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Control of dengue disease: a case study in Cape Verde

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Abstract

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 (adulticide spray) in order to combat the mosquito. The model presents three possible equilibria: two disease-free equilibria (DFE) — where humans, with or without mosquitoes, live without the disease — and another endemic equilibrium (EE). In the literature 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 a minimum level of insecticide is applied, then it is possible to maintain the basic reproduction number below unity. A case study, using data of the outbreak that occured in 2009 in Cape Verde, is presented.

Key words: dengue, basic reproduction number, stability, Cape Verde, control.
MSC 2000: 92B05, 93C95, 93D20.

1 Introduction

Dengue is a mosquito-borne infection that has become a major international public health concern. According to the World Health Organization, 50 to 100 million dengue infections occur yearly, including 500000 Dengue Haemorrhagic Fever cases and 22000 deaths, mostly among children [10]. Dengue is found in tropical and sub-tropical regions around the world, predominantly in urban and semi-urban areas.

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

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*. The life cycle of a mosquito presents four distinct stages: egg, larva, pupa and adult. In the case of *Aedes aegypti* the first three stages take place in or near water while air is the medium for the adult stage [6]. The adult stage of the mosquito is considered to last an average of eleven 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 acquire the virus while feeding on the blood of an infected person. After virus incubation for eight to ten days, an infected mosquito is capable, during probing and blood feeding, of transmitting the virus for the rest of its life.

The organization of this paper is as follows. A mathematical model of the interaction between human and mosquito populations is presented in Section 2. Section 3 is concerned with the equilibria of the epidemiological model and their stability. In Section 4 the results obtained in the previous section are applied to a study case. Finally, some concluding notes are given in Section 5.

2 The mathematical model

Considering the work of [7], the relationship between humans and mosquitoes are now rather complex, taking into account the model presented in [4]. The novelty in this paper is the presence of the control parameter related to adult mosquito spray.

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 other four 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 analyze the effects of campaigns to combat the mosquito, there is also a control variable:

$c(t)$	level of insecticide campaigns

Some assumptions are made in this model:

- the total human population (N_h) is constant, which means that we do not consider births and deaths;
- there is no immigration of infected individuals to 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 do 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 used in our 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)
$1/\mu_h$	average lifespan of humans (in days)
$1/\eta_h$	mean viremic period (in days)
$1/\mu_m$	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)
$1/\eta_m$	extrinsic incubation period (in days)
$1/\nu_h$	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

$$\begin{cases} \frac{dS_h}{dt}(t) = \mu_h N_h - (B\beta_{mh}\frac{I_m}{N_h} + \mu_h)S_h \\ \frac{dE_h}{dt}(t) = B\beta_{mh}\frac{Im}{N_h}S_h - (\nu_h + \mu_h)E_h \\ \frac{dI_h}{dt}(t) = \nu_h E_h - (\eta_h + \mu_h)I_h \\ \frac{dR_h}{dt}(t) = \eta_h I_h - \mu_h R_h \end{cases} \quad (1)$$

and vector population

$$\begin{cases} \frac{dA_m}{dt}(t) = \mu_b(1 - \frac{A_m}{K})(S_m + E_m + I_m) - (\eta_A + \mu_A)A_m \\ \frac{dS_m}{dt}(t) = -(B\beta_{hm}\frac{I_h}{N_h} + \mu_m)S_m + \eta_A A_m - cS_m \\ \frac{dE_m}{dt}(t) = B\beta_{hm}\frac{I_h}{N_h}S_m - (\mu_m + \eta_m)E_m - cE_m \\ \frac{dI_m}{dt}(t) = \eta_m E_m - \mu_m I_m - cI_m \end{cases} \tag{2}$$

with the initial conditions

$$\begin{array}{llll} S_h(0) = S_{h0}, & E_h(0) = E_{h0}, & I_h(0) = I_{h0}, & R_h(0) = R_{h0}, \\ A_m(0) = A_{m0}, & S_m(0) = S_{m0}, & E_m(0) = E_{m0}, & I_m(0) = I_{m0}. \end{array} \tag{3}$$

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.

3 Equilibrium points and Stability

Let the set

$$\Omega = \{(S_h, E_h, I_h, A_m, S_m, E_m, I_m) \in \mathbb{R}^7_+ : S_h + E_h + I_h \le N_h, A_m \le kN_h, S_m + E_m + I_m \le mN_h\}$$

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

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

$$\mathcal{M} = -\left(c(\eta_A + \mu_A) + \mu_A\mu_m + \eta_A(-\mu_b + \mu_m)\right).$$

The system (1)–(2) admits, at most, three equilibrium points:

- *if $\mathcal{M} \le 0$, there is a Disease-Free Equilibrium (DFE), called Trivial Equilibrium, $E_1^* = (N_h, 0, 0, 0, 0, 0, 0)$;*
- *if $\mathcal{M} > 0$, there is a Biologically Realistic Disease-Free Equilibrium (BRDFE), $E_2^* = \left(N_h, 0, 0, \frac{kNh\mathcal{M}}{\eta_A\mu_b}, \frac{kNh\mathcal{M}}{\mu_b\mu_m}, 0, 0\right)$ or an Endemic Equilibrium (EE), $E_3^* = (S_h^*, E_h^*, I_h^*, A_m^*, S_m^*, E_m^*, I_m^*)$.*

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 [5]. Following [9], we prove:

Proposition 2. *If $\mathcal{M} > 0$, then the basic reproduction number associated to (1)–(2) is $\mathcal{R}_0^2 = \frac{B^2 k\beta_{hm}\beta_{mh}\eta_m\nu_h\mathcal{M}}{\mu_b(\eta_h + \mu_h)(c+\mu_m)^2(c+\eta_m+\mu_m)(\mu_h+\nu_h)}$.*

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

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.

We want to find c such that $\mathcal{R}_0 < 1$.

4 Dengue in Cape Verde

The simulations were carried out using the following values: $N_h = 480000$, $B = 1$, $\beta_{mh} = 0.375$, $\beta_{hm} = 0.375$, $\mu_h = 1/(71 * 365)$, $\eta_h = 1/3$, $\mu_m = 1/11$, $\mu_b = 6$, $\mu_A = 1/4$, $\eta_A = 0.08$, $\eta_m = 1/11$, $\nu_h = 1/4$, , $m = 6$, $k = 3$, $K = k * N_h$. The initial conditions for the problem were: $S_{h0} = m * N_h$, $E_{h0} = 216$, $I_{h0} = 434$, $R_{h0} = 0$, $A_{m0} = k * N_h$, $S_{m0} = m * N_h$, $E_{m0} = 0$, $I_{m0} = 0$. The final time was $t_f = 84$ days. The values related to humans describes the reality of an infected period in Cape Verde [1]. However, since it was the first outbreak that happened in the archipelago it was not possible to collect any data for the mosquito. Thus, for the *aedes Aegypti* we have selected information from Brazil where dengue is already a reality long known [8, 11].

Proposition 3. *Let us consider the parameters listed above and consider c as a constant. Then* $\mathcal{R}_0 < 1$ *if and only if* $c > 0.0837$.

For our computations let us consider $c = 0.084$. The results indicate that use of the control c is crucial to prevent that an outbreak could transform an epidemiological episode to an endemic disease. The computational experiences were carried out using Scilab [2].

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

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

The number of infected mosquitoes is close to zero in a situation where control is present. Note that we do not intend to eradicate the mosquitoes but instead the number of infected mosquitoes.

5 Conclusions

It is very difficult to control or eliminate the *Aedes aegypti* mosquito because it makes adaptations to the environment and becomes resistant to natural phenomena (e.g. droughts) or human interventions (e.g. control measures).

During outbreaks emergency vector control measures can also include broad application of insecticides. It has been shown here that with a steady spray campaign it is

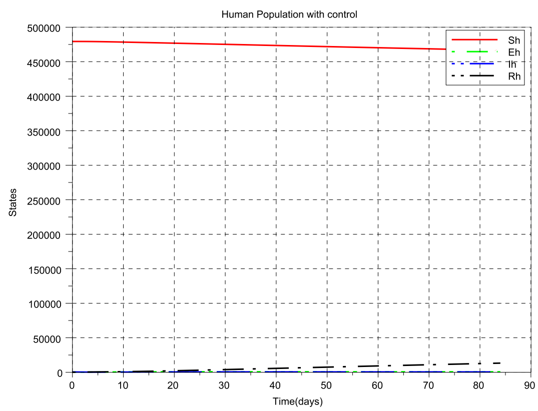

Figure 1: Human compartments using control

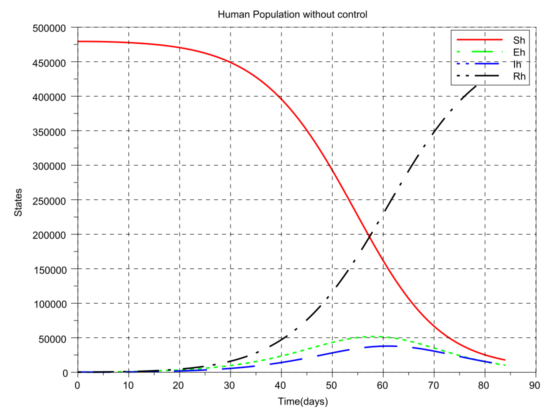

Figure 2: Human compartments with no control

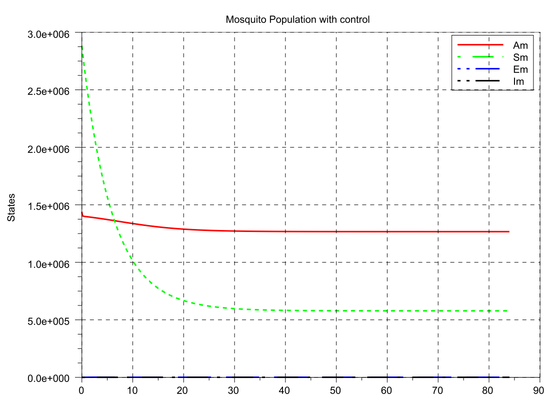

Figure 3: Mosquito compartments using control

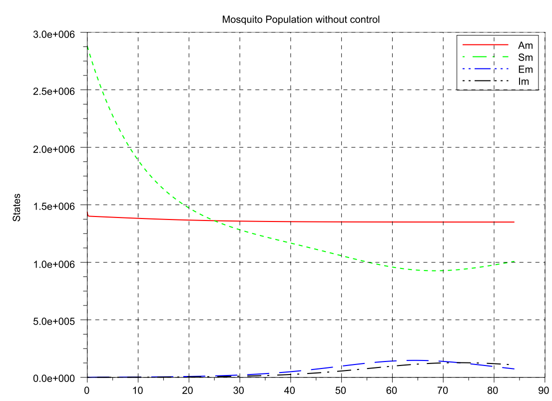

Figure 4: Mosquito compartments with no control

possible to reduce the number of infected humans and mosquitoes. Active monitoring and surveillance of the natural mosquito population should accompany control efforts to determine programme effectiveness.

Acknowledgements

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