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Some Optimal Control Applications in Biology and Biomedicine

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Abstract: We present two optimal control applications in biology and biomedicine. A critical issue in such control models is the appropriate choice of an objective functional. While many authors use L^2-type objectives with quadratic control, we argue that L^1-type objectives with linear control are more appropriate in a biological framework. Pontryagin's Maximum Principle then implies that optimal controls are concatenations of bang-bang and singular arcs. The first model treats an epidemiological SEIR model of disease transmission, while the second model considers the phase-tracking of circadian rhythms by model-based optimal control. We use discretisation and NLP methods to compute solutions that satisfy the necessary optimality conditions with high accuracy. In the case of a pure bang-bang control, we are able to verify second-order sufficient conditions which recently have been obtained in the literature.

Keywords: optimal control with control appearing linearly, bang-bang and singular controls, SEIR model in epidemiology, phase-tracking of circadian rhythms.

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The talk focuses on two applications of optimal control in biology and biomedicine. First, we present the optimal solution of a SEIR model in epidemiology under control and state constraints. While Biswas et al. [1] consider L^2-objectives for this problem, we argue that L^1-objectives, which are linear in control, are more appropriate in a biological framework. The control variable is the fraction of susceptibles individuals which are vaccinated. We also impose constraints on the total number of vaccines and th number of vaccines at each time t. A detailed numerical study of this control problem may be found in Maurer and de Pinho [4].

The second example is based on the fundamental work of Leloup and Goldbeter [2] who present a system of 10 ODEs for describing the dynamics of the circadian rhythm (inner clock) of drosophila. The model involves 38 parameters that can be fitted so as to provide a periodic solution with a period of 24 hours. This model has been used in Shaik, Sager, Slaby and Lebiez [6] to develop phase-tracking techniques for the targeted manipulation of circadian rhythms using model-based optimal control techniques. The control variable is the light stimulus entering one of the ODEs. We develop optimization methods to accurately determine the period of the periodic solution and present a more detailed study of optimal phase-tracking control strategies.

Both problems can be formulated as optimal control problem with control appearing linearly. Let $x \in \mathbb{R}^n$ denote the state vector, let $u \in \mathbb{R}^m$ be the control variable and let $t_f > 0$ be the terminal time which is fixed or free. Then the optimal control problem is to determine a measurable control function $u : [0, t_f] \to \mathbb{R}^m$ that *minimizes* the cost functional

$$J(x,u) = h(x(t_f)) + \int_0^{t_f} (f_o(x(t),u(t)) + g_0(x(t),u(t)))\,dt \tag{1}$$

subject to the differential constraint

$$\dot{x}(t) = f(x(t), u(t)) + g(x(t), u(t)), \quad x(0) = x_0,\ \psi(x(t_f)) = 0, \tag{2}$$

and control constraints

$$u_{min} \le u(t) \le u_{max} \quad \forall\ t \in [0, t_f]\,. \tag{3}$$

In practice it suffices to determine a piecewise continuous control function. Since the control variable u appears linearly in thy system dynamics and objective, the minimization of the Hamiltonian leads to bang-bang and singular controls; cf., e.g., [5]. For pure bang-bang controls, second-order sufficient conditions (SSC) have been derived in [5]. The numerical verification of SSC is based on solving the Induced Optimization Problem with respect to the switching times [3, 5]. These techniques are used to obtain a highly accurate solution to the SEIR control problem, resp., the phase-tracking problem of the circadian rhythm.

The methods can also be used to determine optimal control strategies for the tuberculosis model in Silva, Torres [7] when L^1-objectives are considered.

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