Tikhonov regularization for a spatiotemporal model of the human monkeypox outbreak

Marouane K., Ben Rhila S., Kouidere A., Rachik M.

Laboratory of Analysis Modeling and Simulation, Department of Mathematics and Computer Science,
Faculty of Sciences Ben M'sik, Hassan II University of Casablanca, Morocco

Monkeypox is a contagious disease caused by the monkeypox virus. There is currently an outbreak of monkeypox in the U.S. and other countries where the virus is not usually seen. We develop and analyze a deterministic mathematical model for the monkeypox virus by proposing a spatiotemporal model describing the dynamics of the virus between humans. The existence, the positivity, and the boundedness of the solutions have been proved. Moreover, with the help of the optimal control, we add two different controls (blocking of contact and treatment in the case of infection) to prevent the propagation of monkeypox between humans. Finally, we present brief comments and numerical simulations to illustrate our findings. The results show that keeping diseased people apart from the general population minimizes the spread of disease.

Keywords: *spatial-temporal transmission; Human Monkeypox; Tikhonov regularization; optimal control; numerical simulation.*

2010 MSC: 93C15, 34H05, 37N35   **DOI:** 10.23939/mmc2023.03.875

1. Introduction

Numerous instances of monkeypox have been found and reported to the World Health Organization (WHO) since May 13, 2022, in around 12 non-African nations where the infection is not endemic [14,26]. The monkeypox disease is widespread in West and Central Africa, but ongoing reports from a couple of countries outside of Africa suggest that the study of disease transmission is changing and evolving [8,17]. The situation with expanding cases will keep on changing as reconnaissance and checking of monkeypox infection disease spreads to non-endemic nations and more cases will be recognized, which could pose a serious danger to worldwide general well-being [26]. The monkeypox infection is a two-fold abandoned DNA infection with two unmistakable clades: the West African clade and the Congo Basin (Central African) clade. It is an individual from the Orthopoxvirus variety and is connected with the smallpox infection [9]. The primary human to get the monkeypox zoonotic infection, which was first distinguished in monkeys in a Danish research center in 1958 [6,14,25,26], contracted it in the Democratic Republic of the Congo in 1970. In the post-smallpox time, individuals younger than 40 have diminished cross-defensive resistance, which is changing the study of disease transmission of the human monkeypox infection and its geographic circulation in West and Central Africa [7–9,13]. In May 2022, a larger than usual number of non-endemic countries detailed different instances of monkeypox infection disease [14]. As of May 21, there were 92 research centers affirmed instances of monkeypox and 28 thought cases, with most of the cases happening in the UK, Portugal, and Spain [26]. Furthermore, cases of monkeypox have been reported in the UK, Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Portugal, Spain, Sweden, and the United States of America (USA). No deaths have been attributed to the monkeypox infection in these countries. As per news sources dated May 23rd, 2022, monkeypox cases have been accounted for in Switzerland and Austria, as per news sources.

Human-to-human Kissing, cuddling, kneading, oral, butt-centric, and vaginal sex can all bring about transmission. You could come into contact with contaminated sheet material or different materials during or after sexual action. To forestall the spread of the infection, all nations should rapidly
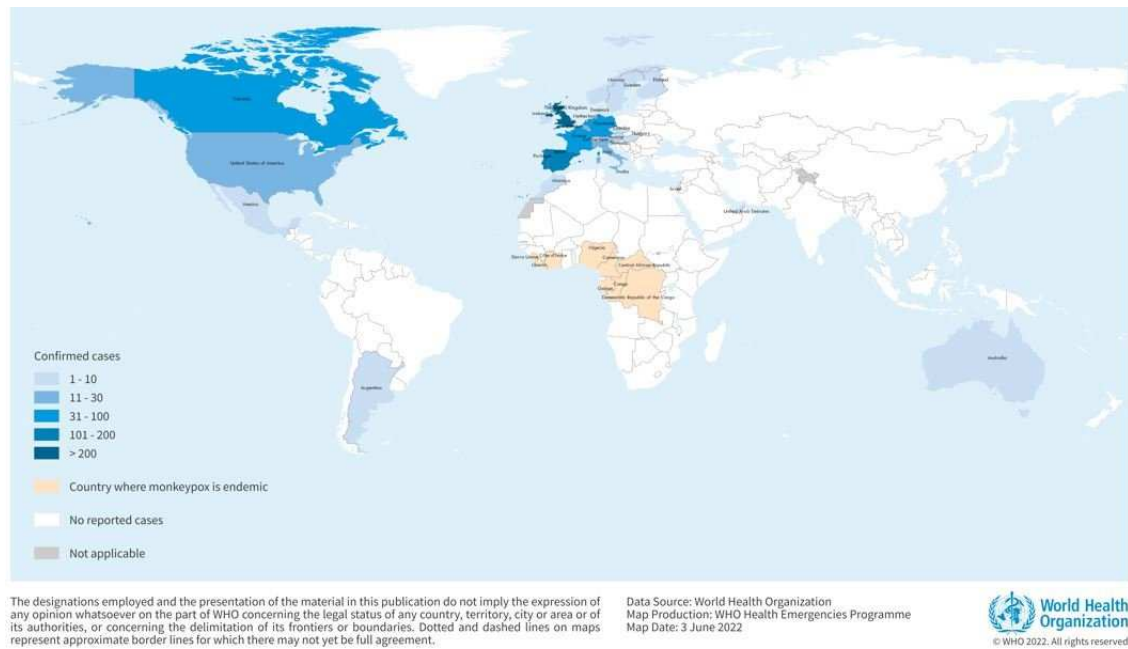
Fig. 1. Reported cases of the human monkeypox epidemic in each nation in June 23, 2022.

search for instances of monkeypox. Recognition, finding, and separation of monkeypox cases are vital for safeguarding cutting edge medical care laborers and research facility experts to keep away from new cases and lay out effective therapy ways to deal with end of flow flare-ups. On account of the sickness' absence of consideration before, its transmission components are ineffectively known. Nonetheless, a couple of scientists have endeavored to comprehend the elements of the monkeypox infection by utilizing numerical models. The research by Bhunu and Mushayabasa (see [4]) serves as the basis for an inquiry into the pox-like dynamics of the monkeypox virus. The writers of Bhunu et al. [3] have proved that the disease will be eradicated from both non-human primates and humans with the planned therapeutic intervention. Usman and Adamu [24] examine the dynamics of the monkeypox virus in rats and humans using stability analysis. TeWinkel [23], Somma et al. [21], Bankuru et al. [2], and Grant et al. all offer major additions [11]. We added spatial diffusion into our model to better model, assess, and regulate the transmission of the human monkeypox virus, as early epidemiological models frequently assumed that the population was evenly distributed throughout the area under study, which is not true. Furthermore, our primary goal is to limit the transmission of the virus by reducing the number of exposed and infected people, decreasing interactions between susceptible people and lowering the cost of treating sick people. For more studies on compartment systems using various optimal control techniques, we refer to the following references [27–30].

The structure of this paper is the following: Section 2 is staunched to the basic mathematical model problem. Section 3, we demonstrate some fundamental properties of solutions. In Section 4, we discuss the optimal control of partial differential equations. As application, the numerical results related to our control problem are given in Section 5. In the end, we conclude the article in Section 6.

2. The basic mathematical model

In this paper, we suggest an optimal control problem utilizing a spatiotemporal epidemic model. There is no doubt that the environment in which we live is spatially heterogeneous, where individuals tend to move about and where their densities depend on space. We write $S(t,x)$, $S_M(t,x)$, $S_W(t,x)$, $E_M(t,x)$, $E_W(t,x)$, $I(t,x)$, and $R(t,x)$ to show that the populations reflect the appropriate geographical and temporal behavior for the population densities of susceptible (Men and Women), exposed (Men and Women), infected, and removed, respectively. As a strategy of control, two controls $(1 - u(t,x))$ and $v(t,x)$ are introduced which represent respectively the blocking of contacts between susceptible and

exposed persons and the treatment applied on the infected. The time t belongs to a finite interval $[0,T]$, while x varies in a bounded domain $\Omega \subseteq \mathbb{R}^2$. The population dynamics is given by the following system

$$\begin{cases} \dfrac{\partial S}{\partial t} = d_S \Delta S + \Lambda - \alpha S - mS, \\[2mm] \dfrac{\partial S_M}{\partial t} = d_{S_M} \Delta S_M + \varepsilon \alpha S - (1-u)\beta_1 S_M E_M - (1-u)\beta_2 S_M E_W - mS_M, \\[2mm] \dfrac{\partial S_W}{\partial t} = d_{S_W} \Delta S_W + (1-\varepsilon)\alpha S - (1-u)\beta_3 S_W E_M - (1-u)\beta_4 S_W E_W - mS_W, \\[2mm] \dfrac{\partial E_M}{\partial t} = d_{E_M} \Delta E_M + (1-u)\beta_1 S_M E_M + (1-u)\beta_2 S_M E_W - mE_M - \gamma_1 E_M, \\[2mm] \dfrac{\partial E_W}{\partial t} = d_{E_W} \Delta E_W + (1-u)\beta_3 S_W E_M + (1-u)\beta_4 S_W E_W - mE_W - \gamma_2 E_W, \\[2mm] \dfrac{\partial I}{\partial t} = d_I \Delta I + \gamma_1 E_M + \gamma_2 E_W - (g+m+r)I - vI, \\[2mm] \dfrac{\partial R}{\partial t} = d_R \Delta R + (g+v)I - mR, \end{cases} \tag{1}$$

where $(t,x) \in Q = [0,T] \times \Omega$, with the homogenous Neumann boundary conditions

$$\frac{\partial S}{\partial \eta} = \frac{\partial S_M}{\partial \eta} = \frac{\partial S_W}{\partial \eta} = \frac{\partial E_M}{\partial \eta} = \frac{\partial E_W}{\partial \eta} = \frac{\partial I}{\partial \eta} = \frac{\partial R}{\partial \eta} = 0, \quad (t,x) \in \Sigma = [0,T] \times \partial \Omega, \tag{2}$$

where $\frac{\partial}{\partial \eta}$ is the outward normal derivative, and the symbol Δ is the usual Laplacian operator.
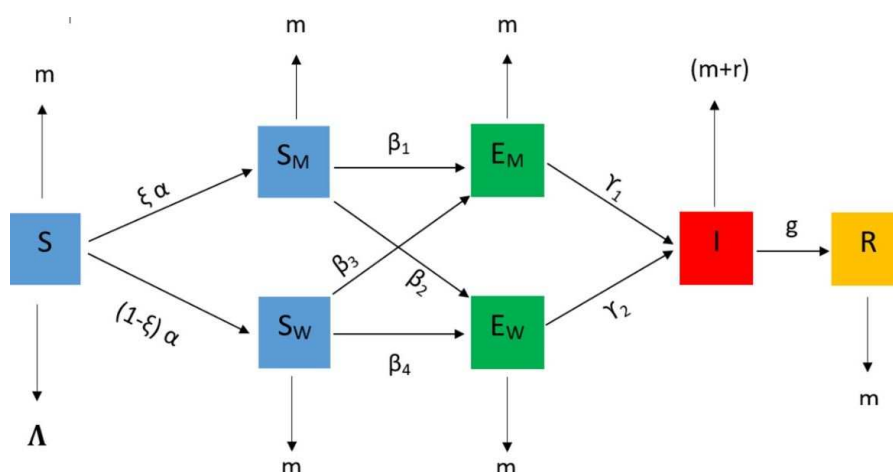

Fig. 2. Schematic representation of the model.

The initial distribution data ϕ_i are non-negative functions for $i = 1,2,3,4,5,6,7$.

$$S(0,x) = \phi_1(x) \geqslant 0, \ S_M(0,x) = \phi_2(x) \geqslant 0, \ S_W(0,x) = \phi_3(x) \geqslant 0, \tag{3}$$
$$E_M(0,x) = \phi_4(x) \geqslant 0, \ E_W(0,x) = \phi_5(x) \geqslant 0, \ I(0,x) = \phi_6(x) \geqslant 0 \text{ and } R(0,x) = \phi_7(x) \geqslant 0.$$

The meanings of the notations are shown in the following table.

3. Fundamental properties of solutions

Firstly, we introduce some notations, let $C = ([0,T], X)$ be the Banach space of continuous functions from $[0,T]$ into X with the usual supremum norm.

In our case, X is the Banach space $C(\overline{\Omega}, R^7)$, where $C(E,F)$ denotes the space of continuous functions from the topological space E into the space F.

Theorem 1. *For any initial data $\phi \in C$ satisfying the condition (3), there exists a unique solution of problem (1)–(3) defined on $[0,+\infty[$ and this solution remains non negative and bounded for all $t \geqslant 0$.*

Table 1. Parameters meaning.

Parameter	Description
Λ	Number of birth
α	probability of becoming susceptible
$\varepsilon\alpha$	Recruitment rate for susceptible men
m	Natural mortality rate
r	Death rate due to the infection
g	Guerison rate
γ_1, γ_2	Proportion of exposed human to infected humans
$\beta_1, \beta_2, \beta_3, \beta_4$	Transmission rates
$(1-\varepsilon)\alpha$	Recruitment rate for susceptible women
$d_S, d_{S_M}, d_{S_W}, d_{E_M}, d_{E_W}, d_I, d_R$	Diffusion rates

Proof. We define $F = (F_1, F_2, \ldots, F_7)\colon C \to X$ by

$$F_1(t,x) = \Lambda - \alpha F_1 - m F_1,$$
$$F_2(t,x) = \varepsilon\alpha F_1 - (1-u)\beta_1 F_2 F_4 - (1-u)\beta_2 F_2 F_5 - m F_2,$$
$$F_3(t,x) = (1-\varepsilon)\alpha F_1 - (1-u)\beta_3 F_3 F_4 - (1-u)\beta_4 F_3 F_5 - m F_3,$$
$$F_4(t,x) = (1-u)\beta_1 F_2 F_4 + (1-u)\beta_2 F_2 F_5 - m F_4 - \gamma_1 F_4,$$
$$F_5(t,x) = (1-u)\beta_3 F_3 F_4 + (1-u)\beta_4 F_3 F_5 - m F_5 - \gamma_2 F_5,$$
$$F_6(t,x) = \gamma_1 F_4 + \gamma_2 F_5 - (g+m+r) F_6 - v F_6,$$
$$F_7(t,x) = (g+v) F_6 - m F_7,$$

then, system (1)–(3) can be rewritten as the following abstract functional differential equation

$$w'(t) = Aw + F(w_t), \quad t > 0, \tag{4}$$
$$w(0) = 0,$$

where $w = (S, S_M, S_W, E_M, E_W, I, R)^T$, $\phi = (\phi_1, \phi_2, \phi_3, \phi_4, \phi_5, \phi_6, \phi_7)^T$, and $Aw = (d_S \Delta S, d_{S_M} \Delta S_M, d_{S_W} \Delta S_W, d_{E_M} \Delta E_M, d_{E_W} \Delta E_W, d_I \Delta I, d_R \Delta R)^T$, it is clear that F is locally Lipshitz in X. From [1, 20], we deduce that system (4) admits a unique local solution on $[0, T_{\max}]$, where $T_{\max}$ is the maximal existence time for solution of system (4).

In addition, we have $S(t,x) \geqslant 0$, $S_M(t,x) \geqslant 0$, $S_W(t,x) \geqslant 0$, $E_M(t,x) \geqslant 0$, $E_W(t,x) \geqslant 0$, $I(t,x) \geqslant 0$, and $R(t,x) \geqslant 0$ because 0 is a sub-solution of each equation of system (1) [12].

Now, we show the boundedness of solution. From (1)–(3)

$$\begin{cases} \dfrac{\partial S}{\partial t} - d_S \Delta S \leqslant \Lambda - mS, \\[2mm] \dfrac{\partial S}{\partial \eta} = 0, \\[2mm] S(0,x) = \phi_1(x) \leqslant \| \phi_1 \|_\infty = \max_{x \in \overline{\Omega}} \phi_1(x) \end{cases}$$

by comparison principale [16], we have $S(t,x) \leqslant S_1(t)$ where $S_1(t) = \phi_1(x)e^{-mt} + \frac{\Lambda}{m}(1 - e^{-mt})$ is the solution of the problem

$$\begin{cases} \dfrac{\partial S_1}{\partial t} = \Lambda - mS_1, \\[2mm] S_1(0) = \|\phi_1\|_\infty, \end{cases}$$

since $S_1(t) \leqslant \max(\frac{\Lambda}{m}, \|\phi_1\|_\infty)$ for $t \in \left[0, +\infty\right[$, we have that $S(t,x) \leqslant \max(\frac{\Lambda}{m}, \|\phi_1\|_\infty), \forall (x,t) \in \overline{\Omega} \times [0, T_{max}]$. From Theorem 3.1 given by Alikakos in [19], to establish the L^∞ boundedness of $S_M(t,x)$, $S_W(t,x)$, $E_M(t,x)$, $E_W(t,x)$, $I(t,x)$ and $R(t,x)$, it is sufficient to show the L^1 uniform boundedness since

$$\frac{\partial S}{\partial \eta} = \frac{\partial S_M}{\partial \eta} = \frac{\partial S_W}{\partial \eta} = \frac{\partial E_M}{\partial \eta} = \frac{\partial E_W}{\partial \eta} = \frac{\partial I}{\partial \eta} = \frac{\partial R}{\partial \eta} = 0$$

and

$$\frac{\partial}{\partial t}(S + S_M + S_W + E_M + E_W + I + R)$$
$$- \Delta(d_S S + d_{S_M} S_M + d_{S_W} \Delta S_W + d_{E_M} E_M + d_{E_W} E_W + d_I I + d_R R)$$
$$< \Lambda - m(S + S_M + S_W + E_M + E_W + I + R),$$

we get

$$\frac{\partial}{\partial t} \int_\Omega (S + S_M + S_W + E_M + E_W + I + R)\, dx \leqslant \Lambda \operatorname{mes}(\Omega) - m \int_\Omega (S + S_M + S_W + E_M + E_W + I + R)\, dx,$$

hence

$$\int_\Omega (S + S_M + S_W + E_M + E_W + I + R)\, dx \leqslant \operatorname{mes}(\Omega) \max\left\{\frac{\Lambda}{m}, \| \phi_1 + \phi_2 + \phi_3 + \phi_4 + \phi_5 + \phi_6 + \phi_7 \|_\infty\right\},$$

which implies that, $\sup\limits_{t>0} \int_\Omega S_M(t,x) \leqslant K = \operatorname{mes}(\Omega) \max\left\{\frac{\Lambda}{m}, \| \phi_1 + \phi_2 \|_\infty\right\}$, analogously for S_W, E_M, E_W, I, R.

Using Theorem 3.1 [19], we deduce that there exists a positive constant K^* that depends on K and on $\|\phi_1 + \phi_2 + \phi_3 + \phi_4 + \phi_5 + \phi_6 + \phi_7\|_\infty$ such that

$$\sup_{t \geqslant 0} \|S_M(t,x)\|_\infty \leqslant K$$

similarly for S_W, E_M, E_W, I, R.

From the above, we have proved that $S(t,x)$, $S_M(t,x)$, $S_W(t,x)$, $E_M(t,x)$, $E_W(t,x)$, $I(t,x)$, and $R(t,x)$ are L^∞ bounded on $\overline{\Omega} \times [0, T_{\max}[$.

Therefore, it follows from the standard theory for semilinear parabolic system (see [5]) that $T_{\max} = +\infty$. ∎

4. The optimal control problem

This section discusses the optimal control of partial differential equations, which was first introduced by J. L. Lions in the 1970s [10, 22].

Let us remind our system of partial differential equations

$$\begin{cases}
\dfrac{\partial S}{\partial t} = d_S \Delta S + \Lambda - \alpha S - mS, \\[2mm]
\dfrac{\partial S_M}{\partial t} = d_{S_M} \Delta S_M + \varepsilon\alpha S - (1-u)\beta_1 S_M E_M - (1-u)\beta_2 S_M E_W - mS_M, \\[2mm]
\dfrac{\partial S_W}{\partial t} = d_{S_W} \Delta S_W + (1-\varepsilon)\alpha S - (1-u)\beta_3 S_W E_M - (1-u)\beta_4 S_W E_W - mS_W, \\[2mm]
\dfrac{\partial E_M}{\partial t} = d_{E_M} \Delta E_M + (1-u)\beta_1 S_M E_M + (1-u)\beta_2 S_M E_W - mE_M - \gamma_1 E_M, \\[2mm]
\dfrac{\partial E_W}{\partial t} = d_{E_W} \Delta E_W + (1-u)\beta_3 S_W E_M + (1-u)\beta_4 S_W E_W - mE_W - \gamma_2 E_W, \\[2mm]
\dfrac{\partial I}{\partial t} = d_I \Delta I + \gamma_1 E_M + \gamma_2 E_W - (g + m + r)I - vI, \\[2mm]
\dfrac{\partial R}{\partial t} = d_R \Delta R + (g + v)I - mR,
\end{cases}$$

where $(t,x) \in Q = [0,T] \times \Omega$, with the homogenous Neumann boundary conditions

$$\frac{\partial S}{\partial \eta} = \frac{\partial S_M}{\partial \eta} = \frac{\partial S_W}{\partial \eta} = \frac{\partial E_M}{\partial \eta} = \frac{\partial E_W}{\partial \eta} = \frac{\partial I}{\partial \eta} = \frac{\partial R}{\partial \eta} = 0, \quad (t,x) \in \Sigma = [0,T] \times \partial\Omega.$$

Our goal is to minimize the density of infected and exposed individuals. Mathematically, we seek to minimize the functional objective. Therefore, we need to apply the Tikhonov regularization [18],

$$J_{\rho_1,\rho_2}(u,v) = \min_{u,v}\left[\frac{1}{2} \int_Q \big(I(t,x) + E_M(t,x) + E_W(t,x)\big)\, dt\, dx\right.$$

$$+ \frac{\rho_1}{2} \int_Q u(t,x)^2 dt\,dx + \frac{\rho_2}{2} \int_Q v(t,x)^2 dt\,dx \Big].$$

Now, let us apply the optimal control theory to find u and v.

Our class of admissible controls

$$U_{ad} = \left\{ (u,v) \in L^2([0,T] \times \Omega), \, 0 \leqslant u,v \leqslant \Gamma_i \text{ for } i = 1,2 \right\}$$

By putting $w = (u,v)$, and $w^* = (u^*,v^*)$, and as $\varepsilon \to 0$ for any $w = (u,v) \in U_{ad}$ and bounded $k = (k_1,k_2)$ such that $(w + \varepsilon k) \in U_{ad}$ for ε small, the derivative (Gateaux differentiable) of the states with respect to w are

$$\lim_{\varepsilon \to 0} \frac{S(w + \varepsilon k) - S(w)}{\varepsilon} = \psi_1, \quad \lim_{\varepsilon \to 0} \frac{S_M(w + \varepsilon k) - S_M(w)}{\varepsilon} = \psi_2$$

simultaneously for S_W, $S_W(t,x)$, $E_M(t,x)$, $E_W(t,x)$, $I(t,x)$, and $R(t,x)$, besides ψ_1, ψ_2, ψ_3, ψ_4, ψ_5, ψ_6, ψ_7 satisfy the linearized state partial differential equation

$$\frac{\partial \psi_1}{\partial t} = d_S \triangle \psi_1 + (-\alpha - m)\psi_1,$$

$$\frac{\partial \psi_2}{\partial t} = d_{S_M} \Delta \psi_2 + \varepsilon \alpha \psi_1 + [-(1-u)\beta_1 E_M - (1-u)\beta_2 E_W - m]\psi_2 - ((1-u)\beta_1 S_M)\psi_4$$
$$- ((1-u)\beta_2 S_M)\psi_5 + k_1\,(\beta_1 S_M E_M + \beta_2 S_M E_W),$$

$$\frac{\partial \psi_3}{\partial t} = d_{S_W} \Delta \psi_3 + (1-\varepsilon)\alpha \psi_1 + [-(1-u)\beta_3 E_M - (1-u)\beta_4 E_W - m]\psi_3 - (1-u)\beta_3 S_W \psi_4$$
$$- (1-u)\beta_4 S_W \psi_5 + k_1\,(\beta_3 S_W E_M + \beta_4 S_W E_W),$$

$$\frac{\partial \psi_4}{\partial t} = d_{E_M} \Delta \psi_4 + [(1-u)\beta_1 E_M + (1-u)\beta_2 E_W]\psi_2 + [(1-u)\beta_1 S_M - m - \gamma_1]\psi_4$$
$$+ ((1-u)\beta_2 S_M)\psi_5 + k_1\,(-\beta_1 S_M E_M - \beta_4 S_M E_W),$$

$$\frac{\partial \psi_5}{\partial t} = d_{E_W} \Delta \psi_5 + [(1-u)\beta_3 E_M + (1-u)\beta_4 E_W]\psi_3 + (1-u)\beta_3 S_W \psi_4 + [(1-u)\beta_4 S_W - m - \gamma_2]\psi_5$$
$$+ k_1\,(-\beta_3 S_W E_M - \beta_4 S_W E_W),$$

$$\frac{\partial \psi_6}{\partial t} = d_I \Delta \psi_6 + \gamma_1 \psi_4 + \gamma_2 \psi_5 - (g + m + r + v)\psi_6 - k_2 I,$$

$$\frac{\partial \psi_7}{\partial t} = d_R \Delta \psi_7 + (g+v)\psi_6 - m\psi_7 + k_2 I$$

with the initial conditions

$$\psi_i(0,x) = 0 \text{ for } i = 1,\ldots,7, \, x \in \Omega,$$

and the boundary conditions

$$\frac{\partial \psi_i}{\partial \eta} = 0 \text{ for } i = 1,\ldots,7, \, (t,x) \in \Sigma.$$

The linearized system changes in the operator form

$$L \begin{pmatrix} \psi_1 \\ \psi_2 \\ \psi_3 \\ \psi_4 \\ \psi_5 \\ \psi_6 \\ \psi_7 \end{pmatrix} = \begin{pmatrix} 0 \\ k_1(\beta_1 S_M E_M + \beta_2 S_M E_W) \\ k_1(\beta_3 S_W E_M + \beta_4 S_W E_W) \\ k_1(-\beta_1 S_M E_M - \beta_4 S_M E_W) \\ k_1(-\beta_3 S_W E_M - \beta_4 S_W E_W) \\ -k_2 I \\ k_2 I \end{pmatrix},$$

where

$$L = (\bar{L} + \theta), \quad \bar{L} = \frac{\partial}{\partial t} - d\Delta,$$

and

$$\theta = \begin{pmatrix} -\alpha - m & 0 & 0 & 0 & 0 & 0 & 0 \\ \varepsilon\alpha & \begin{matrix}-(1-u)\beta_1 E_M- \\ (1-u)\beta_2 E_W - m\end{matrix} & 0 & -(1-u)\beta_1 S_M & \begin{matrix}-(1-u)\beta_2 S_M \\ -(1-u)\beta_2 S_M\end{matrix} & 0 & 0 \\ (1-\varepsilon)\alpha & 0 & \begin{matrix}-(1-u)\beta_3 E_M \\ -(1-u)\beta_4 E_W - m\end{matrix} & -(1-u)\beta_3 S_W & -(1-u)\beta_4 S_W & 0 & 0 \\ 0 & \begin{matrix}(1-u)\beta_1 E_M \\ +(1-u)\beta_2 E_W\end{matrix} & 0 & \begin{matrix}(1-u)\beta_1 S_M \\ -m-\gamma_1\end{matrix} & (1-u)\beta_2 S_M & 0 & 0 \\ 0 & 0 & \begin{matrix}(1-u)\beta_3 E_M+ \\ (1-u)\beta_4 E_W\end{matrix} & (1-u)\beta_3 S_W & \begin{matrix}(1-u)\beta_4 S_W \\ -m-\gamma_2\end{matrix} & 0 & 0 \\ 0 & 0 & 0 & \gamma_1 & \gamma_2 & -(g+m+r+v) & 0 \\ 0 & 0 & 0 & 0 & 0 & g+v & -m \end{pmatrix},$$

we seek the adjoint system, such that

$$\langle L\psi, \lambda \rangle = \langle \psi, L^*\lambda \rangle$$

or

$$\int_Q (L\psi)\lambda \, dt \, dx = \int_Q \psi(L^*\lambda) \, dt \, dx.$$

It will guide us to an integral, and by integration by part we get the result. We presume that $\lambda_i(T) = 0$ so that the state equations and the adjoint equations match.

Knowing that the state equations and the adjoint equations have opposite time orientations, the adjoint operator is

$$\bar{L}^* = -\frac{\partial}{\partial t} - d\Delta \quad \text{and} \quad \theta^* = \theta^T,$$

hence $L^* = \bar{L}^* + \theta^T$.

So, the adjoint partial differential equations becomes

$$L^* \begin{pmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \\ \lambda_4 \\ \lambda_5 \\ \lambda_6 \\ \lambda_7 \end{pmatrix} = \begin{pmatrix} J(w)_S \\ J(w)_{S_M} \\ J(w)_{S_W} \\ J(w)_{E_M} \\ J(w)_{E_W} \\ J(w)_I \\ J(w)_R \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ E_M \\ E_W \\ I \\ 0 \end{pmatrix}$$

with

$$\lambda_i(t, x) = 0 \quad \text{and} \quad \frac{\partial \lambda_i}{\partial \eta} = 0 \quad \text{for} \quad i = 1, \dots, 7. \tag{5}$$

Now, let us assume that $w^* = (u^*, v^*)$ minimize $J_\rho(w)$, then for any direction $k = (k_1, k_2)$

$$0 \leqslant \lim_{\varepsilon \to 0^+} \frac{J(w^* + \varepsilon k) - J(w^*)}{\varepsilon}$$

$$= \lim_{\varepsilon \to 0^+} \frac{1}{\varepsilon} \left[\frac{1}{2} \int_Q I(w^* + \varepsilon k)^2 - I(w^*)^2 dt \, dx + \frac{1}{2} \int_Q E_M(w^* + \varepsilon k)^2 - E_M(w^*)^2 dt \, dx \right.$$

$$\left. + \frac{1}{2} \int_Q E_W(w^* + \varepsilon k)^2 - E_W(w^*)^2 dt \, dx + \rho \int_Q w^* k \, dt \, dx \right]$$

$$= \int_Q \psi_6(I(w^*)) + \psi_4(E_M(w^*)) + \psi_5(E_W(w^*)) dt \, dx + \rho \int_Q w^* k \, dt \, dx$$

$$= \int_Q \begin{pmatrix} \psi_1 & \psi_2 & \psi_3 & \psi_4 & \psi_5 & \psi_6 & \psi_7 \end{pmatrix} L^* \begin{pmatrix} 0 \\ 0 \\ 0 \\ E_M \\ E_W \\ I \\ 0 \end{pmatrix} dt \, dx + \rho \int_Q w^* k \, dt \, dx$$

$$= \int_Q \begin{pmatrix} \psi_1 & \psi_2 & \psi_3 & \psi_4 & \psi_5 & \psi_6 & \psi_7 \end{pmatrix} L^* \begin{pmatrix} \lambda_1 \\ \lambda_2 \\ \lambda_3 \\ \lambda_4 \\ \lambda_5 \\ \lambda_6 \\ \lambda_7 \end{pmatrix} dt \, dx + \rho \int_Q w^* k \, dt \, dx$$

$$
= \int_Q \begin{pmatrix} \lambda_1 & \lambda_2 & \lambda_3 & \lambda_4 & \lambda_5 & \lambda_6 & \lambda_7 \end{pmatrix} \begin{pmatrix} 0 \\ k_1(\beta_1 S_M E_M + \beta_2 S_M E_W) \\ k_1(\beta_3 S_W E_M + \beta_4 S_W E_W) \\ k_1(-\beta_1 S_M E_M - \beta_4 S_M E_W) \\ k_1(-\beta_3 S_W E_M - \beta_4 S_W E_W) \\ -k_2 I \\ k_2 I \end{pmatrix} + \rho_1 k_1 u^* + \rho_2 k_2 v^* dt\, dx
$$

$$
= \int_Q k_1(\beta_1 S_M E_M + \beta_2 S_M E_W)(\lambda_2 - \lambda_4) + (\beta_3 S_W E_M + \beta_4 S_W E_W)(\lambda_3 - \lambda_5) + \rho_1 u^*
$$

$$
+ k_2(-\lambda_6 I + \lambda_7 I + \rho_2 v^*)\, dt\, dx
$$

it holds for every function k.

Then, from the above calculation

$$
u^* = \frac{(\beta_1 S_M E_M + \beta_2 S_M E_W)(\lambda_4 - \lambda_2) + (\beta_3 S_W E_M + \beta_4 S_W E_W)(\lambda_5 - \lambda_3)}{\rho_1},
$$

$$
v^* = \frac{(\lambda_6 - \lambda_7)I}{\rho_2}
$$

as $(u^*, v^*) \in U_{ad}$, we have

$$
u^* = \min\left(1, \max\left(\frac{(\beta_1 S_M E_M + \beta_2 S_M E_W)(\lambda_4 - \lambda_2) + (\beta_3 S_W E_M + \beta_4 S_W E_W)(\lambda_5 - \lambda_3)}{\rho_1}\right)\right),
$$

$$
v^* = \min\left(1, \max\left(\frac{(\lambda_6 - \lambda_7)I}{\rho_2}\right)\right).
$$

5. Numerical Simulations

In this section, we present the numerical results that demonstrate and validate the effectiveness of our control technique. This strategy entails using two words of control, which stand for contact limitation and a treatment plan, to inhibit the spread of human monkeypox disease. To simulate our results, we wrote code in MATLAB and used various data sets. We provide numerical simulations of our optimality system, which is formulated by state equations with initial conditions and boundary conditions, adjoint equations with transversal criteria (5), and a characterization of the optimal control, with regard to the numerical approach. We employ an iterative approach to solve our optimality system called the forward-backward sweep method (FBSM) [15]. The state equations are solved using a direct method in time by employing the Euler explicit method. In order to discretize the second order derivatives ΔS, ΔS_M, ΔS_W, ΔE_M, ΔE_W, ΔI, and ΔR, we use the second order Euler explicit method. Initiation control variables are guessed at the beginning of the iterative method. Next, the adjoint equations are solved backward in time. Finally, the control variables are updated with the current state and adjoint solutions. The iterative process is repeated until a tolerance criterion is reached. To illustrate and show the effect of each control and its influence on the spread of the disease, we choose to adopt two scenarios, in the first scenario we simultaneously optimized the first is to prevent contact between susceptible individuals and those who have been exposed; the second is to treat those who have already contracted the infection

— Case 1: Applying two controls: the blocking of contacts between susceptible and exposed persons and treatment;
— Case 2: Only with treatment control.

Firstly, in Figure 4(d), Figure 4(e), Figure 4(f) and Figure 4(g), we present simulations illustrating the dynamics of exposed men, exposed women, infected and removed in the case where two control variables are considered, representing the blocking of contacts between susceptible and exposed persons and treatment (see differential system (1)). We specify that in all these figures presented here, an idea of the spread of the disease is given by the simulations in the case where the infection starts in the middle, in order to show both the effect of the spatial factor and the contribution of mobility in the transmission of the disease.

Table 2. Initial conditions and parameters values.

Parameter	Value	Description
S_0	45 for Ω_j 40 for Ω_1	Initial susceptible population
E_0	0 for Ω_j 5 for Ω_1	Initial exposed population
I_0	0 for Ω_j 5 for Ω_1	Initial infected population
R_0	0	Initial immune population
α	0.03	probability of becoming susceptible
ε	0.07	Recruitment rate from the probability of becoming susceptible
m	0.5	Natural mortality rate
γ_1, γ_2	0.2	Rate that exposed individuals become in f ectious
g	0.02	Recovery rate
Λ	0.01	birth rate
β_1	0.00035	Men to men contact rate
β_2, β_3	0.00025	Men to women contact rate
β_4	0.0003	Women to women contact rate
r	0.2	Mortality due to infection
$d_i, i = 1, 2, 3, 4, 5, 6, 7$	0.6	Diffusion coefficient
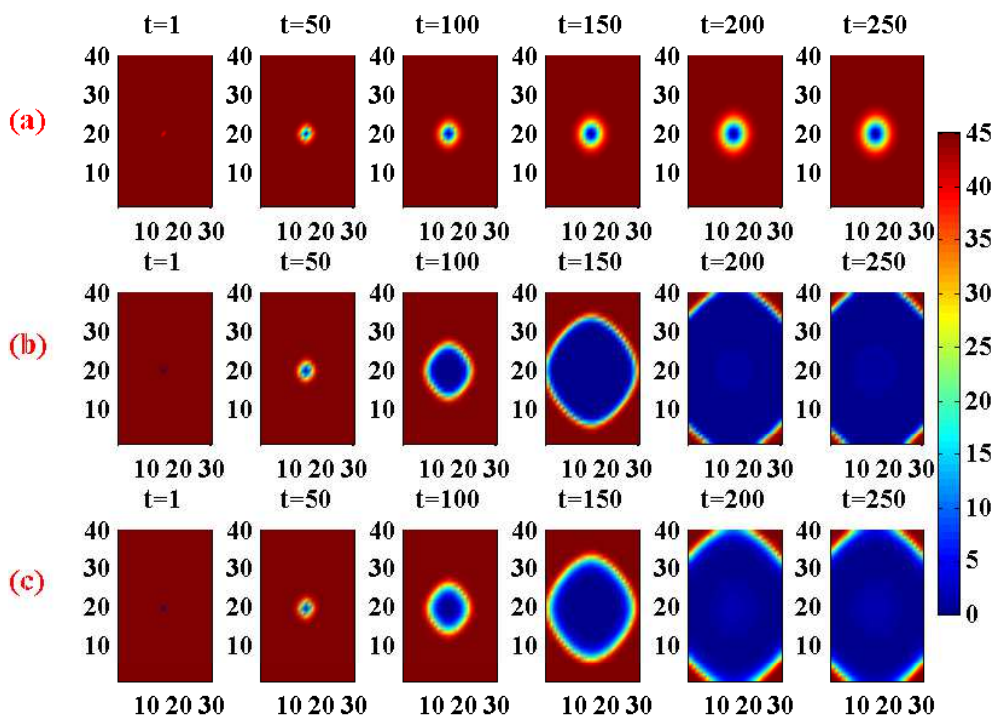
Fig. 3. States of system without controls. (a) Susceptibles behavior without control. (b) Susceptibles Men behavior without control. (c) Susceptibles Women behavior without control.

Figures 3 and 4 show that when we use our spatiotemporal control strategy based on two control words, representing contact limitation and a treatment plan, we can clearly see that the number of infected people decreases. We assume that optimal treatments begin on day $t = 1$, which is the same day that infection is detected in Ω. The impact of the spatiotemporal controls of these two control strategies is quite remarkable in slowing the spread of infection.

In Figure 4(f), the infected population, in the absence of contact limitation and treatment of infectious, increases as the susceptible are infected and reaches its maximum, then gradually decreases and then reaches a steady state where it remains constant. With the adoption of two control strategies, as shown in Figure 6, the infected population decreases and is reduced to low levels as infected individuals
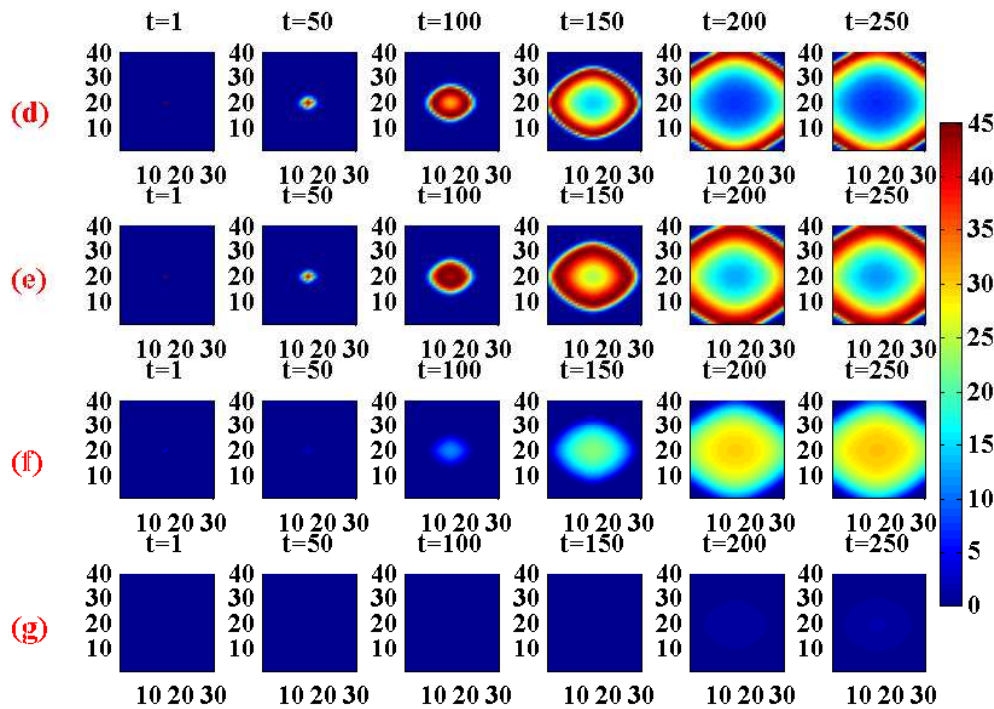
Fig. 4. States of system without controls. (d) Exposed Men behavior without control. (e) Exposed Women behavior without control. (f) Infectives behavior without control. (g) Removed Women behavior without control.

are treated, thereby reducing infectivity. The virus spreads rapidly in the first two Figures (3 and 4), and there is a high level of contagion among the different sections of the population, which causes us to take action to limit its spread. In Figure 6(f), after $t = 250$, the density of the infected population drops from 35 infected in the absence of treatment and from 2 infected in the presence of optimal controls, as shown in Figure 4(f).
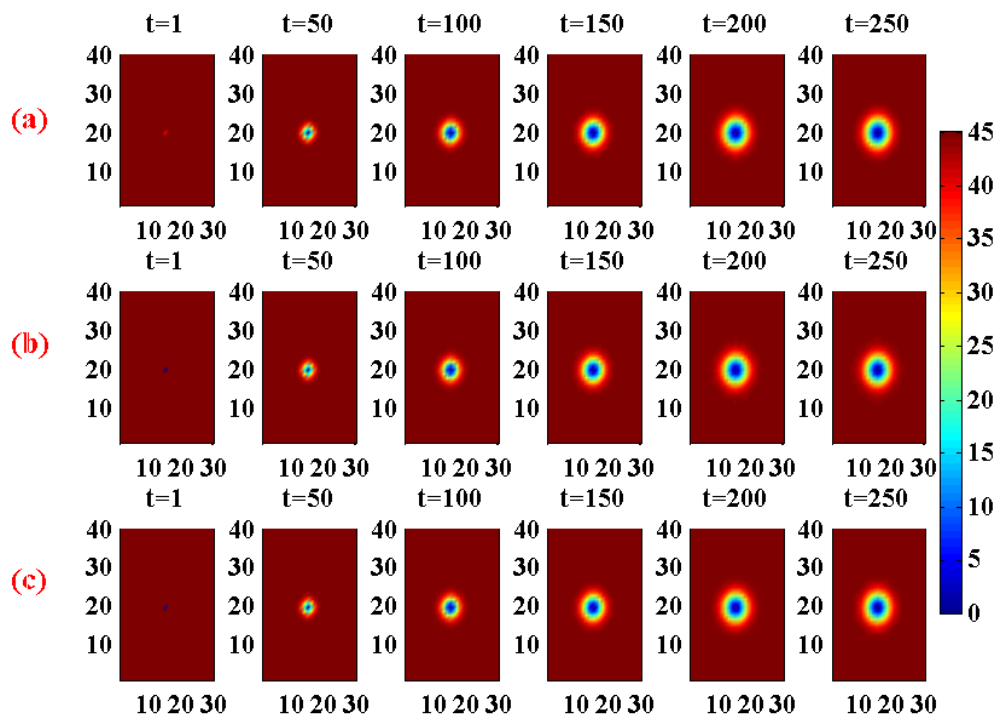

Fig. 5. States of system with controls. (a) Susceptibles behavior with control. (b) Susceptibles Men behavior with control. (c) Susceptibles Women behavior with control.
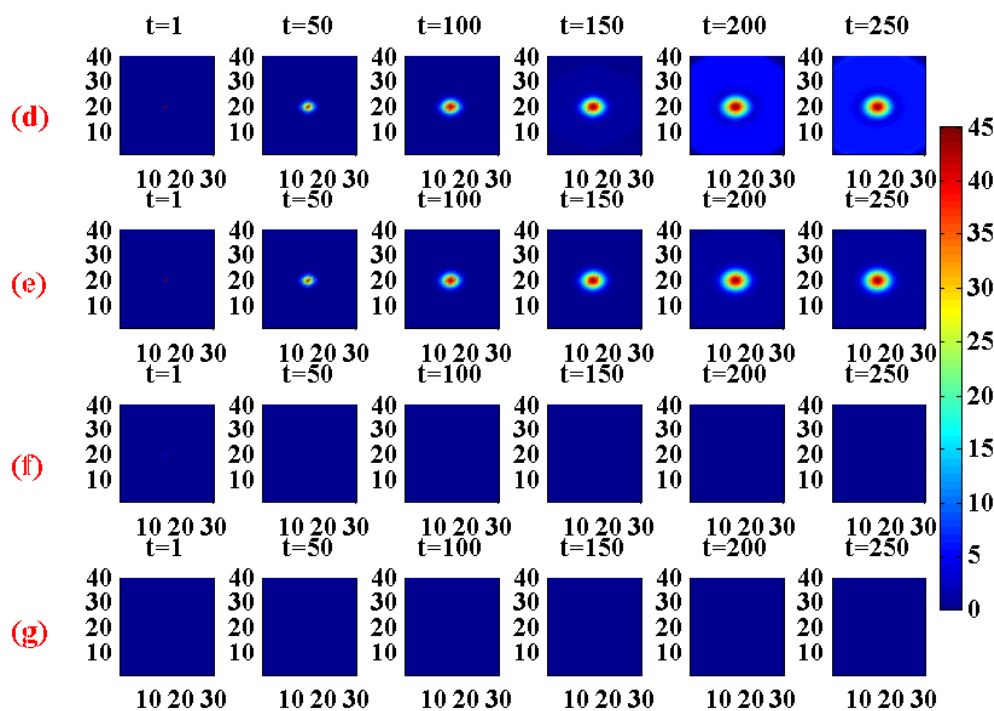
Fig. 6. States of system with controls. (d) Exposed Men behavior with control. (e) Exposed Women behavior with control. (f) Infectives behavior with control. (g) Removed Women behavior with control.
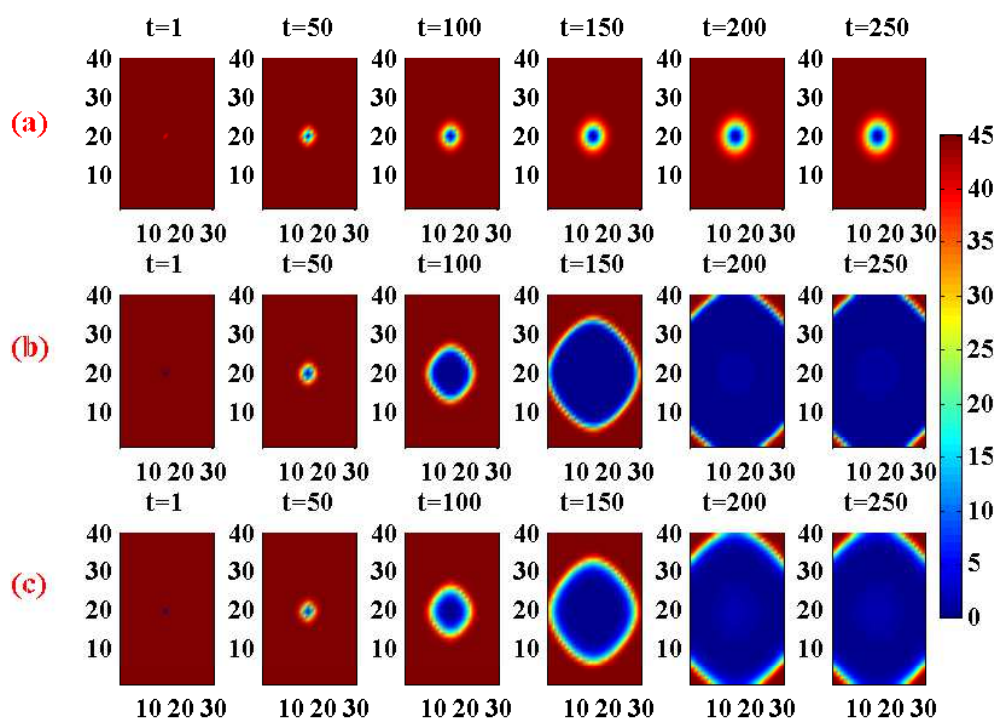

Fig. 7. States of system with treatment control. (a) Susceptibles behavior with control. (b) Susceptibles Men behavior with control. (c) Susceptibles Women behavior with control.

For comparison purposes, only case 2 with treatment control is introduced. Figures 7 and 8 represent only the treatment administered to infected patients in order to demonstrate its efficacy and functioning. Figure 8(g) shows that the maximum number of individuals eliminated reaches about 30 individuals, which is very beneficial and reflects the importance of our control strategy. Although this

control is useful in times of illness, it is important to combine it with another control approach for effective prevention.
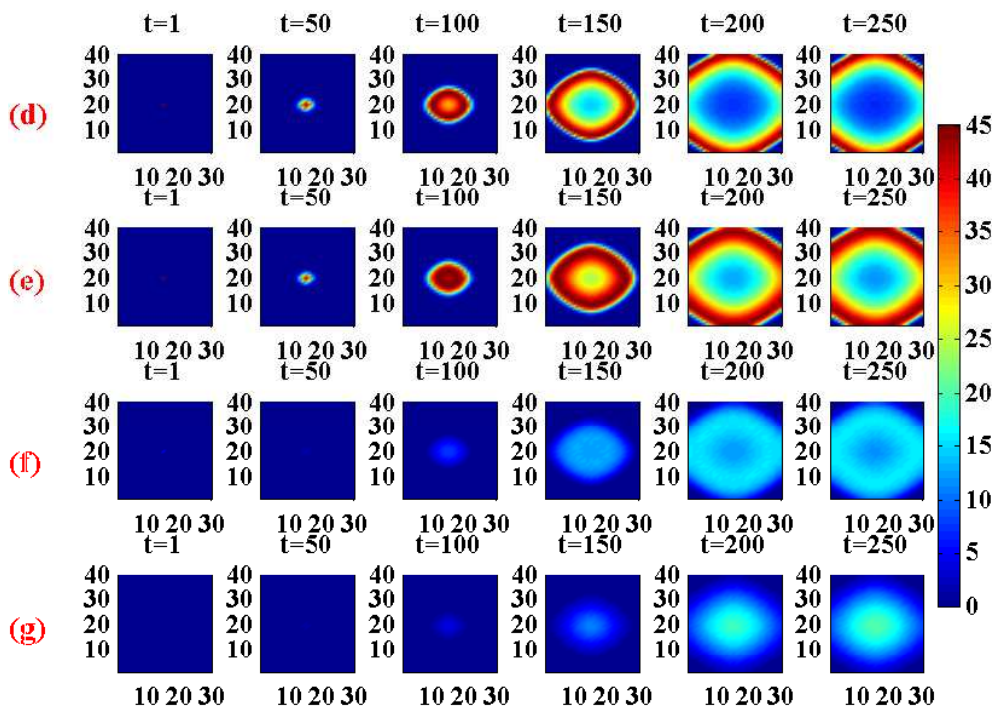

Fig. 8. States of system with treatment control. (d) Exposed Men behavior with control. (e) Exposed Women behavior with control. (f) Infective behavior with control. (g) Removed Women behavior with control.

These results provide important information that the application of both controls is an effective strategy to control the spread of epidemics.

6. Conclusion

In this paper, we present an intriguing application theory to investigate the best combination of contact restriction and treatment for spatiotemporal epidemic models described by a system of partial differential equations. The distribution of contact blocking and treatment in space and time serves as a control variable. The existence, positivity, and boundedness of the solutions of the state system are proved. A numerical simulation is performed to demonstrate the effectiveness of optimal control as a prevention and treatment tool to reduce the total number of infections of human monkeypox.

Data availability

The disciplinary data used to support the findings of this study have been deposited in the Network Repository (http://www.networkrepository.com).

[1] Pazy A. Semigroups of Linear Operators and Applications to Partial Differential Equations. Applied Mathematical Sciences. Vol. 44. Springer, New York, USA(1983).

[2] Bankuru S. V., Kossol S., Hou W., Mahmoudi P., Rychtář J., Taylor D. A game-theoretic model of monkeypox to assess vaccination strategies. PeerJ. **8**, e9272 (2020).

[3] Bhunu C., Garira W., Magombedze G. Mathematical analysis of a two strain HIV/AIDS model with antiretroviral treatment. Acta Biotheoretica. **57** (3), 361–381 (2009).

[4] Bhunu C. P., Mushayabasa S. Modelling the transmission dynamics of pox-like infections. IAENG International Journal of Applied Mathematics. **41** (2), 141–149 (2011).

[5] Henry D. Geometric Theory of Semilinear Parabolic Equations. Lecture Notes in Mathematics. Vol. 840. Springer–Verlag, Berlin, New York (1993).

[6] Mahase E. Monkeypox: what do we know about the outbreaks in Europe and North America? BMJ. **377**, o1274 (2022).

[7] Petersen E., Abubakar I., Ihekweazu C., Heymann D., Ntoumi F., Blumberg L., Asogun D., et al. Monkeypox — enhancing public health preparedness for an emerging lethal human zoonotic epidemic threat in the wake of the smallpox post eradication era. International Journal of Infectious Diseases. **78**, 78–84 (2019).

[8] Beer E. M., Rao V. B. A systematic review of the epidemiology of human monkeypox outbreaks and implications for outbreak strategy. PLoS Neglected Tropical Diseases. **13** (10), e0007791 (2019).

[9] Bunge E. M., Hoet B., Chen L., Lienert F., Weidenthaler H., Baer L. R., et al. The changing epidemiology of human monkeypox — A potential threat? A systematic review. PLoS Neglected Tropical Diseases. **16** (2), e0010141 (2022).

[10] Webb G. F. A reaction-diusion model for a deterministic diffusive epidemic. Journal of Mathematical Analysis and Applications. **84** (1), 150–161 (1981).

[11] Grant R., Nguyen L.-B. L., Breban R. Modelling human-to-human transmission of monkeypox. Bulletin of the World Health Organization. **98** (9), 638 (2020).

[12] Smoller J. Shock Waves and Reaction–Diffusion Equations. Grundlehren der mathematischen Wissenschaften. Vol. 258. Springer–Verlag, Berlin, Germany (1983).

[13] Simpson K., Heymann D., Brown C. S., Edmunds W. J., Elsgaard J., et al. Human monkeypox – after 40 years, an unintended consequence of smallpox eradication. Vaccine. **38** (33), 5077–5081 (2020).

[14] Kozlov M. Monkeypox goes global: why scientists are on alert. Nature. **606**, 15–16 (2022).

[15] McAsey M., Mou L., Han W. Convergence of the forward–backward sweep method in optimal control. Computational Optimization and Applications. **53**, 207–226 (2012).

[16] Protter M. H., Weinberger H. F. Maximum Principles in Differential Equations. Prentice Hall, Englewood Cliffs (1967).

[17] Mauldin M. R., McCollum A. M., Nakazawa Y. J., Mandra A., Whitehouse E. R., Davidson W., et al. Exportation of monkeypox virus from the African continent. Journal of Infectious Diseases. **225** (8), 1367–1376 (2022).

[18] Whitney M. L. Theoretical and numerical study of Tikhonov's regularization and Morozovs discrepancy principle. Thesis, Georgia State University (2009).

[19] Alikakos N. D. An application of the invariance principle to reaction-diffusion equations. Journal of Differential Equations. **33** (2), 201–225 (1979).

[20] Fisher R. A. The wave of advantageous genes. Annals of Eugenics. **7** (4), 353–369 (1937).

[21] Somma S. A., Akinwande N. I., Chado U. D. A mathematical model of monkey pox virus transmission dynamics. Ife Journal of Science. **21** (1), 195–204 (2019).

[22] Lenhart S., Workman J. T. Optimal control applied to biological models. Chapman and Hall/CRC, Boca Raton (2007).

[23] TeWinkel R. E. Stability analysis for the equilibria of a monkeypox model. Thesis and Dissertations, University of Wisconsin (2019).

[24] Usman S., Isa Adamu I. Modeling the transmission dynamics of the monkeypox virus infection with treatment and vaccination interventions. Journal of Applied Mathematics and Physics. **5** (12), 2335–2353 (2017).

[25] WHO, Monkeypox. `https://www.who.int/news-room/fact-sheets/detail/monkeypox` (2022).

[26] WHO, World health organization. Disease outbreak news; multicountry monkeypox outbreak in non-endemic countries. `https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385` (2022).

[27] Khaloufi I., Lafif M., Benfatah Y., Laarabi H., Bouyaghroumni J., Rachik M. A continuous SIR mathematical model of the spread of infectious illnesses that takes human immunity into account. Mathematical Modeling and Computing. **10** (1), 53–65 (2023).

[28] El Youssoufi L., Kouidere A., Kada D., Balatif O., Daouia A., Rachik M. On stability analysis study and strategies for optimal control of a mathematical model of hepatitis HCV with the latent state. Mathematical Modeling and Computing. **10** (1), 101–118 (2023).

[29] Adi Y. A., Irsalinda N., Wiraya A., Sugiyarto S., Rafsanjani Z. A. An epidemic model with viral mutations and vaccine interventions. Mathematical Modeling and Computing. **10** (2), 311–325 (2023).

[30] Kouidere A., Elhia M., Balatif O. A spatiotemporal spread of COVID-19 pandemic with vaccination optimal control strategy: A case study in Morocco. Mathematical Modeling and Computing. **10** (1), 171–185 (2023).

Регуляризація Тихонова для просторово-часової моделі спалаху мавпячої віспи людини

Маруан К., Бен Ріла С., Куідере А., Рачик М.

Лабораторія аналізу, моделювання та симуляції, Кафедра математики та інформатики,
Факультет наук Бен Мсік, Університет Хасана II Касабланки, Марокко

Мавп'яча віспа — інфекційна хвороба, яка спричинена вірусом віспи мавп. Зараз у США та інших країнах, де вірус зазвичай не зустрічається, спостерігається спалах мавп'ячої віспи. Розроблено та проаналізовано детерміновану математичну модель для вірусу мавп'ячої віспи, запропонувавши просторово-часову модель, що описує динаміку вірусу між людьми. Доведено існування, додатність та обмеженість розв'язків. Крім того, за допомогою оптимального керування додано два різних засоби контролю (блокування контакту та лікування у разі зараження), щоб запобігти поширенню мавп'ячої віспи між людьми. Накінець, подано короткі коментарі та чисельне моделювання для ілюстрації отриманих висновків. Результати показують, що ізоляція хворих від населення зводить до мінімуму поширення хвороби.

Ключові слова: *просторово-часова передача; мавпяча віспа людини; регулярізація Тихонова; оптимальне керування; чисельне моделювання.*