Optimization of Dengue Epidemics: a test case with different discretization schemes

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Abstract. The incidence of Dengue epidemiologic disease has grown in recent decades. In this paper an application of optimal control in Dengue epidemics is presented. The mathematical model includes the dynamic of Dengue mosquito, the affected persons, the people's motivation to combat the mosquito and the inherent social cost of the disease, such as cost with ill individuals, educations and sanitary campaigns. The dynamic model presents a set of nonlinear ordinary differential equations. The problem was discretized through Euler and Runge Kutta schemes, and solved using nonlinear optimization packages. The computational results as well as the main conclusions are shown.

Keywords: Optimal Control, Dengue, Nonlinear Programming, Euler Scheme, Runge Kutta Scheme
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INTRODUCTION

Dengue is a mosquito mostly found in tropical and sub-tropical climates worldwide, mostly in urban and semi-urban areas. It can provoque a mosquito-borne infection, that causes a severe flu-like illness, and sometimes a potentially lethal complication called dengue haemorrhagic fever, and about 40% of the world's population are now at risk.

The aim of this paper is to present an attempt to apply quantitative methods in the optimization of investments in the control of Epidemiologic diseases, in order to obtain a maximum of benefits from a fixed amount of financial resources. This model includes the dynamic of the growing of the mosquito, but also the efforts of the public management to motivate the population to break the reproduction cycle of the mosquitoes by avoiding the accumulation of still water in open-air recipients and spraying potential zones of reproduction.

The paper is organized as follows. Next section presents the dynamic model for dengue epidemics, where the variables, parameters and the control system are defined. Then, the numerical implementation and the strategies used to solve the problem are reported. Finally, the numerical results are presented and some conclusions are taken.

DYNAMIC MODEL

The model described in this paper is based on the model proposed in [3].

The notation used in the mathematical model is as follows.

State Variables:

- $x_1(t)$ density of mosquitoes;
- $x_2(t)$ density of mosquitoes carrying the virus;
- $x_3(t)$ number of persons with the disease;
- $x_4(t)$ level of popular motivation to combat mosquitoes (goodwill).

Control Variables:

- $u_1(t)$ investments in insecticides;
- $u_2(t)$ investments in educational campaigns.

Parameters:

α_R average reproduction rate of mosquitoes;
α_M mortality rate of mosquitoes;
β probability of contact between non-carrier mosquitoes and affected persons;
η rate of treatment of affected persons;
μ amplitude of seasonal oscillation in the reproduction rate of mosquitoes;
ρ probability of persons becoming infected;
θ fear factor, reflecting the increase in the population's willingness to take actions to combat the mosquitoes as a consequence of the high prevalence of the disease in the specific social environment;
τ forgetting rate for goodwill of the target population;
φ phase angle to adjust the peak season for mosquitoes;
ω angular frequency of the mosquitoes's proliferation cycle, corresponding to 52 weeks period;
P population in the risk area (usually normalized to yield $P = 1$);
γ_D the instantaneous costs due to the existence of affected persons;
γ_F the costs of each operation of spraying insecticides;
γ_E the cost associated to the instructive campaigns.

The Dengue epidemic can be modeled by the following nonlinear time-varying state equations. Equation (1) represents the variation of the density of mosquitoes per unit time to the natural cycle of reproduction and mortality (α_R and α_M), due to seasonal effects $\mu sin(\omega t+\varphi)$ and to human interference $-x_4(t)$ and $u_1(t)$:

$$\frac{dx_1}{dt} = [\alpha_R(1-\mu sin(\omega t+\varphi)) - \alpha_M - x_4(t)]\,x_1(t) - u_1(t). \tag{1}$$

Equation (2) expresses the variation of the density x_2 of mosquitoes carrying the virus. The term $[\alpha_R(1-\mu sin(\omega t+\varphi)) - \alpha_M - x_4(t)]\,x_2(t)$ represents the rate of the infected mosquitoes and $\beta\,[x_1(t)-x_2(t)]\,x_3(t)$ represents the increase rate of the infected mosquitoes due to the possible contact between the non infected mosquitoes $x_1(t)-x_2(t)$ and the number persons with disease denoted by x_3:

$$\frac{dx_2}{dt} = [\alpha_R(1-\mu sin(\omega t+\varphi)) - \alpha_M - x_4(t)]\,x_2(t) + \beta\,[x_1(t)-x_2(t)]\,x_3(t) - u_1(t). \tag{2}$$

The dynamics of the infectious transmission is presented in equation (3). The term $-\eta x_3(t)$ represents the rate of cure and $\rho x_2(t)\,[P-x_3(t)]$ represents the rate at which new cases spring up. The factor $[P-x_3(t)]$ is the number of persons in the area, that are not infected:

$$\frac{dx_3}{dt} = -\eta x_3(t) + \rho x_2(t)\,[P-x_3(t)]\,. \tag{3}$$

Equation (4) is a model for the level of popular motivation (or goodwill) to combat the reproductive cycle of mosquitoes. Along the time, the level of people's motivation changes and, as consequence, it is necessary to invest in educational campaigns designed to increase consciousness of the population under risk by a proper understanding of the determinants involved with specific disease. The expression $-\tau x_4(t)$ represents the decay of the people's motivation with time, due to forgetting. The expression $\theta x_3(t)$ represents the natural sensibilities of the public due to increase in the prevalence of the disease.

$$\frac{dx_4}{dt} = -\tau x_4(t) + \theta x_3(t) + u_2(t). \tag{4}$$

The goal of the problem is to minimize the cost functional

$$J\,[u_1(.),u_2(.)] = \int_0^{t_f} \{\gamma_D x_3^2(t) + \gamma_F u_1^2(t) + \gamma_E u_2^2(t)\}dt. \tag{5}$$

This functional includes the social costs related to the existence of ill persons, $\gamma_D x_3^2(t)$, the recourses needed for spraying of insecticides operations, $\gamma_F u_1^2(t)$, and for educational campaigns, $\gamma_E u_2^2(t)$. The model for the social cost is based in the concept of goodwill explored by Nerlove and Arrow [8].

Due to computational issues, the optimal control problem (1)-(5) that is in the Lagrange form, was converted into an equivalent Mayer form. Hence, using a standard procedure to rewrite the cost functional [6], the state vector was augmented by an extra component x_5,

$$\frac{dx_5}{dt} = \gamma_D x_3^2(t) + \gamma_F u_1^2(t) + \gamma_E u_2^2(t) \tag{6}$$

leading to the equivalent terminal cost problem of minimizing

$$I[x_5(.)] = x_5(t_f)$$

with given t_f, subject to the control system (1)-(4) and (6).

NUMERICAL IMPLEMENTATION

The simulations were carried out using the following normalized numerical values: $\alpha_R = 0.20$, $\alpha_M = 0.18$, $\beta = 0.3$, $\eta = 0.15$, $\mu = 0.1$, $\rho = 0.1$, $\theta = 0.05$, $\tau = 0.1$, $\varphi = 0$, $\omega = 2\pi/52$, $P = 1.0$, $\gamma_D = 1.0$, $\gamma_F = 0.4$, $\gamma_E = 0.8$, $x_1(0) = 1.0$, $x_2(0) = 0.12$, $x_3(0) = 0.004$, and $x_4(0) = 0.05$. These values are available in the paper [3]. The final time used was $t_f = 52$ weeks.

To solve this problem it was necessary to discretize the problem. Two methods were selected: a first order, the Euler's scheme, and a Runge Kutta's sheme of second order [1]. In both cases, it is assumed that the time $t = nh$ moves ahead in uniform steps of length h. If a differential equation is written like $\frac{dx}{dt} = f(t,x)$, it is possible to make a convenient approximation of this. In the Euler's scheme the update is given by

$$x_{n+1} \simeq x_n + hf(t_n, x_n),$$

while in the Runge Kutta's method is

$$x_{n+1} \simeq x_n + \tfrac{h}{2}\left[f(t_n, x_n) + f(t_{n+1}, x_{n+1})\right].$$

This approximation x_{n+1} of $x(t)$ at the point t_{n+1} has an error depending on h^2 and h^3, for the Euler and Runge Kutta methods, respectively. This discretization process transforms the dengue epidemics problem in a standard nonlinear optimization problem (NLP), with an objective function and a set of nonlinear constraints. This NLP problem was codified, for both discretization schemes, in the AMPL modelling language [4].

Two nonlinear solvers with distinct features were selected to solve the NLP problem: the Knitro and the Snopt. The first one [2] is a software package for solving large scale mathematical optimization problems based mainly on the Interior Point (IP) method. Snopt [5] uses the SQP (Sequential Quadratic Programming) philosophy, with an augmented Lagrangian approach combining a trust region approach adapted to handle the bound constraints. The NEOS Server [7] platform was used as interface with both solvers.

COMPUTATIONAL RESULTS

Table 1 reports the results for both solvers, for each discretization method using three different discretization steps ($h = 0.5, 0.25, 0.125$), rising twelve numerical experiences. The columns # var. and # const. mean de number of variables and constraints, respectively. The next columns refer to the performance measures - number of iterations and total CPU time in seconds (time for solving the problem, for evaluate the objective and the constraints functions and for input/output). The computational experiences were made in the NEOS server platform - in this way the selected machine to run the program remain unknown as well as its technical specifications.

The optimal value reached was $\approx 3E-03$ for all tests. Comparing the general behaviour of the solvers one can conclude that the IP based method (Knitro) presents much better performance than the SQP method (Snopt) in terms of the measures used. Regarding the Knitro results, one realize that the Euler's discretization scheme has better times for $h = 0.25$ and $h = 0.125$ and similar time for $h = 0.5$, when compared to Runge-Kutta's method. Another obvious finding, for both solvers, is that the CPU time increases as far as the problem dimension increases (number of variables and constraints). With respect to the number of iterations, Snopt presents more iterations as the problem dimension

TABLE 1. Numerical results

	Euler's method					Runge Kutta's method				
	h	# var.	# const.	# iter.	time (sec.)	h	# var.	# const.	# iter.	time (sec.)
Knitro	0.5	727	519	113	2.090	0.5	728	520	64	1.980
	0.25	1455	1039	68	2.210	0.25	1456	1040	82	5.550
	0.125	2911	2079	85	7.240	0.125	2912	2080	70	9.740
	h	# var.	# const.	# iter.	time (sec.)	h	# var.	# const.	# iter.	time (sec.)
Snopt	0.5	727	519	175	4.07	0.5	728	520	223	10.52
	0.25	1455	1039	253	19.2	0.25	1456	1040	219	39.7
	0.125	2911	2079	252	105.4	0.125	2912	2080	420	406.67

increases. However this conclusion cannot be taken for Knitro - in fact, doesn't exist a relation between the problem dimension and the number of iterations. The best version tested was Knitro using Runge-Kutta with $h = 0.5$ (best CPU time and fewer iterations), and the second one was Knitro with Euler's method using $h = 0.25$. An important evidence of this numerical experience is that it is not worth the reduction of the discretization step size because no significative advantages are obtained.

CONCLUSIONS

We solved successfully an optimal control problem by direct methods using nonlinear optimization software based on IP and SQP approaches. The effort of the implementation of higher order discretization methods brings no advantages. The reduction of the discretization step and consequently the increase of the number of variables and constraints doesn't improve the performance with respect to the CPU time and to the number of iterations. We can point out the robustness of both solvers in spite of the dimension problem increase.

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