HPU2 Journal of Sciences:
Natural Sciences and Technology

journal homepage: https://sj.hpu2.edu.vn

Article type: Research article

Some notes on the dynamic behavior of COVID-19 epidemic disease governed by modified SEIR epidemic model with saturated treatment function

Thanh-Dung Dao[a*], Van-Huy Kieu[a], Hong-Ngat Kieu Thi[a],
Chi-Nguyen Nguyen[b], Thu-Huyen Dinh Thi[c]

[a]*K45C, Department of Mathematics, Hanoi Pedagogical University 2, 32 Nguyen Van Linh, Phuc Yen, Vinh Phuc, Vietnam*
[b]*K45A, Department of Mathematics, Hanoi Pedagogical University 2, 32 Nguyen Van Linh, Phuc Yen, Vinh Phuc, Vietnam*
[c]*Hanoi Ethnic Boarding High School*

Abstract

In this work, based on theory of differential systems and stability theory, we are in the first stage to study some applications of differential systems in real-world modelling problems. Here, we propose a mathematical epidemic model, namely SEIR epidemic model with saturated treatment to describe the COVID-19 infection. Based on the next–generation matrix method and the theory of Lyapunov stability, we evaluate the basic reproduction number $\Re_0$ and investigate the asymptotic behavior of disease-free equilibrium. Additionally, in the case $\Re_0 > 1$, we also prove the existence of a unique endemic equilibrium. Finally, in order to dicuss the effect of isolation control strategies, we study the optimal control problem for this epidemic model.

Keywords: SEIR epidemic model with saturated treatment, basic reproduction number $\Re_0$, asymptotic stability, disease-free equilibrium, endemic equilibrium, optimal control problem.

1. Introduction

It is well-known that many a physical or real-life problems are formulated by using differential equations and partial differential equations. During three past centuries, a lot of works and publications have proved the importance and significance of differential equations and their applications in various areas of physics, chemistry, biology, engineering, economics and social activies, etc. Stability theory is one of the most important branches in the qualitative theory of

* Corresponding author: Dao Thanh Dung, E-mail: dinhthu19643@gmail.com

https://doi.org/10.56764/hpu2.jos.2022.1.2.3-23

Received date: 29-11-2022 ; Revised date: 21-12-2022 ; Accepted date: 27-12-2022

differential equations. A popular approach in the stability theory is the stability in sense of Lyapunov (1857-1918). Although it has been studied for a long time, the stability theory is still a field of interest to many mathematicians, gaining many important achievements and being widely applied in many fields of sciences such as physics, the process of medicine - biology, economics, mechanics, ecology, computer Science, epidemiology, ... To the best of our knowledge, there are various approaches and method when studying the asymptotic behaviors of typical differential equations. However, with the scope of the undergraduate student's research, we are going to carry out our study by applying a familiar approach that is based on linearization method and Lyapunov candicate method, see [1]. Along with a long history of evolutionary and development of the human, we have had to face with a lot of extremely epidemic diseases such as ebola, measles, SARS or COVID-19, etc. To fight against these pandemics, the first step is to fully study their characteristics and hence, many scientists had proposed various approaches to characterize the properties of epidemic diseases, in which many mathematicians have tried to model the dynamics of epidemic diseases based on differential systems and then, apply the theory of stability to study these mathematical epidemic models. In the last two years, humanity has faced lots of impacts on health and all aspects of human-life due to the acute respiratory infection caused by corona virus. This is the reason why we propose to use the theory of differential equations and its stability to discuss the infection and dynamics of COVID-19 ‘s spread on the community.

In mid-December 2019, in Wuhan city, Hubei province, China, an outbreak of acute pneumonia caused by the first new strain of coronavirus was recorded. Because of its similar genetic structure to SARS-CoV in 2003, this virus was named SARS-Cov 2 by the World Health Organization. On February 12th, 2020, the WHO announced that the official name for acute respiratory infection caused by a new strain of corona virus is COVID-19. 70 days after China reported its first case, the World Health Organization declared COVID-19 a global pandemic on March 11th, 2020 (see [14]). At that time, the whole world had 148,405 people infected, 66,715 infected people were being treated in medical facilities, 4,635 people died from COVID-19 and infection occurred in 117 countries and territories. The WHO's declaration of COVID-19 as a global pandemic reflects the virus ability to spread across geographical areas. As of April 18th, 2022, the World has recorded a total of 504,832,780 virus infections with 6,223,606 deaths and 456,058,793 people have recovering (see [16]). As for Vietnam, our country has been experiencing four waves of COVID-19 infection. The first wave of infections peaked on April 2rd, 2020, with 158 people being treated. The second wave of infections peaked on August 17th, 2020, with 492 people being treated. The 3rd wave, starting on January 27th, 2021, in February 2021 the whole country has 631 people being treated. From the end of April 2021, the 4th wave began to break out and by the end of April 18th, 2022, Vietnam had recorded a total of 10,432,547 virus infections with 42,944 deaths and 8.936.846 people have recovering (see [15]).

Based on the negative effects of the pandemic on public health and all aspects of socio-economic life, we can see that the COVID-19 pandemic is of an extremely dangerous nature and an urgent task of governments is control the pandemic quickly. Developing vaccines and specific drugs are the usual solutions that mankind thinks about to deal with the pandemic. However, preparing, researching and developing the vaccines as well as specific drugs request people to understand the characteristics of viruses, the characteristics of infection, and can be able to predict their evolutionary direction. On the other hand, corona virus always has a complicated development with more and more variants have appear to cope with the effectiveness of vaccines and specific drugs. In addition, there is

often an inevitable delay from the time a new variant emerges to the time when the corresponding drug or vaccine is developed, and during this time, the disease can be transmitted strongly in the community. Therefore, the most important things to minimize the rapid spread of diseases before developing drugs and vaccines is understand the evolutionary laws and govern the spread of disease. One of the effective ways to predict the evolutionary direction of an epidemic disease is using mathematical models. In fact, we have two approaches to mathematical modeling of infection processes in populations, communities and networks, namely graph-based modeling (see [12]) and non-graph-based modeling (see [10]). For the scope of student inquiry, we choose non-graph-based modeling derived from the ideas of Kermack and McKendrick (see [10]). In this paper, authors have proposed a differential equation model containing three classes SIR to describe the spread of disease in the community. After the differential equation model is established, authors have determined the the basic reproduction number, disease-free equilibrium, disease equilibrium. Next, authors have used mathematical stability theory to investigate the asymptotic behavior of the model. Inspired by the work [10], many subsequent studies also established different mathematical models to investigate the behavior of infectious processes with assumptions, constraints and efficiency evaluation of treatments (see [3, 5, 7, 8, 9, 11]). Especially, it should be noted that when a healthy person directly contacts with an infectious person, he will get infected at a certain rate but he doesn't immediately become an infectious one, i.e., he is in the state of infected but not infectious. And we call this state is exposure state. Some recent works have applied this idea for better modelling the transmission of COVID-19 epidemic disease, such as [5, 7, 8]. Furthermore, due to the fact that the financial and medical resources of each populations or country are finite, it only has a certain maximal capacity for the treatment, isolation or immunization against an epidemic disease and moreover, as the number of infected cases reaches the maximal capacity, it leads to an unexpected scenario that there have a number of infected being delayed for treatment or immunization. As a result, we can see that the use of a saturated treatment function seems more realistic than the linear one used in some classical models, see [13].

Motivated by aforesaid, this paper aims to extend our knowledge on the theory of differential equation and its stability along with apply them to study some initial results on the analysis properties of an epidemic disease. For this aim, we proposed a modified SEIR epidemic model with saturated treatment function to describe the corona virus's infection and to investigate the asymptotic behavior of the proposed epidemic model. Futhermore, we also apply the theory of constrainted extrema to study an optimal isolation control problem subject to dynamical constraints to demonstrate the effect of quarantine treatment on the prevention of corona virus spread.

2. Preliminaries

2.1. The existence and uniqueness of the solution to an initial value problem

Consider an initial value problem.(IVP)

$$(IVP) \qquad \begin{cases} y'(t) = f\left(t, y(t)\right) \\ y(t_0) = y_0 \end{cases}$$

where $y_0 \in \mathbb{R}^n$ is the initial condition and the function $f : J \times \Omega \subset \mathbb{R} \times \mathbb{R}^n \to \mathbb{R}^n$ is a continuous function on a set $J \times \Omega$ containing the point (t_0, y_0).

Theorem 2.1 (see [1, Theorem 1] and [2, Theorem 1]). (Picard – Lindelof Theorem) Suppose that the function $f : [t_0 - a, t_0 + a] \times B[y_0, b] \to \mathbb{R}^n$ is a vector-valued function satisfying

(i) The function $f(t,y)$ is continuous on the set $[t_0-a,t_0+a]\times B[y_0,b]$. As a result, there exists a constant $M>0$ such that for any $(t,y)\in[t_0-a,t_0+a]\times B[y_0,b]$, we have $\|f(t,y)\|\le M$.

(ii) The function $f(t,y)$ satisfies the Lipschitz condition with respect to the variable y uniformly in t, i.e., there exists a constant $L>0$ such that

$$\|f(t,y)-f(t,\bar{y})\|\le L\|y-\bar{y}\|$$

for all $(t,y),(t,\bar{y})\in[t_0-a,t_0+a]\times B[y_0,b]$.

Then the problem (IVP) has a unique solution $y(t)$ defined on $[t_0-h,t_0+h]$, where $h=\min\left\{a,\frac{b}{M}\right\}$.

2.2. A comparison theorem of differential equations

Theorem 2.2 (see [4, Theorem 1]): Suppose that the functions $f,g:\mathbb{R}\times\mathbb{R}^n\to\mathbb{R}^n$ are continuous on the domain

$$D=\left\{(t,y)\in\mathbb{R}^2\,\middle|\,|t-t_0|<a,\|y-y_0\|<b\right\}$$

and denote $y_0(t),z_0(t)$ by two any solutions of the initial value problems

$$(P_1)\quad y'(t)=f(t,y);\ y_0(t_0)=y_0$$
$$(P_2)\quad z'(t)=g(t,z);\ z_0(t_0)=y_0,$$

respectively. Then, if the initial value problem (P_1) has a unique solution then the inequality $f(t,y)\ge g(t,y)$ in D implies the inequality $y_0(x)\ge z_0(x)$ for all $x>x_0$.

2.3. Some fundamental results on the stability theory of differential equations

Consider the following differential equations

$$x'(t)=f(t,x(t)),\quad t\ge 0 \tag{1.1}$$

where $x(t)\in\mathbb{R}^n$ is the state vector of the system, $f:\mathbb{R}^+\times\mathbb{R}^n\to\mathbb{R}$ is a given vector-valued function satisfying all assumptions of Theorem 2.1. Then, we recall from [1] some following concepts

Definition 2.1. An equilibrium (or equilibrium point) of a dynamical system generated by an autonomous system of ordinary differential equations (ODEs) is a solution that does not change with time.

Definition 2.2 (see [1, Definition 1.1]) Assume that $\bar{x}(t)$ is an equilibrium point of the differential equations (1.1) defined on the interval $[t_0,+\infty)$. The equilibrium point $\bar{x}(t)$ is said to be:

(i) ***stable*** if for all $\varepsilon>0$, there exists $\delta>0$ such that all solutions $y(t)$ of the differential equations (1.1) with $\|y(t_0)-\bar{x}(t_0)\|<\delta$ exist over the interval $[t_0,+\infty)$ and satisfy

$$\|y(t)-\bar{x}(t)\|<\varepsilon \text{ for all } t\ge t_0.$$

(ii) ***asymptotically stable*** if it is stable and there exists a constant $\beta>0$ such that all solutions $y(t)$ of the differential equations (1.1) with $\|y(t_0)-x(t_0)\|<\beta$ satisfies

$$\lim_{x\to\infty}\left\|y(t)-x(t)\right\|=0.$$

Remark: If the numbers α,β in the above definition do not depend on the initial time t_0 then we have the definitions of uniformly stability, uniformly asymptotically stable.

Now, we consider a linear differential system

$$x'(t)=Ax(t),\quad t\ge t_0, \tag{1.2}$$

where $x(t)\in\mathbb{R}^n$ and A is a constant real matrix of order n. Then, we have the following theorem:

Theorem 2.3 (see [1, Theorem 1.2]) Denote $\sigma(A)=\max\left\{\mathrm{Re}(\lambda):\lambda \textit{ is the eigenvalue of } A\right\}$. Then, we have

(i) The solution 0 of (1.2) is asymptotically stable if $\sigma(A)<0.$

(ii) The solution 0 of (1.2) is unstable if $\sigma(A)>0.$

(iii) If $\sigma(A)=0$ and all eigenvalues of A whose real parts are equal to $0,$ are half-simple then the solution 0 is stable.

Next, we study the stability of the system of differential equations whose the main part is regard as linear:

$$x'(t)=Ax(t)+g(t,x(t)). \tag{1.3}$$

Theorem 2.4 (see [1, Theorem 1.3]) Let A be a constant matrix and $g(t,x(t))$ be a continuous function for all $t\ge 0,$ $\|x\|\le\alpha$ and $\lim\limits_{\|x\|\to 0}\dfrac{\|g(t,x(t))\|}{\|x\|}=0$ for all $t\ge 0.$ Then,

(i) If $\mathrm{Re}\,\sigma(A)<0$ then the solution 0 of the system (1.3) is asymptotically stable.

(ii) If $\mathrm{Re}\,\sigma(A)>0$ then the solution of the system (1.3) is unstable.

Next, we consider the following autonomous nonlinear differential equations

$$x'(t)=f(x(t)), \tag{1.4}$$

Assume that $f\in C^1(D)$, where $D\subset\mathbb{R}^n$ is an open set containing the origin 0 and 0 is a critical point of the function f, i.e. $f(0)=0$. Denote A by the Jacobi matrix $Df(0)$ at the point 0. Then, the autonomous nonlinear system (1.4) can be rewritten as

$$x'(t)=Ax(t)+g(x(t)). \tag{1.5}$$

where the function $g(x(t))=f(x(t))-Df(0)x(t).$ Note that

$$\lim_{\|x\|\to 0}\frac{\|g(x(t))\|}{\|x\|}=0.$$

As a consequence of Theorem 2.4, we have the following result:

Theorem 2.5 (see [1, Theorem 1.5]) (Linearization principle). The equilibrium $x\equiv 0$ of the autonomous nonlinear equation (1.4) is asymptotically stable if $\mathrm{Re}\,\sigma(Df(0))<0$ and not stable if $\mathrm{Re}\,\sigma(Df(0))>0$.

2.4. The existence of optimal solution of the optimal control problem

Let us recall from Theorem 4.1 in [6] some results on the optimal control problem and the existence of its optimal solution. Indeed, we consider the following optimal control problem (OCP)

$$\min J(u) = \int_0^T L\left[x(t), u(t)\right] dt,$$

subject to the differential constraints and initial conditions:

$$\begin{cases} x'(t) = g\left(x(t), u(t)\right) \\ x(0) = x_0. \end{cases} \tag{1.6}$$

Denote the set $U_{ad} = \left\{u = (u_1, u_2) \in L^2[0,T] \times L^2[0,T] : 0 < u_i(t) \le u_0,\ i = \overline{1,2};\ t \in [0,T]\right\}$. Then, the optimal control problem (OCP) has an optimal solution u^* if the following conditions are satisfied:

(i) There exists an element $u \in U_{ad}$ such that Cauchy problem (1.6) has at least one solution $x(t)$.

(ii) The set U_{ad} is convex and closed.

(iii) The function $g\left(x(t), u(t)\right)$ is bounded by a linear function with respect to x.

(iv) The function $L\left[x(t), u(t)\right]$ is convex in U_{ad}.

(v) There exist constants $\beta > 1; c_1 > 0$ and c_2 such that:

$$L\left[x(t), u(t)\right] \ge C_1 \left|u(t)\right|^{\beta} + C_2.$$

3. The SEIR epidemic model with saturated treatment function

3.1. The formulation of the SEIR epidemic model

In the work, a four-compartment mathematical model for the spread and transmission of SARS-CoV-2 on the community is formulated according to some general control strategies such as immunization or quarantine, namely controlled SEIR epidemic model with saturated treatment function. In fact, the SEIR model has some limitations for the real situations, but it provides a basic model for the research of different kinds of epidemic. Motivated by aforesaid, we divide the whole population into four following groups:

- (S): is the group of susceptible people and they are the potential target of virus attack.

- (E): is the group of people who have been infected by coronavirus but have not yet been able to transmit the epidemic disease to others.

- (I): is the group of people who have been infected and are capable of transmitting the disease to those who come into contact with them.

- (R): is the group of people who have been cured and recovered from the epidemic disease.

Next, we denote $S(t), E(t), I(t), R(t)$ by the densities of people in Susceptible, Exposed, Infectious and Recovered states at time t, respectively. Then, the state transitions between four states of this epidemic model can be characterized in Figure 1.

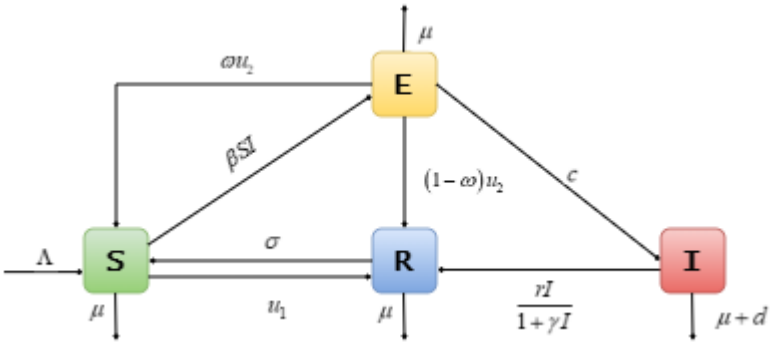

Figure 1. The flowchart of epidemic model among four compartments: Susceptible, Exposed, Infectious, Recovered

In many epidemic models, the treatment rate of infectious people is often considered to be linear, that is, it is proportional to the number of the infectious ones. However, it is a fact that each government and epidemic control strategy have just a certain maximal capacity for the treatment of the epidemic disease infection. That is the reason why in this work, we take into account a nonlinear treatment function, namely saturated treatment function, which was firstly proposed by Zhang et al. [13]. In addition, the parameters used in the COVID-19 transmission model are given in Table 1 .

Table 1. Description of model parameters

Λ	Natural birth rate.
μ	Natural death rate.
d	Death rate due to the disease.
β	The rate of transmission from S to E due to contact with I .
r	The cure rate.
u_1	Control variable representing the vaccination rate for susceptible people.
ωu_2	The control variable represents the infection-free rate of the exposed people.
$(1-\omega)u_2$	The rate of infection but self-healing of the exposed people.
c	The rate of being infectious of an exposed person.
σ	The rate of the vaccine expires, the recovery node returns to the susceptible node.

Based on these above parameters and descriptions, the controlled SEIR epidemic model can be formulated by the following differential equations:

$$\begin{cases} S'(t) = \Lambda - \beta IS - u_1 S + \omega u_2 E + \sigma R - \mu S \\ E'(t) = \beta IS - \mu E - u_2 E - cE \\ I'(t) = cE - \dfrac{rI}{1+\gamma I} - (\mu + d) I \\ R'(t) = \dfrac{rI}{1+\gamma I} - \mu R - \sigma R + u_1 S + (1-\omega) u_2 E, \end{cases} \tag{1.7}$$

where all model's parameters are assumed to be positive.

3.2. The existence of a non-negative solution of the proposed model

First of all, we will show that the solution of the propsed controlled SEIR epidemic model (1.7) are always non-negative for all $t \geq 0$. For this aim, we denote

$$x(t) = \begin{bmatrix} S(t) & E(t) & I(t) & R(t) \end{bmatrix}^T$$
$$\Sigma^+ = \left\{ x(t) \in \mathbb{R}^4_+ \middle| S(t) + E(t) + I(t) + R(t) \leq \frac{\Lambda}{\mu} \right\}.$$

Now, we will prove that:

Theorem 3.1. If $x(0) \in \Sigma^+$ then $x(t) \in \Sigma^+$ for all $t > 0$.

Proof. By the assumption that $x(0) \in \Sigma^+$, we can assume that $S(0) > 0, E(0) \geq 0, I(0) \geq 0, R(0) \geq 0$. Now, we will assume by contrary that the function $S(t)$ is not always positive for all $t > 0$, i.e., there exists a time $t_0 > 0$ and a constant $\varepsilon > 0$ small enough such that:

$$\begin{cases} S(t_0) = 0 \\ S(t) > 0 \ \forall t \in [0, t_0) \\ S(t) < 0 \ \forall t \in [t_0, t_0 + \varepsilon). \end{cases}$$

Then, we consider the following two cases:

Case 1: If the function $I(t)$ is non-negative for all $t \in [0, t_0]$ then the second differential equation of the SEIR epidemic model (1.7) satisfies

$$E'(t) = \beta I(t) S(t) - (\mu + u_2 + c) E(t) \geq -(\mu + u_2 + c) E(t), \quad t \in [0, t_0].$$

According to the comparison principle (see [4]), we have

$$E(t) \geq E(0) e^{-(\mu + u_2 + c)t} \geq 0, \quad \forall t \in [0, t_0].$$

Additionally, the fourth differential equation of (1.7) becomes

$$R'(t) = \frac{rI(t)}{1 + \gamma I(t)} + u_1 S(t) + (1 - \omega) u_2 E(t) - (\mu + \sigma) R(t) \geq -(\mu + \sigma) R(t), \quad t \in [0, t_0],$$

which implies that $R(t) \geq R(0) e^{-(\mu + \sigma)t} \geq 0$ for all $t \in [0, t_0]$. Finally, we directly obtain

$$\begin{aligned} S'(t_0) &= \Lambda - \beta I(t_0) S(t_0) - (u_1 + \mu) S(t_0) + \sigma R(t_0) + \omega u_2 E(t_0) \\ &= \Lambda + \sigma R(t_0) + \omega u_2 E(t_0) > 0. \end{aligned}$$

This inequality leads to $S(t) > S(t_0) = 0$ for all $t_0 < t \leq t_0 + \varepsilon$ with a constant $\varepsilon > 0$ is sufficiently small, which contradicts to our assumption.

Case 2: Assume that there exist a time $t_1 \in (0, t_0)$ and a constant $\varepsilon_1 > 0$ small enough such that

$$\begin{cases} I(t_1) = 0 \\ I(t) > 0, \ \forall t \in (0, t_1) \\ I(t) < 0, \ \forall t \in (t_1, t_1 + \varepsilon_1). \end{cases}$$

Then, by doing similar arguments, we can prove that $E(t), R(t) \geq 0 \ \forall t \in [0, t_1] \subset [0, t_0]$ and it is obvious

that the function $S(t) > 0$ for all $t \in [0, t_1]$. The third differential equation of the model (1.7) becomes

$$I'(t_1) = cE(t_1) - (\mu + d) I(t_1) + \frac{rI(t_1)}{1 + \lambda I(t_1)} = cE(t_1) \geq 0,$$

i.e., there exists $\tau_1 > 0$ such that $I(t) \leq I(t_1) = 0, \forall t \in (t_1 - \tau_1, t_1)$. However, this contradicts to our assumption that the function $I(t) > 0, \ \forall t \in (0, t_1)$. Hence, we deduce that the function $S(t) > 0$ for all $t > 0$. By the similar arguments, we can also show that $I(t), E(t), R(t)$ are all non-negative for all $t > 0$.

On the other hand, by summing up sides by sides of the model (1.7), we have

$$\big(S(t) + E(t) + I(t) + R(t)\big)' = \Lambda - \mu\big(S(t) + E(t) + I(t) + R(t)\big) - dI(t).$$

Denote $N(t) = S(t) + E(t) + I(t) + R(t)$. Then, we receive

$$N'(t) = \Lambda - \mu N(t) - dI(t) \leq \Lambda - \mu N(t).$$

According to the comparison principle, we get

$$N(t) \leq e^{-\mu t}\left[N(0) + \frac{\Lambda}{\mu}\left(e^{\mu t} - 1\right)\right] = \frac{\Lambda}{\mu} + e^{-\mu t}\left[N(0) - \frac{\Lambda}{\mu}\right].$$

In addition, since $x(0) \in \Sigma^+$ then $N(0) = S(0) + E(0) + I(0) + R(0) \leq \frac{\Lambda}{\mu}$. So we get

$$N(t) \leq \frac{\Lambda}{\mu} + e^{-\mu t}\left[N(0) - \frac{\Lambda}{\mu}\right] \leq \frac{\Lambda}{\mu}.$$

Finally, we can conclude that the set Σ^+ is a positively invariant set of the system (1.7).

3.3. Equilibrium points and the basic reproduction number $\Re_0$

It should be noted that the equilibrium points of the propsosed controlled SEIR epidemic model, including the disease-free equilibrium point and endemic equilibrium points, are the solution of the following system:

$$\begin{cases} \Lambda - \beta IS - u_1 S + \omega u_2 E + \sigma R - \mu S = 0 \\ \beta IS - \mu E - u_2 E - cE = 0 \\ cE - \dfrac{rI}{1 + \gamma I} - (\mu + d) I = 0 \\ \dfrac{rI}{1 + \gamma I} - \mu R - \sigma R + u_1 S + (1 - \omega) u_2 E = 0. \end{cases} \tag{1.8}$$

3.3.1. The disease-free equilibrium point

We denote $E_0 = (S^0, E^0, I^0, R^0)$ by a disease-free equilibrium point of the propsosed controlled SEIR epidemic model. Note that since the equilibrium point E_0 is disease-free, it is true that $E^0 = I^0 = 0$. Next, we consider the first and fourth equations of the system (1.8):

$$\begin{cases} \Lambda - u_1 S + \sigma R - \mu S = 0 \\ -(\mu + \sigma) R + u_1 S = 0. \end{cases}$$

By using the substitution, we get $S = \frac{\Lambda(\mu+\sigma)}{\mu(\mu+u_1+\sigma)}$ and $R = \frac{u_1\Lambda}{\mu(\mu+u_1+\sigma)}$. Therefore, we have the coordinate of the disease-free equilibrium point as follows:

$$E^0 = \left(\frac{\Lambda(\mu+\sigma)}{\mu(\mu+u_1+\sigma)}, 0, 0, \frac{u_1\Lambda}{\mu(\mu+u_1+\sigma)} \right).$$

3.3.2. The basic reproduction number $\Re_0$

In the epidemiological theory, the basic reproduction number $\Re_0$ is an important threshold value, that represents the number of cases directly caused by an infectious individual throughout its infectious period. In order to find the basic reproduction number $\Re_0$, we will apply the next-generation matrix method at the disease-free equilibrium point E_0. Indeed, let us consider the gain terms and lost terms of the controlled SEIR epidemic model (1.7) as follows:

$$\begin{bmatrix} \beta IS \\ 0 \end{bmatrix} \qquad \begin{bmatrix} (\mu+u_2+c)E \\ -cE + \frac{rI}{1+\gamma I} + (\mu+d)I \end{bmatrix}.$$

Then, we receive the rate matrix of new infection's appearance at the equilibrium point E_0 and the transition matrix V of infected states as follows:

$$F = \begin{pmatrix} 0 & \beta S \\ 0 & 0 \end{pmatrix} \qquad V = \begin{pmatrix} \mu+u_2+c & 0 \\ -c & \mu+d+r \end{pmatrix}$$

Next, we can find the matrix FV^{-1} as follows:

$$F.V^{-1} = \begin{pmatrix} 0 & \frac{\beta\Lambda(\mu+\sigma)}{\mu(\mu+u_1+\sigma)} \\ 0 & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{\mu+u_2+c} & 0 \\ \frac{c}{(\mu+u_2+c)(\mu+d+r)} & \frac{1}{\mu+d+r} \end{pmatrix}$$

$$= \begin{pmatrix} \frac{\beta\Lambda(\mu+\sigma)c}{\mu(\mu+u_1+\sigma)(\mu+u_2+c)(\mu+d+r)} & \frac{\beta\Lambda(\mu+\sigma)}{\mu(\mu+u_1+\sigma)(\mu+d+r)} \\ 0 & 0 \end{pmatrix}.$$

Consider the characteristic equations

$$\left| F.V^{-1} - \lambda I_2 \right| = \begin{vmatrix} \frac{\beta\Lambda(\mu+\sigma)c}{\mu(\mu+u_1+\sigma)(\mu+u_2+c)(\mu+d+r)} - \lambda & \frac{\beta\Lambda(\mu+\sigma)}{\mu(\mu+u_1+\sigma)(\mu+d+r)} \\ 0 & -\lambda \end{vmatrix} = 0,$$

whose solutions are

$$\lambda_1 = \frac{\beta\Lambda(\mu+\sigma)c}{\mu(\mu+u_1+\sigma)(\mu+u_2+c)(\mu+d+r)}, \qquad \lambda_2 = 0.$$

Note that the basic reproduction number $\Re_0$ is the largest eigenvalue of FV^{-1}, that means

$$\Re_0 = \frac{\beta\Lambda(\mu+\sigma)c}{\mu(\mu+u_1+\sigma)(\mu+u_2+c)(\mu+d+r)}.$$

3.3.3. The existence of the endemic equilibrium point E_*

In the following, we will prove that the basic reproduction number $\Re_0$ plays a key role in the existence of a unique endemic equilibrium point $E_* = \left(S^*, E^*, I^*, R^*\right)$ of the proposed epidemic model.

Theorem 3.1. *If the basic reproduction number* $\Re_0 > 1$ *then the controlled SEIR epidemic model (1.7) has exactly a unique endemic equilibrium point* $E_* = \left(S^*, E^*, I^*, R^*\right)$.

Proof. Let us denote $E_* = \left(S^*, E^*, I^*, R^*\right)$ by an endemic equilibrium point of the controlled SEIR epidemic model (1.7). Then, by applying the substitution for the third equations of the system (1.8), we get

$$E = \frac{1}{c}\left[\frac{r}{1+\gamma I} + (\mu + d)\right] I.$$

Next, by substituting the expression E into the second equation of the system (1.8), we have

$$S = \frac{1}{\beta I}(\mu + u_2 + c)E = \frac{1}{c\beta}(\mu + u_2 + c)\left[\frac{r}{1+\gamma I} + (\mu + d)\right].$$

As a consequence, the forth equation of the system (1.8) implies that

$$\begin{aligned} R &= \frac{1}{\mu + \sigma}\left[\frac{rI}{1+\gamma I} + u_1 S + (1-\omega)u_2.E\right] \\ &= \frac{r}{\mu + \sigma}.\frac{I}{1+\gamma I} + \frac{(1-\omega)u_2}{(\mu+\sigma)c}\left(\frac{r}{1+\gamma I} + (\mu + d)\right) I + \frac{u_1}{c\beta(\mu+\sigma)}\left[\frac{r}{1+\gamma I} + (\mu + d)\right](\mu + u_2 + c). \end{aligned}$$

Finally, by substituting the terms E, S, R into the first equation of the system (1.8), we immediately obtain

$$\begin{aligned} I\left[\frac{\mu}{c\beta}\left(\frac{r}{1+\gamma I} + \mu + d\right)(\mu + u_2 + c) + \frac{\mu}{c}\left(\frac{r}{1+\gamma I} + \mu + d\right) + \mu\left(1 + \frac{d}{\mu}\right) + \frac{\mu r}{(\mu+\sigma)(1+\gamma I)}\right. \\ \left. + \frac{\mu u_1}{c\beta I(\mu+\sigma)}\left(\frac{r}{1+\gamma I} + \mu + d\right)(\mu + u_2 + c)\right] = \Lambda, \end{aligned}$$

or equivalently,

$$\begin{aligned} c\beta\Lambda + c\beta\Lambda\gamma I = \beta\mu\gamma(\mu + d)I^2 + \gamma\mu(\mu + d)(\mu + u_2 + c)\left(1 + \frac{u_1}{\mu+\sigma}\right) I + \beta\mu(\mu + d + r)I \\ + \mu\gamma c\beta\left(1 + \frac{d}{\mu}\right) I^2 + \mu c\beta\left(1 + \frac{d}{\mu}\right) I + \frac{\mu r c\beta}{(\mu+\sigma)} I + \alpha_1\alpha_2, \end{aligned}$$

where $\nu_1 = \mu + d + r;\ \nu_2 = \mu(\mu + u_2 + c)\left(1 + \frac{u_1}{\mu+\sigma}\right)$.

Then, we receive the following quadratic equation

$$\begin{aligned} I^2\left[\beta\gamma(\mu + d)(\mu + c)\right] + (\nu_1\nu_2 - \beta c\Lambda) \\ + I\left[-\gamma\beta c\Lambda + \beta\mu(\mu + d + r) + \beta\mu c\left(1 + \frac{d}{\mu}\right) + \frac{\mu r c\beta}{(\mu+\sigma)} + \gamma\mu(\mu + d)(\mu + u_2 + c)\left(1 + \frac{u_1}{\mu+\sigma}\right)\right] = 0. \end{aligned}$$

Here, we can see that the controlled SEIR epidemic model (1.7) admits a unique endemic equilibrium point if the above quadratic equation has a unique positive real solution. Indeed, if the coefficient

$\nu_1\nu_2 - \beta c\Lambda < 0$ then the above quadratic equation has two distinct solutions with opposite signs. As a result, we deducae that

$$\beta c\Lambda > \mu(\mu + c + u_2)(\mu + d + r)\left(1 + \frac{u_1}{\mu + \sigma}\right)$$

which is equivalent to $\Re_0 = \dfrac{\beta c\Lambda(\mu + \sigma)}{\mu(\mu + c + u_2)(\mu + d + r)(\mu + u_1 + \sigma)} > 1.$ Hence, the proof is completed.

3.3.4. The asymptotic behavior of the disease-free equilibrium

Theorem 3.2. *The disease-free equilibrium* E_0 *is locally asymptotically stable if* $\Re_0 < 1$ *and unstable if* $\Re_0 > 1$. *In the case* $\Re_0 = 1$, *the equilibrium point* E_0 *is stable but not asymptotically unstable.*

Proof. In order to investigate the local asymptotic stability of the disease-free equilibrium E_0, we will apply the linearization method proposed in Section 4 in [1]. With the disease-free equilibrium point $E_0 = (S^0, E^0, I^0, R^0)$, the Jaccobian matrix at the disease-free equilibrium point E_0 is

$$J(E^0) = \begin{pmatrix} -u_1 - \mu & \omega u_2 & -\beta S_0 & \sigma \\ 0 & -\mu - u_2 - c & \beta S_0 & 0 \\ 0 & c & -r - \mu - d & 0 \\ u_1 & (1-\omega)u_2 & r & -\mu - \sigma \end{pmatrix}.$$

For simplicity in representation, we denote $\alpha_1 = -u_1 - \mu, \alpha_2 = -\mu - u_2 - c, \alpha_3 = -r - \mu - d, \alpha_4 = -\mu - \sigma.$ Then

$$J(E^0) = \begin{pmatrix} -\alpha_1 & \omega u_2 & -\beta S_0 & \sigma \\ 0 & -\alpha_2 & \beta S_0 & 0 \\ 0 & c & -\alpha_3 & 0 \\ u_1 & (1-\omega)u_2 & r & -\alpha_4 \end{pmatrix}.$$

The characteristic polynomial of the above Jacobi matrix is given by

$$\begin{aligned} |\lambda I - J(E_0)| &= \begin{vmatrix} \lambda + \alpha_1 & -\omega u_2 & \beta S_0 & -\sigma \\ 0 & \lambda + \alpha_2 & -\beta S_0 & 0 \\ 0 & -c & \lambda + \alpha_3 & 0 \\ -u_1 & -(1-\omega)u_2 & -r & \lambda + \alpha_4 \end{vmatrix} \\ &= (\lambda + \alpha_1)\begin{vmatrix} \lambda + \alpha_2 & -\beta S_0 & 0 \\ -c & \lambda + \alpha_3 & 0 \\ -(1-\omega)u_2 & -r & \lambda + \alpha_4 \end{vmatrix} + u_1 \begin{vmatrix} -\omega u_2 & \beta S_0 & -\sigma \\ \lambda + \alpha_2 & -\beta S_0 & 0 \\ -c & \lambda + \alpha_3 & 0 \end{vmatrix} \\ &= (\lambda + \alpha_1)(\lambda + \alpha_4)\left[(\lambda + \alpha_2)(\lambda + \alpha_3) - \beta c S_0\right] - u_1\sigma\left[(\lambda + \alpha_2)(\lambda + \alpha_3) - \beta c S_0\right] \\ &= \left[(\lambda + \alpha_2)(\lambda + \alpha_3) - \beta c S_0\right]\left[(\lambda + \alpha_1)(\lambda + \alpha_4) - u_1\sigma\right]. \end{aligned}$$

It should be noted that

$$\begin{aligned} (\lambda + \alpha_1)(\lambda + \alpha_4) - u_1\sigma &= (\lambda + \mu + u_1)(\lambda + \mu + \sigma) - u_1\sigma \\ &= (\lambda + \mu)(\lambda + \mu + \sigma + u_1), \\ (\lambda + \alpha_2)(\lambda + \alpha_3) - \beta c S_0 &= (\lambda + (u_2 + c + \mu))(\lambda + (\mu + d + r)) - \beta c S_0 \\ &= \lambda^2 + (\alpha_2 + \alpha_3)\lambda + \alpha_2\alpha_3(1 - \Re_0). \end{aligned}$$

Therefore, we can conclude that

If the reproduction number $\Re_0 = 1$, the characteristic equation $|\lambda I - J(E_0)| = 0$ has three negative eigenvalues and a zero eigenvalue with multiple one. Thus, the disease-free equilibrium E_0 is stable but not asymptotically stable.

If the reproduction number $\Re_0 > 1$, the characteristic equation $|\lambda I - J(E_0)| = 0$ has three negative eigenvalues and a positive eigenvalue $\lambda > 0$. Thus, the disease-free equilibrium E_0 is unstable.

In the case of the reproduction number $\Re_0 < 1$, the equation $\lambda^2 + (\alpha_2 + \alpha_3)\lambda + \alpha_2\alpha_3(1 - \Re_0)$ has

$$\Delta = (\alpha_2 + \alpha_3)^2 - 4\alpha_2\alpha_3(1 - \Re_0) = (\alpha_2 - \alpha_3)^2 + 4\alpha_2\alpha_3\Re_0 > 0.$$

It follows that the equation $\lambda^2 + (\alpha_2 + \alpha_3)\lambda + \alpha_2\alpha_3(1 - \Re_0) = 0$ has two distinct real solution whose sum is negative and product is positive, which means that this equation admits two negative real solutions. Thus, the disease-free equilibrium E_0 is locally asymptotically stable.

4. The optimal control problem for the controlled SEIR epidemic model

4.1. The formulation of optimal control problem (OCP)

In this section, we study the effectiveness of immunization and isolation treatments for reducing the number of infectious people and exposed people on the community. For this aim, we assume that the interval $[0,T]$ is the time period over which the treatments are applied and consider the admissible set

$$U_{ad} = \left\{ u = (u_1, u_2) \in L^2[0,T] \times L^2[0,T] \middle| 0 < u_i(t) \le u_0, t \in [0,T] \right\} \quad (i = \overline{1,2}).$$

Here, we call the set U_{ad} the admissible set for the problem (OCP). Next, the optimal control problem (OCP) for the controlled SEIR epidemic model can be descibed as follows:

$$\min J(u) = \int_0^T \left[I(t) + E(t) + \frac{1}{2} b_1 u_1^2 + \frac{1}{2} b_2 u_2^2 \right] dt$$

subject to the constraint in form of the following differential system

$$\begin{cases} S'(t) = \Lambda - \beta IS - u_1 S + \omega u_2 E + \sigma R - \mu S \\ I'(t) = \beta IS - \mu E - u_2 E - cE \\ E'(t) = cE - \dfrac{rI}{1+\gamma I} - (\mu + d) I \\ R'(t) = \dfrac{rI}{1+\gamma I} - \mu R - \sigma R + u_1 S + (1-\omega) u_2 E \end{cases} \tag{1.9}$$

and initial condition

$$S(0) = S_o, E(0) = E_0, I(0) = I_0, R(0) = R_0, \tag{1.10}$$

where b_1, b_2 are positive constants to keep a balance in the size of infections and input controls.

4.2. The existence of an optimal solution to the problem (OCP)

Next, for simplicity in representation, we denote

$$x(t)=\begin{pmatrix} S(t) & E(t) & I(t) & R(t)\end{pmatrix}^T$$
$$F(x(t))=\begin{pmatrix} \Lambda-\beta IS & \beta IS & -\dfrac{rI}{1+\gamma I} & \dfrac{rI}{1+\gamma I}\end{pmatrix}^T.$$

Then, we can rewrite the differential system (1.7) in the following compact form

$$\begin{aligned} x'(t)&=\begin{bmatrix} -(u_1+\mu)S+\omega u_2E+\sigma R \\ -(\mu+u_2+c)E \\ cE-(\mu+d)I \\ -(\mu+\sigma)R+u_1S+(1-\omega)u_2E\end{bmatrix}+\begin{bmatrix} \Lambda-\beta IS \\ \beta IS \\ -\dfrac{rI}{1+\gamma I} \\ \dfrac{rI}{1+\gamma I}\end{bmatrix} \\ &=\begin{bmatrix} -(u_1+\mu) & \omega u_2 & 0 & \sigma \\ 0 & -(\mu+u_2+c) & 0 & 0 \\ 0 & c & -(\mu+d) & 0 \\ u_1 & (1-\omega)u_2 & 0 & -(\mu+\sigma)\end{bmatrix}x(t)+F\left(x(t)\right) \\ &=G\left(x(t),u(t)\right).\end{aligned}$$

It is easy to prove that the functions $\Phi_1=\beta IS;\ \Phi_2=\dfrac{rI}{1+\gamma I}$ satisfy the Lipschitz condition. Thus, we get

$$\left|G\left(x(t),u(t)\right)-G\left(\bar{x}(t),u(t)\right)\right|\le L_0\left|X(t)-\overline{X}(t)\right|.$$

Therefore, Cauchy problem for the controlled SEIR epidemic model (1.7) always has a solution for all $u\in U_{ad}$. In order to find the optimal solution u^* of the problem (OCP), we consider the Lagrange function and the Hamiltonian function given by

$$L\left[x(t),u(t)\right]=I(t)+E(t)+\frac{1}{2}b_1u_1^2(t)+\frac{1}{2}b_2u_2^2(t)$$
$$H\left[x(t),u(t),\lambda(t)\right]=L\left[x(t),u(t)\right]+\lambda^T(t)\cdot x'(t),$$

where $\lambda^T(t)=\left(\lambda_1(t),\lambda_2(t),\lambda_3(t),\lambda_4(t)\right)^T$ is called the Lagrange multiplier. Firstly, we prove the existence of an optimal control $u^*(t)$ such that $J\left(u^*\right)=\min\left\{J(u)\right\}$. The proof of this assertion is obtained by the following lemmas:

Lemma 4.1. *For each input control $u\in U_{ad}$, the solution $x(t)$ of Cauchy problem for the controlled SEIR epidemic model (1.7) always exists, i.e. the set $\Omega=\{(x,u):u\in U_{ad}\}$ is non-empty.*

Lemma 4.2. *The admissible set U_{ad} is convex and closed.*

Proof. Let $u,\bar{u}\in U_{ad}$ and $\eta\in(0,1)$. Due to the fact that the space $L^2[0,T]\times L^2[0,T]$ is a vector space, it directly gets that

$$0<\eta u_i(t)\le\eta u_0,\quad 0<(1-\eta)\overline{u_i}(t)\le(1-\eta)u_0\quad \left(i=\overline{1,2}\right).$$

The above inequalities lead to

$$0<\eta u_i(t)+(1-\eta)\overline{u_i}(t)\le u_0\ \left(i=\overline{1,2}\right).$$

Thus, the admissible set U_{ad} is a convex subset of the space $L^2[0,T]\times L^2[0,T]$.

In order to prove the admissible set U_{ad} is closed, we choose an element $u=(u_1,u_2)\in L^2[0,T]\times L^2[0,T]$ such that u is the limit point of the functional sequences

$$u^{(n)}=\left(u_1^{(n)},u_2^{(n)}\right)\in U_{ad}.$$

Then, there exists an index $N_0\in\mathbb{N}$ such that for all $n\geq N_0$, it yields

$$\left\|u^{(n)}-u\right\|_2=\left[\int_0^T\left\|u^{(n)}(t)-u(t)\right\|^2dt\right]^{\frac{1}{2}}<\frac{1}{n}.$$

Hence, from the completeness of the space $L^2[0,T]\times L^2[0,T]$, we get

$$\lim_{n\to\infty}u^{(n)}=u\in L^2[0,T]\times L^2[0,T].$$

On the other hand, since $0<u_1(t)=\lim_{n\to\infty}u_1^{(n)}(t)\leq u_0$, $0<u_2(t)=\lim_{n\to\infty}u_2^{(n)}(t)\leq u_0$, we deduce that $u\in U_{ad}$, i.e., the admissible set U_{ad} is a closed set.

Lemma 4.3. There exist $C_1>0, C_2\geq 0$ and $\beta>1$ such that the inequality $L[x,u]\geq C_1\|u(t)\|^{\beta}+C_2$ holds.

Proof. Using the assumption that the functions $I(t),E(t)\geq 0,\ \forall t\in[0,T]$, we have

$$\begin{aligned}L[x(t),u(t)]&=I(t)+E(t)+\frac{1}{2}b_1u_1^2+\frac{1}{2}b_2u_2^2\\&\geq\frac{1}{2}\min\{b_1,b_2\}\{u_1^2(t)+u_2^2(t)\}\\&=\frac{1}{2}\min\{b_1,b_2\}\left[\sqrt{u_1^2(t)+u_2^2(t)}\right]^2\\&=\frac{1}{2}\min\{b_1,b_2\}\|u(t)\|^2,\end{aligned}$$

where $C_1=\frac{1}{2}\min\{b_1,b_2\}>0, C_2=0$ and $\beta=2.$

Lemma 4.4. $L[x(t),u(t)]$ is a convex function in $u\in U_{ad}$.

Proof. It is straightforward since the functional $L[x(t),u(t)]$ is a sum of two convex functions.

Lemma 4.5. The function $G(x(t),u(t))$ *is bounded by a linear function of the state variable.*

Proof. Indeed, for each $x\in\sum^+$ and $u\in U_{ad}$, we have

$$G\big(x(t),u(t)\big)=\begin{bmatrix}\Lambda-\beta IS-\mu S+\sigma R\\ \beta IS-(\mu+c)E\\ cE-(\mu+d)I-\dfrac{rI}{1+\gamma I}\\ \dfrac{rI}{1+\gamma I}-(\mu+\sigma)R\end{bmatrix}+\begin{bmatrix}-S\\0\\0\\S\end{bmatrix}u_1(t)+\begin{bmatrix}\omega E\\E\\0\\(1-\omega)E\end{bmatrix}u_2(t)$$
$$=\begin{bmatrix}G_1\big(x(t),u(t)\big)\\G_2\big(x(t),u(t)\big)\\G_3\big(x(t),u(t)\big)\\G_4\big(x(t),u(t)\big)\end{bmatrix}.$$

Then, for each $t\in[0,T]$, we have

$$\Lambda-\beta\frac{\Lambda}{\mu}S-u_0S+\sigma R<G_1\big(x(t),u(t)\big)\le\Lambda+\sigma R+\omega u_0E$$
$$-u_0E-(\mu+c)E\le G_2\big(x(t),u(t)\big)\le\beta\frac{\Lambda}{\mu}S-(\mu+c)E$$
$$cE-(\mu+d)I-\frac{rI}{1+\gamma I}<G_3\big(x(t),u(t)\big)\le cE-(\mu+d)I$$
$$-(\mu+\sigma)R\le G_4\big(x(t),u(t)\big)\le rI-(\mu+\sigma)R.$$

Therefore, the proof is completed.

Finally, we have the following theorem:

Theorem 4.6. *The optimal control problem* (OCP) *for the controlled SEIR epidemic model* (1.7) *always has an optimal solution* $u^*\in U_{ad}$.

Proof. Indeed, by using the results of some lemmas (from Lemma 1 to Lemma 5) and Theorem 4.1 in [6], we immediately obtained the desired conclusion.

4.3. The sufficient condition for an optimal pair $\left(x^*,u^*\right)$

Theorem 4.7. Suppose that $\left(x^*,u^*\right)\in\sum^+\times U_{ad}$ is an optimal pair of the problem (OCP) under differential constraint system (1.9) and the initial condition (1.10). Then, the triplet $\left(x^*,u^*,\lambda\right)$ satisfies the following conditions

(i)
$$\begin{cases}S^{*\prime}(t)=\Lambda-\beta I^*(t)S^*(t)-u_1^*(t)S^*(t)+\omega u_2^*(t)E^*(t)+\sigma R^*(t)-\mu S^*(t)\\ E^{*\prime}(t)=\beta I^*(t)S^*(t)-\left(\mu+u_2^*(t)+c\right)E^*(t)\\ I^{*\prime}(t)=cE^*(t)-\dfrac{rI^*(t)}{1+\gamma I^*(t)}-(\mu+d)I^*(t)\\ R^{*\prime}(t)=\dfrac{rI^*(t)}{1+\gamma I^*(t)}-(\mu+\sigma)R^*(t)+u_1^*(t)S^*(t)+(1-\omega)u_2^*(t)E^*(t).\end{cases}$$

(ii) $$\begin{bmatrix}\lambda_1'(t)\\ \lambda_2'(t)\\ \lambda_3'(t)\\ \lambda_4'(t)\end{bmatrix}=\begin{bmatrix}-\beta I^*(t)\lambda_1(t)-u_1^*(t)-\mu+\beta I^*(t)\lambda_2(t)+\lambda_4(t)u_1^*(t)\\ 1+\omega\lambda_1(t)u_2^*(t)-\left(\mu+c+u_2^*(t)\right)\lambda_2(t)\\ 1-\beta S^*(t)\lambda_1(t)+\beta S^*(t)\lambda_2(t)-(\mu+d)\lambda_3(t)-\dfrac{r}{\left(1+\gamma I^*(t)\right)^2}\lambda_3(t)+\dfrac{r}{\left(1+\gamma I^*(t)\right)^2}\lambda_4(t)\\ \sigma\lambda_1(t)-(\mu+\sigma)\lambda_4(t)\end{bmatrix}.$$

(iii) $x^*(0)=x_0=(S_0,E_0,I_0,R_0).$

(iv) $\lambda(T)=\lambda(0)=0.$

Proof. According to the definition of Hamiltonian function, we have

$$J(u)=\int_0^T\left\{H\left(x(t),u(t),\lambda(t)\right)-\lambda^T(t)\cdot x'(t)\right\}dt.$$

Next, we apply the Pontryagin extremum principle (see [6]) to investigate the sufficient conditions for the optimality of the problem (OCP). Next, let $u(t)=u^*(t)+\delta u(t)$ and $x(t)=x^*(t)+\delta x(t)$. Then

$$\begin{aligned}\Delta J\left(u^*\right)&=J(u)-J\left(u^*\right)\\&=\int_0^T\left[\left\{H\left(x(t),u(t),\lambda(t)\right)-\lambda^T(t)\cdot x'(t)\right\}-\left\{H\left(x^*(t),u^*(t),\lambda(t)\right)-\lambda^T(t)\cdot x^{*\prime}(t)\right\}\right]dt\\&=\int_0^T\left[H\left(x^*(t)+\delta x(t),u^*(t)+\delta u(t),\lambda(t)\right)-H\left(x^*(t),u^*(t),\lambda(t)\right)\right]dt\\&\qquad-\int_0^T\lambda^T(t)\cdot\left[x^*(t)+\delta x(t)-x^{*\prime}(t)\right]dt\\&=\left\{\int_0^T\left[\frac{\partial H}{\partial x}\left(x^*(t),u^*(t),\lambda(t)\right)\right]^T\cdot\delta x(t)+\int_0^T\left[\frac{\partial H}{\partial u}\left(x^*(t),u^*(t),\lambda(t)\right)\right]^T\cdot\delta u(t)\right\}dt\\&\qquad-\int_0^T\lambda^T(t)\cdot\left(\delta x(t)\right)'dt+o\left(\left\|x^*(t)\right\|^2\right)+o\left(\left\|u^*(t)\right\|^2\right).\end{aligned}$$

Moreover, we have

$$\int_0^T\lambda^T(t)\cdot\left(\delta x(t)\right)'dt=\lambda^T(t)\cdot\delta x(t)\Big|_0^T-\int_0^T\left(\lambda^T(t)\right)'\cdot\delta x(t)dt=\lambda^T(t)\cdot\delta x(t)\Big|_0^T-\int_0^T\left(\lambda'(t)\right)^T\cdot\delta x(t)dt.$$

Then, the pair that $\left(x^*,u^*\right)$ minimizes the functional $J(u)$ if the following expression is fulfilled

$$\int_0^T\left[\frac{\partial H}{\partial x}-\lambda'(t)\right]^T\cdot\delta x(t)+\left[\frac{\partial H}{\partial u}\right]^T\cdot\delta u(t)dt+\lambda^T(x)\cdot\delta x(t)\Big|_0^T=0,\quad\forall\delta x,\delta u.$$

Therefore, we receive the following system:

$$\begin{cases} \dfrac{\partial H}{\partial x} = \lambda'(t) \\ \dfrac{\partial H}{\partial u} = 0 \\ \lambda^T(x)\cdot \delta x(t)\Big|_0^T = 0. \end{cases} \tag{1.11}$$

Note that

$$H = I + E + \frac{1}{2}b_1 u_2^2 + \lambda_1(t)\left[\Lambda - \beta IS - (u_1+\mu)S + \omega u_2 E + \sigma R\right] + \lambda_2(t)\left[\beta IS - (\mu + c + u_2)E\right]$$
$$+ \lambda_1(t)\left[cE - (\mu + d)I - \frac{rI}{1+\gamma I}\right] + \lambda_4(t)\left[\frac{rI}{1+\gamma I} - (\mu+\sigma)R + u_1 S + (1-\omega)u_2 E\right]$$

Hence, the differential equation $\dfrac{\partial H}{\partial x} = \lambda'(t)$ is equivalent to

$$\begin{bmatrix} \lambda_1'(t) \\ \lambda_2'(t) \\ \lambda_3'(t) \\ \lambda_4'(t) \end{bmatrix} = \begin{bmatrix} -\beta I(t)\lambda_1(t) - u_1(t) - \mu + \beta I(t)\lambda_2(t) + \lambda_4(t)u_1(t) \\ 1 + \omega\lambda_1(t)u_2(t) - (\mu + c + u_2(t))\lambda_2(t) \\ 1 - \beta S(t)\lambda_1(t) + \beta S(t)\lambda_2(t) - (\mu+d)\lambda_3(t) - \dfrac{r}{(1+\gamma I(t))^2}\lambda_3(t) + \dfrac{r}{(1+\gamma I(t))^2}\lambda_4(t) \\ \sigma\lambda_1(t) - (\mu+\sigma)\lambda_4(t) \end{bmatrix}.$$

In addition, the differential equation $\dfrac{\partial H}{\partial u} = 0$ can be rewritten as

$$\begin{bmatrix} \dfrac{\partial H}{\partial u_1} \\ \dfrac{\partial H}{\partial u_2} \end{bmatrix} = \begin{bmatrix} b_1 u_1 - \lambda_1(t)S(t) + \lambda_4(t)S(t) \\ b_2 u_2 + \omega\lambda_1(t)E(t) - \lambda_2(t)E(t) + (1-\omega)\lambda_4(t)R(t) \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}.$$

Hence, the proof is completed.

Remark 4.7. The system of conditions (1.11) represents the Euler-Lagrange equations for the optimal control problem (OCP) to the controlled SEIR epidemic model, which gives the sufficient conditions for the optimality of the considered problem (OCP).

5. Some simulations and discussions:

In this section, we are going to present some discussions based on the realistic data of Vietnam's population and COVID-19 pandemic statistical data in Vietnam (see [15 – 17] for more details) to demonstrate the effectiveness of theoretical results. Since our aim is to study the coronavirus epidemic disease when it is a pandemic and is reaching a peak, we will use the data on April 6th, 2022 to estimate the model's parameters and provide the initial inputs for the proposed epidemic model. Indeed, since the natural birth rate in Vietnam at this time is 15,502 children per 1000 persons and the natural birth rate is 6,546 per 1000 persons (see [17]). According to the data in [17], the total population of Vietnam on April 6th, 2022 is $N =$ 98,878,883. In addition, according to the statistical data in [15], the number of dead persons due to coronavirus is 42.768, the number of confirmed COVID-19 infected persons is 495,358,778 and the number of recovered persons is 8,455,673. (These data is counted from the beginning of the pandemic). Therefore, we can estimate some parameters as

follows:

$$\Lambda = \frac{15,502}{N}\times 1000 = \frac{15,502}{98,878,883}\times 1000 = 0.15678$$

$$\mu = \frac{6,546}{98,878,883}\times 1000 = 0.0662$$

$$d = \frac{42,768}{10,135,789} = 4,2195\times 10^{-3}$$

$$r = \frac{8,455,675}{10,135,789} = 0.834.$$

These other parameters are assumed to be $\sigma = 0.18, \beta = 1.1\times 10^{-2}, c = 0.0102, \omega = 0.7, \gamma = 6.$ In addition, at this time, it is informed that the number of infectious persons is 49,124, the number of recovered is 130,273 and assume that the number of exposed persons that are being quarantined or self-quarantined is 1,760,061. Thus, we set up the initial data for the proposed controlled SEIR epidemic model as follows:

$$S(0) = N - \left(E(0) + I(0) + R(0)\right) = 96,939,425$$
$$E(0) = 1,760,061; \quad I(0) = 49,124; \quad R(0) = 130,273.$$

The sensitivity analysis of parameters studies how different uncertainty sources contribute to an epidemic model's overall uncertainty and the sensitivity indices allow us to estimate the relative change of the basic reproduction number $\Re_0$ when a parameter changes. Now, based on the work of Nakul et al. (see [9]), the sensitivity index of a quantity X depending on a parameter λ can be determined by:

$$\Phi_\lambda^{\Re_0} = \frac{\partial \Re_0}{\partial \lambda}\cdot\frac{\lambda}{\Re_0}.$$

According to the definition of $\Re_0$, we can see that the basic reproduction number $\Re_0$ directly depends on these parameters $\beta, \Lambda, \mu, \sigma, c, d, r$ and two control inputs $u_1, u_2.$ Then, by some direct computations, we have

$$\Phi_\Lambda^{\Re_0} = \frac{\partial \Re_0}{\partial \Lambda}\cdot\frac{\Lambda}{\Re_0} = 1, \qquad \Phi_\beta^{\Re_0} = \frac{\partial \Re_0}{\partial \beta}\cdot\frac{\beta}{\Re_0} = 1,$$

$$\Phi_d^{\Re_0} = \frac{\partial \Re_0}{\partial d}\cdot\frac{d}{\Re_0} = -\frac{d}{\mu+d+r}, \qquad \Phi_r^{\Re_0} = \frac{\partial \Re_0}{\partial r}\cdot\frac{r}{\Re_0} = -\frac{r}{\mu+d+r},$$

$$\Phi_{u_1}^{\Re_0} = \frac{\partial \Re_0}{\partial u_1}\cdot\frac{u_1}{\Re_0} = -\frac{u_1}{\mu+u_1+\sigma}, \qquad \Phi_{u_2}^{\Re_0} = \frac{\partial \Re_0}{\partial u_2}\cdot\frac{u_2}{\Re_0} = -\frac{u_2}{\mu+u_2+c},$$

$$\Phi_\sigma^{\Re_0} = \frac{\partial \Re_0}{\partial \sigma}\cdot\frac{\sigma}{\Re_0} = \frac{\sigma u_1}{(\mu+\sigma)(\mu+u_1+\sigma)}, \qquad \Phi_c^{\Re_0} = \frac{\partial \Re_0}{\partial c}\cdot\frac{c}{\Re_0} = \frac{(\mu+u_2)}{(\mu+u_2+c)},$$

$$\Phi_\mu^{\Re_0} = \frac{\partial \Re_0}{\partial \mu}\cdot\frac{\mu}{\Re_0} = -\left[\frac{\sigma}{\mu+\sigma} + \frac{\mu}{\mu+u_1+\sigma} + \frac{\mu}{\mu+u_2+c} + \frac{\mu}{\mu+d+r}\right].$$

From the above computations, we can conclude that the threshold value $\Re_0$ is the most sensitive with the natural birth rate Λ and the disease transmission rate $\beta.$ Indeed, each increase of 10% in the value of these parameters will experience an increase of the basic reproduction number $\Re_0$ at the

same percentage. On the other hand, it is true that the increases of three parameters r, d, μ and two input controls will stifle the epidemic disease spread since they make the basic reproduction number become smaller, while the bigger values of the parameters c and σ will make the value of basic reproduction number go up. In order to illustrate the effects of the model's parameters to the basic reproduction number, the readers can see Figure 2.

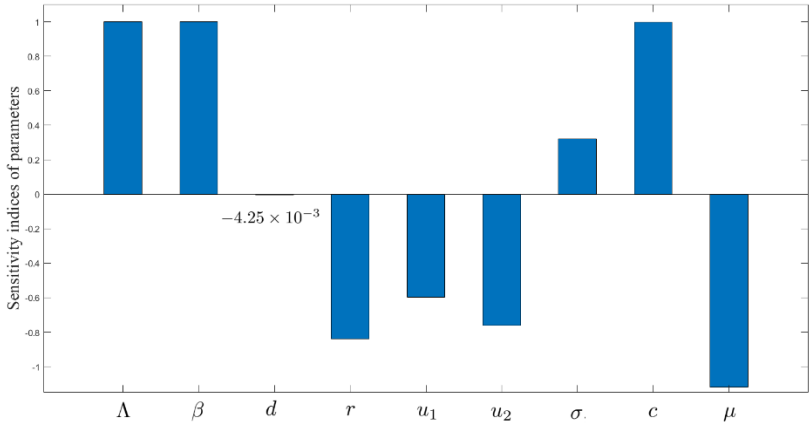

Figure 2. The sensitivity indices of the epidemic model's parameters

6. Conclusions

In this paper, we investigated a modified SEIR epidemic model with nonlinear treatment function to study the transmission of COVID -19 in the community. We evaluated the basic reproduction number $\Re_0$, that is an important threshold value in the epidemiological theory and proved the relationship between this value and the local asymptotic stability of disease-free equilibrium as well as the existence of a unique epidemic equilibrium. Furthermore, we also formulated an isolation and immunization optimal control problem for the proposed SEIR epidemic model. These theoretical results along with numerical simulations proved that applying the quarantine treatment and immunization for exposed and infectious individuals is an effective way to control and fight against the pandemic.

7. Acknowledgments

This research is funded by Hanoi Pedagogical University 2 under grant number SV.2022.HPU2.05.

References

A. References in Vietnamese

[1] C.T.Anh, *Cơ sở lí thuyết phương trình vi phân*, NXB Đại học Sư phạm, 2015.

[2] N.T. Hoàn, P. Phu, *Cơ sở phương trình vi phân và lý thuyết ổn định*, NXB Giáo dục, 2000.

B. References in English

[3] A.J. Arenas, G.G. Parra, B.M. Chen-Charpentier, *Construction of nonstandard finite difference schemes for the SI and SIR epidemic models of fractional order*, Math. Comput. Simulat., 121 (2015), 48-63.

[4] M. Budincevic, *A Comparison theorem of differential equations*, Novi Sad J. Math, 40 (2010), 55 – 56.

[5] N.N. Chung, L.Y. Chew, *Modelling Singapore COVID-19 pandemic with a SEIR multiplex network*

model, Sci. Rep., 11 (2021)**,** 10122.

[6] W. Fleming, R. Rishel, *Deterministic and Stochastic Optimal Control*, Springer – Verlag, Berlin, 1975.

[7] L. López, X. Rodó, *A modified SEIR model to predict the COVID-19 outbreak in Spain and Italy: Simulating control scenarios and multi-scale epidemics*, Results in Physics, 21 (2021), 103746.

[8] S. Mwalili, M. Kimathi, V. Ojiambo, D. Gathungu, R. Mbogo, *SEIR model for COVID-19 dynamics incorporating the environment and social distancing*, BMC Res Notes, 13 (2020), 352.

[9] C. Nakul, J.M. Hyman, J.M. Cushing, *Determining important parameters in the spread of malaria through the sensitivity analysis of a mathematical model*, Bull. Math. Biol., 70 (2008), 1272-96.

[10] W.O. Kermack, A.G. McKendrick, *A Contribution to the Mathematical Theory of Epidemics*, Proc. Roy. Soc. Lond. A, 115 (1927), 700-721.

[11] H. Kheiri, M. Jafari, *Fractional optimal control of an HIV/AIDS epidemic model with random testing and contact tracing*, J. Applied Math. Comp., 60 (1-2) (2018).

[12] C.H. Li, C.C. Tsai, S.Y. Yang, *Analysis of epidemic spreading of an SIRS model in complex heterogeneous networks*, Commun. Nonlinear Sci. Numer. Simulat., 19 (4) (2014), 1042-1054.

[13] X. Zhang, X. Liu, *Backward bifurcation of an epidemic model with saturated treatment function*, J. Math. Anal. Appl., 348 (1) (2008), 433-443.

C. Webpage

[14] https://baochinhphu.vn/who-tuyen-bo-covid-19-la-dai-dich-toan-cau-102269461.html/

[15] COVID – 19's Statistics. (2022). https://covid19.ncsc.gov.vn/

[16] World Ometer: COVID-19 Coronavirus pandemic. https://www.worldometers.info/

[17] Macrotrends: Vietnam Death Rate , Birth Rate 1950-2022. https://www.macrotrends.net/