Application of optimal control theory to an SEIR model with immigration of infectives

Mohamed El hia, Omar Balatif, Mostafa Rachik, J. Bouyaghroumni

Laboratory of Analysis Modeling and Simulation,
Department of Mathematics and Computer Science,
Faculty of Sciences Ben M.Sik, University Hassan II
Mohammedia, BP 7955, Sidi Othman, Casablanca, Morocco

Abstract

Optimal control theory is applied to an SEIR model that includes a constant inflow of infective immigrants. Seeking to reduce the latent and infectious groups, we use two controls representing the effort that reduces the contact between the infectious and susceptible individuals, and a therapeutic treatment. The objective function is based on a combination of minimizing the number latent and infected individuals and the cost. The optimal controls are obtained by solving the optimality system. The results were analyzed and interpreted numerically using MATLAB.

Keywords: *Optimal control, SEIR model, Immigration, Pontryagin's maximum principle.*

1. Introduction

Due to a combination of factors including social, economic and demographic inequalities, whether in terms of employment opportunities, resources, education or human rights; people leave their countries in search of a safer or better life. In recent decades, global human mobility, or international migration, is a growing phenomenon affecting almost all countries in the world. According to recent DESA estimates there were, in 2011, some 214 million international migrants worldwide, representing three per cent of the total global population [1]. In epidemiology, it is well established that human mobility plays an important role in the spread of an epidemic. Indeed, some communicable diseases like HIV, SARS, avian influenza and measles; may be introduced into a population through the migration of infective individuals from outside into the host population.

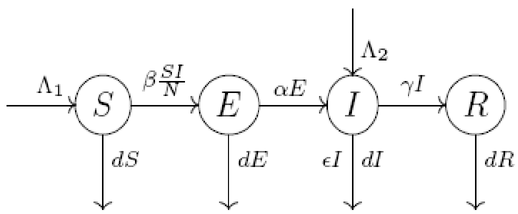
In literature, a variety of models have been formulated and mathematically analyzed to describe the behavior of an epidemic disease when spreading into a population with immigrants. Brauer and van den Driessche [2] considered simple models for disease transmission that include immigration of infective individuals and variable population size. Ram et al. [3] propose and analyze a nonlinear mathematical model of the spread of HIV/AIDS in a population of varying size with immigration of infectives. Wenjuan Wang et al. [4] incorporate the immigration of susceptible individuals into an SEIR epidemic model. An SEIR that includes the immigration of distinct compartments is formulated in [5]. Also, there has been some work where the immigrants are considered as a separate subpopulation [6,7,8].

One of the purposes of modelling epidemics is to provide a rational basis for policies designed to control the spread of a disease. The inclusion of practical control strategies in models allows assessing the intervention of public health authorities. There are two major types of control strategies available to curtail the spread of infectious diseases: pharmaceutical interventions (drugs, vaccines) and non-pharmaceutical interventions (social distancing, quarantine and a campaign for information and education). In this spirit, the focus of this study is to investigate an effective strategy to control the spread of infectious diseases by setting an optimal control problem in the SEIR model when there is immigration with some infectives. Two controls representing the effort that reduces the contact between the infectious and susceptible individuals, and a therapeutic treatment are considered in order to minimize the number of exposed and infected individuals during the course of an epidemic and also the cost of this strategy.

The paper is organized as follows. In section 2, we present a mathematical model including a constant inflow of infective immigrants and control terms. The analysis of optimization problem is presented in section 3. In section 4, we give a numerical appropriate method and the simulation corresponding results. Finally, the conclusions are summarized in section 5.

2. Mathematical model

In this paper, we consider an SEIR epidemic model with a constant inflow of infective immigrants. The population is divided into four disease-state compartments: susceptible individuals *(S)*, people who can catch the disease; exposed individuals *(E)*, people whose body is a host for the infectious agent but are not yet able to transmit the disease; infectious (infective) individuals *(I)*, people who have the disease and can transmit the disease; recovered individuals *(R)*, people who have recovered from the disease. We assume that an individual can be infected only through contacts with infectious individuals and that immunity is permanent. Schematically, the flow between compartments is represented as



The population dynamics is given by the following system of ordinary differential equations subject to non-negative initial conditions.

$$\begin{cases} \dfrac{dS}{dt} = \Lambda_1 - \beta S \dfrac{I}{N} - dS \\ \dfrac{dE}{dt} = \beta S \dfrac{I}{N} - (\alpha + d) E \\ \dfrac{dI}{dt} = \Lambda_2 + \alpha E - (\varepsilon + \gamma + d) I \\ \dfrac{dR}{dt} = \gamma I - dR \end{cases} \qquad (1)$$

Here $N(t) = S(t) + E(t) + I(t) + R(t)$ is the total population number at time *t* and the parameters are defined as follows

Table 1: Parameter definition

Parameter	Definition
β	Effective contact rate
Λ_1	Recruitment rate of susceptibles
Λ_2	Constant inflow of infectives rate
d	Natural mortality rate
α	Rate that exposed individuals become infectious
γ	Recovery rate
ε	Disease induced death rate

Into the model (1) we include two controls *u* and *v* that represent, respectively, the effort that reduces the contact between the infectious and susceptible individuals, and the rate at which infectious individuals are treated at each time period. We assume that *vI* individuals per time are removed from the infected class and added to the recovered class. The mathematical system with controls is given by the nonlinear differential equations

$$\begin{cases} \dfrac{dS}{dt} = \Lambda_1 - (1-u)\beta S \dfrac{I}{N} - dS \\ \dfrac{dE}{dt} = (1-u)\beta S \dfrac{I}{N} - (\alpha + d) E \\ \dfrac{dI}{dt} = \Lambda_2 + \alpha E - (\varepsilon + \gamma + d + v) I \\ \dfrac{dR}{dt} = \gamma I - dR + vI \end{cases} \qquad (2)$$

with $S(0) \geq 0$, $E(0) \geq 0$, $I(0) \geq 0$ and $R(0) \geq 0$ are given.

3. The optimal control problem

In this section we use the optimal control theory to analyze the behavior of the model (2). Our goal is to minimize the number of exposed and infected individuals during the course of an epidemic and the cost of this strategy. Mathematically, for a fixed terminal time t_f , the problem is to minimize the objective functional

$$J(u,v) = \int_0^{tf} \left\{ E(t) + I(t) + \frac{A_1}{2} u^2(t) + \frac{A_2}{2} v^2(t) \right\} dt \qquad (3)$$

where the parameter $A_1 \geq 0$ and $A_2 \geq 0$ denote weights that balance the size of the terms.

In other words, we seek the optimal control (u^*, v^*) such that

$$J(u^*, v^*) = \min \{ J(u,v) : \ (u,v) \in U \} \qquad (4)$$

Where U is the set of admissible controls defined by

$$U = \{ (u,v) : 0 \leq u,v \leq 1, \ t \in [0, t_f], \\ u \text{ and } v \text{ are Lebesgue mesurable} \}$$

The Pontryagin's maximum principle [9] converted (2), (3), (4) into problem of minimizing an Hamiltonian, *H*, defined by

$$H = E(t) + I(t) + \frac{A_1}{2} u^2(t) + \frac{A_2}{2} v^2(t) + \sum_{i=1}^{4} \lambda_i f_i \qquad (5)$$

where f_i is the right side of the differential equation of the i^{th} state variable. By applying the Pontryagin's maximum principle [9] and the existence result of optimal control from [10], we obtain the following theorem:

Theorem 1

There exists an optimal control $(u^*, v^*) \in U$, *and corresponding solution* S^*, E^*, I^* *and* R^*, *that minimizes* $J(u,v)$ *over U. Moreover, there exists adjoint functions,* λ_1, λ_2, λ_3 *and* λ_4 *verifying*

$$\dot{\lambda}_1 = \lambda_1 d + (\lambda_1 - \lambda_2)(1 - u^*)\beta \frac{I^*}{N^*}$$

$$\dot{\lambda}_2 = -1 + (\lambda_2 - \lambda_3)\alpha + \lambda_2 d$$

$$\dot{\lambda}_3 = -1 + (\lambda_1 - \lambda_2)(1 - u^*)\beta \frac{S^*}{N^*} + (\varepsilon + d)\lambda_3 + (\lambda_3 - \lambda_4)(\gamma + v^*)$$

$$\dot{\lambda}_4 = \lambda_4 d$$

with the transversality conditions

$$\lambda_1(t_f) = \lambda_2(t_f) = \lambda_3(t_f) = \lambda_4(t_f) = 0$$

Furthermore, the optimal control pair (u^*, v^*) *is given by*

$$\begin{aligned} u^* &= \min\left(1, \max\left(0, \frac{(\lambda_2 - \lambda_1)}{A_1}\beta \frac{I^* S^*}{N^*}\right)\right) \\ v^* &= \min\left(1, \max\left(0, \frac{(\lambda_3 - \lambda_4)}{A_2} I^*\right)\right) \end{aligned} \tag{6}$$

Proof.
The existence of optimal control can be proved by using the results from [10] (see Theorem 2.1). The adjoint equations and transversality conditions can be obtained by using Pontryagin's Maximum Principle such that

$$\begin{cases} \dot{\lambda}_1 = -\dfrac{\partial H}{\partial S}, & \lambda_1(t_f) = 0 \\ \dot{\lambda}_2 = -\dfrac{\partial H}{\partial E}, & \lambda_2(t_f) = 0 \\ \dot{\lambda}_3 = -\dfrac{\partial H}{\partial I}, & \lambda_3(t_f) = 0 \\ \dot{\lambda}_4 = -\dfrac{\partial H}{\partial R}, & \lambda_4(t_f) = 0 \end{cases}$$

The optimal control pair (u^*, v^*) can be solve from the optimality condition

$$\frac{\partial H}{\partial u} = 0 \text{ and } \frac{\partial H}{\partial v} = 0$$

By the bounds in U of the controls, it is easy to obtain (u^*, v^*) in the form of (6).

4. Numerical simulations

In this section we present the results obtained by solving numerically the following optimality system

$$\begin{cases} \dfrac{dS}{dt} = \Lambda_1 - \left\{1 - \min\left(1, \max\left(0, \dfrac{(\lambda_2 - \lambda_1)}{A_1}\beta \dfrac{IS}{N}\right)\right)\right\}\beta S \dfrac{I}{N} - dS \\ \dfrac{dE}{dt} = \left\{1 - \min\left(1, \max\left(0, \dfrac{(\lambda_2 - \lambda_1)}{A_1}\beta \dfrac{IS}{N}\right)\right)\right\}\beta S \dfrac{I}{N} - (\alpha + d)E \\ \dfrac{dI}{dt} = \Lambda_2 + \alpha E - \left(\varepsilon + \gamma + d + \min\left(1, \max\left(0, \dfrac{(\lambda_3 - \lambda_4)}{A_2} I\right)\right)\right) I \\ \dfrac{dR}{dt} = \gamma I - dR + \min\left(1, \max\left(0, \dfrac{(\lambda_3 - \lambda_4)}{A_2} I\right)\right) I \\ \dot{\lambda}_1 = \lambda_1 d + (\lambda_1 - \lambda_2)\left\{1 - \min\left(1, \max\left(0, \dfrac{(\lambda_2 - \lambda_1)}{A_1}\beta \dfrac{IS}{N}\right)\right)\right\}\beta \dfrac{I}{N} \\ \dot{\lambda}_2 = -1 + (\lambda_2 - \lambda_3)\alpha + \lambda_2 d \\ \dot{\lambda}_3 = -1 + (\lambda_1 - \lambda_2)\left\{1 - \min\left(1, \max\left(0, \dfrac{(\lambda_2 - \lambda_1)}{A_1}\beta \dfrac{IS}{N}\right)\right)\right\}\beta \dfrac{S}{N} \\ \qquad + (\varepsilon + d)\lambda_3 + (\lambda_3 - \lambda_4)\left(\gamma + \min\left(1, \max\left(0, \dfrac{(\lambda_3 - \lambda_4)}{A_2} I\right)\right)\right) \\ \dot{\lambda}_4 = \lambda_4 d \end{cases} \tag{7}$$

with $S(0) = S_0$, $E(0) = E_0$, $I(0) = I_0$, $R(0) = R_0$ and $\lambda_i(t_f) = 0 \ (i = 1, \ldots, 4)$

In this formulation, there were initial conditions for the state variables and terminal conditions for the adjoints. That is, the optimality system is a two-point boundary value problem, with separated boundary conditions at times $t=0$ and t_f. An efficient method to solve the optimality system (7) consists in the following semi-implicit finite difference method. We discretize the interval $[t_0, t_f]$ at the points $t_i = t_0 + ih \ (= 0, 1, \ldots, n)$, where h is the time step such that $t_n = t_f$, [11]. Then, we define the state and adjoint variables $S(t)$, $E(t)$, $I(t)$, $R(t)$, λ_1, λ_2, λ_3, λ_4 and the controls u and v in terms of nodal points $S_i, E_i, I_i, R_i, \lambda_1^i, \lambda_2^i, \lambda_3^i, \lambda_4^i, u^i$ and v^i. A combination of forward and backward difference approximation is used as follows:
The Method, developed by [12] and presented in [13] and [14], is then read as:

$$\frac{S_{i+1}-S_i}{h}=\Lambda_1-\left(1-u^i\right)\beta S_{i+1}\frac{I_i}{N}-dS_{i+1}$$
$$\frac{E_{i+1}-E_i}{h}=\left(1-u^i\right)\beta S_{i+1}\frac{I_i}{N}-\left(\alpha+d\right)E_{i+1}$$
$$\frac{I_{i+1}-I_i}{h}=\Lambda_2+\alpha E_{i+1}-\left(\varepsilon+\gamma+d+v^i\right)I_{i+1}$$
$$\frac{R_{i+1}-R_i}{h}=\gamma I_{i+1}-dR_{i+1}+v^iI_{i+1}$$

By using a similar technique, we approximate the time derivative of the adjoint variables by their first-order backward-difference and we use the appropriate scheme as follows

$$\frac{\lambda_1^{n-i}-\lambda_1^{n-i-1}}{h}=\lambda_1^{n-i-1}d+\left(\lambda_1^{n-i-1}-\lambda_2^{n-i}\right)\left(1-u^i\right)\beta\frac{I_{i+1}}{N}$$

$$\frac{\lambda_2^{n-i}-\lambda_2^{n-i-1}}{h}=-1+\left(\lambda_2^{n-i-1}-\lambda_3^{n-i}\right)\alpha+\lambda_2^{n-i-1}d$$
$$\frac{\lambda_3^{n-i}-\lambda_3^{n-i-1}}{h}=-1+\left(\lambda_1^{n-i-1}-\lambda_2^{n-i-1}\right)\left(1-u^i\right)\beta\frac{S_{i+1}}{N}+\left(\varepsilon+\gamma+d+v^i\right)\lambda_3^{n-i-1}-\left(\gamma+v^i\right)\lambda_4^{n-i}$$
$$\frac{\lambda_4^{n-i}-\lambda_4^{n-i-1}}{h}=\lambda_4^{n-i-1}d$$

The algorithm describing the approximation method to obtain the optimal control is the following

Algorithm 2

Step 1: $S(0)=S_0$, $E(0)=E_0$, $I(0)=I_0$, $R(0)=R_0$, $\lambda_i\left(t_f\right)=0\ \left(i=1,\dots,4\right)$ and $u(0)=v(0)=0$

Step 2: *For* $i=0,\dots,n-1$, *do*

$$S_{i+1}=\frac{S_i+h\Lambda_1}{1+h\left(d+\left(1-u^i\right)\beta\frac{I_i}{N}\right)}$$
$$E_{i+1}=\frac{E_i+h\left(1-u^i\right)\beta S_{i+1}\frac{I_i}{N}}{1+h\left(\alpha+d\right)}$$
$$I_{i+1}=\frac{I_i+h\left(\Lambda_2+\alpha E_{i+1}\right)}{1+h\left(\varepsilon+\gamma+d+v^i\right)}$$
$$R_{i+1}=\frac{R_i+h\left(\gamma+v^i\right)I_{i+1}}{1+hd}$$
$$\lambda_1^{n-i-1}=\frac{\lambda_1^{n-i}+h\left(1-u^i\right)\lambda_2^{n-i}\beta\frac{I_{i+1}}{N}}{1+h\left(d+\left(1-u^i\right)\beta\frac{I_{i+1}}{N}\right)}$$
$$\lambda_2^{n-i-1}=\frac{\lambda_2^{n-i}+h\left(1+\alpha\lambda_3^{n-i}\right)}{1+h\left(\alpha+d\right)}$$
$$\lambda_3^{n-i-1}=\frac{\lambda_3^{n-i}+h\left(1+\left(\lambda_1^{n-i-1}-\lambda_2^{n-i-1}\right)\left(1-u^i\right)\beta\frac{S_{i+1}}{N}+\left(\gamma+v^i\right)\lambda_4^{n-i}\right)}{1+h\left(\varepsilon+\gamma+d+v^i\right)}$$
$$\lambda_4^{n-i-1}=\frac{\lambda_4^{n-i}}{1+hd}$$
$$M^{i+1}=\frac{\left(\lambda_2^{n-i-1}-\lambda_1^{n-i-1}\right)}{A_1}\beta\frac{I_{i+1}S_{i+1}}{N}$$
$$T^{i+1}=\frac{\left(\lambda_3^{n-i-1}-\lambda_4^{n-i-1}\right)}{A_2}I_{i+1}$$
$$u^{i+1}=\min\left(1,\max\left(0,M^{i+1}\right)\right)$$
$$v^{i+1}=\min\left(1,\max\left(0,T^{i+1}\right)\right)$$

End for

Step 3:

For $i=0,\dots,n$, *write*

$S^*(t_i)=S_i$, $E^*(t_i)=E_i$, $I^*(t_i)=I_i$, $R^*(t_i)=R_i$, $u^*(t_i)=u^i$ and $v^*(t_i)=v^i$

End for

The simulations were carried out using the following values taken from [15]:

$$\Lambda_1=42930,\ \beta=0.3253,\ d=0.0005917\ \alpha=1/60,\ \varepsilon=0.005,\ \gamma=0.5,$$

the initial conditions for the ordinary differential system were

$S(0)=28000000$, $E(0)=10543$, $I(0)=200$, $R(0)=7500$,

the transversality conditions for the ordinary differential system were $\lambda_i\left(t_f\right)=0\ \left(i=1,\dots,4\right)$

the computer simulation is also performed for the following value of Λ_2:

$$\Lambda_2=500,\ \Lambda_2=1000\ ,\Lambda_2=2000,$$

Figures 1-3 represent the number of exposed individuals *(E)* with and without controls for different value of Λ_2. When there are no controls (dashed curve), a steady increase in the curve has been observed in the first six months. Then it starts to grow efficiently. In presence of controls, the number *E* (solid curve) starts to decrease steadily in the beginning. Then, it continues its decrease but faster.

Similarly, figures 4-6 represent the number of infected individuals *(I)* with and without controls for different value of Λ_2 . When there are no controls (dashed curve), a sharp increase in the number of infected individuals has been noticed. In presence of controls, the number I (solid curve) starts to increase steadily during the first year. Then, it continues its increase, but very slowly.

Figure 7-8 gives the optimal control pair (u^*, v^*) for different values of Λ_2 .

Finally, table 2 presents a comparison of the number of latent and infected individuals at the final time $t_f = 5$ (years) in both cases with and without controls.

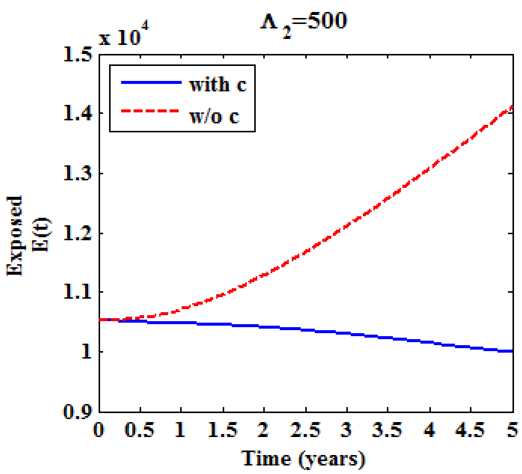


Fig. 1 The function E with and without controls when $\Lambda_2 = 500$

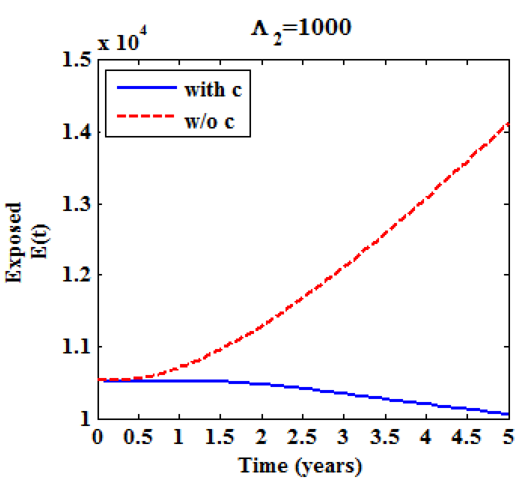


Fig. 2 The function E with and without controls when $\Lambda_2 = 1000$

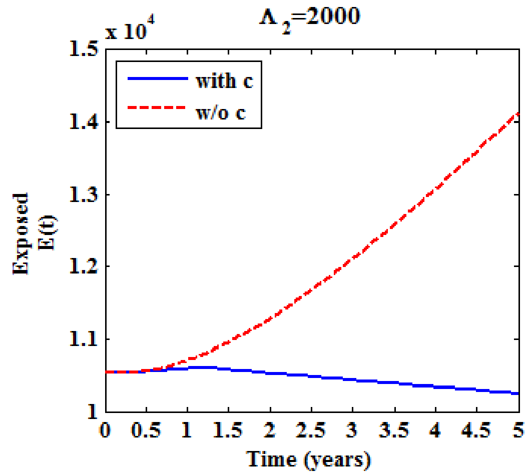


Fig. 3 The function E with and without controls when $\Lambda_2 = 2000$

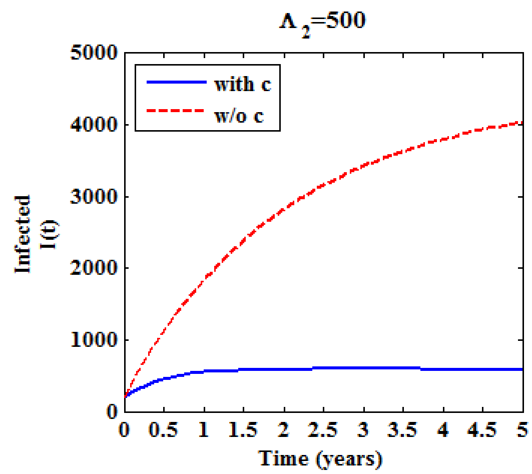


Fig. 4 The function I with and without controls when $\Lambda_2 = 500$

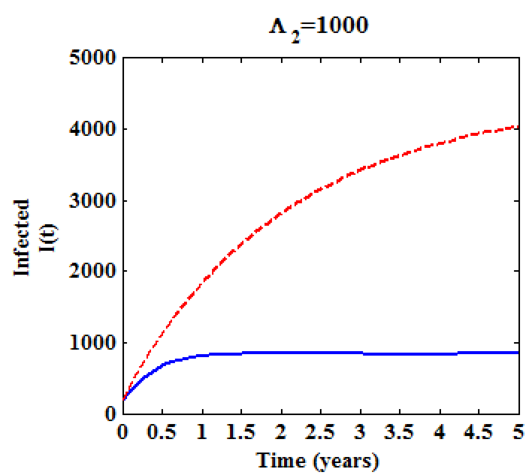


Fig. 5 The function I with and without controls when $\Lambda_2 = 1000$

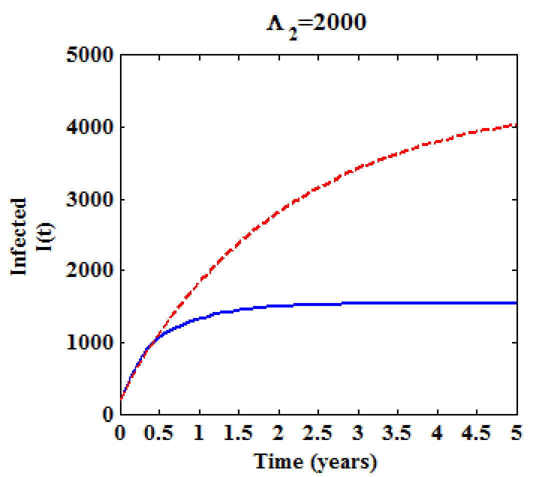


Fig. 6 The function I with and without controls when $\Lambda_2 = 2000$

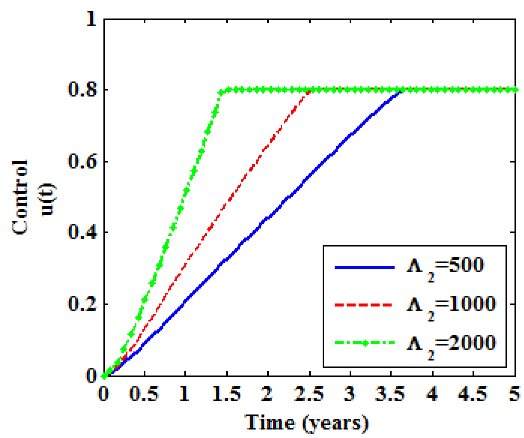


Fig. 7 The optimal control u^*

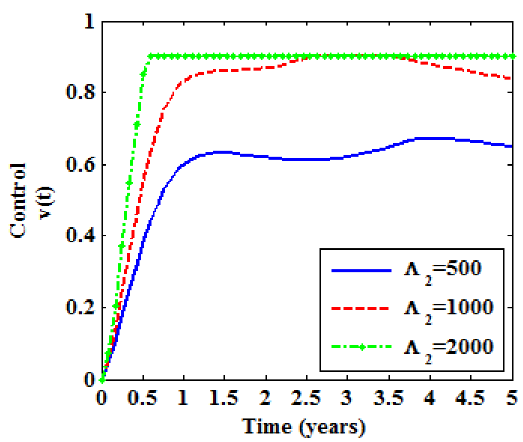


Fig. 8 The optimal control v^*

Table 2: the number of latent and infected individuals at the final time

Λ_2	Latent individuals		Infectious individuals	
	w/o controls	with controls	w/o controls	with controls
500	14130	9987	4040	574
1000	14130	10060	4040	854
2000	14130	10250	4040	1545

5. Conclusion

In this paper, we proposed an effective strategy to reduce the number of exposed and infected individuals when there is a constant inflow of infective immigrants. The optimal control theory has been applied in the context of an SEIR model with immigration of infective; and that includes two controls representing the effort reducing the contact between the infectious and susceptible individuals, and a therapeutic treatment. By using the Pontryagin's maximum principle, the explicit expression of the optimal controls was obtained. Simulation results indicate that despite the presence of a constant inflow of infective immigrants, the proposed control strategy is effective in reducing the number of patients.

Acknowledgments

Research reported in this paper was supported by the Moroccan Systems Theory Network.

References

[1] United Nations Department of Economic and Social Affairs, Trends in International Migration Stocks: Migrants by Age and Sex (New York, 2011)
[2] F. Brauer, P. van den Driessche, Models for transmission of disease with immigration of infectives, Mathematical Biosciences .154-143 (2001)171
[3] Ram Naresh, , Agraj Tripathi , Dileep Sharma, Modelling and analysis of the spread of AIDS epidemic with immigration of HIV infectives. Mathematical and Computer Modelling, 49(5-6):880-892, 2009.
[4] Wenjuan Wang, Jingqi Xin, and Fengqin Zhang, Persistence of an SEIR Model with Immigration Dependent on the Prevalence of Infection. Discrete Dynamics in Nature and Society, Volume 2010, Article ID 727168, 7 pages
[5] Zhang Juan, Li Jianquan, Ma Zhien, Global dynamics of an SEIR epidemic model with immigration of different compartments, Acta Mathematica Scientia 2006,26B(3):551-567
[6] Z. W. Jia, G. Y. Tang, Z. Jin et al., Modeling the impact of immigration on the epidemiology of tuberculosis, Theoretical Population Biology, vol. 73, no. 3, pp. 437-448, 2008.

[7] Ibrahim H. I. Ahmed, Peter J. Witbooi, and Kailash Patidar., Modeling the Dynamics of an Epidemic under Vaccination in Two Interacting Populations, Journal of Applied Mathematics Volume 2012, Article ID 275902, 14 pages

[8] C. Piccolo III and L. Billings., The Effect of Vaccinations in an Immigrant Model, Mathematical and Computer Modelling 42 299-291 (2005)

[9] L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze, E. F. Mishchenko, The Mathematical Theory of Optimal Processes, Wiley, New York, 1962.

[10] H.Raj joshi, S. Lenhart, M Y Li, L. Wang, Optimal control methods applied to disease models-Contemporary Mathematics, Volume 410, 2006

[11] A. B. Gumel, K. C. Patidar, and R. J. Spiteri, editors, Asymptotically Consistent Non-standard Finite-Difference Methods for Solving Mathematical Models Arising in Population Biology, R. E. Mickens and Worl Scientific, Singapore, 2005.

[12] A. B. Gumel, P. N. Shivakumar, and B. M. Sahai, A mathematical model for the dynamics of HIV-1 during the typical course of infection, Third world congress of nonlinear analysts, (2001), 47:20732083.

[13] J. Karrakchou, M. Rachik, and S. Gourari, Optimal control and Infectiology: Application to an HIV/AIDS Model, Applied Mathematics and Computation, (2006), 177:807818.

[14] M. El hia , O. Balatif , J. Bouyaghroumni, E. Labriji, M. Rachik, Optimal Control Applied to the Spread of Influenza A(H1N1), Applied Mathematical Sciences, Vol. 6, 2012, no. 82, 4057 - 4065

[15] Y. Zhou, K. Khan, Z. Feng, and J. Wu, Projection of tuberculosis incidence with increasing immigration trends, Journal of Theoretical Biology, vol. 254, no. 2, pp. 215-228, 2008.