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ESTIMATING THE NUMBER OF SWITCHINGS OF THE OPTIMAL INTERVENTIONS STRATEGIES FOR SEIR CONTROL MODELS OF EBOLA EPIDEMICS

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Abstract. We consider on a given time interval two various SEIR control models describing Ebola epidemics in a population of a constant size. Each of these models contains four bounded controls. The common SEI control subsystem is allocated in these models, and for it the problem of minimizing the sum of total fractions of exposed and infected individuals and total weighted costs of control constraints over a given time interval is stated. For the analysis of the corresponding optimal controls, the Pontryagin maximum principle is used. According to it, these controls are bang-bang functions determined by the corresponding switching functions. For these functions the linear non-homogeneous non-autonomous system of differential equations is obtained. Some properties of the switching functions related to the analysis of this system are studied. In order to estimate the number of zeros of these functions using such system, two new approaches are proposed. It is found that the possible types of the optimal controls obtained by each of these approaches are identical. The corresponding conclusions are made.

1. Introduction

Ebola is a severe virus that has taken thousands of lives in several African countries, mainly Guinea, Sierra Leone, and Liberia. The latest outbreak of Ebola was the largest and deadliest infectious disease outbreak in modern history. As a result of its high mobility, Ebola is not only a concern for African countries, but has been transmitted to some countries in Europe and even to Texas in the United States ([11, 58]). Currently there is a lack of licensed treatment vaccines and a high mortality rate associated with the Ebola virus. Although, there are some vaccines that are not widely available or properly licensed in all affected countries. The best hope for stopping the spread and transmission of Ebola is the practical control interventions of public health.

Mathematical models are an effective tool for studying the dynamics and spread of the Ebola virus. These models allow carrying out a quantitative assessment of the epidemiological situation; studying the impact of various external and internal factors on the spread of an Ebola epidemic; making the forecast of the population

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morbidity level; and assessing the consequences of various management actions. Together with modern information computer systems, mathematical models provide a powerful basis for effective monitoring and incidence analysis, epidemiological risk assessment, forecasting of possible consequences, and management of the epidemiological situation. Following [51], models are distinguished by four different categories related to increasing levels of epidemiological realism and, consequently, increasing difficulties in the systematic analysis ([15, 19, 51]):

(i) deterministic models in the form of ordinary differential or partial differential equations, which describe the coarse-grained dynamics of Ebola epidemics at the population level;
(ii) stochastic models, which include stochastic parameters and variables;
(iii) individual-based models with "memory", which introduce the uniqueness of the individual behavior in a general population ([20]);
(iv) dynamic "social" network-based or agent-based models, which include delayed effects of the interactions between individuals ([29, 47, 52]).

Deterministic and stochastic mathematical models are most frequently used to describe the transmission and spread of the Ebola virus as well as the impact of intervention control measures. Two types of so-called compartment models, namely, SIR and SEIR models ([6, 7, 13, 26, 63]), define these models. In such models, the studied human population is divided into compartments. For the SIR model, the population consists of the susceptible, infectious and recovery compartments. In addition to the already mentioned compartments, the SEIR model also contains the exposed compartment. The interactions between the compartments in both models are described by mathematical relations in accordance with their categories. Moreover, for a more precise description of the transmission and spread of the Ebola virus in SIR and SEIR models, the auxiliary compartments, such as isolated, hospitalized, buried, removed, etc can be added. Such models are still considered SIR and SEIR models.

Considerable attention has been and continues to be given to the calculation of a threshold, also called a basic reproductive number for deterministic and stochastic SIR and SEIR models. At the same time, the dynamics of transmission of the Ebola disease have been studied in terms of the reduction of the basic reproductive number. For stochastic models such investigations are present in [12, 14, 31, 36, 54, 60], and for deterministic models in [1, 2, 9, 18, 34, 59].

In recent years, much attention has been given to the so-called deterministic SIR and SEIR control models. They include a variety of control functions, which reflect practical measures of a manageable impact on the Ebola epidemic. In turn, optimal control problems associated with such models are an important tool to develop the most effective measures against the epidemic. These problems, for example, determine the optimal schedules for vaccine of susceptible individuals, treatment of exposed and infected individuals, and produce the best modes of distribution of public funds related to the educational, quarantine, and other large-scale preventive measures ([3, 5, 10, 24, 27, 32, 41, 44, 46]).

Next, we focus our attention only on such deterministic SIR and SEIR control models in which the interactions between their compartments are described by ordinary differential equations. The set of admissible controls consists of all possible Lebesgue measurable and bounded functions in these models. Traditionally, available controls describe treatment, detection, and isolation of the exposed and infectious individuals; vaccination of susceptible individuals; and other indirect epidemiological measures, such as quarantine and educational campaigns. Finally, each optimal control problem contains an objective function (functional) that mathematically represents a goal that allows deducing the optimal strategies aimed at curtailing the spread and transmission of an Ebola disease. Typically, an objective function is a sum of the total fractions (or the quantities) of exposed and infected, or only infected individuals (depending on the model), and the total weighted costs of the control constraints on the given time interval. The cost of the control constraints represents either the integral of this control, the integral of the square of this control, or the integral of the product of this control and the corresponding phase variable. Further, we will analyze the optimal control problems depending on the type of integrals used for the description of the total weighted costs of the control constraints.

Let for SIR or SEIR control model the corresponding functional contains integrals of controls for describing the total weighted costs of the control constraints. It is shown in [27, 32, 41] that the corresponding optimal controls can contain so-called singular portions, when the value of the optimal control cannot be determined uniquely from the used as necessary condition Pontryagin maximum principle ([48]). As it was noted in [49], in this case the problem of finding optimal solutions becomes complex mathematical problem. In [49], the authors discuss all possible difficulties of the search of such solutions. After establishing the fact that an optimal control can have singular portions, after checking for these portions the corresponding optimality conditions ([48]), finding the ways of possible concatenations of singular and nonsingular portions, finding specific optimal solutions in the considered optimal control problem can be done only numerically ([49]).

Let us now consider such SIR or SEIR control model for which the corresponding functional contains integrals from the squares of controls in order to describe the total weighted costs of the control constraints. It is emphasized in [49] that such terms in the functional, do not reflect any better the total weighted costs of the control constraints than integrals of controls. After application of the Pontryagin maximum principle, the optimal control problem is reduced to a two point boundary value problem for the maximum principle, which can be easily solved numerically because the right hand sides of the corresponding differential equations of the boundary value problem are Lipschitz functions of the phase and adjoint variables. Methods of numerical solution of such boundary value problems are well-developed ([4, 28, 35, 43]). A drawback here is the lack of theoretical investigation of the uniqueness of a solution of the considered boundary value problem. Uniqueness is established only for small time intervals ([22, 28]). Though, the techniques and methods are proposed, allowing to study such uniqueness numerically ([4, 39]). A great existing mathematical software along with big memory computers allow this problem to be the most popular among the researchers modeling epidemics ([8, 22, 50, 53, 61, 62]), in particular Ebola epidemics ([5, 40, 43, 44, 45, 46]).

Finally, let us consider an optimal control problem for SIR or SEIR control model, the corresponding functional for which either does not have any integrals related to controls or contains integrals of controls or integrals of product of controls and corresponding phase variables. The latter integrals, as it was mentioned in [10], also determine the total weighted costs of the control constraints. In this case, such optimal control problems are considered for which the optimal controls have no singular portions, so the number of switchings of such controls can be estimated using either by analysis of the switching functions or by analysis of the differential equations for these functions ([3, 10, 23, 24, 25, 38, 55, 56]). After analysis of the number of switchings of the optimal controls, the original optimal control problem is reduced to a simpler problem of the finite dimensional optimization, for which numerical methods are well-known ([23, 24]). The problem considered in this paper and all investigations related to it, concern the latter type of the optimal control problems.

This paper is organized as follows. In Section 2 we describe two different SEIR control models describing Ebola epidemics in a population of a constant size. Each of these models contains four bounded controls. Two of them reflect the efforts to protect susceptible individuals from infected and exposed individuals. Other two controls depending on the model define the efforts either for the treatment, or for the detection and isolation of exposed and infected individuals. Then, a common SEI control subsystem is extracted in these models. For this subsystem, an optimal control problem of minimizing the total fractions of exposed and infected individuals and the total weighted costs of the control constraints on the given time interval is stated. A discussion of the existence of the optimal controls in the considered minimization problem is also provided in this Section. For the analysis of the corresponding optimal controls, the Pontryagin maximum principle is used, which is formulated in Section 3. Regarding this principle, the behavior of the optimal controls is completely determined by the behavior of the switching functions. Therefore, in this Section we also give a Cauchy problem for such functions. The corresponding system of differential equations is linear non-homogeneous and non-autonomous. Using analysis of this Cauchy problem, in Section 4, we establish some important properties of the switching functions and the corresponding optimal controls. Section 5 is a main section of this article because it contains a detailed discussion of the two new approaches for estimating the number of zeros of the switching functions. The first approach, described in detail in Subsection 5.1, is based on the analysis of the Cauchy problems for the derivatives of the switching functions. It is shown that each switching function has at most one zero on the given time interval, which means that the corresponding optimal control has at most one switching. The second approach described in Subsection 5.2, concerns with the usage of constancy of the Hamiltonian on the optimal solution of the original problem for reducing by one of the order of the system of differential equations for the switching functions. This approach results in obtaining the linear non-homogeneous non-autonomous system of differential equations for each switching function and its corresponding auxiliary function. Then, in each such a system the special substitutions of variables are made in order to reduce its matrix to an upper-triangular form on the entire time interval. The functions that perform such substitutions, satisfy the corresponding non-autonomous differential Riccati equations. Therefore, there is the problem to prove the existence of such solutions of these equations that are defined on the entire time interval as well. The considered differential Riccati equations are of the same type: the coefficient of square of a function and the free coefficient are definite sign on the given interval, and furthermore, opposite in sign functions. Such properties of the coefficients of the Riccati equations are sufficient to prove the existence of the required solutions. Then, the corresponding to each Riccati equation transformed linear system is also defined on the entire time interval. Application to it of the generalized Rolle's theorem allows us to find the estimate of the number of zeros for each switching function. It is shown that each such a function has at most one zero on the given time interval and hence, the corresponding optimal control has at most one switching as well. Moreover, the results obtained for each switching function using the first and second approaches coincide. This means that if as the result of using the first approach it is obtained that the optimal control is constant over the entire time interval, then, this optimal control would have the same type after application of the second approach. On the other hand, if the first approach shows that the optimal control is piecewise constant function with at most one switching, then this type of the optimal control is confirmed by the second approach and vise versa. This conclusion is the main result of Section 6. Additionally, in this Section, there are other conclusions related to the behavior of the optimal controls of the original problem.

2. SEIR models and problem formulation

Over a given time interval $[0, T]$ let us consider a SEIR model described by the following system of differential equations:

$$\begin{cases} \dot{S}(t) = -N^{-1}\left(\beta I(t) + \alpha E(t)\right) S(t), \\ \dot{E}(t) = N^{-1}\left(\beta I(t) + \alpha E(t)\right) S(t) - (\sigma + \lambda) E(t), \\ \dot{I}(t) = \sigma E(t) - (\gamma + \nu) I(t), \\ \dot{R}(t) = \lambda E(t) + (\gamma + \nu) I(t), \\ S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0,\ R(0) = R_0; \\ S_0,\ E_0,\ I_0,\ R_0 > 0. \end{cases} \tag{2.1}$$

Such model describes the spread of an Ebola epidemic in a population of constant size N. Indeed, considering that the equality

$$S_0 + E_0 + I_0 + R_0 = N \tag{2.2}$$

holds, we add together the equations of system (2.1). Then, using equality (2.2), we find the relationship:

$$S(t) + E(t) + I(t) + R(t) = N. \tag{2.3}$$

Let us note that if $\alpha = 0$, then system (2.1) is a standard SEIR model. Therefore, further we focus on the case $\alpha > 0$.

As it follows from system (2.1) and formula (2.3), the total host population is partitioned into susceptible, exposed, infectious, and removed (recovery or died) individuals, respectively denoted by $S(t)$, $E(t)$, $I(t)$, and $R(t)$ at time t, which form the compartments of the same names. After one unit time, a susceptible individual can be infected through contacting with the exposed or infectious individuals and enter the exposed compartment, or is still in the susceptible compartment. An exposed individual may become infectious and enter the infectious compartment, or may be treated and enter the removed compartment, or still stay in the exposed compartment. An infectious individual may be treated and enter the removed compartment, or die because of disease and enter the removed compartment as well, or stay in the infectious compartment. A treated individual may recover by effective treatment. The individual recovery from Ebola depends on good supportive care and the patients immune response. People who recover from an Ebola infection develop antibodies and are not susceptible to this disease in the future. Therefore, a recovery individual only may stay in removed compartment. Here, we unite the recovered and deceased individuals in one compartment, $R(t)$, because there has not been a case in which an individual who survived Ebola contracts this disease again.

At system (2.1) the positive parameters α and β are the rates of the effective contact between susceptible and exposed, between susceptible and infectious individuals, respectively, and $\beta \geq \alpha$; σ denotes the transfer rate between the exposed and infectious compartments; γ is the rate of disease-caused death; λ and ν denote the rates of the treatment effectiveness in the exposed and infectious compartments, respectively. Moreover, in the equations of system (2.1) there are no the terms related to the natural mortality or fertility because of the short time-span of an Ebola epidemic.

Now, we will make controlled the SEIR model described by system (2.1). For this, we introduce four control functions: two of which, $u(t)$ and $v(t)$, define the efforts of preventing susceptible individuals from becoming infectious individuals as a result of contact with infectious and exposed ones, respectively; the other two, $w(t)$ and $z(t)$, imply the corresponding efforts for the treatment of exposed and infectious individuals. For these controls we have the following constraints:

$$\begin{array}{ll} 0 < u_{\min} \leq u(t) \leq u_{\max}, & 0 < v_{\min} \leq v(t) \leq v_{\max}, \\ w_{\min} \leq w(t) \leq w_{\max} < 1, & z_{\min} \leq z(t) \leq z_{\max} < 1, \end{array} \tag{2.4}$$

where $u_{\max} = \beta$, $v_{\max} = \alpha$, $w_{\min} = \lambda$, $z_{\min} = \nu$.

Thus, we have the following control model:

$$\begin{cases} \dot{S}(t) = -N^{-1}\left(u(t)I(t) + v(t)E(t)\right)S(t),\ t \in [0,T], \\ \dot{E}(t) = N^{-1}\left(u(t)I(t) + v(t)E(t)\right)S(t) - (\sigma + w(t))E(t), \\ \dot{I}(t) = \sigma E(t) - (\gamma + z(t))I(t), \\ S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0, \\ S_0,\ E_0,\ I_0 > 0;\ S_0 + E_0 + I_0 < N, \end{cases} \tag{2.5}$$

in which the equation for the function $R(t)$ is excluded, and this function easily can be found from equality (2.3).

Now, let us consider over a given time interval $[0, T]$ another SEIR model described by the following system of differential equations:

$$
(2.6) \qquad \begin{cases} \dot{S}(t) = -N^{-1}\left(\beta I(t) + \alpha E(t)\right) S(t), \\ \dot{E}(t) = N^{-1}\left(\beta I(t) + \alpha E(t)\right) S(t) - (\sigma + \lambda) E(t), \\ \dot{I}(t) = \sigma E(t) - (\gamma + \nu) I(t), \\ \dot{H}(t) = \lambda E(t) + \nu I(t) - \mu H(t), \\ \dot{R}(t) = \gamma I(t) + \mu H(t), \\ S(0) = S_0,\ E(0) = E_0,\ I(0) = I_0,\ H(0) = H_0,\ R(0) = R_0; \\ S_0,\ E_0,\ I_0,\ H_0,\ R_0 > 0. \end{cases}
$$

Such model also describes the spread of an Ebola epidemic in a population of constant size N ([30, 37]). Similar to (2.2) we consider that the equality

$$
(2.7) \qquad S_0 + E_0 + I_0 + H_0 + R_0 = N
$$

holds. Adding together the equations of system (2.6) and then using equality (2.7), we obtain the relationship:

$$
(2.8) \qquad S(t) + E(t) + I(t) + H(t) + R(t) = N.
$$

Comparing systems (2.1), (2.6) and formulas (2.2), (2.8), we see that one more compartment is added to the original SEIR model, namely $H(t)$, uniting individuals from exposed and infectious compartments, which are isolated from susceptible individuals at time t. It is called the isolated compartment. Next, we specify the differences between the SEIR models given by systems (2.1) and (2.6). The arguments related to the susceptible compartment are the same. Then, after one unit time, an exposed individual may become infectious and enter the infectious compartment, or may be detected and enter the isolated compartment, or still stay in the exposed compartment. An infectious individual may be detected and enter the isolated compartment, or die because of disease and enter the removed compartment, or stay in the infectious compartment. An isolated individual may die because of disease and enter the removed compartment, or stay in the isolated compartment. Finally, a recovery individual only may stay in the removed compartment.

In system (2.6) the meaning of the parameters α, β, σ, γ is the same. Positive parameter μ, as well as γ, denotes the rate of disease-caused death; the parameters λ and ν are the detection-isolation rates for exposed and infectious individuals, respectively.

Now, we will also make controlled the SEIR model described by system (2.6). For this, we introduce four control functions: $u(t)$, $v(t)$, $w(t)$, $z(t)$ as well. The first two functions, $u(t)$ and $v(t)$, have the same meaning as in model (2.5). The meaning of the other two functions, $w(t)$ and $z(t)$, changes. They define the efforts for the detection and isolation of exposed and infectious individuals, respectively. Restrictions (2.4) are imposed on these controls. As a result, we have the control model of type (2.5) in which the equation for the function $R(t)$ is excluded, and this function easily can be found from equality (2.8). Moreover, in the first three equations of system (2.6) the function $H(t)$ is absent. Therefore, this function is excluded from system (2.5) as well. It is obtained separately as the solution of the following Cauchy problem:

$$\begin{cases} \dot{H}(t) = w(t)E(t) + z(t)I(t) - \mu H(t),\ t \in [0,T], \\ H(0) = H_0 \end{cases}$$

after the controls $w(t)$, $z(t)$ are defined, and the functions $E(t)$, $I(t)$ are found from system (2.5).

Thus, from the SEIR models described by systems (2.1) and (2.6), we allocate common control system (2.5), which is considered below.

Next, in system (2.5) we introduce the new variables:

$$s(t) = N^{-1}S(t),\ \ e(t) = N^{-1}E(t),\ \ i(t) = N^{-1}I(t)$$

with corresponding initial values:

$$s_0 = N^{-1}S_0,\ \ e_0 = N^{-1}E_0,\ \ i_0 = N^{-1}I_0,$$

for which the following inequalities hold:

$$s_0,\ e_0,\ i_0 > 0;\ \ s_0 + e_0 + i_0 < 1.$$

These variables are the fractions of the quantities $S(t)$, $E(t)$, $I(t)$ in a population of size N.

Then, for the variables $s(t)$, $e(t)$, $i(t)$ we obtain the following nonlinear control system:

$$\begin{cases} \dot{s}(t) = -(u(t)i(t) + v(t)e(t))s(t),\ t \in [0,T], \\ \dot{e}(t) = (u(t)i(t) + v(t)e(t))s(t) - (\sigma + w(t))e(t), \\ \dot{i}(t) = \sigma e(t) - (\gamma + z(t))i(t), \\ s(0) = s_0,\ e(0) = e_0,\ i(0) = i_0, \\ s_0,\ e_0,\ i_0 > 0;\ s_0 + e_0 + i_0 < 1. \end{cases} \tag{2.9}$$

For this system the set of all admissible controls consists of all possible Lebesgue measurable functions $u(t)$, $v(t)$, $w(t)$, $z(t)$, which for almost all $t \in [0,T]$ satisfy constraints (2.4).

Now, we define a region:

$$\Omega = \Big\{(s,e,i) : s > 0,\ e > 0,\ i > 0,\ s + e + i < 1\Big\},$$

Initial conditions for system (2.9) imply the following inclusion:

$$(s_0, e_0, i_0) \in \Omega. \tag{2.10}$$

The following lemma ensures the positiveness, boundedness, and continuation of the solutions for system (2.9).

Lemma 2.1. *For any admissible controls $u(t)$, $v(t)$, $w(t)$, $z(t)$ the corresponding solutions $s(t)$, $e(t)$, $i(t)$ for system* (2.9) *are defined on the entire interval* $[0,T]$ *and satisfy the inclusion:*

$$(s(t), e(t), i(t)) \in \Omega, \quad t \in (0,T]. \tag{2.11}$$

Proof of this lemma is standard and so we omit it. Proofs of similar statements are given for example in [22, 32]. Inclusions (2.10), (2.11) imply that the region Ω is a positive invariant set for system (2.9).

Next, for system (2.9) on the set of all admissible controls we consider the following functionals:

$$J_1(u,v,w,z) = \int\limits_0^T \Big(e(t) + i(t)\Big)dt, \tag{2.12}$$

$$\begin{aligned} J_2(u,v,w,z) = {} & p\int\limits_0^T \Big[(\alpha - v(t))e(t) + (\beta - u(t))i(t)\Big]dt \\ & + q\int\limits_0^T \Big[(w(t) - \lambda)e(t) + (z(t) - \nu)i(t)\Big]dt. \end{aligned} \tag{2.13}$$

Functional (2.12) defines the sum of the total fractions of exposed and infected individuals on the given interval $[0,T]$. Functional (2.13) implies the sum of the total weighted costs of control constraints (2.4), where p, q are the non-negative weighted coefficients. Functionals of type (2.13) were used previously for the analysis of SIR control models in [3, 10].

Finally, for system (2.9) on the set of all admissible controls we consider the optimal control problem of minimization the sum of functionals (2.12) and (2.13):

$$\begin{aligned} \min_{u(\cdot),v(\cdot),w(\cdot),z(\cdot)} \Big\{ J(u,v,w,z) = \int\limits_0^T \Big[& \Big(1 + p(\alpha - v(t)) + q(w(t) - \lambda)\Big)e(t) \\ & + \Big(1 + p(\beta - u(t)) + q(z(t) - \nu)\Big)i(t)\Big]dt \Big\}. \end{aligned} \tag{2.14}$$

Here, depending on the values of the weighted coefficients p and q we simultaneously consider the following four problems:

(i) let $p = 0$ and $q = 0$, then problem (2.14) implies the minimization of the sum of the total fractions of exposed and infected individuals on the interval $[0,T]$;

(ii) let $p > 0$ and $q = 0$, then problem (2.14) implies the simultaneous minimization of the sum of the total fractions of exposed and infected individuals and the total weighted costs of the constraints for the controls $u(t)$, $v(t)$ on the interval $[0,T]$;

(iii) let $p = 0$ and $q > 0$, then problem (2.14) is similar to the previous one with the difference that there are controls $w(t)$, $z(t)$ instead of the controls $u(t)$, $v(t)$;

(iv) let $p > 0$ and $q > 0$, then problem (2.14) is similar to the two previous ones with the difference that it takes into account the total weighted costs of the constraints for all controls, that is $u(t)$, $v(t)$, $w(t)$, $z(t)$.

Remark 2.2. Problem (ii) for the system (2.9) without the controls $w(t)$, $z(t)$ was previously considered in [24], and the analysis of the problem (iiii) was partially presented at the XX International Symposium on Mathematical Methods Applied to the Sciences (SIMMAC), 2016, Costa Rica.

In problem (2.9), (2.14) the optimal controls $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ and corresponding optimal solutions $s_*(t)$, $e_*(t)$, $i_*(t)$ for system (2.9) exist. This fact follows from Lemma 2.1 and Theorem 4 ([33], Chapter 4).

3. Pontryagin maximum principle

For analysis of optimal control problem (2.9), (2.14) we use the Pontryagin maximum principle [42]. First, we write the Hamiltonian as

$$\begin{aligned} H(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= (ui+ve)s(\psi_2-\psi_1)+\sigma e(\psi_3-\psi_2) \\ &- we\psi_2-(\gamma+z)i\psi_3-\Big(1+p(\alpha-v)+q(w-\lambda)\Big)e \\ &- \Big(1+p(\beta-u)+q(z-\nu)\Big)i, \end{aligned}$$

where ψ_1, ψ_2, ψ_3 are the adjoint variables. Secondly, let us calculate for this Hamiltonian the required partial derivatives:

$$\begin{aligned} \frac{\partial H}{\partial s}(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= (ui+ve)(\psi_2-\psi_1), \\ \frac{\partial H}{\partial e}(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= vs(\psi_2-\psi_1)+\sigma(\psi_3-\psi_2)-w\psi_2 \\ &\quad -\Big(1+p(\alpha-v)+q(w-\lambda)\Big), \\ \frac{\partial H}{\partial i}(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= us(\psi_2-\psi_1)-(\gamma+z)\psi_3 \\ &\quad -\Big(1+p(\beta-u)+q(z-\nu)\Big), \\ \frac{\partial H}{\partial u}(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= si\Big((\psi_2-\psi_1)+ps^{-1}\Big), \\ \frac{\partial H}{\partial v}(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= se\Big((\psi_2-\psi_1)+ps^{-1}\Big), \\ \frac{\partial H}{\partial w}(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= e(-\psi_2-q), \\ \frac{\partial H}{\partial z}(s,e,i,\psi_1,\psi_2,\psi_3,u,v,w,z) &= i(-\psi_3-q). \end{aligned}$$

Then, according to the Pontryagin maximum principle for the optimal controls $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ and corresponding optimal solutions $s_*(t)$, $e_*(t)$, $i_*(t)$ for system (2.9) there necessary exists the vector-function $\psi_*(t)=(\psi_1^*(t),\psi_2^*(t),\psi_3^*(t))$ such that:

(i) $\psi_*(t)$ is the nontrivial solution of the adjoint system:

$$\text{(3.1)}\quad \begin{cases} \dot\psi_1^*(t) = -(u_*(t)i_*(t)+v_*(t)e_*(t))(\psi_2^*(t)-\psi_1^*(t)),\ t\in[0,T], \\ \dot\psi_2^*(t) = -v_*(t)s_*(t)(\psi_2^*(t)-\psi_1^*(t))-\sigma(\psi_3^*(t)-\psi_2^*(t)) \\ \qquad\quad +w_*(t)\psi_2^*(t)+(1+p(\alpha-v_*(t))+q(w_*(t)-\lambda)), \\ \dot\psi_3^*(t) = -u_*(t)s_*(t)(\psi_2^*(t)-\psi_1^*(t))+(\gamma+z_*(t))\psi_3^*(t) \\ \qquad\quad +(1+p(\beta-u_*(t))+q(z_*(t)-\nu)), \\ \psi_1^*(T)=0,\ \psi_2^*(T)=0,\ \psi_3^*(T)=0; \end{cases}$$

(ii) the controls $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ maximize the Hamiltonian

$$H(s_*(t), e_*(t), i_*(t), \psi_1^*(t), \psi_2^*(t), \psi_3^*(t), u, v, w, z)$$

with respect to $u \in [u_{\min}, u_{\max}]$, $v \in [v_{\min}, v_{\max}]$, $w \in [w_{\min}, w_{\max}]$, $z \in [z_{\min}, z_{\max}]$ for almost all $t \in [0, T]$, and therefore the following relationships hold:

$$u_*(t) = \begin{cases} u_{\max} & \text{, if } \quad L_0(t) > 0, \\ \forall u \in [u_{\min}, u_{\max}] & \text{, if } \quad L_0(t) = 0, \\ u_{\min} & \text{, if } \quad L_0(t) < 0, \end{cases} \tag{3.2}$$

$$v_*(t) = \begin{cases} v_{\max} & \text{, if } \quad L_0(t) > 0, \\ \forall v \in [v_{\min}, v_{\max}] & \text{, if } \quad L_0(t) = 0, \\ v_{\min} & \text{, if } \quad L_0(t) < 0, \end{cases} \tag{3.3}$$

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

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

where the functions:

$$\begin{aligned} L_0(t) &= (\psi_2^*(t) - \psi_1^*(t)) + p s_*^{-1}(t), \\ L_w(t) &= -\psi_2^*(t) - q, \quad L_z(t) = -\psi_3^*(t) - q, \end{aligned} \tag{3.6}$$

by Lemma 2.1, are the switching functions, which define the types of the optimal controls $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ according to formulas (3.2)–(3.5);

(iii) the Hamiltonian

$$H(s_*(t), e_*(t), i_*(t), \psi_1^*(t), \psi_2^*(t), \psi_3^*(t), u_*(t), v_*(t), w_*(t), z_*(t)),$$

which, by formulas (3.6), is rewritten as

$$\begin{aligned} H_*(t) = e_*(t)\Big(& v_*(t)s_*(t)L_0(t) + (\sigma + w_*(t))L_w(t) - \sigma L_z(t) \\ & - (1 + \alpha p - \lambda q)\Big) \\ + i_*(t)\Big(& u_*(t)s_*(t)L_0(t) + (\gamma + z_*(t))L_z(t) \\ & - (1 + \beta p - (\nu + \gamma)q)\Big), \end{aligned} \tag{3.7}$$

is constant on the given interval $[0, T]$.

Now, applying the first equation of system (2.9) and the equations of system (3.1), we write the differential equations for the switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$ as follows

$$\begin{cases} \dot{L}_0(t) = (u_*(t)i_*(t) + v_*(t)e_*(t) - v_*(t)s_*(t))L_0(t) \\ \qquad\qquad -(\sigma + w_*(t))L_w(t) + \sigma L_z(t) + (1 + \alpha p - \lambda q), \\ \dot{L}_w(t) = v_*(t)s_*(t)L_0(t) + (\sigma + w_*(t))L_w(t) \\ \qquad\qquad -\sigma L_z(t) - (1 + \alpha p - \lambda q), \\ \dot{L}_z(t) = u_*(t)s_*(t)L_0(t) + (\gamma + z_*(t))L_z(t) \\ \qquad\qquad -(1 + \beta p - (\nu + \gamma)q). \end{cases}$$

Using the initial conditions for system (3.1) and formulas (3.6), we find the corresponding initial conditions for the functions $L_0(t)$, $L_w(t)$, $L_z(t)$:

$$L_0(T) = ps_*^{-1}(T), \;\; L_w(T) = -q, \;\; L_z(T) = -q.$$

Combining the differential equations and the initial conditions obtained above, we finally have the Cauchy problem for the switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$:

$$\begin{cases} \dot{L}_0(t) = (u_*(t)i_*(t) + v_*(t)e_*(t) - v_*(t)s_*(t))L_0(t) \\ \qquad\qquad -(\sigma + w_*(t))L_w(t) + \sigma L_z(t) + (1 + \alpha p - \lambda q), \\ \dot{L}_w(t) = v_*(t)s_*(t)L_0(t) + (\sigma + w_*(t))L_w(t) \\ \qquad\qquad -\sigma L_z(t) - (1 + \alpha p - \lambda q), \\ \dot{L}_z(t) = u_*(t)s_*(t)L_0(t) + (\gamma + z_*(t))L_z(t) \\ \qquad\qquad -(1 + \beta p - (\nu + \gamma)q), \\ L_0(T) = ps_*^{-1}(T), \; L_w(T) = -q, \; L_z(T) = -q. \end{cases} \tag{3.8}$$

This system will be actively used in further arguments.

Also, applying the second and third equations of system (3.8) we rewrite relationship (3.7) in a more convenient form:

$$e_*(t)\dot{L}_w(t) + i_*(t)\dot{L}_z(t) = H_*(T), \;\; t \in [0, T]. \tag{3.9}$$

4. Properties of the switching functions

We have the statements that describe the properties of the switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$.

Lemma 4.1. *For all $t \in [0, T]$ the following equality holds:*

$$\frac{d}{dt}(s_*(t)L_0(t)) = -s_*(t)\dot{L}_w(t). \tag{4.1}$$

The validity of this fact directly follows from the first equation of system (2.9) as well as the first and second equations of system (3.8).

Lemma 4.2. *For the switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$ depending on the values of the weighted coefficients p, q we have the following statements.*

(1) *Let $p > 0$ and $q > 0$. Then there exists the value $t_1 \in (0, T)$ such that the following inequalities are simultaneously satisfied:*

$$L_0(t) > 0, \quad L_w(t) < 0, \quad L_z(t) < 0, \quad t \in (t_1, T]. \tag{4.2}$$

(2) *Let $p > 0$ and $q = 0$. Then there exists the value $t_2 \in (0, T)$ such that the following inequalities are simultaneously satisfied:*

$$L_0(t) > 0, \;\; t \in (t_2, T]; \quad L_w(t) > 0, \;\; L_z(t) > 0, \;\; t \in (t_2, T). \tag{4.3}$$

(3) *Let $p = 0$ and $q > 0$. Then there exists the value $t_3 \in (0, T)$ such that the following inequalities are simultaneously satisfied:*

$$L_0(t) < 0, \ \ t \in (t_3, T); \quad L_w(t) < 0, \ \ L_z(t) < 0, \ \ t \in (t_3, T]. \tag{4.4}$$

(4) *Let $p = 0$ and $q = 0$. Then there exists the value $t_4 \in (0, T)$ such that the following inequalities are simultaneously satisfied:*

$$L_0(t) < 0, \quad L_w(t) > 0, \quad L_z(t) > 0, \quad t \in (t_4, T). \tag{4.5}$$

Proof. Let us consider the various cases depending on the values of p and q.

Case 1. Let $p > 0$ and $q > 0$. Inequalities (4.2) are the consequence of continuity of the functions $L_0(t)$, $L_w(t)$, $L_z(t)$ as well as their initial conditions of system (3.8).

Case 2. Let $p > 0$ and $q = 0$. The first inequality in (4.3) follows from continuity of the function $L_0(t)$ and its initial condition of system (3.8). In order to justify the other inequalities in (4.3), we integrate in system (3.8) the differential equations for the functions $L_w(t)$, $L_z(t)$ with the corresponding initial conditions. As a result, the following formulas hold:

$$L_w(t) = \int_t^T e^{-\int_t^\chi (\sigma + w_*(\xi))d\xi} \Big\{ 1 + \sigma L_z(\chi) + \Big(\alpha p - v_*(\chi) s_*(\chi) L_0(\chi) \Big) \Big\} d\chi,$$

$$L_z(t) = \int_t^T e^{-\int_t^\chi (\gamma + z_*(\xi))d\xi} \Big\{ 1 + \Big(\beta p - u_*(\chi) s_*(\chi) L_0(\chi) \Big) \Big\} d\chi. \tag{4.6}$$

By continuity of the functions $s_*(t)$, $L_0(t)$, $L_z(t)$ and initial conditions of system (3.8), a small left half-neighborhood of the value $t = T$ is defined, in which the expressions in braces in formulas (4.6) are positive. Thus, in this neighborhood the functions $L_w(t)$, $L_z(t)$ take positive values. Now, this implies the required fact.

Case 3. Let $p = 0$ and $q > 0$. The last two inequalities in (4.4) follow from continuity of the functions $L_w(t)$, $L_z(t)$ and their initial conditions of system (3.8). In order to justify the first inequality in (4.4), we integrate in system (3.8) the differential equation for the function $L_0(t)$ with the corresponding initial condition. As a result, the following formula is true:

$$\begin{aligned} L_0(t) = -\int_t^T e^{-\int_t^\chi \widehat{a}_0(\xi)d\xi} \Big\{ & 1 + \sigma \Big(L_z(\chi) - L_w(\chi) \Big) \\ & - \Big(w_*(\chi) L_w(\chi) + \lambda q \Big) \Big\} d\chi, \end{aligned} \tag{4.7}$$

where $\widehat{a}_0(t) = u_*(t) i_*(t) + v_*(t) e_*(t) - v_*(t) s_*(t)$. By continuity of the functions $L_w(t)$, $L_z(t)$ and their initial conditions of system (3.8), there exists a small left half-neighborhood of the value $t = T$, in which the expression in braces in formula (4.7) is positive. Therefore, in this neighborhood the function $L_0(t)$ takes negative values. Now, this implies the required fact as well.

Case 4. Let $p = 0$ and $q = 0$. We integrate in system (3.8) all differential equations with the corresponding initial conditions, and, as a result, have the following formulas:

$$L_0(t) = -\int_t^T e^{-\int_t^\chi \widehat{a}_0(\xi)d\xi}\Big\{1 + \sigma\Big(L_z(\chi) - L_w(\chi)\Big) - w_*(\chi)L_w(\chi)\Big\}d\chi,$$

$$L_w(t) = \int_t^T e^{-\int_t^\chi (\sigma + w_*(\xi))d\xi}\Big\{1 + \sigma L_z(\chi) - v_*(\chi)s_*(\chi)L_0(\chi)\Big\}d\chi, \tag{4.8}$$

$$L_z(t) = \int_t^T e^{-\int_t^\chi (\gamma + z_*(\xi))d\xi}\Big\{1 - u_*(\chi)s_*(\chi)L_0(\chi)\Big\}d\chi.$$

By continuity of the functions $s_*(t)$, $L_0(t)$, $L_w(t)$, $L_z(t)$ and initial conditions of system (3.8), a small left half-neighborhood of the value $t = T$ is defined, in which the expressions in braces in formulas (4.8) are positive. Thus, in this neighborhood the function $L_0(t)$ takes negative values as well as the functions $L_w(t)$, $L_z(t)$ take positive values. Now, this implies the required fact. The proof is complete. □

Corollary 4.3. *Inequalities* (4.2)–(4.5) *of Lemma 4.2 and formulas* (3.2)–(3.5) *yield the following relationships for the optimal controls* $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$*:*

(1) *if* $p > 0$ *and* $q > 0$*, then:*

$$\begin{aligned} &u_*(t) = u_{\max}, \quad v_*(t) = v_{\max}, \\ &w_*(t) = w_{\min}, \quad z_*(t) = z_{\min}, \quad t \in (t_1, T]; \end{aligned} \tag{4.9}$$

(2) *if* $p > 0$ *and* $q = 0$*, then:*

$$\begin{aligned} &u_*(t) = u_{\max}, \quad v_*(t) = v_{\max}, \\ &w_*(t) = w_{\max}, \quad z_*(t) = z_{\max}, \quad t \in (t_2, T]; \end{aligned} \tag{4.10}$$

(3) *if* $p = 0$ *and* $q > 0$*, then:*

$$\begin{aligned} &u_*(t) = u_{\min}, \quad v_*(t) = v_{\min}, \\ &w_*(t) = w_{\min}, \quad z_*(t) = z_{\min}, \quad t \in (t_3, T]; \end{aligned} \tag{4.11}$$

(4) *if* $p = 0$ *and* $q = 0$*, then:*

$$\begin{aligned} &u_*(t) = u_{\min}, \quad v_*(t) = v_{\min}, \\ &w_*(t) = w_{\max}, \quad z_*(t) = z_{\max}, \quad t \in (t_4, T]. \end{aligned} \tag{4.12}$$

Lemma 4.4. *For any values of the weighted coefficients* p *and* q *the derivatives of the switching functions* $L_w(t)$, $L_z(t)$ *satisfy the following equalities:*

$$\dot{L}_w(T) = -1, \quad \dot{L}_z(T) = -1. \tag{4.13}$$

Proof. Using in system (3.8) the second and third differential equations as well as the necessary initial conditions, we find the relationships for the corresponding derivatives:

$$\begin{aligned} \dot{L}_w(T) &= -1 - \Big(\alpha - v_*(T)\Big)p - \Big(w_*(T) - \lambda\Big)q, \\ \dot{L}_z(T) &= -1 - \Big(\beta - u_*(T)\Big)p - \Big(z_*(T) - \nu\Big)q. \end{aligned} \tag{4.14}$$

Thereafter, let us consider the various cases depending on the values of p and q.

Case 1. Let $p > 0$ and $q > 0$. Then, by (2.4) and (4.9), we find the equalities:

$$u_*(T) = \beta, \;\; v_*(T) = \alpha, \;\; w_*(T) = \lambda, \;\; z_*(T) = \nu.$$

Using them in formulas (4.14) we find equalities (4.13).

Case 2. Let $p > 0$ and $q = 0$. Then, by (2.4) and (4.10), we obtain the equalities:

$$u_*(T) = \beta, \quad v_*(T) = \alpha.$$

Using them in formulas (4.14) we find equalities (4.13).

Case 3. Let $p = 0$ and $q > 0$. Then, by (2.4) and (4.11), we find the equalities:

$$w_*(T) = \lambda, \quad z_*(T) = \nu.$$

Using them in formulas (4.14) we find equalities (4.13).

Case 4. Let $p = 0$ and $q = 0$. Then equalities (4.13) are immediately obtained from formulas (4.14). This completes the proof. □

Corollary 4.5. *By Lemma 2.1 and equalities* (4.13), *we have for formula* (3.9) *the following relationship:*

$$H_*(T) = -\Big(e_*(T) + i_*(T)\Big) < 0. \tag{4.15}$$

Lemma 4.6. *The switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$ are not equal to zero on any finite interval of* $[0, T]$.

Proof. First, let us consider the function $L_0(t)$. We suppose the contrary. It means that there is the interval $\Delta_0 \subset [0, T]$ on which

$$L_0(t) = 0. \tag{4.16}$$

Then, by Lemma 2.1, we find from formula (4.1) that for all $t \in \Delta_0$ the following equality is true:

$$\dot{L}_w(t) = 0. \tag{4.17}$$

From this, again by Lemma 2.1 and relationships (3.9) and (4.15), we conclude that on the interval Δ_0 the following inequality holds:

$$\dot{L}_z(t) < 0. \tag{4.18}$$

Now, from (4.17) it follows that

$$L_w(t) = L_w^0 = \mathrm{Const}, \quad t \in \Delta_0. \tag{4.19}$$

We consider the possible cases depending on the value of L_w^0.

Case 1. Let $L_w^0 = 0$. Then, by equalities (4.16) and (4.17), the second equation of system (3.8) is transformed to the expression:

$$L_z(t) = -\sigma^{-1}(1 + \alpha p - \lambda q) = \mathrm{Const}, \quad t \in \Delta_0.$$

From this, we conclude that on the interval Δ_0 the equality

$$\dot{L}_z(t) = 0, \tag{4.20}$$

holds, which contradicts (4.18). Hence, this case is impossible.

Case 2. Let $L_w^0 \neq 0$. Then, by (3.4), from (4.19) we obtain that $w_*(t) = w_* \in \{w_{\min}; w_{\max}\}$ on the interval Δ_0. Again by equalities (4.16) and (4.17), the second equation of system (3.8) is reduced to the form:

$$L_z(t) = \sigma^{-1}\Big((\sigma + w_*)L_w^0 - (1 + \alpha p - \lambda q)\Big) = \text{Const}, \quad t \in \Delta_0.$$

From this, we find the contradictory equality (4.20). Therefore, this case is impossible as well. Our assumption is wrong and the switching function $L_0(t)$ does not vanish on any interval of $[0, T]$.

Secondly, let us consider the function $L_w(t)$. Again we suppose the contrary. It implies that there exists the interval $\Delta_w \subset [0, T]$ on which

$$L_w(t) = 0. \tag{4.21}$$

Then, on this interval the equality (4.17) is true. By Lemma 2.1 and relationships (3.9) and (4.15), from this it follows inequality (4.18).

Now, from (4.1) and (4.17) we find the formula:

$$s_*(t)L_0(t) = L_0^0 = \text{Const}, \quad t \in \Delta_w. \tag{4.22}$$

We consider the possible cases depending on the value of L_0^0.

Case 1. Let $L_0^0 = 0$. Then, by equalities (4.17) and (4.21), the second equation of system (3.8) is transformed to the expression:

$$L_z(t) = -\sigma^{-1}(1 + \alpha p - \lambda q) = \text{Const}, \quad t \in \Delta_w.$$

From this, it follows equality (4.20) executing on the interval Δ_w, which contradicts (4.18). Hence, this case is impossible.

Case 2. Let $L_0^0 \neq 0$. Then from (4.22) we find that the function $L_0(t) = L_0^0 s_*^{-1}(t)$ takes the same sign on the interval Δ_w. Hence, by (3.3), we conclude that $v_*(t) = v_* \in \{v_{\min}; v_{\max}\}$ on this interval. Then, again by equalities (4.17) and (4.21), the second equation of system (3.8) is reduced to the form:

$$L_z(t) = \sigma^{-1}\Big(v_* L_0^0 - (1 + \alpha p - \lambda q)\Big) = \text{Const}, \quad t \in \Delta_w.$$

From this, we find the contradictory equality (4.20). Therefore, this case is impossible as well. Our assumption is wrong and the switching function $L_w(t)$ does not vanish on any interval of $[0, T]$.

Finally, let us consider the function $L_z(t)$. Again we argue by contradiction. Then, there is the interval $\Delta_z \subset [0, T]$ on which

$$L_z(t) = 0. \tag{4.23}$$

Hence, on this interval equality (4.20) holds. From this, by Lemma 2.1 and relationships (3.9) and (4.15), we obtain the inequality:

$$\dot{L}_w(t) < 0 \tag{4.24}$$

executing on the interval Δ_z.

Now, by equalities (4.20) and (4.23), the third equation of system (3.8) is transformed to the expression:

$$u_*(t)s_*(t)L_0(t) = 1 + \beta p - (\nu + \gamma)q, \quad t \in \Delta_z. \tag{4.25}$$

We consider the possible cases depending on the value of $(1 + \beta p - (\nu + \gamma)q)$.

Case 1. Let $1+\beta p-(\nu+\gamma)q=0$. Then we have equality $s_*(t)L_0(t)=0$, $t\in\Delta_z$ from which, by Lemma 2.1 and formula (4.1), we obtain the equality:

$$\dot{L}_w(t)=0, \quad t\in\Delta_z, \tag{4.26}$$

which contradicts (4.24). Hence, this case is impossible.

Case 2. Let $1+\beta p-(\nu+\gamma)q\neq 0$. Then, by (4.25), we see that the function

$$L_0(t)=\Big(1+\beta p-(\nu+\gamma)q\Big)u_*^{-1}(t)s_*^{-1}(t)$$

takes the same sign on the interval Δ_z. Therefore, by (3.2), we conclude that $u_*(t)=u_*\in\{u_{\min};u_{\max}\}$ on this interval. Hence, again by (4.25), the following equality holds:

$$s_*(t)L_0(t)=\Big(1+\beta p-(\nu+\gamma)q\Big)u_*^{-1}, \quad t\in\Delta_z.$$

Again using formula (4.1) we find the contradictory equality (4.26). Therefore, this case is impossible as well. Our assumption is wrong and the switching function $L_z(t)$ does not vanish on any interval of $[0,T]$. This completes the proof. □

Corollary 4.7. *Lemma 4.6 and formulas* (3.2)–(3.5) *show that the optimal controls* $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ *are bang-bang functions taking values* $\{u_{\min};u_{\max}\}$, $\{v_{\min};v_{\max}\}$, $\{w_{\min};w_{\max}\}$, $\{z_{\min};z_{\max}\}$, *respectively. Moreover, the controls* $u_*(t)$, $v_*(t)$ *switch from maximum values to minimum values and vice versa at the same moments of switching.*

5. Estimating the number of zeros of the switching functions

We consider two new approaches for estimating the number of zeros of the switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$. The first approach is based on the analysis of the solutions of the Cauchy problems for the derivatives of the switching functions $L_w(t)$ and $L_z(t)$. The second approach implies using the constancy of the Hamiltonian on the optimal solution of the original problem (2.9), (2.14) for reducing by one of the order of system (3.8). Next, we describe in detail these approaches.

5.1. Cauchy problems for derivatives of the switching functions.

Let us obtain the differential equations for the functions $\dot{L}_w(t)$, $\dot{L}_z(t)$. In order to make this, we have to be sure in the possibility of differentiation of these functions almost everywhere on the interval $[0,T]$. Analyzing the second and third equations of system (3.8) we conclude that for differentiability of the functions $\dot{L}_w(t)$, $\dot{L}_z(t)$ it is sufficient if the functions $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ are piecewise constant functions. It implies that they must have a finite number of switchings on the interval $(0,T)$. In turn, it means that the corresponding switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$ have a finite number of zeros on the interval $[0,T]$. Hence, we assume that the following condition holds.

Condition 5.1. *Let the switching functions* $L_0(t)$, $L_w(t)$, $L_z(t)$ *have a finite number of zeros on the interval* $[0,T]$.

Further we will demonstrate that this condition is correct. Condition 5.1 ensures that the functions $\dot{L}_w(t)$, $\dot{L}_z(t)$ are differentiable almost everywhere on the interval $[0,T]$.

Now, let us consider the switching function $L_w(t)$. Using the second equation of system (3.8) we calculate the derivative of the function $\dot{L}_w(t)$. After this, in the obtained relationship we use formulas (3.9) and (4.1). Adding the first formula from (4.13) as the corresponding initial condition, finally, we obtain the Cauchy problem for the function $\dot{L}_w(t)$:

$$(5.1)\qquad \begin{cases} \ddot{L}_w(t) = \widehat{a}_w(t)\dot{L}_w(t) - \sigma H_*(T)i_*^{-1}(t), \ \ t \in [0,T], \\ \dot{L}_w(T) = -1, \end{cases}$$

where $\widehat{a}_w(t) = \sigma + w_*(t) + \sigma e_*(t)i_*^{-1}(t) - v_*(t)s_*(t)$.

Integrating Cauchy problem (5.1), we find the formula:

$$\dot{L}_w(t) = -e^{-\int_t^T \widehat{a}_w(\xi)d\xi} + \sigma H_*(T)\int_t^T e^{-\int_t^\chi \widehat{a}_w(\xi)d\xi} i_*^{-1}(\chi)d\chi, \ t \in [0,T],$$

which, by Lemma 2.1 and (4.15), implies that

$$(5.2)\qquad \dot{L}_w(t) < 0, \quad t \in [0,T].$$

Hence, the function $L_w(t)$ decreases from value $L_w(0)$ to value $L_w(T) = -q \le 0$. Therefore, depending on the values of q and $L_w(0)$ the switching function $L_w(t)$ has at most one zero on the interval $(0,T)$:

$$(5.3)\qquad \text{if } \ q = 0, \text{ then } \ L_w(t) > 0, \quad t \in [0,T);$$

$$(5.4)\qquad \text{if } \ q > 0 \ \text{ and } \ L_w(0) \le 0, \quad \text{then} \quad L_w(t) < 0, \ \ t \in (0,T];$$

$$(5.5)\qquad \text{if } \ q > 0 \ \text{ and } \ L_w(0) > 0, \quad \text{then} \quad L_w(t) \begin{cases} > 0 & , \text{ for } \ 0 \le t < \tau_*, \\ = 0 & , \text{ for } \ t = \tau_*, \\ < 0 & , \text{ for } \ \tau_* < t \le T, \end{cases}$$

where $\tau_* \in (0,T)$ is a zero of the function $L_w(t)$.

Now, let us consider the switching function $L_z(t)$. Using the third equation of system (3.8) we calculate the derivative of the function $\dot{L}_z(t)$. Then, in the obtained expression we use formula (4.1). Adding the second formula from (4.13) as the corresponding initial condition, finally we find the Cauchy problem for the function $\dot{L}_z(t)$:

$$(5.6)\qquad \begin{cases} \ddot{L}_z(t) = (\gamma + z_*(t))\dot{L}_z(t) - u_*(t)s_*(t)\dot{L}_w(t), \ \ t \in [0,T], \\ \dot{L}_z(T) = -1. \end{cases}$$

Integrating Cauchy problem (5.6), we obtain the formula:

$$\dot{L}_z(t) = -e^{-\int_t^T (\gamma + z_*(\xi))d\xi} + \int_t^T e^{-\int_t^\chi (\gamma + z_*(\xi))d\xi} u_*(\chi)s_*(\chi)\dot{L}_w(\chi)d\chi, \ t \in [0,T],$$

which, by constraints (2.4), Lemma 2.1 and inequality (5.2), implies that $\dot{L}_z(t) < 0$ for all $t \in [0,T]$. Hence, the function $L_z(t)$ decreases from value $L_z(0)$ to value $L_z(T) = -q \le 0$. Therefore, depending on the values of q and $L_z(0)$ the switching function $L_z(t)$ has at most one zero on the interval $(0,T)$:

$$\text{if } q=0, \text{ then } L_z(t)>0, \quad t\in[0,T); \tag{5.7}$$

$$\text{if } q>0 \text{ and } L_z(0)\le 0, \text{ then } L_z(t)<0, \quad t\in(0,T]; \tag{5.8}$$

$$\text{if } q>0 \text{ and } L_z(0)>0, \text{ then } L_z(t)\begin{cases} >0 & \text{, for } 0\le t<\eta_*, \\ =0 & \text{, for } t=\eta_*, \\ <0 & \text{, for } \eta_*<t\le T, \end{cases} \tag{5.9}$$

where $\eta_*\in(0,T)$ is a zero of the function $L_z(t)$.

Finally, let us consider the switching function $L_0(t)$. By relationships (4.1) and (5.2), we conclude that the inequality $\frac{d}{dt}(s_*(t)L_0(t))>0$ is valid for all $t\in[0,T]$. Hence, the function $\widetilde{L}_0(t)=s_*(t)L_0(t)$ increases from value $\widetilde{L}_0(0)$ to value $\widetilde{L}_0(T)=p\ge 0$. Therefore, depending on the values of p and $\widetilde{L}_0(0)$ the function $\widetilde{L}_0(t)$ has at most one zero on the interval $(0,T)$:

$$\text{if } p=0, \text{ then } \widetilde{L}_0(t)<0, \quad t\in[0,T); \tag{5.10}$$

$$\text{if } p>0 \text{ and } \widetilde{L}_0(0)\ge 0, \text{ then } \widetilde{L}_0(t)>0, \quad t\in(0,T]; \tag{5.11}$$

$$\text{if } p>0 \text{ and } \widetilde{L}_0(0)<0, \text{ then } \widetilde{L}_0(t)\begin{cases} <0 & \text{, for } 0\le t<\theta_*, \\ =0 & \text{, for } t=\theta_*, \\ >0 & \text{, for } \theta_*<t\le T, \end{cases} \tag{5.12}$$

where $\theta_*\in(0,T)$ is a zero of the function $\widetilde{L}_0(t)$. By Lemma 2.1, we see that the relationships (5.10)–(5.12) hold for the switching function $L_0(t)$. Adding here relationships (5.3)–(5.5) and (5.7)–(5.9) obtained previously for the switching functions $L_w(t)$, $L_z(t)$, we conclude that Condition 5.1 is correct.

Now, by formulas (3.2)–(3.5) and relationships (5.3)–(5.5), (5.7)–(5.9) and (5.10)–(5.12), we make conclusions about the behavior of optimal controls $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ depending on the values of the weighted coefficients p and q. The following theorems hold.

Theorem 5.2. *Let $p>0$ and $q>0$. Then optimal controls $u_*(t)$, $v_*(t)$ are either constant functions of the type:*

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

or piecewise constant functions with one switching of the type:

$$u_*(t),v_*(t)=\begin{cases} u_{\min},v_{\min} & \text{, for } 0\le t\le\theta_*, \\ u_{\max},v_{\max} & \text{, for } \theta_*<t\le T. \end{cases}$$

Optimal control $w_*(t)$ is either constant function of the type:

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

or piecewise constant function with one switching of the type:

$$w_*(t)=\begin{cases} w_{\max} & \text{, for } 0\le t\le\tau_*, \\ w_{\min} & \text{, for } \tau_*<t\le T. \end{cases}$$

Optimal control $z_*(t)$ is either constant function of the type:

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

or piecewise constant function with one switching of the type:

$$z_*(t) = \begin{cases} z_{\max} & , \textit{for} \quad 0 \leq t \leq \eta_*, \\ z_{\min} & , \textit{for} \quad \eta_* < t \leq T. \end{cases}$$

Theorem 5.3. *Let $p > 0$ and $q = 0$. Then optimal controls $u_*(t)$, $v_*(t)$ are either constant functions of the type:*

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

or piecewise constant functions with one switching of the type:

$$u_*(t), v_*(t) = \begin{cases} u_{\min}, v_{\min} & , \textit{for} \quad 0 \leq t \leq \theta_*, \\ u_{\max}, v_{\max} & , \textit{for} \quad \theta_* < t \leq T. \end{cases}$$

Optimal controls $w_*(t)$, $z_*(t)$ are constant functions of the type:

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

Theorem 5.4. *Let $p = 0$ and $q > 0$. Then optimal controls $u_*(t)$, $v_*(t)$ are constant functions of the type:*

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

Optimal control $w_*(t)$ is either constant function of the type:

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

or piecewise constant function with one switching of the type:

$$w_*(t) = \begin{cases} w_{\max} & , \textit{for} \quad 0 \leq t \leq \tau_*, \\ w_{\min} & , \textit{for} \quad \tau_* < t \leq T. \end{cases}$$

Optimal control $z_*(t)$ is either constant function of the type:

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

or piecewise constant function with one switching of the type:

$$z_*(t) = \begin{cases} z_{\max} & , \textit{for} \quad 0 \leq t \leq \eta_*, \\ z_{\min} & , \textit{for} \quad \eta_* < t \leq T. \end{cases}$$

Theorem 5.5. *Let $p = 0$ and $q = 0$. Then optimal controls $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ are constant functions of the type:*

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

Remark 5.6. In [21] for estimating the number of switchings of the optimal control in the model of malignant tumor treatment with the immune reaction the properties of the first and second derivatives of the corresponding switching function were also used.

5.2. **Constancy of the Hamiltonian on the optimal solution.** As in the previous approach, here we will have to differentiate the control functions $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$. In order to do this, they must be piecewise constant functions with a finite number of switchings on the interval $(0,T)$. In turn, it implies that the corresponding switching functions $L_0(t)$, $L_w(t)$, $L_z(t)$ must have a finite number of zeros on the interval $[0,T]$. Therefore, further we consider that Condition 5.1 is satisfied.

Now, let us rewrite formula (3.7) expressing the constancy of the Hamiltonian on the optimal solution of the original problem (2.9), (2.14) as follows

$$\begin{aligned} e_*(t)\Big(v_*(t)s_*(t)L_0(t) + (\sigma + w_*(t))L_w(t) - \sigma L_z(t) \\ - (1+\alpha p - \lambda q)\Big) \\ + i_*(t)\Big(u_*(t)s_*(t)L_0(t) + (\gamma + z_*(t))L_z(t) \\ - (1+\beta p - (\nu+\gamma)q)\Big) = H_*(T), \quad t \in [0,T]. \end{aligned} \tag{5.13}$$

Next, we express from this the term $(\sigma + w_*(t))L_w(t)$ and substitute it into the first equation of system (3.8). After the corresponding transformations and addition of the third equation of this system, we have the following system of differential equations for the switching functions $L_0(t)$, $L_z(t)$:

$$\begin{cases} \dot{L}_0(t) = \Big(u_*(t)i_*(t) + v_*(t)e_*(t) + u_*(t)i_*(t)e_*^{-1}(t)s_*(t)\Big)L_0(t) \\ \qquad\quad + (\gamma + z_*(t))i_*(t)e_*^{-1}(t)L_z(t) \\ \qquad\quad - \Big(H_*(T)e_*^{-1}(t) + (1+\beta p - (\nu+\gamma)q)i_*(t)e_*^{-1}(t)\Big), \\ \dot{L}_z(t) = u_*(t)s_*(t)L_0(t) + (\gamma + z_*(t))L_z(t) \\ \qquad\quad - (1+\beta p - (\nu+\gamma)q), \\ L_0(T) = p s_*^{-1}(T), \quad L_z(T) = -q. \end{cases} \tag{5.14}$$

For the convenience of the subsequent analysis of this system, we will get rid of the non-homogeneity in the first equation. To do this, we introduce in system (5.14) the auxiliary function:

$$G(t) = (\gamma + z_*(t))L_z(t) - \Big(H_*(T)i_*^{-1}(t) + (1+\beta p - (\nu+\gamma)q)\Big).$$

Then, the first equation of system (5.14) is rewritten as

$$\begin{aligned} \dot{L}_0(t) = \Big(u_*(t)i_*(t) + v_*(t)e_*(t) + u_*(t)i_*(t)e_*^{-1}(t)s_*(t)\Big)L_0(t) \\ + i_*(t)e_*^{-1}(t)G(t). \end{aligned} \tag{5.15}$$

Then, using the third equation of system (2.9) and the second equation of system (5.14) we find the corresponding differential equation for the function $G(t)$:

$$\begin{aligned} \dot{G}(t) = (\gamma + z_*(t))u_*(t)s_*(t)L_0(t) + (\gamma + z_*(t))G(t) \\ + \sigma H_*(T)e_*(t)i_*^{-2}(t). \end{aligned} \tag{5.16}$$

Now, let us introduce in equations (5.15) and (5.16) the following functions:

$$\begin{aligned} a_0(t) &= u_*(t)i_*(t) + v_*(t)e_*(t) + u_*(t)i_*(t)e_*^{-1}(t)s_*(t), \\ b_0(t) &= i_*(t)e_*^{-1}(t), \quad c_0(t) = (\gamma + z_*(t))u_*(t)s_*(t). \end{aligned} \tag{5.17}$$

Then, gathering together equations (5.15) and (5.16), we finally have the system of equations for the switching function $L_0(t)$ and its corresponding auxiliary function $G(t)$:

$$\begin{cases} \dot{L}_0(t) = a_0(t)L_0(t) + b_0(t)G(t), \quad t \in [0,T], \\ \dot{G}(t) \ = c_0(t)L_0(t) + (\gamma + z_*(t))G(t) + \sigma H_*(T)e_*(t)i_*^{-2}(t). \end{cases} \tag{5.18}$$

We will use this system in following arguments for the analysis of the number of zeros of the function $L_0(t)$.

Now, let us obtain a system of equations similar to (5.18) for the analysis of the number of zeros of the function $L_z(t)$. To do this, we introduce in system (5.14) the auxiliary function:

$$Q(t) = u_*(t)L_0(t) - (1 + \beta p - (\nu + \gamma)q)s_*^{-1}(t).$$

Then, the second equation of system (5.14) takes the form:

$$\dot{L}_z(t) = (\gamma + z_*(t))L_z(t) + s_*(t)Q(t). \tag{5.19}$$

Then, using the first equations of systems (2.9) and (5.14) we obtain the corresponding differential equation for the function $Q(t)$:

$$\begin{aligned} \dot{Q}(t) = {} & (\gamma + z_*(t))u_*(t)i_*(t)e_*^{-1}(t)L_z(t) \\ & + \Big(u_*(t)i_*(t) + v_*(t)e_*(t) + u_*(t)i_*(t)e_*^{-1}(t)s_*(t)\Big)Q(t) \\ & - H_*(T)u_*(t)e_*^{-1}(t). \end{aligned} \tag{5.20}$$

Now, by (5.17), let us introduce in equation (5.20) the following functions:

$$a_z(t) = a_0(t), \quad c_z(t) = (\gamma + z_*(t))u_*(t)i_*(t)e_*^{-1}(t). \tag{5.21}$$

Then, gathering together equations (5.19) and (5.20), we finally have the required system of equations for the switching function $L_z(t)$ and its corresponding auxiliary function $Q(t)$:

$$\begin{cases} \dot{L}_z(t) = (\gamma + z_*(t))L_z(t) + s_*(t)Q(t), \quad t \in [0,T], \\ \dot{Q}(t) \ = c_z(t)L_z(t) + a_z(t)Q(t) - H_*(T)u_*(t)e_*^{-1}(t). \end{cases} \tag{5.22}$$

Finally, let us obtain a system of equations similar to (5.18) and (5.22) for the analysis of the number of zeros of the function $L_w(t)$. To do this, we express the term $s_*(t)L_0(t)$ from equality (5.13) and first substitute it into the second equation of system (3.8) and then into the third equation. After corresponding transformations we have the following system of differential equations for the switching functions

$L_w(t)$, $L_z(t)$:

$$
(5.23)\qquad \begin{cases} \dot{L}_w(t) = (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1}\Big\{(\sigma + w_*(t))u_*(t)i_*(t)L_w(t) \\ \qquad -(\sigma u_*(t) + (\gamma + z_*(t))v_*(t))i_*(t)L_z(t) \\ \qquad -(1 + \alpha p - \lambda q)u_*(t)i_*(t) \\ \qquad +(1 + \beta p - (\nu + \gamma)q)v_*(t)i_*(t) + H_*(T)v_*(t)\Big\}, \\ \dot{L}_z(t) = (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1}\Big\{-(\sigma + w_*(t))u_*(t)e_*(t)L_w(t) \\ \qquad +(\sigma u_*(t) + (\gamma + z_*(t))v_*(t))e_*(t)L_z(t) \\ \qquad +(1 + \alpha p - \lambda q)u_*(t)e_*(t) \\ \qquad -(1 + \beta p - (\nu + \gamma)q)v_*(t)e_*(t) + H_*(T)u_*(t)\Big\}. \end{cases}
$$

Again, for the convenience of the subsequent analysis of this system, we will get rid of the non-homogeneity in the first equation. To do this, we introduce in system (5.23) the auxiliary function:

$$
\begin{aligned} P(t) &= (\sigma u_*(t) + (\gamma + z_*(t))v_*(t))L_z(t) + (1 + \alpha p - \lambda q)u_*(t) \\ &\quad - (1 + \beta p - (\nu + \gamma)q)v_*(t) - H_*(T)v_*(t)i_*^{-1}(t). \end{aligned}
$$

Then, the first equation of system (5.23) is rewritten as

$$
(5.24)\qquad \begin{aligned} \dot{L}_w(t) = (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1}\Big\{&(\sigma + w_*(t))u_*(t)i_*(t)L_w(t) \\ &- i_*(t)P(t)\Big\}. \end{aligned}
$$

Next, using the third equation of system (2.9) and the second equation of system (5.23) we find the corresponding differential equation for the function $P(t)$:

$$
(5.25)\qquad \begin{aligned} \dot{P}(t) &= (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1} \\ &\quad \times \Big\{-(\sigma + w_*(t))(\sigma u_*(t) + (\gamma + z_*(t))v_*(t))u_*(t)e_*(t)L_w(t) \\ &\quad + (\sigma u_*(t) + (\gamma + z_*(t))v_*(t))e_*(t)P(t)\Big\} \\ &\quad + \sigma H_*(T)(u_*(t)i_*(t) + v_*(t)e_*(t))i_*^{-2}(t). \end{aligned}
$$

Now, let us introduce in equations (5.24) and (5.25) the following functions:

$$
(5.26)\qquad \begin{aligned} a_w(t) &= (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1}(\sigma + w_*(t))u_*(t)i_*(t), \\ b_w(t) &= (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1}i_*(t), \\ c_w(t) &= (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1} \\ &\qquad \times (\sigma + w_*(t))(\sigma u_*(t) + (\gamma + z_*(t))v_*(t))u_*(t)e_*(t), \\ d_w(t) &= (u_*(t)i_*(t) + v_*(t)e_*(t))^{-1} \\ &\qquad \times (\sigma u_*(t) + (\gamma + z_*(t))v_*(t))e_*(t). \end{aligned}
$$

Then, gathering together equations (5.24) and (5.25), we finally have the required system of equations for the switching function $L_w(t)$ and its corresponding auxiliary function $P(t)$:

$$
\left\{\begin{array}{l}
\dot{L}_w(t) = a_w(t)L_w(t) - b_w(t)P(t), \quad t \in [0,T], \\
\dot{P}(t) \ = -c_w(t)L_w(t) + d_w(t)P(t) \\
\qquad\qquad +\sigma H_*(T)(u_*(t)i_*(t) + v_*(t)e_*(t))i_*^{-2}(t).
\end{array}\right. \tag{5.27}
$$

Next, we execute in systems (5.18), (5.22) and (5.27) the corresponding changes of variables:

$$\widetilde{L}_0(t) = L_0(t), \quad \widetilde{G}(t) = G(t) + h_0(t)L_0(t), \tag{5.28}$$

$$\widetilde{L}_z(t) = L_z(t), \quad \widetilde{Q}(t) = Q(t) + h_z(t)L_z(t), \tag{5.29}$$

$$\widetilde{L}_w(t) = L_w(t), \quad \widetilde{P}(t) = P(t) - h_w(t)L_w(t). \tag{5.30}$$

Here the functions $h_0(t)$, $h_z(t)$ and $h_w(t)$ satisfy the corresponding non-autonomous Riccati equations:

$$\dot{h}_0(t) \ = \ b_0(t)h_0^2(t) - (a_0(t) - (\gamma + z_*(t)))h_0(t) - c_0(t), \tag{5.31}$$

$$\dot{h}_z(t) \ = \ s_*(t)h_z^2(t) + (a_z(t) - (\gamma + z_*(t)))h_z(t) - c_z(t), \tag{5.32}$$

$$\dot{h}_w(t) \ = \ b_w(t)h_w^2(t) - (a_w(t) - d_w(t))h_w(t) - c_w(t). \tag{5.33}$$

Now, we will show that equations (5.31)–(5.33) have the solutions $\widetilde{h}_0(t)$, $\widetilde{h}_z(t)$ and $\widetilde{h}_w(t)$ defined on the entire interval $[0,T]$. For this, we establish the validity of the following lemma.

Lemma 5.7. *Let there be given a non-autonomous Riccati equation:*

$$\dot{h}(t) = a(t)h^2(t) + b(t)h(t) + c(t), \tag{5.34}$$

where $a(t)$, $b(t)$, $c(t)$ are the piecewise continuous functions defined on the interval $[0,T]$, and the functions $a(t)$, $c(t)$ satisfy the following inequalities:

$$a(t) > 0, \quad c(t) < 0, \quad t \in [0,T]. \tag{5.35}$$

Then, there exists the piecewise differentiable solution $\bar{h}(t)$ for equation (5.34) *satisfying the initial condition:*

$$\bar{h}(T) = h_T > 0, \tag{5.36}$$

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

Proof. By Theorem 1A ([33], Chapter 1), there exists the solution $\bar{h}(t)$ for equation (5.34) with the initial condition (5.36) defined on the interval (t_0,t_1), which is the maximum possible interval for the existence of such solution. If the inclusion $[0,T] \subset (t_0,t_1)$ is valid, then the required fact is established. Now, let the inequalities $0 \le t_0 < T < t_1$ hold. In order for the required fact to be true, according to Corollary from Lemma ([16], § 14, Chapter 4) it suffices to show the boundedness of the solution $\bar{h}(t)$ on the interval (t_0,t_1).

For this, we execute in equation (5.34) the change of variable:

$$\widetilde{h}(t) = e^{\int_t^T b(\xi)d\xi}\bar{h}(t).$$

It is easy to see that the function $\widetilde{h}(t)$ satisfies the differential equation:

$$\dot{\widetilde{h}}(t) = \widetilde{a}(t)\widetilde{h}^2(t) + \widetilde{c}(t), \quad t \in (t_0,t_1), \tag{5.37}$$

and, by (5.36), the initial condition:

$$\widetilde{h}(T) = h_T > 0. \tag{5.38}$$

Here the functions:

$$\widetilde{a}(t) = e^{-\int\limits_t^T b(\xi)d\xi} a(t), \quad \widetilde{c}(t) = e^{\int\limits_t^T b(\xi)d\xi} c(t)$$

satisfy inequalities (5.35) as well as the functions $a(t)$, $c(t)$.

From the analysis of equation (5.37) we conclude that the function $\widetilde{h}(t)$, firstly, takes only positive values for all $t \in (t_0, T]$, and, secondly, satisfies the following differential inequalities:

$$\dot{\widetilde{h}}(t) > \widetilde{c}(t), \quad \dot{\widetilde{h}}(t) < \widetilde{a}(t)\widetilde{h}^2(t), \quad t \in (t_0, t_1).$$

Let us integrate these inequalities on the interval $[t, T]$, $t \in (t_0, T)$ with initial condition (5.38). We obtain the inequalities:

$$\widetilde{h}(t) < h_T - \int\limits_t^T \widetilde{c}(\chi)d\chi \leq h_T - \int\limits_0^T \widetilde{c}(\chi)d\chi,$$

$$\widetilde{h}(t) > \left[h_T^{-1} + \int\limits_t^T \widetilde{a}(\chi)d\chi\right]^{-1} \geq \left[h_T^{-1} + \int\limits_0^T \widetilde{a}(\chi)d\chi\right]^{-1},$$

which, by relationships (5.35) and (5.38), imply the required boundedness. This completes the proof. □

Remark 5.8. Justification of Lemma 5.7 is based on the ideas presented in [57].

Thus, the existence of the required solutions $\widetilde{h}_0(t)$, $\widetilde{h}_z(t)$ and $\widetilde{h}_w(t)$ follows from constraints (2.4), formulas (5.17), (5.21) and (5.26), equations (5.31)–(5.33) and Lemmas 2.1 and 5.7.

Moreover, we consider that for each of the solutions $\widetilde{h}_0(t)$, $\widetilde{h}_z(t)$, $\widetilde{h}_w(t)$ the value h_T in (5.36) is given by one of the following equalities:

$$h_T^0 = \beta s_*(T), \tag{5.39}$$

$$h_T^z = (\nu + \gamma)s_*^{-1}(T), \tag{5.40}$$

$$h_T^w = (\lambda + \sigma)u_*(T). \tag{5.41}$$

Next, system (5.18) in new variables (5.28) and with the function $\widetilde{h}_0(t)$ is given by

$$\begin{cases} \dot{\widetilde{L}}_0(t) = \Big(a_0(t) - b_0(t)\widetilde{h}_0(t)\Big)\widetilde{L}_0(t) + b_0(t)\widetilde{G}(t), \quad t \in [0, T], \\ \dot{\widetilde{G}}(t) = \Big((\gamma + z_*(t)) + b_0(t)\widetilde{h}_0(t)\Big)\widetilde{G}(t) + \sigma H_*(T)e_*(t)i_*^{-2}(t). \end{cases} \tag{5.42}$$

Now, system (5.22) in new variables (5.29) and with the function $\widetilde{h}_z(t)$ is written as follows

$$\begin{cases} \dot{\widetilde{L}}_z(t) = \Big((\gamma + z_*(t)) - s_*(t)\widetilde{h}_z(t)\Big)\widetilde{L}_z(t) + s_*(t)\widetilde{Q}(t), \quad t \in [0, T], \\ \dot{\widetilde{Q}}(t) = \Big(a_z(t) + s_*(t)\widetilde{h}_z(t)\Big)\widetilde{Q}(t) - H_*(T)u_*(t)e_*^{-1}(t). \end{cases} \tag{5.43}$$

Finally, system (5.27) in new variables (5.30) and with the function $\widetilde{h}_w(t)$ has the following form:

$$
\left\{
\begin{aligned}
\dot{\widetilde{L}}_w(t) &= \Big(a_w(t) - b_w(t)\widetilde{h}_w(t)\Big)\widetilde{L}_w(t) - b_w(t)\widetilde{P}(t), \quad t \in [0, T], \\
\dot{\widetilde{P}}(t) &= \Big(d_w(t) + b_w(t)\widetilde{h}_w(t)\Big)\widetilde{P}(t) \\
&\quad +\sigma H_*(T)\Big(u_*(t)i_*(t) + v_*(t)e_*(t)\Big)i_*^{-2}(t).
\end{aligned}
\right.
\tag{5.44}
$$

Let us consider systems (5.42)–(5.44). We show that for the corresponding functions $\widetilde{G}(t)$, $\widetilde{Q}(t)$, $\widetilde{P}(t)$ the following lemma is true.

Lemma 5.9. *For the functions $\widetilde{G}(t)$, $\widetilde{Q}(t)$, $\widetilde{P}(t)$, which satisfy systems* (5.42)–(5.44) *together with the corresponding functions $\widetilde{L}_0(t)$, $\widetilde{L}_z(t)$, $\widetilde{L}_w(t)$, the following inequalities hold:*

$$
\widetilde{G}(t) > 0, \quad \widetilde{Q}(t) < 0, \quad \widetilde{P}(t) > 0, \quad t \in [0, T]. \tag{5.45}
$$

Proof. First, let us consider the function $\widetilde{G}(t)$. From constraints (2.4), Corollary 4.3, formula (4.15), the corresponding initial condition of system (5.14) and the definition of the function $G(t)$ we find the equality:

$$
G(T) = e_*(T)i_*^{-1}(T) - \beta p.
$$

Then, by Lemma 2.1, the corresponding initial condition of system (5.14), formulas (5.28) and (5.39), we obtain the relationship:

$$
\widetilde{G}(T) = e_*(T)i_*^{-1}(T) > 0.
$$

Now, let us integrate the following Cauchy problem for the function $\widetilde{G}(t)$:

$$
\left\{
\begin{aligned}
&\dot{\widetilde{G}}(t) = \widetilde{k}_0(t)\widetilde{G}(t) + \sigma H_*(T)e_*(t)i_*^{-2}(t), \quad t \in [0, T], \\
&\widetilde{G}(T) = e_*(T)i_*^{-1}(T),
\end{aligned}
\right.
$$

where $\widetilde{k}_0(t) = (\gamma + z_*(t)) + b_0(t)\widetilde{h}_0(t)$. As a result, we have the following formula:

$$
\begin{aligned}
\widetilde{G}(t) &= e_*(T)i_*^{-1}(T)e^{-\int_t^T \widetilde{k}_0(\xi)d\xi} \\
&\quad - \sigma H_*(T)\int_t^T e^{-\int_t^\chi \widetilde{k}_0(\xi)d\xi} e_*(\chi)i_*^{-2}(\chi)d\chi, \quad t \in [0, T],
\end{aligned}
$$

which, by Lemma 2.1 and Corollary 4.5, implies the positiveness of the function $\widetilde{G}(t)$ on the interval $[0, T]$.

Now, let us consider the function $\widetilde{Q}(t)$. Again, from constraints (2.4), Corollary 4.3, the corresponding initial condition of system (5.14) and the definition of the function $Q(t)$ we obtain the equality:

$$
Q(T) = -s_*^{-1}(T) + (\nu + \gamma)qs_*^{-1}(T).
$$

Then, by Lemma 2.1, the corresponding initial condition of system (5.14), formulas (5.29) and (5.40), we find the relationship:

$$
\widetilde{Q}(T) = -s_*^{-1}(T) < 0.
$$

Now, let us integrate the following Cauchy problem for the function $\widetilde{Q}(t)$:

$$\begin{cases} \dot{\widetilde{Q}}(t) = \widetilde{k}_z(t)\widetilde{Q}(t) - H_*(T)u_*(t)e_*^{-1}(t), \quad t \in [0,T], \\ \widetilde{Q}(T) = -s_*^{-1}(T), \end{cases}$$

where $\widetilde{k}_z(t) = a_z(t) + s_*(t)\widetilde{h}_z(t)$. As a result, we have the following formula:

$$\begin{aligned} \widetilde{Q}(t) = & - s_*^{-1}(T)e^{-\int_t^T \widetilde{k}_z(\xi)d\xi} \\ & + H_*(T)\int_t^T e^{-\int_t^\chi \widetilde{k}_z(\xi)d\xi} u_*(\chi)e_*^{-1}(\chi)d\chi, \quad t \in [0,T], \end{aligned}$$

which, by constraints (2.4), Lemma 2.1 and Corollary 4.5, implies the negativeness of the function $\widetilde{Q}(t)$ on the interval $[0,T]$.

Finally, let us consider the function $\widetilde{P}(t)$. From formula (4.15), the corresponding initial condition of system (5.14) and the definition of the function $P(t)$ we find the equality:

$$\begin{aligned} P(T) = & - (\sigma u_*(T) + (\gamma + z_*(T))v_*(T))q + (\alpha p - \lambda q)u_*(T) \\ & - (\beta p - (\nu + \gamma)q)v_*(T) + (u_*(T) + v_*(T)e_*(T)i_*^{-1}(T)). \end{aligned}$$

Then, by the corresponding initial condition of system (5.14), formulas (5.30) and (5.41), we obtain the equality:

$$\begin{aligned} \widetilde{P}(T) = & p(\alpha u_*(T) - \beta v_*(T)) - qv_*(T)(z_*(T) - \nu) \\ & + (u_*(T) + v_*(T)e_*(T)i_*^{-1}(T)). \end{aligned}$$

By constraints (2.4) and Corollary 4.3, we find that the first two terms in this expression are equal to zero. Thus, by Lemma 2.1, we finally have the following relationship:

$$\widetilde{P}(T) = u_*(T) + v_*(T)e_*(T)i_*^{-1}(T) > 0.$$

Now, let us integrate the following Cauchy problem for the function $\widetilde{P}(t)$:

$$\begin{cases} \dot{\widetilde{P}}(t) = \widetilde{k}_w(t)\widetilde{P}(t) + \sigma H_*(T)\Big(u_*(t)i_*(t) + v_*(t)e_*(t)\Big)i_*^{-2}(t), \quad t \in [0,T], \\ \widetilde{P}(T) = u_*(T) + v_*(T)e_*(T)i_*^{-1}(T), \end{cases}$$

where $\widetilde{k}_w(t) = d_w(t) + b_w(t)\widetilde{h}_w(t)$. As a result, we have the following formula:

$$\begin{aligned} \widetilde{P}(t) = & \Big(u_*(T) + v_*(T)e_*(T)i_*^{-1}(T)\Big)e^{-\int_t^T \widetilde{k}_w(\xi)d\xi} \\ & - \sigma H_*(T)\int_t^T e^{-\int_t^\chi \widetilde{k}_w(\xi)d\xi}\Big(u_*(\chi)i_*(\chi) + v_*(\chi)e_*(\chi)\Big)i_*^{-2}(\chi)d\chi, \end{aligned}$$

which is valid for all $t \in [0,T]$. By constraints (2.4), Lemma 2.1 and Corollary 4.5, this formula implies the positiveness of the function $\widetilde{P}(t)$ on the interval $[0,T]$. This completes the proof. □

Then, applying to the first equations of systems (5.42)–(5.44) the generalized Rolle's Theorem ([17]) and taking into account the corresponding inequalities (5.45), we conclude that for the functions $L_0(t) = \widetilde{L}_0(t)$, $L_z(t) = \widetilde{L}_z(t)$, $L_w(t) = \widetilde{L}_w(t)$ the following lemma holds.

Lemma 5.10. *The switching functions $L_0(t)$, $L_z(t)$, $L_w(t)$ have at most one zero on the interval $[0, T]$.*

This statement shows that Condition 5.1, the validity of which we have previously suggested, is satisfied.

Analyzing again the first equations of systems (5.42)–(5.44), and taking into account the results of Lemmas 4.2, 5.9 and 5.10, we imply the validity of relationships (5.3)–(5.5), (5.7)–(5.9) and (5.10)–(5.12) for the corresponding switching functions $L_0(t)$, $L_z(t)$, $L_w(t)$. Then, using formulas (3.2)–(3.5), we conclude that depending on the values of the weighting coefficients p and q Theorems 5.2–5.5 about the types of the optimal controls $u_*(t)$, $v_*(t)$, $w_*(t)$, $z_*(t)$ hold for this approach as well.

6. Conclusion

In this paper, we considered two various SEIR control models describing the spread of an Ebola epidemic in a population of a constant size. These models are nonlinear, deterministic and involve four bounded controls implying intervention control strategies for stopping Ebola transmission and spreading. Two of them reflect the efforts to protect susceptible individuals from exposed and infected individuals. The other two controls, depending on the model, define the efforts or for the treatment, or for the detection and isolation of exposed and infected individuals. In the considered SEIR control models, the common SEI subsystem was allocated for which the minimization problem of the sum of total fractions of exposed and infected individuals and total weighted costs of control constraints over a given time interval was stated. The corresponding two weighted coefficients are non-negative values that allow us to study several optimal control problems. Using the Pontryagin maximum principle, the analysis of the optimal controls was conducted analytically. It related to the established properties of the switching functions, which completely determined the behavior of the optimal controls. By these properties, we stated that the optimal controls were bang-bang, and then proposed two new approaches for estimating the number of zeros of the switching functions. The basis of all these studies is the linear non-homogeneous non-autonomous system of differential equations for these functions. The first approach relates to the analysis of the Cauchy problems for the derivatives of the switching functions. The second approach is based on using the constancy of the Hamiltonian on the optimal solution of the original problem for reducing by one of the order of the mentioned system for the switching functions. The estimates of the number of switchings of the optimal controls for each considered approach were found. Possible behavior of these controls depending on the values of the weighted coefficients is focused in Theorems 5.2–5.5.

The important conclusion that can be made for the original problem based on the study presented above, is the coincidence of the behavior of the optimal controls obtained by applying the first and second approaches. This means that if as a result of using the first approach some optimal control is a constant function, then this control has the same type as a result of applying the second approach. If as a result of using the first approach some optimal control is a piecewise constant function with one switching, then this control has the same type as a result of applying the second approach as well.

Finally, we will give the epidemiological interpretation of the results presented in Theorems 5.2–5.5. If the weighted coefficients are zero, then we consider the problem of minimizing the total fractions of exposed and infected individuals on the given time interval. The optimal intervention strategies found in this case, correspond to the maximum efforts that can be made. If the weighted coefficients are positive, then we consider the problem of minimizing the sum of the total fractions of exposed and infected individuals and the total weighted costs of the control constraints on the given time interval. All optimal intervention strategies are the piecewise constant functions with at most one switching (each control has its own switching). Before the corresponding switchings, these strategies correspond to the maximum efforts that can be made and after to minimum efforts. If one of the weighted coefficients is zero and the other is not, then we consider the problem of minimizing the sum of the total fractions of exposed and infected individuals and the total weighted costs of the control constraints corresponding to the positive weighted coefficient on the given time interval. The optimal intervention strategies relating to the zero weighted coefficient imply the maximum efforts that can be made, and the optimal intervention strategies corresponding to the positive weighted coefficient are the piecewise constant functions with at most one switching of the type described above.

References

[1] C.L. Althaus, N. Low, E.O. Musa, F. Shuaib and S. Gsteiger, *Ebola virus disease outbreak in Nigeria: transmission dynamics and rapid control*, Epidemics **11** (2015), 80–84.

[2] M.V. Barbarossa, A. Dénes, G. Kiss, Y. Nakata, G. Röst and Z. Vizi, *Transmission dynamics and final epidemic size of Ebola disease outbreaks with varying interventions*, PLoS One **10** (2015), 1–21.

[3] H. Behncke, *Optimal control of deterministic epidemics*, Optim. Contr. Appl. Met. **21** (2000), 269–285.

[4] M. H. A. Biswas, L. T. Paiva and M. R. de Pinho, *A SEIR model for control of infectious diseases with constraints*, Math. Biosci. Eng. **11** (2014), 761–784.

[5] E. Bonyah, K. Badu and S. K. Asiedu-Addo, *Optimal control application to an Ebola model*, Asian Pac. J. Trop. Biomed. **6** (2016), 283–289.

[6] F. Brauer and C. Castillo-Chavez, *Mathematical Models in Population Biology and Epidemiology*, Texts in Applied Mathematics, vol. 40, Springer-Verlag, New York, 2001.

[7] F. Brauer, P. Driessche and J. Wu, *Mathematical Epidemiology*, Mathematical Biosciences Subseries, Lecture Notes in Mathematics, vol. 1945, Springer, Dordrecht, 2008.

[8] B. Buonomo, D. Lacitignola and C. Vargas-De-Leon, *Qualitative analysis and optimal control of an epidemic model with vaccination and treatment*, Math. Comput. Simulat. **100** (2014), 88–102.

[9] A. Camacho, A.J. Kucharski, S. Funk, J. Breman, P. Piot and W.J. Edmunds, *Potential for large outbreaks of Ebola virus disease*, Epidemics **9** (2014), 70–78.

[10] C. Castilho, *Optimal control of an epidemic through educational compaigns*, Electr. J. Differ. Equ. **2006** (2006), 1–11.

[11] Centers for Disease Control and Prevention. Ebola (Ebola virus disease). Atlanta: Centers for Disease Control and Prevention, 2015 [Online] Available from: http://www.cdc.gov/vhf/ebola/transmission/index.html [Accessed on 24th August, 2015].

[12] G. Chowell, N. W. Hengartner, C. Castillo-Chavez, P. W. Fenimore and J. M. Hyman, *The basic reproductive number of Ebola and the effects of public health measures: the cases of Congo and Uganda*, J. Theor. Biol. **229** (2004), 119–126.
[13] G. Chowell, J. M. Hayman, L. M. A. Bettencourt and C. Castillo-Chavez, *Mathematical and Statistical Estimation Approaches in Epidemiology*, Springer, Dordrecht, 2009.
[14] G. Chowell and H. Hishiura, *Transmission dynamics and control of Ebola virus disease (EVD): a review*, BMC Med. **12** (2014), 1–16.
[15] J.-P. Chretien, S. Riley and D. B. George, *Mathematical modeling of the West Africa Ebola epidemic*, eLife **4** (2015), 1–15.
[16] B. P. Demidovich, *Lectures on Stability Theory*, Nauka, Moscow, Russia, 1967.
[17] A. V. Dmitruk, *A generalized estimate on the number of zeros for solutions of a class of linear differential equations*, SIAM J. Control Optim. **30** (1992), 1087–1091.
[18] T. S. Do and Y. S. Lee, *Modeling the spread of Ebola*, Osong Public Health Res. Perspect. **7** (2016), 43–48.
[19] F. Dong, D. Xu, Z. Wang and M. Dong, *Evaluation of Ebola spreading in West Africa and decision of optimal medicine delivery strategies based on mathematical models*, Infect. Genet. Evol. **36** (2015), 35–40.
[20] J. M. Drake, R. B. Kaul, L. W. Alexander, S. M. O'Regan, A. M. Kramer, J. T. Pulliam, M. J. Ferrari and A. W. Park, *Ebola cases and health system demand in Liberia*, PLoS Biol. **13** (2015), 1–20.
[21] I. Ye. Egorov, *Optimal feedback control in a mathematical model of malignant tumor treatment with the immune reaction taken into account*, Mathematical Biology and Bioinformatics **9** (2014), 257–272 (in Russian).
[22] H. Gaff and E. Schaefer, *Optimal control applied to vaccination and treatment strategies for various epidemiological models*, Math. Biosci. Eng. **6** (2009), 469–492.
[23] E. V. Grigorieva and E. N. Khailov, *Optimal vaccination, treatment and preventive campaigns in regard to the SIR epidemic model*, Math. Model. Nat. Phenom. **9** (2014), 105–121.
[24] E. V. Grigorieva and E. N. Khailov, *Optimal intervention strategies for a SEIR control model of Ebola epidemics*, Mathematics **3** (2015), 961–983.
[25] E. Hansen and T. Day, *Optimal control of epidemics with limited resources*, J. Math. Biol. **62** (2011), 423–451.
[26] H. W. Hethcote, *The mathematics of infectious diseases*, SIAM Review **42** (2000), 599–653.
[27] H. R. Joshi, S. Lenhart, S. Hota and F. Agusto, *Optimal control of an SIR model with changing behavior through an educational campaign*, Electr. J. Differ. Equ. **2015** (2015), 1–14.
[28] H. R. Joshi, S. Lenhart, M. Y. Li and L. Wang, *Optimal control methods applied to disease models*, in: AMS Volume on Mathematical Studies on Human Disease Dynamics: Emerging Paradigms and Challenges, AMS Contemporary Mathematics Series, vol. 410, 2006, pp. 187–207.
[29] M. Kiskowski and G. Chowell, *Modeling household and community transmission of Ebola virus disease: epidemic growth, spatial dynamics and insights for epidemic control*, Virulence **7** (2016), 163–173.
[30] P. R. Koya and D. K. Mamo, *Ebola epidemic disease: modelling, stability analysis, spread control technique, simulation study and data fitting*, J. Multidis. Engin. Sci. Tech. **2** (2015), 476–483.
[31] P. E. Lecone and B. F. Finkenstädt, *Statistical inference in a stochastic epidemic SEIR model with control intervention: Ebola as a case study*, Biometrics **62** (2006), 1170–1177.
[32] U. Ledzewicz and H. Schättler, *On optimal singular controls for a general SIR-model with vaccination and treatment*, Discret. Contin. Dyn. S. **supplement** (2011), 981–990.
[33] E. B. Lee and L. Marcus, *Foundations of Optimal Control Theory*, John Wiley & Sons, New York NY, USA, 1967.
[34] J. Legrand, R. F. Grais, P. Y. Boelle, A. J. Valleron and A. Flahault, *Understanding the dynamics of Ebola epidemics*, Epidemiol. Infect. **135** (2007), 610–621.
[35] S. Lenhart and J. T. Workman, *Optimal Control Applied to Biological Models*, CRC Press, Taylor & Francis Group, London, 2007.

[36] J. A. Lewnard, M. L. Ndeffo-Mbah, J. A. Alfaro-Murillo, F. L. Altice, L. Bawo, T. G. Nyenswah and A. P. Galvani, *Dynamics and control of Ebola virus transmission in Montserrado, Liberia: a mathematical modelling analysis*, Lancet Infect. Dis. **14** (2014), 1189–1195.

[37] D. K. Mamo and P. R. Koya, *Mathematical modeling and simulation study of SEIR disease and data fitting of Ebola epidemic spreading in West Africa*, J. Multidis. Engin. Sci. Tech. **2** (2015), 106–114.

[38] R. Morton and K. H. Wickwire, *On the optimal control of a deterministic epidemic*, Adv. Appl. Probab. **6** (1974), 622–635.

[39] R. M. Neilan and S. Lenhart, *An introduction to optimal control with an application in disease modeling*, in: DIMACS Series in Discrete Mathematics, vol. 75, 2010, pp. 67–81.

[40] S. D. D. Njankou and F. Nyabadza, *An optimal control model for Ebola virus disease*, J. Biol. Syst. **24** (2016), 29–49.

[41] M. R. de Pinho, I. Kornienko and H. Maurer, *Optimal control of a SEIR model with mixed constraints and L_1 cost*, in: Controllo'2014 – Proceedings of the 11th Portuguese conference on automatic control, Lecture Notes in Electrical Engineering, vol. 321, Springer, Switzerland, 2015, pp. 135–145.

[42] L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze and E. F. Mishchenko, *Mathematical Theory of Optimal Processes*, John Wiley & Sons, New York NY, USA, 1962.

[43] A. Rachah and D. F. M. Torres, *Mathematical modeling, simulation, and optimal control of 2014 Ebola outbreak in West Africa*, Discrete Dyn. Nat. Soc. article ID 842792 (2015), 1–9.

[44] A. Rachah and D. F. M. Torres, *Optimal control strategies for the spread of Ebola in West Africa*, J. Math. Anal. **7** (2016), 102–114.

[45] A. Rachah and D. F. M. Torres, *Predicting and controlling the Ebola infection*, Math. Method Appl. Sci. doi: 10.1002/mma.3841 (2016), 1–10.

[46] A. Rachah and D. F. M. Torres, *Dynamics and optimal control of Ebola transmission*, Math. Comput. Sci. doi: 10.1007/s11786-016-0268-y (2016), 1–12.

[47] A. Rizzo, B. Pedalino and M. Porfiri, *A network model for Ebola spreading*, J. Theor. Biol. **394** (2016), 212–222.

[48] H. Schättler and U. Ledzewicz, *Geometric optimal control. Theory, methods and examples*, Springer, New York-Heidelberg-Dordrecht-London, 2012.

[49] H. Schättler and U. Ledzewicz, *Optimal control for mathematical models of cancer therapies. An application of geometric methods*, Springer, New York-Heidelberg-Dordrecht-London, 2015.

[50] O. Sharomi and T. Malik, *Optimal control in epidemiology*, Ann. Oper. Res. doi: 10.1007/s10479-015-1834-4 (2015), 1–17.

[51] C.I. Siettos and L. Russo, *Mathematical modeling of infectious dynamics*, Virulence **4** (2013), 295–306.

[52] C. Siettos, C. Anastassopoulou, L. Russo, C. Grogoras and E. Mylonakis, *Forecasting and control policy assessment for the Ebola virus disease (EVD) epidemic in Sierra Leone using small-world networked model simulations*, BMJ Open **6**, e008649, doi: 10.1136/bmjopen-2015-008649 (2016), 1–7.

[53] R. Ullah, G. Zaman, S. Islam and I. Ahmad, *Dynamical features and vaccination strategies in an SEIR epidemic model*, Res. J. Recent Sci. **2** (2013), 48–56.

[54] L.D. Valdez, H.H. Aragão Rêgo, H.E. Stanley and L.A. Braunstein, *Predicting the extinction of Ebola spreading in Liberia due to mitigation strategies*, Sci. Rep. **5**, article 12172, doi: 10.1038/srep12172 (2015), 1–10.

[55] K. H. Wickwire, *Optimal isolation policies for deterministic and stochastic epidemics*, Math. Biosci. **26** (1975), 325–346.

[56] K. H. Wickwire, *Mathematical models for the control of pests and infectious diseases: a survey*, Theor. Popul. Biol. **11** (1977), 182–238.

[57] W. Wong, *Existence of global solution of Riccati equation*, http://math. stackexchange.com/ questions/155180/existence-of-global-solution-of-riccati-equation.

[58] World Health Organization. Ebola situation reports. Geneva: World Health Organization, 2015. [Online] Available from: http://apps.who.int/ebola/current-situation/ebola-situation-report-16-december-2015 [Accessed on 18th December, 2015].

[59] Z.-Q. Xia, S.-F. Wang, S.-L. Li, L.-Y. Huang, W.-Y. Zhang, G.-Q. Sun, Z.-T. Gai and Z. Jin, *Modeling the transmission dynamics of Ebola virus disease in Liberia*, Sci. Rep. **5**, article 13857, doi: 10.1038/srep13857 (2015), 1–13.

[60] D. Yamin, S. Gertler, M.L. Ndeffo-Mbah, L.A. Skrip, M. Fallah, T.G. Nyenswah, F.L. Altice and A.P. Galvani, *Effect of Ebola progression on transmission and control in Liberia*, Ann. Intern. Med. **162** (2015), 11–17.

[61] T. T. Yusuf and F. Benyah, *Optimal control of vaccination and treatment for a SIR epidemiological model*, World Journal of Modelling and Simulation **8** (2012), 194–204.

[62] G. Zaman, Y. Han Kang and I. Hyo Jung, *Stability analysis and optimal vaccination of an SIR epidemic model*, Biosystems **93** (2008), 240–249.

[63] D. Zeng, H. Chen, C. Castillo-Chavez, W.B. Lober and M. Thurmond, *Infectious Disease Informatics and Biosurveillance*, Integrated Series in Information Systems, vol. 27, Springer, New York, 2011.

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