

## FRACTIONAL DIFFERENTIAL EQUATION MODEL FOR COVID-19 EPIDEMIC

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### ABSTRACT.

An epidemic disease caused by coronavirus has spread all over the world with a strong contagion rate. We present simulations of epidemic models constructed using real data to give a clear perspective and confirmation on the effect of quarantine on the evolution of the infection and the number of infected, recovered, and dead because of this epidemic in South Carolina in a time window (December 1, 2020, to June 1, 2021) when the epidemic was relatively strong. We use CDC data for infected and dead populations covering the period December 1, 2020, to June 1, 2021 in South Carolina to develop models and do simulations. There were no data available for recovered populations in this period. Part of our goal is to estimate the number of recovered for the entire period. The models and results are consistent with the data. The infection and recovery increasing in South Carolina do not show improvement in this period. The number of dead people in this period tended to increase although by small amount. Optimal control methodologies are considered where transmission, recovery, relapse of immunity and death rates are considered as decision variables in minimizing the difference between the real and computed COVID-19 infection and dead data. Effect of quarantine as intervention strategy is also considered as it is critical issue. What we want to show is what could have been the outcome if quarantine had been implemented from the very beginning. The progress of an infection in general is related not only to the present states, but also to its historical states. To account for the effect of past evolution we add fractional differential equations models.

**AMS (MOS) Subject Classification.** 34H05, 34D20, 68T07, 92B20 **Key Words and Phrases.** Optimal control, Reproduction number.

### 1. INTRODUCTION

The rapid spread of a disease in regions (epidemic) or the global outbreak of a disease (pandemic), can have a detrimental effect on health systems and economical activities locally and globally. Measures to reduce the pandemic spread include curtailing close interactions between people using social distancing and face masks and vaccinations. Social distancing has negative economic effects. It is useful to understand the significance of these interventions, ([4], [39], [53], [59]).

Mathematical models have been used in epidemiology for many years, going back to the eighteenth century. Most of the models are compartmental models, with the population divided into classes and with assumptions being made about the rate of transfer from one class to another. Here we start by considering a Susceptible-Infectious-Recovered (SIR) model to describe the spread of the virus and compute the number of infected and dead individuals. There are models that include exposed and migration. The goal is to compute the number of infected, recovered, and dead individuals on the basis of the number of contacts, probability

of disease transmission, incubation period, recovery rate, and fatality rate. The epidemic disease models help predict a peak of infected and dead individuals as a function of time when dealing with a very short period of time. The population members decrease due to the disease as dictated by the fatality rate of the disease. Generally the differential equations are solved with a forward Euler scheme, ([29]).

In this paper we want to include memory effect. There are different mathematical ways of dealing with memory issue. Modeling of memory effect in epidemic modeling has been done in various areas of epidemiology. To give perspective one of the important applications is in the modeling of HIV. There has been a continued effort in the mathematical modeling of the dynamics and control of human immunodeficiency virus (HIV) by various authors ([11], [14], [16], [19], [20], [33], [34], [47], [52], [56], [62], [67]). One of the earliest models dealing with HIV is due to Perelson, Kirschner and De Boer ([47]). They consider the interaction of HIV with CD4+ T-cells where the CD4+ T-cells consist of four population groups: uninfected T-cells, latently infected T cells, actively infected T cells, and free virus. Much effort has been put toward the study of the global dynamics of the HIV differential equation models. There has also been a number of studies where optimal control techniques are employed ([9], [20], [27], [33], [63]). Memory is an important feature in immune response ([19], [55]). To include memory in the model fractional differential equations(FDE) have been used([19], [20], [27]).

Besides applications in HIV modeling fractional differential equations(FDE) have proved to be valuable tools in the modeling of many phenomena in engineering, physics, and economics ([24], [25], [26], [40], [42], [48], [61]). Fractional differential equations have also been useful in biology, fluid mechanics, modeling of viscoelasticity. The most fundamental characteristics in these models is their nonlocal characteristics. That is, the future aspect of the model relates not only to the present states, but also to its historical states.

A decision maker, leader must carry out various responsibilities such as controlling epidemic while adhering to economics, budget, employment, industry requirements. The goals that a decision maker has to accomplish are generally complex and involve conflicting objectives, budget, scheduling. To deal with these types of situations, in addition to fractional differential equation models, one could also consider impulsive control problems, optimization, neural networks, multiobjective programming ([6], [7], [12], [14], [22], [23], [32], [43], [44], [45], [49], [50], [60]).

We proceed by starting with a standard mathematical model using data mentioned above and then introduce quarantine, quarantine and memory effects using FDE. The data we have does not have all that we need. Our models need to be consistent with the available data while giving us reliable information on unavailable data and significance of an intervention, quarantine in this case. Quarantine was not very popular as was face mask in the period considered.

## 2. MATHEMATICAL MODELS

Mathematical and statistical methods provide essential input for governmental decision making that aims at controlling an epidemic outbreak. Statistical methods frequently aim at early detection of disease outbreaks ([53]). Another approach is to develop models that indicate the outbreak dynamics using compartmental models ([53]). In compartmental models we consider a fraction of the population to be susceptible, a fraction to be infected, a fraction that has recovered. In some models exposed group is part of the model. Compartmental models have been used to model HIV epidemic, malaria, and corona virus outbreak, ([28], [31], [41], [53], [56],[60]). In this paper we start by considering SIR model. SIR model can be modified in several ways, for example, by including demographics, deceased populations, hidden population, i.e., exposed populations (SEIR). In an accelerating epidemic outbreak contact tracing, the SEIR model needs to be modified to account for it. In the current paper our objectives are to consider SIR and SIR-plus-quarantine models based on real data and control methods and show the effectiveness of quarantine intervention to control the epidemic. We first consider a model with no quarantine and then one with quarantine. Optimal control, optimization/neural network approaches for the estimation of the parameters of the SIR models using real time series data are important tools. We start with an SIR model with no quarantine. The SIR model is formulated in terms of three populations of individuals. The susceptible population,  $z_1$ , consists of all individuals susceptible to the infection of concern. The infected population,  $z_2$ , comprises the infected individuals. These persons have the disease and can transmit it to the susceptible individuals. The recovered population,  $z_3$ , represents the immune individuals, who cannot become infected and cannot transmit the disease to others.

We use CDC data covering the period December 1, 2020, to June 1, 2021. In this period vaccination has been available although not taken advantage of by a lot of people. In addition, social distancing and face making were not widely accepted interventions. We have data for infected population and dead population. The recovered population for Dec. 1, 2020, is known to be 115152. Constrained optimization and neural network(deep/reinforcement learning in lieu of curse of dimensionality) methodologies are relevant in dealing with discrete models ([10],[54], [58], [63]). Neural network methodology can be used to come up with recovery, contact, and reproduction rates. Number of recovered for the period was not available from the CDC data.

We first present discrete model followed by basic SIR epidemic disease model where there is no quarantine in either case. The total (initial) population,  $N$ , is categorized into four classes, namely, susceptible,  $z_1(t)$ , infected-infectious,  $z_2(t)$ , and recovered,  $z_3(t)$ , where  $t$  is the time variable.

$$\begin{array}{ll}
 \text{The initial} & \text{value problem} \\
 \text{we} & \text{consider is} \\
 \frac{dz_1}{dt} &= \lambda_{SC} \cdot z_1 - (\mu_{SC})z_1 - u \cdot z_1 z_2(1/N), \\
 \frac{dz_2}{dt} &= u \cdot z_1 z_2(1/N) - (v + w)z_2 - (\mu_{SC})z_2 + u \cdot z_2 z_3(1/N) \\
 \frac{dz_3}{dt} &= v \cdot z_2 - (\mu_{SC})z_3 - u \cdot z_2 z_3(1/N), \quad , \\
 \end{array}
 \tag{2.1}$$

where  $\lambda_{SC}$  = birth rate,  $\mu_{SC}$  = natural death rate,  $u$ =transmission rate,  $v$ =recovery rate,  $w$ = death rate of infected,  $N=5149000$ , susceptible population in SC.

We solve the above system of differential equations by using MATLAB Euler-scheme. Simulations of the results are shown below. To determine the necessary parameters, we used data obtained from CDC and optimal control methodology.

### 3. DISCRETE MODEL

We use data covering the period December 1, 2020, to June 1, 2021. In this period vaccination has been available although not taken advantage of by a lot of people. In addition, social distancing and face masking have not been widely accepted. The discrete model is useful to determine transmission, recovery, relapse, immunity, death rates from the infection for the period considered day by day. We will refer to these parameters as the dynamic parameters.

We consider the following discrete model covering the period December 1, 2020, to June 1, 2021. We have data for infected population and dead population for this model. We are going to rely on our model to estimate the recovered populations day by day covering this period. The recovered population for Dec. 1, 2020, is known to be 115152. Constrained optimization and neural network(deep/reinforcement learning in lieu of curse of dimensionality) methodologies are relevant in dealing with the discrete models ([54], [58], [63]).

$$\begin{aligned}
 z_1(i+1) &= (1 - vc) \cdot \lambda_{SC} \cdot N + z_1(i) - \mu_{SC} \cdot z_1(i) \\
 &\quad - (1/(1 + \exp(-u(i))))z_1(i)z_2(i)(1/N) + (1/(1 + \exp(-s(i))))z_3(i), \\
 z_2(i+1) &= z_2(i) + u(i)z_1(i)z_2(i)/N - (v(i) + 1/(1 + \exp(-w(i))) + \mu_{SC})z_2(i) \\
 &\quad + 1/(1 + \exp(-r(i))) \cdot z_3(i), \\
 z_3(i+1) &= vc \cdot \lambda_{SC} \cdot N + z_3(i) + (1/(1 + \exp(-v(i)))) \cdot z_2(i) - (\mu_{SC} \\
 (3.1) \quad &\quad + 1/(1 + \exp(-r(i))) + 1/(1 + \exp(-s(i)))) \cdot z_3(i),
 \end{aligned}$$

In this model,  $\lambda_{SC} = .058$  birth rate;  $\mu_{SC} = .0095$ , natural death rate  $vc = .40$ ,  $vc \cdot N$  represents proportion of vaccinated people,  $N$ =the susceptible population, 5149000, transmission rate= $1/(1+\exp(-u(i)))$ , recovery rate= $1/(1+\exp(-v(i)))$ , relapse rate= $1/(1+\exp(-r(i)))$ , immunity rate= $1/(1+\exp(-s(i)))$ , death rate from infection= $1/(1+\exp(-w(i)))$ .

Thus, the number of recovered compartment,  $z_3$ , increases by  $vc \cdot N$ , whereas the susceptible compartment  $z_1$  increases by  $(1 - vc) \cdot \lambda_{SC} \cdot N$ . We see the recovery, relapse, and death rates are numbers between zero and 1. The optimization model determines what are appropriate. The number of infections arising from an infected individual is then modeled by the number  $R_0(i)$  given below.

$$\begin{aligned}
 A(i) &= (u(i)z(i, 1)/N)/(v(i) + w(i) + \mu_{SC}) \\
 R_0(i) &= (A(i) + 1/2\sqrt{A(i)^2 + 4v(i)r(i)/((v(i) + w(i) + \mu_{SC})(\mu_{SC} + r(i) + s(i)))})
 \end{aligned}$$

The dynamic parameters of interest are obtained by minimizing the objective function

$$\sum_i (C(i)^2 + D(i)^2 + E(i)^2)$$

where

$$\begin{aligned} C(i) &= (z_2(i) - Inf(i)), \\ D(i) &= ((1/(1 + \exp(-w(i)))) \cdot z_2(i) - Dead(i)), \\ E(i) &= (z_2(i) - z_3(i)). \end{aligned}$$

subject to the discrete model above. In the objective function above,  $Inf(i)$  is the number of infected people at or on the  $i$ -th date after December 1, 2020. The numbers are gotten from CDC. Likewise  $Dead(i)$  represents the number of dead people. The quantity  $E(i)$  represents the difference between the number of infected people according to our model  $z_2(i)$ , and infected people,  $Inf(i)$ , gotten from CDC data. We represent the recovered people by  $z_3(i)$ . Infected and recovered and contact rates based on the discrete model are shown in Fig. 1 and Fig. 2

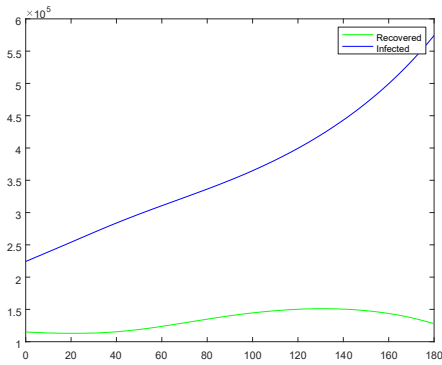


Figure 1. Infected Recovered, Discrete Model.

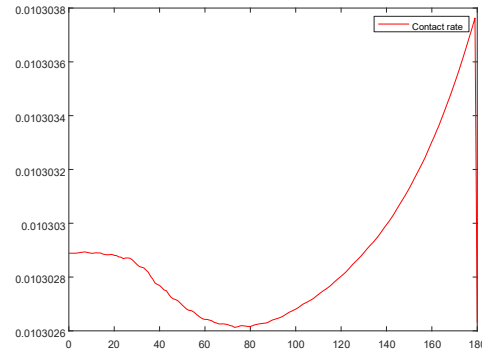


Figure 2. Transmission rates Discrete Model

Thus, the number of recovered compartment,  $z_3$ , increases by  $vc \cdot N$ , whereas the susceptible compartment  $z_1$  increases by  $(1 - vc) \cdot \lambda_{sc} \cdot N$ . We see the recovery, relapse, and death rates are numbers between zero and 1. The number of infections arising from an infected individual is modeled by the reproduction number  $R_0(i)$  given below. The average basic reproduction number is 1.6133. We note that it is slightly bigger than 1 consistent with the infected-recovered graph.

#### 4. CONTINUOUS MODEL-OPTIMAL CONTROL APPROACH

Mathematical models are important in analyzing the spread and control of infectious diseases. The model formulation requires carefully designed models with appropriate assumptions, and variable parameters. Mathematical models have been critical in the study of infectious diseases ([13], [21], [29], [53], [54]). They have been used in studying tuberculosis ([50]), HIV ([31]), and dengue fever ([3]) models, etc. The aim here is to start with appropriate model and relevant parameters to be determined. Among the parameters of importance to be determined are contact rates  $u$ , recovery rates  $v$ , relapse rates  $r$ , infection reproduction rates  $R_0$ , death rates  $w$ , immunity rates  $s$ . We also include the role of vaccination. The dynamic parameters obtained in the discrete model serve as starting parameters in the model here and the later ones. Although vaccinated people are unlikely to be infected contributing to immunity, there is still a possibility of relapse. In the continuous models we use a slightly different objective function from the discrete model where the aim is for infected population in the model to follow the data of CDC infected people. In the continuous model the CDC data of dead people is included in relation to the susceptible and infected people. We expect the infected population to go down due to quarantine and so it should not be expected to align with the CDC data of infected people. Optimal control related epidemic models are also considered in ([5], [8], [14], [15], [34], [35], [36], [37], [38], [46], [50], [51], [64]).

We first consider dynamics with no quarantine. We would like to consider the following problem.

$$\min \left\{ \int_0^T \{ (w(t)z_1(t) - Dead(t))^2 + (v(t)z_2(t) - z_3(t))^2 + (u(t)z_1(t) - z_2(t))^2 \} dt \right\}$$

subject to

$$\begin{aligned} \frac{dz_1}{dt} &= (1 - vc) \cdot \lambda_{SC} \cdot N - \mu_{SC} z_1 - uz_1 z_2 (1/N) + s \cdot z_3 = f_1 \\ \frac{dz_2}{dt} &= uz_1 z_2 (1/N) - (v + w) z_2 - \mu_{SC} z_2 + rz_3 = f_2, \\ \frac{dz_3}{dt} &= vc \cdot \lambda_{SC} \cdot N + vz_2 - \mu_{SC} z_3 - rz_2 - sz_3 = f_3. \end{aligned}$$

,

(4.1)

The adjoint equation is

$$\begin{aligned} dP_1/dt &= 2(uz_1 - z_2)u + (\mu_{SC} + uz_2/N)P_1 - (uz_2/N)P_2, \quad dP_2/dt = \\ &2(wz_2 - Dead(t))w + 2(vz_2 - z_3)v - 2(uz_1 - z_2) + (uz_1/N)P_1 \\ &\quad - (uz_1/N - v - w - \mu_{SC})P_2 - vP_3, \\ (4.2) \quad dP_3/dt &= -2(vz_2 - z_3) - sP_1 - rP_2 + (\mu_{SC} + r + s)P_3. \end{aligned}$$

Next we construct the Hamiltonian.

Set

$$f_0(t) = (w(t)z_1 - Dead(t))^2 + (v(t)z_2 - z_3)^2 + (u(t)z_1 - z_2)^2.$$

Next,

$$\partial f_0 / \partial u = 2(u z_1 - z_2) z_1,$$

$$\partial f_0 / \partial v = 2(v z_2 - z_3) z_2,$$

$$\partial f_0 / \partial w = 2(w z_2 - Dead(t)) z_2.$$

$$\partial f_1 / \partial u = -z_1 z_2 / N,$$

$$\partial f_1 / \partial v = 0,$$

$$\partial f_1 / \partial w = 0.$$

$$\partial f_2 / \partial u = z_1 z_2 / N,$$

$$\partial f_2 / \partial v = -z_2,$$

$$\partial f_2 / \partial w = -z_2.$$

$$\partial f_3 / \partial u = 0,$$

$$\partial f_3 / \partial v = z_2, \partial f_3 / \partial w =$$

$$0.$$

$$\partial H / \partial u(t) = f_0(t)u(t) - P_1 \partial f_1 / \partial u - P_2 \partial f_2 / \partial u - P_3 \partial f_3 / \partial u,$$

$$\partial H / \partial v(t) = f_0(t)v(t) - P_1 \partial f_1 / \partial v - P_2 \partial f_2 / \partial v - P_3 \partial f_3 / \partial v,$$

$$\partial H / \partial w(t) = f_0(t)w(t) - P_1 \partial f_1 / \partial w - P_2 \partial f_2 / \partial w - P_3 \partial f_3 / \partial w.$$

Finally we update our control variables.

$$u(t) = u(t) - del_1 \cdot \partial H / \partial u(t),$$

$$w(t) = w(t) - del_2 \cdot \partial H / \partial w(t),$$

$$v(t) = v(t) - del_3 \cdot \partial H / \partial v(t).$$

Again, we use the CDC data of infected population and dead people day by day from December 1, 2020, to June 1, 2021. We use our model to estimate the number of recovered people. The following figure (Fig. 3) represents the recovered (green) and infected (blue) populations confirming what we expect.

We see that the number of infected populations increases until mid-April. The number of recovered populations follows the pattern of infected populations. The number of recovered

people becomes closer to the number of infected populations. Recovery rates, transmission rates and reproductions rates are also presented. Corresponding infected, recovered and susceptible states are shown in Fig. 3, Fig. 4 and transmission, recovery and reproduction rates are in Fig. 5, 6, 7, and the average transmission rate=0.0391, average recovery rate=0.0405. From the state equation (4.1) we consider

$$(4.3) \quad \begin{aligned} \frac{dz_2}{dt} &= uz_1z_2(1/N) - (v+w)z_2 - \mu_{SC}z_2 + rz_3, \\ \frac{dz_3}{dt} &= vz_2 - (\mu_{SC})z_3 - rz_2 - sz_3. \end{aligned}$$

We rewrite this equations as

$$(4.4) \quad \frac{dz}{dt} = (F + V)z, \text{ where}$$

$$(4.5) \quad F = \begin{bmatrix} uz_1/N & r \\ v & 0 \end{bmatrix},$$

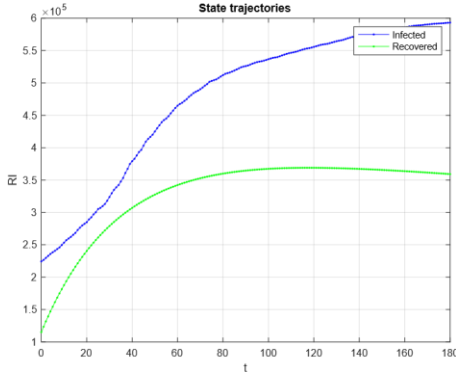


Figure 3. Infected Recovered States, no quarantine

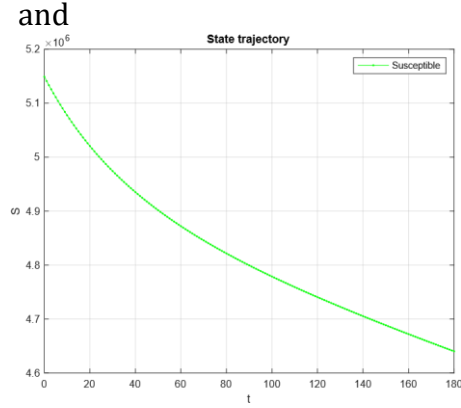


Figure 4. Susceptible State, no quarantine.

$$(4.6) \quad V = \begin{bmatrix} -v - w - \mu_{SC} & 0 \\ 0 & -\mu_{SC} - r - s \end{bmatrix}.$$

Now,

$$(4.7) \quad -FV^{-1} = \begin{bmatrix} uz_1/(v+w+\mu_{SC}) & r/(\mu_{SC}+r+s) \\ v/(v+w+\mu_{SC}) & 0 \end{bmatrix}.$$



$$\begin{aligned}
 A(i) &= (u(i)z(i, 1)/N)/(v(i) + w(i) + \mu_{SC}), \\
 R_0(i) &= A(i) + 1/2\sqrt{A(i)^2 + 4v(i)r(i)/((v(i) + w(i) + \mu_{SC})(\mu_{SC} + r(i) + s(i)))} \\
 (4.8)
 \end{aligned}$$

The dominant eigenvalue of  $-FV^{-1}$  is  $R_0$  (4.8) and the average of  $R_0(i)$  is 1.0314 which is less than what had in the discrete model. A sketch of the reproduction number is shown. We have evaluated the reproduction number for each day. We note it is slightly bigger than 1 consistent with the infected-recovered graph. Below, Table 1 shows for the first 10 days of May 2021 the number of susceptible, infected, dead, and recovered when there is no quarantine in our model from the beginning Dec. 1, 2020 to the end of our data June 1, 2021.

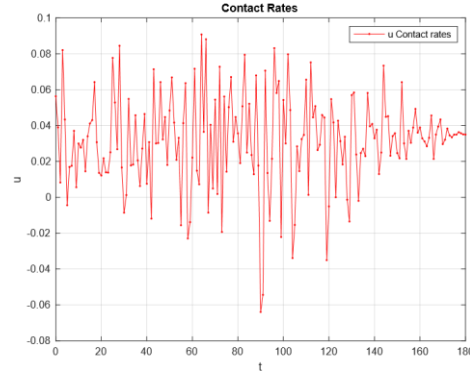


Figure 5. Tansmission Rates

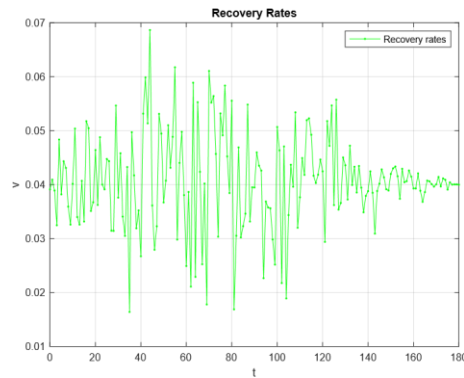


Figure 6. Recovery rates.

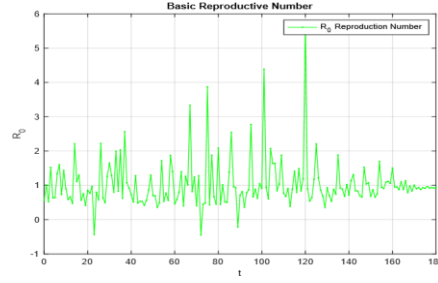


Figure 7. Reproduction Number.

Table 1

<i>Susceptible</i>	<i>Infected</i>	<i>Dead</i>	<i>Recovered</i>
4654300	580560	9560	365670
4652700	581290	9570	365500
4651100	581800	9590	365310
4649500	582230	9590	365130
4647900	582830	9600	364940
4646400	583480	9600	364750
4644800	584190	9610	364560
4643200	584950	9620	364360
4641700	585670	9630	364160
4640100	585810	9640	363960

**4.1. EFFECT OF QUARANTINE.** In the infected and recovered figure resulting from the SIR model above we see that the number of infected people is increasing. The figure of infected people shown is in complete agreement to the data gotten from CDC. It is not acceptable to see the number is increasing. It is known that the disease of COVID-19 is transmitted through different mechanisms, such as hand contamination followed by mucosal inoculation, and droplets or aerosols disseminated by coughing and sneezing. Some measures that control the transmission of COVID-19 involve simple habits such as washing one's hands continuously, sneezing into one's hand or elbow, use of face mask low mobility, quarantine. Quarantine includes all of these measures. From now on we introduce quarantine. What we want to show is what could have been the outcome if quarantine had been implemented from the very beginning. We will see a model where an initial quarantine of 50,000 susceptible people, which decreases, leads to a significant decrease in the infected population and corresponding increase in the recovered population. We modify (4.1) to include quarantine of a small fraction of the population. We can contrast the effect of quarantine by comparing Fig. 1, Fig. 3, 4, where there is no quarantine to Fig. 8, 9, Fig. 10,11,12 where there is quarantine, which is our objective. We now consider our quarantine model:

$$\begin{aligned}
\frac{dz_1}{dt} &= (1 - vc) \cdot \lambda_{SC} \cdot N - \mu_{SC} z_1 - u z_1 z_2 (1/N) + s \cdot z_3 - \lambda_1 z_1 z_4 (1/N) + \theta_1 z_4 \\
\frac{dz_2}{dt} &= u z_1 z_2 (1/N) - (v + w) z_2 - \mu_{SC} z_2 + r z_3, \\
\frac{dz_3}{dt} &= vc \cdot \lambda_{SC} \cdot N + v z_2 - \mu_{SC} z_3 - r z_2 - s z_3, \\
(4.9) \quad \frac{dz_4}{dt} &= \lambda_1 z_1 z_4 (1/N) - \theta_1 z_4 - \mu_{SC} z_4.
\end{aligned}$$

In this quarantine model we use the dynamic parameters for contact, recovery, relapse and immunity rates that were obtained in the discrete/optimal methods as starting parameters in our control problem. The parameters  $\lambda_1, \theta_1$  are chosen to be .01. Next, we proceed to solve the differential equation (4.9). The simulations of the infected, recovered and quarantine populations are shown in Fig. 8 and Fig. 9. The simulations confirm what we expect that quarantine has a positive effect.

## 5. PRELIMINARIES FOR FRACTIONAL DIFFERENTIAL EQUATION MODEL

To account for the fact that the immune response involves memory we will consider a control problem governed by fractional differential equations. For information on fractional differential equation we recommend the references([1], [2], [19], [20], [48]). Let  $f: [0, \infty) \rightarrow \mathbb{R}$ . For  $-\infty < a < b < \infty$  the fractional integral of order  $\alpha > 0$  of  $f$  with lower limit zero is defined as

$${}_a I_t^\alpha f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t \frac{f(s)}{(t-s)^{1-\alpha}} ds.$$

The left Riemann-Liouville fractional derivative of order  $\alpha$  of  $f$  is given as

$${}_a^L D_t^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \frac{d^n}{dt^n} \int_0^t \frac{f(s)}{(t-s)^{\alpha+1-n}} ds, \quad t > 0, \quad n-1 < \alpha < n.$$

The right Riemann-Liouville fractional derivative of order  $\alpha$  of  $f$  is given as

$${}_t^L D_b^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \left(-\frac{d}{dt}\right)^n \int_t^b \frac{f(s)}{(s-t)^{\alpha+1-n}} ds, \quad t > 0, \quad n-1 < \alpha < n.$$

The right Caputo derivative of  $f$  of order  $\alpha$  with lower limit zero is given as

$${}_0^C D_t^\alpha f(t) = {}_0^L D_t^\alpha [f(t) - \sum_{k=0}^{n-1} \frac{t^k}{k!} f^{(k)}(0)], \quad t > 0, \quad n-1 < \alpha < n.$$

The right and left Caputo derivatives, in integral form, are given as

$${}_a^C D_t^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \int_a^t \frac{f(s)}{(t-s)^{\alpha+1-n}} ds,$$

$${}_t^C D_b^\alpha f(t) = \frac{1}{\Gamma(n-\alpha)} \int_t^b \frac{f(s)}{(s-t)^{\alpha+1-n}} ds.$$

Fractional differential equations and models are considered in ([17], [18], [30], [57], [65], [66]).

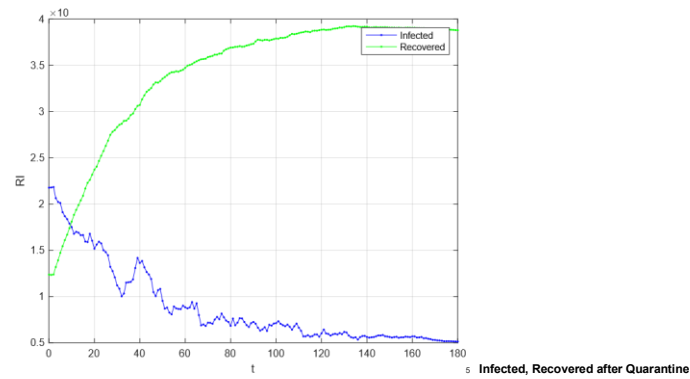


Figure 8. Infected Recovered after Quarantine

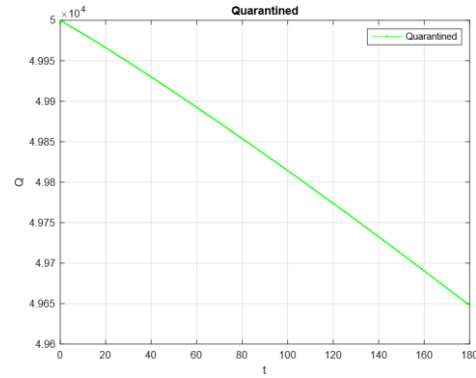


Figure 9. Quarantined.

The initial value problem

$$\begin{aligned}
 {}^C_0 D_t^\alpha f(t) &= f(t, x(t)), \quad 0 < \alpha < 1 \\
 x(t_0) &= x_0
 \end{aligned}
 \tag{5.1}$$

is equivalent to the nonlinear Volterra integral equation([48]):

$$x(t) = x_0 + \frac{1}{\Gamma(\alpha)} \int_0^t (t-s)^{\alpha-1} f(s, x(s)) ds.$$

In this paper we take  $\alpha = 0.9$ .

## 6. PROBLEM STATEMENT

Let the functions  $f : [t_0, T] \times \mathbb{R}^4 \times \mathbb{R}^3 \rightarrow \mathbb{R}$  be such that  $f(\cdot, x, u, v, w)$  is measurable for fixed  $(x, u, v, w)$ . For fixed  $t$  and  $u, v, w$ , the function  $f$  is continuously differentiable in  $x$ . For fixed  $t$ ,  $f(t, \cdot)$  is continuous. We also assume that

$$\begin{aligned} & \| \partial_x f(t, x_2, u_2, v_2, w_2) - \partial_x f(t, x_1, u_1, v_1, w_1) \| + \| f(t, x_2, u_2, v_2, w_2) - f(t, x_1, u_1, v_1, w_1) \| \\ & \leq K \{ \|x_2 - x_1\| + \| (u_2, v_2, w_2) - (u_1, v_1, w_1) \| \}, \end{aligned}$$

where  $K$  is a fixed constant.

Now, we consider the following fractional differential equation

$$\begin{aligned} {}^C_0 D_t^q x(t) &= f(t, x(t), u(t), v(t), w(t)), \quad 0 < q < 1, \quad 0 = t_0 < t < T, \\ (6.1) \quad x(t_0) &= x_0. \end{aligned}$$

Suppose we consider the following optimal control problem

$$(\mathcal{P}) \quad \min \{ J(x, u, v, w) = \int_0^T \{ F_0(x(t), u(t), v(t), w(t)) \} dt \}$$

subject to

$$\begin{aligned} {}^C_0 D_t^q f(t) &= f(t, x(t), u(t), v(t), w(t)), \quad 0 < q < 1, \quad 0 = t_0 < t < T, \\ (6.2) \quad x(t_0) &= x_0. \end{aligned}$$

Assume that problem (P) has a solution  $(\bar{x}, (\bar{u}, \bar{v}, \bar{w}))$ .

The adjoint equation has the form

$$(6.3) \quad P(s) = \frac{1}{\Gamma(q)} \int_s^T (\xi - s)^{q-1} [P(\xi) \partial_x f(\xi, \bar{x}(\xi), \bar{u}(\xi), \bar{v}(\xi), \bar{w}(\xi)) + \partial_x F_0(\xi, \bar{x}(\xi), \bar{u}(\xi), \bar{v}(\xi), \bar{w}(\xi))] d\xi$$

We now define the Hamiltonian by

$$(6.4) \quad H(t, x(t), P(t), u(t), v(t), w(t)) = P(t) \cdot f(t, x(t), u(t), v(t), w(t)) + F_0(t, x(t), u(t), v(t), w(t)).$$

Then, for any  $(u, v, w) \in U$ ,

$$(6.5) \quad H(t, \bar{x}(t), P(t), u(t), v(t), w(t)) \geq H(t, \bar{x}(t), P(t), \bar{u}(t), \bar{v}(t), \bar{w}(t)) \text{ a.e. } t.$$

## 7. APPLICATION TO QUARANTINE MODEL

We consider the optimal control problem

$$(\mathcal{P}) \quad \min \{J(z, u, v, w) = \int_0^T \{(w(t)z_1(t) - Dead(t))^2 + (v(t)z_2(t) - z_3(t))^2 + (u(t)z_1(t) - z_2(t))^2\} dt\}$$

subject to

$$\begin{aligned} {}^C_0 D_t^q z_1(t) &= (1 - vc) \cdot \lambda_{sc} \cdot N - \mu_{sc} z_1 - u z_1 z_2 (1/N) + s \cdot z_3 - \lambda_1 z_1 z_4 (1/N) + \theta_1 z_4, \\ {}^C_0 D_t^q z_2(t) &= u z_1 z_2 (1/N) - (v + w) z_2 - \mu_{sc} z_2 + r z_3, \\ {}^C_0 D_t^q z_3(t) &= vc \cdot \lambda_{sc} \cdot N + v z_2 - \mu_{sc} z_3 - r z_2 - s z_3, \\ {}^C_0 D_t^q z_4(t) &= \lambda_1 z_1 z_4 (1/N) - \theta_1 z_4 - \mu_{sc} z_4. \end{aligned}$$

where  $z_1$  represents susceptible population,  $z_2$  infected population,  $z_3$  recovered population,  $z_4$  quarantined population. The control  $u$  is transmission rate,  $v$  death rate,  $w$  recovery rate,  $r$  relapse rate,  $s$  immunity rate. To numerically solve the control problem we employ the control updating procedure we used in the previous control problem.

Using the control problem the simulations of infected, recovered, quarantined, susceptible during quarantine are shown in Fig. 10, 11, 12.

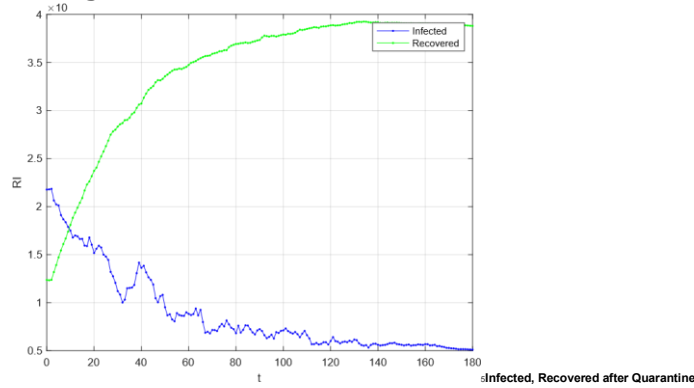


Figure 10. Quarantine Infected Recovered FDE Model

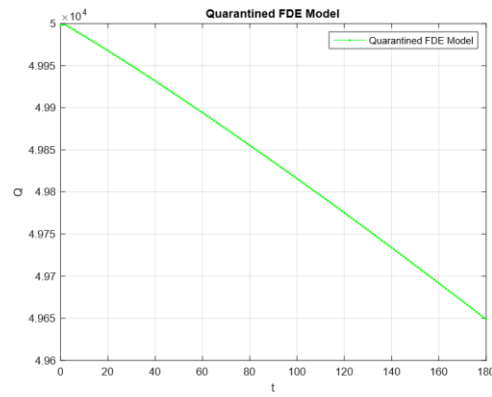


Figure 11. Quarantined FDE Model.

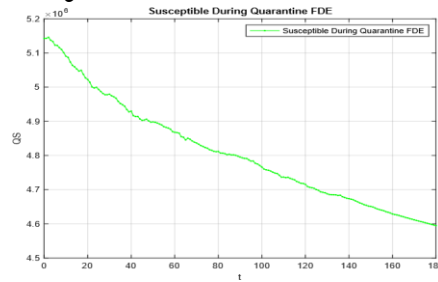


Figure 12. Susceptible During Quarantine FDE model

Table 2 uses the first 10 days of May 2021 if quarantine were applied from the beginning, i.e., December 1, 2020. There is a significant difference in the number of infected and recovered from what we see in Table 1 when there is no quarantine. The number of dead people is slightly lower than in the model without quarantine and slightly less does not fluctuate much.

Table 2

<i>Susceptible</i>	<i>Infected</i>	<i>Dead</i>	<i>Recovered</i>
4673400	58500	9600	369300
4671300	58200	9600	369300
4669700	57800	9600	369300
4667800	57700	9600	369300
4665400	58200	9600	369100

4663200	58700	9600	369100
4661700	58400	9600	369400
4660300	57600	9600	369600
4658700	56900	9600	369900
4656100	56700	9600	369800

## 8. CONCLUSION

The worldwide spread of corona virus exerts enormous pressure on healthcare systems, societies, and governments. Therefore, predicting the epidemic dynamics is an important problem from a data science and mathematical modeling perspective. The motivation of the current work was to explore the potential of sequential data assimilation to create a regional epidemic model as a forecasting tool and effectiveness of interventions such as quarantine. The standard epidemic SIR-type models implement a compartmental description under the assumption of homogeneous mixing of individuals.

More realistic modeling approaches must account for spatial heterogeneity due to time varying disease onset times, regionally different contact rates, and the time dependence of the contact rates due to the implementation of containment strategies. However, extensive data are not currently available. Thus, we must construct models where control theory, optimization, and neural network methodologies to approximate missing and necessary data are used. In the work we did relating to data from December 1, 2020, to June 1, 2021, we rely only on available data of infected and dead populations to have some ideas on the transmission, recovery, and relapse rates and the relevance of certain interventions such as quarantine.

In Fig. 1, 3, 4, where there is no quarantine, we see an increase in infection although not significant and the recovered population increases and then levels off and tends to decrease. This is in contrast to Fig. 8, 10, where we see the infected population goes down and the recovered population tends upward when quarantine is introduced. In Fig. 4 the susceptible population decreases not as much as when there is quarantine intervention Fig. 12. We can infer from these simulations that quarantine would make a significant impact in decreasing infection population and decreasing the susceptible population, i.e., susceptible people are protected. Thus, quarantine is an effective tool in curbing the spread of the virus.

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## REFERENCES

- [1] O. P. Agarwal, Fractional variational calculus and the transversality conditions, J. Phys. A, Math. Gen. 39 (2006) pp. 10375-10384.
- [2] E. Ahmed, A. S. Elgazzar, On fractional order differential equations model for nonlocal epidemics, Phys. A, Vol. 379 (2007) pp. 607-714.
- [3] D. Aldila, T. Gotz, E. Soewono, An optimal Control problem arising from a dengue disease transmission model, Math. Biosci. 242 (1)(2013), 9-16.
- [4] Anastassopoulou C, et.al, Anastassopoulou C, Russo L, Tsakris A, Siettos C. Data-based analysis, modelling and forecasting of the COVID-19 outbreak. PLoS ONE 15(3): e0230405. <https://doi.org/10.1371/journal.pone.0230405>
- [5] S. A. Attiya, V. Azhmyakov, J. Raisch, State jump optimization for a class of hybrid autonomous Systems, Proceedings of the 2007 IEEE Multiconference on Systems and Control, Singapore, 2007, pp. 1408-1413.



- [6] V. Azhmyakov, S. A. Attiya, J. Raisch, On The Maximum Principle for the Impulsive Hybrid System, *Lec. Notes in Computer Science*, Vol. 4981, Springer, Berlin, 2008, pp. 30-42.
- [7] V. Azhmyakov, V. G. Boltyanski, A. Poznyak, Optimal control of impulsive hybrid systems, *Nonlinear Analysis: Hybrid Systems* 2(2008) pp. 1089-1097.
- [8] F. G. Ball, E. S. Knock, P.D. O'Neil, Control of emerging infectious diseases using responsive imperfect vaccination and isolation, *Math. Biosci.* 216 (1) (2008), 100-113.
- [9] M. Barao, J. M. Lemos, Nonlinear control of HIV-1 infection with a singular perturbation model, *Biomed. Signal Process Control*, Vol. 2, (2007), pp. 248-257.
- [10] Marcus de Barros Braga, et al, Artificial neural networks for short-term forecasting of cases, deaths, and hospital beds occupancy in the COVID-19 pandemic at the the Brazilian Amazon, *PLOS—*  
<https://doi.org/10.1371/journal.pone.0248161> March 2021.
- [11] M. E. Brandt, G. Chen, Feedback control of a biodynamical model of HIV-1, *IEEE Tans. Biomed. Eng.*, Vol. 48, No. 7 (2001), pp. 754-758.
- [12] M. S. Branicky, V. S. Borkar, S. K. Mitter, A unified framework for hybrid control: Model and optimal control theory, *IEEE Transactions on Automatic Control* 43(1998) pp. 31-45.
- [13] C. Castilho, Optimal Control of an epidemic through educational campaigns, *Electron. J. Differ. Equ.* 2006 (2006), 1-11.
- [14] H. Chang, A. Astolfi, Activation of immune response in disease dynamics via controlled drug scheduling, *IEEE Trans. Autom. Sci. Eng.*, Vol. 6, No. 2 (2009) pp. 248-255.
- [15] H. J. Chang, H. Shim, J. H. Seo Control of immune response of HIV infection model by gradual reduction of drug dose: In *Proceedings of the 43rd Conference on Decision and Control*, pp. 1048-1054 (1974).
- [16] R. V. Culshaw, S. Ruan, A delay-differential equation model of HIV infection of CD4+ T-cells, *Math. Biosci.*, Vol. 165 (2000) pp. 27-39.
- [17] K. Diethelm, N. J. Ford, A. D. Freed, A Predictor-Corrector Approach for the Numerical Solution of Fractional Differential Equation, 29: 3-22, 2002.
- [18] K. Diethelm, *The Analysis of Fractiona Differential Equations*, Lecture Notes in Mathematics 2004.
- [19] Y. S. Ding, H. Ye, A fractional-order differential equation model of HIV infection of CD4+ T-cells, *Math. Comput. Model.*, Vol. 50 (2009), pp. 386-392.
- [20] Y. S. Ding, Z. Wang, Haiping Ye, Optimal Control of a Fractional-Order HIV-Immune System With Memory, *Vol. 20, No. 3*, (2012), pp. 763-769.
- [21] H. Gaff, E. Schaefer, Optimal control applied to vaccination and treatment strategies for various epidemiological models, *Math. Biosci. Eng.* 6 (3) (2009), 469-492.
- [22] K. Ganesh, M. Punniyamoorthy, Optimization of continuous-time production planning using hybrid genetic algorithms-simulated annealing, *The International Jour. of Advanced Manufacturing Technology*, Vol. 26, No. 1-2, 2005, pp. 148-154.
- [23] M. Garavello, B. Piccoli, Hybrid necessary principle, *SIAM Jour. on Cpntrl and Optimization* 43(2005), pp. 1867-1887.
- [24] L. Gaul, P. Klein, S. Kempfle, Damping description involving fractional operators, *Mech. Syst. Signal Process*, 5, 81-88 (1991).
- [25] E. G. Gilbert, G. A. Hardy, A class of fixed-time fuel optimal impulsive control problems and an efficient algorithm for their solution, *IEEE Trans. Autom. Control* AC-16(1971).
- [26] W. G. Glockle, T. F. Nonnenmacher, A fractional calculus approach of selfsimilar proten dynamics, *Biophys J.* 68, 46-53(1995).
- [27] Tinag Liang Guo, The Necessary Conditions of Fractional Optimal Control in the Sense of Caputo, *J. Optim Theory Appl* (2013) 156:115-126.
- [28] K. Hattaf, N. Yousfi, Optimal Control of a delayed HIV infection model with immune response using an efficient numerical method, *Int. Sch. Res. Netw.* (2012), 1-7.
- [29] Hethcote, The mathematics of infectious diseases. *SIAM Rev.* Vol. 42, 2006, 599-653.
- [30] R. Hilfer, *Applications of Fractional Calculus in Physics*, World Scientific, Singapore, 2000.
- [31] Hail-Fung Huo et. al., Modeling and stability of HIV/AIDS epidemic model with treatment, Hail-Feng Huo, Rui Chen, Xun-Yang Wang, *Applied Mathematical Modelling* 40(2016) 6550-6559.
- [32] S. H. Hou, K. H. Wong, Optimal Impulsive Control Problem with Application to Human Immunodeficiency Virus Treatment, *J. Optim Theory Appl* (2011) 151: 385-401.

- [33] A. M. Jeffrey, X. H. Xia, I. K. Craig, When to initiate HIV therapy: A control theoretic approach, *IEEE Trans. Biomed., Eng.*, Vol. 50, No. 11 (2003) pp. 1213-1220.
- [34] D. E. Kirschner, Using mathematics to understand HIV immune dynamics, *Notices of Amer. Math. Soc.*, Vol 43 (1996) pp. 191-202.
- [35] D. Kirschner, S. Lenhart, S. Serbin, Optimal control of chemotherapy of HIV, *Jour. Math. Biol.* Vol. 35 (1997), pp. 775-792.
- [36] H. Kwon, Optimal treatment strategies derived from a HIV model with drug-resistant mutants, *Appl. Math. Comput.*, Vol. 188, (2007) pp. 1193-1204.
- [37] H. Laarabi, A. Abta, K. Hattaf, Optimal Control of a delayed SIRS epidemic model with vaccination and treatment, *Acta Biotheor.* 63 (15) (2015), 87-97
- [38] M. L. Lazo, D. F. M. Torres, The DuBois-Reymond Fundamental Lemma of the Fractional Calculus of Variations and an Euler-Lagrange Equation Involving Only Derivatives of Caputo, *J. Optim Theory Appl* (2013) 156: 56-67.
- [39] Lin Q, et.al, Lin Q, Zhao S, Gao D, Lou Y, Yang S, Musa SS, Wang MH, Cai Y, Wang W, Yang L, He D. A conceptual model for the coronavirus disease 2019 (COVID-19) outbreak in Wuhan, China with individual reaction and governmental action. *Int J Infect Dis.* Vol. 93, 2020; pp. 211-216.
- [40] J. C. Luo, E. B. Lee, Time-optimal control of the swing using impulsive control actions. In *Proceedings of American Control Conference*, pp. 200-204(1998).
- [41] Macdonald, G. The epidemiology and control of malaria. Oxford University, 1957, Mandal, S. et al.
- [42] F. Mainardi, Fractional calculus: Some basic problems in continuum and statistical mechanics, *Fractals and Fractional Calculus in Continuum Mechanics* (editors: Carpinteri, Mainardi), Springer Verlag (1997) pp. 291-348.
- [43] Malaria Review, Mathematical Models of Malaria - A Review, *Malaria Journal* (2011).
- [44] Aniela Maria, Christopher Mattson, Amir Ismail-Yahaya, Achille Messac, Linear physical programming for production planning optimization *Eng. Opt.*, 2003, Vol. 35(1), pp. 19-37.
- [45] Achille Messac, W. Batayneh, Amir Ismail-Yahaya, Production Planning Optimization with Physical Programming *Eng. Opt.*, 2002, No. 4, Vol. 34, pp. 323-340.
- [46] P. Ogren, C. F. Martin, Vaccination strategies for epidemics in highly mobile populations. *Appl. Math. Comput.* 127 (2002), 261-276.
- [47] A. S. Perelson, D. E. Kirschner, R. De Boer, Dynamics of HIV infection of CD4+ T cells, *Math. Biosci.*, Vol. 165 (1993) pp. 81-125.
- [48] I. Podlubny, *Fractional Differential Equations*, Academic Press, New York, 1999.
- [49] M. S. Shaikh, P. E. Caines, On the hybrid optimal control problem: Theory and algorithms, *IEEE Transaction on Automatic Control* 52(2007) pp. 1587-1683.
- [50] G. N. Silva, R. B. Vinter, Necessary Conditions for Optimal Impulsive Control Problems, *Proceedings of the 36th Conf. on Decision Control* 1197, pp. 2086-2090.
- [51] C. J. Silva, D. F. Torres, Optimal Control strategies for tuberculosis treatment: a case study in angola, *Numer. Algebra Control Optim.* 2 (3) (2012), 601-617
- [52] R. F. Stengel, Mutation and control of the human immunodeficiency virus, *Math. Biosci.*, Vol. 213 (2008) pp. 93-102.
- [53] Unkel S, et.al, Statistical methods for the prospective detection of infectious disease outbreaks: a review. *J R Stat Soc, Ser A, Stat Soc.* 2012;175(1):49-82.
- [54] Valeri M. Mladenov, Nicholas G. Maratos, Neural Networks for Solving Constrained Optimization Problems, *Proc. of CSCC'00*, Athens, Greece.
- [55] J. Velasco-Hernandez, J. Garcia, and D. Kirschner, Remarks on modeling host-viral dynamics and treatment, *Math. Approaches for Emerg. Reemerg. Infectious Diseases I, An Introduction to Models, Methods, Theory*, Vol. 125 (2001) pp. 287-308.
- [56] L. Wang, M. Y. Li, Mathematical analysis of the global dynamics of a model for HIV infection of CD4+ T-cells, *Math. Biosci.*, Vol. 200 (2006) pp. 44-57.
- [57] J. Wang, Y. Zhou, A class of fractional evolution equations and optimal controls, *Nonlinear Anal., Real World Appl.* Vol. 12 (2011), pp. 262-272.
- [58] Wang, S. Second-Order necessary and sufficient conditions in multiobjective programming, *Numer. Func. Anal. and Optimiz.*, 12(1&2), 237-252 (1991.)

- [59] Wu JT et.al, Estimating clinical severity of COVID-19 from the transmission dynamics in Wuhan, China. *Nature Medicine* Vol. 26, 2020, pp. 506-510.
- [60] C. Z. Wu, K. L. Teo, Yi Zhao, W. Y. Yan, An optimal control problem involving impulsive integrodifferential systems, *Optimization Methods and Software*, Vol. 22. No. 3, June 2007, pp. 531-549.
- [61] T. Yang, *Impulsive Control Theory*, Lecture Notes in Control and Information Sciences, Vol. 272, Springer, Berlin ( 2001).
- [62] H. Ye, Y. S. Ding Dynamical analysis of a fractional-order HIV model, *Comput. Model. Eng. Sci.*, Vol 49, No. 3 (2009), pp. 255-268.
- [63] H. Ying, F. Lin, R. D. MacArthur, J. A. Cohn, D. C. Barth-Jones, H. Ye, and L. R. Crane, A fuzzy discrete even system approach to determining optimal HIV/AIDS treatment regimens, *IEEE Tans. Inform. Technol. Biomed.*, Vol 10, No. 4 (2006), pp. 663-676.
- [64] G. Zaman, Y.H. Kang, J.H. Jung, Optimal treatment of an SIR epidemic model with time delay , *Biosystems* 98 (1) (2009), 43-50.
- [65] S. Zhang, Existence of positive solution for some class of nonlinear fractional differential equations, *Jour. Math. Anal. Appl.* Vol. 278 ( 2003), pp. 136-148.
- [66] Y. Zhou, F. Jiao, Nonlocal Cauchy problem for fractional evolution equations, *Nonlinear Anal., Real Word Appl.* Vol. 11 ( 2010), pp. 4465-4475.
- [67] X. Zhou, X. Song, X. Shi, A differential equation model of HIV infection of CD4+ T-cells with cure rate, *Jour. Math. Anal. Appl.* Vol. 342 ( 2008), pp. 1342-1355.