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IFAC PapersOnLine 51-2 (2018) 1–6

Numerical optimal control applied to an epidemiological model

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Abstract: A previously published SIR-ASI optimal control model of dengue fever is described and the optimal control problem is solved in this paper by an alternative solution approach, namely by a direct transcription method. In this method, the optimal control problem is substituted by a nonlinear programming problem. The nonlinear programming problem is solved by an interior point method. In the following an a posteriori check of the necessary optimality conditions of optimal control, which has not yet been done, is performed with the discretized states, adjoints, and controls. The check shows some accordance with the numerical results, but unfortunately in this setting a seldom discrepancy is observed, which seems to be connected with the modeling of the mechanical control.

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Keywords: Dengue fever, mechanical control, insecticide, optimal control, direct transcription, a posteriori verification of numerical results

1. INTRODUCTION

Dengue fever is an infectious disease which occurs in tropical and subtropical areas. According to the World Health Organization (WHO (2017)) about 50% of the world population is nowadays at risk. Dengue fever is caused by viruses and transmitted to humans by the bite of an infected mosquito, mainly of the species Aedes aegypti. The symptoms of dengue fever include high fever, severe headache, muscle and joint pains, and nausea. Complications occur in seldom cases, but may lead to severe dengue, a potentially lethal course of the disease. A first vaccine against dengue fever has only recently been made available and several other vaccines are under development. Furthermore, there is no specific anti-viral treatment for dengue. For these reasons the best protection against dengue fever at present is avoiding the contact with infected mosquitoes, including the control of mosquitoes and their eggs as described in WHO (2009).

The course of the disease in a population can be simulated with mathematical models in order to make statements about future developments and to suggest possible strategies to attenuate the spread of the disease. The investigation of a model describing an epidemic outbreak of dengue fever in Cape Verde is the subject matter in Rodrigues et al. (2013b). In this paper three vector control operations are considered: larvicides which are distributed in the water reservoirs in order to combat the mosquitoes in the aquatic phase (eggs, larvae, and pupae); adulticides against the adult mosquitoes which can be sprayed in buildings or outdoor to achieve a fast and significant decrease in the mosquito population; and the mechanical control including the removal of standing waters and small water reservoirs to get rid of possible breeding grounds. The aim of using control measures is to keep the number of infected individuals as low as possible. This also leads to less medical treatment, hospitalizations, and absences from work due to illness and thus to less costs. On the other hand, the costs caused by the use of the controls should also be as low as possible, including the development and distribution of insecticides and search for breeding areas and their subsequent elimination. The goal is to optimize the tradeoff between costs and effectiveness.

Rodrigues et al. (2013a) consider an optimal control problem and solve it numerically, but no verification of the results is done. We apply an alternative numerical approach for the solution of this optimal control problem by direct transcription into a nonlinear programming problem, see e.g. Betts (2001). The message along the line of Vanderbei (2001); Dussault (2014) is that one has to be careful when applying the direct transcription approach to optimal problems which are non-convex in the controls which is the case here for one of the three controls. We use the solver IPOPT of Wächter and Biegler (2006) and compare our results to Rodrigues et al. (2013a) to investigate if our approach yields better outcomes. Furthermore, an a posteriori verification of the necessary optimality conditions of optimal control is performed. We present analytical control laws obtained from Pontryagin's minimum principle and use them to validate our numerical results.

In Section 2 the model is described. The numerical results and the verification are shown in Section 3.

2. DENGUE SIR-ASI-MODEL

We firstly describe the model from Rodrigues et al. (2013b). We consider a human population of N_h individuals and a mosquito population. Both populations are split

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Peer review under responsibility of International Federation of Automatic Control.
10.1016/j.ifacol.2018.03.001

into disjoint groups (compartments). The human population is divided into three groups, the susceptibles S_h, the infected and infectious I_h, and the recovered R_h. These variables denote total numbers. By birth, all humans are assumed to be susceptible which means they have not yet been infected by dengue fever. Once they have been bitten by an infected mosquito and become carriers of the virus, they are infected and able to transmit the virus to mosquitoes. After recovery the humans are healthy and cannot contract the disease again. The total human population N_h is assumed to be constant over time t, so $N_h = S_h(t)+I_h(t)+R_h(t)$. The mosquitoes are also divided into three groups. For this classification it is necessary to know the life cycle of the mosquitoes: Female mosquitoes bite humans and lay their eggs in small water containers, like empty cans or old car tyres. After a few days larvae hatch from the eggs and mature further to pupae. The adult mosquitoes emerge from the pupae. The first group of the mosquitoes, A_m, refers to the mosquitoes in the aquatic phase and includes the egg, larva, and pupa stages. The other two groups characterize the adult mosquitoes, the susceptibles S_m and the infected I_m. The mosquitoes get infected and become vectors of the disease by taking a blood meal from an infectious human. After that they are able to transmit the virus to humans by biting them. The mosquitoes live to briefly to become immune. Due to this six compartments the model is also called an SIR-ASI model. Individuals in one group are assumed to be homogeneous and they can change between compartments during the course of the disease. The dynamics of the flow between the compartments is described using differential equations. The mosquito population is affected by the use of vector control measures. The three control variables considered in this model include

- c_m, the proportion of adulticides, $(0 \leq c_m \leq 1)$,
- c_A, the proportion of larvicides, $(0 \leq c_A \leq 1)$, and
- α, the proportion of mechanical control $(0 < \alpha_{\min} \leq \alpha \leq 1)$.

Table 1. Parameters and values in the model according to Rodrigues et al. (2013b)

Parameter	Value	Description
N_h	$480000[-]$	total human population
B	$0.8\left[\frac{\text{bite}}{\text{day}}\right]$	average number of bites of a mosquito per day
$\frac{1}{\mu_h}$	$71 \cdot 365[\text{day}]$	average lifespan of humans in days
β_{mh}	$0.375\left[\frac{1}{\text{bite}}\right]$	probability of disease transmission from mosquitoes to humans per bite
β_{hm}	$0.375\left[\frac{1}{\text{bite}}\right]$	probability of disease transmission from humans to mosquitoes per bite
$\frac{1}{\eta_h}$	$3[\text{day}]$	duration of the infection in days
φ	$6\left[\frac{1}{\text{day}}\right]$	number of eggs at each deposit per mosquito per day
$\frac{1}{\mu_m}$	$10[\text{day}]$	average lifespan of adult mosquitoes in days
μ_A	$\frac{1}{4}\left[\frac{1}{\text{day}}\right]$	natural mortality rate of larvae per day
η_A	$0.08\left[\frac{1}{\text{day}}\right]$	maturation rate from larvae to adult per day
m	$3[-]$	number of female mosquitoes per human
k	$3[-]$	total number of larvae per human

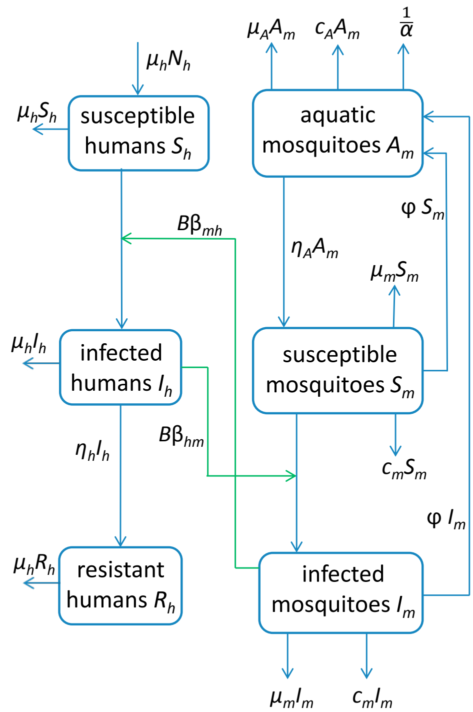

Fig. 1. SIR for humans – ASI for mosquitoes

The first control combats the adult mosquitoes in the compartments S_m and I_m, while the latter two are directed against the mosquitoes in the aquatic phase A_m. The maximal use of insecticides is attained at $c_m = 1$ and $c_A = 1$. Since $\alpha \neq 0$, because it appears in a denominator in the model, we introduce $\alpha_{\min}$ as a lower bound which corresponds to the maximal use of mechanical control. Here $\alpha_{\min} = 0.001$ is chosen. Note that the case $c_m = 0$, $c_A = 0$, and $\alpha = 1$ means no control at all. The parameters used in the model are summarized in Table 1 with the values of the Cape Verde data from Rodrigues et al. (2013b). The state variables are S_h, I_h, R_h, A_m, S_m, and I_m. Together with the control variables and the transition and contact rates between the groups, the model is described and a nonlinear system of differential equations is obtained. Fig. 1 shows a scheme of this model. For the analysis we use the normalized system. The following transformations are carried out: $s_h = \frac{S_h}{N_h}$, $i_h = \frac{I_h}{N_h}$, $r_h = \frac{R_h}{N_h}$, $a_m = \frac{A_m}{kN_h}$, $s_m = \frac{S_m}{mN_h}$, and $i_m = \frac{I_m}{mN_h}$. The model is thus given by:

$$
\begin{aligned}
\frac{ds_h}{dt} &= \mu_h - (B\beta_{mh} m i_m + \mu_h)\, s_h \\
\frac{di_h}{dt} &= B\beta_{mh} m i_m s_h - (\eta_h + \mu_h) i_h \\
\frac{dr_h}{dt} &= \eta_h i_h - \mu_h r_h \\
\frac{da_m}{dt} &= \varphi \frac{m}{k}\left(1 - \frac{a_m}{\alpha}\right)(s_m + i_m) - (\eta_A + \mu_A + c_A) a_m \\
\frac{ds_m}{dt} &= \eta_A \frac{k}{m} a_m - (B\beta_{hm} i_h + \mu_m + c_m)\, s_m \\
\frac{di_m}{dt} &= B\beta_{hm} i_h s_m - (\mu_m + c_m) i_m
\end{aligned}
\tag{1}
$$

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