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MULTI-REGION OPTIMAL IMPULSE CONTROL THROUGH EXAMPLE OF IMMUNIZATION POLICY AT LARGE GEOGRAPHICAL SCALE WITH DISCUSSION OF THE CLOSURE CASE

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Abstract. Most epidemiological studies prefer to rely on differential systems because of their mathematical tractability, however, in addition to the need to control modeling framework that takes into account factors of interconnections, there is also a need to rely on the practical pulsed controls. For that, we define first a susceptible-immunized-infected-removed (SVIR) multi-region control differential system, then we explain how this problem is reformulated after the introduction of discrete impulse controls via the compartment of the V variable and that is associated to the example of the immunization policy whose goals can be reached either by following those who recommend the application of discrete-time awareness seasonally or those who advise to use some potentially effective antiviral medications. Then, we characterize our sought optimal controls in the multi-region impulse case. Finally, we take the example of three interconnected regions and conclude that prompt control measures are not always necessary as we observe that even when their values are not that significant in the first six weeks, there is a decrease in infection and which may be also due to natural immunity and that could lead to some herd immunity

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later enhanced by impulse controls for other months. We also discuss in the end, the pandemic crisis scenario when impulse closure policies are needed to enhance the effectiveness of the impulse immunization strategy.

Keywords: multi-region model; impulsive differential model; impulsive control; immunization; closure policy.

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1. INTRODUCTION

1.1. Impulsive control: Literature limitations and recent developments. When compared to conventional strategies, the immunization pulse strategy has the potential to eradicate some epidemics at relatively low vaccination rates through either awareness campaigns or potentially efficient medical interventions like vaccines or antiviral drugs. This potential was theoretically demonstrated and investigated very early by Shulgin et al. in [1] and Agur et al. in [2]. The efficiency and significance of such vaccination regimens were examined by the authors in the first mentioned reference and also in [3], and more recently in the paper of Yang and Xiao [4] where the authors discussed the effectiveness and importance of such immunization programs by referring to many theoretical and applicable results in literature, as in the case of poliomyelitis studied by De Quadros et al. [5], or in the case of measles treated by Albert Bruce Sabin in [6].

Many mathematicians have been interested in the study of the complexity of epidemic models in the presence of impulsive vaccination, for example see Zhou and Liu in [8], Nistal et al. in [7], Zhao Zeng with Sun Chen in [9] and again with Hua Sun in [10]. However, there have been only very few studies that tried to develop from these studies and suggest a mathematical framework that could help to find optimized impulse interventions. In fact, optimal control procedures have proven to be very good candidates in such development when they have been subjects to continuous-time systems as in [11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21], or discrete-time systems as in [22, 23, 24, 25], or even stochastic systems as in [26, 27, 28], but there have been only very few initiatives as in [29] with a numerical method for the impulsive control case, or as in [30] where the authors proved an impulse version for the application of optimal control in an example of epidemic control model with short-term immunity. This is not to say that limitations of this topic in literature would leave researchers not interested in developing the theoretical framework of the optimal impulse control and that in our opinion, has an important potential to get involved in the resolution of many real-world problems that are described with hybrid equations. In fact, just very recently, Hugo Leiva published a paper about optimal control of nonlinear impulsive differential equations [31], and this makes a good sign for more development of this context that has been lacking in research for many years.

1.2. Multi-region control modeling: Treated cases and goal of the paper.

Recent multi-region models have been interested in the study of the infection spread at large geographical scales either by using discrete-time multi-region control systems as in [32, 34, 35, 36, 37, 38, 39, 40, 41, 43, 44] or deterministic continuous-time multi-region control systems as studied in the cases of HIV/AIDS and Ebola [33, 42], or more recently with the stochastic multi-region control systems [26, 28]. Nevertheless, the authors in [45] saw that despite the many forms of the control policies in literature, this is not enough as any strategy would fail if there is no serious focus on the health educational system. In the same context, no control approach has been suggested to study the same phenomena in the more realistic case, namely when the controls are introduced as discrete pulses, because as we have just explained above and before talking about the interconnected regions, there is a lack of such control frameworks even if we consider just one region within itself. In front of this problem, we try here to benefit from the research initiated in [30] and we contribute to its development by considering now the multi-region impulse case. In order to reach our goal, we first consider a multi-region susceptible-infected-removed (SIR) epidemic model with an additional compartment to represent the immunized population. Since our controls are introduced in discrete times and the state dynamics are based on a continuous-time system, the proposed model becomes in the form of an S-Immunized-IR (SVIR) differential hybrid system where the V variable is associated to the immunization pulsed policy that can be achieved either by applying discrete-time awareness or by using some potentially effective antiviral medications.

As described in the epidemic control systems [17, 22, 30], or as in [46] for the case of COVID-19 where the authors reported that there is still no proper vaccine that is necessarily 100% effective, and people may get reinfected if the virus induced short-term immunity. As a different modeling approach to the SIRS framework as in [22] and where people in the removed class can move again to the susceptible one, we suppose here in our multi-region model that the impulse immunization policy could only lead to temporary immunity as in [30], and then people in the immunized class are not moving to the removed class as we could not be sure about the effect of control as just explained and we suppose then it is very limited when it about recovery. In fact, only the natural immunity that is prioritized and taken into account here for moving to the R compartment, while the pulsed immunization discrete functions are only responsible for controlling the infection spread between regions. Thus, we proceed by using a hybrid version of Pontryagin's maximum principle in order to find our optimal impulse controls. Finally, we apply the hybrid regression-progressive iterative schemes first suggested in [30] in order to generate numerical simulations of our example.

Our paper is organized as follows, the theoretical modeling framework is defined in section 2., while the impulse control procedure that enables us to characterize our optimal impulse controls, is presented in section 3. Finally, we provide a numerical example in section 4.

2. Multi-Region Control Model With Short-Term Immunity

2.1. Model description in continuous-time case.

In this part, we consider a multi-region epidemic control model where the vaccination strategy is described using a constant parameter and it has a limited effect on people who receive it.

We need first to define the following four compartments

· S^{Ω_j}: the number of individuals in Ω_j who are susceptible people to infection or who are not yet infected,

· V^{Ω_j}: the number of susceptible people in Ω_j and who are temporary immunized so they can not move to the removed class due for example to the limited effect of vaccine [22, 30],

· I^{Ω_j}: the number of infected people in Ω_j and who are capable of spreading the epidemic to those in the susceptible and temporary controlled categories,

· R^{Ω_j}: the number of removed people from the epidemic in Ω_j.

For all t belonging to an interval $[0,T]$ and when the immunization policy is only presented by a constant parameter of control θ, the model takes the form of the following differential system

$$(1)\qquad \begin{cases} \dot{S}^{\Omega_j}(t) &=& \Pi_j(t) - \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) - a\theta_j S^{\Omega_j}(t) - \mu_j S^{\Omega_j}(t) \\ \dot{V}^{\Omega_j}(t) &=& a\theta_j S^{\Omega_j}(t) - b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \mu_j V^{\Omega_j}(t) \\ \dot{I}^{\Omega_j}(t) &=& \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) + b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \gamma_j I^{\Omega_j}(t) - \mu_j I^{\Omega_j}(t) \\ \dot{R}^{\Omega_j}(t) &=& \gamma_j I^{\Omega_j}(t) - \mu_j R^{\Omega_j}(t) \end{cases}$$

with initial conditions $S^{\Omega_j}(0) = S_0^{\Omega_j} > 0$, $V^{\Omega_j}(0) = V_0^{\Omega_j} \geq 0$, $I^{\Omega_j}(0) = I_0^{\Omega_j} \geq 0$ and $R^{\Omega_j}(0) = R_0^{\Omega_j} \geq 0$ and where $\Pi_j(t) = \mu_j N^{\Omega_j}(t)$ with $N^{\Omega_j}(t) = S^{\Omega_j}(t) + V^{\Omega_j}(t) + I^{\Omega_j}(t) + R^{\Omega_j}(t)$, giving the newborn people.

$a\theta$ $(0 \leq a \leq 1)$ is the fraction of controlled people with "a" modeling the reduced chances of a susceptible individual to be controlled.

Also, $\beta_{jj} = \frac{\kappa_{jj}}{N(t)}$ with κ_{jj} the infection transmission rate in Ω_j, μ_j is the natural death rate, $b\theta_j$ $(0 \leq b \leq 1)$ is the infection transmission rate even in the presence of θ_j with "b" modeling the reduced chances of a temporary controlled individual to be infected, and γ_j is the recovery rate.

The population size N is constant because $\dot{N}^{\Omega_j}(t) = \dot{S}^{\Omega_j}(t) + \dot{V}^{\Omega_j}(t) + \dot{I}^{\Omega_j}(t) + \dot{R}^{\Omega_j}(t) = 0$, hence, $\Pi_j(t) = \Pi_j = \mu_j N_0^{\Omega_j}$ knowing that $N^{\Omega_j}(0) = N_0^{\Omega_j}$.

We note that $\theta_j = 0$ will denote no immunization and $\theta_j = 1$ will denote the use of immunization having of an initial number of susceptible people $S(0)$.

2.2. Model formulation in impulsive-time case.

Let t_1, t_2, ..., t_n be the times at which the new immunization is followed. n is for example the total number of vaccines utilized.

Let the immunization strategy to be described now using a control function of time $\theta_j(t)$. The continuous-time model in (1) is now converted to the following hybrid system with impulse immunizations

$$(2)\qquad \begin{cases} \dot{S}^{\Omega_j}(t) &=& \Pi_j - \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) - a\sum_{i=1}^{n} \delta(t-t_i)\theta_j(t) S^{\Omega_j}(t) - \mu_j S^{\Omega_j}(t) \\ \dot{V}^{\Omega_j}(t) &=& a\sum_{i=1}^{n} \delta(t-t_i)\theta_j(t) S^{\Omega_j}(t) - b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \mu_j V^{\Omega_j}(t) \\ \dot{I}^{\Omega_j}(t) &=& \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) + b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \gamma_j I^{\Omega_j}(t) - \mu_j I^{\Omega_j}(t) \\ \dot{R}^{\Omega_j}(t) &=& \gamma_j I^{\Omega_j}(t) - \mu_j R^{\Omega_j}(t) \end{cases}$$

where $\delta(t-t_i)$ is the Dirac-delta function. Thus, we understand the following conditions.

If $t \neq t_i\ \forall i$, then the system (2) is changed to:

$$\text{(3)} \qquad \begin{cases} \dot{S}^{\Omega_j}(t) &=& \Pi_j - \sum\limits_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) - \mu_j S^{\Omega_j}(t) \\ \dot{V}^{\Omega_j}(t) &=& -b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \mu_j V^{\Omega_j}(t) \\ \dot{I}^{\Omega_j}(t) &=& \sum\limits_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) + b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \gamma_j I^{\Omega_j}(t) - \mu_j I^{\Omega_j}(t) \\ \dot{R}^{\Omega_j}(t) &=& \gamma_j I^{\Omega_j}(t) - \mu_j R^{\Omega_j}(t) \end{cases}$$

and

If $t = t_i\ \forall i$, then we can obtain the following equations

$$\text{(4)} \qquad \begin{cases} S^{\Omega_j}(t_i^+) &=& S^{\Omega_j}(t_i) - a\theta_j(t_i) S^{\Omega_j}(t_i) \\ V^{\Omega_j}(t_i^+) &=& V^{\Omega_j}(t_i) + a\theta_j(t_i) S^{\Omega_j}(t_i) \\ I^{\Omega_j}(t_i^+) &=& I^{\Omega_j}(t_i) \\ R^{\Omega_j}(t_i^+) &=& R^{\Omega_j}(t_i) \end{cases}$$

where t_i representing the immunization time and $\theta_j(t_i)$ the impulse control at this time, while $S^{\Omega_j}(t_i) = S^{\Omega_j}(t_i^-)$, $V^{\Omega_j}(t_i) = V^{\Omega_j}(t_i^-)$, $I^{\Omega_j}(t_i) = I^{\Omega_j}(t_i^-)$ and $R^{\Omega_j}(t_i) = R^{\Omega_j}(t_i^-)$ are defined as the old numbers of susceptible, immunized, infected and removed people respectively, while $S^{\Omega_j}(t_i^+)$, $V^{\Omega_j}(t_i^+)$, $I^{\Omega_j}(t_i^+)$ and $R^{\Omega_j}(t_i^+)$ defining these same numbers just after t_i. Thus, (4) means we have abandoned the old immunization and used a new immunization for the number of susceptible people $S(t_i)$.

3. Optimal Impulse Immunization Control Approach

3.1. Theoretical framework. At time t and for $j = 1, ..., p$, let define for every region Ω_j, the following state and control variables

$$x^{\Omega}(t) = x^{\Omega_j}(t) = \begin{pmatrix} S^{\Omega_j}(t) \\ I^{\Omega_j}(t) \\ R^{\Omega_j}(t) \end{pmatrix}$$

$\theta^{\Omega}(t) = \theta^{\Omega_j}(t) = \theta_j(t)$.

In this part of paper, we define our objective by determining the optimal values of the impulse control $\theta_j(t_i)$ that minimizes a given criterion, but before this, we present hereafter the theoretical steps for reaching this goal.

Based on results in [47], we try here to derive an analogous necessary conditions of optimality that will be associated to our particular form of the impulsive system (2).

We start then first by presenting a general formulation of our optimal control problem that can be adapted to the form (3)-(4) as follows

$$\min_{n,t_i,\theta_j(t_i)} \int_0^T F(t,x^{\Omega_j}(t)) + \sum_{i=1}^{n} G(x^{\Omega_j}(t_i^-,\theta_j(t_i),t_i)) + \phi(x^{\Omega_j}(T^+)) \tag{5}$$

subject to

$$\dot{x}^{\Omega_j}(t) = f(t,x^{\Omega_j}(t)),\ t \notin \{t_1,...,t_n\}$$

$$x^{\Omega_j}(t_i^+) - x^{\Omega_j}(t_i^-) = g(x^{\Omega_j}(t_i^-,\theta_j(t_i),t_i)),\ i \in \{1,...,n\}$$

$$x^{\Omega_j} \in \mathbb{R}^N, \theta_j(t_i) \in \Theta_j,\ x^{\Omega_j}(0^-) = x_0^{\Omega_j}, t_i \in [0,T]$$

where x^{Ω_j} is the state variable, a piece-wise continuous function of time, and $\theta_j(t_i)$ is the impulse control variable.

n is the number of pulses, t_i is the instant of the ith pulse and t_i^-, t_i^+ are the instants just before and after the impulse, (i.e. $x^{\Omega_j}(t_i^-)$, $x^{\Omega_j}(t_i^+)$ represent the first and second limit sides of x^{Ω_j} respectively). The final time is noted $T > 0$ while T^+ is the instant that comes just after T.

The system gain is given by $F(t,x^{\Omega_j}(t))$, $G(x^{\Omega_j}(t_i^-,\theta_j(t_i),t_i))$ is the gain function associated to the ith pulse, and $\phi(x^{\Omega_j}(T^+))$ is the final cost function associated to the system just after T.

Finally, $f(t,x^{\Omega_j}(t))$ is the continuous change of the state variable through time between pulses points and $g(x^{\Omega_j}(t_i^-,\theta_j(t_i),t_i))$ is the function that represents the instantaneous or finite change of the state variable when there is a pulse.

We admit that Θ_j is bounded convex control set, and we impose that F, f, g and G are continuously differentiable functions in x^{Ω_j} on $\mathbb{R}^N$ and in $\theta_j(t_i)$ on Θ, $\phi(x^{\Omega_j}(T^+))$ is continuously differentiable in $x^{\Omega_j}(T^+)$ on $\mathbb{R}^N$,and that g and G are continuous on t. Finally, when there is no pulse, i.e. $\theta_j(t_i) = 0$, we assume that $g(x(t),0,t) = 0$ for all x and t.

Consider the Hamiltonian function defined by

$$H^{\Omega_j}(t,x^{\Omega_j}(t),\lambda_j(t)) = F(t,x^{\Omega_j}(t)) + \lambda_j(t)^T f(t,x^{\Omega_j}(t))$$

and the impulse Hamiltonian function defined by

$$H^I_j(t,x^{\Omega_j}(t),\theta_j(t_i),\lambda_j(t)) = G(t,x^{\Omega_j}(t),\theta_j(t_i)) + \lambda_j(t)^T g(t,x^{\Omega_j}(t),\theta_j(t_i))$$

where $\lambda_j(t)$ represent the adjoint state variable.

As we have defined the general formulation of our objective that can be associated to the form of impulsive system (2), we follow similar steps as in [48, 49, 50] to obtain the following theorem which states the necessary conditions of optimality associated to our special case of optimal impulse control problem (5).

Theorem 3.1.1. Let $(x^{\Omega_j*}(t),n,t_1^*,...,t_k^*,\theta_j^*(t_1),...,\theta_j^*(t_k))$ be optimal solutions of the minimization problem (5), then there exists an adjoint variable such that the following conditions is satisfied

$$\dot{\lambda}_j(t) = -\frac{\partial H^{\Omega_j}}{\partial x^{\Omega_j}}(t,x^{\Omega_j*}(t),\lambda_j(t)). \tag{6}$$

In the points of pulse, we have

$$\frac{\partial H^I_j}{\partial \theta_j(t_i)}(t_i^*,x^{\Omega_j*}(t_i^{*-}),\theta_j(t_i),\lambda_j(t_i^{*+}))(\theta_j(t_i)-\theta_j^*(t_i)) \leq 0, \tag{7}$$

$$\lambda_j(t_i^{*+}) - \lambda_j(t_i^{*-}) = \frac{\partial H^I_j}{\partial x^{\Omega_j}}(t_i^*,x^{\Omega_j*}(t_i^{*-}),\theta^*(t_i),\lambda(t_i^{*+})) \tag{8}$$

3.2. Optimal impulse control problem. As the most evident objective in such cases of epidemic control as done for models in [17, 22], we aim also here to minimize the number of infected people while minimizing the cost of immunization, we define the objective function to be minimized as

$$J(\theta_j) = \int_0^T A_j I^{\Omega_j}(t)dt + \sum_{i=1}^{n} \frac{B_j}{2}\theta_j^2(t_i) \tag{9}$$

In other words, we are seeking an optimal control θ^* such that

$$J(\theta_j^*) = \min\{J(\theta_j)/\theta_j \in \Theta_j\}$$

with

$$\Theta_j([0,T]) = \{\theta_j(t_i)\ \ measurable | 0 \leqslant \theta_j(t_i) \leqslant 1, t_i \in [0,T]\}$$

subject to

$$(10)\qquad \begin{cases} \dot{S}^{\Omega_j}(t) = \Pi_j - \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) - a \sum_{i=1}^{n} \delta(t-t_i)\theta_j(t_i) S^{\Omega_j}(t) - \mu_j S^{\Omega_j}(t) \\ \dot{V}^{\Omega_j}(t) = a \sum_{i=1}^{n} \delta(t-t_i)\theta_j(t_i) S^{\Omega_j}(t) - b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \mu_j V^{\Omega_j}(t) \\ \dot{I}^{\Omega_j}(t) = \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) + b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \gamma_j I^{\Omega_j}(t) - \mu_j I^{\Omega_j}(t) \\ \dot{R}^{\Omega_j}(t) = \gamma_j I^{\Omega_j}(t) - \mu_j R^{\Omega_j}(t) \\ S_0, V_0, I_0, R_0 \ given \\ 0 \leqslant \theta_j(t_i) \leqslant 1 \end{cases}$$

Or, our optimal pulse control problem can be stated as follows

$$\begin{cases} \qquad \min_{\theta_j \in \Theta} \left\{ \int_0^T A_j I^{\Omega_j}(t) dt + \sum_{i=1}^{n} \frac{B_j}{2} \theta^2(t_i) \right\} \\ \qquad subject\ to \\ \qquad \dot{S}^{\Omega_j}(t) = \Pi_j - \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) - \mu_j S^{\Omega_j}(t) \\ \qquad \dot{V}^{\Omega_j}(t) = -b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \mu_j V^{\Omega_j}(t) \\ \qquad \dot{I}^{\Omega_j}(t) = \sum_{k=1}^{p} \beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) + b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \gamma_j I^{\Omega_j}(t) - \mu_j I^{\Omega_j}(t) \\ \qquad \dot{R}^{\Omega_j}(t) = \gamma_j I^{\Omega_j}(t) - \mu_j R^{\Omega_j}(t) \ when\ t \neq t_i \\ \\ and \\ \qquad S^{\Omega_j}(t_i^+) = S^{\Omega_j}(t_i) - a\theta_j(t_i) S^{\Omega_j}(t_i) \\ \qquad V^{\Omega_j}(t_i^+) = V^{\Omega_j}(t_i) + a\theta_j(t_i) S^{\Omega_j}(t_i) \\ \qquad I^{\Omega_j}(t_i^+) = I^{\Omega_j}(t_i) \\ \qquad R^{\Omega_j}(t_i^+) = R^{\Omega_j}(t_i) \ when\ t = t_i \\ \qquad S_0^{\Omega_j}, V_0^{\Omega_j}, I_0^{\Omega_j}, R_0^{\Omega_j} \ given \\ \qquad 0 \leqslant \theta_j(t_i) \leqslant 1 \end{cases}$$

In order to resolve this problem, we follow these steps.

We construct the Hamiltonian H without control as the function defined as

$$
\begin{aligned}
&H^{\Omega_j}(S^{\Omega_j}(t),V^{\Omega_j}(t),I^{\Omega_j}(t),R^{\Omega_j}(t),\lambda_{1,j}(t),\lambda_{2,j}(t),\lambda_{3,j}(t))\\
&=A_jI^{\Omega_j}(t)+\lambda_{1,j}(t)(\Pi_j-\sum_{k=1}^{p}\beta_{jk}S^{\Omega_j}(t)I^{\Omega_k}(t)-\mu_jS^{\Omega_j}(t))-\lambda_{2,j}(t)(b\beta_{jj}V^{\Omega_j}(t)I^{\Omega_j}(t)+\mu_jV^{\Omega_j}(t))\\
&+\lambda_{3,j}(t)(\sum_{k=1}^{p}\beta_{jk}S^{\Omega_j}(t)I^{\Omega_k}(t)+b\beta_{jj}V^{\Omega_j}(t)I^{\Omega_j}(t)-\gamma_jI^{\Omega_j}(t)-\mu_jI^{\Omega_j}(t))+\lambda_{4,j}(t)(\gamma_jI^{\Omega_j}(t)-\mu_jR^{\Omega_j}(t))
\end{aligned}
$$

and the impulse Hamiltonian function H^{p,Ω_j} defined as

$$
\begin{aligned}
H^{p,\Omega_j}(S^{\Omega_j}(t),V^{\Omega_j}(t),I^{\Omega_j}(t),R^{\Omega_j}(t),\theta_j(t_i)) &= \frac{B_j}{2}\theta_j^2(t_i)-a\lambda_{1,j}(t^+)\theta_j(t)S^{\Omega_j}(t)\\
&\quad +a\lambda_{2,j}(t^+)\theta_j(t_i)S^{\Omega_j}(t)
\end{aligned}
\tag{11}
$$

We can announce the impulse maximum principle as follows.

Theorem 3.2.1. Given an impulse optimal control $\theta^*(t_i),\ i=1,...,n$ where $t_i>t_{i-1}>0$ and which minimizes (9) along with the optimal trajectories S^*, V^*, I^* and R^* associated to the differential system in (10), then there exist adjoint variables λ_k, $k=1,2,3,4$ as notations of $\lambda_k(t)$ and which satisfy for $t\neq t_i$ the following adjoint differential system

$$
\left\{
\begin{aligned}
\dot{\lambda_{1,j}}(t) &= \lambda_{1,j}(t)(\sum_{k=1}^{p}\beta_{jk}I^{\Omega_j*}(t)+\mu_j)-\lambda_{3,j}(t)\sum_{k=1}^{p}\beta_{jk}I^{\Omega_j*}(t)\\
\dot{\lambda_{2,j}}(t) &= \lambda_{2,j}(t)(b\beta_{jj}I^{\Omega_j*}(t)+\mu_j)-b\lambda_{3,j}(t)\beta_{jj}I^{\Omega_j*}(t)\\
\dot{\lambda_{3,j}}(t) &= -A_j+\lambda_{1,j}(t)\beta_{jj}S^{\Omega_j*}(t)+b\lambda_{2,j}(t)\beta_{jj}V^{\Omega_j*}(t)\\
&\quad -\lambda_{3,j}(t)(\beta_{jj}(S^{\Omega_j*}(t)+bV^{\Omega_j*}(t))-\mu-\gamma)-\lambda_{4,j}(t)\gamma\\
\dot{\lambda_{4,j}}(t) &= \lambda_{4,j}(t)\mu_j
\end{aligned}
\right.
\tag{12}
$$

with the transversality conditions $\lambda_k(T)=0$, $k=1,2,3,4$ and we have,

$$
\left\{
\begin{aligned}
\lambda_{1,j}(t_i) &= \lambda_{1,j}(t_i^+)-a\lambda_{1,j}(t_i^+)\theta_j(t_i)+a\lambda_{2,j}(t_i^+)\theta_j(t_i)\\
\lambda_{2,j}(t_i) &= \lambda_{2,j}(t_i^+)\\
\lambda_{3,j}(t_i) &= \lambda_{3,j}(t_i^+)\\
\lambda_{4,j}(t_i) &= \lambda_{4,j}(t_i^+)
\end{aligned}
\right.
\tag{13}
$$

Furthermore, we have

$$
\theta_j^*(t_i)=\min\left(\max\left(0,\frac{aS^{\Omega_j*}(t_i)(\lambda_{1,j}(t_i^+)-\lambda_{2,j}(t_i^+))}{B_j}\right),1\right)
\tag{14}
$$

Proof. We have the Hamiltonian function H is defined above as

$$\begin{aligned} H^{p,\Omega_j}(S^{\Omega_j}(t),V^{\Omega_j}(t),I^{\Omega_j}(t),R^{\Omega_j}(t),\theta_j(t_i)) &= \frac{B_j}{2}\theta_j^2(t_i) - a\lambda_{1,j}(t^+)\theta_j(t_i)S^{\Omega_j}(t) \\ &\quad + a\lambda_{2,j}(t^+)\theta_j(t)S^{\Omega_j}(t_i) \end{aligned}$$

Then, using the impulse version of Pontryagin's maximum principle in [47], then we have, for $t \neq t_i$

$$\begin{aligned} \dot{\lambda_{1,j}}(t) &= \lambda_{1,j}(t)(\sum_{k=1}^{p}\beta_{jk}I^{\Omega_j*}(t)+\mu_j) - \lambda_{3,j}(t)\sum_{k=1}^{p}\beta_{jk}I^{\Omega_j*}(t) \\ \dot{\lambda_{2,j}}(t) &= \lambda_{2,j}(t)(b\beta_{jj}I^{\Omega_j*}(t)+\mu_j) - b\lambda_{3,j}(t)\beta_{jj}I^{\Omega_j*}(t) \\ \dot{\lambda_{3,j}}(t) &= -A_j + \lambda_{1,j}(t)\beta_{jj}S^{\Omega_j*}(t) + b\lambda_{2,j}(t)\beta_{jj}V^{\Omega_j*}(t) \\ &\quad -\lambda_{3,j}(t)(\beta_{jj}(S^{\Omega_j*}(t)+bV^{\Omega_j*}(t)) - \mu - \gamma) - \lambda_{4,j}(t)\gamma \\ \dot{\lambda_{4,j}}(t) &= \lambda_{4,j}(t)\mu_j \end{aligned}$$

while the transversality conditions defined as minus the derivative of the final gain function with respect to the state variables S, V, I and R. Since the final gain function in (9) does not contain any term of these variables, then $\lambda_{k,j}(T) = 0$, $k = 1,2,3,4$.

Since the impulse Hamiltonian function H^p is defined above as

$$H_j^p(S^{\Omega_j},V^{\Omega_j},I^{\Omega_j},R^{\Omega_j},\theta_j) = \frac{B_j}{2}\theta_j^2 - a\lambda_{1,j}(t^+)\theta_jS^{\Omega_j} + a\lambda_{2,j}(t^+)\theta_jS^{\Omega_j}$$

Then, we have also at $t = t_i$

$$\begin{cases} \lambda_{1,j}(t_i) = \lambda_{1,j}(t_i^+) + H^p_{S^{\Omega_j}}(S^{\Omega_j},V^{\Omega_j},I^{\Omega_j},R^{\Omega_j},\theta_j) = \lambda_{1,j}(t_i^+) \\ \qquad -a\lambda_{1,j}(t_i^+)\theta_j(t_i) + a\lambda_{2,j}(t_i^+)\theta_j(t_i) \\ \lambda_{2,j}(t_i) = \lambda_{2,j}(t_i^+) + H^p_{V^{\Omega_j}}(S^{\Omega_j},V^{\Omega_j},I^{\Omega_j},R^{\Omega_j},\theta_j) = \lambda_{2,j}(t_i^+) \\ \lambda_{3,j}(t_i) = \lambda_{3,j}(t_i^+) + H^p_{I^{\Omega_j}}(S^{\Omega_j},V^{\Omega_j},I^{\Omega_j},R^{\Omega_j},\theta_j) = \lambda_{3,j}(t_i^+) \\ \lambda_{4,j}(t_i) = \lambda_{4,j}(t_i^+) + H^p_{R^{\Omega_j}}(S^{\Omega_j},V^{\Omega_j},I^{\Omega_j},R^{\Omega_j},\theta_j) = \lambda_{4,j}(t_i^+) \end{cases}$$

The optimality condition at $\theta_j = \theta_j^*$ implies that $\dfrac{\partial H_j^p}{\partial \theta_j(t_i)} = 0$.

Then, after setting $S^{\Omega_j} = S^{\Omega_j *}$, we have

$B_j\theta_j(t_i) - aS(t_i)\lambda_{1,j}(t_i^+) + aS(t_i)\lambda_{2,j}(t_i^+) = 0 \Rightarrow \theta_j(t_i) = \dfrac{aS(t_i)(\lambda_{1,j}(t_i^+) - \lambda_{2,j}(t_i^+))}{B}$.

Using the bounds on controls, we obtain

$$\theta_j^*(t_i) = \min\left(\max\left(0, \frac{aS^{\Omega_j *}(t_i)(\lambda_{1,j}(t_i^+) - \lambda_{2,j}(t_i^+))}{B_j}\right), 1\right)$$

□

4. Numerical Results

In Figure 9.1. we present simulations of the number of susceptible people in the absence and presence of the control and we can observe that when we choose $\theta_j = 0$, the number of susceptible people has decreased from its initial condition to numbers close to 7.5, 8 and 9 in regions Ω_1, Ω_2 and Ω_3 respectively, while the optimal state S^* associated to $\theta_j \neq 0$ decreases to a value that is close to zero after just 10 days.

Simultaneously in Figure 9.2., the number of removed people increases to only a value close to values close to 100, 75 and 50 people in regions Ω_1, Ω_2 and Ω_3 respectively, due to natural recovery, while it reaches a value higher than this number with a maximal peak equaling to 650, 1200 and 450 in regions Ω_1, Ω_2 and Ω_3 respectively when $\theta_j \neq 0$. As regards to the number of infected people, it remains stabilized in an important value close to its initial condition in Ω_1, increased to 1150 and 1180 in Ω_1 and Ω_2 respectively, while it decreases towards values very close to 300, 400 and 500 in regions Ω_1, Ω_2 and Ω_3 respectively after the introduction of the control θ_j.

We can observe the relationship between the number of controlled people and the optimal values taken by θ_j in Figure 9.3., so when this is increasing, the optimal state V^* is also increasing. In fact, we can deduce that with only one pulse value of θ_j, we reach our goal by minimizing I function, and maximizing R function while the total number of the susceptible who received the control along T.

Figure 9.2. also explains how an impulse vaccination can be followed when we suppose that all pulse immunizations are equal. In all weeks except week 3, it is recommended to follow immunizations by their maximal values.

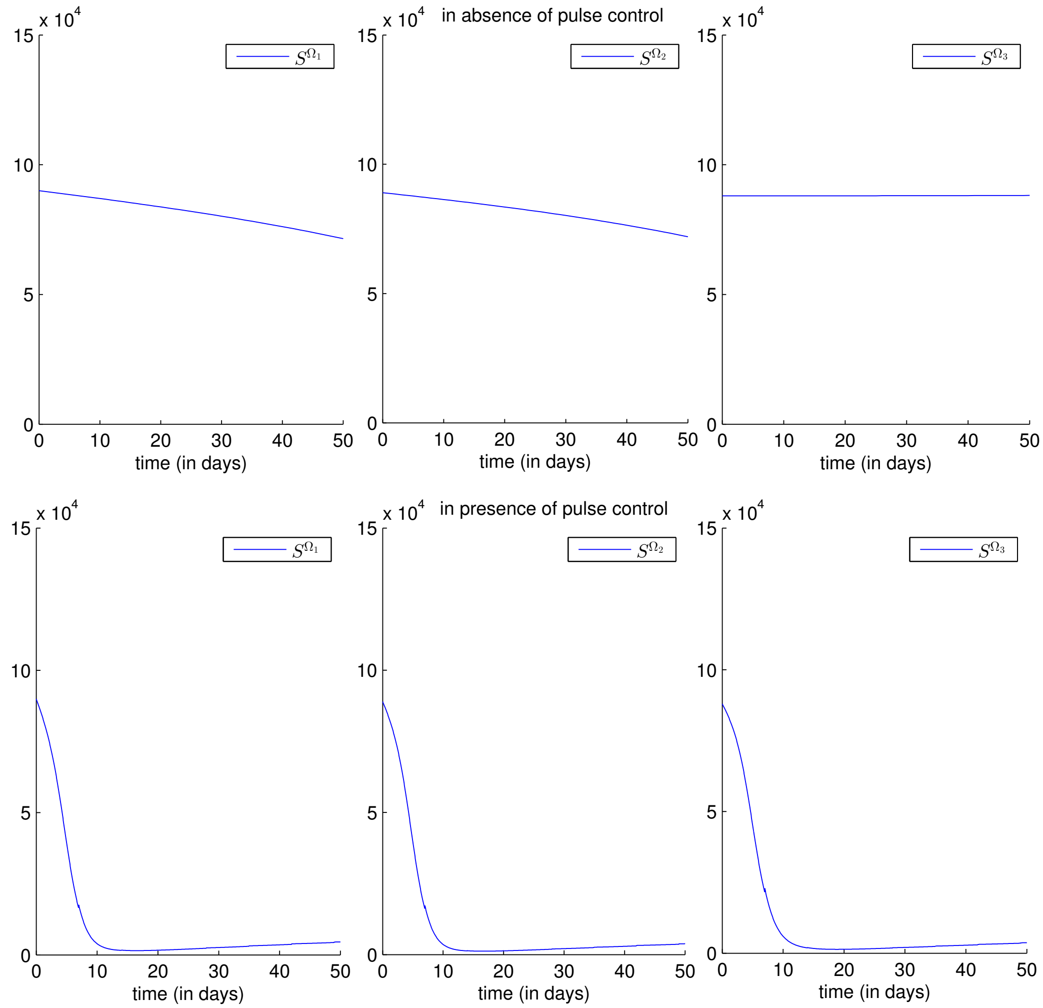

FIGURE 1. Number of susceptible people without and with pulse immunization

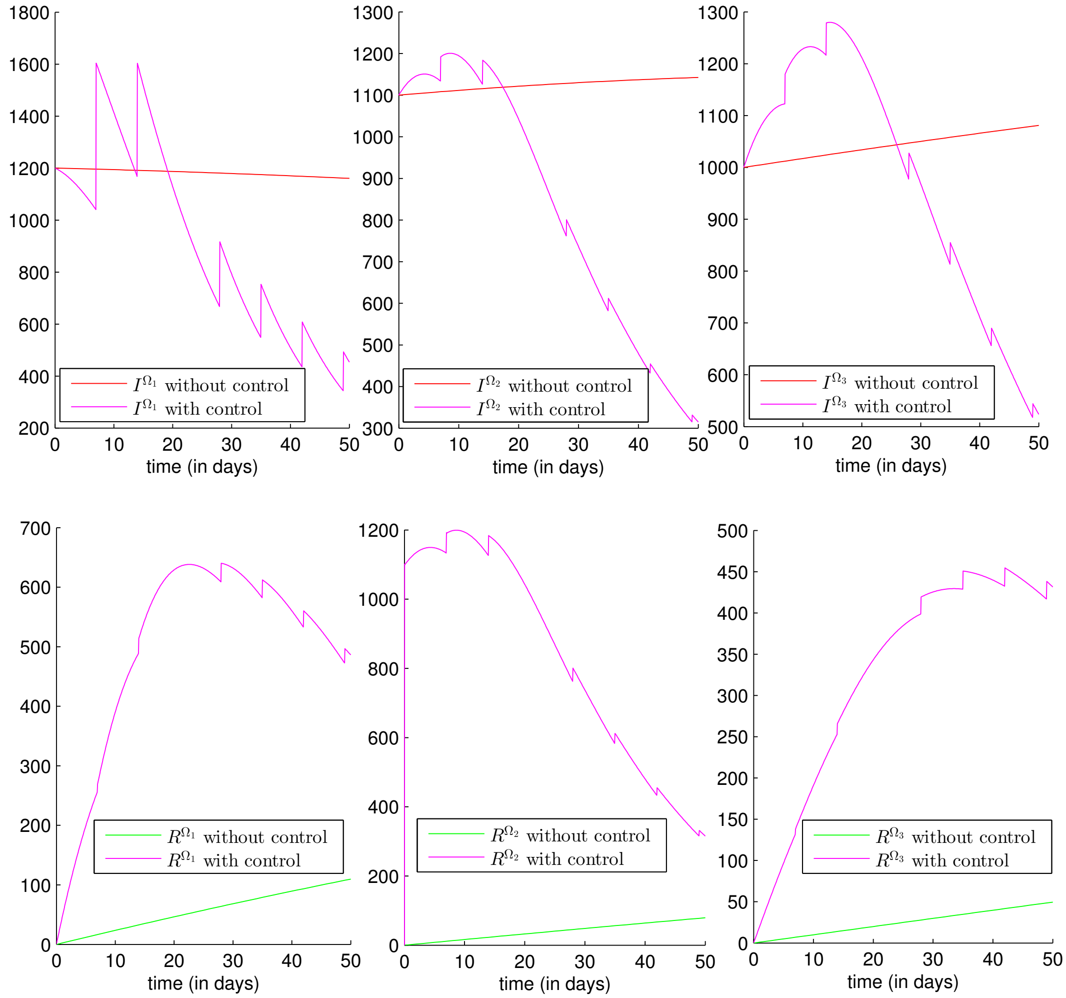

FIGURE 2. Number of infected and removed people without and with pulse immunization

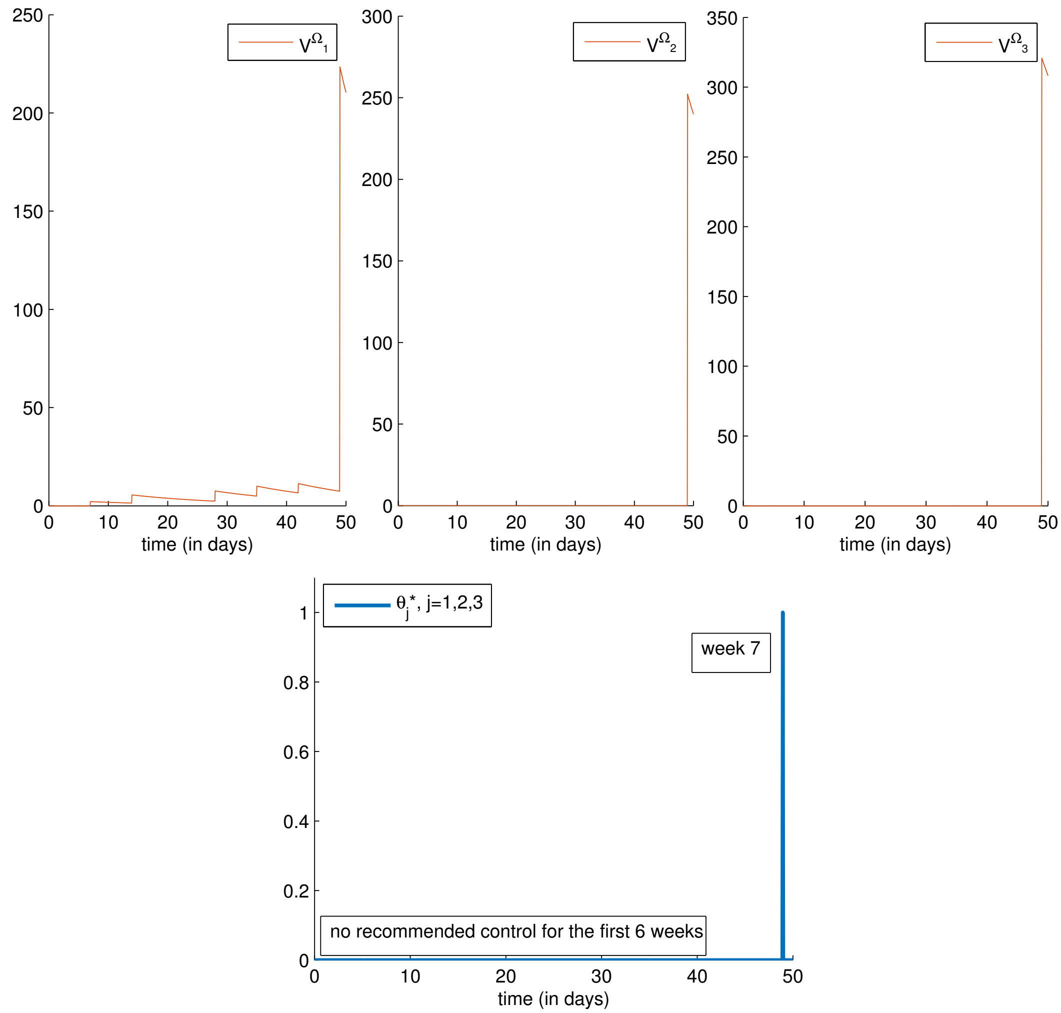

FIGURE 3. The number of immunized people and the pulse immunization recommended

5. Discussion of the Pandemic Crisis Scenario With Closure Policy

Let $I = \{1, ..., p\}$ and $I_H \subset I$ the set of indices of regions at high-risk and then, having the ability to spread the epidemic to other regions. Here, we study the case when a given region Ω_j is under impulse vaccination control θ_j and at the same time under threat of infection coming from other regions. For this, we add to the vaccination strategy, an other control denoted as $\zeta^{j\Omega_k}$ to characterize the effectiveness of movement restriction operations, in order to prevent infected of regions Ω_k, $k \in I_H$ to come to the controlled region Ω_j, where

$$\begin{cases} \zeta^{j\Omega_k} \neq 0 \quad \forall k \in I_H \quad k \neq j \\ \zeta^{j\Omega_k} = 0 \quad \text{elsewhere} \end{cases} \tag{15}$$

Then, if the functional (9) is changed to

$$J(\theta_j, \zeta^{j\Omega}) = \int_0^T A_j I^{\Omega_j}(t)dt + \sum_{k \in I_H} \sum_{i=1}^n \frac{C_k}{2} (\zeta^{j\Omega_k}(t_i))^2 + \sum_{i=1}^n \frac{B_j}{2} \theta_j^2(t_i) \tag{16}$$

Thus, the problem changes to searching the optimal control θ^* and $\zeta^{j\Omega} = \left(\zeta^{j\Omega_k}\right)_{k \in I_H}$ belonging to the control set $Z_j^{I_H}$ defined as

$$Z_j^{I_H}([0,T]) = \{\zeta^{j\Omega}(t_i) \ \ measurable | 0 \leqslant \zeta^{j\Omega_k}(t_i) \leqslant 1, k \in I_H, t_i \in [0,T]\}$$

such that

$$J(\theta_j^*, \zeta^{j\Omega *}) = \min\{J(\theta_j, \zeta^{j\Omega_k}) / (\theta_j, \zeta^{j\Omega_k}) \in \Theta_j \times Z_j^{I_H}\}$$

subject to

$$\begin{cases} \dot{S}^{\Omega_j}(t) = \Pi_j - \sum_{k=1}^p \sum_{i=1}^n \delta(t-t_i)(1-\zeta^{j\Omega_k}(t_i))\beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) - a \sum_{i=1}^n \delta(t-t_i)\theta_j(t_i) S^{\Omega_j}(t) \\ \qquad -\mu_j S^{\Omega_j}(t) \\ \dot{V}^{\Omega_j}(t) = a \sum_{i=1}^n \delta(t-t_i)\theta_j(t_i) S^{\Omega_j}(t) - b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \mu_j V^{\Omega_j}(t) \\ \dot{I}^{\Omega_j}(t) = \sum_{k=1}^p \sum_{i=1}^n \delta(t-t_i)(1-\zeta^{j\Omega_k}(t_i))\beta_{jk} S^{\Omega_j}(t) I^{\Omega_k}(t) + b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \gamma_j I^{\Omega_j}(t) - \mu_j I^{\Omega_j}(t) \\ \dot{R}^{\Omega_j}(t) = \gamma_j I^{\Omega_j}(t) - \mu_j R^{\Omega_j}(t) \\ S_0, V_0, I_0, R_0 \ given \\ 0 \leqslant \theta_j(t_i) \leqslant 1, \ 0 \leqslant \zeta^{j\Omega_k}(t_i) \leqslant 1 \end{cases} \tag{17}$$

Or, our optimal pulse control problem can be stated as follows

$$\begin{cases} \quad \min_{(\theta_j, \zeta^{j\Omega_k}) \in \Theta_j \times Z_j^{I_H}} \left\{ \int_0^T A_j I^{\Omega_j}(t)dt + \sum_{k \in I_H} \sum_{i=1}^{n} \frac{C_k}{2} (\zeta^{j\Omega_k}(t_i))^2 + \sum_{i=1}^{n} \frac{B_j}{2} \theta_j^2(t_i) \right\} \\ \quad subject\ to \\ \quad \dot{S}^{\Omega_j}(t) = \Pi_j - \mu_j S^{\Omega_j}(t) \\ \quad \dot{V}^{\Omega_j}(t) = -b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \mu_j V^{\Omega_j}(t) \\ \quad \dot{I}^{\Omega_j}(t) = b\beta_{jj} V^{\Omega_j}(t) I^{\Omega_j}(t) - \gamma_j I^{\Omega_j}(t) - \mu_j I^{\Omega_j}(t) \\ \quad \dot{R}^{\Omega_j}(t) = \gamma_j I^{\Omega_j}(t) - \mu_j R^{\Omega_j}(t)\ when\ t \neq t_i \\ and \\ \quad S^{\Omega_j}(t_i^+) = S^{\Omega_j}(t_i) - \sum_{k=1}^{p} (1 - \zeta^{j\Omega_k}(t_i)) \beta_{jk} S^{\Omega_j}(t_i) I^{\Omega_k}(t_i) - a\theta_j(t_i) S^{\Omega_j}(t_i) \\ \quad V^{\Omega_j}(t_i^+) = V^{\Omega_j}(t_i) + a\theta_j(t_i) S^{\Omega_j}(t_i) \\ \quad I^{\Omega_j}(t_i^+) = I^{\Omega_j}(t_i) + \sum_{k=1}^{p} (1 - \zeta^{j\Omega_k}(t_i)) \beta_{jk} S^{\Omega_j}(t_i) I^{\Omega_k}(t_i) \\ \quad R^{\Omega_j}(t_i^+) = R^{\Omega_j}(t_i)\ when\ t = t_i \\ \quad S_0^{\Omega_j}, V_0^{\Omega_j}, I_0^{\Omega_j}, R_0^{\Omega_j}\ given \\ \quad 0 \leqslant \theta_j(t_i) \leqslant 1,\ 0 \leqslant \zeta^{j\Omega_k}(t_i) \leqslant 1 \end{cases}$$

In order to resolve this problem, we follow the same previous steps when there was no closure policy.

Thus, using the bounds on controls, we obtain

$$\theta_j^*(t_i) = \min\left(\max\left(0, \frac{aS^{\Omega_j *}(t_i)(\lambda_{1,j}(t_i^+) - \lambda_{2,j}(t_i^+))}{B_j} \right), 1 \right) \tag{18}$$

while for $l \in I_H$

$$\zeta^{j\Omega_l *}(t_i) = \min\left(\max\left(0, -\frac{(\lambda_{1,j}(t) - \lambda_{3,j}(t))\beta_{jl} I^{\Omega_l *} S^{\Omega_j *}}{C_l} \right), 1 \right),$$

As a numerical result, we can observe from Figure 4. that movement restriction approach is slightly more effective than immunization alone. The difference between the number of infected people when there is only pulse immunization and this number when there there is pulse closure policy, takes the values 0.07, 7.7×10^{-4} and 10^{-3} in regions Ω_1, Ω_2 and Ω_3 in the final time respectively. In fact, in the first seek weeks, as we have observed in Figure 3. when no control is recommended, we have $I^{\Omega_j}_{without} \approx I^{\Omega_j}_{with} \approx 0$, however once both impulse controls θ^*_j and $\zeta^{j\Omega_k *}$ are introduced with bigger values tending just to 0.1, we can observe that $I^{\Omega_j}_{without} - I^{\Omega_j}_{with} > 0$ which gives $I^{\Omega_j}_{with} < I^{\Omega_j}_{without}$, thus, $\zeta^{j\Omega_k *}$ is enhancing the immunization policy by reducing the number of infected people more than the case when there has been only θ^*_j.

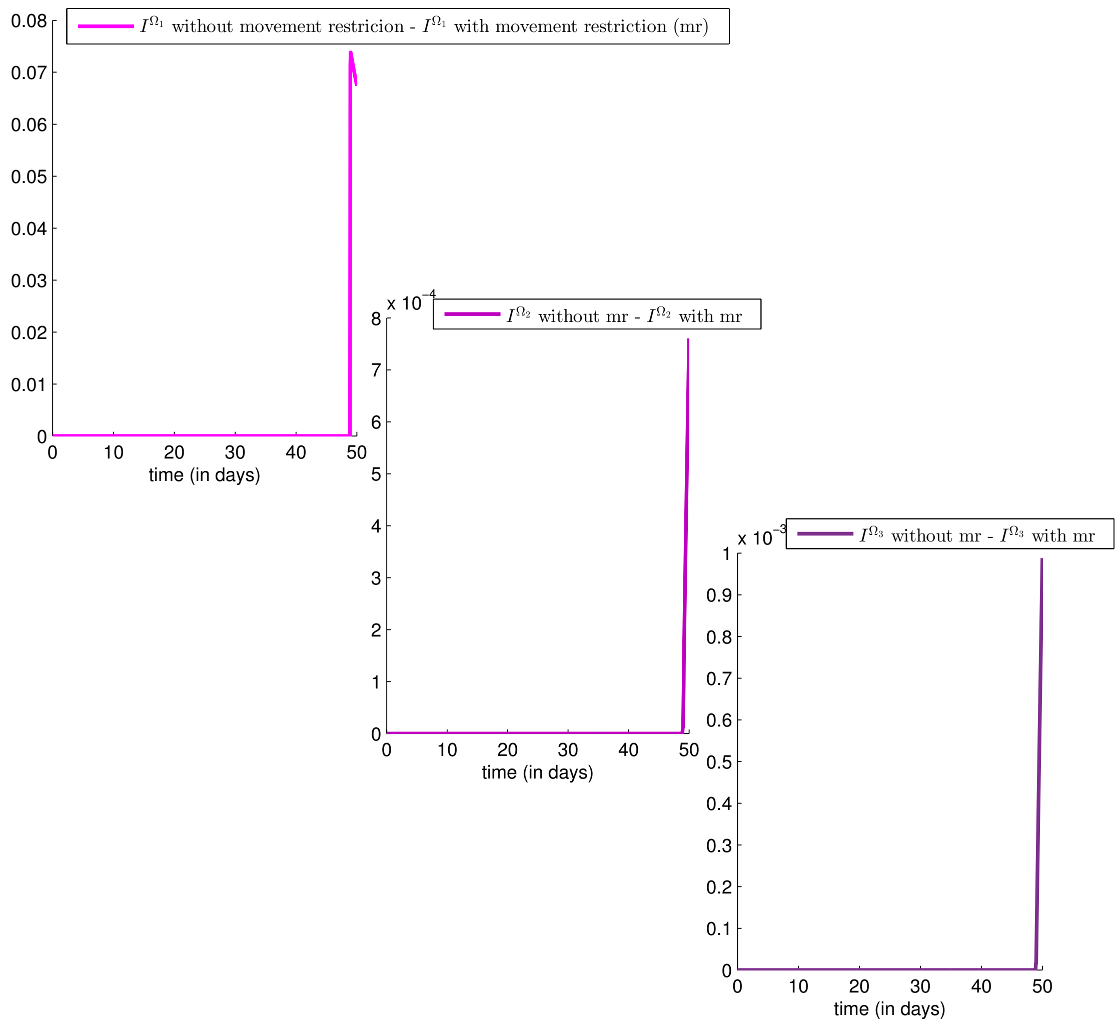

FIGURE 4. Effect of the impulse closure control on infection vs the impulse immunization control through the computation of the difference $I^{\Omega_j}_{without} - I^{\Omega_j}_{with}$.

6. CONCLUSION

In this paper, we have proposed a hybrid control model for the study of infection dynamics when an epidemic emerges in regions that are connected by any factor of mobility, considering immunization pulses for epidemic prevention in a first case, and thereafter, investigating the role of second control pulses and which have represented the closure policy used in the pandemic crisis scenario, in enhancing the effectiveness of the first one. The theoretical control framework suggested here for the multi-region impulse case has also the potential to be applied for other real-world examples.

Conflict of Interests

The authors declare that there is no conflict of interests.

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