Is it Curbing-spread of SARS-CoV-2 Variants by Considering Non-linear Predictive Control?

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ABSTRACT: Although SARS-COV-2 started in 2019, its losses are still significant, and it takes victims. In the present study, the epidemic patterns of SARS-COV-2 disease have been investigated from the point of view of mathematical modeling. Also, the effect of quarantine has been considered. This mathematical model is designed in the form of fractional calculations along with a model predictive control (MPC) to monitor this model. The fractional-order model has the memory and hereditary properties of the system, which can provide more adjustable parameters to the designer. Because the MPC can predict future outputs, it can overcome the conditions and events that occur in the future. The results of the simulations show that the proposed nonlinear model predictive controller (NMPC) of fractional-order has a lower mean squared error in susceptible people compared to the optimal control of fractional-order (~3.6e-04 vs. 47.4). This proposed NMPC of fractional-order can be used for other models of epidemics.

KEYWORDS: Mathematical model, fractional-order calculations, a nonlinear model predictive control, SARS-COV-2

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Introduction

Coronaviruses are a group of viruses that cause disease by infecting the respiratory system of birds and mammals.[1] In November 2002, the first known case of an acute respiratory syndrome (SARS) occurred in China.[2] In addition, another disease called SARS-CoV-2 spread in China for the first time in 2019. In 2020, the World Health Organization (WHO) declared the epidemic caused by SARS-COV-2 as an acute respiratory syndrome.[3,4] Severe infections of this disease can cause the failure of several organs, which in some cases leads to death. The transmission of this disease from one person to another is mainly caused by physical contact with infected areas and respiratory droplets contaminated with this virus.[5] Mathematical models can be the most important tools for analyzing the spread of and determining control measures of infectious diseases. Understanding epidemic mathematical modeling is related to the effectiveness of quarantine. Because using the quarantine rate reduces transmission and eradicates the disease.

At the beginning of the outbreak of COVID-19, the SQEIAR model was selected, which included susceptible people, exposed people, infected people, asymptomatic people, and recovered people. It also includes a new group of people in quarantine. At that time, there was still no vaccine for treatment. In order to help people understand dynamic systems for disease transmission, it can attract the attention of researchers. So far, the optimal control plan has been presented to control the epidemic model.[6] So, one of the epidemic models is the SQEIAR model. The purpose of this SQEIAR model is to reduce the size of the groups of susceptible people, infected people, exposed people, and asymptomatic people, which results in the elimination of infections using two actions: Quarantine and treatment of infected people. The design of strategies for optimal control of the disease of SARS-COV-2 in Yousefpour et al[7] was carried out. In this study, a multi-objective genetic algorithm was proposed to achieve high-quality programs, including various factors such as contact speed and transition rate of symptomatic infected individuals to the quarantined infected class. Optimal policies were successfully designed by changing these factors. In Tang et al[8], ordinary differential equations and Markov Chain Monte Carlo (MCMC) methods were used to estimate the risk of disease transmission and the consequences of public health interventions. The optimal control theory for a SARS-COV-2 transmission model provided by a system of nonlinear ordinary differential equations is presented in Lemecha Obsu & Feyissa Balcha.[9] Thus, optimal control strategies are obtained by minimizing the number of exposed and infected people, considering the implementation cost. In Fatima et al[10], an optimal control mathematical model for analyzing the spread of SARS-COV-2 is proposed. This proposed model depicts multiple transmission pathways in the dynamics of infection and emphasizes the role of environmental resources in disease transmission. In Shaikh et al[11], a SARS-CoV-2 model was analyzed to simulate fractional control measures. The Picard successive approximation technique and Banach's fixed-point theory were used to verify the criteria for the existence and stability of the model. So that in this model, preventive measures, predicting future outbreaks, and estimating disease control strategies. A Susceptible Exposed Infectious Hospitalized Recovered Dead (θ-SEIHRD) model is used in Ivorra et al[4], which includes a new approach. Therefore, the fraction θ considers the diagnosed cases in the total number of infected cases and investigates the importance of this ratio in SARS-COV-2. In Khajji et al[12], the fractional optimal control problem is proposed in the SEIR model, which considers the age structure and uses fractional-order derivatives to obtain a more realistic model. In Yousefpour et al[13], an adaptive terminal sliding state controller was designed along with a neural network estimator to synchronize and stabilize a hyperchaotic economic system in the form of fractional-order differential equations. In Jajarmi et al[14], an active control scheme was developed from a linear and homogeneous feedback controller to control and synchronize a hyperchaotic economic system in the form of fractional order. In Baleanu et al[15], a generalized fractional mathematical model was proposed to investigate the dynamics of HIV/AIDS transmission. Also, an efficient intervention strategy based on optimal control approaches has been investigated. Their results show that the fractional model with ordinary time derivatives performs better than the classical model. Among all control schemes for nonlinear systems, model predictive control (MPC) is an effective scheme that can be applied optimally way for control systems.[16,17] In Jahanshahi et al[18], a chaotic economic system model was investigated using variable fractional-order derivatives. In addition, a nonlinear model predictive controller (NMPC) is designed to over-control the system.

In the present study, the SQEIAR optimal control model is considered first. Fractional-order differential equations are then proposed because they are capable of describing the memory and features of the mathematical model. In this case, they can be more suitable for modeling the SARS-CoV-2 disease in contrast to the correct order. They also provide additional parameters to the controller designer. Also, a novel NMPC has been proposed to control SARS-COV-2. In addition to optimization, the predictive controller can predict the future behavior of the model and establish more control constraints. This controller can recalculate the control parameters for several samples. In addition, in this controller, a cost function is defined in which the tracking error of the output is minimized until the desired goal, and the control effort is minimized. Therefore, by presenting these mathematical models, the control of the epidemic of this disease is performed optimally. So that deaths caused by this disease can be significantly prevented.

Fractional Order Model of SARS-COV-2

The Caputo derivative is a fractional calculus concept that extends traditional calculus to allow non-integer differentiation and integration. This derivative is essential in modeling phenomena that exhibit memory effects and non-local behavior, making it valuable in various epidemiology fields. The Caputo fractional derivative operator with $\tau(\tau \geq 0)$ and $n \in N \cup \{0\}$ is defined as follows:

$$D_t^{\alpha}(u(t)) = \frac{1}{\Gamma(n-\alpha)} \int_0^t (t-\zeta)^{n-\alpha-1} \frac{d^n}{dt^n} u(\zeta) d\zeta, \tag{1}$$

$u(t)$ contains a composite variable representing the different states of infection in the population. It captures the overall dynamics of the spread of COVID-19 while showing the interconnectedness of the other parts of the model. By acknowledging $u(t)$ not only as a count of infections but also as a representation of the evolving state of the population, we can better understand the consequences of disease dynamics, inform public health decisions, and assess the effectiveness of containment measures. Γ is a gamma function that generalizes factorial functions for non-integer values. n is the smallest integer greater than τ. Which in this equation α is $n-1 \leq \alpha < n$.[11] In the present study, the SEIAR model without control is selected based on Abbasi et al[6]. Also, in the current study, the fractional-order derivative was considered equal to $\alpha = 0.99$. These SEIAR fractional-order model equations are as follows.

Where *S(t)* represents the number of susceptible people who have not yet been infected;

$$D^{\alpha} S(t) = -\Lambda \beta(t) S(t) \tag{2}$$

When a susceptible person gets infected, he/she is exposed to infection. Then, they are transferred to the group of exposed people $E(t)$. They are infected but cannot transmit the virus. Eventually, they reach a point where they can transmit the disease at a rate of K.

$$D^{\alpha} E(t) = \beta \Lambda(t) S(t) - kE(t) \tag{3}$$

Also, some person have symptoms that are characterized by $I(t)$. A fraction of the p from exposed people is transferred to the group of infected people, and the infection can be transmitted to others.

$$D^{\alpha} I(t) = (1-z)\eta A(t) - \alpha_1 I(t) + pkE(t) \tag{4}$$

Some others have no visible symptoms. They are called asymptomatic and denoted by $A(t)$. A fraction $(1-p)$ of them belong to the group of asymptomatic people who are infected without symptoms of infection.

$$D^{\alpha} A(t) = (1-p)kE(t) - \eta A(t) \tag{5}$$

The fraction f of people infected with the rate of α recovers, and the remainder of them $(1-f)$ die due to infection. Also, $R(t)$ shows the recovered people.

$$D^{\alpha} R(t) = z\eta A(t) + f\alpha_1 I(t) \tag{6}$$

$$\Lambda(t) = \varepsilon E(t) + (1-q) I(t) + \delta A(t) \tag{7}$$

The SQEIAR model designs an optimal controller using Pontryagin's maximum principle. So that, treatment $(0 \leq U(t) \leq 1)$ and quarantine $(0 \leq \lambda(t) \leq 1)$ are the inputs of this model. Parameters P_1 to P_6 represent specific rates that determine the dynamic behavior of the disease. In this modeling method, optimal control techniques and Hamiltonian analyses are often used to make better decisions about health policies. Hamiltonian is used in optimal control equations to relate system states with optimal controls, which is a function of S, Q, E, I, A, R states and λ(t), U(t) controls in operation. Therefore, in the optimal control of the SQEIAR model, P_1 to P_6 are adjoint variables that are used in the Hamiltonian formula.[6] Here, we consider the fractional-order derivative equal to $\alpha = 0.99$. Fractional-order model equations of SQEIAR with the controller are as follows. The parameters of this model are presented in Tables 1 and 2. The initial values of SQEIAR model parameters are shown in Table 1. Also, the values of the parameters of the epidemic model according to the experimental data are given from Riou and Althaus[19] and Li et al[20]. Figure 1 presents the transition between the modes of the SQEIR model.

$$D^{\alpha} S^{*}(t) = -(\Lambda\beta(t) + \max\{\min\{\frac{S^{*}(t)[p_1(t) - p_2(t)]}{A_6}\}, \lambda^{*}_{max} \quad (8)$$

$$D^{\alpha} Q^{*}(t) = (maxmin\{\frac{S^{*}(t)[p_1(t) - p_2(t)]}{A_6}\}, \lambda^{*}_{max} \quad (9)$$

$$D^{\alpha} E^{*}(t) = \beta\Lambda(t)S^{*}(t) - kE^{*}(t) \quad (10)$$

$$D^{\alpha} I^{*}(t) = (1-z)\eta A^{*}(t) - \alpha I^{*}(t) + pkE^{*}(t) - (\max\{\min\{\frac{I^{*}(t)[p_4(t) - p_6(t)]}{A_4}, U^{*}_{max} \quad (11)$$

$$D^{\alpha} A^{*}(t) = (1-p)kE^{*}(t) - \eta A^{*}(t) \quad (12)$$

$$D^{\alpha} R^{*}(t) = (1-p)kE^{*}(t) - \eta A^{*}(t) \quad (13)$$

In these equations, β is the rate of disease transmission, which indicates the effective contact rate between susceptible people and exposed people, which leads to disease transmission. λ is the quarantine rate, which shows the entry rate of susceptible people into the quarantine group, which can help reduce the transmission of the disease faster. κ is the rate of progression to the infection stage, which shows the speed of transformation of

Table 1. Initial amounts of SQEIAR epidemic model.[6]

STATE VARIABLE	DESCRIPTION	INITIAL VALUE
S_0	Susceptible people	8000
Q_0	Quarantined people	0
E_0	Exposed people	1000
I_0	Infected people	500
A_0	Asymptomatic people	500
R_0	Recovered people	0
N_0	Total population	10,000

Table 2. Values of SQEIAR model.[6]

PARAMETER	VALUES
k	0.54/day
α	0.3/day
η	0.3/day
p	0.1
f	0.965
ε	0
δ	1
q	0.5
z	0.02

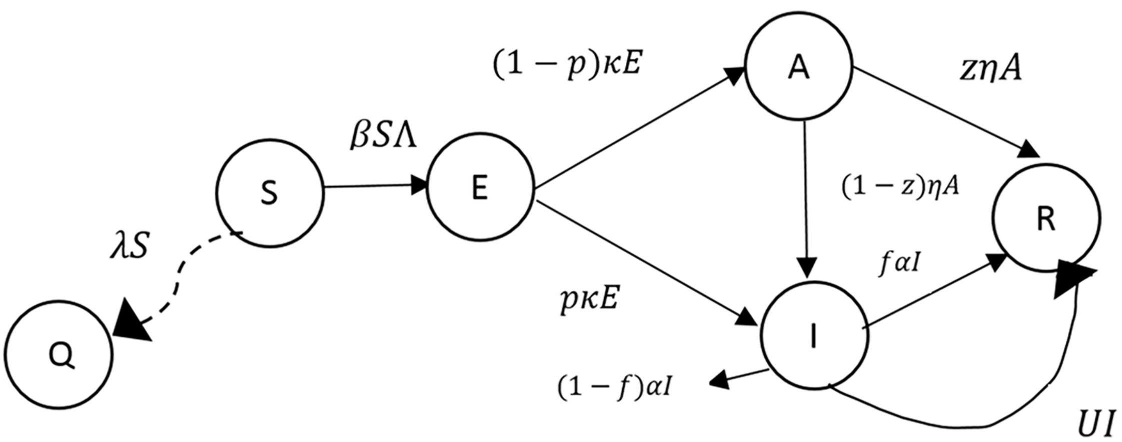

Figure 1. Conceptual flow diagram of SQEIAR dynamic model with controller.

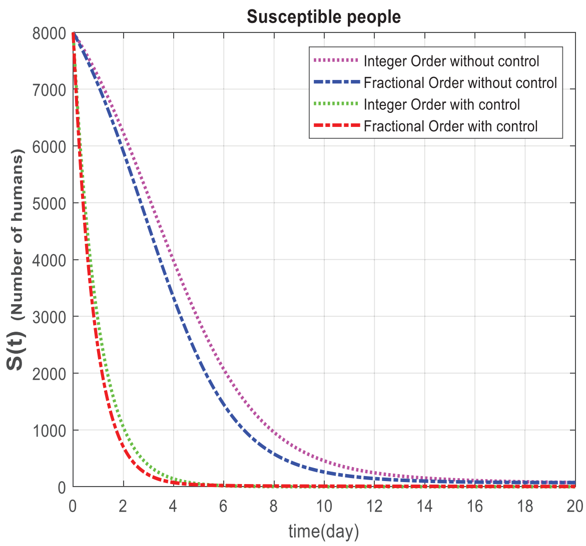

Figure 2. The curve of susceptible people in two cases of integer order and fractional order without controller and with controller.

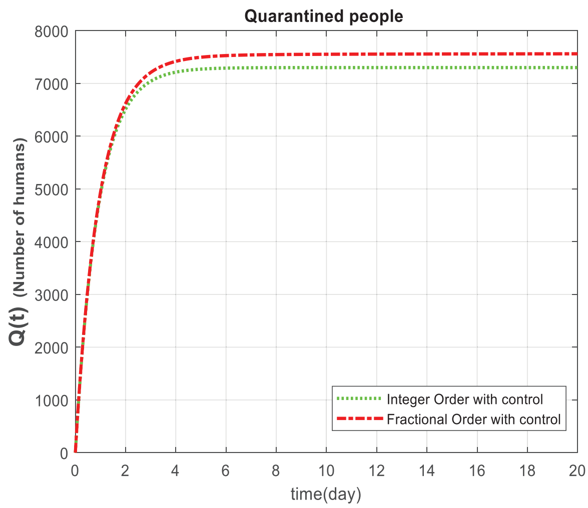

Figure 3. The curve of quarantined people in two cases of integer order and fractional order without controller and with controller.

exposed people into the group of infected people. η is the rate of progression to the recovered group or in the group of asymptomatic people, which determines how fast asymptomatic people recover.

Results and Discussion

Comparison between integer order and fractional order models without controller and with controller

A controller continuously monitors the epidemic situation and adapts strategies based on time data to optimize infection control. A controller is basically an algorithm or device that adjusts a system by adjusting control inputs based on the current state of the system. Its main purpose is to maintain operational stability and guide the system toward the desired performance criteria. In this section, a comparison has been made between integer and fractional order models without and with the controller. Figures 2 to 7 show the curves of susceptible people (S), quarantined people (Q), exposed people (E), infected people (I), asymptomatic people (A), and recovered people (R). These graphs report the number of people by day. It can be seen from Figure 2 that the number of susceptible people started from 8000 people in a sixteen-day period. Fractional order always reports lower values than integer order. Finally, both approaches zero on the 16th day reaches zero. From the first to the fifth day, the number of susceptible people in the fractional order diagram is lower than the integer order. Therefore, these results indicate that the fractional order model performs better with the controller. Figure 3 shows that the number of quarantined people was zero at the beginning in both cases. However, in the case of fractional order, from the third day onwards, about 7500 people were reached, while this number reached about 7200 people in the case of integer order. Therefore, the more quarantined people there are, the better the results will be.

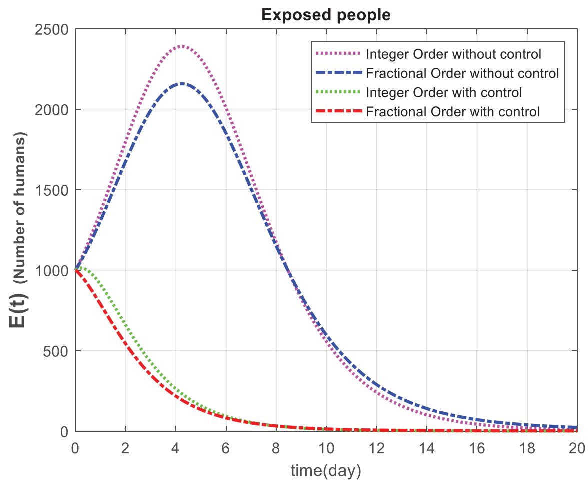

Figure 4. The curve of exposed people in two cases of integer order and fractional order without controller and with controller.

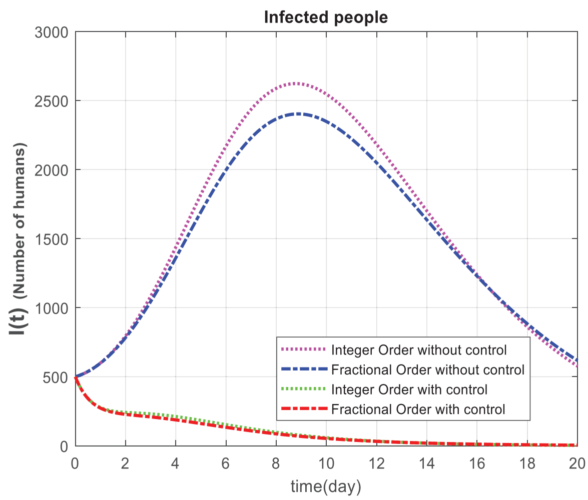

Figure 5. The curve of infected people in two cases of integer order and fractional order without controller and with controller.

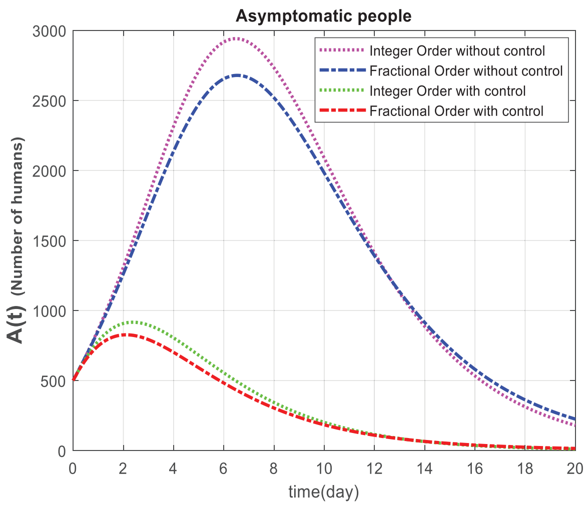

Figure 6. The curve of asymptomatic people in two cases of integer order and fractional order without controller and with controller.

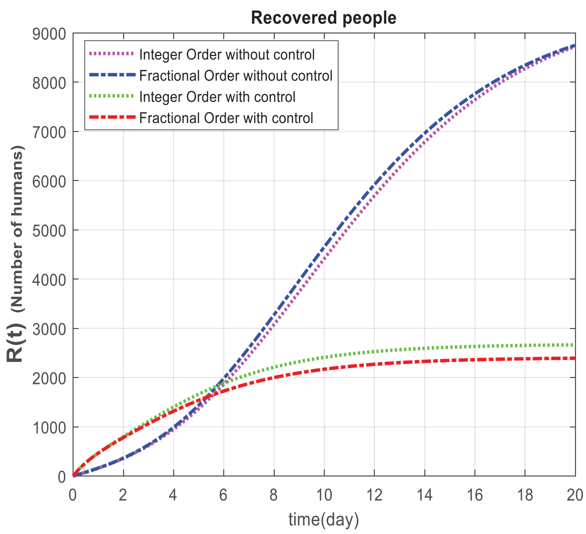

Figure 7. Curve of recovered people in two cases of integer order and fractional order without controller and with controller.

From Figure 4, it can be seen that the number of exposed people, in the case of no controller in both cases, starts from 1000 people and continues to increase until the fourth day. So, the maximum fractional order is less than the integer order and is approximately 2200 people. Also, in both cases, the curve is downward from the fifth day onwards, and on the 20th day, they are close to zero. Also, with the presence of the controller, the start of both integer order and fractional order charts is from 1000. During the journey from zero to the seventh day, the number of exposed people in the fractional order model is less than the integer order. On the 11th day, both graphs reach almost zero. It can be seen from Figure 5 that in the case without a controller, the number of infected people in both cases starts from 500 and increases. The maximum occurs on the 9th day, so it reaches 2400 people in fractional order, which is less than the integer order. In both cases, there is a downward curve from the ninth day onwards. The curve of infected people started from 500 people with the presence of the controller in both cases. From the 1st to the twelfth day, the number of infected people in the fractional order model is less than the integer order model. On the 19th day, both graphs reach zero.

It can be seen from Figure 6 that in the case without a controller, the number of asymptomatic people starts from 500 in both cases, and the curves are upward. So, the number of these people is the highest on the seventh day and becomes 2700 people in the state Fractional order. This value is less than the report of the integer order, and in both cases, the curves are downward from the seventh day onwards. Also, despite the presence of the controller of the number of asymptomatic people, in both cases, it starts from 500 people, and they have an upward trend until they reach their peak on the third day. Then they find a downward trend and finally tend to zero. From the 1st day to the 13th day, the number of asymptomatic people in the fractional order is less than the integer order and finally reaches zero. It can be seen from Figure 7 that in the case without a controller, the number of recovered people in both cases starts from zero, and the curves are ascending. Fractional order values are higher than integer order on the fourth day onwards. Finally, the number of these people has reached 8800 on the 20th day. Also, with the presence of the controller, the number of recovered people is zero at the beginning of both modes. Both curves are upward, and finally, in fractional order, they tend to reach 2400 people. Also, the number of these people in integer order is 2700 people. Therefore, the number of recovered people in the fractional order model is less than the integer order model.

Therefore, graphs without controllers are not designed for them. This does not mean that the fractional order model must show better results than the integer order model. Also, the graphs with the fractional order model controller report better results than the integer order model in all the graphs in this section.

Comparison between actual data with fractional and integer-order model with controller

In this section, the actual data used in the article[6] related to China has been selected from January 22, 2020, to March 22, 2020. Also, the accuracy of the designed controller has been estimated using actual data from China. To evaluate the SQEIAR epidemic model, a successful model of quarantine control input and treatment has been studied.[6] This section compares the results of this study with real Chinese data to verify the performance of the designed controller.

The controller is applied to this identified model. These results have been compared with the proposed deficit order SQEIAR epidemic model. Figures 8 to 13 show these comparisons. It can be seen from Figure 8 that from the fifth day onwards, the fractional-order model and the integer-order approach zero. In contrast, the actual data has taken much longer to approach zero. As shown in Figure 9, the

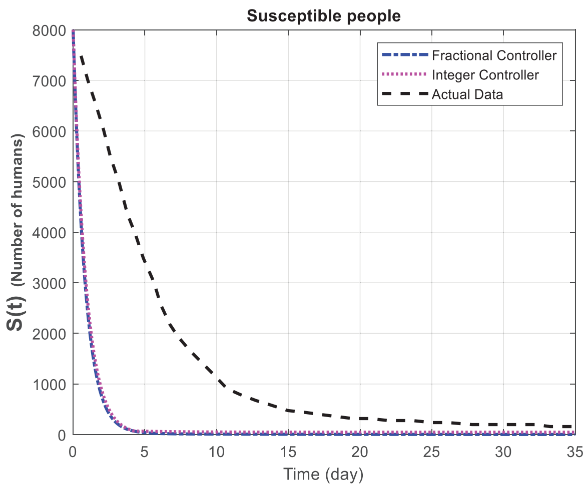

Figure 8. The curve of susceptible people in the control mode of fractional order, integer-order, and actual data.

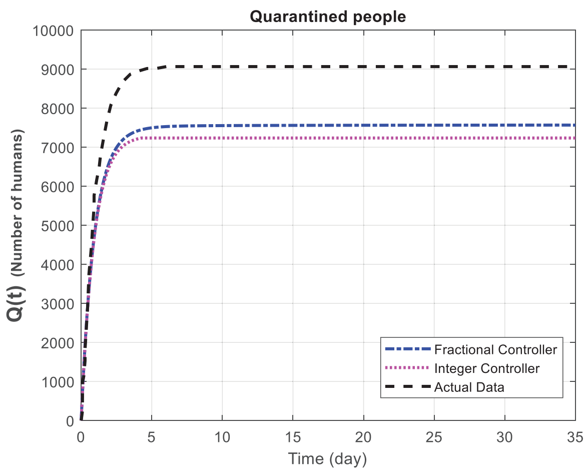

Figure 9. The curve of quarantined people in the control mode of fractional order, integer-order, and actual data.

number of quarantined people in all three cases started from zero and is increasing. So, the value of the fractional-order controller is less than the actual data and greater than the integer-order.

It can be seen from Figure 10 that the number of exposed people in the fractional-order control mode has reached zero earlier than the actual data mode. It can also be seen that around the tenth day, both integer-order and fractional-order curves are close to zero. From Figure 11, as shown in number of infected people in the actual data state first decreased and then reached a peak, and it has been decreasing since the eighth day. It has also tended to zero since about the 30th day. In contrast, the number of these people in the controller of fractional-order and integer-order is less than the actual data and has reached zero on the 20th day.

From Figure 12, the number of asymptomatic people in the fraction order reached earlier than the actual data to zero around the 20th day. Figure 13 shows the decrease in the population of recovered people in the actual data. It can be seen from this figure that the recovery time is longer. In comparison, the number of recovered people in both controllers shows more than the actual data.

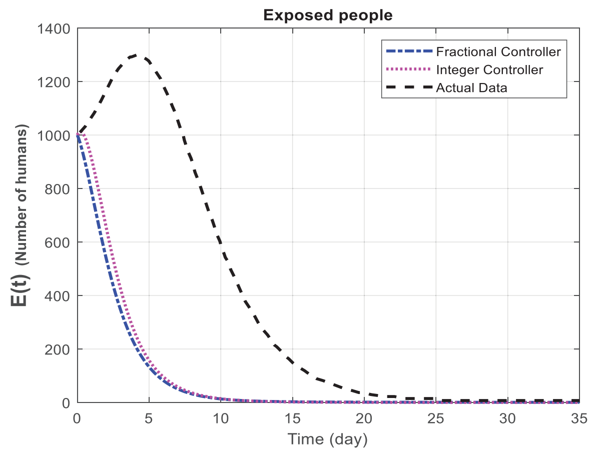

Figure 10. The curve of exposed people in the control mode of fractional order, integer-order, and actual data.

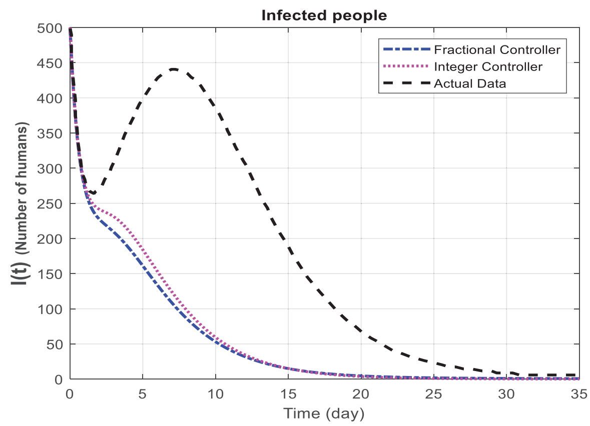

Figure 11. The curve of infected people in the control mode of fractional order, integer-order, and actual data.

Proposal of a novel NMPC by fractional-order type

This section proposes a NMPC for the SQEIAR fractional order model. The optimization will be done in several steps. Depending on the value of the prediction horizon, the proposed controller calls the cost function several times and performs the minimization operation. The cost function includes the control effort and the error of the state signals toward the desired values. Because the transient response does not have an adverse effect on the answers, its effect is not considered in the cost function. Because if the transient response is included in the cost function, the value of the cost function will increase, and the controller will not be adjusted correctly. For this reason, in order to minimize the cost function better, the last half of the simulation time in the cost function is considered as the following equation:

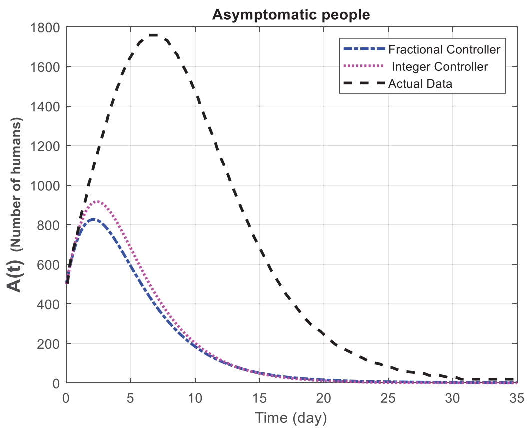

Figure 12. The curve of asymptomatic people in the control mode of fractional order, integer-order, and actual data.

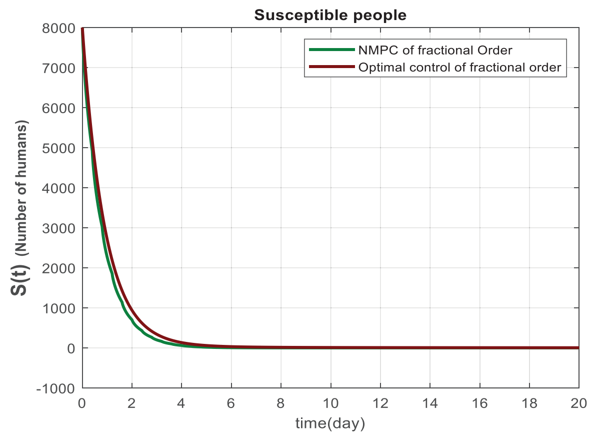

Figure 14. Comparison curve of the number of susceptible people using NMPC of fractional-order and optimal control of fractional order.

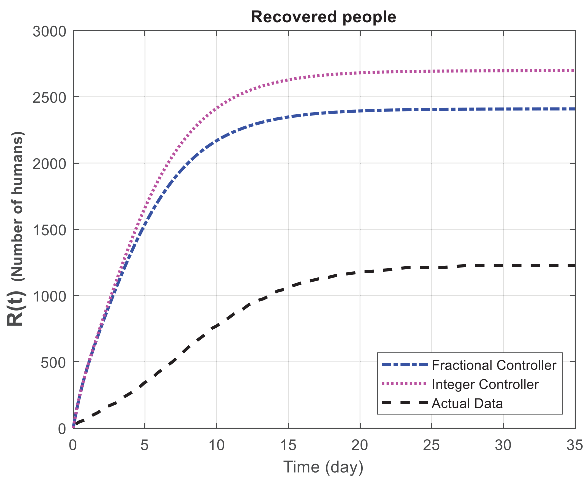

Figure 13. The Curve of recovered people in the control mode of fractional order, integer-order, and actual data.

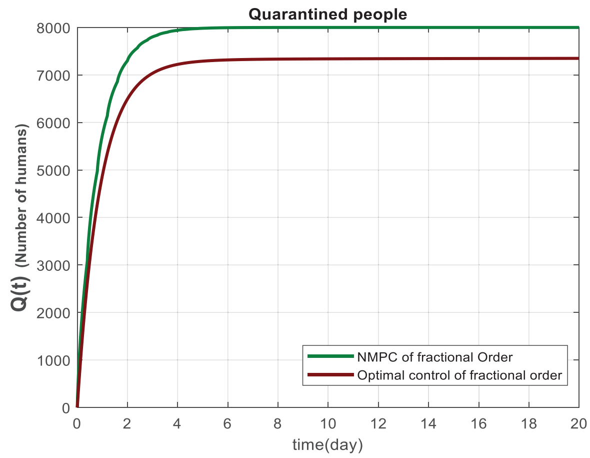

Figure 15. Comparison curve of the number of quarantined people using NMPC of fractional-order and optimal control of fractional order.

$$J = 20mean(S^2) + mean((Q-8000)^2) + mean(E^2) + mean(I^2) + mean(A^2) + mean((R-2663)^2) + 0.01mean(u^2) + 0.01mean(\lambda^2) \quad (14)$$

The constraint of this problem is as follows:

$$\begin{cases} 0 < u < 1 \\ 0 < \lambda < 1 \end{cases} \quad (15)$$

Simulations have been performed for 20 days with a time step of 0.01. The fmincon function optimization tool in MATLAB R2019 b is used to minimize the predicted cost function. The total number of samples is equal to 2000. Considering that the prediction horizon equals 40, this solver is executed 50 times in the entire program. Forty samples of outputs and future control efforts are calculated and stored every time of execution. These steps continue until the completion of calculations for all samples. In each step, the state signals are stored, and the state signals are drawn for the entire simulation time. In the simulations, the value of α for the fractional-order derivative is considered equal to 0.8. In the following, the comparative results between NMPC of fractional-order and optimal control of fractional-order are given. It can be seen from Figure 14 that the number of susceptible people in both cases starts from 8000 people, and the NMPC of fractional-order is lower than the optimal control of fractional-order from the first day to the sixth day. Finally, both curves tend to be zero. In other words, the quarantine of susceptible people in NMPC of fractional order on the first to sixth day reduces the infection of this disease. It can be seen from Figure 15 that the number of quarantined people started from zero in both cases. So the NMPC of fractional-order has increased compared to the optimal control of fractional order. On the fourth day, the number of quarantined people in NMPC of fractional-order equals 8000 people, and in optimal control of fractional order, it is about 7100 people. Obviously, the more the number of quarantined people, led to the better the control of this disease.

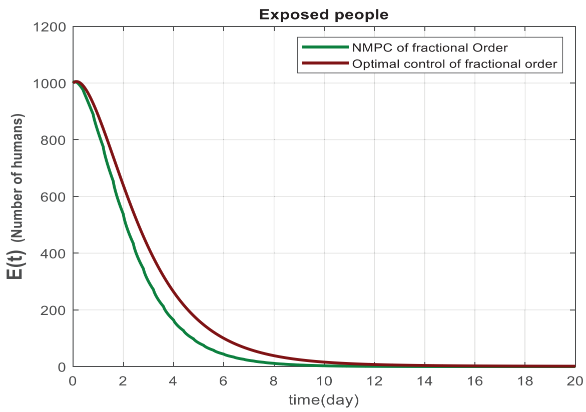

Figure 16. Comparison curve of the number of exposed people using NMPC of fractional-order and optimal control of fractional order.

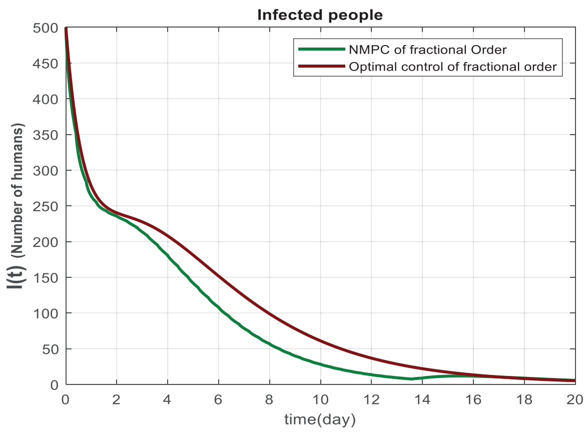

Figure 17. Comparison curve of the number of infected people using NMPC of fractional-order and optimal control of fractional order.

It can be seen from Figure 16 that the number of exposed people in the NMPC of fractional order started from 1000 people and reached zero on the tenth day. This state occurs faster than the optimal control of fractional order. It is also known that the smaller the number of people exposed by the proposed controller and the faster it reaches zero, the more the disease infection will be controlled. It can be seen from Figure 17, the number of infected people in both cases started at 500 people. It can also be seen that until the 16th day, the values of NMPC of fractional-order are almost lower than the optimal control of fractional order. Notably, the lower the number of infected people, the lower the number of infected people.

It can be seen from Figure 18 that the number of asymptomatic people started from 500 people. Until the second day, the NMPC of fractional-order was more than optimal control of fractional order. Also, the NMPC of fractional-order has reached zero faster than the optimal control of fractional order. It is clear that by quarantining susceptible people and treating infected people, the number of asymptomatic people will decrease, which will control this disease. It

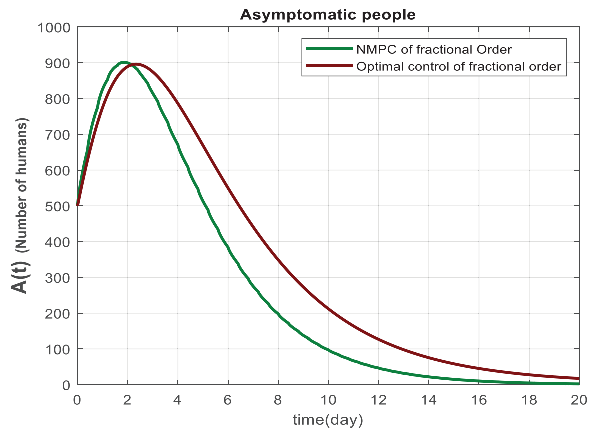

Figure 18. Comparison curve of the number of asymptomatic people using NMPC of fractional-order and optimal control of fractional order.

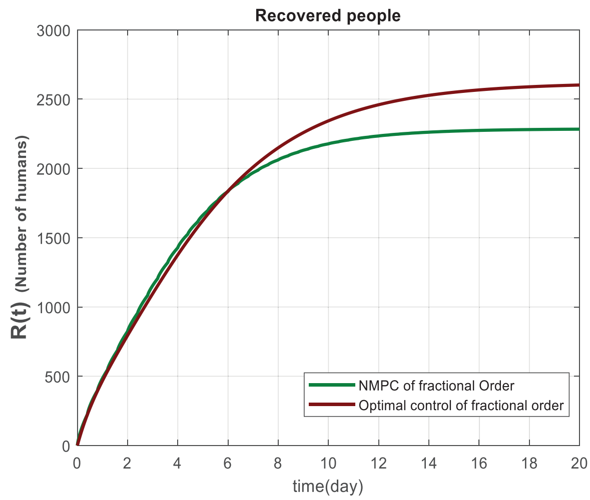

Figure 19. Comparison curve of the number of recovered people using NMPC of fractional-order and optimal control of fractional order.

can be seen from Figure 19 that the number of recovered people started from zero in both cases. Then the number of these people in the NMPC of fractional-order is less than the optimal control of fractional-order from the seventh day onwards. It is obvious that more people are quarantined; as a result, fewer people are infected, which causes the number of recovered people to decrease.

Hence, it can be seen that NMPC of fractional order has better results than the optimal control of fractional order. The advantage of the predictive controller is that it can adapt to future conditions by changing the value of the controller signal. While the fractional optimal controller is executed only once, and if an unexpected event occurs in the model, it may not be able to overcome it and have a suitable resistance against it. Table 3 shows the results of the mean squared error of the number of susceptible people. As shown in Table 3, the mean squared error in the NMPC of the fractional order is much lower than the optimal control of fractional order.

Table 3. The mean squared error of the number of susceptible people in both controllers.

CONTROLLER	MEAN SQUARED ERROR
Optimal control of fractional	47.3990
NMPC of fractional order	3.5769e-04

Conclusion

The present study proposed the model predictive control of the SARS-COV-2 disease with fractional calculations. First, an optimal control model of the fractional order was studied. The results of the fractional- and integer-order models without control were compared. Then, the comparison was made in the optimal control of fractional-order and integer-order. The fractional-order model performed better in both cases than the integer-order model. Comparing these results with the model obtained with real data showed that its performance has successfully controlled the disease and reduced the number of susceptible, infected, and asymptomatic people to zero. Next, the proposed NMPC of fractional-order was designed to control the SQEIAR disease model of SARS-COV-2. Then, the NMPC of fractional order was compared with the optimal control of fractional order. Finally, the NMPC of fractional-order has provided better results and more accuracy. According to the obtained results, the high performance of the NMPC of fractional-order compared to the optimal control of fractional-order was confirmed. In future work, it is suggested to use the proposed NMPC of fractional-order for other variants of SARS-COV-2 disease.

Author Contributions

All author have contributed equally.

Data Availability Statement

Data will be available upon reasonable request.

Institutional Review Board Statement

All procedures performed in studies involving human participants were in accordance with the institutional and/or national research committee's ethical standards and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Statement

Informed consent was obtained from all subjects involved in the study

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