Mathematical Biosciences 258 (2014) 77–84

Contents lists available at ScienceDirect

Mathematical Biosciences

journal homepage: www.elsevier.com/locate/mbs

Review

Multiobjective Genetic Algorithm applied to dengue control

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ARTICLE INFO

Article history:
Received 29 November 2013
Revised 14 August 2014
Accepted 22 August 2014
Available online xxx

Keywords:
Dengue
Multiobjective optimization
Genetic algorithm

ABSTRACT

Dengue fever is an infectious disease caused by a virus of the *Flaviridae* family and transmitted to the person by a mosquito of the genus *Aedes aegypti*. This disease has been a global public health problem because a single mosquito can infect up to 300 people and between 50 and 100 million people are infected annually on all continents. Thus, dengue fever is currently a subject of research, whether in the search for vaccines and treatments for the disease or efficient and economical forms of mosquito control. The current study aims to study techniques of multiobjective optimization to assist in solving problems involving the control of the mosquito that transmits dengue fever. The population dynamics of the mosquito is studied in order to understand the epidemic phenomenon and suggest strategies of multiobjective programming for mosquito control. A Multiobjective Genetic Algorithm (MGA_DENGUE) is proposed to solve the optimization model treated here and we discuss the computational results obtained from the application of this technique.

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1. Introduction

The dengue virus is most commonly transmitted by the mosquito vector *Aedes aegypti*, but can be transmitted by other members of the genus *Aedes* including *Aedes albopictus*. The tropical regions are most affected by dengue fever due to environmental conditions that favor the development and proliferation of *A. aegypti*. In hot and rainy periods there occurs increased density of mosquitoes, causing a greater incidence of dengue fever. This disease is caused by four distinct serotypes known as DEN1, DEN2, DEN3 and DEN4. If a person is infected by one of the four serotypes, he will never again be infected by the same serotype (*homologous immunity*), but loses immunity to the three other serotypes (*heterologous immunity*) in about 12 weeks and then becomes more susceptible to developing dengue hemorrhagic fever [4,6,16].

A female mosquito becomes infected with dengue by feeding on the blood of an infected person and then transmits the virus to other people through subsequent blood feedings. A mosquito remains infected for the duration of its life and females can also transmit the virus to their offspring. According to Health Surveillance Secretariat of Brazil, in 45 days of life, a single mosquito can infect up to 300 people. The incubation of the virus in humans ranges from 3 to 15 days after the bite of the vector, with an average of 6 days [4,16,21].

There is an estimate by the World Health Organization (WHO) that annually from 50 to 100 million people are infected in more than 100 countries on all continents. With nearly half of the world's population at risk of dengue infection, the lack of specific treatment or vaccine increases the severity and risk. It is estimated that 500,000 people with dengue hemorrhage fever (DHF) require hospitalization each year – a large proportion of these are children. It is fatal in approximately 2.5% of those affected [21].

The prevention and control of dengue fever depend on measures that effectively control the mosquito *A. aegypti*. In Brazil, the main controls currently used by the Superintendence of Endemic Disease Control (SUCEN, *Superintendência de Controle de Endemias*) are: physical control, done by public health officials and residents through eliminating breeding; and chemical control, done by applying insecticides. Insecticides play an important part in controlling dengue vectors. However, over the time the vectors acquire resistance, requiring an increase of chemicals, increasing the cost of control and affecting public health [20].

It is very difficult to control or eliminate *A. aegypti* mosquitoes with these control measures. This is due to the fact that they have adaptations to the environment that make them highly resilient. The mosquito has the ability to bounce back rapidly to initial numbers after disturbances resulting from natural phenomena (e.g., droughts) or human interventions. Thus, the control of the mosquito that transmits dengue is the subject of much research.

There are several works with the proposal of assisting in the search for optimal control of the mosquito that transmits dengue. Caetano and Yoneyama [5] present an application of the optimal control theory in dengue epidemics. In this work, the dynamics of this

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http://dx.doi.org/10.1016/j.mbs.2014.08.013
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insect-borne disease are modeled as a set of non-linear ordinary differential equations. These include the effect of educational campaigns organized to motivate the population to break the reproductive cycle of the mosquitoes by avoiding the accumulation of standing water in open-air receptacles. The functional cost is such that it reflects a compromise between the health of the population and the actual spending on insecticides and educational campaigns.

Rodrigues et al. [18] present a dynamic model which describes the dynamics of the dengue mosquito, the number of infected individuals and people's motivation to combat the mosquito. The functional cost depends on the costs of medical treatment of the infected people as well as on the costs related to education and sanitation campaigns. They present two approaches for solving the problem: one using the optimal control theory and the other carried out by first defining the problem and then solving it with nonlinear programming. Other authors have proposed approaches of optimal control which are applied to dengue differently than the approach that will be presented in the present work ([1,2,20] and others).

Brazil has started biological control with genetically modified mosquitoes to fight dengue. In this control, male mosquitoes that have been rendered sterile by irradiation in laboratory are used. This technique is called the Sterile Insect Technique (SIT) and has been shown to be effective in controlling agricultural pests, such as the blowfly eradication program. The sterile males compete with the wild males for female insects. Adult females mate only once in their lifetime and, after mating, reject other males. Additionally, the female lays about 100 eggs. The release is performed gradually and in different places to increase the probability of the birth of mosquitoes. However, if a female mates with a sterile male it will have no offspring, thus reducing the next generation's population [3,8,14,17].

The main aim of the present work is to study techniques of multiobjective optimization that assist in solving problems involving the control of the mosquito that transmits dengue fever. We do not include all biological and mathematical details in order to give greater importance to the multiobjective technique proposed. The population dynamics of the mosquito that transmits dengue fever is studied in order to understand the epidemic phenomenon and suggest new multiobjective programming strategies for the control of the mosquito. A Multiobjective Genetic Algorithm (MGA_DENGUE) is proposed to solve the optimization model treated here and we discuss the computational results obtained from the application of this technique.

2. Mathematical model

Esteva and Yang [9] proposed a mathematical model for analyzing the effect of the introduction of sterile male insects in the environment for control of the mosquito that transmits dengue. In this proposal, the mosquito's life cycle was considered as being divided in two phases: the aquatic phase, when mosquitoes are in the egg, larva and pupa stages; and the terrestrial phase, when mosquitoes are at the adult stage. The size of the mosquito population in the aquatic phase at time t is denoted by $\boldsymbol{A}(t)$. Mosquitoes in the aquatic phase enter the terrestrial phase at a γ per capita rate, with r proportion of the females and $(1-r)$ of the males. In the terrestrial phase, the wild adult mosquitoes were divided into three compartments: immature females (before mating), $\boldsymbol{I}$; natural (or wild) male insects, $\boldsymbol{M}$; and fertilized females, $\boldsymbol{F}$. By inserting sterile mosquitoes into the system, it creates two more compartments: sterile (irradiated or transgenic) insects, $\boldsymbol{S}$; and unfertilized females (removed female), $\boldsymbol{U}$, which are the females that mate with sterile males.

The flows from immature females I to fertilized females F and unfertilized females U compartments depend mainly on the number of encounters with natural and sterile males. Then the probability of an encounter of a female I with natural male insects is given by $(M/(M+S))$ and the per capita rate at which female insects are fertilized is $(\beta M/(M+S))$, where β is the mating rate of the insects. The probability of an encounter of a sterile male S with a female I is given by $(pS/(M+S))$, where p, $0 \le p \le 1$, is the proportion of sterile insects that are released in the appropriate places. The effective fertilization during mating could be diminished due to sterilization, which leads one to assume that the effective mating rate of sterile insects is given by $q\beta$, $0 \le q \le 1$. Putting together the assumptions above, we get that $(\beta_S S/(M+S))$, were $\beta_S = pq\beta$. Finally, α is the rate at which the population of the sterile mosquitoes S is sprayed in the environment.

The net oviposition rate per female insect is proportional to their density, but it is also regulated by a carrying capacity effect depending on the occupation of the available breeder sites. It is assumed that the per capita oviposition rate is given by $\phi(1-A/C)$ where ϕ is the intrinsic oviposition rate and C is the carrying capacity related to the amount of available nutrients and space.

The per capita mortality rates of the aquatic phase, immature females, fertilized females, unfertilized females and sterile male insects are denoted by μ_A, μ_I, μ_F, μ_U, μ_M and μ_S respectively.

The dynamics of this system are illustrated in Fig. 1. The parameters $A(t)$, $S(t)$, $I(t)$, $M(t)$, $U(t)$ and $F(t)$ represent the size of each segment of the mosquito population at time t:

In addition to the biological control with sterile mosquitoes, we also consider chemical control with insecticide, which has played an important role in controlling *A. aegypti*. The insecticide acts only in the adult stage of the mosquito and not in the aquatic phase.

In chemical control, the amount and cost of insecticide used is generally proportional to the area treated and not to the size of the population. However, the damage done by mosquitoes is proportional to the number of individual per unit area. Thus, the cost/benefit ratio of insecticidal control increases as the size of the population increases. In sterile male release programs, the number of sterile male released and their cost is proportional to the size of the population. The cost/benefit ratio decreases with a decrease in size of the population. Then, it can be wise to use integrated insecticidal methods with sterile male technique.

Considering the control variables $u_1 = u_1(t)$ and $u_2 = u_2(t)$, associated respectively with chemical control and biological control, we present the mathematical model (1) for the population dynamics using the insecticide and sterile mosquitoes controls as proposed by Thome et al. [20].

$$\begin{cases} \dfrac{dA}{dt} = \phi\left(1-\dfrac{A}{C}\right)F - (\gamma+\mu_A)A \\ \dfrac{dI}{dt} = r\gamma A - \left[\dfrac{\beta M}{M+S} + \dfrac{\beta_S S}{M+S} + \mu_I + u_1\right]I \\ \dfrac{dF}{dt} = \dfrac{\beta M I}{M+S} - (\mu_F + u_1)F \\ \dfrac{dM}{dt} = (1-r)\gamma A - (\mu_M + u_1)M \\ \dfrac{dS}{dt} = u_2 - (\mu_S + u_1)S. \end{cases} \tag{1}$$

The state variable U, related to removed female mosquitoes, is decoupled from the dynamic system described by

$$\frac{dU}{dt} = \frac{\beta_S S I}{M+S} - \mu_U U - u_1 U.$$

To study the system state (1), Ref. [20] used the initial conditions presented in (2) because these are the equilibrium conditions

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