

Optimal Control of an Influenza Model Using Both Vaccination and Treatment

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Abstract—This paper proposes a modification in the dynamical SVEIR model of infectious diseases. The basic SVEIR model, considers vaccination as the only control method for the disease; while in this work, we have proposed treatment as another means of control, along with vaccination. As a result, a model that uses both vaccination and treatment as the control inputs of the model is derived. After discussing the stability of the model, an optimal control method has been applied to the system, in order to derive an optimal combination of vaccines and treatment, for curing the influenza disease. It is obvious that the treatment charges are higher than the vaccination costs. As a result, a higher weight has been dedicated to treatment ratio and the infected population, in the objective function of the optimization problem. The simulation results, show more efficiency in optimal control of the new SVEIR model, compared to the classic SVEIR model, controlled with a PID controller, or an epidemic disease, controlled just with a constant vaccination ratio and without any treatments.

Keywords—optimal control, SVEIR model, treatment, vaccination, epidemic diseases.

I. INTRODUCTION

Infectious diseases are of the oldest enemies of human health. Some epidemic diseases, like plague and influenza in the past century, have inflicted heavy damages on human society. However, with the development of economic and cultural status, the infectious diseases have become under control and in some cases, such as small pox, they have been eradicated. But, still in many undeveloped countries the infectious diseases are the majority of common diseases.

One of the most important infectious diseases, which could have not been eradicated completely until now is influenza. Statistics show that influenza pandemics have periodically affected humanity since ancient times; they are rare but recurring events. Influenza spreads around the world in a yearly outbreak, resulting in about three to five million cases of severe illness and about 250 to 500 thousand deaths.

In the Northern and Southern parts of the world, outbreaks occur mainly in winter while in areas around the equator, outbreaks may occur at any time of the year. Death occurs

mostly in the young, the old and those with other health problems. Larger outbreaks known as pandemics are less frequent. In the 20th century three influenza pandemics occurred: Spanish influenza in 1918, Asian influenza in 1958, and Hong Kong influenza in 1968; each resulting in more than a million deaths. The World Health Organization, WHO, declared an outbreak of a new type of influenza A/H1N1 to be a pandemic in June 2009 [1]. There are three types of flu viruses, namely, A, B, and C. Among these influenza types, the type A viruses is more severe than others for human populations. Most influenza outbreaks and epidemics, including all pandemics of the last century, have been caused by the influenza A type viruses of a specific HA and NA subtypes. It has been the cause of excessive morbidity and mortality.

Because of the high risks of illness and high numbers of death, associated with influenza, much attention has been focused on understanding the influenza disease dynamics, and different dynamical models have been derived, in order to model this epidemic disease [2], [3]. Each model can be used as a tool to obtain a specific purpose. For example, the mathematical model uses mathematical language to describe the system. Therefore, mathematical modeling has become an important and powerful tool in understanding the dynamics of disease transmission.

The mathematical models come in many forms, from simple models to very complex ones; but all of the models must comply with the three important principles, namely, accuracy, understandability and flexibility. The mathematical models that describe the infectious diseases can be modeled in the form of ordinary differential equations (ODEs), partial differential equations (PDEs), or sometimes both [4]. The simplest model, in infectious diseases, which was first introduced in [5] is the SIR model, that includes three state variables; namely, susceptible, infected and recovered [6]–[9]. After the development of this model, a lot of mathematical models have been presented for different infectious diseases, for example the SEIR model, which includes an extra state, representing the exposed population [10]–[13]. One of the most common methods, to control the infectious diseases is

vaccination, which has been modeled either as a function or as a separate state in the literature.

A good example of dynamic models of epidemic diseases, that has considered the vaccinated population in the form of a separate state is the SVEIR dynamical model [14]–[16]. Some authors, have modeled vaccination as pulse function in their papers [17], [18]. But the vaccination is not the only way for controlling infectious diseases and sometimes it is not an efficient way either. For instance, to prevent the spread of the severe acute respiratory syndrome (SARS) during 2003-2004, scientists used quarantine method and quarantined and isolated those infected with SARS[19]. The mathematical model, SEQIHRs, which contains the additional states of quarantined and hospitalized, is another model for infectious diseases which uses quarantine as a control measure in its equations [20]. The other mathematical tool that can be used to control the spread of infectious diseases is optimal control theory. Optimal control has a long history in biomedicine, particularly, in models for cancer chemotherapy [21]. It is often used for cases in which, either vaccine or treatment is available. For example, Gaff and Schaefer [22] applied the optimal control theory to find the most effective control strategy to minimize the number of individuals who become infected. Zaman et al. [23] did a related work, but concentrated on an SIR model using only vaccination as their control strategy.

In this paper, first the SVEIR dynamic model of infectious diseases has been modified, adding a treatment ratio to the equations, in order to consider treatment of infected individuals, as another control input along with vaccination. The stability of the model has also been discussed. Then, an optimal control strategy has been applied to this new dynamic model and it has been shown that the proposed optimization on this model, provides better results compared to other control strategies, with vaccination as the only control input at hand.

The paper is organized in the following format. In section II, the SVEIR dynamical model and its normalized version are introduced thoroughly. In section III, the stability of this model is presented and discussed. Section IV, first modifies the SVEIR model, to include treatment as another important control input, and then presents the proposed optimal control strategy, while in section V, the simulation results are presented. Section VI, concludes the paper.

II. MODEL FORMULATION

In this work, the SVEIR model introduced in [3] will be used as the dynamical model of the infectious diseases. In this model, the total population is divided into five subgroups: susceptible, S, vaccinated, V, exposed, E, infective, I, and recovered, R. The total population size is denoted by $N=S+V+E+I+R$. The SVEIR dynamical model is presented by the following equations:

$$\frac{dS}{dt} = -\beta\beta_E \frac{ES}{N} - \beta\beta_I \frac{IS}{N} - \varphi S - \mu S + \delta R + \theta V + rN \quad (1)$$

$$\frac{dV}{dt} = -\beta\beta_E \beta_V \frac{EV}{N} - \beta\beta_I \beta_V \frac{IV}{N} - \mu V - \theta V + \varphi S \quad (2)$$

$$\frac{dE}{dt} = \beta\beta_E \frac{ES}{N} + \beta\beta_I \frac{IS}{N} - \beta\beta_E \beta_V \frac{EV}{N} + \beta\beta_I \beta_V \frac{IV}{N} - (\mu + k + \sigma) E \quad (3)$$

$$\frac{dI}{dt} = \sigma E - (\mu + \alpha + \gamma) I \quad (4)$$

$$\frac{dR}{dt} = kE + \gamma I - \mu R - \delta R \quad (5)$$

The biological definition of the parameters of the model in (1)-(5), are specified in Table 1.

TABLE I. MODEL PARAMETERS

Parameter	Description
β	Contact rate
β_E	Ability to cause infection by exposed individuals
β_I	Ability to cause infection by infectious individuals
$1-\beta_V$	Factor by which the vaccine reduces infection
σ^{-1}	Mean duration of latency
γ^{-1}	Mean recovery time for clinically ill
δ^{-1}	Duration of immunity loss
μ	Natural mortality rate
r	Birth rate
κ	Recovery rate of latents
α	Flu induced mortality rate
θ^{-1}	Duration of vaccine-induced immunity loss
φ	Rate of vaccination
ν	Rate of treatment

Fig.1, depicts a transfer diagram of this model, which shows the relations between these epidemic classes graphically.

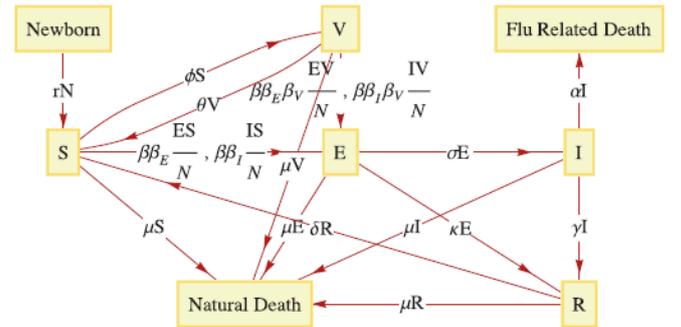


Figure 1. The flow diagram of the SVEIR model [3].

In order to analyze the SVEIR model, here we have used the normalized form of this model, which is signified the fraction of the classes S, V, E, I and R. Here we have placed $s=S/N$, $v=V/N$, $e=E/N$, $i=I/N$ and $r=R/N$ instead of SVEIR, respectively. Thus, the SVEIR model presented in (1)-(5) will be rewritten in the following normalized form [3]:

$$\frac{ds}{dt} = -\beta\beta_E ES + \beta\beta_I IS + \alpha IS - \varphi s - r s + \delta R + \theta v + r \quad (6)$$

$$\frac{dv}{dt} = -\beta\beta_E \beta_V EV - \beta\beta_I \beta_V IV + \alpha IV + \varphi s - r v - \theta v \quad (7)$$

$$\frac{dE}{dt} = \beta\beta_E ES + \beta\beta_I IS + \beta\beta_E\beta_V EV + \beta\beta_I\beta_V IV + \alpha IE - (\tau + k + \sigma)E \quad (8)$$

$$\frac{dI}{dt} = \sigma E - (\tau + \alpha + \gamma)I + \alpha I^2 \quad (9)$$

$$\frac{dR}{dt} = kE + \gamma I - \tau R - \sigma R + \alpha I \quad (10)$$

$$N = S + V + E + I + R = 1 \quad (11)$$

III. STABILITY ANALYSIS

In order to derive the equilibrium points of the system formulated in (6)-(11), the following equation should be solved:

$$\frac{dS}{dt} = \frac{dV}{dt} = \frac{dE}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0 \quad (12)$$

For deriving the disease free equilibrium, we should assume I, E, and R to be equal to zero. This results in the number of susceptible and vaccinated populations, in the absence of diseases, to be calculated as:

$$S_{df} = \frac{\tau + \theta}{\tau + \theta + \phi} \quad (13)$$

$$V_{df} = \frac{\phi}{\tau + \theta + \phi} \quad (14)$$

Now, with regards to the aforementioned fact that: $E_{df} = I_{df} = R_{df} = 0$, and with the use of (13), and (14), the disease free equilibrium of the model will be:

$$EQ_{df} = (S_{df}, V_{df}, 0, 0, 0) = \left(\frac{\tau + \theta}{\tau + \theta + \phi}, \frac{\phi}{\tau + \theta + \phi}, 0, 0, 0 \right) \quad (15)$$

Another equilibrium of the system is the endemic equilibrium point, an equilibrium in which the infected, exposed and recovered populations are not assumed to be zero, in other words, the equilibrium at the presence of the disease. This equilibrium, $EQ_{en} = (S^*, V^*, E^*, I^*, R^*)$, has been explained in [3].

With the use of the generation approach presented in [3], the next generation matrix FW is derived. In this formulation, F and W are defined as follows:

$$F = \begin{bmatrix} \beta\beta_E & \beta\beta_I \\ 0 & 0 \end{bmatrix}, \quad W = \begin{bmatrix} k + \sigma + \tau & 0 \\ -\sigma & \alpha + \gamma + \tau \end{bmatrix} \quad (16)$$

Therefore, the dominant eigenvalue of FW, called the basic reproduction number, R_0 , is calculated as:

$$R_0 = \frac{\beta(\tau\beta_E + \alpha\beta_E + \gamma\beta_E + \sigma\beta_I)}{(\tau + \alpha + \gamma)(\tau + k + \sigma)} \quad (17)$$

In [3], it has been shown that the basic reproduction number modified by vaccination is:

$$R_{vac} = R_0 (S_{df} + \beta_V V_{df}) \quad (18)$$

Substituting S_{df} and V_{df} from (15), into (18), the reproduction number R_{vac} will be derived as follows:

$$R_{vac} = R_0 \left(\frac{\tau + \theta}{\tau + \theta + \phi} + \beta_V \frac{\phi}{\tau + \theta + \phi} \right) = \frac{\beta(\tau\beta_E + \alpha\beta_E + \gamma\beta_E + \sigma\beta_I)(\tau + \theta + \beta_V\phi)}{(\tau + \alpha + \gamma)(\tau + k + \sigma)(\tau + \theta + \phi)} \quad (19)$$

It has been proved in [3], that the disease free equilibrium point of the SVEIR model in (7)-(10), would be stable for $R_{vac} < 1$. Reference one, has also investigated the stability of the endemic equilibrium point, thoroughly.

IV. OPTIMAL CONTROL FORMULATION

Although vaccination is one of the methods for controlling infectious diseases, a control strategy cannot be effective with the mere use of vaccination. Moreover, vaccination forces a lot of costs on health centers. As a result, in this work, the two strategies of vaccination and treatment have been used simultaneously in order to reduce the number of infected population. Furthermore, in order to optimize the costs we have used an optimal control method.

To reach this goal we add the rate of treatment, v , to the equations (9) and (10), which explain the dynamical behavior of the infected and recovered populations, respectively. Therefore, equations (9) and (10) are modified, and rewritten, as follows:

$$\frac{dI}{dt} = \sigma E - (\tau + \alpha + \gamma)I + \alpha I^2 - \vartheta I \quad (20)$$

$$\frac{dR}{dt} = kE + \gamma I - \tau R - \sigma R + \alpha I R + \vartheta I \quad (21)$$

The treatment expenses are much greater than the vaccination costs, as a result, the main purpose is to reduce the treatment costs. Thus, we define the purpose of the optimal control strategy, performed in this work, to reduce the treatment expenses, and number of the infected individuals; we also try to reduce the vaccination costs, as much as possible. In order to reduce the infected population, I, more individuals have to be vaccinated. This causes the majority of the vaccinated population to become immune against the disease, as a result, the disease becomes controlled and does not prevail.

The objective function of our optimal control strategy, is defined in the following general form:

$$J = \frac{1}{2} \int_0^{t_{end}} (A_1 V^2 + A_2 I^2 + \alpha u_1^2 + b u_2^2) dt \quad (22)$$

where, u_1 and u_2 are the two control inputs of the system, representing the rate of vaccination and rate of treatment, respectively. Moreover, the constants A_1 , A_2 , a , and b should be defined with regards to the fact that, reduction of the treatment charges, is much more important than lowering the vaccination costs, although reducing the vaccination costs is also our second priority.

The optimization strategy used in this work, was implemented, with the use of the "fmincon" function with "active-set" algorithm in MATLAB.

V. SIMULATION SOLUTIONS

In this section, we are going to control Influenza SVEIR model with the use of optimal control. Here we use the

objective function, introduced in (22), with the following constant parameters:

$$A_1 = 0.1, A_2 = 10, a \neq b \neq 0 \quad (23)$$

It is obvious from (23), that a greater weight, A_2 has been considered for the number of infected individuals, compared to other values, also the constant b has been given a value, much greater than A_1 , and that is because in our optimal control design, the most important priority, is to reduce the number of infected individuals, also it is very important to reduce the treatment charges. It is after these two that comes the vaccination costs, which have a lower weight in the objective function.

Also, the initial conditions are assumed to be as follows, and the parameter values used for this simulation, are shown in table. II.

$$S_0 = 0.799, V_0 = 0.197, E_0 = 0, I_0 = 0.004, R_0 = 0, N_0 = 1$$

TABLE II. PARAMETER VALUES

parameter	value
β	0.514
β_E	0.25
β_I	1.00
$1-\beta_V$	0.9
σ^{-1}	2 days
γ^{-1}	5 days
δ^{-1}	365 days
μ	$5.5 \cdot 10^{-8}$
r	$7.14 \cdot 10^{-5}$
κ	$1.857 \cdot 10^{-4}$
α	$9.3 \cdot 10^{-6}$
θ^{-1}	365 days
φ	Variable
v	Variable

Fig.2, shows the dynamical behavior of the Influenza disease, controlled with the optimal control strategy, while Fig.3, and Fig.4, show the behavior of the system, without any control strategies and with a PID controller, respectively. In order to have a better comparison between these three dynamical behaviors, the dynamics of each population has been drawn separately, for all of the three simulations, in Fig.5- Fig.9.

Fig.5, shows that the population of the susceptible individuals, in the case of the modified model with optimal control strategy, changes better, compared to its behavior in the case of PID control. Moreover, the susceptible population with optimal control, is larger compared to the case with no control, which seems to be logical, because, in the case of optimal control, less people get infected or exposed to disease, which

causes a greater proportion of the population to remain susceptible and not infected.

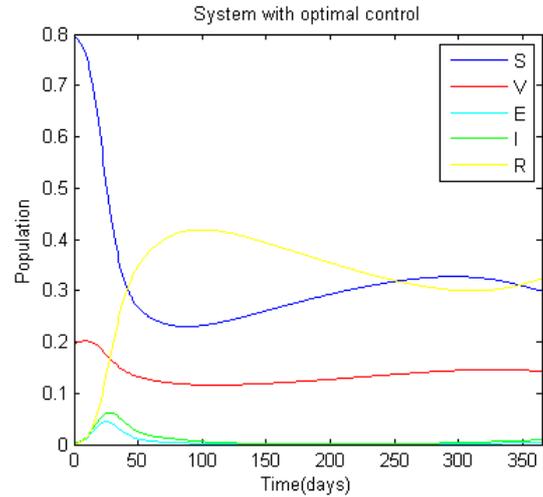


Figure 2. SVEIR model with optimal control

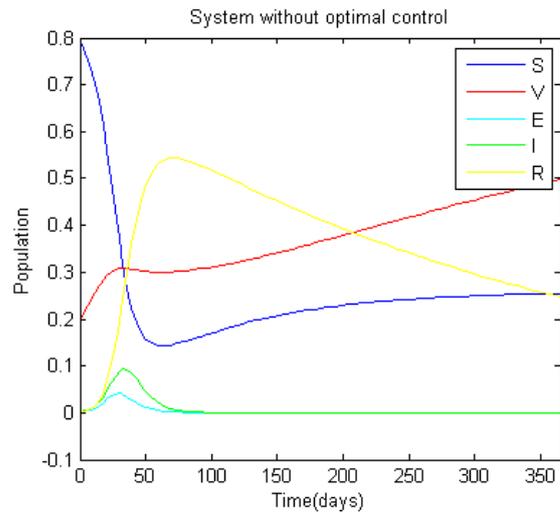


Figure 3. SVEIR model without any control

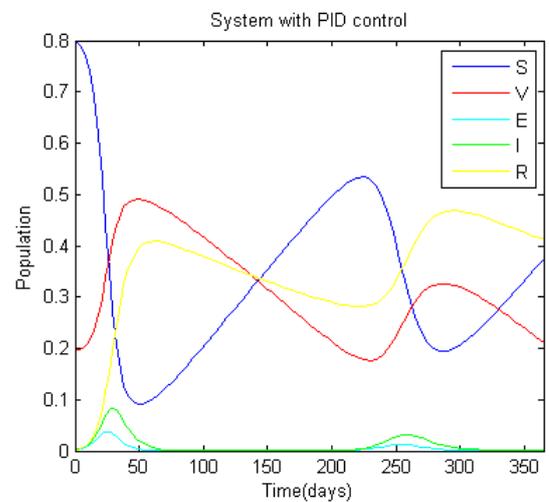


Figure 4. SVEIR model with PID control

It can be seen from Fig.6, that the vaccinated population, reduces dramatically, in the presence of optimal control strategy. This is due to the fact that, with smaller infected population, smaller proportions of the total population need to be vaccinated. This in turn, will result in lower vaccination costs.

Also, it can be seen from Fig.7, and Fig.8, that with optimal control strategy, the infected and exposed populations, have smaller amounts, which is strong representation of the efficacy of the optimal control on the proposed modified SVEIR model.

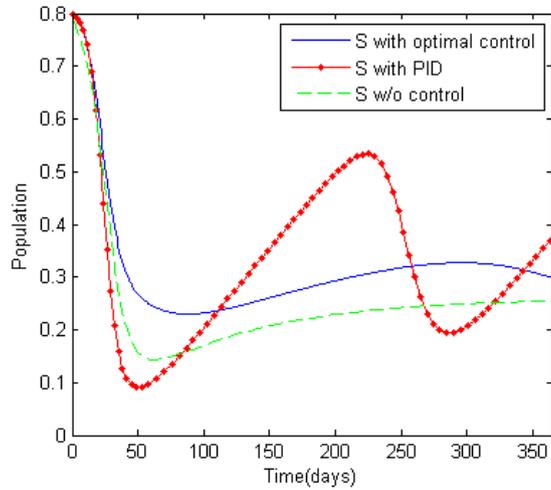


Figure 5. The population of Susceptible

Finally, Fig.9, shows that the recovered population, changes in a better fashion, with the proposed method, compared to the case of PID. Moreover, it has a lower value, compared to the recovered population, in the case with no control strategy; this is due to the fact that, when using optimal control strategies, the populations of the infected and exposed have reduced, and it is obvious that for smaller infected or exposed numbers of individuals, we will also have a smaller recovered population. In other words, there are fewer infected people in the need of being recovered, in the first place.

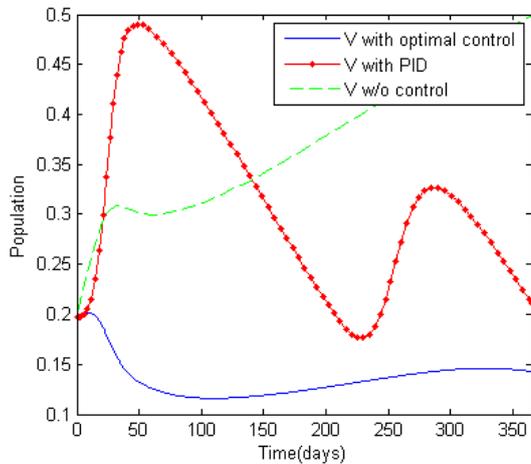


Figure 6. The population of Vaccinated

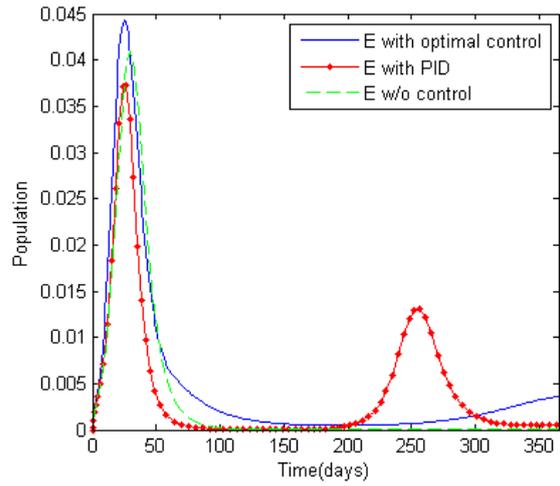


Figure 7. The population of Exposed

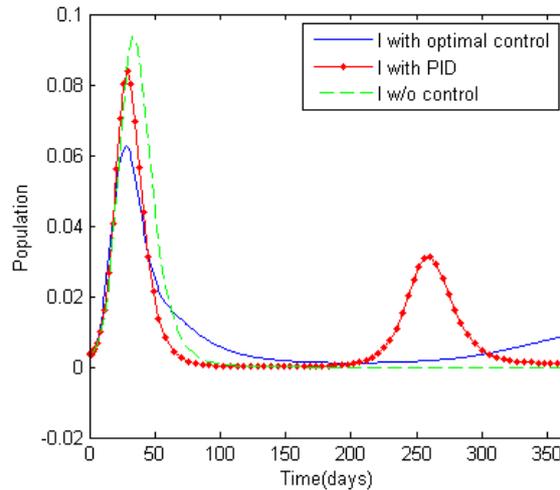


Figure 8. The population of Infected

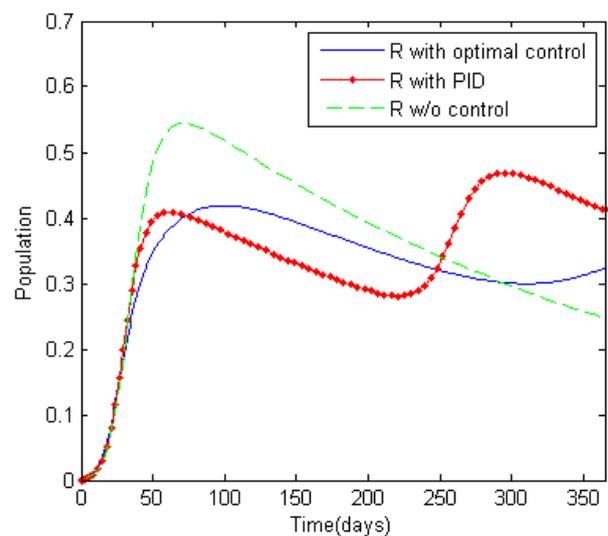


Figure 9. The population of Recovered

VI. CONCLUSION

In this paper, the SVEIR model of dynamic diseases has been considered. First, the dynamics of this system has been modified by adding the treatment ratio to the dynamical equations of the recovered and the infected populations, this enables to transport those of the infectious population who have been cured to the recovered population. After this modification, which makes the dynamical model of the disease, more realistic and applicable to real epidemic cases, the optimization problem of this new SVEIR dynamical model of infectious diseases, has been investigated. Then, an objective function has been defined to optimize the system. It is obvious that the treatment costs are much greater than the vaccination costs; making us want to reduce the treatment costs by dedicating a greater weight to the treatment in the objective function of the optimization problem. The simulation results, performed on the SVEIR model of influenza disease, show the efficacy of this method. The modified version of the SVEIR model, performs better compared to the model, which had vaccination, as its only control means, for overcoming the disease.

REFERENCES

- [1] "WHO | Influenza (Seasonal)," *WHO*. [Online]. Available: <http://www.who.int/mediacentre/factsheets/fs211/en/>. [Accessed: 19-Nov-2015].
- [2] "Interferon," *Wikipedia, the free encyclopedia*. 24-Oct-2014.
- [3] M. Samsuzzoha, M. Singh, and D. Lucy, "A numerical study on an influenza epidemic model with vaccination and diffusion," *Appl. Math. Comput.*, vol. 219, no. 1, pp. 122–141, 2012.
- [4] M. J. Keeling and P. Rohani, *Modeling infectious diseases in humans and animals*. Princeton University Press, 2008.
- [5] J. Mena-Lorcat and H. W. Hethcote, "Dynamic models of infectious diseases as regulators of population sizes," *J. Math. Biol.*, vol. 30, no. 7, pp. 693–716, 1992.
- [6] T. Fayeldi, A. Suryanto, and A. Widodo, "Dynamical Behaviors of a Discrete SIR Epidemic Model with Nonmonotone Incidence Rate," *Int. J. Appl. Math. Stat.*, vol. 47, no. 17, pp. 416–423, 2013.
- [7] L. A. Meyers and N. Dimitrov, "Mathematical approaches to infectious disease prediction and control," *Inf. Tutor. Oper. Res.*, 2010.
- [8] D. Xiao and S. Ruan, "Global analysis of an epidemic model with nonmonotone incidence rate," *Math. Biosci.*, vol. 208, no. 2, pp. 419–429, 2007.
- [9] S. Gakkhar and K. Negi, "Pulse vaccination in SIRS epidemic model with non-monotonic incidence rate," *Chaos Solitons Fractals*, vol. 35, no. 3, pp. 626–638, 2008.
- [10] C. Ozcaglar, A. Shabbeer, S. L. Vandenberg, B. Yener, and K. P. Bennett, "Epidemiological models of Mycobacterium tuberculosis complex infections," *Math. Biosci.*, vol. 236, no. 2, pp. 77–96, 2012.
- [11] H. W. Hethcote, "The mathematics of infectious diseases," *SIAM Rev.*, vol. 42, no. 4, pp. 599–653, 2000.
- [12] H. L. Smith, L. Wang, and M. Y. Li, "Global dynamics of an SEIR epidemic model with vertical transmission," *SIAM J. Appl. Math.*, vol. 62, no. 1, pp. 58–69, 2001.
- [13] X. Meng, L. Chen, and H. Cheng, "Two profitless delays for the SEIRS epidemic disease model with nonlinear incidence and pulse vaccination," *Appl. Math. Comput.*, vol. 186, no. 1, pp. 516–529, 2007.
- [14] M. A. Khan, Z. Ali, L. C. C. Dennis, I. Khan, S. Islam, M. Ullah, and T. Gul, "Stability Analysis of an SVIR Epidemic Model with Non-linear Saturated Incidence Rate," *Appl. Math. Sci.*, vol. 9, no. 23, pp. 1145–1158, 2015.
- [15] S. Liao and W. Yang, "On the dynamics of a vaccination model with multiple transmission ways," *Int. J. Appl. Math. Comput. Sci.*, vol. 23, no. 4, pp. 761–772, 2013.
- [16] L. Gao and H. Hethcote, "Simulations of rubella vaccination strategies in China," *Math. Biosci.*, vol. 202, no. 2, pp. 371–385, 2006.
- [17] I. A. Moneim, "Efficiency of different vaccination strategies for childhood diseases: A simulation study," 2013.
- [18] X. Liu and P. Stechliniski, "SIS models with switching and pulse control," *Appl. Math. Comput.*, vol. 232, pp. 727–742, 2014.
- [19] A. Mubayi, C. K. Zaleta, M. Martcheva, and C. Castillo-Chavez, "A cost-based comparison of quarantine strategies for new emerging diseases," *Math Biosci Eng.*, vol. 7, no. 3, pp. 687–717, 2010.
- [20] G. P. Sahu and J. Dhar, "Dynamics of an SEIQHRS epidemic model with media coverage, quarantine and isolation in a community with pre-existing immunity," *J. Math. Anal. Appl.*, vol. 421, no. 2, pp. 1651–1672, 2015.
- [21] G. W. Swan, "Role of optimal control theory in cancer chemotherapy," *Math. Biosci.*, vol. 101, no. 2, pp. 237–284, 1990.
- [22] H. Gaff and E. Schaefer, "Optimal control applied to vaccination and treatment strategies for various epidemiological models," *Math. Biosci. Eng. MBE*, vol. 6, no. 3, pp. 469–492, 2009.
- [23] G. Zaman, Y. H. Kang, and I. H. Jung, "Stability analysis and optimal vaccination of an SIR epidemic model," *BioSystems*, vol. 93, no. 3, pp. 240–249, 2008.