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# Dynamics models for identifying the key transmission parameters of the COVID-19 disease

Muhammad Shahzad<sup>a</sup>, Abdel-Haleem Abdel-Aty<sup>b,c,\*</sup>, Raghda A.M. Attia<sup>d,e</sup>,  
 Sarbaz H.A. Khoshnaw<sup>f</sup>, Dipo Aldila<sup>g</sup>, Mehboob Ali<sup>a</sup>, Faisal Sultan<sup>a</sup>

<sup>a</sup> Department of Pure and Applied Mathematics, University of Haripur, KP, Pakistan

<sup>b</sup> Department of Physics, College of Sciences, University of Bisha, P.O. Box 344, Bisha 61922, Saudi Arabia

<sup>c</sup> Physics Department, Faculty of Science, Al-Azhar University, Assiut 71524, Egypt

<sup>d</sup> Department of Mathematics, Faculty of Science, Jiangsu University, Zhenjiang 212013, China

<sup>e</sup> Department of Basic Science, Higher Technological Institute, 10th of Ramadan City, El Sharqia 44634, Egypt

<sup>f</sup> Department of Mathematics, University of Raparin, Ranya, Kurdistan Region, Iraq

<sup>g</sup> Department of Mathematics, Universitas Indonesia, Depok 16424, Indonesia

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## KEYWORDS

COVID-19 outbreak;  
 Reduction;  
 Simulations techniques;  
 Sensitivity-analysis

**Abstract** After the analysis and forecast of COVID-19 spreading in China, Italy, and France the WHO has declared the COVID-19 a pandemic. There are around 100 research groups across the world trying to develop a vaccine for this coronavirus. Therefore, the quantitative and qualitative analysis of the COVID-19 pandemic is needed along with the effect of rapid test infection identification on controlling the spread of COVID-19. Mathematical models with computational simulations are the effective tools that help global efforts to estimate key transmission parameters and further improvements for controlling this disease. This is an infectious disease and can be modeled as a system of non-linear differential equations with reaction rates. In this paper, we develop the models for coronavirus disease at different stages with the addition of more parameters due to interactions among the individuals. Then, some key computational simulations and sensitivity analysis are investigated. Further, the local sensitivities for each model state concerning the model parameters are computed using the model reduction techniques: the dynamical models are eventually changed with the change of parameters are represented graphically.

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## 1. Introduction

The COVID-19 becomes an international issue and this virus is spreading very quickly. There are millions of confirmed cases in the infected countries. Therefore, in an affected area of the region, an emergency has been affirmed by the world health organization WHO and a serious health concern has

\* Corresponding authors at: Department of Physics, College of Sciences, University of Bisha, P.O. Box 344, Bisha 61922, Saudi Arabia.

E-mail address: [amabdelaty@ub.edu.sa](mailto:amabdelaty@ub.edu.sa) (A.-H. Abdel-Aty).

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been paid by the WHO. All the countries are making all-out efforts to deal with a rapidly evolving situation which is a challenge for the whole world. Various healthcare strategies have been conducted by the government all over the world to suppress the spread of COVID-19 on their countries, such as with social distancing, international travel restrictions, rapid-test, and even lockdown. They have used many theoretical and practical tools to prevent this from spreading in their countries.

An important theoretical tool that has been used to understand and analyze the disease is mathematical modeling. This is an effective tool that can be used to present COVID-19 transmissions. Mathematical models with computational simulations help global efforts to identify the critical-model transmissions and model-dynamics. Such theoretical approaches may give more suggestions to estimate the model parameters and to predict this spreading. Many mathematical models conclude that lockdown is the best way to reduce the spread of COVID-19 effectively among all the aforementioned control strategies. However, lockdown interventions are very risky for a country's economic stability. Therefore, as a step to prevent the increasing number of infections, social distancing interventions to minimize the successful contact of infections and rapid-test to map the spread of infection into options in various countries, instead of implementing lockdown in their countries. Mathematical modeling is used to analyze the basic imitation numbers and serial intervals. Although many mathematical models are available online for the prediction of coronavirus disease but still need improvement for better control on its spreading. Our models are based on the Mass-Action Law with reaction rate constants and measuring the sensitivities for each model-state relating to model-parameters that improves the outcome.

In complicated modeling of the COVID-19, it's necessary to carefully analyze the model dynamics and identify key critical parameters more accurately and widely. Some proposed theoretical approaches help international efforts for controlling this disease. Firstly, few mathematical models were introduced, like [1], this model describes the interaction between all populations. This study has also proposed the estimation of the model parameters. Then, they updated the suggested model for the new confirmed cases in China, they improved the model further with more explanations [2]. Secondly, the idea of sensitivity analysis has been proposed for the COVID-19 to identify the model sensitive parameters [3]. In the study, three different techniques of sensitivity were applied in computational simulations. More recently, we updated the previous model of the COVID-19, some transmission parameters have been added [4]. In our previous study, the model key critical parameters were investigated and discussed. The reader can see more recently published works in this area in [5–17].

Also, there are many recently published papers related to the application of mathematical modeling and fractional derivatives in systems biology and infectious disease problems. Application non-singular fractional derivative for immune and tumor cells given in [18]; an important numerical approach for fractional model of HIV-1 infection of CD4+ T-cells models presented in [19]; using Haar wavelet and Adams-Bashforth-Moulton methods for fractional Lotka-Volterra population model shown in [20]; fractional predator-prey dynamical system with Chaotic behaviour given in [21]; an efficient numerical method for fractional SIR epidemic model of infectious

disease presented in [22]; a nonlinear fractional model to describe the population dynamics of two interacting species expressed in [23]; numerical approximation for HIV infection of CD4+ T cells mathematical model shown in [24]; an analysis for heat equations arises in diffusion process presented in [25]; a new Rabotnov fractional-exponential function-based fractional derivative for diffusion equation given in [26]; using nonsingular derivative for propagation of classical optical solitons given in [27]; a fractional derivative with two singular kernels shown in [28].

In this paper, we introduce two simple models of the COVID-19 to measure the spreading of the disease and virus transmission dynamically. The idea of graph theory uses to show the model population transmissions. Another novelty in this work is that the proposed models of COVID-19 have been simplified with the help of “model reduction techniques”, MRT. This will help to measure and specify further control/spreading with the recommendation and improvement.

Accordingly, the dynamical models for model states are investigated based on computational simulations. Furthermore, some key critical transmission parameters are identified using three techniques of sensitivity analysis.

## 2. Method

A detailed mechanism may occur through a series of distinct steps, known as a complex mechanism. Each of these steps can be written as an equation, i.e., if we have  $i^{th}$  species (patients)  $\chi_i$ , participating in any model and the process is going on in uni-direction (forward or irreversible) then  $s^{th}$  basic forward stoichiometric mechanisms can be written as:



The formal sums  $\sum_{i=1}^n b_{si} \cdot \chi_i = (b_s, \chi)$  appearing on both sides of the Eq. (1) are the subgroups  $\Xi_i$  while  $a$ ,  $b$  are the constants and are corresponding stoichiometric coefficients, the stoichiometric vectors  $\gamma_s$ :  $\gamma_s = b_s - a_s$  are obtained through there difference at each point.

Also, (1) can be represented as  $\Xi_i^- \rightarrow \Xi_i^+$ . The set of subgroups for the given reaction mechanism will become  $\Xi_i, \dots, \Xi_q$ , while they may be different from each other or coincide in some cases (depending on the type of problems and distinct steps) therefore, we assume  $q < 2n$ .

If there exist any other intermediates between the subgroups, i.e., between the healthy and infected patients groups, there exist any subgroups of patients having mild symptoms of a virus that can either recover towards the healthy or become a part of an infected patient, such that any intermediate auxiliary states  $\Lambda_i$  (patients having mild symptoms). Thus, the extended form of the reaction mechanism may be represented as



i.e., the interaction between the healthy and mildly than in between the mildly then between the mildly and healthy. If the system is open (such that with no social distance or without isolated patients) the concentration  $\chi_i$  will become an intensive variable  $c = N/V$ , where  $V > 0$  is volume. This implies the volume of the system is not constant, then there exist  $\dot{V}$  and

we have a different form. Whereas in case of constant volume we have  $c_i = \chi_i$ . The polynomial form of the reaction rate function is provided by the Mass-Action Law:

$$\mathfrak{R}_s(c) = \mathfrak{R}_s^+(c) - \mathfrak{R}_s^-(c);$$

$$\mathfrak{R}_s^+(c) = K_s^+(T) \prod_{i=1}^n c_i^{\alpha_i}, \quad \mathfrak{R}_s^-(c) = K_s^-(T) \prod_{i=1}^n c_i^{\beta_i} \quad (3)$$

here  $c_{Ai}$ ,  $c_{Bi}$  are the concentration of initial and final(product) substances.

$k_i^+$ ,  $k_i^-$  are the coefficient for the direct and reverse reaction and their ratio  $k_i^+/k_i^- = k_{eq}$  represents equilibrium constants.  $k_i$  will be related to any increasing exponential factor but at the moment we will take any constant.

When there is a reversibility factor involved in the mechanism then we have an equilibrium such that  $\mathfrak{R}_s^+(c^*) = \mathfrak{R}_s^-(c^*)$ .

Thus Eq. (3) along with the stoichiometric vectors provides the kinetic equations, i.e.,

$$\frac{dc}{dt} = J(c) = \gamma \cdot \mathfrak{R}(c) \quad (4)$$

Some other linear constraints also take part during the spreading, i.e., the balancing equations \or involved balancing matrix.

$$Dc = b_c, \dots b_c = b_A \dots b_l \quad (5)$$

The system of Eq. (4) can be written as follows:

$$\frac{dc_j}{dt} = \mathfrak{R}_j(c, \alpha), \quad (6)$$

where  $c \in \mathbb{R}^m$  and  $\alpha \in \mathbb{R}^n$ . Now, the above system (6) can be further analyzed with the help of sensitivity analysis. This approach allows us to investigate the sensitivity of each concerning variable parameter. That can be represented as

$$s_{ip} = \frac{\partial c_j}{\partial \alpha_p} = \lim_{\Delta \alpha_p \rightarrow 0} \frac{c_j(\alpha_p + \Delta \alpha_p) - c_j(\alpha_p)}{\Delta \alpha_p}. \quad (7)$$

The above Eq. (7) implies the time-dependent sensitivities of each involve variables  $\{c_j, j = 1, 2, \dots, m\}$  relating to all parameter values  $\{\alpha_p, p = 1, 2, \dots, n\}$ . Further, the sensitivity of the coefficients can be measured through their differentials, i.e.,

$$\frac{\partial s_{ip}}{\partial t} = \frac{\partial}{\partial t} \left( \frac{\partial c_j}{\partial \alpha_p} \right) = \frac{\partial}{\partial \alpha_p} \left( \frac{\partial c_j}{\partial t} \right) = \frac{\partial}{\partial \alpha_p} (\mathfrak{R}_j(c(t), \alpha)). \quad (8)$$

Eq. (8) is used to identify the local sensitivity of model elements concerning model parameters in systems biology. It means this approach is used to determine which variable or parameter is sensitive to a specific condition which is defined by a variable or parameter.

Differentiate with the help of chain rule, Eq. (8) will become more driven and the Jacobian matrix further takes the sensitivity equations, i.e.,

$$\dot{S} = \mathcal{H}_{\alpha_p} + \mathcal{J} \cdot S, \quad p = 1, 2, \dots, n \quad (9)$$

here the above matrices  $S$ ,  $\mathcal{H}_{\alpha_p}$  and  $\mathcal{J}$  are defined by

$$S = \begin{pmatrix} \frac{\partial c_1}{\partial \alpha_p} \\ \frac{\partial c_2}{\partial \alpha_p} \\ \vdots \\ \frac{\partial c_m}{\partial \alpha_p} \end{pmatrix}, \quad \mathcal{H}_{\alpha_p} = \begin{pmatrix} \frac{\partial \mathfrak{R}_1}{\partial \alpha_p} \\ \frac{\partial \mathfrak{R}_2}{\partial \alpha_p} \\ \vdots \\ \frac{\partial \mathfrak{R}_m}{\partial \alpha_p} \end{pmatrix}, \quad \mathcal{J} = \begin{pmatrix} \frac{\partial \mathfrak{R}_1}{\partial c_1} & \dots & \frac{\partial \mathfrak{R}_1}{\partial c_m} \\ \vdots & \ddots & \vdots \\ \frac{\partial \mathfrak{R}_m}{\partial c_1} & \dots & \frac{\partial \mathfrak{R}_m}{\partial c_m} \end{pmatrix}.$$

Eq. (9) provides the local sensitivity values through the ‘simbiology’ in Matlab by using three different normalization techniques, i.e., half-normalization, full-normalization, and non-normalization. These normalization techniques become more important when we have a complex model of COVID-19 spreading, especially when spreading is in a different direction, i.e., adopting different routes. In that case, we need to apply the model reduction techniques over the multi-routes COVID spreading. This will help to identify the critical parameters of the model to improve the dynamic model. For further details, readers are referred to [29–39].

### 3. Hid model with one reversible reaction

If a simple healthy person ( $H$ ) gets infected ( $k_1^+$ ), this individual will become an infected person ( $I$ ). Then, either infected individual will get to recover ( $k_1^-$ ) and become healthy or after some time die ( $D$ ), denoted by ( $k_2$ ). The model diagram here can be given below:

The model chemical reactions of Fig. 1 can be simply expressed as follows:



For convenience, we take the healthy  $H$  as  $c_1$ , infected  $I$  as  $c_2$  and died people  $D$  as  $c_3$ , then by using the above Eq. (4) the time derivatives of concentrations will become,

$$\begin{aligned} \dot{c}_1 &= \frac{d}{dt} c_1 = -k_1 c_1 + k_1^- c_2 + v_{in} c_1^{in} - v_{out} c_1, \\ \dot{c}_2 &= \frac{d}{dt} c_2 = -k_1 c_1 - (k_1^- + k_2) c_2 + v_{in} c_2^{in} - v_{out} c_2, \\ \dot{c}_3 &= \frac{d}{dt} c_3 = k_2 c_2 + v_{in} c_3^{in} - v_{out} c_3, \end{aligned} \quad (11)$$

At here following parameters are defined for the case of a two-step mechanism

$$\begin{aligned} k_1^+ &= 0.1, \quad k_2^+ = 0.2, \\ c_1^{eq} &= 0.8, \quad c_2^{eq} = 0.2, \quad c_3^{eq} = 0.4 \end{aligned}$$

While the  $v_{in} c_1^{in} - v_{out} c_1$ , depends upon the specified area chosen for study is closed or open. Here we will consider a closed system for a case study, i.e., constant volume.

#### 3.1. Results and discussions

Solving the system (11), we observe that as the number of healthy people decreases the death graph increases, while the infected people contribute on both sides. Some of the infected people get recovers while some infected people die per day (Fig. 2).

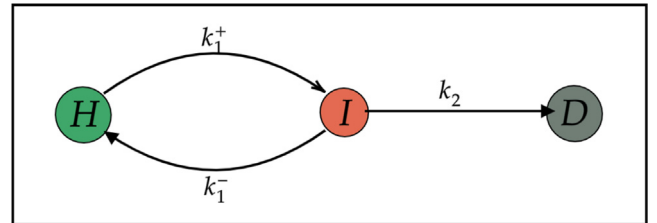
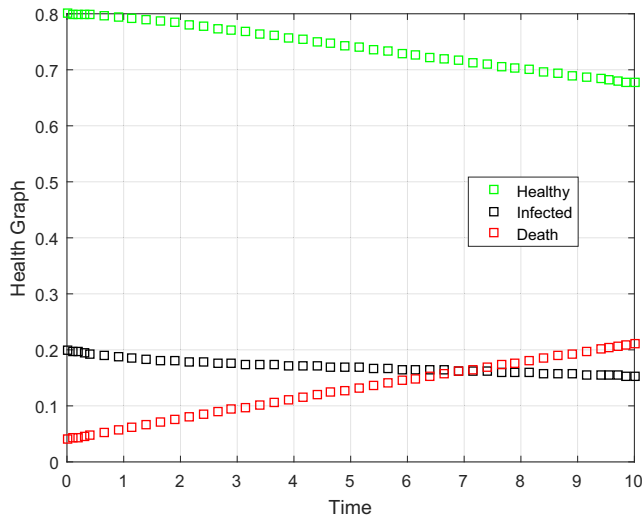
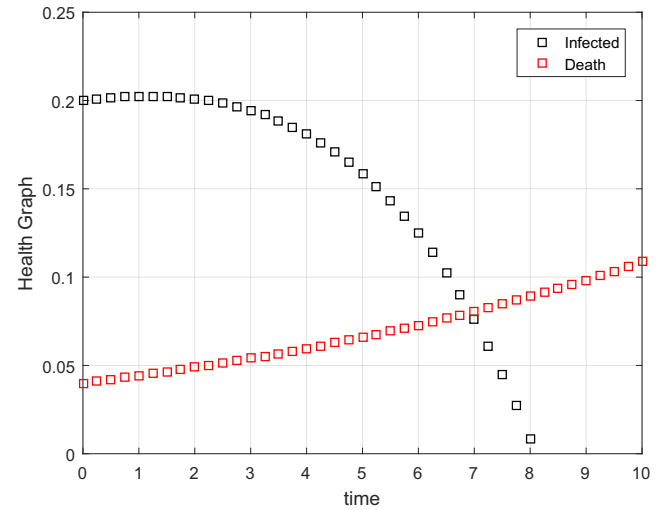


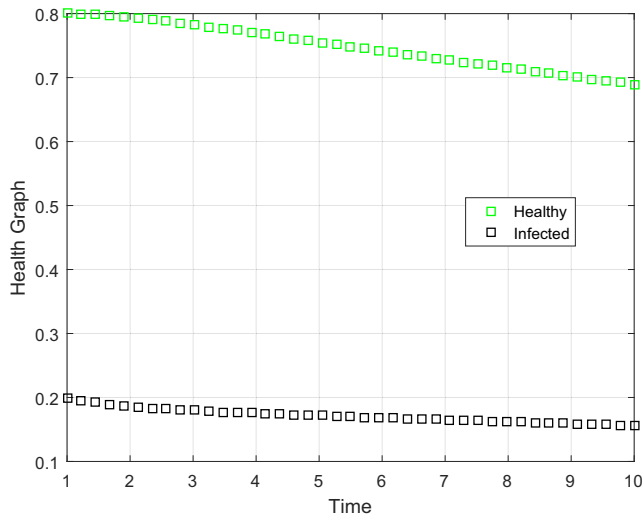
Fig. 1 The HID model diagram of the spreading COVID-19.



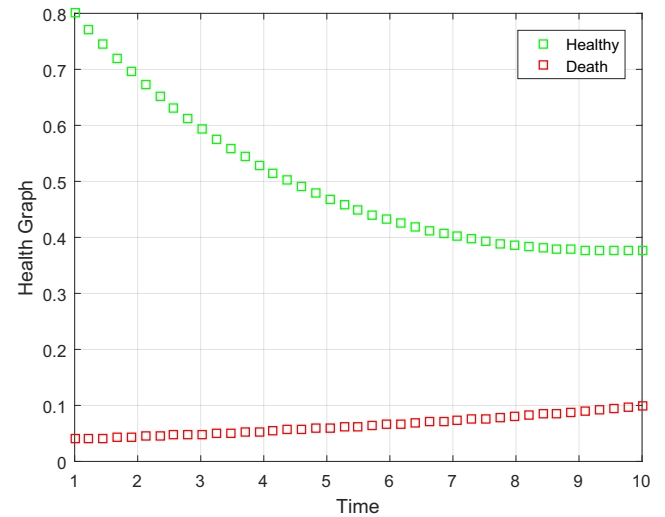
**Fig. 2** The complete behavior of the involved species in the system (11) in computational simulations using initial populations  $H(0) = 0.8$ ,  $I(0) = 0.2$ ,  $D(0) = 0.04$ .



**Fig. 4** Comparison between the infected and the die species (patients) in computational simulations using initial populations  $I(0) = 0.2$ ,  $D(0) = 0.04$ .



**Fig. 3** Comparison of the healthy and infected species in its reduced form in computational simulations using initial populations  $H(0) = 0.8$ ,  $I(0) = 0.2$ .



**Fig. 5** Comparison of healthy and the die patients in computational simulations using initial populations  $H(0) = 0.8$ ,  $D(0) = 0.04$ .

Similarly, the graphs between healthy and infected peoples are shown in Fig. 3.

Fig. 4 indicates that the graph between the infected and the dead peoples.

Fig. 5 shows the graph between the healthy and the dead people. As the number of healthy people reduces the death graph increases and vice versa.

From the figure above, we can easily judge that  $H$  is inversely proportional to  $D$  and the graph  $H$  can be increased in several ways. Firstly, the interaction  $H$  and  $I$  must be reduced, such as by reducing the success probability of infection (medicine, increase the level of immune, use of medical mask, physical distancing, lockdown, etc). Secondly, the recovery factor  $K_1^-$  must be increased, this can be done with the proper medication or vaccinations.

Another way of analyzing the data is its sensitivity analysis presented in Eq. (9). We determine the sensitivity of the model through three different normalization-techniques see Fig. 6. Graphs show that the death class is very sensitive to the parameter  $k_2$  in all suggested techniques, see Fig. 6. Also, healthy individuals are sensitive to  $k_1^+$ , see Fig. 6(a), and infected and death individuals are also very sensitive to  $k_1^+$ , see Fig. 6(c). On the other hand, all model classes are less sensitive to the parameter  $k_1^-$ , see Fig. 6(a) and (b). The proposed method based on the computational simulations technique of simbiology is an effective approach to identify the critical model parameters. A further improvement, interventions, and controlling the spread of disease is also possible by studying the model practically and theoretically.

#### 4. Hisd model with one reversible reaction

Consider another model cause for the spreading of disease, this is called the HISD model. If some healthy and infected people are living together. Among them, some healthy person  $H$  gets infected  $I$  and get recover but some of them reach to the serious conditions  $S$ , i.e., ventilator but still have some chances to get recover otherwise dies  $D$ . The model diagram here is given below:

The model chemical reactions of Fig. 7 can be simply expressed as follows:



The time derivatives of concentrations are given by (4):

$$\begin{aligned} \dot{c}_1 &= \frac{d}{dt} c_1 = -k_1 c_1 c_2 + k_1^- c_3 + k_2 c_3 + v_{in} c_1^{in} - v_{out} c_1, \\ \dot{c}_2 &= \frac{d}{dt} c_2 = -k_1 c_1 c_2 + k_1^- c_3 + v_{in} c_2^{in} - v_{out} c_2, \\ \dot{c}_3 &= \frac{d}{dt} c_3 = k_1 c_1 c_2 - k_1^- c_3 - k_2 c_3 + v_{in} c_3^{in} - v_{out} c_3, \\ \dot{c}_4 &= \frac{d}{dt} c_4 = k_2 c_3 + v_{in} c_4^{in} - v_{out} c_4. \end{aligned} \quad (13)$$

#### 4.1. Results and discussions

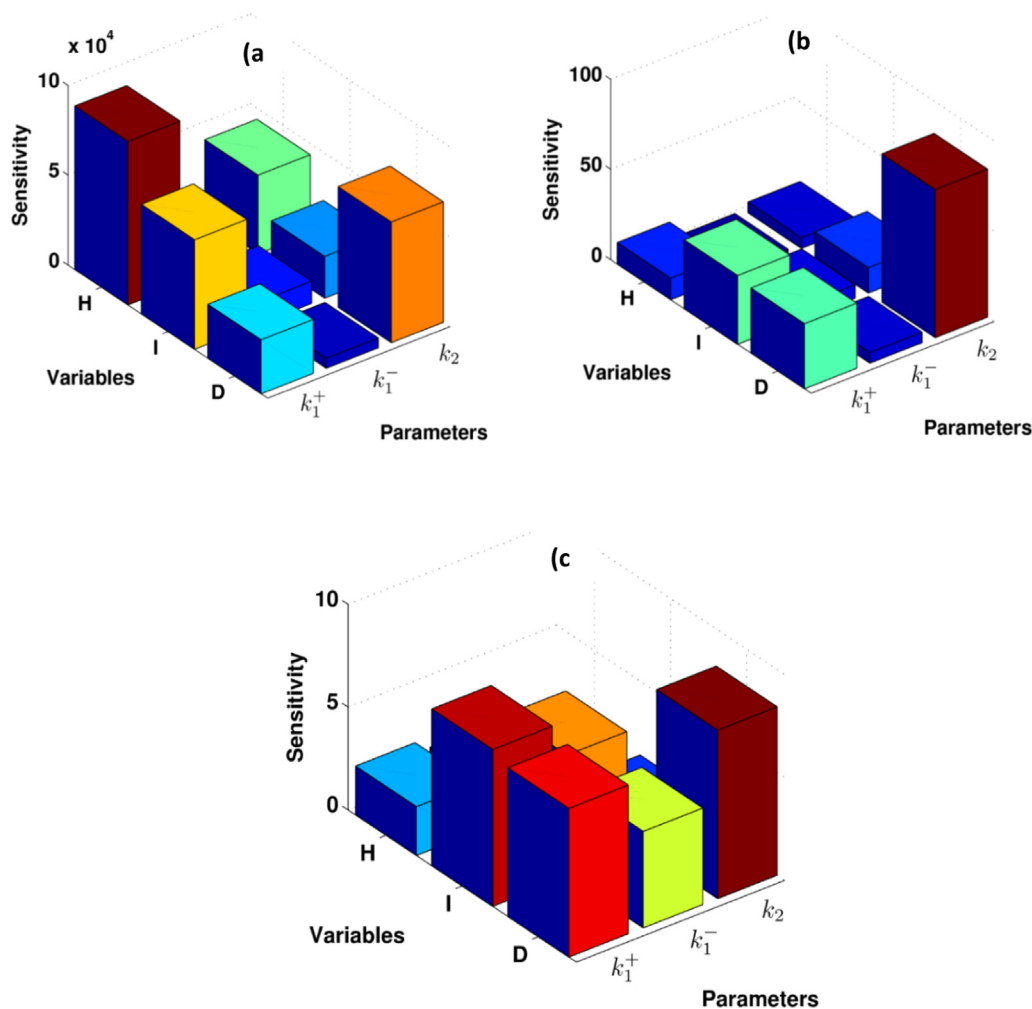
At here following parameters are defined for the case of a two-step mechanism

$$k_1^+ = 1, \quad k_2^+ = 0.4, \\ c_1^{eq} = 0.4, \quad c_2^{eq} = 0.2, \quad c_3^{eq} = 0.1, \quad c_4^{eq} = 0.04$$

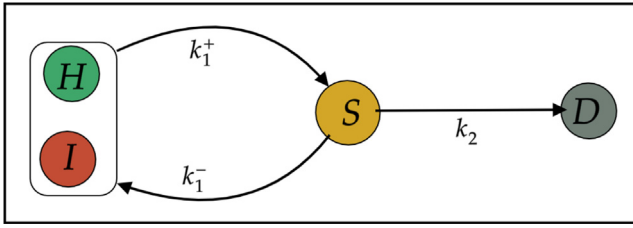
The balance of healthy and the infected patients can be seen among its different stages, i.e.,

BALANCE	HEALTHY	INFECTED	SERIOUS	DEATH
H-	H		H	
BALANCE				
I-		I	I	I
BALANCE				

Now, mathematically speaking we can discuss the behavior of each individual along with the impact of one species over the other. Here we have,



**Fig. 6** The computational simulations for sensitive analysis of the HISD model along with the concerning parameters for the (COVID-19) disease (using initial populations  $H(0) = 10,000$ ,  $I(0) = 200$ ,  $D(0) = 25$  and parameters  $k_1^+ = 0.2$ ,  $k_1^- = 0.8$ ,  $k_2 = 0.1$ ) (a) Non – Normalization sensitivity, (b) Half – Normalization sensitivity, (c) Full – Normalization sensitivity.



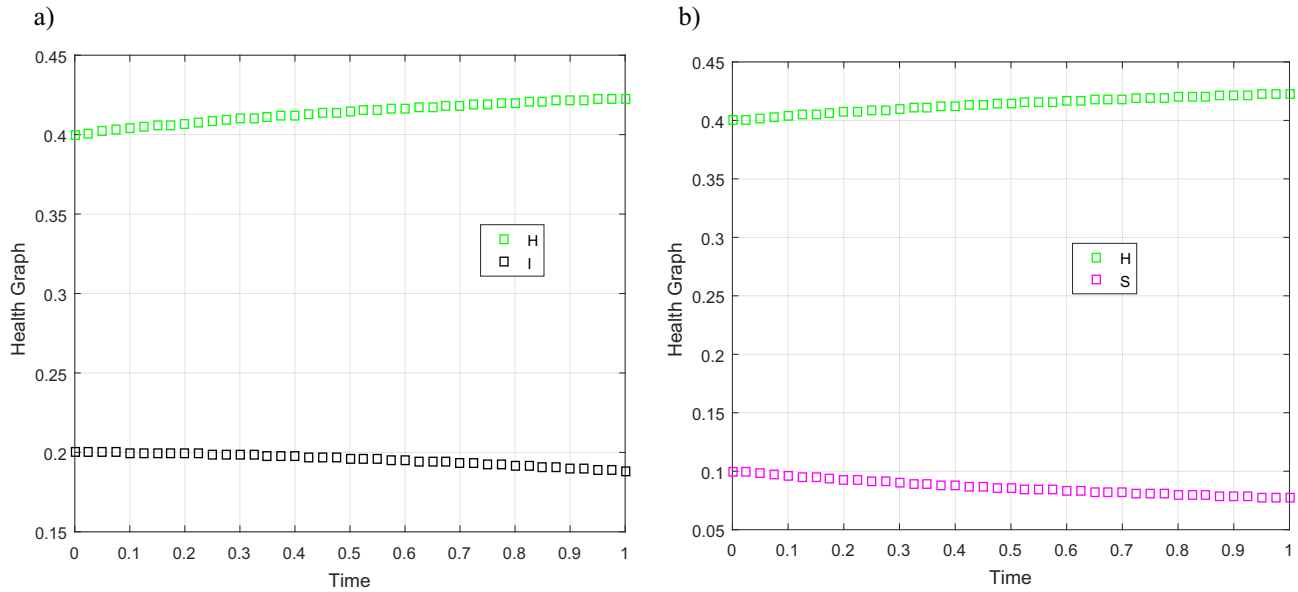
**Fig. 7** The HISD model diagram of the spreading COVID-19.

$$\begin{aligned} C_H + C_S &= b_1, \\ C_I + C_S + C_D &= b_2. \end{aligned} \quad (14)$$

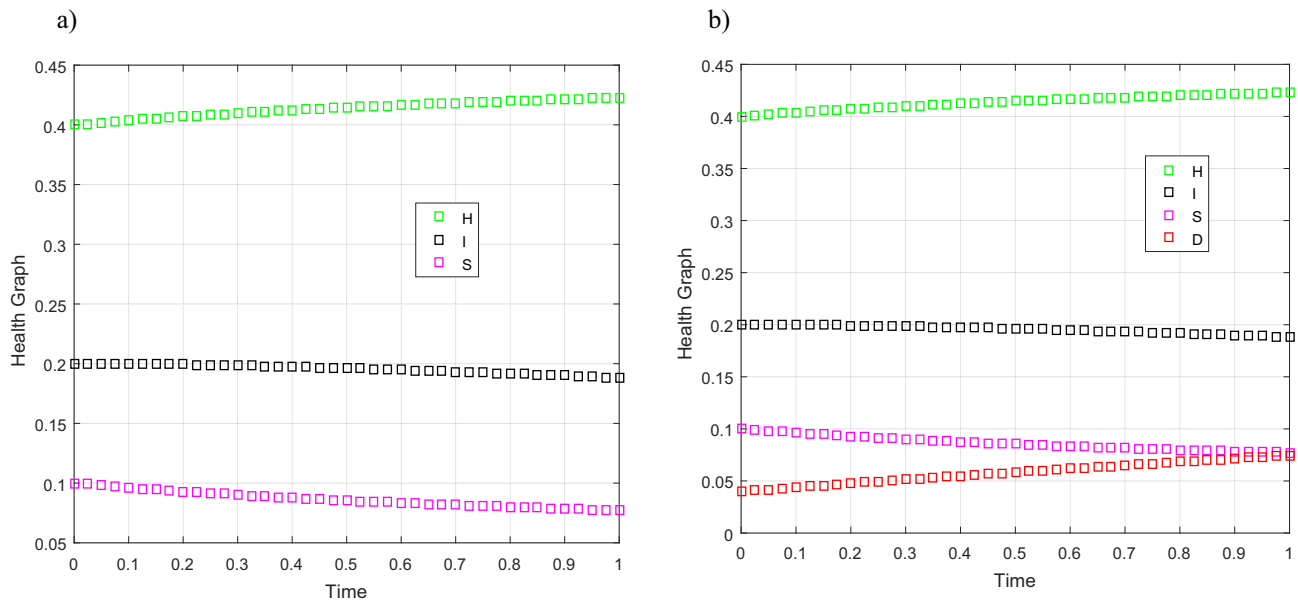
Through this, we will be able to get the finalized form of the involved variables (Fig. 8).

From the above graph, we can see that as the healthy graph increases the number of infected and serious patients graph decreases (Fig. 9).

Let us measure again the sensitivity of the HISD-model using three different techniques for the given system (13). Intestinally, the class S is very sensitive to the parameter  $k_2$  using all three techniques, see Fig. 10. Furthermore, death and healthy classes are also sensitive to  $k_2$ , see Fig. 10(a)–(c), while, the state variables I, S, and D are less sensitive to the parameters  $k_1^+$  and  $k_1^-$ , see Fig. 10. Therefore, the key critical model elements are established computationally and simulated is an effective way to further enhance the model for future advances, interventions, and monitoring the spread of disease.

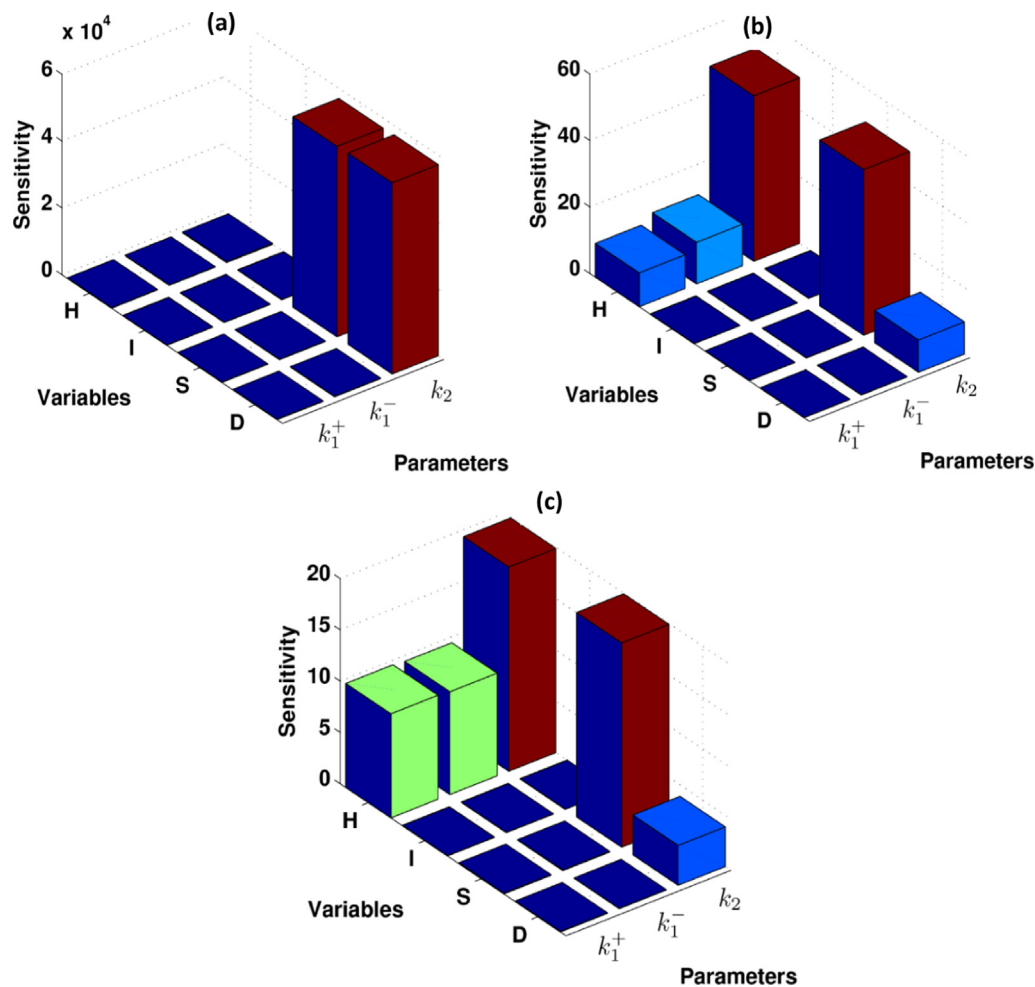


**Fig. 8** Comparison of a) healthy and infected patients and b) healthy and serious patients in its reduced form.



**Fig. 9** Comparison of a) healthy, infected, and serious patients and b) complete behavior of the involved species in the system (13).





**Fig. 10** The computational simulations for sensitive analysis of the HISD model along with the concerning parameters for the coronavirus disease (COVID-19) (using initial populations  $H(0) = 10,000$ ,  $I(0) = 200$ ,  $S(0) = 50$ ,  $D(0) = 10$  and parameters  $k_1^+ = 1$ ,  $k_1^- = 0.8$ ,  $k_2 = 0.4$ ) (a) Non – Normalization sensitivity, (b) Half – Normalization sensitivity, (c) Full – Normalization sensitivity.

## 5. Conclusions

In this paper, we suggested two simple models of the COVID-19 to incorporate the impact of social awareness programs conducted by public health officials with quarantine strategies in hospitals. It has been observed that these awareness programs and quarantine strategy result in human behavioral changes to avoid the risk of disease transmission. These models mainly account for the reduction in disease class due to awareness while we can say the disease goes away due to applied the quarantine it well.

1. These models are presented as a set of mathematical equations. The dynamics of model equations are simplified constructed on the “model reduction computational simulations techniques for the initial populations and parameters’ to evaluate the spreading with the dynamical view of the virus transmission.
2. The idea of local sensitivity is applied to three different techniques, non, half, and full normalization sensitivity. They provide us the sensitivity of each variable relating to

the model parameters. The suggested methods give a major step forward to evaluate the models and identify the key critical parameters.

3. Knowing of critical model-parameters allows the biologist/-chemist to specify/distinguish control strategies to adopt further precaution measures with improvements.
4. Model the problem helps to understand how to reduce the interaction of the peoples of serious/mild-infected individual patients from the community to avoid the spreading of coronavirus widely in the surrounding community.

## Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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