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OPTIMAL CONTROL FOR A SIR EPIDEMIC MODEL WITH NONLINEAR INCIDENCE RATE

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ABSTRACT. The goal of this paper is to explore the impact of non-linearity of functional responses on the optimal control of infectious diseases. In order to address this issue, we consider a problem of minimization of the level of infection at the terminal time for a controlled SIR model, where the incidence rate is given by a non-linear unspecified function $f(S, I)$. In this model, we consider four distinctive control policies, namely the vaccination of the newborn and the susceptible individuals, isolation of the infected individuals and an indirect policy aimed at reduction of the transmission. The Pontryagin maximum principle is used for the problem analysis. We prove that in this problem the optimal controls are bang-bang functions, estimate the maximal possible number of switchings of the controls, and then construct possible types of the optimal controls.

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1. INTRODUCTION

Problems of control, such as pest control, antiviral and antibacterial therapy and cancer therapy, are frequently arise in biosciences and in biomedical practice, and the problem of infectious disease control is probably the most practically relevant and important of these. Historically, the problem of infectious disease control is the oldest of the problems of biological control: the Old Testament (Leviticus, Chapter 13) refers to measures of infectious disease control such as quarantine as to usual established practice. Considering the importance and practical relevance of this problem, as well as other control problems originated in biosciences, it is rather surprising that systematic applications of the optimal control theory to the infectious disease control (as well as to others problems of biological control) started comparatively recently. Nevertheless, for the less than three decades significant progress was made, results were obtained and important

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insights into the problem were gained (see [1, 2, 3, 4, 7, 17, 18, 26, 28, 31, 29, 32, 34, 35] and bibliography therein). However, the majority of these results were obtained numerically, which implies that these results were gained for a specific model and specific values of model's parameters. This leads to a natural question about the reliability and robustness of these results; that is, the question arises about the extends to which these results and conclusions can be be valid, at least qualitatively, for other models and other parameterizations. Besides, due to intrinsic complexity of biological systems (compared, for instance, with technical systems which for long were the major subject of optimal control theory) in biological applications many functional responses are not know in sufficient details and hardly will be known in the feasible future, and even the values of parameters often cannot be measured directly or found with acceptable certainty. This makes answering the question about the robustness and the reliability of the results principally important.

The problem of the insufficient certainty of biological data was recognized fairly early. A.N. Kolmogorov [19] was probably the first who suggested (in 1930th) a possible treatment for this. Since the precise form and the parametrization of the functional responses is not know, Kolmogorov suggested to consider a non-specified functional responses and to “reverse” the problem. That is, instead of studying properties of a specific model with specifically defined functional responses, he suggested to identify the properties which a functional responses should have in order to produce a model exhibiting a certain dynamics. In the content of epidemiological modelling, this concept combined with the direct Lyapunov method was utilized in [20, 21, 22, 23, 24, 25] and later developed by many other. However, since in the framework of this conceptual approach the applicability of numerical simulations is limited and the analysis is the major (and often the only possible) tool, the application of this concept to an optimal control problem is a challenging task.

In this paper, in order to address the issue of the robustness and the reliability and to explore the impact of a general form of non-linearity of a functional response on the optimal control, we consider a reasonably simple SIR model, where the incidence rate is given by a non-specified nonlinear function. We use a very few constraints for this function; in fact, the set of constraints that we impose on the incidence rate is considerably less restrictive than these which are typically used with this kind of models. Apart from the incidence rate, this model and the objective functional are essentially the same as these that was considered in [13]; the similarity of these models and optimal control problems allows us to use results in [13] as a reference case.

The very general form of incidence rate that we consider in this paper makes numerical methods nearly useless. Therefore, to address this problem in this paper we apply the technique developed earlier for control of a biochemical reaction [8, 9, 10, 15] and thereafter extended to antiviral therapy [12, 14] and

to infectious disease control [13, 11]. The idea of this technique comprises the following stages:

- (1) prove that the optimal control is a bang-bang control;
- (2) find the possible number of switchings, or at least good estimations from above for this, and
- (3) find the possible type of controls which can occur with this number of switchings for this model.

When a parametrization is given, the number of switchings known or estimated with a reasonable accuracy allows to reformulate an optimal control problem in the form of a considerably simpler problem of the finite-dimensional optimization. The latter can be completely solve numerically using any of a number of standard solvers.

An obvious limitation of this technique is that it is applicable only to bang-bang controls. However, the authors have a strong reason to believe that this kind of control is fairly common for control problems originated in biosciences.

2. MODEL AND PROBLEM FORMULATION

We consider following SIR epidemic model with a nonlinear incidence rate:

$$\begin{aligned}
 \dot{S}(t) &= \mu - f(S(t), I(t)) - \mu S(t), \\
 \dot{I}(t) &= f(S(t), I(t)) - (\sigma + \mu)I(t), \\
 \dot{R}(t) &= \sigma I(t) - \mu R(t).
 \end{aligned}
 \tag{2.1}$$

In this model, $S(t)$, $I(t)$ and $R(t)$ are, respectively, the fractions of susceptible, infectious and removed (recovered and immune) individuals. We assume that the population size is constant, and

$$S(t) + I(t) + R(t) = 1
 \tag{2.2}$$

holds. The constant population size assumption is typical in mathematical epidemiology and is based on the hypothesis that the time scale of the epidemic processes is considerably faster than that of demographic ones. This assumption and (2.2) enable us to omit the third equation and reduce the system to two equations for $S(t)$ and $I(t)$.

This model assumes that births and natural (that is, not associated with the infection in question) death occur at a per capita rate μ . (The equality of the birth and death rates is only assumed for convenience and is not of principle importance for further analysis.) All the newborn are susceptible and hence enter the susceptible compartment S . The susceptible individuals can be infected with the infectious with rate $f(S, I)$. After the incidence of infection, the individuals immediately enter infectious compartment I . The infectious can infect the susceptibles and are removed (recover or die of the infection) at per capita rate σ . (That is, an average duration of the infectious period is σ^{-1} .)

In this paper, we assume that incidence rate $f(S, I)$ satisfies the following assumptions:

(A1) $f(S, I)$ is a continuous differentiable function;

(A2) $f(S, I) > 0$ for all $S, I > 0$, and $f(0, I) = f(S, 0) = 0$ for all $S, I \geq 0$;

(A3) derivatives $f'_S = \frac{\partial f(S, I)}{\partial S}$ and $f'_I = \frac{\partial f(S, I)}{\partial I}$ are positive for all $S, I > 0$;

(A4) there are constants $M_S = \max_{(S, I) \in \bar{\Omega}} f'_S$ and $M_I = \max_{(S, I) \in \bar{\Omega}} f'_I$, where $\bar{\Omega}$ is a closure of the set $\Omega = \{(S, I) : S > 0, I > 0, S + I < 1\}$.

Properties of this model are well studied [20, 21, 24]. Thus, it is known that the monotonicity of incidence rate $f(S, I)$ ensures the uniqueness of a positive equilibrium state in the model, and that the concavity of the function with respect to I , together with the monotonicity, is sufficient to ensure the global asymptotic stability of the model.

Model (2.1) admits up to four controls, namely: vaccinations of the new borns, with per capita rate $\tilde{u}(t)$; vaccination of the susceptibles, with per capita rate $\tilde{w}(t)$; removal (isolation or treatment) of the infectious individuals, with the per capita rate $\tilde{z}(t)$; indirect measures, such as education, or an imperfect quarantine, aimed at a reduction of the disease transmission, $\tilde{v}(t)$. The action of control $\tilde{v}(t)$ results in a reduction of transmission, $f(S, I)(1 + \tilde{v}(t))^{-1}$.

We assume that the controls are bounded; that is, relationships $\tilde{u}(t) \in [0, \tilde{u}_{\max}]$, $\tilde{v}(t) \in [0, \tilde{v}_{\max}]$, $\tilde{w}(t) \in [0, \tilde{w}_{\max}]$, $\tilde{y}(t) \in [0, \tilde{y}_{\max}]$ and $\tilde{z}(t) \in [0, \tilde{z}_{\max}]$ hold. Here, the lower bounds are the absence of a control, that is zero, whereas the upper bounds, which corresponds to the maximal intensity of a corresponding control, are predetermined by considerations such as the health system capability. Furthermore, for the vaccination of newborns, $\tilde{u}_{\max} \leq 1$ holds. Introducing these controls into model (2.1), we obtain a control model

$$(2.3) \quad \begin{aligned} \dot{S}(t) &= \mu(1 - \tilde{u}(t)) - \frac{f(S(t), I(t))}{1 + \tilde{v}(t)} - (\mu + \tilde{w}(t))S(t), \\ \dot{I}(t) &= \frac{f(S(t), I(t))}{1 + \tilde{v}(t)} - (\sigma + \mu + \tilde{z}(t))I(t), \\ \dot{R}(t) &= \mu\tilde{u}(t) + \tilde{w}(t)S(t) + (\sigma + \tilde{z}(t))I(t) - \mu R(t), \end{aligned}$$

which is defined on the interval $[0, T]$.

Let us denote

$$(2.4) \quad \begin{aligned} u(t) &= \mu(1 - \tilde{u}(t)), \quad v(t) = (1 + \tilde{v}(t))^{-1}, \\ w(t) &= \mu + \tilde{w}(t), \quad z(t) = \sigma + \mu + \tilde{z}(t). \end{aligned}$$

Omitting the third equation in (2.3), we obtain control system

$$(2.5) \quad \begin{aligned} \dot{S}(t) &= u(t) - v(t)f(S(t), I(t)) - w(t)S(t), \\ \dot{I}(t) &= v(t)f(S(t), I(t)) - z(t)I(t). \end{aligned}$$

Here the controls are subjects of constraints:

$$(2.6) \quad \begin{aligned} u(t) &\in [u_{\min}, \mu], & v(t) &\in [v_{\min}, 1], \\ w(t) &\in [w_{\min}, w_{\max}], & z(t) &\in [z_{\min}, z_{\max}], \end{aligned}$$

where

$$(2.7) \quad \begin{aligned} u_{\min} &= \mu(1 - \tilde{u}_{\max}), & v_{\min} &= (1 + \tilde{v}_{\max})^{-1}, & w_{\min} &= \mu, \\ w_{\max} &= \mu + \tilde{w}_{\max}, & z_{\min} &= \sigma + \mu, & z_{\max} &= \sigma + \mu + \tilde{z}_{\max}. \end{aligned}$$

Control system (2.5) is defined on time interval $[0, T]$ and should be complemented by initial conditions:

$$S(0) = S_0, \quad I(0) = I_0, \quad S_0, I_0 > 0, \quad S_0 + I_0 < 1.$$

Let set $D(T)$ be the set of admissible controls; that is, $D(T)$ is the set of all possible Lebesgue measurable functions $(u(t), v(t), w(t), z(t))$, which for almost all $t \in [0, T]$ satisfy (2.6). The following Lemma ensures the boundedness, positiveness and continuity of solutions for system (2.5):

Lemma 1. *Let $(S_0, I_0) \in \Omega$ be held. Then for any admissible controls $(u(t), v(t), w(t), z(t))$ the corresponding solutions $(S(t), I(t))$ to system (2.5) are defined on the entire interval $[0, T]$, and $(S(t), I(t)) \in \Omega$ holds for all $t \in [0, T]$. (That is, set Ω is a positively invariant set of system (2.5).)*

The proof is fairly straightforward, and we omit it.

For control system (2.5) and for the set of admissible controls $D(T)$, we consider the problem of minimizing the level of infection at the end of time interval $[0, T]$. That is, we consider this system together with the objective functional

$$(2.8) \quad J(u, v, w, z) = I(T).$$

Lemma 1 and Theorem 4 in [27] (Chapter 4) ensure the existence of optimal controls $(u_*(t), v_*(t), w_*(t), z_*(t))$ and corresponding optimal solutions $(S_*(t), I_*(t))$ for this problem.

3. PONTRYAGIN MAXIMUM PRINCIPLE

To analyze optimal control problem (2.5, 2.8), we apply the Pontryagin maximum principle [30]. Let us define Hamiltonian

$$H(S, I, u, v, w, z, \psi_1, \psi_2) = (u - vf(S, I) - wS)\psi_1 + (vf(S, I) - zI)\psi_2,$$

where ψ_1 and ψ_2 are adjoint variables.

By the Pontryagin maximum principle, for the optimal controls

$$(u_*(t), v_*(t), w_*(t), z_*(t))$$

and the corresponding optimal solutions $(S_*(t), I_*(t))$, there exists on interval $[0, T]$ a non-trivial solution $\psi_*(t) = (\psi_1^*(t), \psi_2^*(t))$ of adjoint system

$$(3.1) \quad \begin{aligned} \dot{\psi}_1^*(t) &= w_*(t)\psi_1^*(t) - v_*(t)f'_S(S_*(t), I_*(t))(\psi_2^*(t) - \psi_1^*(t)), \\ \dot{\psi}_2^*(t) &= z_*(t)\psi_2^*(t) - v_*(t)f'_I(S_*(t), I_*(t))(\psi_2^*(t) - \psi_1^*(t)), \\ \psi_1^*(T) &= 0, \quad \psi_2^*(T) = -1, \end{aligned}$$

such that optimal controls $(u_*(t), v_*(t), w_*(t), z_*(t))$ maximize Hamiltonian $H(S_*(t), I_*(t), u, v, w, z, \psi_1^*(t), \psi_2^*(t))$ with respect to variables $u \in [u_{\min}, \mu]$, $v \in [v_{\min}, 1]$, $w \in [w_{\min}, w_{\max}]$, and $z \in [z_{\min}, z_{\max}]$ for almost all $t \in [0, T]$, and hence satisfy conditions

$$(3.2) \quad u_*(t) = \begin{cases} \mu & , \text{ if } L_u(t) > 0, \\ \forall u \in [u_{\min}, \mu] & , \text{ if } L_u(t) = 0, \\ u_{\min} & , \text{ if } L_u(t) < 0; \end{cases}$$

$$(3.3) \quad v_*(t) = \begin{cases} 1 & , \text{ if } L_v(t) > 0, \\ \forall v \in [v_{\min}, 1] & , \text{ if } L_v(t) = 0, \\ v_{\min} & , \text{ if } L_v(t) < 0; \end{cases}$$

$$(3.4) \quad w_*(t) = \begin{cases} w_{\max} & , \text{ if } L_w(t) > 0, \\ \forall w \in [w_{\min}, w_{\max}] & , \text{ if } L_w(t) = 0, \\ w_{\min} & , \text{ if } L_w(t) < 0; \end{cases}$$

$$(3.5) \quad z_*(t) = \begin{cases} z_{\max} & , \text{ if } L_z(t) > 0, \\ \forall z \in [z_{\min}, z_{\max}] & , \text{ if } L_z(t) = 0, \\ z_{\min} & , \text{ if } L_z(t) < 0. \end{cases}$$

Here, by (A2) and Lemma 1, the switching functions

$$(3.6) \quad \begin{aligned} L_u(t) &= \psi_1^*(t), \quad L_v(t) = \psi_2^*(t) - \psi_1^*(t), \\ L_w(t) &= -\psi_1^*(t), \quad L_z(t) = -\psi_2^*(t) \end{aligned}$$

entirely determine the corresponding optimal controls $(u_*(t), v_*(t), w_*(t), z_*(t))$.

Please note that in (3.6)

$$(3.7) \quad L_u(t) = -L_w(t)$$

holds, and hence it suffices to establish properties of one of these two functions. Furthermore, from (3.6) follows that

$$(3.8) \quad L_v(t) = L_w(t) - L_z(t).$$

Differential equations for functions $L_v(t)$, $L_w(t)$ and $L_z(t)$ immediately follow from system (3.1) and (3.6):

$$\begin{aligned}
 \dot{L}_w(t) &= w_*(t)L_w(t) + v_*(t)f'_S(S_*(t), I_*(t))L_v(t), \\
 (3.9) \quad \dot{L}_z(t) &= z_*(t)L_z(t) + v_*(t)f'_I(S_*(t), I_*(t))L_v(t), \\
 \dot{L}_v(t) &= [v_*(t)(f'_S(S_*(t), I_*(t)) - f'_I(S_*(t), I_*(t))) + z_*(t)]L_v(t) \\
 &\quad - (z_*(t) - w_*(t))L_w(t), \\
 L_w(T) &= 0, \quad L_z(T) = 1, \quad L_v(T) = -1.
 \end{aligned}$$

(Function $L_u(t)$ is to be found from equality (3.7).)

The following Lemma is of principal importance for problem (2.5,2.8):

Lemma 2. *Adjoint functions $\psi_1^*(t)$ and $\psi_2^*(t)$ are not equal identically to zero on any finite subinterval of interval $[0, T]$.*

Proof. Let consider function $\psi_1^*(t)$ and assume, by contradiction, that there is a subinterval $\Delta_1 \subset [0, T]$ such that $\psi_1^*(t) = 0$ for all $t \in \Delta_1$. Then $\dot{\psi}_1^*(t) = 0$ must hold almost everywhere on Δ_1 as well. Substituting these two equalities into the first equation of system (3.1), we obtain, by (A2), that $\psi_2^*(t) = 0$ necessary holds for all $t \in \Delta_1$ as well. However, system (3.1) is a system of linear non-autonomous homogeneous differential equations, and hence $\psi_*(t) = (\psi_1^*(t), \psi_2^*(t)) = 0$ on $\Delta_1 \subset [0, T]$ implies that $\psi_*(t) = 0$ for all $t \in [0, T]$. This contradicts to the existence of the non-trivial solution $\psi_*(t)$, and hence the hypothesis is incorrect.

The same arguments, applied to function $\psi_2^*(t)$ and the second equation of system (3.1), yield that if $\psi_2^*(t) = 0$ holds on a finite subinterval $\Delta_2 \subset [0, T]$, then $\psi_*(t) = (\psi_1^*(t), \psi_2^*(t)) = 0$ necessary holds for all $t \in [0, T]$. This contradict to the existence of a non-trivial solution. This completes the proof. \square

Lemma 2 combined with relationships (3.4–3.6) immediately leads to the following Corollary:

Corollary 3. *Optimal controls $w_*(t)$ and $z_*(t)$ are bang-bang controls, which take only values $\{w_{\min}, w_{\max}\}$ and $\{z_{\min}, z_{\max}\}$, respectively.*

An important property which we would like to stress is that these controls have no singularities (see [31] for details), and they are entirely determined by the corresponding switching functions $L_w(t)$ and $L_z(t)$.

For a particular case $z_{\max} = w_{\max}$, the following Lemma allows to immediately establish behavior of functions $L_v(t)$, $L_w(t)$ and $L_z(t)$.

Lemma 4. *If $z_{\max} = w_{\max}$ holds, then*

$$(3.10) \quad L_v(t) < 0, \quad t \in [0, T]; \quad L_w(t) > 0, \quad t \in (0, T); \quad L_z(t) > 0, \quad t \in (0, T].$$

Proof. By the continuity of function $L_z(t)$ and the initial condition for this function in (3.9) follows that there is $t_z \geq 0$ such that $L_z(t) > 0$, and hence

$z_*(t) = z_{\max}$ holds for all $t \in [t_z, T]$. Likewise, by continuity and the initial condition for $L_v(t)$, there is $t_v \geq 0$ such that $L_v(t) < 0$, and hence $v_*(t) = v_{\min}$ holds for all $t \in [t_v, T]$. Integrating of the equation for $L_w(t)$ in (3.9) yields that $L_w(t) > 0$ for $t \in [t_w, T]$. Therefore, there is interval (t_w, T) , where $0 \leq t_w \leq t_v$, where $L_w(t) > 0$, and hence $w_*(t) = w_{\max}$ for all $t \in [t_w, T]$.

Let $t_0 = \max\{t_w, t_z\}$. If $t_0 = 0$, then the second and the third inequalities in (3.10) hold, and then the first inequality immediately follows from the third equation in (3.9). Let assume that $t_0 > 0$. For certainty, let assume that $t_0 = t_w$. Then $L_w(t_0) = 0$, and $L_v(t) < 0$ for all $t \in [t_0, T]$. The integration of the first equation in (3.9) yields

$$0 = L_w(T) - L_w(t_0) = \int_{t_0}^T e^{\int_{t_0}^{\chi} w_*(\xi) d\xi} v_*(\chi) f'_S(S_*(\chi), I_*(\chi)) L_v(\chi) d\chi < 0,$$

which means contradiction. Hence such case is not valid, and (3.10) are correct. \square

Lemma 4 implies that if $z_{\max} = w_{\max}$ holds, then

$$u_*(t) = u_{\min}, v_*(t) = v_{\min}, w_*(t) = w_{\max}, z_*(t) = z_{\max}, t \in [0, T].$$

Since the optimal controls for the case $z_{\max} = w_{\max}$ are now found, further in this paper we assume that

$$(3.11) \quad z_{\max} \neq w_{\max}$$

holds.

To establish for function $L_v(t)$ and control $v_*(t)$ the same properties as those that are provided for functions $L_w(t)$ and $L_z(t)$ and controls $w_*(t)$ and $z_*(t)$ by Lemma 2 and Corollary 3, we have to prove the following Lemma:

Lemma 5. *Switching function $L_v(t)$ is not equal identically to zero on any finite subinterval of interval $[0, T]$.*

Proof. By contradiction, let us assume that there is a subinterval $\Delta_0 \subset [0, T]$ where $L_v(t) = \psi_2^*(t) - \psi_1^*(t) = 0$. Then, as in the proof of Lemma 2, equalities

$$(3.12) \quad \psi_1^*(t) = \psi_2^*(t), \quad \dot{\psi}_1^*(t) = \dot{\psi}_2^*(t)$$

necessary hold. Moreover, on subinterval Δ_0 the equations of system (3.1) are

$$(3.13) \quad \begin{aligned} \dot{\psi}_1^*(t) &= w_*(t)\psi_1^*(t), \\ \dot{\psi}_2^*(t) &= z_*(t)\psi_2^*(t). \end{aligned}$$

Please note that function $\psi_1^*(t)$ can not be equal to zero at any point of the interval Δ_0 , because, if the opposite is correct, then it follows from the first equation of (3.13) that $\psi_1^*(t) = 0$ for all $t \in \Delta_0$. Moreover, by (3.12), in this case $\psi_2^*(t) = 0$ on this interval as well. Hence, as well as in the proof of Lemma 2, we come to a contradiction. Therefore, $\psi_1^*(t) \neq 0$ on Δ_0 , and, by (3.12), functions $\psi_1^*(t)$ and

$\psi_2^*(t)$ are of the same sign. Then, by (3.4,3.5), on subinterval Δ_0 controls $w_*(t)$ and $z_*(t)$ takes values either $\{w_{\min}, z_{\min}\}$, or $\{w_{\max}, z_{\max}\}$, respectively.

Finally, equalities (3.12,3.13) yield

$$z_*(t) = w_*(t), \quad t \in \Delta_0.$$

which implies

$$w_{\min} = z_{\min}, \quad w_{\max} = z_{\max}.$$

However, by (2.7) and (3.11), neither of these equalities is possible, and hence we gain a contradiction and the initial assumption is not correct, and function $L_v(t)$ is not equal to zero on any finite subinterval of the interval $[0, T]$. This completes the proof. \square

Lemma and (3.3) immediately lead to the Corollary:

Corollary 6. *Optimal control $v_*(t)$ is a bang-bang control, which take only values $\{v_{\min}, 1\}$ on interval $[0, T]$. The control has no singularities (see [31]), and is entirely determined by switching functions $L_v(t)$.*

4. OPTIMAL CONTROLS

In previous Section, we show that in problem (2.5,2.8) the optimal controls $v_*(t)$, $w_*(t)$, $z_*(t)$ are bang-bang controls with values $\{v_{\min}, 1\}$, $\{w_{\min}, w_{\max}\}$, and $\{z_{\min}, z_{\max}\}$, respectively. If we would be able to estimate the maximum possible number of switchings of the controls, then we can immediately reduce the optimal control problem to a considerably simpler problem of the finite dimensional optimization, which then can be solved numerically (see e.g. [13, 14, 15, 12, 11]). We will not do this in this paper, as for a numerical procedure requires a specific parametrization for the incidence rate $f(S, I)$, whereas our goal is to study the impact of a general nonlinearity to the controls.

Formulas (3.2–3.5) imply that to estimate the number of switchings of the controls we have to estimate the number of zeros of the corresponding switching functions $L_v(t)$, $L_w(t)$, $L_z(t)$ defined by system (3.9). We start at the estimation of the number of zeros for function $L_v(t)$, and then proceed to $L_w(t)$ and $L_z(t)$.

Function $L_v(t)$ and $L_w(t)$ satisfy differential equations

$$(4.1) \quad \begin{aligned} \dot{L}_v(t) &= g(t)L_v(t) - r(t)L_w(t), \\ \dot{L}_w(t) &= p(t)L_v(t) + w_*(t)L_w(t), \\ L_v(T) &= -1, \quad L_w(T) = 0, \end{aligned}$$

where

$$\begin{aligned} g(t) &= v_*(t)(f'_S(S_*(t), I_*(t)) - f'_I(S_*(t), I_*(t))) + z_*(t), \\ p(t) &= v_*(t)f'_S(S_*(t), I_*(t)), \quad r(t) = z_*(t) - w_*(t). \end{aligned}$$

Please note that, by (A3) and (2.7), $p(t) > 0$.

We consider two cases.

Case 1. Let $w_{\max} \leq z_{\min}$ (that is, $\tilde{w}_{\max} \leq \sigma$), and hence $r(t) \geq 0$. Then substitution

$$\tilde{L}_v(t) = L_v(t), \quad \tilde{L}_w(t) = L_w + q(t)L_v(t)$$

yields

$$(4.2) \quad \begin{aligned} \dot{\tilde{L}}_v(t) &= (g(t) + r(t)q(t))\tilde{L}_v(t) - r(t)\tilde{L}_w(t), \\ \dot{\tilde{L}}_w(t) &= [\dot{q}(t) + p(t) + (g(t) - w_*(t))q(t) + r(t)q^2(t)]\tilde{L}_v(t) \\ &\quad + (w_*(t) - r(t)q(t))\tilde{L}_w(t). \end{aligned}$$

Let us define function $q(t)$ by Riccati equation

$$\dot{q}(t) = -r(t)q^2(t) - (g(t) - w_*(t))q(t) - p(t).$$

If this equation has a solution on $[0, T]$, then the square brackets in the second equation of system (4.2) are equal to zero, and the system takes the upper-triangular form.

Functions

$$\tilde{a}(t) = -r(t), \quad \tilde{b}(t) = -(g(t) - w_*(t)), \quad \tilde{c}(t) = -p(t)$$

satisfy, by (2.7), the following estimates:

$$\begin{aligned} |\tilde{a}(t)| &= |r(t)| \leq (z_{\max}^2 + w_{\max}^2)^{\frac{1}{2}} = \tilde{A}, \\ |\tilde{b}(t)| &= |g(t) - w_*(t)| \leq (2v_{\max}^2(M_S^2 + M_I^2) + 2(z_{\max}^2 + w_{\max}^2))^{\frac{1}{2}} = \tilde{B}, \\ |\tilde{c}(t)| &= |p(t)| \leq (v_{\max}^2 M_S^2)^{\frac{1}{2}} = \tilde{C}. \end{aligned}$$

Hence, constants \tilde{A} , \tilde{B} , and \tilde{C} can serve as estimates from above for coefficients $\tilde{a}(t)$, $\tilde{b}(t)$ and $\tilde{c}(t)$ of the Riccati equation

$$(4.3) \quad \dot{q}(t) = \tilde{a}(t)q^2(t) + \tilde{b}(t)q(t) + \tilde{c}(t).$$

Furthermore, constants \tilde{A} , \tilde{B} , and \tilde{C} satisfy the inequality

$$\begin{aligned} \tilde{B}^2 - 4\tilde{A}\tilde{C} &= 2v_{\max}^2(M_S^2 + M_I^2) + 2(z_{\max}^2 + w_{\max}^2) \\ &\quad - 4(z_{\max}^2 + w_{\max}^2)^{\frac{1}{2}}(v_{\max}^2 M_S^2)^{\frac{1}{2}} \\ &\geq 2v_{\max}^2(M_S^2 + M_I^2) + 2(z_{\max}^2 + w_{\max}^2) - 2v_{\max}^2 M_S^2 \\ &\quad - 2(z_{\max}^2 + w_{\max}^2) = 2v_{\max}^2 M_I^2 > 0. \end{aligned}$$

Therefore, Riccati equation (4.3) has a solution $\tilde{q}(t)$ on the entire interval $[0, T]$ (see [13, 15]), and system (4.2) takes on this interval the upper-triangular form

$$(4.4) \quad \begin{aligned} \dot{\tilde{L}}_v(t) &= (g(t) + r(t)\tilde{q}(t))\tilde{L}_v(t) - r(t)\tilde{L}_w(t), \\ \dot{\tilde{L}}_w(t) &= (w_*(t) - r(t)\tilde{q}(t))\tilde{L}_w(t). \end{aligned}$$

Here function $\tilde{L}_v(t)$ satisfies initial condition $\tilde{L}_v(T) = L_v(T) = -1 < 0$.

Our next objective is to prove that function $\tilde{L}_v(t) = L_v(t)$ has not more than one zero on interval $[0, T]$. Let assume, by contradiction, that function $\tilde{L}_v(t)$ has at least two zeros τ_1 and τ_2 , such that $0 \leq \tau_1 < \tau_2 < T$ hold. Note that for a non-negative function $r(t)$ inequality

$$(4.5) \quad \int_{\tau_1}^{\tau_2} r(t) dt > 0$$

holds. Indeed, otherwise $r(t) = 0$ must hold almost everywhere on $[\tau_1, \tau_2]$, and then, from the first equation of (4.4), $\tilde{L}_v(t) = L_v(t) = 0$ for all $t \in [\tau_1, \tau_2]$. Besides, at any point t_0 from the set of a non-zero measure where $r(t) = 0$, $L_w(t_0) > 0$ and $L_z(t_0) < 0$ hold, and hence, by (3.8), $L_v(t_0) > 0$. Therefore, (4.5) is correct. Therefore, by the generalized Rolle's theorem (see [6]) applied to the first equation of system (4.4), function $\tilde{L}_w(t)$ has at least one zero $\eta \in (\tau_1, \tau_2)$. But $\tilde{L}_w(t)$ satisfies a linear homogeneous differential equation, and hence in this case $\tilde{L}_w(t) = 0$ must hold on the entire interval $[0, T]$. Substituting $\tilde{L}_w(t) = 0$ in the first equation of (4.4) we come to the conclusion that in this case $\tilde{L}_v(t) = 0$ must hold for all $t \in [0, T]$ as well. This contradicts to the initial condition for $\tilde{L}_v(T)$, and hence the hypothesis is incorrect, and function $\tilde{L}_v(t) = L_v(t)$ has at most one zero on interval $[0, T]$.

Now we have to consider two subcases.

Subcase 1.1. Function $L_v(t)$ has no zero on interval $(0, T]$. In this case, by the initial condition, $L_v(t) < 0$ holds for all $t \in (0, T]$. Furthermore, by (3.9), $L_w(t) > 0$ and $L_u(t) < 0$ hold for $t \in (0, T)$, and $L_z(t) > 0$ holds for $t \in (0, T]$. Hence the controls have no switchings and are

$$u_*(t) = u_{\min}, v_*(t) = v_{\min}, w_*(t) = w_{\max}, z_*(t) = z_{\max}, t \in [0, T].$$

The corresponding physical controls are

$$\tilde{u}_*(t) = \tilde{u}_{\max}, \tilde{v}_*(t) = \tilde{v}_{\max}, \tilde{w}_*(t) = \tilde{w}_{\max}, \tilde{z}_*(t) = \tilde{z}_{\max}.$$

Subcase 1.2. Function $L_v(t)$ has a single zero, τ_* , on interval $(0, T)$. Then, by the initial condition,

$$L_v(t) \begin{cases} > 0 & , \quad \text{if } 0 \leq t < \tau_*, \\ = 0 & , \quad \text{if } t = \tau_*, \\ < 0 & , \quad \text{if } \tau_* < t \leq T. \end{cases}$$

Hence the optimal control $v_*(t)$ is

$$\tilde{v}_*(t) = \begin{cases} 1 & , \quad \text{if } 0 \leq t \leq \tau_*, \\ v_{\min} & , \quad \text{if } \tau_* < t \leq T. \end{cases}$$

It is easy to see that each of functions $L_w(t)$ and $L_z(t)$ can have for this subcase not more than one zero on interval $[0, \tau_*)$, and have no zeros outside of this interval. Hence for each of these functions there are two variants. For $L_w(t)$, either

$$L_w(t) > 0, \quad t \in (0, T),$$

or

$$L_w(t) \begin{cases} < 0 & , \quad \text{if } 0 \leq t < \theta_*, \\ = 0 & , \quad \text{if } t = \theta_*, t = T \\ > 0 & , \quad \text{if } \theta_* < t \leq T. \end{cases}$$

Likewise, for $L_z(t)$, either

$$L_z(t) > 0, \quad t \in (0, T],$$

or

$$L_z(t) \begin{cases} < 0 & , \quad \text{if } 0 \leq t < \eta_*, \\ = 0 & , \quad \text{if } t = \eta_*, \\ > 0 & , \quad \text{if } \eta_* < t \leq T. \end{cases}$$

Here $\theta_*, \eta_* < \tau_*$ are the corresponding zeros of functions $L_w(t)$ and $L_z(t)$, respectively. Taking into consideration that, by (3.8), $L_w(0) < L_z(0)$, there are three possible variants for controls $u_*(t)$, $w_*(t)$ and $z_*(t)$, namely: either

$$w_*(t) = w_{\max}, \quad z_*(t) = z_{\max}, \quad t \in [0, T];$$

or

$$z_*(t) = z_{\max}, \quad t \in [0, T], \quad w_*(t) = \begin{cases} w_{\min} & , \quad \text{if } 0 \leq t \leq \theta_*, \\ w_{\max} & , \quad \text{if } \theta_* < t \leq T, \end{cases}$$

or

$$z_*(t) = \begin{cases} z_{\min} & , \quad \text{if } 0 \leq t \leq \eta_*, \\ z_{\max} & , \quad \text{if } \eta_* < t \leq T; \end{cases} \quad w_*(t) = \begin{cases} w_{\min} & , \quad \text{if } 0 \leq t \leq \theta_*, \\ w_{\max} & , \quad \text{if } \theta_* < t \leq T. \end{cases}$$

For the first variant, control $u_*(t)$ is

$$u_*(t) = u_{\min}, \quad t \in [0, T];$$

for the second and third variants it is

$$u_*(t) = \begin{cases} \mu & , \quad \text{if } 0 \leq t \leq \theta_*, \\ u_{\min} & , \quad \text{if } \theta_* < t \leq T. \end{cases}$$

Case 2. Let $w_{\max} > z_{\min}$ (that is, $\tilde{w}_{\max} > \sigma$). In this case the sign of function $r(t)$ can be as positive as negative. This makes a straightforward application

of the Rolle's theorem impossible and hence the analysis of this case is more difficult, compared with Case 1.

Denoting $G(t) = r(t)L_w(t)$, we can rewrite the first equation of system (4.1) as

$$(4.6) \quad \dot{L}_v(t) = g(t)L_v(t) - G(t).$$

To obtain the differential equation for $G(t)$, we have to be sure that $G(t)$ is differentiable almost everywhere on $[0, T]$. For the differentiability of $G(t)$, it suffices if $w_*(t)$ and $z_*(t)$ are piecewise constant functions; that is they must have a finite number of switchings on this interval. In turn, this implies that the corresponding switching functions $L_w(t)$ and $L_z(t)$ have finite numbers of zeros on interval $[0, T]$. From (3.9) it follows that this is possible if $L_v(t)$ has a finite number of zeros. Hence, we assume that the following proposition holds:

Proposition 7. *Let the switching function $L_v(t)$ has a finite number of zeros on interval $[0, T]$.*

Further we will demonstrate that this proposition is correct.

Proposition 7 ensures that function $G(t)$ is differentiable almost everywhere on $[0, T]$, and hence satisfies differential equation

$$(4.7) \quad \dot{G}(t) = x(t)L_v(t) + w_*(t)G(t),$$

where

$$x(t) = v_*(t)(z_*(t) - w_*(t))f'_S(S_*(t), I_*(t)).$$

Gathering equations (4.6,4.7) together, we obtain the system

$$(4.8) \quad \begin{aligned} \dot{L}_v(t) &= g(t)L_v(t) - G(t), \\ \dot{G}(t) &= x(t)L_v(t) + w_*(t)G(t). \end{aligned}$$

Substitution in system (4.8)

$$\bar{L}_v(t) = L_v(t), \quad \bar{G}(t) = G(t) + q(t)L_v(t),$$

where, as in Case 1, function $q(t)$ is to be defined later, yields the system of differential equations

$$(4.9) \quad \begin{aligned} \dot{\bar{L}}_v(t) &= (g(t) + q(t))\bar{L}_v(t) - \bar{G}(t), \\ \dot{\bar{G}}(t) &= [\dot{q}(t) + x(t) + (g(t) - w_*(t))q(t) + q^2(t)] \bar{L}_v(t) \\ &\quad + (w_*(t) - q(t))\bar{G}(t). \end{aligned}$$

Let function $q(t)$ satisfy Riccati equation

$$\dot{q}(t) = -q^2(t) - (g(t) - w_*(t))q(t) - x(t);$$

then the expression in the square brackets is equal to zero, and system (4.9) has the upper triangular form. Let denote

$$\bar{a}(t) = -1, \quad \bar{b}(t) = -(g(t) - w_*(t)), \quad \bar{c}(t) = -x(t).$$

Functions $\bar{a}(t)$, $\bar{b}(t)$ and $\bar{c}(t)$ satisfy

$$|\bar{a}(t)| = 1 = \bar{A},$$

$$|\bar{b}(t)| = |g(t) - w_*(t)| \leq (2v_{\max}^2(M_S^2 + M_I^2) + 2(z_{\max}^2 + w_{\max}^2))^{\frac{1}{2}} = \bar{B},$$

$$|\bar{c}(t)| = |x(t)| \leq (v_{\max}^2(z_{\max}^2 + w_{\max}^2)M_S^2)^{\frac{1}{2}} = \bar{C}.$$

Hence constants \bar{A} , \bar{B} and \bar{C} can serve as estimates for coefficients $\bar{a}(t)$, $\bar{b}(t)$ and $\bar{c}(t)$, respectively, of the Ricatti equation

$$(4.10) \quad \dot{q}(t) = \bar{a}(t)q^2(t) + \bar{b}(t)q(t) + \bar{c}(t).$$

Furthermore, constants \bar{A} , \bar{B} and \bar{C} satisfy

$$\begin{aligned} \bar{B}^2 - 4\bar{A}\bar{C} &= 2v_{\max}^2(M_S^2 + M_I^2) + 2(z_{\max}^2 + w_{\max}^2) \\ &\quad - 4(z_{\max}^2 + w_{\max}^2)^{\frac{1}{2}}(v_{\max}^2 M_S^2)^{\frac{1}{2}} \\ &\geq 2v_{\max}^2(M_S^2 + M_I^2) + 2(z_{\max}^2 + w_{\max}^2) - 2v_{\max}^2 M_S^2 \\ &\quad - 2(z_{\max}^2 + w_{\max}^2) = 2v_{\max}^2 M_I^2 > 0. \end{aligned}$$

Therefore, by the same arguments as in Case 1, the Ricatti equation (4.10) has a solution $\bar{q}(t)$ defined on the entire interval $[0, T]$, and hence system (4.9) takes the upper-triangular form

$$(4.11) \quad \begin{aligned} \dot{\bar{L}}_v(t) &= (g(t) + \bar{q}(t))\bar{L}_v(t) - \bar{G}(t), \\ \dot{\bar{G}}(t) &= (w_*(t) - \bar{q}(t))\bar{G}(t). \end{aligned}$$

Here function $\bar{L}_v(t)$ satisfies initial condition

$$(4.12) \quad \bar{L}_v(T) = L_v(T) = -1 < 0.$$

It is easy to see that function $\bar{L}_v(t) = L_v(t)$ has not more than one zero on interval $[0, T]$. Indeed, let us assume, by contradiction, that $\bar{L}_v(t)$ has at least two different zeros τ_1 and τ_2 , such that $0 \leq \tau_1 < \tau_2 < T$ hold. Then the generalized Rolle's theorem applied to the first equation of system (4.11) yields that function $\bar{G}(t)$ has on interval (τ_1, τ_2) at least one zero ξ . But $\bar{G}(t)$ satisfies a linear homogeneous differential equation, and hence if $\bar{G}(\xi) = 0$ holds then $\bar{G}(t) = 0$ holds everywhere on $[0, T]$. By the same arguments, and substituting $\bar{G}(t) = 0$ into the first equation of (4.11), $\bar{L}_v(t) = 0$ everywhere on $[0, T]$ as well. This contradicts to initial condition (4.12), and hence the hypothesis is incorrect, and function $L_v(t) = \bar{L}_v(t)$ has at most one zero interval $[0, T]$.

This also confirms that Proposition 7 is correct.

The arguments above show that the numbers of switchings in Case 2 are the same as these in Case 1, and hence the possible type of the optimal controls $u_*(t)$, $v_*(t)$, $w_*(t)$ and $z_*(t)$ are the same as in Case 1. That is, for both Cases when

$w_{\max} \neq z_{\min}$, if control $\tilde{v}_*(t)$ has no switchings, then all for physical controls are maximal on entire interval $[0, T]$:

$$\tilde{u}_*(t) = \tilde{u}_{\max}, \tilde{v}_*(t) = \tilde{v}_{\max}, \tilde{w}_*(t) = \tilde{w}_{\max}, \tilde{z}_*(t) = \tilde{z}_{\max}.$$

If control $\tilde{v}_*(t)$ has one switching, then

$$\tilde{v}_*(t) = \begin{cases} 0 & , \text{ if } 0 \leq t \leq \tau_*, \\ \tilde{v}_{\max} & , \text{ if } \tau_* < t \leq T, \end{cases}$$

whereas physical controls $\tilde{u}_*(t)$, $\tilde{w}_*(t)$ and $\tilde{z}_*(t)$ belong to one of three following possible variants:

either (i)

$$\tilde{u}_*(t) = \tilde{u}_{\max}, \tilde{w}_*(t) = \tilde{w}_{\max}, \tilde{z}_*(t) = \tilde{z}_{\max}, \quad t \in [0, T];$$

or (ii)

$$\tilde{z}_*(t) = \tilde{z}_{\max}, \quad t \in [0, T]; \quad \tilde{u}_*(t), \tilde{w}_*(t) = \begin{cases} 0 & , \text{ if } 0 \leq t \leq \theta_*, \\ \tilde{u}_{\max}, \tilde{w}_{\max} & , \text{ if } \theta_* < t \leq T; \end{cases}$$

or (iii)

$$\tilde{z}_*(t) = \begin{cases} 0 & , \text{ if } 0 \leq t \leq \eta_*, \\ \tilde{z}_{\max} & , \text{ if } \eta_* < t \leq T, \end{cases}$$

$$\tilde{u}_*(t), \tilde{w}_*(t) = \begin{cases} 0 & , \text{ if } 0 \leq t \leq \theta_*, \\ \tilde{u}_{\max}, \tilde{w}_{\max} & , \text{ if } \theta_* < t \leq T. \end{cases}$$

5. DISCUSSION AND CONCLUSION

The major conclusion that can be withdrawn from the results of the previous sections is that for all incidence rates satisfying assumptions (A1–A4) (that is, for all biologically feasible incidence rates) the maximal number of switchings of the optimal controls, as well as the order of switchings, do not depend on a specific form of the nonlinearity of the incidence rate. For the SIR model considered in this paper with any incidence rate satisfying assumptions (A1–A4), either of four controls considered in this paper (and in fact possible for this model) has at most one switching. For the considered control problem there are two principal variants: either all controls should be implemented at the maximal rate for the whole period from the begin, or, when the indirect measures are initially absent and are switched to the maximal rate at a later moment, the other control should be switched to their maximum rates before this moment. A conclusion that can be made regarding a specific version of the controls for a specific problem is that this would more depend on the values of derivatives $f'_S(S, I)$ and $f'_I(S, I)$ than on a type of the nonlinearity of the incidence rate. Moreover, we conjecture that in a specific case the initial conditions, and in particular the sign of derivative $I'(0)$, have a larger impact on an implementation of a specific variant of the optimal

control, than on a nonlinearity of the incidence rate. We have to stress, however, that this conjecture does not follow from our analysis and its proof is highly nontrivial. Therefore, we left it as an open challenge.

It might be noteworthy that if $f'_S(S, I)$ or $f'_I(S, I)$ is equal to zero in the feasible region $\bar{\Omega}$ (that is, if (A3) is not held), than one or several of the switching functions can be identically equal to zero on a subinterval of $[0, T]$. This, in turn, implies that the corresponding optimal controls cannot be precisely found from (3.2–3.5), and singularities can arise on this subinterval [31].

In this paper we considered the impact of nonlinearity of only one functional response, namely this of the incidence rate. However, an epidemic model comprises several functional responses. Thus, in model considered in this paper, apart from the incidence rate these are (i) the demographic dynamic given by the rate $\mu(1 - S(t))$ and (ii) the removal of the infectious individuals defined by the rate $\sigma I(t)$. The linearity of both these rates is no more than a convenient assumption. Numerical experiments shows that the incidence rate is the most important of the functional responses in an epidemic model, and hence the conjecture that nonlinearities of the other functional responses would affect the control at a considerably smaller scale appears to be sufficiently safe. However, so far the question about possible impacts of nonlinearities of other functional responses on the optimal controls remains open.

In this paper, the above mentioned results were gained for the problem of minimizing the level of infection at the end of a given time interval. This objective corresponds to the concept of elimination of an infection by reducing the level of infection below its survival level. Another feasible objectives, which corresponds to the goal of protecting a population during an epidemic, is minimizing the cumulative number of the infected for a given period. The question whether our conclusions would be valid for this second objective, as well as for other possible objective functionals, also remains open. In particular, it can be expected that for control problems with objective functionals, which include controls, the controls (which for such kind of control problems are very sensitive) would explicitly depend on the nonlinearities of the functional responses.

Another practically relevant conclusion that follows from our analysis is that the vaccination the newborn and the susceptible should be started, carried out and ended simultaneously. This means that these two controls must be considered as one control. There still remains a question the vaccination of which of these two groups will give the better outcome. However, the answer to this question could be not entirely of mathematical nature, as this answer can depend on a level of danger of a particular infection for different age groups.

Furthermore, our analysis shows that the vaccination and the removal (isolation) of the infected are connected only by the indirect measures. That is, the implementation of each of these two types of controls depends only on the implementation of the indirect measures and is independent on the implementation of

the another type. This also implies that the controls of each of these types can be considered independently of the another type.

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