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Multiobjective synthesis of robust vaccination policies

André R. da Cruz [a,b], Rodrigo T.N. Cardoso [c], Ricardo H.C. Takahashi [d,*]

[a] Dep. de Computação e Construção Civil – Centro Federal de Educação Tecnológica de Minas Gerais, R. Dezenove de Novembro, 121, Centro, Timóteo, MG, Brazil
[b] Programa de Pós-Graduação em Engenharia Elétrica – Universidade Federal de Minas Gerais, Av. Antônio Carlos 6627, 31270-901 Belo Horizonte, MG, Brazil
[c] Dep. de Física e Matemática – Centro Federal de Educação Tecnológica de Minas Gerais, Av. Amazonas, 7675, Nova Gameleira, Belo Horizonte, MG, Brazil
[d] Dep. de Matemática – Universidade Federal de Minas Gerais, Av. Pres. Antônio Carlos, 6627, Pampulha, Belo Horizonte, MG, Brazil

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ABSTRACT

This paper deals with the optimal planning of vaccination campaigns, using an evolutionary multiobjective optimization algorithm and a stochastic simulation of the epidemics dynamics in order to determine robust vaccination policies. A biobjective model is formulated, considering the minimization of control costs and number of infected individuals. The decision variables include number of campaigns, percentage of vaccination and time interval between each campaign. A SIR (Susceptible-Infected-Recovered) model and an IBM (Individual-Based Model) are employed for representing the epidemics. A two-stage optimization process is proposed: a set of nondominated steady-state regimes is obtained and one of them is selected to be concatenated to the transient regime vaccination policies. An evolutionary multiobjective optimization algorithm is proposed, with a local search procedure based on quadratic approximation supported by a hash table information storage. The resulting nondominated solutions are simulated in the IBM, in order to detect and discard the non-robust solutions. Final results show that optimal robust vaccination campaigns with different trade-offs can be designed, allowing policymakers to choose the best strategy according to the monetary cost and the expected efficacy.

1. Introduction

An epidemic is defined as the occurrence of cases of a disease in excess of what is normally expected in a population. An endemic is a relatively stable pattern of occurrence of a transmissible disease in a population group with relatively high prevalence and incidence. A big challenge in public health is related to the planning of vaccination campaigns which aim to eradicate a disease, or to control its spread avoiding large epidemic peaks or significant endemic states, with the minimum possible cost [24]. This paper presents a multiobjective framework, considering a compromise between cost and effectiveness, to determine *nondominated* and *robust* policies to control a disease through impulsive vaccination. A nondominated solution is not worse than any other possible one in both cost and effectiveness, and a robust solution does not degrade significantly its performance when different realizations of the underlying stochastic processes are considered.

Many works have applied control theory to develop optimal strategies to control infectious diseases [25,28,26,27]. Most of them used pulse vaccination, defined as an impulsive control composed by the repeated application of a fixed vaccination ratio in discrete instants [2,20,12]. Stochastic programming frameworks and mono-objective optimization techniques have also been used [31–34]. Different methodologies to the optimization of vaccination campaigns can be found in the literature [29–31,26].

From the modelling perspective, some articles consider generic epidemic models (such as SIR) [28,25], while other ones use specific models of some specific epidemics such as influenza [29,31,32]. In [32], genetic algorithms were applied with specific operators and stochastic epidemic simulations to find good vaccine distributions to minimize the number of illnesses or deaths in the population, considering an influenza pandemic with age-specific illness attack, given limited quantities of vaccine. More recently, [26] proposed a mono-objective strategy using a Differential Evolution algorithm and a SEIR model with age-structure in order to find the optimal vaccine distribution that minimizes the total number of infected. The work [27] applied a standard multiobjective genetic algorithm to control dengue epidemic using insecticide and sterile males,

* Corresponding author.
E-mail address: taka@mat.ufmg.br (R.H.C. Takahashi).

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minimizing both social and economic costs via alternated step-size control.

The trade-off between the effectiveness of policies to control the epidemics and the cost of its implementation has been already recognized in some other works, which already employed multiobjective optimization approaches for the synthesis of vaccination policies. This work, developed within this framework, also presents the following specific methodological contributions:

(i) Every epidemics process will present two rather distinct dynamic regimes: a transient phase and a steady-state phase. Whilst the transient phase will require a time-varying control policy in order to perform an optimal control, the steady-state phase will be tackled better by a steady-state control, since its synthesis will become more precise under a smaller number of degrees of freedom. In this work, the control policy is built as a concatenation of a transient control sequence followed by a time-invariant sequence. This allows an enhanced efficiency of the control policy, as illustrated in Section 6. The usual methodology of promoting a single vaccination policy along all the duration of the epidemic process leads to policies that can be far from the optimality [24,23,12]. Compared to the previous works, the approach presented here adds new degrees of freedom to the problem by allowing different sizes of pulse control action in different instants and also allowing the application of pulses at arbitrary time instants in the two phases. Given a time horizon, a control policy solution is represented here by the number of vaccination campaigns, the time instants when each one should be performed as well as the number of individuals to be immunized in each campaign. The search space used in this work includes the intervals found in reference [20], which theoretically guarantee that the infected population tends to zero over time.

(ii) The synthesis of control policy is performed using a differential equation based epidemics model, which represents the average behavior of the epidemics on the population. The simulation of this model is computationally affordable, which makes this kind of model suitable for being used inside an optimization algorithm in which the model is run several times. Although this work considers Susceptible-Infected-Recovered endemic model (SIR) [15,2,12], it should be noticed that the general methodology proposed here can be employed using other differential equation models.

(iii) However, as the actual behavior of the epidemics on a finite-size population will be endowed with a stochastic variation, a simulation that takes such effects into account becomes necessary in order to perform a more realistic evaluation of the outcome of the application of the vaccination policy. An Individual-Based Model (IBM) [11] which corresponds in average to the differential equation model is employed here in order to evaluate the set of policies that emerge from the multiobjective optimization, in order to assess the sensitivity of each policy to the stochasticity. This model is also employed in order to estimate some stochastic performance measures of the vaccination policy, such as the probability of disease eradication. Such an analysis was not performed in any former work.

In addition to the new methodology, some computational improvements have been proposed too. The hybrid multiobjective strategy was improved with the inclusion of a hash table to avoid re-evaluating of repeated solutions and some modifications in genetic operators. Finally, an enhanced IBM version is applied to find a robust nondominated set of polices. The probabilities of disease control and extinction for each policy are computed now. The new framework to epidemics control proposed here can be seen as an evolution of some previous works by the authors. In [6], a canonical NSGA-II was used to solve a multiobjective problem whose solutions were transient-phase vaccination campaigns. The objectives represented the cost and the efficacy of the control. Also, a rudimentary IBM version was applied to simulate the random behavior of the final solutions, re-evaluating the optimal polices in order to consider just their median values in a classical nondominated sorting procedure. In [8], the performance of an NSGA-II algorithm with quadratic local search was compared with the performance of its canonical version in order to solve the epidemic control problem, still considering only the transient-phase vaccination campaigns.

This paper is organized as follows: Section 2 describes the epidemiological models; Section 3 presents the multiobjective optimization models developed in this work; Section 4 shows the proposed optimization engine; Section 5 presents the experiment planning; Section 6 shows the results of the case study; before finalize this paper, Section 7 indicates that the proposed optimization engine is superior than the canonical version in many disease configurations; and Section 8 concludes the paper.

2. Epidemiological models

The next two subsections explain the SIR model and its stochastic version IBM.

2.1. SIR model

The SIR model describes the dynamics of the susceptible, infected and recovered individuals in a population during the evolution of the disease, in an average way. It can be used to describe contagious viruses that can be transmitted among individuals, like measles and rubella. The virus infects susceptible individuals who become infectious, and after some time they recover and become immune. When a vaccine exists and is applied to a susceptible individual, this also becomes a “recovered” [12].

The SIR model uses the strategy of compartments, related by a system of three differential equations. The initial value problem is presented in Eq. (1). The variables S, I and R represent, respectively, the number of susceptible, infected and recovered individuals. The term N represents the number of individuals, which is supposed to be constant, $S(t)+I(t)+R(t)=N, \forall\, t \geq 0$. The constant parameters are the transmission rate β, the recovery rate of infected individuals γ, and the birth/mortality rate μ. The measurement units of these parameters are the inverse of time unit. The birth rate and the mortality rate are assumed to be equal, in order to keep the population size constant. The values $1/\gamma$ and $1/\mu$ represent the average time of infection and the average lifetime of an individual, respectively, in time units (t.u.), w.l.g.. This model is realistic and mathematically and epidemiologically well-conditioned [12].

$$\begin{aligned} \frac{dS}{dt} &= \mu N - \mu S - \frac{\beta IS}{N}, \quad S(0) \geq 0, \\ \frac{dI}{dt} &= \frac{\beta IS}{N} - \gamma I - \mu I, \qquad I(0) \geq 0, \\ \frac{dR}{dt} &= \gamma I - \mu R, \qquad\qquad R(0) \geq 0, \end{aligned} \tag{1}$$

By dividing Eq. (1) by N, considered constant, the system becomes expressed by the fraction of susceptible, s, and infected, i. This leads to Eq. (2). Therefore, the recovered fraction is computed as $r(t) = 1 - s(t) - i(t)$.

$$\begin{aligned} \frac{ds}{dt} &= \mu - \mu s - \beta is, \quad s(0) \geq 0, \\ \frac{di}{dt} &= \beta is - \gamma i - \mu i, \quad i(0) \geq 0, \end{aligned} \tag{2}$$