OPTIMAL CONTROL OF AN EPIDEMIC MODEL WITH INCLUSION OF GAME THEORY IN VACCINATION

By

Wenzhong Wang

Senior Honor Thesis
Department of Mathematics
University of North Carolina at Chapel Hill

May 4, 2021

Approved:

Christopher Jones, Thesis Advisor

Stephen Schecter, Reader

Christian Sampson, Reader

ABSTRACT

WENZHONG WANG. Optimal control of an epidemic model with inclusion of game theory in vaccination. (Under the supervision of CHRISTOPHER JONES)

An SIR epidemic model is expanded to include a game theory characterization of changes in human vaccination acceptance. Using the vaccination capacity as a control, we apply optimal control theory to the model and minimize the infected population and social cost simultaneously. We conduct numerical simulations and analyze different scenarios to control COVID-19. Numerical results suggest that the scenario with an optimal control on vaccination capacity may offer a feasible approach for eliminating the epidemic with minimal cost and time. We give a specific vaccination plan based on the optimal control scenario.

ACKNOWLEDGEMENTS

I would like to express my very great appreciation to my advisor Professor Christopher K.R.T. Jones for his patient guidance, constructive suggestions, and valuable critiques of the senior honor research work as well as my independent study during my sophomore and junior years. I would also like to thank Professor Stephen Schecter for his help in the research background and model design.

I would like to extend my thanks to Professor Mary Silber and John Gemmer, my advisors at the Mathematics and Climate Research Network, for their advice and assistance in my research on dynamical systems and El Niño models, and to Dr. Christian Sampson for his support in my MCRN research work.

This project was supported by the Alexandre Honors Carolina Expendable Fund administered by Honors Carolina. Special thanks should be given to the Fund for covering the cost of computer software.

Finally, I wish to thank my parents for their financial support and encouragement throughout my undergraduate study abroad.

TABLE OF CONTENTS

CHAPTER 1: INTRODUCTION

The COVID-19 outbreak at the end of 2019 had a huge negative impact on global public health and economic development. Scientists have been long using optimal control on the SIR model to study the spread of epidemics and investigate various control strategies. Some studies take education campaigns, social distancing, and quarantine as available policies and indicate that one can find policy known as a maximum control by using optimal control theory [3, 6, 8]. Other scientists have also taken vaccination into consideration [7]. With limited control resources, Hansen and Day applied bang-bang control to a combination of the optimal isolation-only policy and the optimal vaccination-only policy, where more than one control variable was utilized in their model [4].

Additionally, a particular approach to formulating an SIR model based on game theory recently became popular in epidemic model studies. Human behavior changes greatly affect the spread of diseases. An analysis on imitation dynamics and vaccination policy showed that game theoretical models are feasible for appropriating the population dynamics of vaccinating behaviour [2]. Poletti et al. proposed an SIR model including eight classifications of population as well as two different time scales in the disease transmission process and the imitation process [11]. Other studies develop Poletti's model and conduct a geometric singular perturbation theory analysis to explore model performances [12].

We adapt optimal control on an SIR model and include imitation dynamics in human behavior towards vaccination. To my knowledge, there have been no previous uses of both optimal control theory and imitation dynamics in epidemic models. We

are investigating a model design which includes the two techniques and reflects some key aspects of the actual situation under COVID-19.

Chapter 2 of this thesis describes the model design and analyses the feasibility of optimal control. Chapter 3 discusses the choice of parameter values. Chapter 4 gives numerical illustrations and analysis on different scenarios of the model, and the last Chapter is the conclusion.

CHAPTER 2: MATHEMATICAL MODEL

We start with an SIR model in epidemiology, where S refers to the susceptible proportion of the population, whether vaccinated or not. I is the infected proportion of the population, and R is the naturally immune proportion of the population. Suppose the population will not increase or decrease. Since $S + I + R \equiv 1$, we could eliminate the equation for R. In the system of differential equations of the model, the control variable u is the maximum number of people that can be vaccinated at a time instant, which represents the vaccination capacity. Denote α as the relative frequency of people who accept vaccines and x as the relative frequency of vaccine coverage. We consider an ordinary differential equation model, which describes the vaccination "game" with imitation dynamics and control on vaccination capacity, as following:

$$\begin{aligned} S' &= -[(1-\eta)x + (1-x)]SI\beta \\ I' &= [(1-\eta)x + (1-x)]SI\beta - \gamma I \\ \alpha' &= k\alpha(1-\alpha)(f_v - f_n) \\ x' &= udx(1 - \frac{x}{\alpha}) \end{aligned} \tag{2.1}$$

Here, η is the efficacy of vaccines, supposed to be very high. β is the mean transmission rate and γ is the recovery rate. The third equation describes the imitation dynamics of vaccination in game theory [2]. In this equation, k is the combined imitation rate at which individuals mimic others and switch strategies. The perceived payoff f_v for vaccinators is

$$f_v = -r_v - (1-\eta)r_i mI \tag{2.2}$$

where r_v is the perceived probability of significant morbidity from the vaccine, r_i is the perceived probability of suffering significant morbidity upon infection, and m is a constant measuring the sensitivity of vaccinating behaviour to changes in prevalence of people who accept vaccines. The perceived payoff f_n for non-vaccinators is

$$f_n = -r_i m I \tag{2.3}$$

The fourth equation, which is a logistic equation, describes the relationship between vaccine coverage, vaccine acceptance, and vaccine capacity during the whole vaccination [13]. The number of people vaccinated will not exceed the number of people accepting the vaccine. The parameter d is a proportion constant in this equation.

Plugging into these equations, we have

$$\begin{aligned} S' &= -(1-\eta x)SI\beta \\ I' &= (1-\eta x)SI\beta - \gamma I \\ \alpha' &= k\alpha(1-\alpha)(-r_v + \eta r_i m I) \\ x' &= udx(1-\frac{x}{\alpha}) \end{aligned} \tag{2.4}$$

We assume the control variable is bounded as $u_a \leq u \leq u_b$. The cost function considers the social cost of both vaccination and treatment for people infected, which is in the form of

$$J(u) = \int_0^T pu^2 + I(t)dt \tag{2.5}$$

where p is a positive constant measuring the proportion of vaccination cost to treatment cost, in order to make the two costs comparable to each other.

The Hamiltonian is

$$\begin{aligned} H =& \lambda_1 S' + \lambda_2 I' + \lambda_3 \alpha' + \lambda_4 x' + L \\ =& \lambda_1[-(1-\eta x)SI\beta] + \lambda_2[(1-\eta x)SI\beta - \gamma I] + \lambda_3 k\alpha(1-\alpha)(-r_v + \eta r_i m I) \\ &+ \lambda_4 u d x(1-\frac{x}{\alpha}) + pu^2 + I \end{aligned} \tag{2.6}$$

By Pontryagin's Maximum Principle [5, 9], we verify sufficient conditions for our optimal control and corresponding states. We have

$$H_u = \lambda_4 d x(1-\frac{x}{\alpha}) + 2pu \tag{2.7}$$

Then $H_{uu} = 2p > 0$, hence this optimal control problem is indeed minimization. The optimality condition is

$$H_u = 0 \Rightarrow u^* = -\frac{1}{2p}\lambda_4 d x(1-\frac{x}{\alpha}) \tag{2.8}$$

Given an optimal control u^*, there exist adjoint functions, $\lambda_1, \lambda_2, \lambda_3, \lambda_4$, corresponding to the states S, I, α, x such that

$$\begin{aligned} \lambda_1' &= -\frac{\partial H}{\partial S} = (\lambda_1 - \lambda_2)(1-\eta x) I\beta \\ \lambda_2' &= -\frac{\partial H}{\partial I} = \lambda_1(1-\eta x)S\beta - \lambda_2[(1-\eta x)S\beta - \gamma] - \lambda_3 k\alpha(1-\alpha)\eta r_i m - 1 \\ \lambda_3' &= -\frac{\partial H}{\partial \alpha} = -\lambda_3 k(-r_v + \eta r_i m I)(1-2\alpha) - \lambda_4 u d\frac{x^2}{\alpha^2} \\ \lambda_4' &= -\frac{\partial H}{\partial x} = (\lambda_2 - \lambda_1) SI\beta\eta + 2\lambda_4 u d\frac{x}{\alpha} \end{aligned} \tag{2.9}$$

Due to both necessary clinics and limited resources in vaccination, we apply bang-bang control in the model. Since u is bounded as $u_a \le u \le u_b$, if $H_u > 0$, we have $u(t) = u_b$; if $H_u < 0$, we have $u(t) = u_a$; otherwise, we have $u(t) = -\frac{1}{2p}\lambda_4 d x(1-\frac{x}{\alpha})$ as

the optimality condition above. We use Runge-Kutta method in order 4 to solve the ODE system (2.4), (2.8), and (2.9), with initial conditions $S(0) = S_0, I(0) = I_0, \alpha(0) = \alpha_0, x(0) = x_0$. The transversality condition is $\lambda_1(0) = \lambda_2(0) = \lambda_3(0) = \lambda_4(0) = 0$.

In the phase space, this dynamical system has two line segments of equilibria. One is a disease-free, complete vaccine acceptance but pure non-vaccinator (nobody vaccinated) line $(S_1, 0, 1, 0)$ for any $0 \leq S_1 \leq 1$. The other is a disease-free, complete vaccine acceptance, and pure vaccinator (everybody vaccinated) line $(S_2, 0, 1, 1)$ for any $0 \leq S_2 \leq 1$.

CHAPTER 3: PARAMETERS

We estimate the baseline parameters of the model from available COVID-19 data and reasonable speculations. Since the real-world Pfizer-BioNTech COVID-19 Vaccine (BNT162b2) effectiveness estimates align with the 95% vaccine efficacy in clinical trials [10], we set $\eta = 0.95$, which is very high. For two other epidemiological parameters, we set $\beta = 0.1$ and $\gamma = 0.04$, then the basic reproduction number $R_0 = \dfrac{\beta}{\gamma} = 2.5$, which is in line with the estimation in the early phase of the COVID-19 outbreak in Wuhan, China [14].

Earlier research has determined the value of imitaion dynamics parameters r_v and r_i for its numerical simulations [2]. However, this research has conducted non-dimensionalization to reduce the number of parameters and to further explore underlying Hopf bifurcation, so we are not clear about the exact values of r_v and r_i. We currently set $r_v = 0.0001$ and $r_i = 0.02$ to make them consistent with the situation in Bauch's study.

For other baseline parameters, we consider $k = 1, m = 10, d = 6$. We use p to adjust the influence of vaccination cost and treatment cost, and it is currently estimated to be $p = 1200$. We set the baseline control bounds as $u_a = 0.005$ and $u_b = 0.012$.

CHAPTER 4: ANALYSIS

We conduct numerical simulations in MATLAB to solve the optimal control system. The unit of time in simulations is days. We set initial conditions $S(0) = 0.95, I(0) = 0.05, \alpha(0) = 0.3, x(0) = 0.01, u(0) = 0.008$. We use the baseline parameters except when otherwise stated.

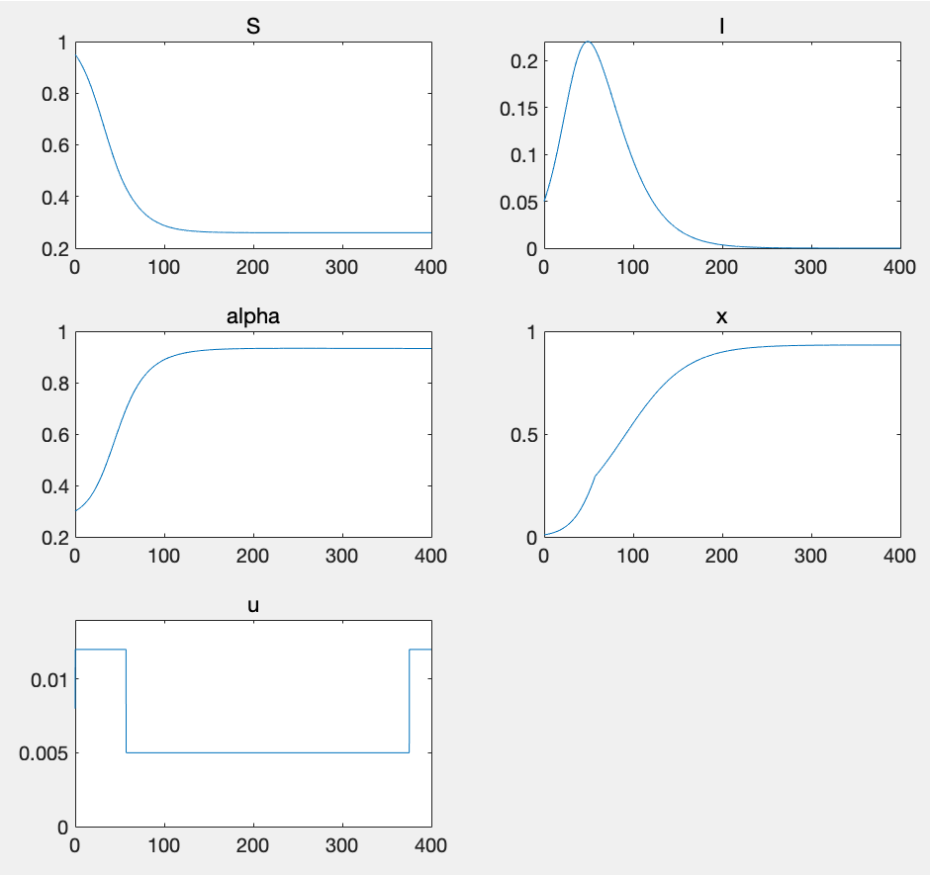

Figure 4.1: Results using the baseline parameters.

Figure 4.1 and 4.2 show the 'bang-bang' control using the baseline parameters. The

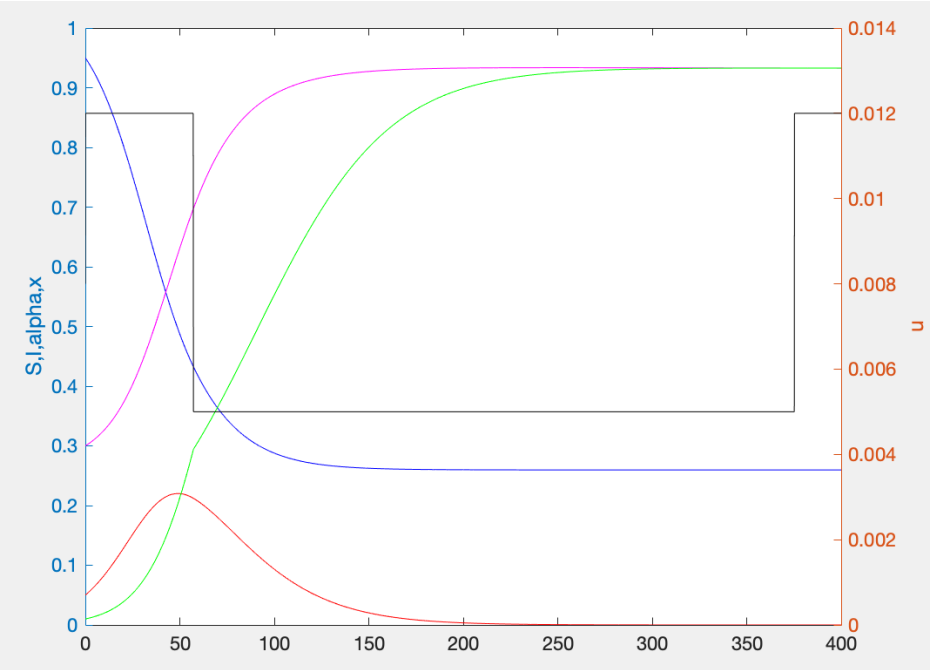

Figure 4.2: Results using the baseline parameters. (Blue) S. (Red) I. (Purple) α. (Green) x. The above four variables correspond to the left coordinate axis. (Black) u, corresponding to the left coordinate axis.

bang-bang control refers the case that the control variable u switches between only the upper and lower bounds [9]. In the numerical simulation, u stays at the upper bound from the beginning, switches to the lower bound at $t = 57.3$, switches back to the upper bound at $t = 375.4$, nearly one year after the epidemic breakout, then still stays at the upper bound. In Figure 4.2, we observe that near $t = 57.3$, the peak of the first wave of epidemic has just passed, so it is reasonable to reduce the vaccination capacity from the maximum. Meanwhile, the growth rate of the relative frequency of vaccinators has slowed down.

Recall that $H_u = \lambda_4 dx(1 - \frac{x}{\alpha}) + 2pu$ from (2.7), the switching time also depends on the value of u, hence it is possible to have more than one switch. When $57.3 \leq t \leq 375.4$, simulation results show that $H_u < 0$. Near $t = 375.4$, the value of x is close enough to α, then H_u becomes positive again. The adjoint function is the Lagrange

multiplier for the constraint of the state variables [5], and the value of the function doesn't contain meaningful information in the actual epidemic problem. We speculate that after the control variable reducing to the lower bound, its weight in the cost function is also reduced. Though the infected proportion of the population is relatively low at this time, the value of $I(t)$ dominates the cost integral. When $I(t)$ stays at a very low level and the vaccine coverage almost equals to vaccine acceptance, almost no one comes to get vaccinated, so the control variable jumps to the upper bound again in order to further eliminate the epidemic while the vaccine cost is no longer important. We observe that about 90% of the population choose to be vaccinated at the end of the epidemic, which is in accordance with herd immunity [1]. We consider two important statistics in each numerical simulation: using the baseline parameters, the time required to reduce I below 2% is $T = 150.4$ days, and the cost is $J = 30.6096$.

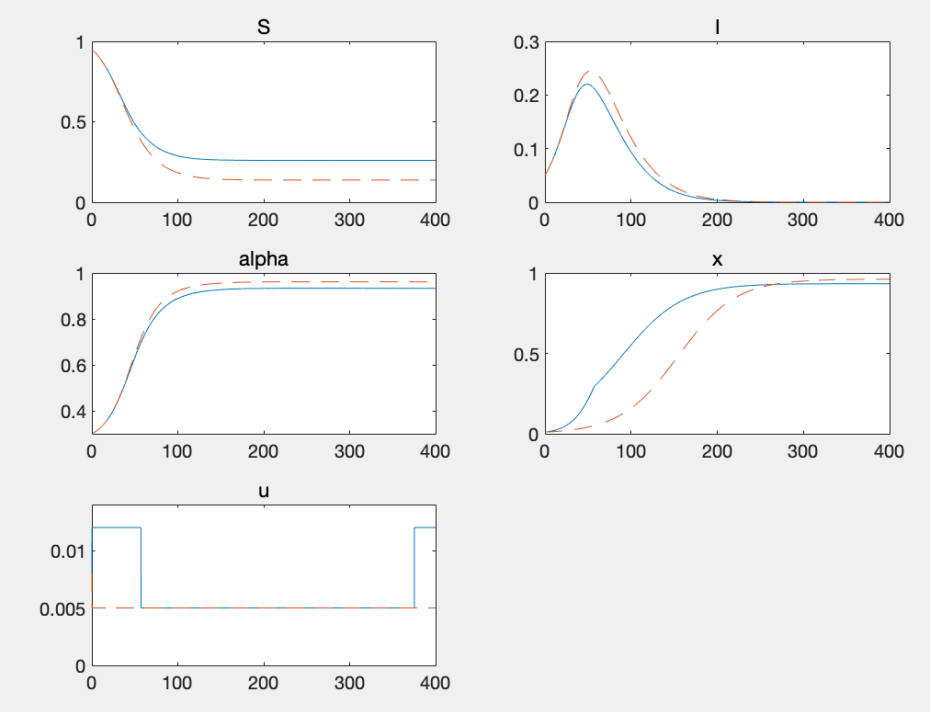

Figure 4.3: Results for two cases. (Solid lines) With optimal control. (Dashed lines) Without optimal control and $u = 0.005$.

In Figure 4.3, we compare the epidemic system with optimal control to the one without optimal control. In this case, we set the control variable $u = u_a = 0.005$ as the constant lower bound. The peak of the wave of epidemic is higher, and the duration is longer. Due to the increase in infected population, however, more people choose to be vaccinated in the "game". Though limited by the vaccination capacity, the initial vaccination is slow, but the final vaccination coverage is higher than the baseline case. The time required to reduce I below 2% is $T = 161.3$ days, extended by 7.25%. The cost is $J = 25.8295$, decreased by 15.62%. This is due to the cost of vaccination has dropped.

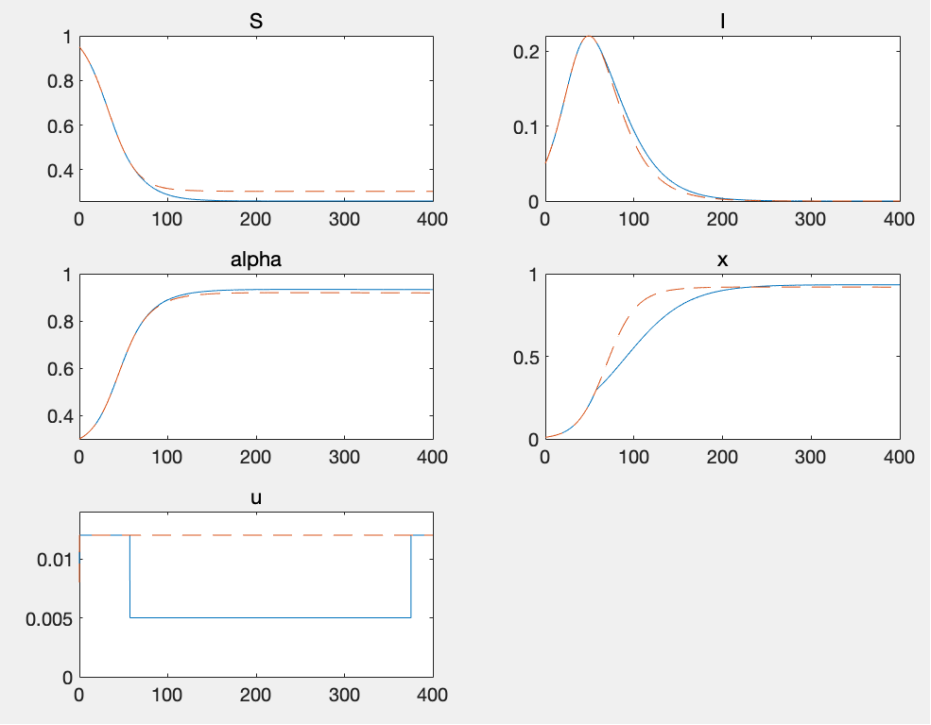

Figure 4.4: Results for two cases. (Solid lines) With optimal control. (Dashed lines) Without optimal control and $u = 0.012$.

In Figure 4.4, we again compare the epidemic system with optimal control to the one without optimal control, and now we set $u = u_b = 0.012$ as the constant upper bound. In contrast, the shape of the wave of epidemic and its duration are similar to

the baseline case. Due to the constant high vaccination capacity, the initial vaccination is faster, while the final vaccination coverage keeps the same. The time required to reduce I below 2% is $T = 140$ days, shortened by 6.91%. The cost is $J = 41.0585$, significantly increased by 34.14%.

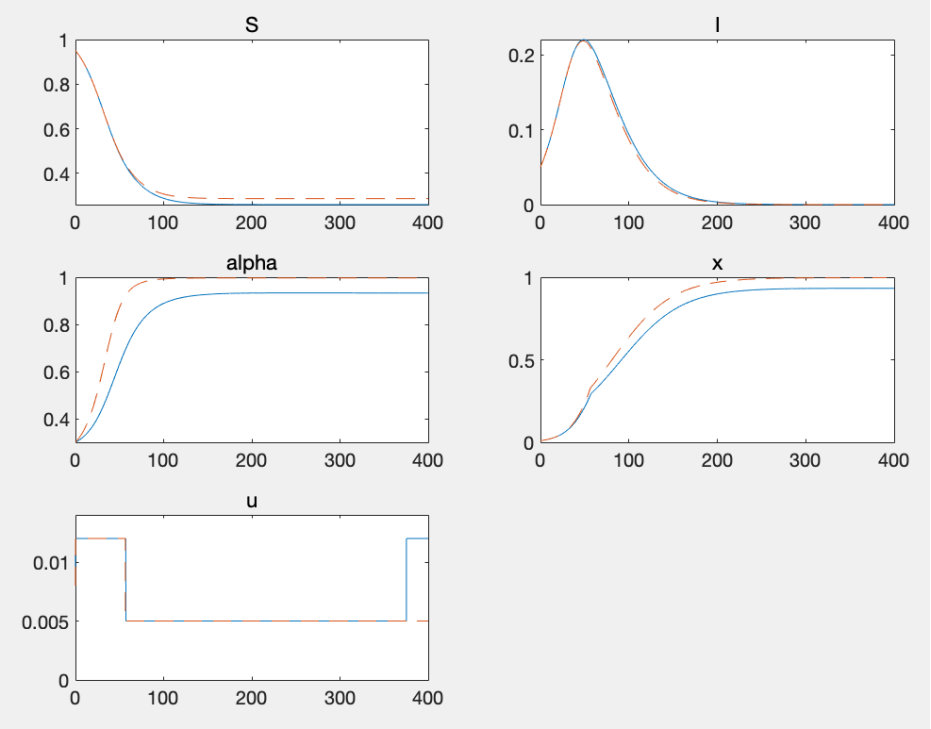

Figure 4.5: Results for varying the imitation rate k. (Solid lines) $k = 1$. (Dashed lines) $k = 2$.

In Figure 4.5, we compare the epidemic system with a normal combined imitation rate to the one with a higher combined imitation rate, as k doubled. The shape of the wave of epidemic and its duration are similar to the baseline case. At the beginning of the epidemic, with the acceleration of the dynamics of imitation process [11], the vaccine acceptance increased much faster than the baseline case, almost approaching the ideal situation where everyone is willing to get vaccinated. The bang-bang control happens again, while the second switching time is around $t = 443.9$ and is not shown in the figure. The time required to reduce I below 2% is $T = 145.8$ days and the cost

is $J = 29.7382$, not much different from the baseline case.

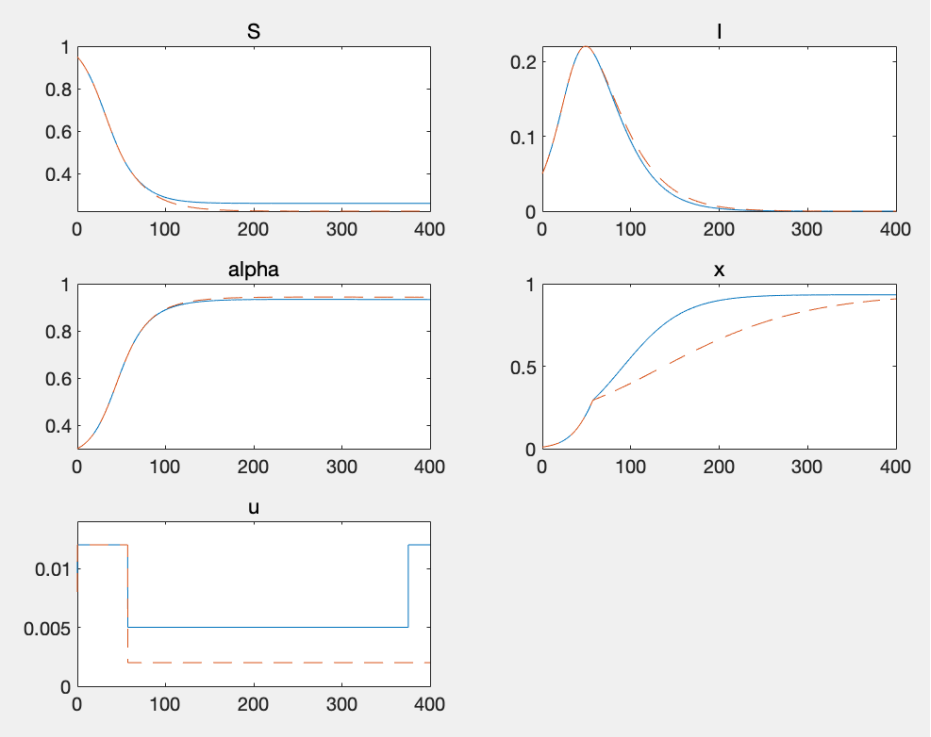

Figure 4.6: Results for varying the control lower bound u_a. (Solid lines) $u_a = 0.005$. (Dashed lines) $u_a = 0.002$.

In Figure 4.6, we assume a scenario where vaccine supply is insufficient. We compare the epidemic system with the baseline control lower bound to a smaller control lower bound, as $u_a = 0.002$. The shape of the wave of epidemic is similar. After the first switch of the control variable, the value of u is smaller, so the increase of x is significantly slower than in the baseline control bounds case. Besides, the second switch of the control variable comes much later, around $t = 763.9$, also not shown in the figure. The time required to reduce I below 2% is $T = 160.9$ days, extended by 6.98%. However, the cost is $J = 29.1473$, decreased by 4.78%.

Lastly, we vary the constant in the cost function which measures the proportion of vaccination cost to treatment cost. In Figure 4.7, the shape of the wave of epidemic is still similar to the baseline case, and the duration is slightly longer. As long as

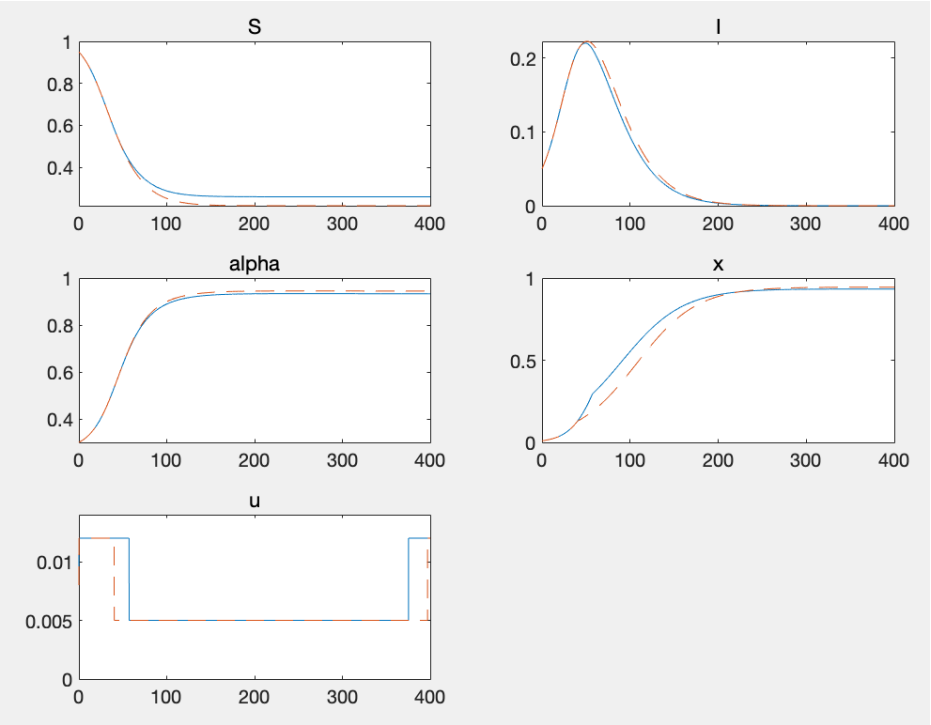

Figure 4.7: Results for varying the constant p in the cost function. (Solid lines) $p = 1200$. (Dashed lines) $p = 200$.

the weight of vaccination cost decreases, the system tends to make u switches to the lower bound earlier and switches back to the upper bound later. The time required to reduce I below 2% is $T = 155.2$ days, extended by 3.19%.

CHAPTER 5: CONCLUSION

We investigated optimal controls for several scenarios with an expanded SIR model. The proposed SIR model with the inclusion of optimal control and game theory in vaccination acceptance could reflect characteristics of the herd immunity with appropriate parameter values under the condition of COVID-19. Compared to the case without optimal control and having constant vaccination capacity, the optimal control scenario achieves less cost and time needed to control the epidemic. The vaccination strategy of this optimal control scenario is to first determine the upper and lower bounds of the vaccination capacity, i.e. the maximum number of people who can be vaccinated at a time instant. During the beginning stage and the peak of the epidemic, the vaccination capacity should be kept at its upper bound. When the infected proportion starts to decrease from the maximum, we need to continuously calculate the partial derivative of Hamiltonian with respect to the vaccination capacity, where the calculation requires us to collect real-time vaccinated proportion, infected proportion, and the value of one of the adjoint functions. The vaccination capacity should be immediately adjusted to the lower bound while the sign of the partial derivative changes. Later, we shall adjust the capacity to the upper bound while the sign changes again to consolidate the effect of herd immunity. In the case that vaccine supply is insufficient, reducing the lower bound of vaccination capacity or accelerating the imitation process are feasible strategies to control COVID-19.

In future work, we will have more classifications of population to consider the asymptomatic infected, quarantine, social distancing, etc. We will also include vaccine hesitancy and emergencies in the imitation dynamics equation.

REFERENCES

[1] R. M. Anderson and R. M. May. Vaccination and herd immunity to infectious diseases. *Nature*, 318(6044):323–329, 1985.

[2] C. T. Bauch. Imitation dynamics predict vaccinating behaviour. *Proceedings of the Royal Society B*, 272(1573):1669–1675, 2005.

[3] H. Behncke. Optimal control of deterministic epidemics. *Optimal Control Applications and Methods*, 21(6):269–285, 2000.

[4] E. Hansen and T. Day. Optimal control of epidemics with limited resources. *Mathematical Biology*, 62(3):423–451, 2011.

[5] D. G. Hull. *Optimal Control Theory for Applications*. Springer, New York, 2003.

[6] H. R. Joshi, S. Lenhart, S. Hota, and F. Agusto. Optimal control of an SIR model with changing behavior through an education campaign. *Electronic Journal of Differential Equations*, 2015(50):1–14, 2015.

[7] T. K. Kar and A. Batabyal. Stability analysis and optimal control of an SIR epidemic model with vaccination. *Biosystems*, 104(2–3):127–135, 2011.

[8] T. Kruse and P. Strack. Optimal control of an epidemic through social distancing. Cowles Foundation Discussion Paper No. 2229, 2020.

[9] S. Lenhart and J. T. Workman. *Optimal Control Applied to Biological Models*. Chapman & Hall/CRC, Boca Raton, FL, 2007.

[10] Pfizer Inc. Real-world evidence confirms high effectiveness of Pfizer-BioNTech COVID-19 vaccine and profound public health impact of vaccination one year after pandemic declared, 2021.

[11] P. Poletti, M. Ajelli, and S. Merler. Risk perception and effectiveness of uncoordinated behavioral responses in an emerging epidemic. *Mathematical Biosciences*, 238(2):80–89, 2012.

[12] S. Schecter. Geometric singular perturbation theory analysis of an epidemic model with spontaneous human behavioral change, 2020.

[13] P.-F. Verhulst. Recherches mathématiques sur la loi d'accroissement de la population. *Nouv. mém. de l'Academie Royale des Sci. et Belles-Lettres de Bruxelles*, 18:1–41, 1845.

[14] S. Zhao, Q. Lin, J. Ran, S. S. Musa, G. Yang, W. Wang, Y. Lou, D. Gao, L. Yang, D. He, and M. H. Wang. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: A data-driven

analysis in the early phase of the outbreak. *International Journal of Infectious Diseases*, 92:214–217, 2020.