

## ON OPTIMAL CONTROL FOR A GENERAL SIR-MODEL WITH VACCINATION AND TREATMENT

URSZULA LEDZEWICZ

Dept. of Mathematics and Statistics,  
Southern Illinois University at Edwardsville,  
Edwardsville, Il, 62026-1653, USA

HEINZ SCHÄTTLER

Dept. of Electrical and Systems Engineering,  
Washington University,  
St. Louis, Mo, 63130-4899, USA

(Communicated by the associate editor name)

**ABSTRACT.** A general SIR-model with vaccination and treatment is considered as a multi-input optimal control problem over a fixed time horizon. Existence and local optimality of singular controls is investigated. It is shown that the optimal vaccination schedule can be singular, but that treatment schedules are not.

**1. Introduction.** In spite of the improvement in sanitation, developments of antibiotics and vaccines, infectious diseases still contribute significantly to deaths worldwide. While the earlier recognized diseases like cholera or the plague still sometimes create problems in underdeveloped countries erupting occasionally in epidemics, in the developed countries new diseases are emerging like AIDS (1981), hepatitis C or E (1989-1990). Additionally some of the diseases that we generally seem to have under control like tuberculosis, pneumonia, or gonorrhea developed antibiotic-resistant strains. Malaria or yellow fever continue to be a major problem in regions with climate changes. New threads constantly appear like the recent bird flue (SARS) epidemic in Asia or the very dangerous Ebola virus in Africa. Overall, infectious diseases continue to be one of the most important health problems worldwide.

Modeling of epidemiological phenomena has a very long history with the first model for smallpox formulated by Daniel Bernoulli in 1760. Starting from the beginning to the twentieth century, in response to epidemics of various infectious diseases, a large number of models has been constructed and analyzed starting a field known as epidemiology modeling; for example, see [7, 8]. Although many of these models are disease specific, like models for measles, smallpox, malaria, gonorrhea or HIV/AIDS (e.g., [9, 19]) there are also common characteristics of all models which allows to analyze a general framework without actually specifying what disease we have in mind [8].

---

2000 *Mathematics Subject Classification.* Primary: 49K15; Secondary: 92B05.

*Key words and phrases.* optima control, epidemiology, SIR-model, singular controls.

This work is supported by NSF collaborative research grants DMS 1008209 and 1008221.

With years mathematical models have become an important tool in describing the dynamics of the spread of an infectious disease and the effect of vaccination and treatments on its dynamics. As such, these models can be particularly useful in comparing the effect of various prevention, therapy and control programs. Since a variety of these programs are available, it is a natural objective to design optimal programs in terms of some pre-assumed criterion. This brings the application of the tools of optimal control to these problems. Optimal control has a long history of being applied to problems in biomedicine, particularly, to models for cancer chemotherapy. This research, that started in the seventies and eighties, e.g., [5, 16, 17], has continued uninterrupted to the present day [11, 14, 18] and has taken on new forms as mathematical models for novel therapies such as tumor anti-angiogenesis are formulated and analyzed, for example [12, 13]. But until recently little attention has been given to models in epidemiology. Gaff and Schaefer [6] consider several variations of standard epidemiologic models with an objective that takes into account vaccination and treatment. They compute optimal controls numerically and investigate the sensitivity of the optimal solutions to parameter values. Behncke also analyzes SIR epidemiological models numerically and finds controls that exert maximum effort on some initial interval [1]. In this paper, for a SIR-model with vaccination and treatment, we investigate the optimality of singular controls theoretically. These are controls that correspond to time-varying administration schedules and while we show that they cannot be optimal for treatment protocols, depending on the growth model taken they are an option for optimal vaccination schedules.

**2. Epidemiologic Models.** The standard models in epidemiology includes five compartments typically denoted by  $M$ ,  $S$ ,  $E$ ,  $I$  and  $R$  corresponding to five classes of individuals [6]. The most typical epidemiology model is of  $SIR$  type, that only includes three of these classes. The class  $S$  represents the susceptible individuals,  $I$  stands for the class of infected ones and  $R$  denotes the recovered class of those who went through infection and emerge with permanent or temporary infection-acquired immunity. This model can be extended by adding a class  $M$  which represents infants with passive immunity. This is not a highly relevant class because maternal antibodies disappear relatively quickly from the body and the infant enters the class  $S$ . Another class which could be taken into account is the class  $E$  (located between the classes  $S$  and  $I$ ) which stands for exposed individuals who are in the latent stage, i.e., have been infected, but are not yet infectious. Clearly, the classes  $M$  and  $E$  are of minor importance and since the effectiveness of our theoretical analysis depends on the dimension of the system, here we will consider an  $SIR$  type model. Also, depending on the type of disease, the immunity in the class  $R$  may not be permanent and the class  $R$  should be followed by the class  $S$  of individuals who regain their susceptibility when temporary immunity ends. Again, we will not take this into account in our model below and we shall assume that immunity is permanent.

Let  $S(t)$  represent the number of susceptibles at time  $t$ ,  $I(t)$  the number of infectives at  $t$  and  $R(t)$  the number of recovered individuals in time. We also denote the total number of individuals by  $N$ ,  $N = S + I + R$ , and assume that all new births (new growth) enter the susceptible class  $S$ . Different from classical formulations of  $SIR$ -models in the literature, however, we will not formulate the dynamics in terms of the variables  $S$ ,  $I$ , and  $R$ , but we prefer to replace  $R$  by the total number of individuals,  $N$ . We believe this somewhat simplifies the structure of the equations

and better brings out the theoretical connections between the equations. Therefore we consider the following dynamics similar to [6]:

$$\dot{N} = F(N) - \delta I, \quad (1)$$

$$\dot{S} = F(N) - \beta \frac{IS}{N} - Su \quad (2)$$

$$\dot{I} = \beta \frac{IS}{N} - (\gamma + \delta)I - Iv \quad (3)$$

The first equation describes the overall growth of the population with  $F : [0, K] \rightarrow \mathbb{R}$  denoting a general growth function. We only assume that

**(F):**  $F$  is a continuously differentiable function that satisfies  $F(0) = 0$  and is positive on the interval  $(0, K)$  with  $K \leq \infty$  denoting a fixed carrying capacity for the population.

All standard growth models have these properties; e.g., with  $\mu$  being the growth rate and  $K$  the carrying capacity, exponential growth given by  $F(N) = \mu N$  ( $K = \infty$  here), logistic or generalized logistic growth,  $F(N) = \mu N \left(1 - \left(\frac{N}{K}\right)^\alpha\right)$ ,  $\alpha > 0$ , or Gompertzian growth,  $F(N) = -\mu N \log\left(\frac{N}{K}\right)$ . The function  $F$  describes the normal growth of the population without any epidemic present and the term  $\delta I$  represents additional decrease through higher deaths of infectious individuals. It is assumed that the natural growth of the population corresponds to the susceptible individuals and therefore the term  $F(N)$  also enters the dynamics for  $S$ . The main term in this dynamics,  $\beta \frac{IS}{N}$ , represents the number of susceptible individuals from class  $S$  being infected by individuals from class  $I$  with the parameter  $\beta$  standing for the average number of adequate contacts (i.e., contacts sufficient for transmission) of a person per unit of time. In the  $I$ -dynamics,  $\gamma I$  and  $\delta I$  represent the individuals that recover without intervention respectively die from the infection with  $\gamma$  and  $\delta$  being the recovery and the death rate accordingly. The initial numbers of individuals in each of the populations are positive numbers denoted by

$$N(0) = N_0, \quad S(0) = S_0, \quad \text{and} \quad I(0) = I_0.$$

Note that if there are no infected individuals initially,  $I_0 = 0$ ,  $I$  remains identically zero. The model thus does not represent an onset of infection, but only its course.

There are two possible mechanisms available as controls: immunization of the susceptible individuals and treatment of the infected ones. We represent these actions by two controls  $u$  and  $v$  that for mathematical reasons are taken as Lebesgue-measurable functions. The control  $u$  represents the rate at which susceptible individuals are vaccinated and  $v$  measures the rate at which infectious individuals are treated at each time period. Both controls take values in compact intervals of the form  $0 \leq u \leq u_{\max}$  and  $0 \leq v \leq v_{\max}$  where  $u_{\max}$  and  $v_{\max}$ , respectively, denote the maximum vaccination and treatment rates. The action of both controls enriches the class  $R$  of the recovered individuals by removing them from the class of susceptible and infected, respectively. The class  $R$  is defined as  $R = N - I - S$ . For the model to be realistic, we need to make sure that all the variables including  $R$  remain positive.

**Proposition 1. (positive invariance)** *The region*

$$\mathcal{R} = \{(N, S, I) : 0 < N, 0 < S, 0 < I, S + I < N\},$$

is positive invariant; that is, for any admissible control the solutions exist for all times and remain in  $\mathcal{R}$ .

**Proof.** Suppose  $(N_0, S_0, I_0) \in \mathcal{R}$  and let  $u$  and  $v$  be any two Lebesgue-measurable functions with values in the control sets  $[0, u_{\max}]$  and  $[0, v_{\max}]$  respectively. Equation (3) has the equilibrium solution  $I = 0$  and thus as long as solutions exist  $I(t)$  will be positive. Let  $\tau$  be the supremum over all times  $a > 0$  so that solutions exist and  $N$  is positive on  $[0, a]$ . Then all the variables are positive on  $[0, \tau)$ . For, if  $S(t) = 0$ , then  $\dot{S}(t) = F(N(t)) > 0$  and thus  $S$  cannot turn negative in  $[0, \tau)$ . Furthermore,  $R = N - S - I$  and thus

$$\dot{R} = \dot{N} - \dot{S} - \dot{I} = \gamma I + Su + Iv > 0$$

so that  $R$  is increasing on  $[0, \tau)$ . Hence  $S(t) + I(t) < N(t)$  for all  $t \in [0, \tau)$ . Thus the system can leave  $\mathcal{R}$  forward in time only through  $N(\tau) = 0$ .

But this is not possible in finite time  $\tau < \infty$ : Let  $M = M(t)$  be the solution to the initial value problem

$$\dot{M} = F(M) - \delta M, \quad M(0) = N_0 > 0.$$

Then we have

$$\dot{M}(0) = F(N_0) - \delta N_0 < F(N_0) - \delta I_0 = \dot{N}(0)$$

and it follows from standard comparison results (see, e.g., [10]) that the solution  $M(t)$  will always lie below  $N(t)$ . Since  $F \in C^1$  and  $F(0) = 0$ , we can write  $F$  in the form  $F(M) = M\phi(M)$  with some continuous function  $\phi$ . In a given small neighborhood  $W$  of  $M = 0$  the right-hand side of the differential equation is therefore continuously differentiable and linearly bounded. Hence solutions are unique,  $\bar{M}(t) \equiv 0$  is an equilibrium solution and the solution  $M(t)$  can only approach  $\bar{M}(t) \equiv 0$  as  $t \rightarrow \infty$ . In particular, it is bounded away from 0 on any finite interval. Hence  $N(t) > M(t)$  will be positive for all finite times.  $\square$

**3. Formulation as an Optimal Control Problem.** Our goal is to solve the following problem: *given the initial population sizes of all three classes,  $S_0$ ,  $I_0$  and  $R_0$ , find the best strategy in terms of combined efforts of vaccination and treatment that would minimize the number of people who die from the infection while at the same time also minimizing the cost of vaccination and treatment of the population.* Naturally, there are various ways of expressing such a goal mathematically. In this paper, for a fixed terminal time  $T$ , we consider the following objective:

$$J(u, v) = \int_0^T aI(t) + bu(t) + cv(t)dt \quad (4)$$

The first term in the objective,  $aI(t)$ , represents the number of people who become infected and this also is a measure for the deaths associated with the outbreak which is taken proportional to the number of individuals infected in this model. The terms,  $bu(t)$  and  $cv(t)$  represent the cost of vaccination and treatment, respectively, and are assumed to be proportional to the vaccination and treatment rates. This is a simplified first approach and does not reflect, for example, that the cost of efforts needed of vaccinating the population will increase drastically the closer we get to the saturation value  $K$ . Real life data show that the cost of vaccinating the first 80% of the population is relatively small compared with the cost for the remaining 20% (see [6]). But our model will be realistic if such high rates of vaccination are not reached.

We shall apply methods of geometric optimal control theory to analyze the relations between optimal vaccination and treatment schedules. These techniques become more transparent if the problem is formulated as a Mayer-type optimal control problem; that is, one where we only minimize a penalty term at the terminal point. Such a structure can easily be achieved at the cost of one more dimension if the objective is adjoined as an extra variable. Defining

$$\dot{Z} = aI + bu + cv, \quad Z(0) = 0, \quad (5)$$

we therefore consider the following optimal control problem:

**[OC]:** For a fixed terminal time  $T$ , minimize the value  $Z(T)$  subject to the dynamics

$$\begin{aligned} \dot{Z} &= aI + bu + cv, & Z(0) &= 0, \\ \dot{N} &= F(N) - \delta I, & N(0) &= N_0, \\ \dot{S} &= F(N) - \beta \frac{IS}{N} - Su, & S(0) &= S_0, \\ \dot{I} &= \beta \frac{IS}{N} - (\gamma + \delta)I - Iv, & I(0) &= I_0, \end{aligned}$$

over all Lebesgue measurable functions  $u : [0, T] \rightarrow [0, u_{\max}]$  and  $v : [0, T] \rightarrow [0, v_{\max}]$ .

Introducing the state  $x = (Z, N, S, I)^T$ , the dynamics of the system is a multi-input control-linear system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v$$

with drift vector field  $f$  given by

$$f(x) = \begin{pmatrix} aI \\ F(N) - \delta I \\ F(N) - \beta \frac{IS}{N} \\ \beta \frac{IS}{N} - (\gamma + \delta)I \end{pmatrix} \quad (6)$$

and control vector fields  $g_1$  and  $g_2$  given by

$$g_1(x) = \begin{pmatrix} b \\ 0 \\ -S \\ 0 \end{pmatrix} \quad \text{and} \quad g_2(x) = \begin{pmatrix} c \\ 0 \\ 0 \\ -I \end{pmatrix}. \quad (7)$$

We call an admissible control pair  $(u, v)$  with corresponding solution  $x$  a *controlled trajectory* of the system.

**4. Necessary Conditions for Optimality.** First-order necessary conditions for optimality of a controlled trajectory are given by the *Pontryagin Maximum Principle* [4, 15]: For a row-vector  $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4) \in (\mathbb{R}^4)^*$ , we define the Hamiltonian  $H = H(\lambda, x, u, v)$  as

$$\begin{aligned} H &= \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle \\ &= \lambda_1 (aI + bu + cv) + \lambda_2 (F(N) - \delta I) + \lambda_3 \left( F(N) - \beta \frac{IS}{N} - Su \right) \\ &\quad + \lambda_4 \left( \beta \frac{IS}{N} - (\gamma + \delta)I - Iv \right). \end{aligned} \quad (8)$$

Then, if  $(u_*, v_*)$  is an optimal control defined over the interval  $[0, T]$  with corresponding trajectory  $x_* = (Z_*, N_*, S_*, I_*)^T$ , there exists an absolutely continuous co-vector,  $\lambda : [0, T] \rightarrow (\mathbb{R}^4)^*$ , such that the following conditions hold<sup>1</sup>:

(a)  $\lambda$  satisfies the adjoint equations

$$\dot{\lambda} = -\langle \lambda, Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_* \rangle \quad (9)$$

with transversality conditions

$$\lambda(T) = (1, 0, 0, 0), \quad (10)$$

(b) for almost every time  $t \in [0, T]$  the optimal controls  $(u_*(t), v_*(t))$  minimize the Hamiltonian along  $(\lambda(t), x_*(t))$  over the control set  $[0, u_{\max}] \times [0, v_{\max}]$  and

(c) the Hamiltonian is constant along the optimal solution.

We call a pair  $(x, (u, v))$  consisting of admissible controls  $(u, v)$  with corresponding trajectory  $x$  for which there exist multipliers  $\lambda$  such that the conditions of the Maximum Principle are satisfied an *extremal* (pair) and the triple  $(x, (u, v), \lambda)$  is an extremal lift (to the cotangent bundle).

Note that the dynamics does not depend on the auxiliary variable  $Z$  and thus by the adjoint equation (9) the multiplier  $\lambda_1$  is constant; by the transversality condition (10) it is thus given by  $\lambda_1(t) \equiv 1$ . In particular, the overall multiplier  $\lambda(t)$  is never zero. For almost any time  $t$  the optimal controls  $(u_*(t), v_*(t))$  minimize the Hamiltonian  $H(\lambda(t), x_*(t), u, v)$  over the compact interval  $[0, u_{\max}] \times [0, v_{\max}]$ . Since  $H$  is linear in the controls, this minimization problem splits into two separate one-dimensional problems that can easily be solved. Defining the so-called *switching functions*  $\Phi_1$  and  $\Phi_2$  as

$$\Phi_1(t) = \langle \lambda(t), g_1(x_*(t)) \rangle = b - \lambda_3(t)S_*(t) \quad (11)$$

and

$$\Phi_2(t) = \langle \lambda(t), g_2(x_*(t)) \rangle = c - \lambda_4(t)I_*(t), \quad (12)$$

it follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & \text{if } \Phi(t) > 0 \\ u_{\max} & \text{if } \Phi(t) < 0 \end{cases} \quad \text{and} \quad v_*(t) = \begin{cases} 0 & \text{if } \Phi(t) > 0 \\ v_{\max} & \text{if } \Phi(t) < 0 \end{cases}. \quad (13)$$

The minimum condition alone does not determine the control at times when  $\Phi_i(t) = 0$ . If  $\Phi_i(\tau) = 0$ , but  $\dot{\Phi}_i(\tau) \neq 0$ , then the control switches between the value 0 and its maximum value depending on the sign of  $\dot{\Phi}_i(\tau)$ . Controls with this property are called bang-bang controls and we refer to the constant controls with values in the endpoints of the control intervals as *bang* controls. The other extreme occurs when a switching function vanishes over an open interval. In this case also all derivatives of  $\Phi_i(t)$  must vanish and this typically allows to actually compute such a control. Controls of this kind are called *singular* [2]. While the name (which has historical reasons) might give the impression that these controls are less important, quite the contrary is true. Typically singular controls (if they exist) are either the best (minimizing) or the worst (maximizing) strategies and in either case they are essential in determining the structure of optimal controls. These typically then need to be synthesized from bang and singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories and in this paper we analyze their existence and local optimality for the problem [OC].

<sup>1</sup>Compared with a general formulation of the Maximum Principle in our case all extremals are normal and we already have incorporated this into our statement.

An essential tool in this analysis is the Lie bracket of vector fields which naturally arises in the formulas for the derivatives of the switching function. Given two differentiable vector fields  $f$  and  $g$  defined on a common open subset of  $\mathbb{R}^n$ , their *Lie bracket* can be defined as

$$[f, g](x) = Dg(x)f(x) - Df(x)g(x)$$

where  $Df$  and  $Dg$  denote the matrices of the partial derivatives of  $f$  and  $g$ , respectively. The Lie-bracket is anti-commutative, i.e.,  $[f, g] = -[g, f]$ , and for arbitrary vector fields  $f$ ,  $g$  and  $h$  satisfies the Jacobi identity [3]

$$[f, [g, h]] + [g, [h, f]] + [h, [f, g]] \equiv 0. \quad (14)$$

The following result provides an elegant and important framework for efficient computations of the derivatives of the switching functions. It is easily verified by a direct computation.

**Proposition 2.** *Let  $(x, (u, v))$  be a controlled trajectory of the system and let  $\lambda$  be a solution to the corresponding adjoint equations. Given a continuously differentiable vector field  $h$ , define*

$$\Psi(t) = \langle \lambda(t), h(x(t)) \rangle. \quad (15)$$

*Then the derivative of  $\Psi$  is given by*

$$\dot{\Psi}(t) = \langle \lambda(t), [f + g_1u + g_2v, h](x(t)) \rangle. \quad (16)$$

□

**5. The Structure of Singular Controls.** We investigate the existence and local optimality of singular controls for the system [OC]. By Proposition 2 the derivatives of the switching functions  $\Phi_1(t) = \langle \lambda(t), g_1(x(t)) \rangle$  and  $\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle$  are given by

$$\begin{aligned} \dot{\Phi}_1(t) &= \langle \lambda(t), [f + g_1u + g_2v, g_1](x(t)) \rangle, \\ \dot{\Phi}_2(t) &= \langle \lambda(t), [f + g_1u + g_2v, g_2](x(t)) \rangle. \end{aligned}$$

By anti-commutativity of the Lie bracket  $[g_i, g_i] \equiv 0$  and a simple computation verifies that the control vector fields  $g_1$  and  $g_2$  commute, i.e.,  $[g_1, g_2] \equiv 0$ . We thus have that

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f, g_1](x(t)) \rangle \quad \text{and} \quad \dot{\Phi}_2(t) = \langle \lambda(t), [f, g_2](x(t)) \rangle. \quad (17)$$

Elementary calculations verify that

$$[f, g_1](x) = \begin{pmatrix} 0 \\ 0 \\ -F(N) \\ \beta \frac{IS}{N} \end{pmatrix} \quad \text{and} \quad [f, g_2](x) = \begin{pmatrix} 0 \\ -\delta I \\ -\beta \frac{IS}{N} \\ 0 \end{pmatrix}. \quad (18)$$

**Proposition 3.** *The controls  $u$  and  $v$  cannot be singular simultaneously on an open interval  $I$ .*

**Proof.** In this case both switching functions  $\Phi_1$  and  $\Phi_2$  and their derivatives  $\dot{\Phi}_1$  and  $\dot{\Phi}_2$  must vanish on  $I$ . But the vector fields  $g_1$ ,  $g_2$ ,  $[f, g_1]$  and  $[f, g_2]$  are linearly independent and thus this implies that  $\lambda(t) \equiv 0$  on  $I$ . But  $\lambda_1(t) \equiv 1$ . Contradiction.

□

We first analyze the control  $u$ , i.e., vaccination schedules. Applying Proposition 2 once more to  $\dot{\Phi}_1$ , we get

$$\ddot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, [f, g_1]](x(t)) \rangle. \quad (19)$$

A direct calculation shows that  $g_2$  and  $[f, g_1]$  commute as well,

$$[g_2, [f, g_1]] \equiv 0, \quad (20)$$

and that

$$[g_1, [f, g_1]](x) = \begin{pmatrix} 0 \\ 0 \\ -F(N) \\ -\beta \frac{IS}{N} \end{pmatrix}. \quad (21)$$

The relation

$$\dot{\Phi}_1(t) \equiv -\lambda_3(t)F(N(t)) + \lambda_4(t)\beta \frac{I(t)S(t)}{N(t)} \equiv 0 \quad (22)$$

implies that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_3(t)F(N(t))$$

and  $\Phi_1(t) = b - \lambda_3(t)S(t) \equiv 0$  gives that  $\lambda_3(t)$  must be positive along a singular arc. Hence we have that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_3(t)F(N(t)) < 0.$$

Singular controls for which  $\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle$  does not vanish are said to be of order 1 and it is a second-order necessary condition for minimality, the so-called *Legendre-Clebsch condition*, that this quantity be negative [2]. Thus singular controls  $u$  are locally optimal. Furthermore, in this case (and taking into account that  $[g_2, [f, g_1]] \equiv 0$ ) we can compute the singular control as

$$u_{\sin}(t) = -\frac{\langle \lambda(t), [f, [f, g_1]](x(t)) \rangle}{\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle}. \quad (23)$$

Evaluating the vector fields, this equation can be simplified. A direct, but somewhat lengthy computation shows that for some smooth functions  $\varphi$  and  $\psi$  we can write

$$[f, [f, g_1]](x) = \delta\beta \frac{IS}{N} \begin{pmatrix} 0 \\ 1 \\ 0 \\ 0 \end{pmatrix} + \varphi(x)[f, g_1](x) + \psi(x)[g_1, [f, g_1]](x) \quad (24)$$

where

$$\begin{aligned} \psi(x) = & \frac{1}{2} \left[ F'(N) \left( 1 - \frac{\delta I}{F(N)} \right) + \beta \frac{I}{N} \left( 1 - \beta \frac{S^2}{NF(N)} \right) \right. \\ & \left. - F(N) \left( \frac{2}{S} - \frac{1}{N} \right) + I(\beta - \delta) \right] \end{aligned} \quad (25)$$

Since  $\langle \lambda(t), [f, g_1]](x(t)) \equiv 0$ , it follows that

$$u_{\sin}(t) = \frac{1}{2} \frac{\lambda_2(t)}{\lambda_3(t)} \frac{\delta\beta I(t)S(t)}{N(t)F(N(t))} - \psi(x(t)).$$

Once more using (22) the first term can be simplified to  $\frac{1}{2}\delta\frac{\lambda_2}{\lambda_4}$  and we obtain the following result:

**Proposition 4.** *A singular control  $u$  is of order 1 and satisfies the Legendre-Clebsch condition for minimality. The singular control is given as a function depending both on the state and the multiplier in the form*

$$u_{\text{sin}}(t) = \frac{1}{2} \delta \frac{\lambda_2(t)}{\lambda_4(t)} - \psi(x)$$

with  $\psi$  given by (25).  $\square$

**Proposition 5.** *The control  $v$  cannot be singular.*

**Proof.** Suppose  $v$  is singular on an open interval  $I$ . Then it follows from Proposition 3 that the control  $u$  cannot be singular on any subinterval of  $I$  and thus  $u$  must be bang-bang. Consider a subinterval where  $u$  is constant given by  $u = 0$  or  $u = u_{\text{max}}$  and without loss of generality let it be  $I$ .

The second derivative of the switching function  $\Phi_2$  is given by

$$\ddot{\Phi}_2(t) = \langle \lambda(t), [f + g_1 u + g_2 v, [f, g_2]](x(t)) \rangle.$$

It follows from the Jacobi identity that  $[g_1, [f, g_2]] = [g_2, [f, g_1]]$  and thus by (20) also the vector fields  $g_1$  and  $[f, g_2]$  commute. Another direct calculation shows that

$$[g_2, [f, g_2]](x) = \begin{pmatrix} 0 \\ \delta I \\ \beta \frac{IS}{N} \\ 0 \end{pmatrix} = -[f, g_2](x). \quad (26)$$

Since  $v$  is singular on  $I$ , we have  $\langle \lambda(t), [f, g_2](x(t)) \rangle \equiv 0$  and thus also

$$\langle \lambda(t), [g_2, [f, g_2]](x(t)) \rangle \equiv 0.$$

Hence we have that

$$\ddot{\Phi}_2(t) = \langle \lambda(t), [f, [f, g_2]](x(t)) \rangle \equiv 0. \quad (27)$$

A singular control  $v$  is therefore of order higher than 1. However, its order is not intrinsic [2] and therefore additional non-trivial relation will be imposed by differentiating (27) further. These conditions typically prevent the existence of singular arcs. This also holds here. Differentiating once more, we obtain

$$\Phi_2^{(3)}(t) = \langle \lambda(t), [f + g_1 u + g_2 v, [f, [f, g_2]]](x(t)) \rangle \equiv 0. \quad (28)$$

Using the Jacobi identity once more, we get

$$[g_2, [f, [f, g_2]]](x) = [f, [g_2, [f, g_2]]](x).$$

The relation (26) thus implies that

$$[g_2, [f, [f, g_2]]](x) = -[f, [f, g_2]](x)$$

and hence

$$\langle \lambda(t), [g_2, [f, [f, g_2]]](x(t)) \rangle = -\langle \lambda(t), [f, [f, g_2]](x(t)) \rangle \equiv 0.$$

Thus we have that

$$\Phi_2^{(3)}(t) = \langle \lambda(t), [f + g_1 u, [f, [f, g_2]]](x(t)) \rangle \equiv 0. \quad (29)$$

Hence along a singular control  $v$  the multiplier  $\lambda(t)$  must vanish against the vector fields  $g_2$ ,  $[f, g_2]$ ,  $[f, [f, g_2]]$  and  $[f + g_1 u, [f, [f, g_2]]]$  where  $u$  is either 0 or  $u_{\text{max}}$ . But in each case these four vector fields are linearly independent and thus  $\lambda(t)$  cannot vanish against all of them.  $\square$

**6. Conclusion.** In this paper we initiated the analysis of an optimal control problem for an *SIR*-model with with vaccination and treatment. We analyzed the structure of singular controls, but it still remains to complete this analysis by determining the structure of possible concatenations with bang-bang controls in order to determine an optimal synthesis of controlled trajectories. Based on our computations so far it is expected that the optimal treatment schedule will be bang-bang, most likely with just one switch from  $u_{max}$  to  $u = 0$  while we expect a singular regimen for the optimal vaccination strategy.

**Acknowledgement.** This material is based upon research supported by the National Science Foundation under collaborative research grants DMS 1008209 and 1008221. U. Ledzewicz's research also was partially supported by an SIUE "STEP" grant in Summer 2010.

#### REFERENCES

- [1] H. Behncke, *Optimal control of deterministic epidemics*, Optimal Control Applications and Methods, **21**, (2000), 269–285.
- [2] B. Bonnard and M. Chyba, "Singular Trajectories and their Role in Control Theory", Springer Verlag, Paris, 2003.
- [3] W.M. Boothby, "An Introduction to Differentiable Manifolds and Riemannian Geometry", Academic Press, 1975.
- [4] A. Bressan and B. Piccoli, "Introduction to the Mathematical Theory of Control", American Institute of Mathematical Sciences, 2007.
- [5] M. Eisen, "Mathematical Models in Cell Biology and Cancer Chemotherapy," Lecture Notes in Biomathematics, Vol. **30**, Springer Verlag, 1979.
- [6] H. Gaff and E. Schaefer, *Optimal control applied to vaccination and treatment strategies for various epidemiologic models*, Mathematical Biosciences and Engineering (MBE), **6**, (2009), 469–492.
- [7] H. Hethcote, *The Mathematics of Infectious Diseases*, SIAM Review, **42**, (2000), 599–653.
- [8] H. Hethcote, A thousand and one epidemic models, in "Frontiers in Theoretical Biology, (Ed. S.A. Levin), Springer-Verlag, (1994), 504–515.
- [9] E. Kaplan, D. Craft, L. Wein, *Emergency response to the smallpox attack: The case of mass vaccination*, Proceedings of the National Academy of Sciences of the United States of America, **99**, (2002), 10935–10940.
- [10] H.K. Khalil, "Nonlinear Systems", 3rd. ed., Prentice Hall, 2002.
- [11] U. Ledzewicz and H. Schättler, *Optimal bang-bang controls for a 2-compartment model in cancer chemotherapy* J. of Optimization Theory and Applications, **114**, (2002), 609–637.
- [12] U. Ledzewicz and H. Schättler, *Anti-Angiogenic therapy in cancer treatment as an optimal control problem* SIAM J. Control and Optimization, **46**, (2007), 1052–1079.
- [13] U. Ledzewicz and H. Schättler, *Optimal and suboptimal protocols for a class of mathematical models of tumor anti-angiogenesis*, J. of Theoretical Biology, **252**, (2008), 295–312.
- [14] R. Martin and K.L. Teo, "Optimal control of drug administration in cancer chemotherapy", World Scientific, Singapore, 1994.
- [15] L.S. Pontryagin, V.G. Boltyanskii, R.V. Gamkrelidze and E.F. Mishchenko, "The Mathematical Theory of Optimal Processes," MacMillan, New York, 1964.
- [16] G. W. Swan, *Role of optimal control in cancer chemotherapy*, Mathematical Biosciences, **101** (1990), 237–284.
- [17] A. Swierniak, *Optimal treatment protocols in leukemia - modelling the proliferation cycle*, Proceedings of the 12th IMACS World Congress, Paris, **4**, (1988), 170–172.
- [18] A. Swierniak, *Cell cycle as an object of control* J. of Biological Systems, **3**, (1995), 41–54.
- [19] W. Wang and S. Ruan, *Simulating the SARS outbreak in Beijing with limited data*, Journal of Theoretical Biology, **227**, (2004), 369–379.

Received xxxx 20xx; revised xxxx 20xx.

*E-mail address:* uledzew@siue.edu

*E-mail address:* hms@wustl.edu