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Optimal Control of an "SIR" Epidemic Model in a Chemostat Using Some Suitable Protein Doses

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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Abstract

A modified "SIR" epidemic model is proposed taking into account of suitable protein doses that are applied on the total population as a control to manage a disease outbreak when treatments are not available. The proteins cause a change in behavior resulting in three susceptible classes. The stability analysis is studied and the optimal control theory is applied to the system of differential equations to achieve the goal of minimizing the infected population (while minimizing the cost). Some numerical simulations are given in order to illustrate the obtained results.

Keywords: "SIR" epidemic model; optimal control; Pontryagin's Maximum Principle.

2010 Mathematics Subject Classification: 34D23, 35N25, 37B25, 49K40, 60H10, 65C30, 91B70.

1 Introduction

Understanding how an epidemic develops once it has emerged is crucial if we want to hope to control it. To do this, various models have been developed which highlight (in particular) the crucial role played by the parameter $\mathcal{R}_0$, describing the average number of new infections due to a sick individual. As one can imagine, if this number is less than 1 then the epidemic will tend to go out, whereas it will be able to persist even to extend to the entire population if $\mathcal{R}_0 > 1$. However,

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these classical models obviously have their limits and the parameter $\mathcal{R}_0$ does not really describe on its own the future of an epidemic in a real population (assuming that we know how to find it in this case). For example, the fact that a population is always finished induces random effects all the more marked that the population is small. On the other hand, most populations also have a structure in the form of groups within which bacteria are closer (and therefore more easily infected) than between groups. All this requires finer models and the development of the tools necessary for their study.
In a chemostat, an epidemic model can also be understood as a competition model where various pathogen strains compete for the the same susceptible host as only resource [1, 2]. Such models predict the strain with the largest basic reproduction number to be the winner. In [2], it is proved that this prediction amount to the same if the per capita functional responses of infective bacteria to the density of susceptible are proportional to each other but that they are different if the functional responses are non-proportional.
The effects of changing behavior is important in epidemic outcomes, and now such effects are beginning to be included in models [3, 4]. Management strategies of how to motivate bacteria to make such behavior changes will become increasingly important.

The present article is a contribution to this question. More precisely, a proposed investigating for the level of suitable protein doses that are applied on the population as a control to manage a disease outbreak when the treatments are not available or too costly to be widely used. The model is adapted from [5] to have three susceptible classes depending on behavior and having different transmission rates and with time-varying protein doses. With limited resources, the balance between benefits of lower numbers of infected and the cost of the protein doses is investigated using optimal control theory on this system of differential equations, the protein doses is taken as the control.
In the next section, the model is formulated and discuss briefly its stability analysis. The optimal control problem is formulated as an objective functional in section 3. Finally, some numerical simulations are given in section 4 with some concluding comments.

2 Mathematical Model and Analysis

An optimal control model is developped of Susceptible, Infected and Recovered- an SIR type model. In this optimal control problem, the used control is the protein doses, which helps to change the behavior of some bacteria in the susceptible class.
It has been taked into account of the dilution rate only and all individual specific mortality (maintenance) rates are neglected. Only susceptible bacteria are introduced into the reactor with a constant dilution rate D and an input concentration S_{in} (Fig. 1).

This change in behavior leads to subdividing susceptible into three subclasses, namely S, S_1 and S_2. A proportion of the susceptible populations, S, decide to change their behavior due to an effect of the protein doses and thus enter in the S_1 or S_2 class. These two classes, S_1 and S_2, have lower transmission rates than the S class and will contribute to lower the number of new infections and thus also lower the recovered/removed population (Fig. 2).

The proposed model is given by the following system of ordinary differential equations describing the effect of protein doses on Susceptible as following:

$$\begin{cases} \dot{S} &= DS_{in} - (a_1 + a_2)PS - bSI - DS \\ \dot{S}_1 &= a_1 PS - b_1 S_1 I - DS_1 \\ \dot{S}_2 &= a_2 PS - b_2 S_2 I - DS_2 \\ \dot{I} &= \big(bS + b_1 S_1 + b_2 S_2 - (D+\gamma)\big)I \\ \dot{R} &= \gamma I - DR \end{cases} \tag{2.1}$$

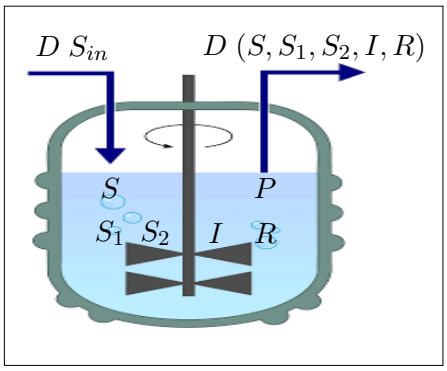

Fig. 1: A modified "SIR" epidemic model taking into account of some suitable protein doses that are applied to all bacteria as a control variable.

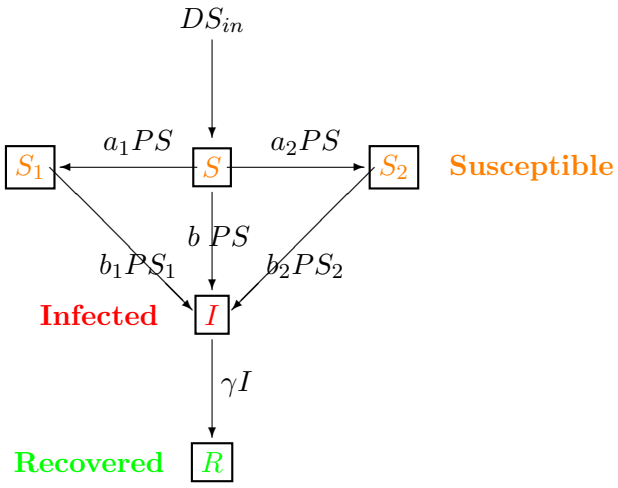

Fig. 2: A modified "SIR" epidemic model taking into account of some suitable protein doses that are applied to all bacteria as a control to manage a disease outbreak when treatments are not available.

with initial conditions S_0, S_{10}, S_{20}, I_0, and R_0. The input concentration of Susceptible into the reactor is given by S_{in} and with a dilution rate D. Since there is three susceptible classes, three infection rates b, b_1, b_2 are proposed for S, S_1, and S_2 respectively for their interactions with the Infected class I. Notice that, as a result of interactions of bacteria in class S with the control, protein doses P, a proportion of the susceptible leave the general susceptible class S and move to S_1 and S_2. The rate of moving into class S_i for $i = 1, 2$ is $a_i PS$. Also, as a result of each susceptible class interacting with the infected class we have bacteria leaving at their respective rates and moving to the infected class. The rate γ is the transition rate where bacteria leave the infected class I and move to the removed class R. The removed class R could represent recovered, infected or removed

bacteria due to disease related deaths.

Since model (2.1) represents bacterial populations, all parameters in the model are non-negative and one can show that the solutions of the system are non-negative, given non-negative initial values [6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18].

$\mathbb{R}^5_+$, the closed non-negative cone in $\mathbb{R}^5$, is positively invariant by the system (2.1). More precisely,

Proposition 1.

1. For all initial condition in $\mathbb{R}^5_+$, the solution of system (2.1) is bounded and has positive components and thus is defined for all $t > 0$.
2. System (2.1) admits a positive invariant attractor set of all solution given by $\Omega = \{(S, S_1, S_2, I, R) \in \mathbb{R}^5_+ \ / \ S + S_1 + S_2 + I + R = S_{in}\}$.

Proof. 1. The positivity of the solution is proved by the fact that :
If $S = 0$ then $\dot{S} = DS_{in} > 0$ and if $S_1 = 0$ then $\dot{S}_1 = a_1PS > 0$. If $S_2 = 0$ then $\dot{S}_2 = a_2PS > 0$ and if $I = 0$ then $\dot{I} = 0$. Finally, if $R = 0$ then $\dot{R} = \gamma I > 0$.
Next one has to prove the boundedness of solutions of (2.1). By adding all equations of system (2.1), one obtains, for $T = S + S_1 + S_2 + I + R - S_{in}$, a single equation for total populations :

$$\begin{aligned} \dot{T} &= \dot{S} + \dot{S}_1 + \dot{S}_2 + \dot{I} + \dot{R} \\ &= D(S_{in} - S - S_1 - S_2 - I - R) \\ &= -DT \end{aligned}$$

then

$$S + S_1 + S_2 + I + R = S_{in} + \Big(S_0 + S_{10} + S_{20} + I_0 + R_0 - S_{in}\Big)e^{-Dt}. \tag{2.2}$$

Since all terms of the sum are positive, then the solution of system (2.1) is bounded.

2. The second point is simply a direct consequence of equality (2.2)

□

To consider the stability of the model, it is temporarily assumed that the control P is just a constant parameter. Under this assumption, $P(t) = p$, where p is a constant and the model (2.1) has a disease free equilibrium, obtained by setting the right-hand sides of the equations in the model to zero, given by

$$\mathcal{E}_0 = (S^*, S_1^*, S_2^*, I^*, R^*) = \Big(\frac{DS_{in}}{(a_1 + a_2)p + D}, \frac{a_1pS_{in}}{(a_1 + a_2)p + D}, \frac{a_2pS_{in}}{(a_1 + a_2)p + D}, 0, 0\Big).$$

The stability of $\mathcal{E}_0$ can be established using the next generation operator method on the system (2.1). As I is the infected compartment, then using the notation in [19], the Jacobian matrices F and V for the new infection terms and the remaining transfer terms are respectively given by,

$$J_1 = [bS^* + b_1S_1^* + b_2S_2^*] \ \text{ and } \ J_2 = [D + \gamma].$$

It follows that the basic reproduction number of the system (2.1), denoted by $\mathcal{R}_0$, is given by

$$\mathcal{R}_0 = \rho(J_1J_2^{-1}) = \frac{bS^* + b_1S_1^* + b_2S_2^*}{(D + \gamma)} = \frac{Db + (a_1b_1 + a_2b_2)p}{(D + \gamma)((a_1 + a_2)p + D)}S_{in}, \tag{2.3}$$

where ρ is the spectral radius.

Further, using [19, Theorem 2], the following result is established.

Lemma 1. The disease free equilibrium of system (2.1) (with $P(t) = p$), given by $\mathcal{E}_0$, is locally asymptotically stable if $\mathcal{R}_0 < 1$, and unstable if $\mathcal{R}_0 > 1$.

The basic reproduction number ($\mathcal{R}_0$) measures the average number of new infections generated by a single infected individual in a completely susceptible population [20, 19]. Thus, Lemma 1 implies that the infection can be eliminated from the population (when $\mathcal{R}_0 < 1$) if the initial sizes of the sub-populations are in the basin of attraction of the disease free equilibrium, $\mathcal{E}_0$. The endemic equilibrium does not considered here since the case when a disease outbreak has just started was considered.

3 Optimal Control Problem via Suitable Protein Doses

In this section, let focus on the optimal control problem using a time-varying control function $P(t)$ describing suitable protein doses applied on susceptible bacteria to change their behavior. The control set $\mathbf{P_{ad}}$ is

$$\mathbf{P_{ad}} = \{P(t) : 0 \leq P_{\min} \leq P(t) \leq P_{\max} < 1,\ 0 \leq t \leq T,\ P(t) \text{ is Lebesgue measurable}\}.$$

The goal is to find the control $P(t)$ and associated state variables $S(t)$, $S_1(t)$, $S_2(t)$, $I(t)$, and $R(t)$ to minimize the following objective functional:

$$J[P] = \int_0^T \Big(I(t) - \alpha\big(S(t) + S_1(t) + S_2(t)\big) + \beta P(t)\Big)\, dt.$$

By choosing appropriate positive balancing constants α and β, the goal is to minimize the infected population, and maximize the susceptible population while minimizing the cost of the control. If one only wants to minimize the infected population and not be concerned with the level of the S, S_1 and S_2 populations, one would take $\alpha = 0$, The structure of this model bounded solutions for finite final time T. This objective functional and the differential equations are linear in the control with bounded states, and one can show by standard results that an optimal control and corresponding optimal states exist [21].

By applying Pontryagin's Maximum Principle [21, 22, 23] we derive necessary conditions for our optimal control and corresponding states. The Hamiltonian is

$$\begin{aligned} H = {} & I - \alpha(S + S_1 + S_2) + \beta P + \lambda_1(-a_1PS - a_2PS - bSI + DS_{in} - DS) + \lambda_2(a_1PS - b_1S_1I - DS_1) \\ & + \lambda_3(a_2PS - b_2S_2I - DS_2) + \lambda_4(bSI + b_1S_1I + b_2S_2I - DI - \gamma I) + \lambda_5(\gamma I - DR) \end{aligned} \tag{3.1}$$

For a given optimal control P^*, there exist adjoint functions, $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$, corresponding to the states S, S_1, S_2, I, and R such that:

$$\begin{aligned} \dot{\lambda}_1 &= -\frac{\partial H}{\partial S} = -[-\alpha + \lambda_1(-a_1P - a_2P - bI - D) + a_1\lambda_2P + a_2\lambda_3P + b\lambda_4I], \\ \dot{\lambda}_2 &= -\frac{\partial H}{\partial S_1} = -[-\alpha + \lambda_2(-b_1I - D) + b_1\lambda_4I], \\ \dot{\lambda}_3 &= -\frac{\partial H}{\partial S_2} = -[-\alpha + \lambda_3(-b_2I - D) + b_2\lambda_4I], \\ \dot{\lambda}_4 &= -\frac{\partial H}{\partial I} = -[1 + \lambda_1(-bS) + \lambda_2(-b_1S_1) - b_2\lambda_3S_2 + \lambda_4(bS + b_1S_1 + b_2S_2 - D - \gamma) + \gamma\lambda_5], \\ \dot{\lambda}_5 &= -\frac{\partial H}{\partial R} = -D\lambda_5, \end{aligned} \tag{3.2}$$

where $\lambda_1(T) = 0, \lambda_2(T) = 0, \lambda_3(T) = 0, \lambda_4(T) = 0$, and $\lambda_5(T) = 0$ are the transversality conditions.

The Hamiltonian is minimized with respect to the control variable at P^*. Since the Hamiltonian is linear in the control, one must consider if the optimal control is bang-bang (at its lower or upper bound), singular or a combination. The singular case could occur if the slope or the switching function,

$$\frac{\partial H}{\partial P} = \beta + [-(a_1+a_2)\lambda_1 + a_1\lambda_2 + a_2\lambda_3]S, \tag{3.3}$$

is zero on non-trivial interval of time. Note that the optimal control would be at its upper bound or its lower bound according to:

$$\frac{\partial H}{\partial P} < 0 \quad \text{or} \quad > 0.$$

To investigate the singular case, suppose that $\dfrac{\partial H}{\partial P} = 0$ on some non-trivial interval. In this case, by calculating

$$\frac{d}{dt}\left(\frac{\partial H}{\partial P}\right) = 0$$

and then one can see that control is not present in that equation. To solve for the value of the singular control, let further calculate

$$\frac{d^2}{dt^2}\left(\frac{\partial H}{\partial P}\right) = 0.$$

The above equation can be written in the form (see Appendix A)

$$\frac{d^2}{dt^2}\left(\frac{\partial H}{\partial P}\right) = f_1(t)P(t) + f_2(t) = 0$$

and then the singular control is expressed as

$$P_{\text{singular}}(t) = -\frac{f_2(t)}{f_1(t)},$$

if

$$f_1(t) \neq 0 \quad \text{and} \quad P_{\min} \leq -\frac{f_2(t)}{f_1(t)} \leq P_{\max}$$

with

$$\begin{aligned}
&f_1(t)\\
&= -DS_{in}[(a_1+a_2)^2\lambda_1 - (a_1+a_2)(a_1\lambda_2+a_2\lambda_3)] - \big[a_1(b_1-b)\lambda_2\\
&\quad + a_2(b_2-b)\lambda_3 + (a_1(b-b_1)+a_2(b-b_2))\lambda_4\big](a_1+a_2)SI\\
&= -DS_{in}[(a_1+a_2)^2\lambda_1 - (a_1+a_2)(a_1\lambda_2+a_2\lambda_3)]\\
&\quad - [a_1(b-b_1)(\lambda_4-\lambda_2) + a_2(b-b_2)(\lambda_4-\lambda_3)](a_1+a_2)SI\\
&= -DS_{in}(a_1+a_2)\frac{\beta}{S} - [a_1(b-b_1)(\lambda_4-\lambda_2) + a_2(b-b_2)(\lambda_4-\lambda_3)](a_1+a_2)SI
\end{aligned}$$

and

$$\begin{aligned}
&f_2(t)\\
&= -DS_{in}\Big\{[b(a_1+a_2)\lambda_1 - a_1b_1\lambda_2 - a_2b_2\lambda_3 + (a_1(b_1-b)+a_2(b_2-b))\lambda_4]I\\
&\quad + D\frac{\beta}{S}\Big\} + \Big\{a_1(b_1-b)(b_1I+D)\lambda_2 + a_2(b_2-b)(b_2I+D)\lambda_3 + (a_1b_1(b-b_1)\\
&\quad + a_2b_2(b-b_2))\lambda_4 I - (a_1(b-b_1)+a_2(b-b_2))((bS+b_1S_1+b_2S_2\\
&\quad - D-\gamma)\lambda_4 + 1 + \alpha - b\lambda_1 S - b_1\lambda_2 S_1 - b_2\lambda_3 S_2 + \gamma\lambda_5)\Big\}SI + \big[a_1(b_1-b)\lambda_2\\
&\quad + a_2(b_2-b)\lambda_3 + (a_1(b-b_1)+a_2(b-b_2))\lambda_4\big]\Big\{(bS+b_1S_1+b_2S_2\\
&\quad - (D+\gamma))SI + (-bSI + DS_{in} - DS)I\Big\}
\end{aligned}$$

To check the generalized Legendre-Clebsch condition for the singular control to be optimal, it require $\frac{d}{dP}\frac{d^2}{dt^2}\left(\frac{\partial H}{\partial P}\right) = f_1(t)$ to be negative [24]. To summarize, the control characterization is: On a nontrivial interval,

$$\begin{aligned}
&\text{if } \frac{\partial H}{\partial P} < 0 \text{ at } t, \text{ then } P^*(t) = P_{\max},\\
&\text{if } \frac{\partial H}{\partial P} > 0 \text{ at } t, \text{ then } P^*(t) = P_{\min},\\
&\text{if } \frac{\partial H}{\partial P} = 0, \text{ then } P_{\text{singular}}(t) = -\frac{f_2}{f_1}.
\end{aligned}$$

Hence, the control is optimal at t provided $f_1(t) < 0$ and $P_{\min} \leq -\frac{f_2(t)}{f_1(t)} \leq P_{\max}$.

4 Numerical Results and Conclusions

Consider a subdivision of the time interval $[0, T]$ as follows

$$[0,T] = \bigcup_{n=0}^{N-1} [t_n, t_{n+1}], \quad t_n = n\delta t, \quad \delta t = T/N$$

Let $S^n, S_1^n, S_2^n, I^n, R^n, \lambda_1^n, \lambda_2^n, \lambda_3^n, \lambda_4^n, \lambda_5^n$ and P^n be an approximation of $S(t), S_1(t), S_2(t), I(t), R(t)$, $\lambda_1(t)$, $\lambda_2(t), \lambda_3(t)$ and the control $P(t)$ at the time t_n. $S^0, S_1^0, S_2^0, I^0, R^0, \lambda_1^0, \lambda_2^0, \lambda_3^0, \lambda_4^0, \lambda_5^0$ and P^0 as the state and adjoint variables and the controls at initial time. $S^N, S_1^N, S_2^N, I^N, R^N, \lambda_1^N, \lambda_2^N, \lambda_3^N, \lambda_4^N, \lambda_5^N$ and P^N as the state and adjoint variables and the control at final time T.
In order to resolve the stae system, a created improving the Gauss-Seidel-like implicit finite-difference method was applied.
For the adjoint system, a first-order backward-difference is applied and then the following appropriated scheme was adapted:

$$\begin{cases}
\frac{S^{n+1} - S^n}{\delta t} &= D\, S_{in} - DS^n - (a_1 + a_2)P^n S^n - bS^n I^n,\\
\frac{S_1^{n+1} - S_1^n}{\delta t} &= a_1 P^n S^n - b_1 S_1^n I^n - DS_1^n,\\
\frac{S_2^{n+1} - S_2^n}{\delta t} &= a_2 P^n S^n - b_2 S_2^n I^n - DS_2^n,\\
\frac{I^{n+1} - I^n}{\delta t} &= bS^n I^n + b_1 S_1^n I^n + b_2 S_2^n I^n - (D+\gamma) I^n,\\
\frac{R^{n+1} - R^n}{\delta t} &= \gamma I^n - DR^n,\\
\frac{\lambda_1^{N-n-1} - \lambda_1^{N-n}}{\delta t} &= -\Big[-\alpha + \lambda_1^{N-n}(-a_1 P^n - a_2 P^n - bI^{n+1} - D) + a_1 \lambda_2^{N-n} P^n\\
&\quad + a_2 \lambda_3^{N-n} P^n + b\lambda_4^{N-n} I^{n+1}\Big],\\
\frac{\lambda_2^{N-n-1} - \lambda_2^{N-n}}{\delta t} &= -\Big[-\alpha + \lambda_2^{N-n}(-b_1 I^{n+1} - D) + b_1 \lambda_4^{N-n} I^{n+1}\Big],\\
\frac{\lambda_3^{N-n-1} - \lambda_3^{N-n}}{\delta t} &= -\Big[-\alpha + \lambda_3^{N-n}(-b_2 I^{n+1} - D) + b_2 \lambda_4^{N-n} I^{n+1}\Big],\\
\frac{\lambda_4^{N-n-1} - \lambda_4^{N-n}}{\delta t} &= -\Big[1 + \lambda_1^{N-n}(-bS^{n+1}) + \lambda_2^{N-n}(-b_1 S_1^{n+1}) - b_2 \lambda_3^{N-n} S_2^{n+1}\\
&\quad + \lambda_4^{N-n}(bS^{n+1} + b_1 S_1^{n+1} + b_2 S_2^{n+1} - D - \gamma) + \gamma \lambda_5^{N-n}\Big],\\
\frac{\lambda_5^{N-n-1} - \lambda_5^{N-n}}{\delta t} &= -D\lambda_5^{N-n}.
\end{cases}$$

Hence, the algorithm given in Appendix B will be applied under MATLAB software to solve the optimality system and then one deduces the optimal control.

Table 1: Description of the variables and parameters for model (2.1)

Variable	Description	
$S(t)$	Susceptible bacteria	
$S_1(t),\ S_2(t)$	Susceptible bacteria who change their behavior due to protein doses	
$I(t)$	Infected bacteria	
$R(t)$	Removed bacteria	
Parameter	**Description**	**Value**
D	Dilution rate	0.0015
S_{in}	Input concentration of susceptible	10/3
$a_1\ a_2$	Transfer rate of protein doses	0.0019, 0.0152
$b,\ b_1,\ b_2$	Infection rate	0.0040, 0.0002, 0.0016
γ	Removal rate	0.005
$P_{\min},\ P_{\max}$	Control lower and upper bound	0, 0.85
$\alpha,\ \beta$	Balancing constant	0, 5×10^{-2}

The numerical simulation of system (2.1) are done using parameter values in Table 1 and initial conditions, $S_0 = 1.5$, $S_{10} = 0$, $S_{20} = 0$, $I_0 = 1.2$, $R_0 = 0.05$, $P(0) = 0.5$, except when otherwise stated. With no control, the basic reproductive number $\mathcal{R}_0$ is 2.0513, thus, indicating the disease free equilibrium is unstable. Here S_0, S_{10}, S_{20}, I_0 and R_0, as well as the corresponding states in the figures, are in millions of bacteria.

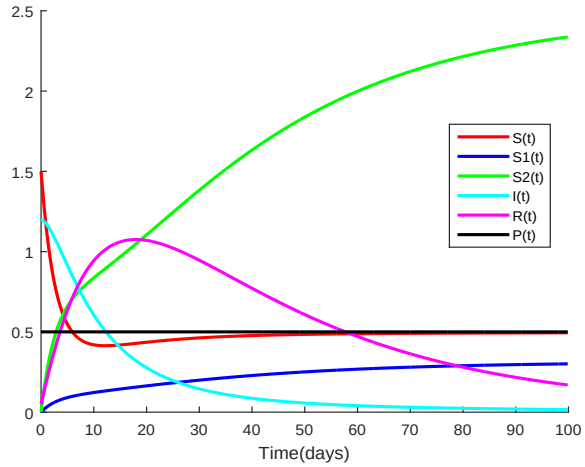

Fig. 3: Numerical simulations for system (2.1), using the parameter values in Table 1.

Fig. 4 shows a higher number of susceptible bacteria in the absence of vitamin (without control) compared to the application of vatamin doses (with control). This is due to the fact that susceptible bacteria in the community are not changing their behavior which causes them to move to either of the two other susceptible classes S_1 and S_2.

By increasing a_2, the S_2-class increases and then the reduction in the total number of infected

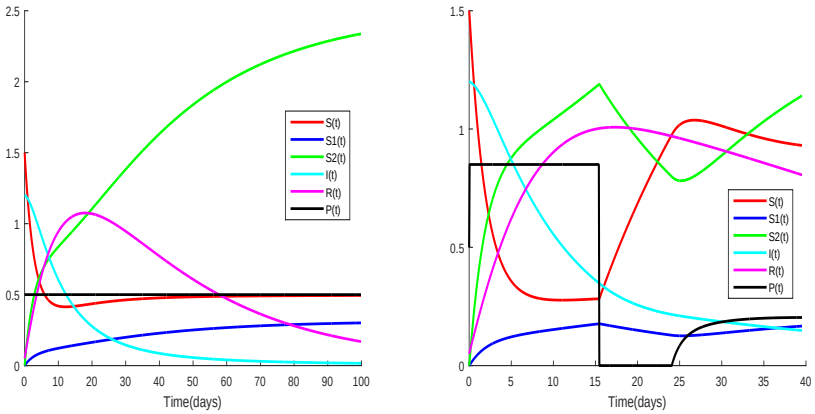

Fig. 4: Numerical simulation of system (2.1) without control ($P(t) = p$, constant) compared to the application of vatamin doses (with control $P(t)$).

bacteria(Fig. 5).

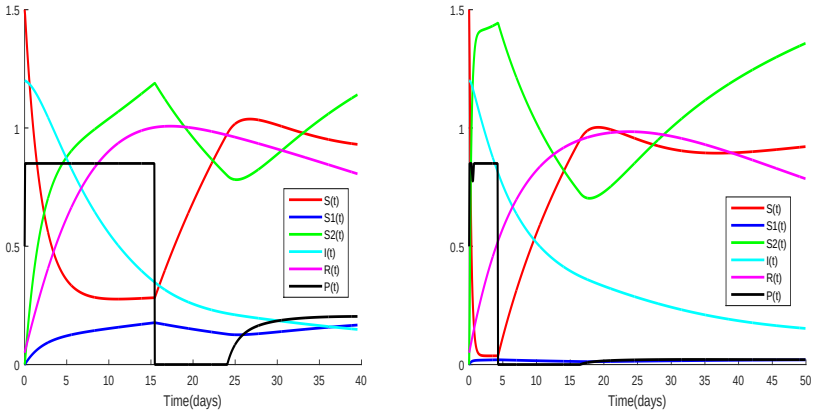

Fig. 5: $a_2 = 0.0152$ left and $a_2 = 0.152$ right.

Same by increasing the input concentration of susceptible $S_{in} = 20/3$, one need more time to obtain an efficient effect of the strategy (Fig. 6).

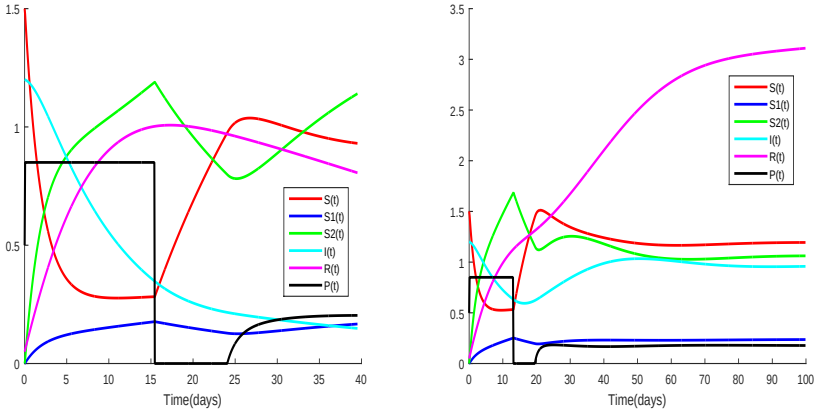

Fig. 6: $S_{in} = 10/3$ left and $S_{in} = 20/3$ right.

Next by increasing the upper bound $P_{\max} = 1.75$, the S-compartment decreases however the S_1- and S_2-compartments increase and then a reduction of infected bacteria and a decrease of the time control (Fig. 7).

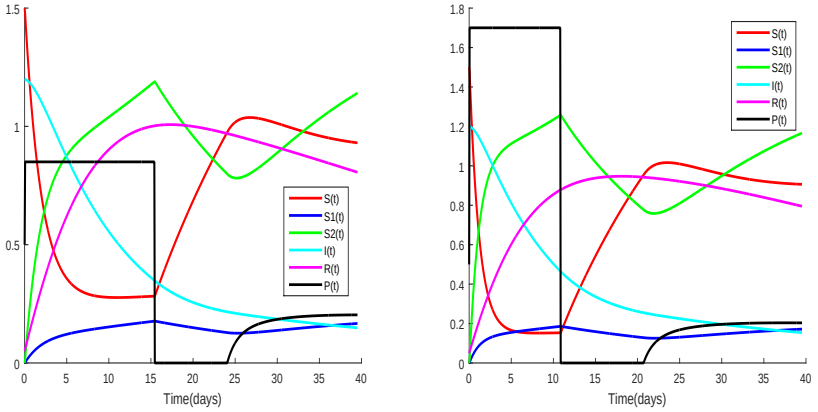

Fig. 7: $P_{\max} = 0.085$ left and $P_{\max} = 1.7$ right.

To conclude, an optimal control for a model with three susceptible classes due to changing behavior has been illustrated. The behavior changes result from an application of some protein doses to susceptible. This work demonstrates an optimal control tool allowing to slow down an epidemic with a strategy by applying a protein doses process in a continuous reactor.

Competing Interests

Author has declared that no competing interests exist.

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Appendices

A Singular control

By simplifying the time derivative of $\frac{\partial H}{\partial P}$,

$$\begin{aligned} 0 &= \frac{d}{dt}\left(\frac{\partial H}{\partial P}\right) = \frac{d}{dt}\{\beta + [-(a_1+a_2)\lambda_1 + a_1\lambda_2 + a_2\lambda_3]S\} \\ &= [-(a_1+a_2)\lambda_1 + a_1\lambda_2 + a_2\lambda_3]\dot{S} + [-(a_1+a_2)\dot{\lambda}_1 + a_1\dot{\lambda}_2 + a_2\dot{\lambda}_3]S \end{aligned} \tag{A.1}$$

Both sums can be calculated separately and then added together. The first sum can be written as:

$$\begin{aligned} &[-(a_1+a_2)\lambda_1 + a_1\lambda_2 + a_2\lambda_3]\dot{S} \\ &= [-(a_1+a_2)\lambda_1 + a_1\lambda_2 + a_2\lambda_3][-(a_1+a_2)PS - bSI + DS_{in} - dS] \\ &= (a_1+a_2)^2\lambda_1 PS + b(a_1+a_2)\lambda_1 SI - (DS_{in} - dS)(a_1+a_2)\lambda_1 \\ &\quad - a_1(a_1+a_2)\lambda_2 PS - a_1 b\lambda_2 SI + (DS_{in} - dS)a_1\lambda_2 \\ &\quad - a_2(a_1+a_2)\lambda_3 PS - a_2 b\lambda_3 SI + (DS_{in} - dS)a_2\lambda_3 \end{aligned}$$

The second sum can be written as:

$$\begin{aligned} &(a_1+a_2)\{-\alpha + \lambda_1[-(a_1+a_2)P - bI - D] + a_1\lambda_2 P + a_2\lambda_3 P + b\lambda_4 I\}S \\ &- a_1[-\alpha + \lambda_2(-b_1 I - D) + b_1\lambda_4 I]S - a_2[-\alpha + \lambda_3(-b_2 I - D) + b_2\lambda_4 I]S \\ &= -(a_1+a_2)^2\lambda_1 PS - b(a_1+a_2)\lambda_1 IS - D(a_1+a_2)\lambda_1 S + a_1(a_1+a_2)\lambda_2 PS \\ &\quad + a_2(a_1+a_2)\lambda_3 PS + b(a_1+a_2)\lambda_4 SI + a_1(b_1 I + D)\lambda_2 S - a_1 b_1\lambda_4 SI \\ &\quad + a_2(b_2 I + D)\lambda_3 S - a_2 b_2\lambda_4 SI \end{aligned}$$

Thus combining, one has

$$\begin{aligned} 0 = \frac{d}{dt}\left(\frac{\partial H}{\partial P}\right) &= -DS_{in}(a_1+a_2)\lambda_1 - a_1 b\lambda_2 SI + DS_{in}a_1\lambda_2 \\ &\quad - a_2 b\lambda_3 SI + DS_{in}a_2\lambda_3 + b(a_1+a_2)\lambda_4 SI \\ &\quad + a_1 b_1\lambda_2 SI - a_1 b_1\lambda_4 SI + a_2 b_2\lambda_3 SI - a_2 b_2\lambda_4 SI \\ &= [-DS_{in}(a_1+a_2)\lambda_1 + DS_{in}a_1\lambda_2 + DS_{in}a_2\lambda_3] + (a_1 b_1 - a_1 b)\lambda_2 SI \\ &\quad + (a_2 b_2 - a_2 b)\lambda_3 SI + [b(a_1+a_2) - a_1 b_1 - a_2 b_2]\lambda_4 SI \\ &= DS_{in}[a_1(\lambda_2 - \lambda_1) + a_2(\lambda_3 - \lambda_1)] \\ &\quad + \{a_1(b_1 - b)\lambda_2 + a_2(b_2 - b)\lambda_3 + [a_1(b - b_1) + a_2(b - b_2)]\lambda_4\}SI. \end{aligned}$$

It can be seen that the control does not explicitly show in this expression, so next let calculate the second derivative with respect to time.

$$\begin{aligned} 0 &= \frac{d^2}{dt^2}\left(\frac{\partial H}{\partial P}\right) \\ &= DS_{in}[a_1(\dot{\lambda}_2 - \dot{\lambda}_1) + a_2(\dot{\lambda}_3 - \dot{\lambda}_1)] + \Big\{a_1(b_1 - b)\dot{\lambda}_2 + a_2(b_2 - b)\dot{\lambda}_3 \\ &\quad + [a_1(b - b_1) + a_2(b - b_2)]\dot{\lambda}_4\Big\}SI + \Big\{a_1(b_1 - b)\lambda_2 \\ &\quad + a_2(b_2 - b)\lambda_3 + [a_1(b - b_1) + a_2(b - b_2)]\lambda_4\Big\}(S\dot{I} + \dot{S}I) \end{aligned} \tag{A.2}$$

Using systems (2.1) and (3.2), then simplify (A.2) as follows

$$
\begin{aligned}
0 &= \frac{d^2}{dt^2}\left(\frac{\partial H}{\partial P}\right) \\
&= -DS_{in}\Big\{[b(a_1+a_2)\lambda_1 - a_1b_1\lambda_2 - a_2b_2\lambda_3 + (a_1(b_1-b)+a_2(b_2-b))\lambda_4]I \\
&\quad + D[(a_1+a_2)\lambda_1 - a_1\lambda_2 - a_2\lambda_3] + \left[(a_1+a_2)^2\lambda_1\right. \\
&\quad \left. - (a_1+a_2)(a_1\lambda_2+a_2\lambda_3)\right]P\Big\} + \Big\{a_1(b_1-b)(b_1I+D)\lambda_2 \\
&\quad + a_2(b_2-b)(b_2I+D)\lambda_3 + (a_1b_1(b-b_1)+a_2b_2(b-b_2))\lambda_4 I \\
&\quad - (a_1(b-b_1)+a_2(b-b_2))((bS+b_1S_1+b_2S_2-D-\gamma)\lambda_4 \\
&\quad + 1+\alpha - b\lambda_1 S - b_1\lambda_2 S_1 - b_2\lambda_3 S_2 + \gamma\lambda_5)\Big\}SI \\
&\quad + [a_1(b_1-b)\lambda_2 + a_2(b_2-b)\lambda_3 + (a_1(b-b_1)+a_2(b-b_2))\lambda_4] \\
&\quad \times \Big\{(bS+b_1S_1+b_2S_2-(d+\gamma))SI + (-(a_1+a_2)PS - bSI + DS_{in} - DS)I\Big\}.
\end{aligned}
$$

The above equation can be written in the form

$$\frac{d^2}{dt^2}\left(\frac{\partial H}{\partial P}\right) = f_1(t)P(t) + f_2(t) = 0$$

and then solve for the singular control as

$$P_{\text{singular}}(t) = -\frac{f_2(t)}{f_1(t)},$$

if

$$f_1(t) \neq 0 \quad \text{and} \quad P_{\min} \leq -\frac{f_2(t)}{f_1(t)} \leq P_{\max}$$

B Algorithm for the optimal control resolution

Algorithm B.1.

1: $S^0 \leftarrow S_0, S_1^0 \leftarrow S_{10}, S_2^0 \leftarrow S_{20}, I^0 \leftarrow I_0, R^0 \leftarrow R_0, \lambda_1^N \leftarrow 0, \lambda_2^N \leftarrow 0, \lambda_3^N \leftarrow 0, \lambda_4^N \leftarrow 0, \lambda_5^N \leftarrow 0,$
$P^0 \leftarrow P(0),$

2: **for** $n = 0$ *to* $N-1$ **do**

$$
\begin{array}{lcl}
S^{n+1} & \leftarrow & S^n + \delta t\Big(D\ S_{in} - DS^n - (a_1+a_2)P^nS^n - bS^nI^n\Big),\\
S_1^{n+1} & \leftarrow & S_1^n + \delta t\Big(a_1P^nS^n - b_1S_1^nI^n - DS_1^n\Big),\\
S_2^{n+1} & \leftarrow & S_2^n + \delta t\Big(a_2P^nS^n - b_2S_2^nI^n - DS_2^n\Big),\\
I^{n+1} & \leftarrow & I^n + \delta t\Big(bS^nI^n + b_1S_1^nI^n + b_2S_2^nI^n - (D+\gamma)I^n\Big),\\
R^{n+1} & \leftarrow & R^n + \delta t\Big(\gamma I^n - DR^n\Big),\\
\lambda_1^{N-n-1} & \leftarrow & \lambda_1^{N-n} - \delta t\Big[-\alpha + \lambda_1^{N-n}(-a_1P^n - a_2P^n - bI^{n+1} - D) + a_1\lambda_2^{N-n}P^n\\
 & & +a_2\lambda_3^{N-n}P^n + b\lambda_4^{N-n}I^{n+1}\Big],\\
\lambda_2^{N-n-1} & \leftarrow & \lambda_2^{N-n} - \delta t\Big[-\alpha + \lambda_2^{N-n}(-b_1I^{n+1} - D) + b_1\lambda_4^{N-n}I^{n+1}\Big],\\
\lambda_3^{N-n-1} & \leftarrow & \lambda_3^{N-n} - \delta t\Big[-\alpha + \lambda_3^{N-n}(-b_2I^{n+1} - D) + b_2\lambda_4^{N-n}I^{n+1}\Big],\\
\lambda_4^{N-n-1} & \leftarrow & \lambda_4^{N-n} - \delta t\Big[1 + \lambda_1^{N-n}(-bS^{n+1}) + \lambda_2^{N-n}(-b_1S_1^{n+1}) - b_2\lambda_3^{N-n}S_2^{n+1}\\
 & & +\lambda_4^{N-n}(bS^{n+1} + b_1S_1^{n+1} + b_2S_2^{n+1} - D - \gamma) + \gamma\lambda_5^{N-n}\Big],\\
\lambda_5^{N-n-1} & \leftarrow & \lambda_5^{N-n} - \delta tD\lambda_5^{N-n},\\
f_1^{n+1} & \leftarrow & -DS_{in}(a_1+a_2)\dfrac{\beta}{S^{n+1}} - [a_1(b-b_1)(\lambda_4^{N-n-1} - \lambda_2^{N-n-1})\\
 & & +a_2(b-b_2)(\lambda_4^{N-n-1} - \lambda_3^{N-n-1})](a_1+a_2)S^{n+1}I^{n+1}\\
f_2^{n+1} & \leftarrow & -DS_{in}\Big\{[b(a_1+a_2)\lambda_1^{N-n-1} - a_1b_1\lambda_2^{N-n-1} - a_2b_2\lambda_3^{N-n-1}\\
 & & +(a_1(b_1-b)+a_2(b_2-b))\lambda_4^{N-n-1}]I^{n+1} + D\dfrac{\beta}{S^{n+1}}\Big\}\\
 & & +\Big\{a_1(b_1-b)(b_1I^{n+1}+D)\lambda_2^{N-n-1} + a_2(b_2-b)(b_2I^{n+1}+D)\lambda_3^{N-n-1}\\
 & & +(a_1b_1(b-b_1)+a_2b_2(b-b_2))\lambda_4^{N-n-1}I^{n+1} - (a_1(b-b_1)\\
 & & +a_2(b-b_2))((bS^{n+1} + b_1S_1^{n+1} + b_2S_2^{n+1} - D - \gamma)\lambda_4^{N-n-1} + 1 + \alpha\\
 & & -b\lambda_1^{N-n-1}S^{n+1} - b_1\lambda_2^{N-n-1}S_1^{n+1} - b_2\lambda_3^{N-n-1}S_2^{n+1} + \gamma\lambda_5^{N-n-1})\Big\}S^{n+1}I^{n+1}\\
 & & +\big[a_1(b_1-b)\lambda_2^{N-n-1} + a_2(b_2-b)\lambda_3^{N-n-1} + (a_1(b-b_1)\\
 & & +a_2(b-b_2))\lambda_4^{N-n-1}]\Big\{(bS^{n+1} + b_1S_1^{n+1} + b_2S_2^{n+1} - (D+\gamma))S^{n+1}I^{n+1}\\
 & & +(-bS^{n+1}I^{n+1} + DS_{in} - DS^{n+1})I^{n+1}\Big\}\\
P^{n+1} & \leftarrow & \max(\min(-\dfrac{f_2^{n+1}}{f_1^{n+1}}, P_{\max}), P_{\min}),\\
S^*(n+1) & \leftarrow & S^{n+1}, S_1^*(n+1) \leftarrow S_1^{n+1}, S_2^*(n+1) \leftarrow S_2^{n+1},\\
I^*(n+1) & \leftarrow & I^{n+1}, R^*(n+1) \leftarrow R^{n+1}, P^*(n+1) \leftarrow P^{n+1}.
\end{array}
$$

end

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