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Multiple Optimal Control Strategies in a Vector-Borne Reaction-Diffusion Model

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Abstract. Mathematical models aim to help predictions and possible contention of disease spread, in particular vector-borne diseases. We have been working with a reaction-diffusion model that considers spatial movement of humans and vectors, with local contact transmission of Zika virus. Control measures, namely vaccination, human and vector contact reduction and vector elimination, are introduced in order to characterize an optimal strategy that minimizes the costs associated with infections and interventions. The optimal control characterization for each control variable is obtained in terms of state and adjoint equations. Numerical simulations are carried out using data for the initial 2015 Zika outbreak in the state of Rio Grande do Norte in Brazil. Several scenarios are simulated and analyzed in terms of number of new infections and costs, showing that the optimal control application is successful.

Keywords Optimal control, Epidemiology, Zika virus, Partial differential equations, Numerical methods.

1 Introduction

Mathematical models have been widely used in epidemiology, including vector-borne diseases, in order to obtain a better understanding that can help prediction and intervention. Dengue, Chikungunya, Zika, are examples of vector-borne diseases with worldwide concern, as they are transmitted by the same mosquitoes, *Aedes aegypti* and *Aedes albopictus*. Also, Zika virus can be transmitted directly between human, through sexual relations, for example, and is associated with neurological conditions in newborn babies from infected mothers [10]. In an ongoing project, we have been working in the application of optimal control of a hypothetical vaccine in a reaction-diffusion vector-borne model applied to Zika virus [6]. This partial differential equation (PDE) model accounts for spatial spread of the virus in humans and mosquitoes. Although the application of

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vaccination alone is capable of lowering the number of infections in a Zika outbreak, it is also important to consider other kinds of control measures, such as human and vector contact reduction, and mosquito elimination. In the present work, we apply these intervention measures by extending the model studied in our previous work [6], using numerical simulations and optimal control theory to obtain a strategy that gives a minimum cost associated to adopted measures and resulting infections.

2 Mathematical modeling and optimal control

We developed a reaction-diffusion PDE system model to study the spread of Zika virus, using SIR (Susceptible – Infected – Removed) dynamics for humans and SI (Susceptible – Infected) for mosquitoes (vectors). The model consists of five compartments: Susceptible (S), Infected (I) and Immune (R) humans, and Susceptible (S_v) and Infected (I_v) mosquitoes/vectors [3]. The word "infected" is used to denote that a human or a vector in its corresponding class is able to transmit the virus. All populations are able to spatially move, which is described in the model by diffusion. The control rates $\boldsymbol{u} = (u_1, u_2, u_3, u_4)$ are defined as follows: u_1 is vaccination, u_2 is vector contact reduction in humans, such as use of repellents, u_3 is human contact reduction, as prophylaxis, and u_4 is vector elimination, by use of insecticide and elimination of breeding sites. A flow chart for the model is shown in Figure 1. Due to the studied periods the model does not include birth and death of human population, but logistic growth is considered for vectors.

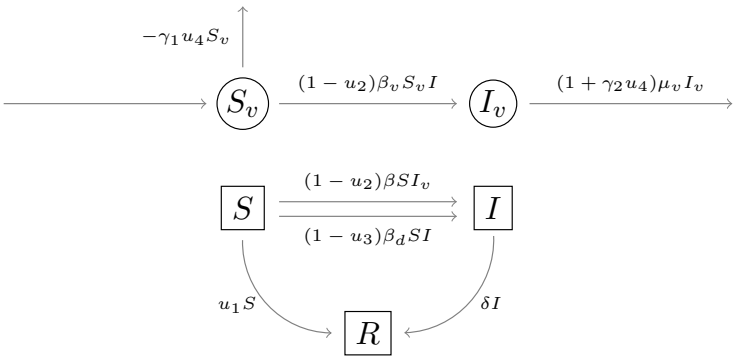

Figure 1: Flow chart for model (1). Squares denote humans and circles mosquitoes. S, I, R denote susceptible, infected, and immune, respectively

The state system is given by (1) in $Q = \Omega \times (0, T)$, and a summary of its parameters and meanings can be found in Table 1. All populations S, I, R, S_v, I_v and the controls u_1, u_2, u_3, u_4 are functions of space $\boldsymbol{x} = (x, y)$ and time $t \in (0, T)$, with spatial domain $\Omega \subset \mathbb{R}^2$ and smooth boundary $\partial\Omega$. Boundary conditions are no flux, with derivatives in the outward normal direction $\boldsymbol{n}$ equal to zero [7]. Initial conditions S_0, I_0, R_0, S_{v0} and I_{v0} are properly defined in each situation of interest. In the model, α, α_I and α_v are diffusion coefficients, β, β_d and β_v are vector to human, human to human, and human to vector transmission rates, δ is the disease recovery rate, r_v is the mosquito birth rate, κ_v

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is the mosquito carrying capacity, μ_v is the mosquito death rate, γ_1 and γ_2 are mosquito mortality rates associated to control u_4.

$$\begin{cases} \dfrac{\partial S}{\partial t} - \nabla \cdot (\alpha \nabla S) = -(1-u_2)\beta S I_v - (1-u_3)\beta_d S I - u_1 S, \\ \dfrac{\partial I}{\partial t} - \nabla \cdot (\alpha_I \nabla I) = (1-u_2)\beta S I_v + (1-u_3)\beta_d S I - \delta I, \\ \dfrac{\partial R}{\partial t} - \nabla \cdot (\alpha \nabla R) = u_1 S + \delta I, \\ \dfrac{\partial S_v}{\partial t} - \nabla \cdot (\alpha_v \nabla S_v) = -(1-u_2)\beta_v S_v I + (1-u_4) r_v \left(S_v + I_v\right)\left(1 - \dfrac{S_v + I_v}{\kappa_v}\right) - \gamma_1 u_4 S_v, \\ \dfrac{\partial I_v}{\partial t} - \nabla \cdot (\alpha_v \nabla I_v) = (1-u_2)\beta_v S_v I - (1+\gamma_2 u_4)\mu_v I_v, \text{ in } Q, \\ S(\boldsymbol{x},0) = S_0,\ I(\boldsymbol{x},0) = I_0,\ R(\boldsymbol{x},0) = R_0,\ S_v(\boldsymbol{x},0) = S_{v0},\ I_v(\boldsymbol{x},0) = I_{v0}, \text{ in } \Omega, \\ \dfrac{\partial S}{\partial \boldsymbol{n}} = 0,\ \dfrac{\partial I}{\partial \boldsymbol{n}} = 0,\ \dfrac{\partial R}{\partial \boldsymbol{n}} = 0,\ \dfrac{\partial S_v}{\partial \boldsymbol{n}} = 0,\ \dfrac{\partial I_v}{\partial \boldsymbol{n}} = 0, \text{ in } \partial\Omega \times (0,T). \end{cases} \quad (1)$$

Our goal is to minimize the costs associated to infected humans and mosquitoes, and to all controls during a time interval. Therefore, considering the state system (1) as a constraint, we wish to minimize the cost objective functional given by:

$$J(u) = \int_Q \left(A_1 I + A_2 I_v + (B_1 u_1 + B_2 u_2 + B_3 u_3) S + B_4 u_4 (S_v + I_v) + \sum_{i=1}^{4} C_i u_i^2 \right) d\boldsymbol{x} dt, \quad (2)$$

where A_1, A_2, B_1, B_2, B_3, B_4, C_1, C_2, C_3, C_4, are constant weights representing costs. A_1 are A_2 are related to costs of infected humans and mosquitoes, respectively; B_i are related to u_i application costs; and C_i are related to u_i nonlinear logistic and production costs of the controls themselves, $i = 1, \ldots, 4$, respectively.

All controls are bounded, non-negative and belong to $L^2(Q)$. It is possible to show that, in the appropriate weak sense, a solution of system (1) exists and is unique, as well as a solution for the optimal control problem for a sufficiently small time [5]. Solutions of the optimal control problem are obtained by solving an optimality system consisting of the state PDEs, adjoint PDEs (in the adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$), and a characterization of the optimal control. After a careful derivation procedure very similar to that performed in [4, 6, 8], the optimal control characterizations are given by:

$$\begin{aligned} u_1^* &= \min\left(u_{1\max}, \max\left(0, \frac{(\lambda_1 - \lambda_3 - B_1)S^*}{2C_1}\right)\right). \\ u_2^* &= \min\left(u_{2\max}, \max\left(0, \frac{(\beta(-\lambda_1 + \lambda_2)I_v^* - B_2)S^* + \beta_v(-\lambda_4 + \lambda_5)S_v^* I^*}{2C_2}\right)\right). \\ u_3^* &= \min\left(u_{3\max}, \max\left(0, \frac{(\beta_d(-\lambda_1 + \lambda_2)I^* - B_3)S^*}{2C_3}\right)\right). \\ u_4^* &= \min\left(u_{4\max}, \max\left(0, \frac{(r_v\left(1 - (S_v^* + I_v^*)/\kappa_v\right)\lambda_4 - B_4)(S_v^* + I_v^*) + \gamma_1\lambda_4 S_v^* + \gamma_2\mu_v\lambda_5 I_v^*}{2C_4}\right)\right). \end{aligned} \quad (3)$$

Where $\boldsymbol{u}_{\max} = (u_{1\max}, u_{2\max}, u_{3\max}, u_{4\max})$ are upper bounds on the controls, the adjoint variables $\lambda_1, \lambda_2, \lambda_3, \lambda_4, \lambda_5$ are obtained by solving the adjoint system, and the * superscript denotes optimality.

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3 Numerical Simulations

We use MATLAB (version R2015a) PDE toolbox to obtain numerical simulations for the optimality system, combined with the Forward-Backward Sweep, an iterative method that updates the state and adjoint systems, and the controls using characterization (3) until convergence is reached [4]. We based our simulations in the initial 2015 Zika epidemic in Rio Grande do Norte state, for which there is available data [9]. Parameter estimates were obtained from literature [1, 2], estimated, or assumed. Transmission rates β and β_v were estimated using a least squares approach, in order to find parameters for model (1) that produce results close to data. Cost weights related to controls were assumed based on real life costs. All parameters values are shown in Table 1.

Table 1: Parameters with values used in simulations

	Value	Unit		Value	Unit
β	1.28×10^{-5}	1/(mosq./km^{2}days)	γ_2	0.1	1/days
β_v	1.55×10^{-2}	1/(hum./km^{2}days)	A_1	66.67	(\$/hum.)/days
β_d	7.81×10^{-5}	1/(hum./km^{2}days)	A_2	2.38	(\$/mosq.)/days
$1/\delta$	15	days	B_1	175	\$/hum.
$1/r_v$	14	days	B_2	1	(\$/hum.)/days
$1/\mu_v$	14	days	B_3	0.1	(\$/hum.)/days
κ_v	321.4	mosq./km^2	B_4	0.02	(\$/mosq.)/days
α	5	km^2/days	C_1	1000	\$/(km^2/days)
α_I	5	km^2/days	C_2	10	(\$/km^2)/days
α_v	0.3	km^2/days	C_3	10	(\$/km^2)/days
γ_1	0.1	1/days	C_4	500	(\$/km^2)/days

Table 2: Optimal control results

	$\boldsymbol{u} = \mathbf{0}$	$\boldsymbol{u} = \boldsymbol{u}_{\max}$	$\boldsymbol{u} = \boldsymbol{u}^*$
Total incidence	4.5238×10^5	3.8691×10^4	1.0256×10^5
$J(\boldsymbol{u})$	6.2397×10^8	1.0731×10^9	2.0410×10^8

We considered a final time of 140 days, corresponding to available data. Several scenarios were considered, but we show graphical results for only one of them, with all optimal controls starting to be applied 35 days after the beginning of the simulation. Plots for infected humans are in Figure 2, and for all controls in Figure 3, at selected times. Integrating the solutions over space, in Figure 4 we have plots representing the total number of each population and control over time. In order to assess the efficacy of the optimal control, in Table 2 we show the total incidence, or number of new cases, and the cost $J(u)$ for simulations without control ($\boldsymbol{u} = \mathbf{0}$), with constant controls at upper bounds ($\boldsymbol{u} = \boldsymbol{u}_{\max}$), and with optimal control ($\boldsymbol{u} = \boldsymbol{u}^*$). The cost is lowest at the optimal control, as expected, and highest with controls at the upper bounds. Also, the incidence lowers as

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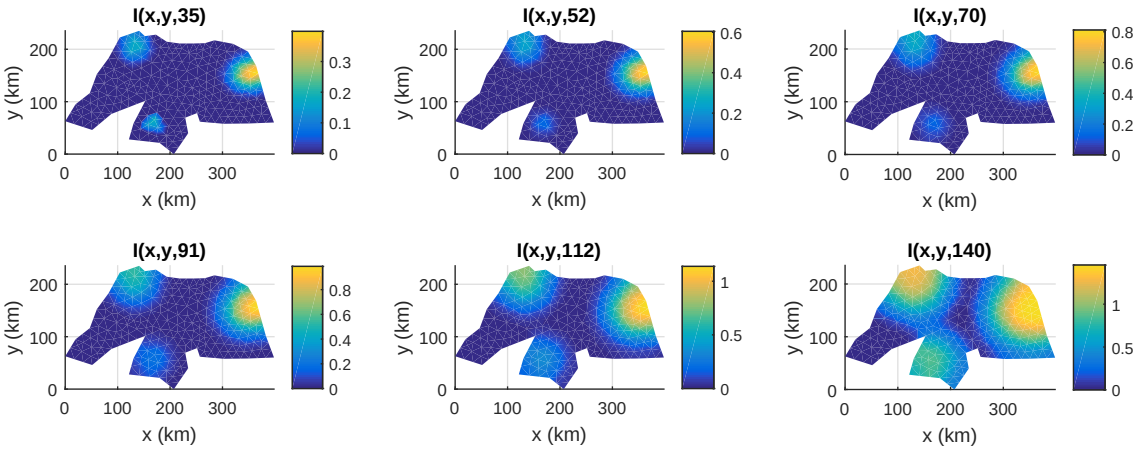

Figure 2: Plots of infected humans at selected times. Each plot has a different scale.

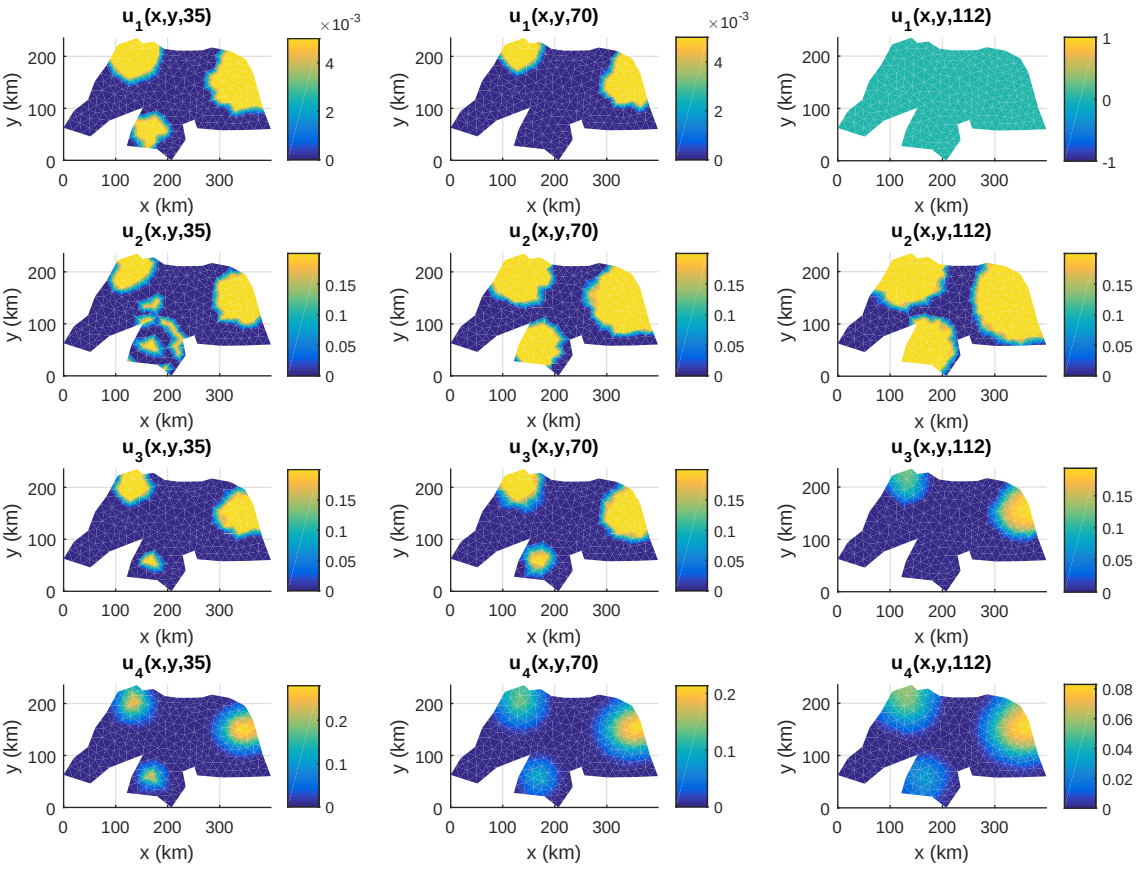

Figure 3: Plots of optimal controls at selected times. Each plot has a different scale.

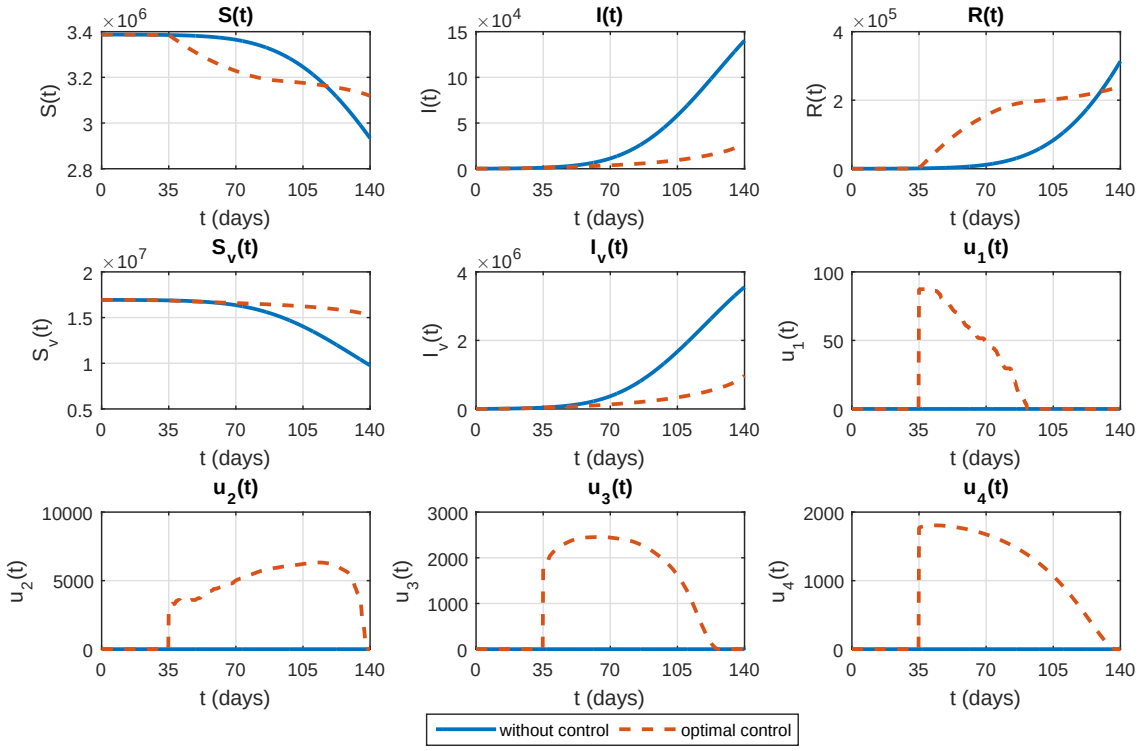

Figure 4: Integrals of state solutions and optimal controls over space.

the controls are applied. Constant controls at the upper bounds result in less incidence, but at a higher cost, almost double the optimal cost. Although this could be a useful strategy, it may not be feasible due to cost limitations.

In Figure 2 we can see the spatial spread of the disease, starting in three small areas and occupying most part of the spatial domain in 140 days. In Figure 3 we can see that all controls are applied in the regions where there are most infected humans, and as time passes, less control is being applied. In Figure 4 we can see that the application of the controls highly reduces the number of infected humans and mosquitoes over time.

4 Conclusions

The applied controls have brought about significant reductions in the number of new infections and overall cost, showing a successful application of the optimal control strategies. The numerical simulations performed were able to assess different realistic scenarios, using real data from Rio Grande do Norte state in the 2015 initial Zika outbreak. Other scenarios could be explored, applying only some of the control measures in different combinations. This work could help public policy decisions in order to implement efficient control measures in a Zika virus outbreak, or even other vector-borne diseases, such as dengue, malaria and yellow fever, with small modifications in the model.

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