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Application of indirect methods to optimal control problems in epidemiology

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Abstract. Currently most of the numerical resolution of optimal control problems is done using direct methods where the increase accuracy of indirect methods is overshadowed by the necessary analytical derivation required beforehand. With recent developments from the *control-toolbox ecosystem* team the application of indirect methods as become more streamline enabling a wider range of problems to be solved, like, for example, optimal control problems applied to the transmission of infectious diseases. In this work, we aim to extend the application of indirect methods to optimal control problems applied to epidemiological models, using the *control-toolbox* [25].

Keywords: Optimal control, Indirect methods, Shooting methods, Epidemiological models, Compartmental models

1 Introduction

Optimal control is a mathematical theory that deals with finding a control for a dynamical system over a period of time such that an objective function is optimized. It has emerged as a field that has profound impact on many scientific domains including engineering, economics and biology, see, e.g., [21, 20, 18].

A general form of an Optimal Control Problem (OCP) can be stated as follows, see e.g. [23]:

$$\begin{aligned} &\text{Minimize} \quad \int_0^{t_f} f^0(t, x(t), u(t))dt + g(t_f, x(t_f)) \\ &\text{subject to:} \quad \dot{x}(t) = f(t, x(t), u(t))\,, \quad u(t) \in \Omega \quad t \in [0, t_f] \text{ a.e.}\,, \\ &\text{with} \quad x(0) \in M_0\,, \quad x(t_f) \in M_1\,, \end{aligned} \tag{OCP}$$

where M_0 and M_1 are two measurable subsets of $\mathbb{R}^n$. We consider the control system $\dot{x}(t) = f(t, x(t), u(t))$ in $\mathbb{R}^n$ where $f : \mathbb{R} \times \mathbb{R}^n \times \mathbb{R}^m \to \mathbb{R}^n$ is of class C^1, and the controls are measurable, essentially bounded functions of time, taking values in some measurable subset $\Omega \in \mathbb{R}^m$ (set of controls), that

is, $u \in L^\infty([0,t_f],\mathbb{R}^m)$. For the cost functional which we aim to minimize, we assume $f^0 : \mathbb{R}\times\mathbb{R}^n\times\mathbb{R}^m \to \mathbb{R}$ and $g : \mathbb{R}\times\mathbb{R}^n \to \mathbb{R}$ to be functions of class C^1.

We consider the (OCP) of determining a trajectory $x(\cdot)$, defined on $[0,t_f]$, corresponding to an admissible control u solution of the control system, such that $x(0) \in M_0$ and $x(t_f) \in M_1$ and minimizing the cost functional over all possible trajectories steering the control system from M_0 to M_1 in time t_f.

For results on the existence and uniqueness of the solution of the OCP, see e.g. [23] and references cited therein.

Real-world problems are typically too complex for analytical solutions, highlighting the importance of computational algorithms for solving optimal control problems [15]. In optimal control, there are two main types of numerical methods: direct methods and indirect methods.

Direct methods work by first discretizing the problem, then solving it. This is done by transcribing the optimal control problem into a nonlinear optimization problem. The discretization process involves breaking down the time horizon into small intervals and approximating the control and state trajectories. Once the problem is discretized, a non linear optimization solver like IPOPT [24] can be used to find the solution [4]. Direct methods offer several advantages, including ease of implementation, flexibility in handling constraints, and a broad domain of convergence [23, 4]. However, they also come with drawbacks. One significant disadvantage is their potential computational cost, particularly for large-scale problems [23, 4]. Additionally, direct methods tend to be less accurate compared to indirect methods, with solution accuracy dependent on the level of discretization. While finer discretization can lead to more accurate solutions, it also escalates computational costs. Despite these drawbacks, the simplicity, versatility, and reliability of direct methods often make them often a preferred choice [23, 4]. Direct methods have been studied in many works, see e.g. [2, 7], and references cited therein.

On the other hand, indirect methods are based on the application of Pontryagin's Maximum Principle (PMP) [19] (see e.g. [23] for a complete formulation of the PMP), by transforming the optimal control problem into a two-point boundary value problem (TBVP), and by solving numerically the TBVP by a shooting method. Indirect methods in optimal control offer certain advantages. Firstly, they tend to provide highly accurate solutions since they rely on the necessary optimality conditions (PMP). Secondly, they are often more efficient when dealing with small-scale problems. However, these methods also come with drawbacks. Their main disadvantage lies in their complexity, as they require the derivation of the necessary optimality conditions, which can be challenging. Moreover, they are sensitive to the initial guess of the solution, potentially converging to local optima. Additionally, indirect methods may encounter difficulty in effectively managing constraints [23, 5]. However, some of these challenges can be addressed within the indirect framework, as seen in e.g. [10, 11, 9, 12].

In this work, we solve numerically optimal control problems applied to epidemiological models. Our goal is to enlarge the range of examples of optimal control problems solved with shooting methods. For the application of the shooting

method we based on the works and tools developed by [6] and the *control-toolbox ecosystem* [25].

2 Optimal control problems applied to epidemiological models

Epidemiological models are mathematical models used in epidemiology and biomathematics to better understand the spread of diseases in populations. We focus on two deterministic compartmental models, namely on the general SEIR (Susceptible-Exposed-Infective-Recovered) model [1] and the SICA compartmental model for HIV/AIDS trasmission [22]. We consider two optimal control problems where the control systems are the SEIR and SICA models, respectively, where a control function was introduced representing transmission control measures for the eradication of the disease.

2.1 SEIR optimal control problem

In this example, we consider a SEIR compartmental model, studied in [1], that is a variation of the well known SIR model, firstly introduced by Kermack and McKendrick in 1927 [17]. In the SEIR model the total population is divided into four compartments: susceptible (S), those able to contract the disease; exposed (E), those who have been infected but are not yet infectious; infected (I), those capable of transmitting the disease; and recovered (R), those who have become immune. For the construction of the model, the following assumptions are considered: the total population is assumed to be constant and S, E, I, R are smooth functions of time t, such that $S(t) + E(t) + I(t) + R(t) = 1$ for all time; the birth and death rates μ are equal; an exposed individual's probability of becoming infectious, in a specified time interval, is independent of time after initial contact, and $1/\alpha$ is the mean latent period; the mean infectious period of an infected individual I is $1/\gamma$; recovered individuals are permanently immune. An exposure of a susceptible by an infected is an encounter in which the infection is transmitted. The contact rate, β, is the average number of susceptible in a given population contacted per infected per unit time. Thus, we consider the SEIR model governed by the following system of differential equations:

$$\begin{cases} \dot{S}(t) = \mu - \beta S(t)I(t) - \mu S(t), \\ \dot{E}(t) = \beta S(t)I(t) - (\mu + \alpha)E(t), \\ \dot{I}(t) = \alpha E(t) - (\mu + \gamma)I(t). \end{cases} \tag{1}$$

The value of R is determined by the normalizing condition, i.e., $S + E + I + R = 1$. To construct the control system, a control function u is introduced in the SEIR model (1), representing distancing and preventive transmission measures. The chosen objective function will be maximizing the uninfected population (susceptible individuals) while minimizing the infected individuals and the cost

associated to the distancing/preventive (control) measures. This results on the following optimal control problem:

$$\begin{cases} \int_0^{t_f} S(t) - I(t) - u(t)^2 dt \to \max, \\ \text{subject to} \\ \dot{S}(t) = \mu - (1-u(t))\beta S(t) I(t) - \mu S(t), \\ \dot{E}(t) = (1-u(t))\beta S(t) I(t) - (\mu+\alpha) E(t), \\ \dot{I}(t) = \alpha E(t) - (\mu+\gamma) I(t), \\ \text{and} \\ u(t) \in [0, u_{\max}],\ t \in [t_0, t_f] \ \text{ a.e.}, \\ S(t_0) = S_0,\ E(t_0) = E_0,\ I(t_0) = I_0. \end{cases} \tag{OCP-SEIR}$$

Consider the parameter values (with time unit in days), from [1], $\mu = 0.02/365$, $\alpha = 35.84/365$, $\gamma = 100/365$, $\beta = 1800/365$ and take $u_{\max} = 0.5$, $t_0 = 0$, $t_f = 20$ and initial conditions $S_0 = 0.6$, $E_0 = 0.2$, $I_0 = 0.1$.

Our goal is to apply the control-toolbox ecosystem [25] to problem (OCP-SEIR). The control-toolbox ecosystem [25] is a collection of packages for mathematical control and applications written in the Julia programming language [3]. Its root package is *OptimalControl.jl* and aims to be the sequel to previous developments, notably *Bocop* [26] and *Hampath* [6]. *OptimalControl.jl* aims to provide tools to solve optimal control problems by both direct and indirect methods. It allows users to model an optimal control problem with fixed boundary conditions and final times, subject to control and state constraints. The package is designed to be user-friendly and efficient, making it a valuable resource for those working in the field of optimal control.

The first step to solve any optimal control problem using *OptimalControl.jl* is defining the model, this can be easily done writing the (OCP-SEIR) according with the examples provided in https://control-toolbox.org/. The implementation of the direct method, after having defined the problem, may be done with only one line of code. For the direct solution of (OCP-SEIR), see Figure 2.

As for the implementation of the indirect shooting method, when using the control-toolbox, the first step is to import the solutions from the direct method, this is done to provide a sufficient accurate initial guess (as the indirect method is more sensible as stated previously) and in order to understand the structure of the optimal control. From the direct solution (see Figure 2), it is possible to conclude that the control has a singular arc for all time interval. With that we may define the structure of the flow defined by the singular control (see, for example, the Goddard example in [25] and the documentation for the definition of flows).

According to the Pontryagin Maximum Principle, the Hamiltonian is given by

$$H(x, p, u) = \langle p, f \rangle + p^0 f^0$$

where the components of f are given by the right-hand side of the control system, f^0 is the integrand function of the cost, and $p(\cdot) : [0, t_f] \to \mathbb{R}^3$ is an absolutely continuous mapping called *adjoint vector*, with $\left(p(\cdot), p^0\right) \neq (0, 0)$, such that

$$\dot{x}(t) = \frac{\partial H}{\partial p}\left(t, x(t), p(t), p^0, u(t)\right), \quad \dot{p}(t) = -\frac{\partial H}{\partial x}\left(t, x(t), p(t), p^0, u(t)\right)$$

almost everywhere on $[0, t_f]$. We assume that there are no abnormal extremals, that is, $p^0 = -1$. Considering the control derived from Pontryagin Maximum Principle's maximization condition

$$H(t, x(t), p(t), p^0, u(t)) = \max_{v \in [0, u_{\max}]} H(t, x(t), p(t), p^0, v) \quad \text{a. e. on} \quad [0, t_f]\,,$$

and plugging it in feedback form into the Hamiltonian, the problem is reduced to an extremal system of the form $\dot{z}(t) = F\left(t, z(t)\right)$, where $z(t) = (x(t), p(t))$, and the initial, final and transversality conditions $p(t_f) = 0$, can be written in the form $R(z(0), z(t_f)) = 0$. We thus end up with a boundary value problem of the form

$$\begin{cases} \dot{z}(t) = F\left(t, z(t)\right) \\ R\left(z(0), z(t_f)\right) = 0\,. \end{cases} \tag{2}$$

Let $z(t, z_0)$ denote the solution of the Cauchy problem $\dot{z}(t) = F(t, z(t))$, $z(0) = z_0$, and let $G(z_0) = R(z_0, z(t_f, z_0))$. The boundary value problem (2) is equivalent to finding a zero of the function G that is $G(z_0) = 0$, see e.g. [7, 6] for a more detailed explanation. For our epidemic optimal control problem (OCP-SEIR) we have

$$\begin{aligned} G : \mathbb{R}^3 &\to \mathbb{R}^3 \\ p = \begin{bmatrix} p_S(0) \\ p_E(0) \\ p_I(0) \end{bmatrix} &\mapsto G(p) = \begin{bmatrix} p_S(tf) - 0 \\ p_E(tf) - 0 \\ p_I(tf) - 0 \end{bmatrix}. \end{aligned}$$

The shooting function $G(p(0))$ essentially measures the violation of the transversality condition for a given initial guess p_0. When the shooting function returns a zero vector, it means that the transversality condition is satisfied, and the corresponding control is optimal according to Pontryagin's Maximum Principle. The solution found using the shooting method with the control-toolbox [25] is plotted in Figure 1.

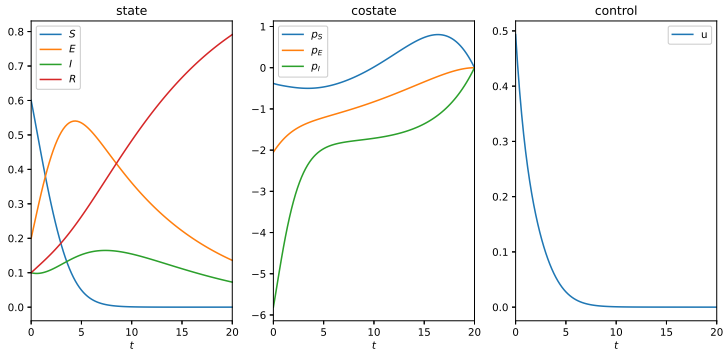


Fig. 1. Optimal states $x = (S, E, I, R)$, adjoint vector $p = (p_S, p_E, p_I)$ and control u for the problem (OCP-SEIR) using the shooting method with the control-toolbox [25].

In Figure 2, we compare both solutions derived from the direct and indirect method with the control-toolbox in *OptimalControl.jl* [25], and it is possible to see that they overlap.

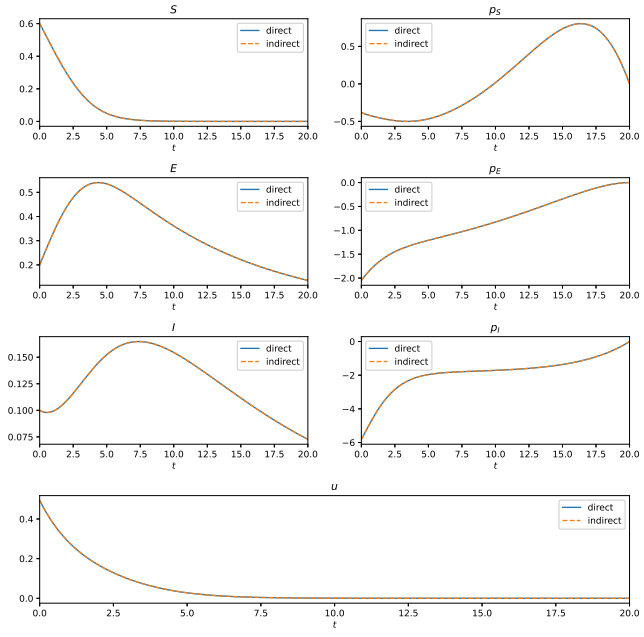


Fig. 2. Solution of problem (OCP-SEIR) using direct and indirect methods with the control-toolbox [25].

2.2 SICA optimal control problem

The SICA model is a mathematical model for HIV/AIDS transmission and it was first introduced in [22]. It is a compartmental epidemic model where the total population, denoted by N, is divided into four categories: $S(t)$, susceptible individuals; $I(t)$, HIV-infected individuals with no clinical symptoms of AIDS; $C(t)$, HIV-infected individuals under treatment for HIV infection; $A(t)$, HIV-infected individuals with AIDS clinical symptoms.

The equations governing the model are:

$$\begin{cases} \dot{S}(t) = \Lambda - \lambda(t)S(t) - \mu S(t), \\ \dot{I}(t) = \lambda(t)S(t) - (\rho + \phi + \mu)I(t) + \alpha A(t) + \omega C(t), \\ \dot{C}(t) = \phi I(t) - (\omega + \mu)C(t), \\ \dot{A}(t) = \rho I(t) - (\alpha + \mu + d)A(t), \end{cases}$$

where the parameters have the following meaning: Λ, recruitment rate of individuals (assumed susceptible) into the population; $\lambda(t)$, The rate at which susceptible individuals acquire HIV infection, following effective contact with people infected with HIV; μ, constant rate of natural death; ρ, rate at which HIV-infected individuals (with no AIDS symptoms) progress to the AIDS class A; ϕ, rate at which HIV-infected individuals (with no AIDS symptoms) progress to the class of individuals with HIV infection under treatment C; α, rate at which HIV-infected individuals with AIDS symptoms are treated for HIV; d, rate of induced death suffered by HIV-infected individuals with AIDS symptoms; ω, rate at which individuals in the class C leave to the class I; β, effective contact rate for HIV transmission; η_A, modification parameter indicating that individuals with AIDS symptoms are more infectious than HIV-infected individuals (pre-AIDS); η_C, modification parameter indicating the partial restoration of immune function of individuals with HIV infection that use Antiretroviral Therapy (ART) correctly.

Additionaly, $N(t) = S(t)+I(t)+A(t)+C(t)$ and $\lambda(t) = \frac{\beta}{N(t)}(I(t)+\eta_C C(t)+\eta_A A(t))$.

For the SICA optimal control problem formulation, we consider the normalized *sica* model (see [8] for more details), a linear objective function and we introduce a control u representing preventive measures for the HIV:

$$\begin{cases} \int_0^T (s(t) - i(t) - u(t))\ dt \to \max, \\ \\ \dot{s}(t) = b(1 - s(t)) - (1 - u(t))\beta(i(t) + \eta_C c(t) + \eta_A a(t))s(t) + da(t)s(t), \\ \dot{i}(t) = (1 - u(t))\beta(i(t) + \eta_C c(t) + \eta_A a(t))s(t) - (\rho + \phi + b)i(t) + \alpha a(t) + \omega c(t) + da(t)i(t), \\ \dot{c}(t) = \phi i(t) - (\omega + b)c(t) + da(t)c(t), \\ \dot{a}(t) = \rho i(t) - (\alpha + b + d)a(t) + da^2(t), \\ \\ u \in [0, u_{\max}],\ t \in [t_0, t_f] \text{ a.e.}, \\ s(t_0) = s_0,\ i(t_0) = i_0,\ c(t_0) = c_0,\ a(t_0) = a_0. \end{cases} \tag{OCP-SICA}$$

For the implementation of the numerical methods we consider the following parameter values, from [8]: $\mu = 1/69.54$, $b = 2.1\mu$, $\beta = 1.9$, $\omega = 0.09$, $\rho = 0.1$, $\phi = 1.0$, $\alpha = 0.33$, $d = 1.0$, $\eta_C = 0.015$, $\eta_A = 1.3$ and initial conditions $s_0 = 0.6$, $i_0 = 0.2$, $c_0 = 0.1$, $a_0 = 0.1$. In this case, the shooting function takes the following form:

$$G : \mathbb{R}^5 \to \mathbb{R}^5$$
$$p = \begin{bmatrix} p_S(0) \\ p_I(0) \\ p_C(0) \\ p_A(0) \\ t_1 \end{bmatrix} \mapsto G(p) = \begin{bmatrix} p_S(tf) - 0 \\ p_I(tf) - 0 \\ p_C(tf) - 0 \\ p_A(tf) - 0 \\ \Phi(x, p) \end{bmatrix},$$

where $\Phi(x, p) = \frac{dH}{du}(x, p) = 0$ denotes the switching function and t_1 is the switching time, at which the switching function vanishes and changes sign. Analogously to the previous example, the initial guess was provided from the direct solution computed using the integrated IPOPT solver [24] in the control-toolbox [25]. From the application of the direct method, we conclude that the solution is a bang-bang control and the switching function, Φ, is firstly positive and then negative, switching at time t_1 (see Figure 4 for the solutions using the direct method). With this information, two flows may be defined, one corresponding to the system with maximum control applied and the other corresponding to no control being applied.

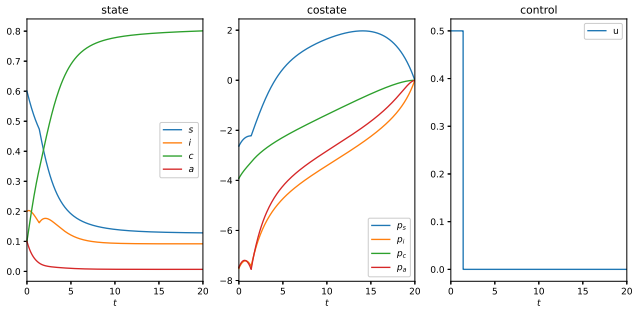


Fig. 3. SICA optimal control problem solutions using the indirect shooting method with the control-toolbox [25].

In Figure 4, we compare the solutions obtained when applying the direct and indirect shooting method, using the control-toolbox [25]. We conclude that they overlap.

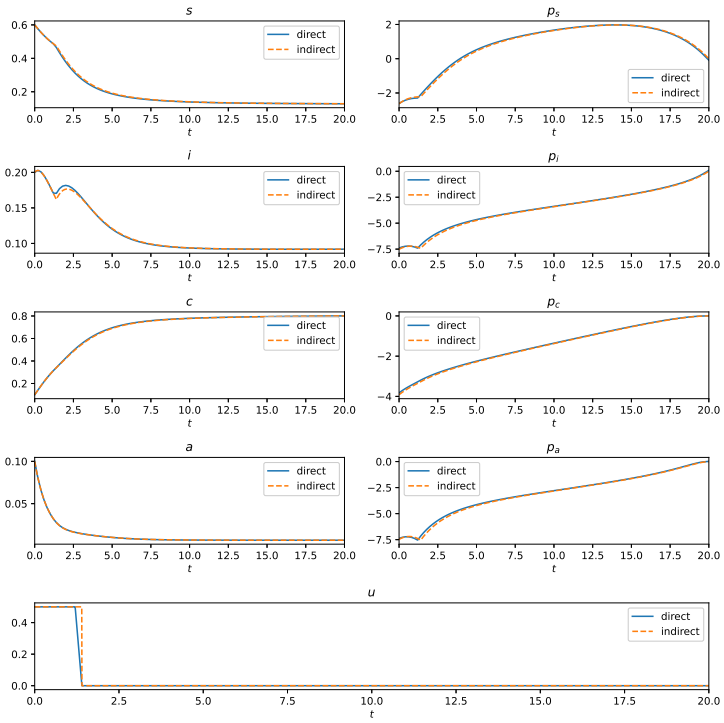


Fig. 4. SICA optimal control problem solutions applying direct and indirect methods with the control-toolbox [25].

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