COVID-19: Development of A Robust Mathematical Model and Simulation Package with Consideration for Ageing Population and Time Delay for Control Action and Resusceptibility

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Abstract

The current global health emergency triggered by the COVID-19 pandemic is one of the greatest challenges mankind face in this generation. Computational simulations have played an important role to predict the development of the current pandemic. Such simulations enable early indications on the future projections of the pandemic and is useful to estimate the efficiency of control action in the battle against the SARS-CoV-2 virus. The SEIR model is a well-known method used in computational simulations of infectious viral diseases. It has been widely used to model other epidemics such as Ebola, MERS (Middle East Respiratory Syndrome), and influenza. A general SEIR model represents an epidemic using four compartments in cascade; susceptible (S), exposed (E), infected (I), and recovery/removed (R), where the model assumes that the epidemic exits with the infected population either recovered or removed due to immunity to the virus. In this work, we present a modified SEIRS model with additional exit conditions in the form of death rates and resusceptibiliy, where we tuned the exit conditions in the model to extend predictions on the projection of the current pandemic into three outcomes; death, recovery, and recovery with a possibility of resusceptibility.

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Owing to huge variations in clinical symptoms exhibited by COVID-19, the proposed model aims to reflect better to the current scenario and case data reported. The model also considers specific information such as ageing factor of the population, time delay on the development of the pandemic due to control action measures, as well as resusceptiblity with temporary immune response. The model is verified with a case study using the real-world data in South Korea.

Keywords: COVID-19, Coronavirus, Respiratory disease, SEIR, SEIRS, Resusceptibility, Modelling, Simulation

1. Introduction

Coronavirus disease (COVID-19) is a respiratory infection disease caused by the newly discovered coronavirus, SARS-CoV-2. COVID-19 outbreak was firstly reported in Wuhan of Hubei Province, China at the end of December 2019. Within just two months, the disease rapidly spreads across global wide and has been declared a global pandemic in early March 2020. As of the data on 1 April 2020, the virus has affected more than 1 million people with close to 53,000 confirmed deaths across 206 countries [1].

The symptoms caused by SARS-CoV-2 have large variations where most people only experience mild to moderate respiratory illnesses while only a smaller group of people would develop complications of respiratory failure or acute respiratory distress syndrome. Study shows that upto approximately 80% of the people infected with SARS-CoV-2 are asymptomatic virus carriers, i.e. they experience no or mild symptoms but are still able to transport the virus to others [2]. This has caused the detection and containment of SARS-CoV-2 virus become much more complicated. As such, social distancing has been widely implemented in most countries aiming to slow down the transportation of the virus through minimising human-to-human contact.

The SEIR (Susceptible-Exposed-Infected-Removed/Recovered) model is the most widely used mathematical model to represent a typical infectious epidemic disease, where susceptible (S) represents the people who have yet to be infected by the virus; exposed (E) stands for the number of people exposed to the virus; infected (I) denotes the number of people infected and demonstrated symptoms and are able to spread the virus to the people in the S compartment. Lastly, removed (R) denotes the number of people who have recovered and assumed to have immune response to the virus [3, 4].

Thus, based on the model, the S compartment will slowly deplete when the outbreak prolongs further, and the virus will eventually die out due to insufficient population within the S compartment.

SARS-CoV-2 is a novel virus in which we have very limited knowledge about this disease, where the immune response of humans to this virus has yet to be fully understood. People who have recovered from COVID-19 after experiencing mild or moderate symptoms are more likely to be resistant to the SARS-CoV-2 virus [5]. However, in rare occasions, there have been clinical findings showing that patients who have recovered from the disease have been reinfected. For instance, in February 2020, a patient in Osaka, Japan, has been tested positive towards the COVID-19 a few days after being discharged from the hospital for treatment with the disease [6].

In this work, we propose a modified SEIRS model by including resusceptibility into the development of the mathematical model and for simulation. In this modified model, the probability of a recovered patient to be reinfected with SARS-CoV-2 is taken into consideration to predict the future projection of COVID-19 cases. Other than that, we also included information such as demographic details for the ageing population, who seem to experience a higher rate of fatality due to COVID-19 [7]. Time delay in the control action representing the time taken for the authorities to act on the virus and also the duration of short-term immunity after recovery, which may lead to resusceptibility, are also considered in the model.

This paper is organised as follows: Section 2 presents the development of the mathematical model; Section 3 presents the design of the simulation package on the Matlab/Simulink platform; Section 4 provides some discussions on the verification of the model using a case study; and Section 5 concludes the paper.

2. Mathematical Modelling of The COVID-19 Using Modified SEIRS

First, let's consider the modified SEIRS model system below,

$$\frac{dS(t)}{dt} = \Lambda - \mu S(t) - \frac{\beta I(t)S(t)}{N} + \sigma\frac{\beta I(t-\tau_\sigma)S(t-\tau_\sigma)}{N} + R_s(t,\tau_\xi), \quad (1)$$

$$\frac{dE(t)}{dt} = \frac{\beta I(t)S(t)}{N} - \sigma\frac{\beta I(t-\tau_\sigma)S(t-\tau_\sigma)}{N} - (\mu+\alpha)E(t), \quad (2)$$

$$\begin{aligned}\frac{dI(t)}{dt} &= (\mu+\alpha)E(t) - (\gamma+\mu)I(t) \\ &\quad - \delta\left[(1-\kappa_{old})N_{old} + (1-\kappa)(1-N_{old})\right]I(t),\end{aligned} \quad (3)$$

$$\frac{dR(t)}{dt} = (\gamma+\mu)I(t) - \mu R(t) - R_s(t,\tau_\xi), \quad (4)$$

$$\frac{dD(t)}{dt} = \delta\left[(1-\kappa_{old})N_{old} + (1-\kappa)(1-N_{old})\right]I(t), \quad (5)$$

where $N, S(t), E(t), I(t), R(t)$, and $D(t)$ represent the stock population, susceptible, exposed, infected, recovered/removed, and deaths compartments, respectively. It is established that $S(t) + E(t) + I(t) + R(t) + D(t) = N$. The constant Λ is the birth rate in the overall population and μ is the death rate due to conditions other than the COVID-19. The parameter β is the rate of transmission per S-I contact, α is the rate of which an exposed person becomes infected, and γ is the recovery rate. Therefore, the incubation and recovery times are $\tau_{inc} = \frac{1}{\alpha}$ and $\tau_{rec} = \frac{1}{\gamma}$, respectively. The basic reproduction number can be expressed using

$$R_0 = \frac{\alpha}{\mu+\alpha}\frac{\beta}{\mu+\gamma}. \quad (6)$$

The constant σ is the efficiency of the control action. It has a direct effect on the reproduction number, such that the new reproduction number with the control action is $R_t = (1-\sigma)R_0$. The time delay $\tau_\sigma = \tau_{pre-\sigma} + \tau_{post-\sigma}$ indicates the time taken for the control action to take effect in flattening the infection curve, where $\tau_{pre-\sigma} \geq 0$ represents the time to initiate the control action after the first confirmed case at $t = 0$, and $\tau_{post-\sigma} \geq 0$ represents the time after the control action has been initiated but before the effects are evidenced in the outputs of the system. In practical scenarios, $\tau_{post-\sigma}$ can be used to model the delay for the population to effectively respond to the rules introduced by the control action, such as social distancing, isolation, and lockdown.

In the worst case scenario where the patient does not recover from the virus, we model the fatality rate with influence of the percentage of elderly population (above 65 years of age) within the community, N_{old}, where the percentages of non-elderly and elderly who recovered κ and κ_{old}, respectively. The time spent hospitalised or infected in fatal cases is $\tau_{hosp} = \frac{1}{\delta}$. In this paper, we establish that $\tau_{hosp} = \tau_{rec}$, assuming that patients spend the same amount of time hospitalised or infected, whether they recover from the virus or not.

The function $R_s(t, \tau_\xi)$ represents the resusceptible stock, which can be computed from the recovered population using

$$R_s(t, \tau_\xi) = \xi R(t - \tau_\xi), \tag{7}$$

where ξ is the percentage of the recovered population who are resusceptible and the time delay $\tau_\xi \geq 0$ represents the duration of temporary immune response from the recovered population.

The number of recovered cases can then be expressed using

$$R_c(t) = R(t) - R_s(t, \tau_\xi). \tag{8}$$

In an ideal situation where population who recovered develop permanent immunitity against the virus, $\xi = 0$ and $\tau_\xi \to \infty$. As a result, (7) becomes $R_s(t, \infty) = 0$ and $R_c(t) = R(t)$.

For the model used in the simulation package presented in this paper, we assume a closed population with negligible birth and death rates, i.e. $\Lambda = 0, \mu = 0$. As a result, the system (1)(5) becomes

$$\frac{dS(t)}{dt} = -\frac{\beta I(t)S(t)}{N} + \sigma\frac{\beta I(t-\tau_\sigma)S(t-\tau_\sigma)}{N} + R_s(t, \tau_\xi), \tag{9}$$

$$\frac{dE(t)}{dt} = \frac{\beta I(t)S(t)}{N} - \sigma\frac{\beta I(t-\tau_\sigma)S(t-\tau_\sigma)}{N} - \alpha E(t), \tag{10}$$

$$\frac{dI(t)}{dt} = \alpha E(t) - \gamma I(t) - \delta\left[(1-\kappa_{old})N_{old} + (1-\kappa)(1-N_{old})\right] I(t), \tag{11}$$

$$\frac{dR(t)}{dt} = \gamma I(t) - R_s(t, \tau_\xi), \tag{12}$$

$$\frac{dD(t)}{dt} = \delta\left[(1-\kappa_{old})N_{old} + (1-\kappa)(1-N_{old})\right] I(t), \tag{13}$$

and the basic reproduction number in (6) becomes $R_0 = \frac{\beta}{\gamma}$. The block diagram of the proposed SEIRS model is shown in Figure 1.

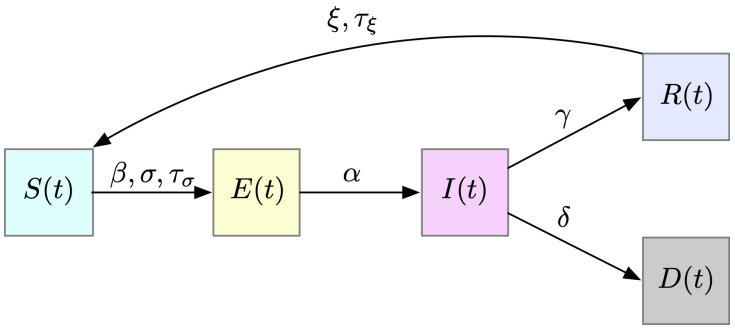


Figure 1: The block diagram of the proposed SEIRS system used in the simulation package.

3. Description of The Simulation Package

Figure 2 shows the graphical user interface (GUI) of the simulation testbed in Matlab. Users can use this interface to set preferred settings for the simulation and also to view simulation results. The simulation kit can be downloaded from `https://github.com/nkymark/COVIDSim`.

3.1. Establishing Simulation Settings

On the top of the GUI are some interactive interfaces available for the user to set key simulation settings, which include the following:

- General Settings:
  - *Stock Data*: Use this to load real-world data of select countries. The data are obtained from [1].
  - *Stock Population*: The stock population N is entered here.
  - *Recovered Cases*: Use this to set the percentage of recovered cases κ.
  - *Elderly Population*: Use this to set the percentage of elderly population (above 65 years of age) N_{old}.
  - *Elderly Fatality Rate*: Use this to set the fatality rate $(1 - \kappa_{old})$ for the elderly population.
  - *SEIR Parameters*: Use this to set the values for $R_0, \tau_{inc}, \tau_{rec}$, the initial infected cases $I(0)$, and the simulation time.
- Resusceptibility Settings:

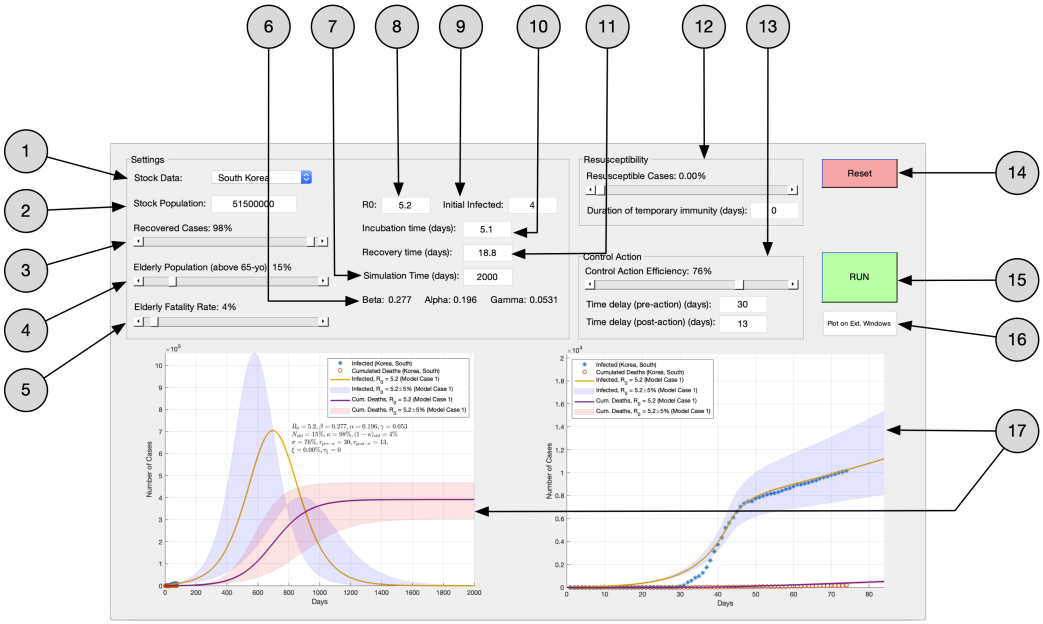


Figure 2: The main graphical user interface of the simulation package in Matlab. ① Load real-world data for the selected country. ② Set the stock population N for simulation. ③ Set the percentage of recovered cases κ. ④ Set the percentage of elderly population N_{old}. ⑤ Set the fatality rate for the elderly population $(1 - \kappa_{old})$. ⑥ Computed values for $\beta = R_0\gamma$, $\alpha = \frac{1}{\tau_{inc}}$, and $\gamma = \frac{1}{\tau_{rec}}$ using values entered for R_0, τ_{inc}, and τ_{rec}. ⑦ Set the simulation time in days. ⑧ Set the value for the basic reproduction number R_0. ⑨ Set the initial number of infected cases $I(0)$. ⑩ Set the incubation time τ_{inc}. ⑪ Set the recovery time τ_{rec}. ⑫ Settings for recusceptibility, including the percentage of resusceptible cases ξ and duration of temporary immunity τ_ξ. ⑬ Settings for control action, including the effeciency rate σ as well as the time delay during pre- and post-control action, $\tau_{pre-\sigma}$ and $\tau_{post-\sigma}$, respectively. ⑭ Reset the GUI and clear all plots. ⑮ Run the simulation. ⑯ Recreate the graphs on external Matlab figure windows. ⑰ Graphical plots from the simulation (left figure for overall simulation while right figure compare initial projections of the model with real-world data).

  - *Resusceptible Cases*: Use this to set the percentage of recovered cases who are resusceptible.
  - *Duration of temporary immunity*: Use this to set the time of short-term immune response τ_ξ, assuming there is no permanent immunity after recovery.

- Control Action Settings:

  - *Control Action Efficiency*: Use this to set the percentage of control

action efficiency σ.

- *Pre-action Time Delay*: Use this to set the time delay for the control action to be introduced after the first confirmed case $\tau_{pre-\sigma}$.
- *Post-action Time Delay*: Use this to set the time delay to mimic the time it takes for the population to respond to the control action $\tau_{post-\sigma}$.

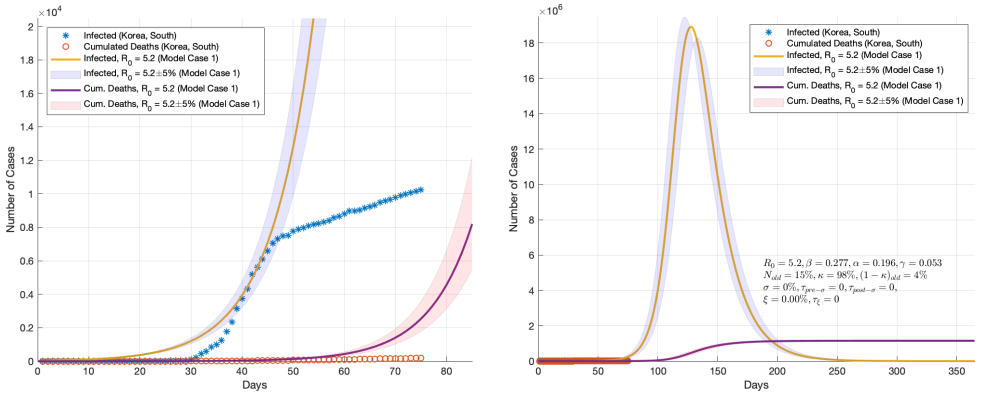
3.2. Simulation Results

The simulation results are displayed at the bottom section of the GUI. The plot on the right shows the initial fit of the model using the settings established in Section 3.1 onto the real-world data of the select country, while the plot on the left shows the simulation results until the simulation stop time.

4. Verification Case Study: South Korea

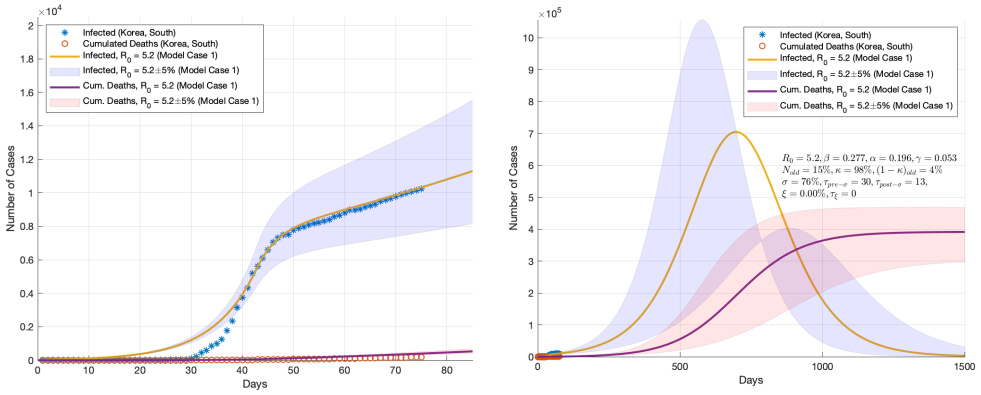
South Korea is used as a case study due to the amount of data available given that it is one of the first few countries to be directly affected by the virus outside of China, with its first confirmed case reported on 20 January 2020 [8]. The other reason being South Korea is also one of the very few countries that managed to effectively flatten the COVID-19 infection curve and it has set itself apart from others in leading the fight against the COVID-19, at least for the moment. For example, the country started vigorous testing among its population with contact tracing, especially those of confirmed and suspected cases during the early stage of the epidemic. The government accomplished this by maintaining a public database keeping track of mobile phone, credit card, and other data of patients who tested positive [9]. Also, on 16 March 2020, the authorities in the country began to screen every person, both domestic and international, who arrived at its airports.

As of 6 April, 2020, there are 10,284 confirmed cases and 186 fatalities in South Korea [1]. As a result, we used the following parameters for our simulation. First, we assumed that the population of South Korea to be approximately $N = 51.5 \times 10^6$ with an elderly population of about 15% ($N_{old} = 0.15$) [10]. We then set the recovery rate of 98% ($\kappa = 0.98$) for the general public [1] and a fatality rate of 8% ($(1 - \kappa_{old}) = 0.08$) for the elderly [11]. We then assumed the incubation time and recovery time to be $\tau_{inc} = 5.1$, and $\tau_{rec} = 18.8$, respectively in accordance with [12]. The basic



(a) (b)

Figure 3: The left subfigure shows the initial fitting of the model onto the data in South Korea and the right subfigure shows the projections of the model when no control action is taken.



(a) (b)

Figure 4: The left subfigure shows the initial fitting of the model onto the data in South Korea and the right subfigure shows the projections of the model when control action with an efficiency of 76% is taken.

reproduction number was set to $R_0 = 5.2$ (95% CI: 3.94–5.46) based on the early growth-rate of the epidemic in South Korea. The initial infected and exposed cases were assumed to be $I(0) = 4$ and $E(0) = 20I(0)$, respectively. Figure 3a shows the initial fitting of the model based on the data in South Korea while Figure 3b shows the projections of the model when no control action is taken.

Once we have the initial fitting of the model, we introduced control action in line with the mitigation and preventive measures taken by the government. Due to the aforementioned vigorous testing, contact tracing, and isolation efforts taken, we assumed that the control action has an efficiency of 76% ($\sigma = 0.76$). As a result, the reproduction number could be be reduced to $R_t = 1.25$. We also assumed that there was a time delay of 30 days since the first confirmed case before the control action was introduced ($\tau_{pre-\sigma} = 30$) and a further delay of approximately 13 days before the control action could be properly executed in the community ($\tau_{post-\sigma} = 13$). Figure 4 shows the simulation results. There are some minor discrepancies between the modelled values and the real-world data during the initial stage of the simulation as seen in Figure 4a. This is absolutely reasonable and acceptable while modelling an actual epidemic as most countries are still coming to terms with the virus during the first month and the data do not usually represent the actual number of cases due to lack of testing for confirmed cases. Nevertheless, Figure 4a shows that the trajectory of the modelled infected and death cases match the real-world data after the control action was introduced. Figure 4b shows the simulation results until the model stabilises assuming no subsequent control action being taken to further reduce the reproduction number.

4.1. Simulation With Resusceptibility

One of the many uncertainties about the COVID-19 is whether patients who have recovered from the virus will be reinfected in the future. There have been reports in the news that a few patients who recovered from the virus were tested positive for a second time after being cleared of the virus [6, 13, 14]. On the other hand, most health authorities believe that patients who recovered may develop an immunity towards the virus. However, it is not sure if the said immunity is short-term or long-term and further research is required to provide clinical proofs to this hypothesis.

As such, we repeated the simulation for the Case Study on South Korea without control action, but with the inclusion of a possibility of resusceptibility. Here, we assumed that 1% of the patients who recovered are resusceptible towards the virus ($\xi = 0.01$), where the patients develop a temporary immunity of $\tau_\xi = 0, 30, 90, 360$ days, respectively after recovering from the initial infection of the virus. Figure 5 shows the simulation results, where the first infection spikes shown in all subfigures are synonymous to the result presented in Figure 3b. The subsequent infection spikes are the result of

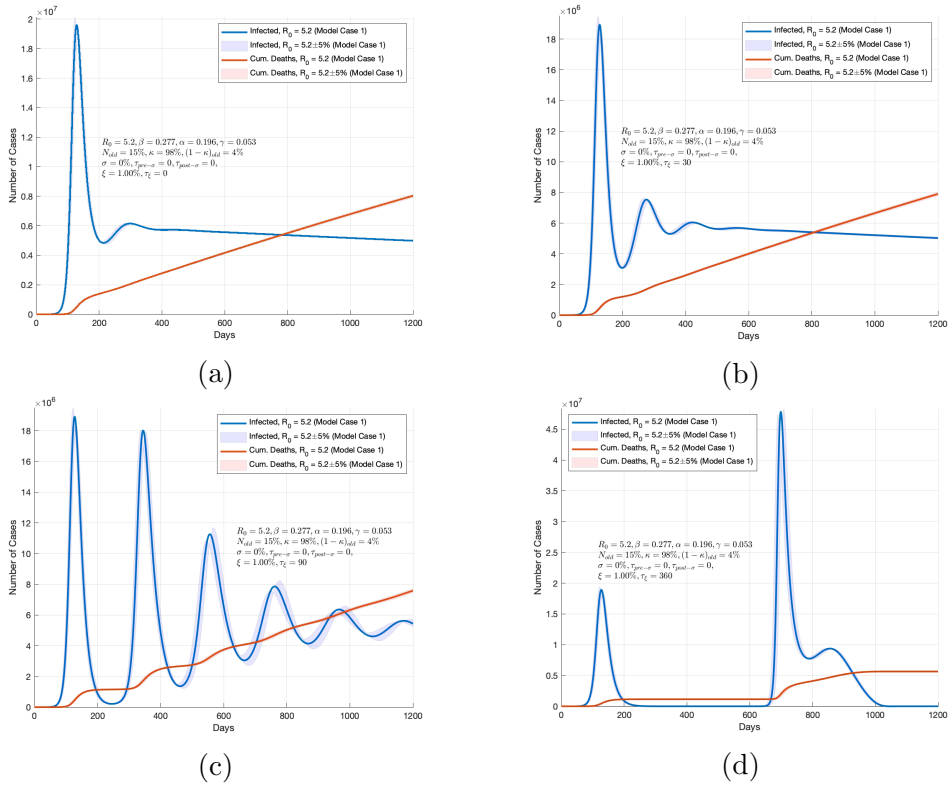


Figure 5: Trajectories for the infected and fatalities in South Korea due to resusceptibility where it is assumed that 1% of the recovered cases are reinfected after a time span of temporary immunity of (a) 0 day, (b) 30 days, (c) 90 days, and (d) 360 days, respectively. However, these results only apply assuming that if there is no control action being taken to flatten the curve.

resusceptibility, depending on the days of temporary immune response. The results show new surges in infection cases after the specific τ_ξ in each case, which diminish over time as more people develop immunity towards the virus. Interestingly, for the result shown in Figure 5d where $\tau_\xi = 360$ days, it could also be used to reflect on the situation where the virus exhibits similar characteristics as the seasonal flu or the pandemic influenza A (pH1N1) that it is most likely active during certain seasons of the year, e.g. autumn/winter for the seasonal flu and spring/summer for the pH1N1, in which case an annual vaccine administration is necessary [15, 16].

5. Conclusion

This paper has presented a robust model for the COVID-19 based on a modified SEIRS method to include considerations for the ageing population, and time delay for control action as well as resusceptibility of the recovered population due to temporary immunity. A case study using real-world data in South Korea was used to verify the model during the initial projection of the virus and also to predict the future trajectories of the outputs.

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