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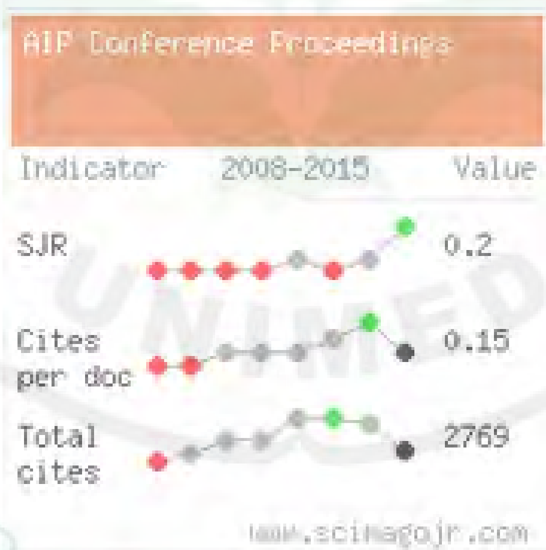

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Faridawaty Marpaung, Yulita M. Rangkuti, and Marlina S. Sinaga

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The Analysis of Optimal Singular Controls for SEIR Model of Tuberculosis

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Abstract. The optimally of singular control for SEIR model of Tuberculosis is analyzed. There are controls that correspond to time of the vaccination and treatment schedule. The optimally of singular control is obtained by differentiate a switching function of the model. The result shows that vaccination and treatment control are singular.

Keywords: SEIR model, Optimal singular control, Switching function, Tuberculosis
PACS: 02.30.Yy; 02.40 Xx; 05.45.-a

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by bacteria Mycobacterium tuberculosis. TB is usually transmitted through contaminated air with Mycobacterium tuberculosis bacteria that are released during coughing TB patients, and in children the source of infection is generally derived from adult TB patients. These bacteria often enter and when accumulated in the lungs will breed a lot (especially in people with a low immune system), and can spread through the blood vessels or lymph nodes. That is why TB infection can infect virtually all body organs such as the lungs, brain, kidneys, gastrointestinal tract, bone, lymph nodes, etc., although the organs most commonly affected are lungs.[1].

Mathematical models have been widely used in different form for studying the transmission dynamics of TB epidemics [2]. Mathematical models have become an important tool in describing the dynamics of the spread of an infectious disease and the effects that vaccination and treatment have on its dynamics. We assume that a susceptible individual goes through a latent period before coming to infectious. The models are conducted as Susceptible Exposed Infected (SEI), Susceptible Exposed Infected Recovery (SEIR) [3] or Susceptible Exposed Infected Susceptible (SEIRS) or so on.

Despite some successes associated with the use of BCG vaccine and some TB treatment therapies, this pandemic has continued to increase and has led to a growing consensus that new control strategies will be needed for disease eradication. The optimal control has a long history of being analyzed to problems in epidemiology problems. Bowong [4] control a tuberculosis model indicating how a control term on the chemoprophylaxis should be introduced in the population to reduce the number of individuals with active TB.Yang et al. [5] focus primarily on controlling the disease using an objective function based on a combination of minimizing the number of TB infections and minimizing the cost of control strategies. In this work, main emphasis is on a complete analysis of the optimally properties corresponding to trajectories. There controls are natural candidates for optimally and are widely used in medical treatment were a maximum dose of treatment is given repeatedly with breaks in between. We develop simple and easily verifiable conditions which allow us to determine the locally of bang-bang control. In this paper, we investigate the optimality singular controls of SEIR models of tuberculosis with vaccination and treatment theoretically. These are controls correspond to time-vary the vaccination and treatment schedules.

EPIDEMIOLOGIC MODELS

The epidemiology model of this paper isSEIR. This model consists of four classes, namely,S represents the susceptible who do not have the disease,E represents the exposed who are infected but are yet to show any sign of symptoms,I represents the infective who have the disease and can transmit it to others, and$R$, denotes the recovered class of those who went through infection and emerge with permanent or temporary infection-acquired immunity.

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In this paper, we consider an SIERmodel[1]. We assume that the treatment in rate s, the recruitment due to immigration in rateγ, the slow and fast progression in rate ϑ, ρ , respectively was omitted.The immunity in the class *R* may not be permanent and the class *R* should be followed by the class *S* of individuals who regain their susceptibility when temporary immunity ends.Therefore we consider the following dynamics:

$$\dot{S} = \pi - \beta IS - \mu S \tag{1}$$

$$\dot{E} = \beta IS - \mu E, \tag{2}$$

$$\dot{I} = DIS + DE - (\mu + \mu_T)I, \tag{3}$$

$$\dot{R} = \varepsilon I - sI - \beta IR - \mu R, \tag{4}$$

Thus, the controlled mathematical model is written as follow

$$\dot{S} = \pi - \beta IS - \mu S - Su, \tag{5}$$

$$\dot{E} = \beta IS - \mu E - Eu, \tag{6}$$

$$\dot{I} = DIS + DE - (\mu + \mu_T)I - Iv, \tag{7}$$

whereπ, represents the rate of recruitment of susceptible individuals, βIS, represents the loss of the number of susceptible individuals that are being infected by individuals from class I with the parameter β standing for the average number of adequate contacts (i.e., contacts sufficient for transmission) of a person per unit of time.

The last term of equation (5), Su represents the effect of vaccination, and it is assumed that vaccination removes the fraction $Su$of individuals from the class S and makes them resistent.In equation (2), the$E$decreasedbynaturaldeath ofthe Eu,andindividualclass $E$to classisinfectious(I)andincreasedas a result ofdisease transmissionβIS, the last term Eu, represents the effect of vaccination of E. The variable$u$ is a control that represents the rate at which susceptible individuals are vaccinated. It takes values in a compact interval, $0 \le u \le u_{max}$. In the I, Eq.3, D, represents detection rate of *TB* . The additional outflow Iv is related to the cure of infected individuals due to treatment and v represents the rate at which infectious individuals are treated at each time period, the second control in the model with values in the interval $0 \le v \le\le v_{max}$.

Thus there are two possible mechanisms as controls: immunization of the susceptible and exposed individuals and treatment of the infected ones. These actions are modeled by the two controls u dan v that for mathematical reasons are taken as Lebesque-measurable functions. The action of both controls enriches the class R of the recovered individuals by removing them from the class of susceptible and infected ones, respectively. The class R is defined as $R = N - I - S - E$. For the model to be realistic, we need to make sure that all the variables including R remain positive. The initial numbers of individuals in each of the populations are positive numbers denoted by

$N(0) = N_0, S(0) = S_0$, $E(0) = E_0$ and $I(0) = I_0$. (8)

Note that if there are no infected individuals initially,$I_0 = 0$,I remains identically zero. The model, thus don't represent the on the set of infection, but only its course.From biological considerations, a closed set

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

where $\mathbb{R}^4$, denote the non-negative cone and its lower dimensional faces. It can be verified that Q is posively invariant with respect to (1-4). We denote by ∂Q and $\dot{Q}$ the boundary and the interior of Q.

FORMULATION AS AN OPTIMAL CONTROL PROBLEM

Let the population sizes of all there classes, S_0, E_0, I_0 and $R_0$are given, find the best strategy in terms of combined efforts of vaccination and treatment that would minimize the number of people who die from the infection while at the same time also minimizing the cost vaccination and treatment of the population.

In this paper, we consider the following objectivefor a fixed terminal time T:

$$J(u, v) = \int_0^T (a_1 + c_1)V + a_2 I(t) + a_3 u(t) + a_4 v(t) dt \tag{9}$$

The first term in the objective, $aE(t)$ represents the number of exposed who are infected but are yet to show any sign of symptoms at time t, $bI(t)$, represents the number of people who are exposed and infected at time t and are taken as *b* measure for the deaths associated with the outbreak. The terms, $cu(t)$ and $dv(t)$ represent the cost of vaccination and treatment, respectively, and are assumed to be proportional to the vaccination and treatment rates.

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

$$\dot{Z} = aE + bI + cu + dv, \qquad Z(0) = 0. \tag{10}$$

We therefore consider the following optimal control problem. For a fixed terminal time , minimize the value $Z(T)$ subject to the dynamics

$$\dot{Z} = aE + bI + cu + dv, \qquad Z(0) = 0, \tag{11}$$
$$\dot{S} = \pi - \beta IS - \mu S - Su \qquad S(0) = 0, \tag{12}$$
$$\dot{E} = \beta IS - \mu E - Eu, \qquad E(0) = 0, \tag{13}$$
$$\dot{I} = DIS + DE - (\mu + \mu_T)I - Iv, \qquad I(0) = 0, \tag{14}$$

Over all Lebesque measurable function

$$u: [O, T] \rightarrow [0, u_{max}] \text{and} v: [0, T] \rightarrow [0, v_{max}]$$

Introducing the state $\dot{x} = (Z, S, E, I)^T$, the dynamics of the system is a multiinput control-affine system of the form

$$\dot{x} = f(x) + g_1(x)u + g_2(x)v, \tag{15}$$

with drift vector field f given by

$$f(x) = \begin{pmatrix} aE + bI \\ \pi - \beta IS - \mu S \\ \beta IS - \mu E \\ DIS + DE - (\mu + \mu_T)I \end{pmatrix}, \tag{16}$$

and control vector fields g_1 and g_2 given by

$$g_1 = \begin{pmatrix} c \\ -S \\ -E \\ 0 \end{pmatrix} \quad \text{and} \quad g_2(x) = \begin{pmatrix} d \\ 0 \\ 0 \\ -I \end{pmatrix}. \tag{17}$$

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

NECESSARY CONDITIONS FOR OPTIMALITY

First-order necessary conditions for optimality of a controlled trajectory by the *Pontryagin maximum principle* [4,15] : For a row-vector $\lambda = (\lambda_1, \lambda_2, \lambda_3, \lambda_4) \epsilon (\mathbb{R}^4)$, we define the Hamiltonian $H = H(\lambda, x, u, v)$ as the dot product, $\langle ., . \rangle$ of the row vector λ with the column vector that defines the dynamics, that is

$$\begin{aligned} H &= \langle \lambda, f(x) + g_1(x)u + g_2(x)v \rangle \\ &= \lambda_1(aE + bI + cu + dv) + \lambda_2(\pi - \beta IS - \mu S - Su) + \lambda_3(\beta IS - \mu E - Eu) \\ &\quad + \lambda_4(DIS + DE - (\mu + \mu_t)I - Iv). \end{aligned} \tag{18}$$

Then, if (u_*, v_*) is an optimal control defined over the interval $[0, T]$ with corresponding trajectory$x_* = (Z_*, S_*, E_*, I_*)^T$, there exists an absolutely continuous co-vector, $\lambda: [0, T] \rightarrow (\mathbb{R}^4)^*$, such that following conditions hold [6]

(a) λsatisfies the adjoin equation (written as row vector and with D_f and D_{gi} denoting the Jacobian matrices of the partial derivatives)

$$\dot{\lambda} = -\lambda(Df(x_*) + Dg_1(x_*)u_* + Dg_2(x_*)v_*), \tag{19}$$

with terminal condition

$$\lambda(T) = \left(\frac{\pi}{\mu}, \quad 0, \quad 0, \quad 0\right) \tag{20}$$

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

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

We call a pair $(x,(u,v))$ consisting of admissible controls (u,v) with corresponding trajectory x for wich there exist multipliers λ such that the conditions of the Maximum Principle are satisfied an *external* (pair) and the triple $(x,(u,v),\lambda)$ is an external lift. Note that the dynamics does not depend on the auxiliary variable Z and thus by the adjoint equation (6) the multiplier λ_1 is constant; by the terminal condition (20) , it is thus given by $\lambda_1(t) \equiv \frac{\pi}{\mu}$. In particular, the overall multiplier $\lambda(t)$ is never zero. For almost any time t, the optimal controls $(u_*(t), v_*(t))$ minimize the Hamiltonian $H(\lambda(t), x_*(t), u, v)$ over the compact interval $[0, u_{max}] \times [0, v_{max}]$. Since H is linear in the controls, this minimization problem s plits into separate one-dimensional problems that can easily be solved. Defining the so-called *switching functions*Φ_1 and Φ_2 as

$$\Phi_1(t) = \langle \lambda(t).\, g_1(x_*(t)) \rangle = c - \lambda_3(t) S_*(t) \tag{21}$$

and

$$\Phi_2(t) = \langle \lambda(t).\, g_2(x_*(t)) \rangle = d - \lambda_4(t) I_*(t) \tag{22}$$

It follows that the optimal controls satisfy

$$u_*(t) = \begin{cases} 0 & if \quad \Phi_1(t) > 0 \\ u_{max} & if \quad \Phi_1 < 0 \end{cases} \text{and} v_*(t) = \begin{cases} 0 & if \quad \Phi_2(t) > 0 \\ v_{max} & if \quad \Phi_2(t) < 0 \end{cases}$$

The minimum condition alone does determine the controls at times when $\Phi_1(t) = 0$. if$\Phi_1(\tau) = 0$, but $\Phi_1(\tau) \neq 0$, then the control switches between the value 0 and its maximum value depending on the sign of $\dot{\Phi_\iota}(\tau)$. Controls with this property are called bang-bang controls and we refer to the constant controls with values in the endpoints of the control intervals as *bang* controls. The other extreme occurs when a switching function vanishes over an open interval. In this case also derivatives of $\Phi_1(t)$ must vanish and this typically allows to compute such a control. Controls of this kind are called *singular* [6]. While the name might give impression that these controls are less important, quite the contrary is true. Singular controls (if they exist) tend to be either that best (minimizing) or the worst (maximizing) strategies and in either case they are essential in determining the structure of optimal controls. This typically needs to be synthesized from bang and singular controls through an analysis of the switching function. Thus singular controls generally play a major role in a synthesis of optimal controlled trajectories and this paper we analyze their existence and local for the problem in Eqs. (11)-(14).

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

$$[f,g](x) = Dg(x)f(x) - Df(x)g(x) \tag{23}$$

The Lie-bracket is anti-commutative, i.e.,$[f,g] = -[g,f]$, and for arbitrary vector fields f, g and h it satisfies the Jacobiidentity [5]

$$[f,[g,h]] + [g,[h,f]] + [h,[f,g]] \equiv 0 \tag{24}$$

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

Proposition 1.*Let $(x,(u,v))$be a controlled trajectory of the system and let λ be a solution to the corresponding adjoint equations. Given a continuously differentiable vector field h , define*

$$\psi(t) = \langle \lambda(t), h(x(t)) \rangle \tag{25}$$

Then the derivative of ψ is given by

$$\dot{\psi}(t) = \langle \lambda(t), [f + g_1 u + g_2 v, h](x(t)) \rangle \tag{26}$$

THE STRUCTURE OF SINGULAR CONTROLS

We investigate the existence and local optimality of singular controls for the system in Eqs (11)-(14). By Propositions 1 the derivatives of the switching functions $\Phi_1(t) = \langle \lambda(t), g_1(x(t)) \rangle$ and $\Phi_2(t) = \langle \lambda(t), g_2(x(t)) \rangle$ are given by

$$\dot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_1] x(t) \rangle \tag{27}$$

$$\dot{\Phi}_2(t) = \langle \lambda(t), [f + g_1 u + g_2 v, g_2] x(t) \rangle \tag{28}$$

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

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

Elementary calculations verify that

$$[f, g_1](x) = \begin{pmatrix} aE \\ -\pi \\ 0 \\ DIS + DE \end{pmatrix} \text{and} [f, g_2](x) = \begin{pmatrix} bI \\ -\beta IS \\ \beta IS \\ -DE \end{pmatrix}.$$

We first analyze the control, i.e., vaccinations schedules. Applying Propositions 2 oncemore to $\dot{\Phi}_1$, it follows that

$$\ddot{\Phi}_1(t) = \langle \lambda(t), [f + g_1 u + g_2 v, [f, g_1]](x(t)) \rangle \tag{29}$$

A direct calculation shows that g_2 and $[f, g_1]$ commute as well, $[g_2, [f, g_1]] \equiv \begin{pmatrix} 0 \\ 0 \\ 0 \\ ED \end{pmatrix}$, and that

$$[g_1, [f, g_1]](x) = \begin{pmatrix} -aE \\ -\pi \\ 0 \\ -DSI - DE \end{pmatrix}.$$

The relation

$$\dot{\Phi}_1 \equiv -\lambda_1(t) aE(t) - \lambda_2(t)\pi(t) + \lambda_4(t)(DSI + DE)(t) \equiv 0 \tag{30}$$

Implies that

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_4(t)(DSI + DE)(t)$$

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

$$\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle = -2\lambda_4(t)(DSI + DE)(t) < 0$$

Singular controls of this type, i.e., for which $\langle \lambda(t), [g_1, [f, g_1]](x(t)) \rangle$ does not vanish, are said to be of order 1 and it is a second-order necessary condition for minimallity, the so-called *Legendre-Clebsh condition,* that this quantity be negative [9]. Thus for this model singular controls u are locally optimal. Furthermore, in this case, we taking into account that $[g_2, [f, g_1]] \equiv \begin{pmatrix} 0 \\ 0 \\ 0 \\ DE \end{pmatrix}$, we can compute the singular control as

$$u_{sin}(t) = -\frac{\langle \lambda(t), [f, [f, g_1]](x(t)) \rangle}{\langle \lambda(t), [g_1, [f, g_1](x(t))] \rangle} \tag{31}$$

Here,

$$[f, [f, g_1]](x) = \begin{pmatrix} a\beta IS - a\mu E - bDIS - bDE \\ -\pi\beta I - \pi\mu + \pi\beta S^2 DI + \pi\beta SDE \\ \pi\beta I - \beta S^2 DI - \beta SDE \\ 2DI\pi - DI^2\beta S - DI\mu S + D\beta IS + \mu_T \end{pmatrix} \tag{32}$$

Since $\langle \lambda(t), [f, g_1](x(t)) \rangle \equiv 0$, it follows from (31) that

$$\mu_{sin}(t) = -\frac{1}{2\lambda_2 \pi}\left[-\lambda_2(a\beta IS + bDIS + bDE) + \psi(t)(\lambda_2 - \lambda_3) - \mu - \frac{\lambda_4}{2\lambda_2}\left(\frac{\mu + \mu_T}{\pi}\right) DE\right], \tag{33}$$

where, $\psi(t) = \beta I\pi - \pi\beta S^2 DI - \pi\beta SDE$. Therefore, we obtain the following result

Proposition 2. *A singular control u is of order* 1 *and satisfies the Legendre-Clebsch condition for minimality. The singular control is given as a function depending both on the state and the multiplier in the form*

$$u_{sin}(t) = -\frac{1}{2\lambda_2\pi}\left[-\lambda_2(\alpha\beta IS + bDIS + bDE) + \psi(t)(\lambda_2 - \lambda_3) - \mu - \frac{\lambda_4}{2\lambda_2}\left(\frac{\mu+\mu_T}{\pi}\right)DE\right]$$

where $\psi(t) = \beta I\pi - \pi\beta S^2 DI - \pi\beta S.$

For treatment control, we define the switching function as

$$\Phi_2(t) = \langle\lambda(t), g_2(x(t))\rangle \quad (34)$$

By using proposition 2, the first derivative of Eq. 34 we have

$$\dot{\Phi}_2(t) = (\lambda(t), [f, g_2](x)(t)) = \lambda_1 bI - \lambda_2\beta IS + \lambda_3\beta IS - \lambda_4 DE \quad (35)$$

As we know, to check the optimally Eq 34, Eq. 35 will be zero, we habe

$$(\lambda(t), [f, g_2](x)(t)) = \lambda_1 bI - \lambda_2\beta IS + \lambda_3\beta IS - \lambda_4 DE = 0. \quad (36)$$

Hence, we have

$$\ddot{\Phi}_2 = (\lambda, f, [f, g_2])$$
$$= -\lambda_1(bI\mu - bDIS - 2bDE + \alpha\beta IS) - \lambda_2(\beta S^2 DI + \beta SDE + \beta^2 I^2 S - \pi\beta SDE)$$
$$+ \lambda_3(\pi\beta I - \mu\beta IS + \beta S^2 DI + 2\beta SDE) - \lambda_4(2D\beta IS - DI^2\beta S - D^2 ES + 2DE\mu_T) < 0$$

It also shows a second-order necessary condition for minimallity, the so-called *Legendre-Clebsh condition,* that this quantity be negative . Thus for this model singular controls are locally optimal. Furthermore, in this case,and taking

$$v_{sin}(t) = -\frac{\langle\lambda(t), [f, [f, g_2]](x(t))\rangle}{\langle\lambda(t), [g_2, [f, g_2]](x(t))\rangle}. \quad (37)$$

Here, we have

$$(\lambda, f, [f, g_2]) = -\lambda_1(bI\mu - bI\mu_T - bDIS - 2bDE + \alpha\beta IS) - \lambda_2(\beta S^2 DI + \mu_T\beta IS + \beta SDE + \beta^2 I^2 S - \pi\beta SDE) + \lambda_3(\pi\beta I - \mu\beta IS + \beta S^2 DI - \mu_T\beta IS + 2\beta SDE) - \lambda_4(2D\beta IS - DI^2\beta S - D^2 ES - DE\mu_T)$$

and $\left(\lambda\left(g_2(f, g_2)\right)\right) = -\lambda_1 bI - \lambda_4$

we can compute the singular control as

$$v_{sin}(t) = \frac{1}{-(\lambda_1 bI + \lambda_4 DE)}(\lambda_1 bDIS + 2\lambda_1 bDE - \lambda_1 bI\mu - \lambda_1 bI\mu_T - \lambda_1\alpha\beta IS - \lambda_2\beta S^2 DI - \lambda_2\beta SDE + \lambda_2\beta SI\mu_T$$
$$- \lambda_2\beta^2 I^2 S + \lambda_2\pi\beta SDE + \lambda_3\pi\beta I - \lambda_3\mu\beta IS + \lambda_3\beta S^2 DI + 2\lambda_3\beta SDE + \lambda_3\beta SI\mu_T - 2\lambda_4 D\beta IS$$
$$+ \lambda_4 DI^2\beta S + \lambda_4 D^2 ES - \lambda_4 DE\mu_T) \quad (38)$$

Therefore, we obtain the following result:

Proposition 3.*The control v issingular.*

CONCLUSION

The optimal singular control problem for an SEIR-model of Tuberculosis was discussed. The structure singular controls was analized to determine singularity properties of the model. We apply Lie bracket of vector field to check whether the second order of switching function was vanish or not. For the calculation we used Maple. Based on our computation, we found that the vaccination and treatment schedulesare singulars. The optimality of vaccination and treatment for other epidemology problem can be analized in future.

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