $\mathcal{M} > 0$ and $\mathcal{R}_0 > 1$, then system (1)–(2) also admits an endemic equilibrium $(EE) : E_3^* = (S_{\mathrm{h}}^*, E_{\mathrm{h}}^*, I_{\mathrm{h}}^*, A_{\mathrm{m}}^*, S_{\mathrm{m}}^*, E_{\mathrm{m}}^*, I_{\mathrm{m}}^*)$, where*

$$
\begin{aligned}
S_{\mathrm{h}}^* &= N_{\mathrm{h}} - \frac{(\mu_{\mathrm{h}} + \nu_{\mathrm{h}})(\mu_{\mathrm{h}} + \eta_{\mathrm{h}})}{\mu_{\mathrm{h}}\nu_{\mathrm{h}}} I_{\mathrm{h}}^*,\\
E_{\mathrm{h}}^* &= \frac{\mu_{\mathrm{h}} + \eta_{\mathrm{h}}}{\nu_{\mathrm{h}}} I_{\mathrm{h}}^*,\\
I_{\mathrm{h}}^* &= \frac{\xi}{\chi},\\
\xi &= N_{\mathrm{h}}\mu_{\mathrm{h}}[-B^2k\beta_{\mathrm{hm}}\beta_{\mathrm{mh}}\nu_{\mathrm{h}}\eta_{\mathrm{m}}\mathcal{M} + \mu_b\mu_{\mathrm{m}}^2(\eta_{\mathrm{m}} + \mu_{\mathrm{m}})(\mu_{\mathrm{h}} + \nu_{\mathrm{h}})(\mu_{\mathrm{h}} + \eta_{\mathrm{h}})\\
&\quad + c^2\mu_b(\eta_{\mathrm{h}} + \mu_{\mathrm{h}})(\mu_{\mathrm{h}} + \nu_{\mathrm{h}})(c + \eta_{\mathrm{m}} + 3\mu_{\mathrm{m}})\\
&\quad + c\mu_b\mu_{\mathrm{m}}(\mu_{\mathrm{h}} + \nu_{\mathrm{h}})(\mu_{\mathrm{h}}(3\mu_{\mathrm{m}} + 2) + \eta_{\mathrm{h}}(2\eta_{\mathrm{m}} + 3\mu_{\mathrm{m}}))],\\
\chi &= B\beta_{\mathrm{hm}}(\eta_{\mathrm{h}} + \mu_{\mathrm{h}})[-\mu_b\mu_{\mathrm{h}}(c + \mu_{\mathrm{m}})(c + \eta_{\mathrm{m}} + \mu_{\mathrm{m}}) - Bk\beta_{\mathrm{mh}}\eta_{\mathrm{m}}\mathcal{M}](\mu_{\mathrm{h}} + \nu_{\mathrm{h}}),\\
A_{\mathrm{m}}^* &= \frac{\mathcal{M}}{\eta_A\mu_b} kN_{\mathrm{h}},\\
S_{\mathrm{m}}^* &= \frac{kN_{\mathrm{h}}^2\mathcal{M}}{\mu_b(cN_{\mathrm{h}} + BI_{\mathrm{h}}^*\beta_{\mathrm{hm}} + N_{\mathrm{h}}\mu_{\mathrm{m}})},\\
E_{\mathrm{m}}^* &= \frac{\mu_{\mathrm{m}} + c}{\eta_{\mathrm{m}}} I_{\mathrm{m}}^*,\\
I_{\mathrm{m}}^* &= \frac{BI_{\mathrm{h}}^*kN_{\mathrm{h}}\beta_{\mathrm{hm}}\eta_{\mathrm{m}}\mathcal{M}}{\mu_b(c + \mu_{\mathrm{m}})(c + \eta_{\mathrm{m}} + \mu_{\mathrm{m}})(cN_{\mathrm{h}} + BI_{\mathrm{h}}^*\beta_{\mathrm{hm}} + N_{\mathrm{h}}\mu_{\mathrm{m}})}.
\end{aligned}
$$

Proof See Appendix 2. ■

From a biological point of view, it is desirable that humans and mosquitoes coexist without the disease reaching a level of endemicity. We claim that proper use of the control c can result in the basic reproduction number remaining below unity and, therefore, making BRDFE stable.

In order to make effective use of achievable insecticide control, and simultaneously to explain more easily to the competent authorities its effectiveness, we assume that c is constant. The goal is to find c such that $\mathcal{R}_0^2 < 1$.

5. Dengue in Cape Verde

An unprecedented outbreak was detected in the Cape Verde archipelago in September 2009 [28]. This is the first report of dengue virus activity in that country. A total of 17,224 cases, including six deaths, were reported from 18 of the 22 municipalities in Cape Verde by the end of 2009. The municipality of Praia, on Santiago island, notified the highest number of cases (13,000 cases) followed by São Felipe in Fogo Island (3000 cases). We used the data for human population related to Cape Verde [6]. There have been no cases of dengue in all the West African countries near Cape Verde islands since 2000 [2]. They speak explicitly about mosquitoes coming from Brazil. Also the information that comes from the Ministry of Health in the capital of Cape Verde, Praia, confirms that the insects responsible for dengue came most probably from Brazil, transported by means of air transport that perform frequent connections between Cape Verde and Brazil, as reported by José Rosa in the Radio of Cape Verde. With respect to *A. aegypti*, we have thus considered data from Brazil [25,30].

The simulations were carried out using the following values: $N_{\mathrm{h}} = 480000$, $B = 1$, $\beta_{\mathrm{mh}} = 0.375$, $\beta_{\mathrm{hm}} = 0.375$, $\mu_{\mathrm{h}} = 1/(71 \times 365)$, $\eta_{\mathrm{h}} = 1/3$, $\mu_{\mathrm{m}} = 1/11$, $\mu_b = 6$, $\mu_{\mathrm{A}} = 1/4$, $\eta_{\mathrm{A}} = 0.08$, $\eta_{\mathrm{m}} = 1/11$, $\nu_{\mathrm{h}} = 1/4$, $m = 6$, $k = 3$, $K = kN_{\mathrm{h}}$. The initial conditions for the problem were: $S_{\mathrm{h0}} = N_{\mathrm{h}} - E_{\mathrm{h0}} - I_{\mathrm{h0}}$, $E_{\mathrm{h0}} = 216$, $I_{\mathrm{h0}} = 434$, $R_{\mathrm{h0}} = 0$, $A_{\mathrm{m0}} = kN_{\mathrm{h}}$, $S_{\mathrm{m0}} = mN_{\mathrm{h}}$.

Considering non-existence of control, i.e. $c = 0$, the basic reproduction number for this outbreak in Cape Verde is approximately $\mathcal{R}_0 = 2.396$, which is in agreement with other studies of dengue in other countries [17]. The control c affects the basic reproduction number, and our aim is to find a control that puts $\mathcal{R}_0$ less than one.

PROPOSITION 1 *Let us consider the parameters listed above and consider c as a constant. Then $\mathcal{R}_0 < 1$ if and only if $c > 0.156961$.*

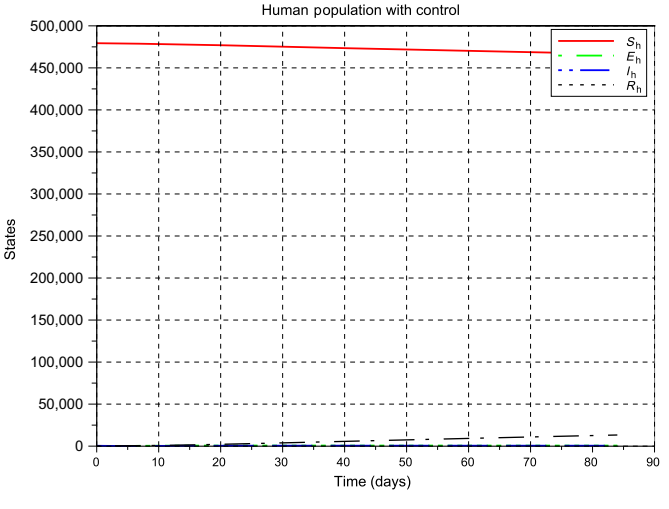

Figure 1. Human compartments using control.

Several computational investigations were carried out.

The software used was Scilab [5]. It is an open source, cross-platform numerical computational package and a high-level, numerically oriented programming language. For our problem, we used the routine `ode` to solve the set of differential equations. By default, `ode` uses the lsoda solver of package ODEPACK. It automatically selects between the non-stiff predictor–corrector Adams method and the stiff backward differentiation formula method. It uses the non-stiff method initially and dynamically monitors data in order to decide which method to use. The graphics were also obtained using this software, using the command `plot`.

Figures 1 and 2 show the curves related to human population, with and without control, respectively. The number of infected persons, even with a small control, is much less than without any insecticide campaign.

Figures 3 and 4 show the difference between a region with control and without control.

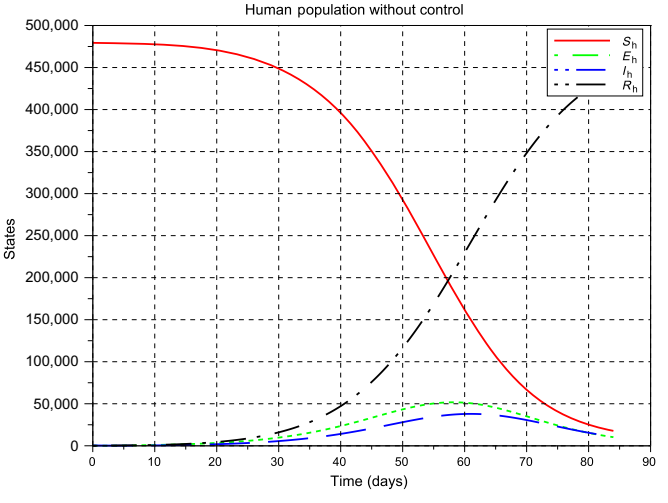

Figure 2. Human compartments without control.

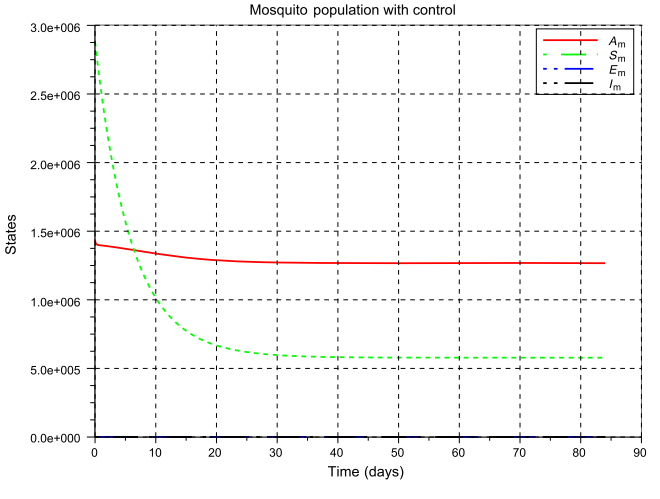

Figure 3. Mosquito compartments using control.

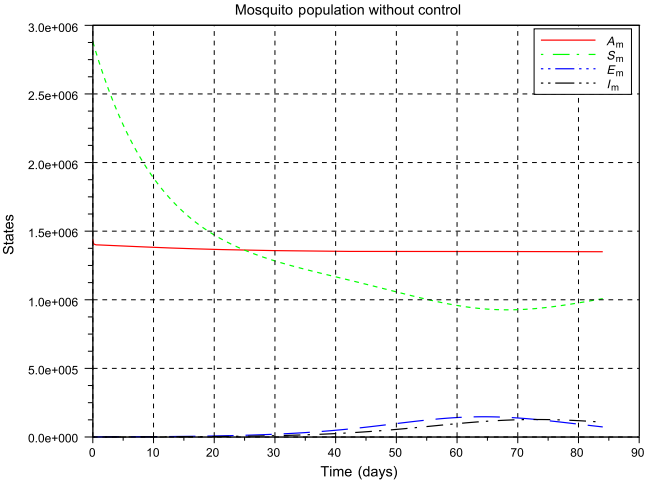

Figure 4. Mosquito compartments without control.

When the control is applied, the number of infected mosquitoes is close to zero. Note that the intention is not to eradicate the mosquitoes but instead the number of infected mosquitoes.

6. Conclusions and future work

In this paper, a model based on two populations, humans and mosquitoes, with insecticide control has been presented. It has been shown that with a steady insecticide campaign, it is possible to reduce the number of infected humans and mosquitoes and can prevent an outbreak that could transform an epidemiological episode to an endemic disease.

It has been proved algebraically that, if a constant minimum level of a control is applied, it is possible to maintain the basic reproduction number below unity, guaranteeing the BRDFE. This is corroborated in another numerical study [20].

In this work, we considered a constant control. In future work, using a theoretical approach [19], we intend to find the best function $c(t)$, using optimal control theory. Instead of finding a constant control, it will be possible to study other types of control, such as piecewise constant or even continuous but not constant. Numerical methods can be used to solve the model [22,23,26]. Additionally, we could consider another strategy, a more practical one: due to logistics and health reasons, it may be more convenient to apply insecticide periodically and at some specific hours at night.

The rapid increase in mosquito resistance to several chemical insecticides, and the damage caused by these to the environment, has resulted in the search for new control alternatives, such as the use of biological agents. Among the alternatives available, the use of *Bacillus thuringiensis israelensis* (Bti) has been adopted by several countries [15]. Laboratory testing shows that Bti has a high larvicide property and its mechanism of action is based on the production of an endotoxin protein that, when ingested by the larvae, causes death. So, in future work, we will also take into account the use of larvicide control.

To ensure the minimization of the outbreaks, educational programmes that are customized for different levels of health care and that reflect local capacity should be supported and implemented widely. The population should also be educated regarding dengue in order to minimize the breeding of the mosquito. Educational campaigns can be included as an extra control parameter in the model.

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Appendix 1. Dynamical properties of Metzler systems

System (1)–(2) can be rewritten in the following way:

$$\frac{\mathrm{d}X}{\mathrm{d}t} = M(X)X + F, \tag{A1}$$

where $X = (S_\mathrm{h}, E_\mathrm{h}, I_\mathrm{h}, A_\mathrm{m}, S_\mathrm{m}, E_\mathrm{m}, I_\mathrm{m})$,

$$M(X) = \begin{pmatrix} -B\beta_\mathrm{mh}\dfrac{I_\mathrm{m}}{N_\mathrm{h}} - \mu_\mathrm{h} & 0 & 0 & 0 & 0 & 0 & 0 \\ B\beta_\mathrm{mh}\dfrac{I_\mathrm{m}}{N_\mathrm{h}} & -\nu_\mathrm{h} - \mu_\mathrm{h} & 0 & 0 & 0 & 0 & 0 \\ 0 & \nu_\mathrm{h} & -\eta_\mathrm{h} - \mu_\mathrm{h} & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -\mu_b\dfrac{S_\mathrm{m} + E_\mathrm{m} + I_\mathrm{m}}{K} - \mu_\mathrm{m} - \eta_\mathrm{m} & \mu_b & 0 & 0 \\ 0 & 0 & 0 & \eta_A & -B\beta_\mathrm{hm}\dfrac{I_\mathrm{h}}{N_\mathrm{h}} - \mu_\mathrm{m} - c & 0 & 0 \\ 0 & 0 & 0 & 0 & B\beta_\mathrm{hm}\dfrac{I_\mathrm{h}}{N_\mathrm{h}} & -\mu_\mathrm{h} & 0 \\ 0 & 0 & 0 & 0 & 0 & \eta_\mathrm{h} & -\mu_\mathrm{h} \end{pmatrix},$$

and $F = (\mu_\mathrm{h} N_\mathrm{h}, 0, 0, 0, 0, 0, 0)^\mathrm{T}$. As $M(X)$ has all off-diagonal entries non-negative, $M(X)$ is a Metzler matrix.

Using the fact that $F \geq 0$, system (A1) is positively invariant in $\mathbb{R}^7_+$ [1], which means that any trajectory of the system starting from an initial state in the positive orthant $\mathbb{R}^7_+$ remains forever in $\mathbb{R}^7_+$.

Appendix 2. Equilibrium points

The equilibrium points are reached when the following equations hold:

$$\begin{aligned} \frac{\mathrm{d}S_\mathrm{h}}{\mathrm{d}t}(t) &= 0 \\ \frac{\mathrm{d}E_\mathrm{h}}{\mathrm{d}t}(t) &= 0 \\ \frac{\mathrm{d}I_\mathrm{h}}{\mathrm{d}t}(t) &= 0 \\ \frac{\mathrm{d}A_\mathrm{m}}{\mathrm{d}t}(t) &= 0 \\ \frac{\mathrm{d}S_\mathrm{m}}{\mathrm{d}t}(t) &= 0 \\ \frac{\mathrm{d}E_\mathrm{m}}{\mathrm{d}t}(t) &= 0 \\ \frac{\mathrm{d}I_\mathrm{m}}{\mathrm{d}t}(t) &= 0. \end{aligned} \tag{A2}$$

Using the Mathematica software to solve system (A2), we obtained four solutions.

The first one is known as the *trivial equilibrium*, since the mosquitoes do not exist, so there is no disease:

$$E_1^* = (N_\mathrm{h}, 0, 0, 0, 0, 0, 0).$$

In the second one, mosquitoes and humans interact, but there is only one outbreak of the disease, i.e. over time the disease goes away without being necessary to kill all the mosquitoes. We have called this equilibrium point a *BRDFE*, since it is a more reasonable situation to find in nature than the previous one:

$$E_2^* = \left(N_\mathrm{h}, 0, 0, \frac{kN_\mathrm{h}(-(c(\eta_A+\mu_A)+\mu_A\mu_\mathrm{m}+\eta_A(-\mu_b+\mu_\mathrm{m})))}{\eta_A\mu_b}, \frac{kN_\mathrm{h}(-(c(\eta_A+\mu_A)+\mu_A\mu_\mathrm{m}+\eta_A(-\mu_b+\mu_\mathrm{m})))}{\mu_b\mu_\mathrm{m}}, 0, 0\right),$$

which is equivalent to

$$E_2^* = \left(N_\mathrm{h}, 0, 0, \frac{kN_\mathrm{h}\mathcal{M}}{\eta_A\mu_b}, \frac{kN_\mathrm{h}\mathcal{M}}{\mu_b\mu_\mathrm{m}}, 0, 0\right).$$

This is biologically interesting only if $\mathcal{M}$ is greater than 0.

The third solution corresponds to a situation where humans and mosquitoes live together but the disease persists in the two populations. So the disease is not anymore an epidemic episode, but transforms into an endemic one. With some algebraic manipulations, we obtain the following point:

$$\begin{aligned}
E_3^* &= (S_\mathrm{h}^*, E_\mathrm{h}^*, I_\mathrm{h}^*, A_\mathrm{m}^*, S_\mathrm{m}^*, E_\mathrm{m}^*, I_\mathrm{m}^*), \text{ where}\\
S_\mathrm{h}^* &= N_\mathrm{h} - \frac{(\mu_\mathrm{h}+\nu_\mathrm{h})(\mu_\mathrm{h}+\eta_\mathrm{h})}{\mu_\mathrm{h}\nu_\mathrm{h}} I_\mathrm{h}^*,\\
E_\mathrm{h}^* &= \frac{\mu_\mathrm{h}+\eta_\mathrm{h}}{\nu_\mathrm{h}} I_\mathrm{h}^*,\\
I_\mathrm{h}^* &= N_\mathrm{h}\mu_\mathrm{h}(-B^2k\beta_\mathrm{hm}\beta_\mathrm{mh}\nu_\mathrm{h}\eta_\mathrm{m}\mathcal{M} + \mu_b\mu_\mathrm{m}^2(\eta_\mathrm{m}+\mu_\mathrm{m})(\mu_\mathrm{h}+\nu_\mathrm{h})(\mu_\mathrm{h}+\eta_\mathrm{h})\\
&\quad + c^2\mu_b(\eta_\mathrm{h}+\mu_\mathrm{h})(\mu_\mathrm{h}+\nu_\mathrm{h})(c+\eta_\mathrm{m}+3\mu_\mathrm{m}) + c\mu_b\mu_\mathrm{m}(\mu_\mathrm{h}+\nu_\mathrm{h})(\mu_\mathrm{h}(3\mu_\mathrm{m}+2)\\
&\quad + \eta_\mathrm{h}(2\eta_\mathrm{m}+3\mu_\mathrm{m})))/(B\beta_\mathrm{hm}(\eta_\mathrm{h}+\mu_\mathrm{h})(-\mu_b\mu_\mathrm{h}(c+\mu_\mathrm{m})(c+\eta_\mathrm{m}+\mu_\mathrm{m}) - Bk\beta_\mathrm{mh}\eta_\mathrm{m}\mathcal{M})(\mu_\mathrm{h}+\nu_\mathrm{h}));\\
A_\mathrm{m}^* &= \frac{\mathcal{M}}{\eta_A\mu_b} kN_\mathrm{h},\\
S_\mathrm{m}^* &= \frac{kN_\mathrm{h}^2\mathcal{M}}{\mu_b(cN_\mathrm{h} + BI_\mathrm{h}^*\beta_\mathrm{hm} + N_\mathrm{h}\mu_\mathrm{m})},\\
E_\mathrm{m}^* &= \frac{\mu_\mathrm{m}+c}{\eta_\mathrm{m}} I_\mathrm{m}^*,\\
I_\mathrm{m}^* &= \frac{BI_\mathrm{h}^*kN_\mathrm{h}\beta_\mathrm{hm}\eta_\mathrm{m}\mathcal{M}}{\mu_b(c+\mu_\mathrm{m})(c+\eta_\mathrm{m}+\mu_\mathrm{m})(cN_\mathrm{h} + BI_\mathrm{h}^*\beta_\mathrm{hm} + N_\mathrm{h}\mu_\mathrm{m})}.
\end{aligned}$$

As before, this equilibrium is only biologically interesting if $\mathcal{M} > 0$.

With the Mathematica software, we obtained a fourth solution. However, some of its components are negative, which means that it does not belong to the Ω set.

Appendix 3. The basic reproduction number: proof of Theorem 2

The basic reproduction number is calculated in a DFE. In this case, we consider the most realistic one, BRDFE.

Following [3,9], we consider the vector $x^\mathrm{T} = (E_\mathrm{h}, I_\mathrm{h}, E_\mathrm{m}, I_\mathrm{m})$ which corresponds to the components related to the progression of the disease.

Thus, the subsystem used is:

$$\begin{aligned}
\frac{\mathrm{d}E_\mathrm{h}}{\mathrm{d}t}(t) &= B\beta_\mathrm{mh}\frac{I_\mathrm{m}}{N_\mathrm{h}}S_\mathrm{h} - (\nu_\mathrm{h}+\mu_\mathrm{h})E_\mathrm{h}\\
\frac{\mathrm{d}I_\mathrm{h}}{\mathrm{d}t}(t) &= \nu_\mathrm{h}E_\mathrm{h} - (\eta_\mathrm{h}+\mu_\mathrm{h})I_\mathrm{h}\\
\frac{\mathrm{d}E_\mathrm{m}}{\mathrm{d}t}(t) &= B\beta_\mathrm{hm}\frac{I_\mathrm{h}}{N_\mathrm{h}}S_\mathrm{m} - (\mu_\mathrm{m}+\eta_\mathrm{m})E_\mathrm{m} - cE_\mathrm{m}\\
\frac{\mathrm{d}I_\mathrm{m}}{\mathrm{d}t}(t) &= \eta_\mathrm{m}E_\mathrm{m} - \mu_\mathrm{m}I_\mathrm{m} - cI_\mathrm{m}.
\end{aligned} \tag{A3}$$

This subsystem can be written as partitioned, $\mathrm{d}x/\mathrm{d}t = \mathcal{F}(x) - \mathcal{V}(x)$, where $x^\mathrm{T} = (E_\mathrm{h}, I_\mathrm{h}, E_\mathrm{m}, I_\mathrm{m})$, $\mathcal{F}(x)$ represents the components related to new cases of disease (in this situation in the exposed compartments) and $\mathcal{V}(x)$ represents the

other components. Thus, subsystem (A3) can be rewritten as

$$\mathcal{F}(x) = \begin{pmatrix} B\beta_{\mathrm{mh}} \dfrac{I_{\mathrm{m}}}{N_{\mathrm{h}}} S_{\mathrm{h}} \\ 0 \\ B\beta_{\mathrm{hm}} \dfrac{I_{\mathrm{h}}}{N_{\mathrm{h}}} S_{\mathrm{m}} \\ 0 \end{pmatrix} \quad \text{and} \quad \mathcal{V}(x) = \begin{pmatrix} (\nu_{\mathrm{h}} + \mu_{\mathrm{h}}) E_{\mathrm{h}} \\ -\nu_{\mathrm{h}} E_{\mathrm{h}} + (\eta_{\mathrm{h}} + \mu_{\mathrm{h}}) I_{\mathrm{h}} \\ (\mu_{\mathrm{m}} + \eta_{\mathrm{m}} + c) E_{\mathrm{m}} \\ -\eta_{\mathrm{m}} E_{\mathrm{m}} + (\mu_{\mathrm{m}} + c) I_{\mathrm{m}} \end{pmatrix}.$$

Let us considerer the Jacobian matrices associated with $\mathcal{F}$ and $\mathcal{V}$:

$$J_{\mathcal{F}(x)} = \begin{pmatrix} 0 & 0 & 0 & B\beta_{\mathrm{mh}} \dfrac{S_{\mathrm{h}}}{N_{\mathrm{h}}} \\ 0 & 0 & 0 & 0 \\ 0 & B\beta_{\mathrm{hm}} \dfrac{S_{\mathrm{m}}}{N_{\mathrm{h}}} & 0 & 0 \\ 0 & 0 & 0 & 0 \end{pmatrix}$$

and

$$J_{\mathcal{V}(x)} = \begin{pmatrix} \nu_{\mathrm{h}} + \mu_{\mathrm{h}} & 0 & 0 & 0 \\ -\nu_{\mathrm{h}} & \eta_{\mathrm{h}} + \mu_{\mathrm{h}} & 0 & 0 \\ 0 & 0 & \mu_{\mathrm{m}} + \eta_{\mathrm{m}} + c & 0 \\ 0 & 0 & -\eta_{\mathrm{m}} & \mu_{\mathrm{m}} + c \end{pmatrix}.$$

According to [9], the basic reproduction number is $\mathcal{R}_0 = \rho(J_{\mathcal{F}(x_0)} J_{\mathcal{V}^{-1}(x_0)})$, where x_0 is a DFE (BRDFE) and $\rho(A)$ defines the spectral radius of a matrix A. Using Mathematica

$$\mathcal{R}_0^2 = \frac{B^2 k \beta_{\mathrm{hm}} \beta_{\mathrm{mh}} \eta_{\mathrm{m}} \nu_{\mathrm{h}} \mathcal{M}}{\mu_b(\eta_{\mathrm{h}} + \mu_{\mathrm{h}}) \mu_{\mathrm{m}} (c + \mu_{\mathrm{m}})(c + \eta_{\mathrm{m}} + \mu_{\mathrm{m}})(\mu_{\mathrm{h}} + \nu_{\mathrm{h}})},$$

and we obtain the value for the threshold parameter, with $\mathcal{M} > 0$.