A Control Approach to Guide Nonpharmaceutical Interventions in the Treatment of COVID-19 Disease Using a SEIHRD Dynamical Model

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The recent worldwide epidemic of COVID-19 disease, for which there are no medications to cure it and the vaccination is still at an early stage, led to the adoption of public health measures by governments and populations in most of the affected countries to avoid the contagion and its spread. These measures are known as nonpharmaceutical interventions (NPIs), and their implementation clearly produces social unrest as well as greatly affects the economy. Frequently, NPIs are implemented with an intensity quantified in an ad hoc manner. Control theory offers a worthwhile tool for determining the optimal intensity of the NPIs in order to avoid the collapse of the healthcare system while keeping them as low as possible, yielding concrete guidance to policymakers. A simple controller, which generates a control law that is easy to calculate and to implement is proposed. This controller is robust to large parametric uncertainties in the model used and to some level of noncompliance with the NPIs.

Keywords: COVID-19 disease; SEIR model; nonlinear systems; proportional control

1. Introduction

The novel SARS-CoV-2 coronavirus, which produces the disease known as COVID-19, was first reported on December 2019 in Wuhan, province of Hubei, China. With amazing speed it spread to the majority of the countries in the world. The outbreak was declared as a public health emergency of international concern by the World

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Health Organization (WHO) on January 30, 2020, and as a pandemic on March 11.

At the moment, there is no effective medicine to cure the disease and vaccination is not yet widespread. Health systems only try to mitigate its consequences to avoid complications and fatal outcomes. This disease has shown a great capacity of contagion and high fatality rates (see updated reports in [1]).

Patients affected by this disease present a number of symptoms, not all clearly identified at the moment, but which are mainly cough, breathing difficulties, fever, loss of taste and smell and extreme tiredness. Frequently, patients develop a form of viral pneumonia that requires hospitalization and artificial mechanical ventilation in intensive care units. The large number of patients affected by this disease threatens to collapse public health systems, increasing the lethality rates due to the lack of available medical assistance.

In this context, it is very important to predict the trend of the epidemic in order to plan effective strategies to avoid its spread and to determine its impact. As the contagion is produced very easily by simple contact between people, several measures were adopted by the governments, public health systems and populations in order to reduce the transmission by reducing contact rates. Examples of these measures, the so-called nonpharmaceutical interventions (NPIs), include the closing of schools, churches, bars and factories, quarantine or physical-distancing policies, confinement of people in their homes and lockdown, among other social impositions that produce discomfort and clearly harm the economy.

This goal has generated many articles and studies published recently on the behavior of the epidemic. A number of them are addressed to determine a mathematical model that represents the dynamics of the different agents involved in a population affected by the disease. The dynamics described by the model aim to make it possible to answer crucial issues, such as the maximum number of individuals who will be affected by the disease and when that maximum will occur, and makes key predictions about the outbreak and eventual recovery from the epidemic. This information allows us to outline public policies and strategies to mitigate the social impact and reduce the fatality rate. The seminal work [2] exemplifies and analyzes different strategies to control the transmission of the virus.

Most of the models adopted to represent the dynamical behavior of COVID-19 are based on the susceptible, infected, recovered (SIR) model, first introduced by Kermack and McKendrick [3]. The SIR model is a basic representation that is widely used, which describes key epidemiological phenomena. It assumes that the epidemic affects a constant population of N individuals. The model neglects demography, that is, births and deaths from other causes unrelated to the disease. (In Argentina, the annual death rate is 7.604 per 1000 people [4].)

The population is broken into three non-overlapping groups corresponding to the stages of the disease:

- Susceptible (S). The population susceptible to acquiring the disease.
- Infected (I). The population that has acquired the virus and can infect other people.
- Recovered (R). The population that has recovered from infection and is presumably no longer susceptible to the disease. (At the moment, in the COVID-19 disease it is an open question if a recovered person can get reinfected. Even though some cases were recently reported, the reinfection rate value appears to be statistically negligible based on early evidence.)

We give a brief description of these compartments now. Susceptible people are those who have no immunity but are not currently infected. An individual in group S can move to group I by infection produced through contact with an infected individual. Group I are peo ple who can spread the disease to susceptible people. Finally, an infected individual recovered from the disease is moved from group I to group R. Some references (e.g., [5–7]) consider group R as removed population, or closed cases, which includes those who are no longer infectious after recovery and those who died from the disease. The summation of these three compartments in the SIR model remains constant and equal to the initial number of population N.

In order to better describe the spread of epidemics, many studies (e.g., [8–10]) adopted the SEIR model. In the SEIR model, a fourth group denoted as exposed (E) is added between group S and group I:

- Exposed (E). The population that has been infected with the virus, but is not yet at an infectious stage capable of transmitting the virus to others.

This compartment is dedicated to those people who are infectious but cannot infect others for a period of time, namely incubation or latent period.

Other studies (e.g., [11]) consider an additional compartment at the end of the SIR or SEIR model to distinguish between recovered and death cases:

- Dead (D). The population dead due to the disease.

Thus, these models become the SIRD or the SEIRD models, respectively.

Other studies, such as [5–7, 12] consider the existence of other groups seeking to match the models proposed with the data obtained from the actual COVID-19 disease.

The work presented in [13] has to be specially mentioned. This work studies the evolution of COVID-19 in Italy, and proposes a model denoted as SIDARTHE, where the letters correspond to eight groups denoted as susceptible, infected, diagnosed, ailing, recognized, threatened, healed and extinct, respectively. All of them are subgroups of those presented in the SEIR model. This model discriminates between detected and undetected cases of infection, either asymptomatic or symptomatic, and also between different illness severity, having a group for moderate or mild cases and another one for critical cases that require hospitalization in intensive care units. The authors affirm that the distinction between diagnosed and undiagnosed cases is important because undiagnosed individuals are more likely to spread the infection than diagnosed ones, since the latter are typically isolated, which can explain misperceptions of the case fatality rate and the seriousness of the epidemic. The fact of considering more groups in the SIDARTHE model than in the SEIR model allows a better discrimination between the different agents involved in the evolution of the epidemic, as well as a better differentiation of the role played by each one. In [7] the authors also consider a model that discriminates between reported and unreported symptomatic cases. However, the fact of increasing the number of groups implies the knowledge of more rates, probabilities and constants that determine the dynamics between the groups. Many of these parameters are difficult to know in practice, as is estimating the population of some groups, such as ailing (symptomatic infected undetected). The authors choose these constants and quantities to fit the values calculated by their model to the actual data. In order to achieve the goal of better determining public policies, we understand that it is not necessary to have some of these groups in the model used.

In order to better guide the determination of public policies to mitigate the spread of the virus, we propose the use of control theory.

Control theory has been successfully implemented in several areas other than physical systems control, for which it was initially designed. For example, in economics, ecological and biological systems, many studies demonstrate the success of its implementation. Of course, regardless of the area focused on, a good control strategy depends on the adequate modeling of the dynamical system to be controlled.

The proposal to use control in this epidemic is not new. It was first presented in [10]. In this paper, the authors use the SEIR model to show that a simple feedback law can manage the response to the pandemic for maximum survival while containing the damage to the economy. However, although the authors illustrate with several examples the benefits of using feedback control, they do not present the mathematical control laws nor do they prove the convergence of the trajectories in the closed-loop system. Examples are implemented by means of several computational experiments that illustrate the different strategies proposed. In [14] an open-loop control action based on two different constant levels of NPIs is applied on the SIR model. The authors analytically calculate the peak of infected people as a function of the day of application of the NPIs and of the duration of these policies. Simulations were also carried out for other epidemic dissemination models proposed in the literature.

In this paper, we propose the use of a simple controller that produces a control signal proportional to an adequate combination of the process variables. Although this is not a proportional controller, since the control signal is not a gain times the values of the process variables, we will denote it as a proportional controller with notation abuse. Proportional control is a standard tool in control theory to calculate the control action. This variable guides how to determine NPIs in order to avoid the collapse of the health system while reducing the damage to the society and the economy that NPIs inevitably produce. Partial and preliminary versions of this paper have been published in [15, 16].

2. The SEIHRD Model

This section is addressed to adequately modeling the disease. A suitable model should avoid making unnecessary classifications in order to obtain key data on the behavior of the epidemic. This data includes number of deaths, maximum number of infected people and time at which the maximum infection rate will occur, among other information useful to prevent and reduce the damage produced by the outbreak.

The SEIR model assumes that exposed people have been infected but are not able to transmit the virus before a latency period. We consider that those people continue to be in the susceptible group S, whereas we consider group E as people who have been infected but still have no symptoms and are able to transmit the virus. Part of this group will present symptoms after an incubation time (moving to group I) and another part will remain asymptomatic. Asymptomatic people who have been diagnosed as positive also are considered in group I, so this group includes all known positive cases, symptomatic or not. Note that our classification highlights the distinction between diagnosed and undiagnosed cases, whether they are symptomatic or not, because reported positive cases tend to be isolated and their contagion capacity is greatly reduced.

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In addition, a critical issue is the number of infected people who need hospitalization, because the public policies must try to keep this number lower than the capacity of the health care system in order to avoid its collapse. Thus we define an extra group:

- Hospitalized (H). The infected population who need hospitalization.

In group H we do not differentiate between people hospitalized in mild condition and those in intensive care units (ICUs), despite the fact that the number of people in the last subgroup is a critical problem due to an even more limited capacity in ICUs. We also consider the population number N as a constant, as the SEIR model does.

The progression of this epidemic can be modeled by the rate processes described in Figure 1.

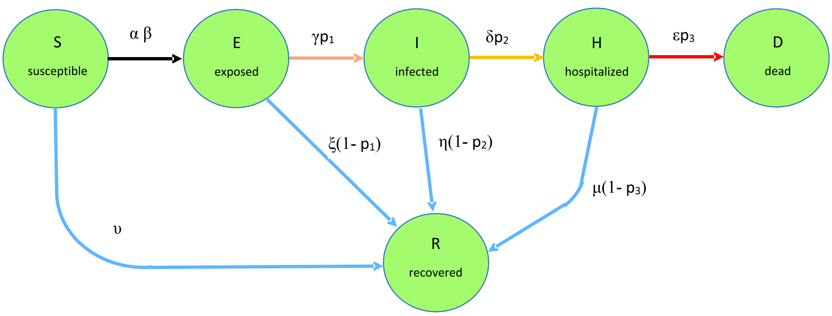

Figure 1. Rate processes that describe the progress between the groups in the SEIHRD model.

The proposed SEIHRD model for the spread of the COVID-19 disease in a uniform population is given by the following deterministic equations, which are normalized with respect to the total population N:

$$\begin{aligned}\dot{S} &= -(1-u)(\alpha SE + \beta SI) - \nu S \\ \dot{E} &= (1-u)(\alpha SE + \beta SI) - (\gamma p_1 + \zeta(1-p_1))E \\ \dot{I} &= \gamma p_1 E - (\delta p_2 + \eta(1-p_2))I \\ \dot{H} &= \delta p_2 I - (\epsilon p_3 + \mu(1-p_3))H \\ \dot{R} &= \nu S + \zeta(1-p_1)E + \eta(1-p_2)I + \mu(1-p_3)H \\ \dot{D} &= \epsilon p_3 H.\end{aligned} \tag{1}$$

The groups S, E, I, R, H and D are the state variables of the dynamical system equation (1). They are always non-negative. The time derivatives $\dot{R}$ and $\dot{D}$ are also non-negative, because the number of recovered and dead people cannot decrease, whereas $\dot{S}$ is always non-positive, because we consider that recovered people cannot be reinfected. This dynamic is represented in Figure 1 because the states R and D only have input arrows and the state S only has output arrows. Equation (2) is a nonlinear system normalized with respect to the constant population N. Hence $S + E + I + H + R + D = 1$ and $\dot{S} + \dot{E} + \dot{I} + \dot{H} + \dot{R} + \dot{D} = 0$.

The rate processes are modeled as follows.

- αSE and βSI are the transmission rates of the virus between the susceptible and the exposed population (respectively, infected population). α and β are the probability of disease transmission in a single contact with exposed (infected) people times the average daily number of contacts per person, and they have units of $1 / \text{day}$. Typically, α is greater than β, assuming that people tend to avoid contact with subjects showing symptoms or diagnosed as positive. Contacts between susceptible people and hospitalized people are neglected, except for healthcare workers. The probability of contagion from dead people is also neglected, despite the fact that some cases have been reported recently. Finally, recovered people are no longer able to transmit the virus.
- $u \in [0, 1]$ is the intensity of NPIs. $u = 0$ means no intervention and the epidemic grows completely free, whereas $u = 1$ implies total elimination of the spread of the disease.
- v is the vaccination rate, at which susceptible people became unable to be infected. Unfortunately, at this early stage of vaccination in most countries, this rate can be neglected, so we consider $v = 0$.
- p_1 is the probability that exposed people develop symptoms, γ^{-1} is the average period to develop symptoms, and ζ^{-1} is the average time to overcome the disease, staying asymptomatic.
- p_2 is the probability that infected people with symptoms require hospitalization, δ^{-1} is the average time between infection and the need for hospitalization, and η^{-1} is the average time in which infected people recover without hospitalization.
- p_3 is the probability of hospitalized people dying, ϵ^{-1} is the average time between hospitalization and death, and μ^{-1} is the average time to recover after hospitalization.

The parameters used in equation (1) are not very precisely determined and even differ greatly in the literature consulted (see [2, 5, 7, 8, 13, 17–19] among many other references). Most of the models adopted in the references adjust these parameters to fit real data from different countries. It must be taken into account that some of these parameters, mainly α and β, are not independent of the populations and their general state of health or their actions.

The parameters α and β are related to the basic reproduction number R_0, defined as the expected number of secondary cases produced by a single (typical) infection in a completely susceptible population

[18]. R_0 is not a fixed number, depending as it does on such factors as the density of a community, the general health of its population, or its medical infrastructure [10]. This is the most important parameter to understand the spread of an epidemic. If $R_0 > 1$, the epidemic grows and the number of infected people increases. If $R_0 < 1$, the epidemic decreases and after a certain time disappears, when a large enough number of people acquire antibodies and the so-called herd immunity occurs.

In the actual COVID-19 disease, R_0 was determined to be 2.6 in Wuhan, China [10] (between 2.2 and 2.7 according to [20]), ranging from 2.76 to 3.25 in Italy [10] and even close to 3.28 [17]. An important remark is that many studies consider R_0 to depend on the NPIs, admitting that these actions tend to reduce this number because the contact rates between people decrease. Note that NPIs always occur even in countries where no government action has been taken, because people spontaneously tend to stay at home and to avoid contact with others. This fact explains the disparity of this number in different countries and reported in the references (see [17]).

Here, we consider R_0 as a constant reproduction number in the absence of any external action, that is, as if the disease could spread completely freely, which, obviously, is an unreal scenario. Specifically, the relation between the rates α and β and R_0 can be calculated in equation (1) as in [13, 18], resulting in

$$R_0 = \frac{\alpha}{(\zeta + \gamma p_1 - p_1 \zeta)} + \frac{\beta \gamma p_1}{(\eta + \delta p_2 - \eta p_2)(\zeta + \gamma p_1 - p_1 \zeta)}. \qquad (2)$$

The intensity of the NPIs is considered in the variable u, which determines the rate at which susceptible people become exposed and infected.

Several studies [5, 6, 9, 12] consider these parameters as time dependent, because incorporated in these parameters is the impact of government actions among other NPIs. Here we will consider them as constants, because the NPIs will be considered in the control action u; hence, equation (1) is a nonlinear time-invariant system.

The incubation period is estimated as $\gamma^{-1} = 5.1$ days [2, 8, 21].

The probability of developing symptoms p_1 will be roughly estimated as 50% [2, 22]. (This probability is the most difficult to determine. According to [23], up to 80% of the cases could be asymptomatic.)

The period to overcome the disease without presenting symptoms is $\zeta^{-1} = 14.7$ days (deduced from [13]).

The infectious period with no need for hospitalization is widely accepted as 14 days, so $\eta = 1 / 14$.

The probability to need hospitalization after the infection is $p_2 = 19\%$ [23, 5, 6], and the time from symptom onset to hospitalization is $\delta^{-1} = 5.5$ days [20].

The probability to die after hospitalization is $p_3 = 15\%$ according to [1, 2], and the average time to die is $\epsilon^{-1} = 11.2$ days [20].

The average time to recovery after hospitalization is $\mu^{-1} = 16$ days [2].

Finally, as noted earlier, we neglect the vaccination rate, so $\nu = 0$.

Remark 1. Most of these parameters are subject to large inaccuracies, and they differ greatly in the literature consulted. However, as we will show below, the proposed control method is robust for such uncertainties as well as for measurement errors characterized as unreported or undiagnosed cases and inaccuracies in the quantities of the groups.

2.1 Analysis of the SEIHRD Model

Equation (1) is a normalized nonlinear system. It presents only one equilibrium point at $\left[SEIHRD\right]^* = \left[\overline{S}000\overline{RD}\right]$, where $\overline{R}$ and $\overline{D}$ are positive constants and $\overline{S}$ is a non-negative constant such that $\overline{S} + \overline{R} + \overline{D} = 1$. These constants depend on the initial conditions, the transmission rates and the constants α and β. The lower the reproduction number R_0, the lower the final number of deaths and people recovered. This equilibrium point may be reached by the trajectories described by the states in equation (1) in infinite time. Note that this equilibrium point is stable, because once $E = I = H = 0$, the virus is no longer circulating among the population, and hence the states S, R and D remain constant.

In order to better understand the system behavior, we divide equation (1) into the following three subsystems

$$\dot{S} = -\overline{u} \tag{3a}$$

$$\dot{\mathbf{x}} = A\mathbf{x} + \mathbf{b}\overline{u} \tag{3b}$$

$$\dot{\mathbf{y}} = C_2\mathbf{x} \tag{3c}$$

where

$$\begin{aligned}
\overline{u} &= S\left(1 - u\right)C_1\mathbf{x} \\
\mathbf{x} &= [EIH]^{\boldsymbol{T}} \\
\mathbf{y} &= [RD]^{\boldsymbol{T}} \\
C_1 &= \left[\alpha\beta 0\right] \\
C_2 &= \begin{bmatrix} \zeta\left(1 - p_1\right) & \eta\left(1 - p_2\right) & \mu\left(1 - p_3\right) \\ 0 & 0 & \epsilon p_3 \end{bmatrix}.
\end{aligned}$$

In the subsystem (3b), the matrix A and the vector $\mathbf{b}$ are defined as

$$A = \begin{bmatrix} -\left(\gamma p_1 + \zeta\left(1 - p_1\right)\right) & 0 & 0 \\ \gamma p_1 & -\left(\delta p_2 + \eta\left(1 - p_2\right)\right) & 0 \\ 0 & \delta p_2 & -\left(\epsilon p_3 + \mu\left(1 - p_3\right)\right) \end{bmatrix}$$

$$\mathbf{b} = \left[100\right]^{\boldsymbol{T}}.$$

Note that $\left[S\mathbf{x}^{\boldsymbol{T}}\mathbf{y}^{\boldsymbol{T}}\right] = \left[SEIHRD\right]^{\boldsymbol{T}} \in \mathrm{R}^6$.

The subsystem (3a) is nonlinear, because of the product $S\mathbf{x}$; the other ones are linear systems. In the system (3b), A is a lower triangular matrix. Its eigenvalues are given by the entries on its main diagonal, which are real and strictly negative, whatever the values of the constants used. Therefore, the subsystem (3b) is globally asymptotically stable [24, c. 6].

Note that the goal of the control strategy is not to lead equation (1) to its equilibrium point, but to keep the number of hospitalized people small enough in order to avoid the collapse of the health care system, as will be shown in the following section.

3. The Control Strategy

We propose the use of control theory to determine public NPIs in order to control the evolution of the epidemic, avoiding the collapse of health care systems while minimizing harmful effects on the population and on the economy.

As noted in [10], "a properly designed feedback-based policy that takes into account both dynamics and uncertainty can deliver a stable result while keeping the hospitalization rate within a desired approximate range. Furthermore, keeping the rate within such a range for a prolonged period allows a society to slowly and safely increase the percentage of people who have some sort of antibodies to the disease because they have either suffered it or they have been vaccinated, preferably the latter."

The action law is given by the control variable u in equation (1). No intervention from the public health agencies means $u = 0$, and the disease evolves naturally without control. On the other hand $u = 1$ means the total impossibility of transmitting the virus, which, of course, is an unreal scenario.

There are several possible choices of the reference signal or set point of the control system. One of them may be a small enough number of hospitalized people to not affect the capacity of the ICUs available in the health care system. This reference signal may be nonconstant; it may increase due to the increase of available beds by capacity additions in the health care system, by creation of provisory field hospitals, among other similar measures. In addition, we must keep in mind that the quantities of each group described in equation (1) are subject to large inaccuracies due to unreported or undiagnosed cases, except for the number of people diagnosed as positive (I) which is quite well known, the number of hospitalized people (H) and the number of deaths (D). For that reason, the output variable to be fed back only can be the infected population I or the hospitalized population H.

Hence, the goal of the control action is to keep the number of hospitalized people lower than the set point, minimizing external interventions that produce social discomfort and clearly harm the economy.

Therefore, the control action should aim to solve the following constrained optimization problem:

$$\begin{aligned} \min \quad & \int_T u(\tau)\partial\tau \\ \text{subject to} \quad & H < SP \end{aligned} \tag{4}$$

where T is a considered period and SP is the reference signal (or set point, in the case where it is considered as a constant). Generally, it is not possible to obtain an analytical expression of the objective function of a constrained minimization problem subject to the dynamics of a nonlinear system. Therefore, solving equation (4) to obtain an expression of the control signal $u(t)$ is not possible. In the experiments shown later, the scalar gain of the controller will be tuned experimentally in order to minimize the area under the curve u versus t.

As a reference, the WHO recommends a number of 80 hospital beds per 10 000 population, which means an index of 0.008, or 0.8%. This number will be used as the SP of the closed-loop control system.

We must also bear in mind that NPIs impact physical contacts between susceptible and infected or exposed people. When an individual is infected, hospitalization may be required after $\delta^{-1} = 5.5$ days or after $\delta^{-1} + \gamma^{-1} = 10.6$ days on average if the infection was recent. Hence, there exists a delay between the adoption of NPIs and their consequences on hospitalization of people. If the control action is calculated based only on the number of hospitalized people, the following 10.6 days, too many people may require hospitalization, exceeding the capacity for medical care. In control jargon, it means that for almost two weeks the system is operating in an open loop. Therefore, the control action should also be calculated as a function of the number of infected people I (the number of exposed people E is quite unknown) in order to avoid future hospitalization requirements in the next 10.6 days at most. This strategy emulates a kind of *predictive control*.

Figure 2 shows the closed-loop control system. The process variables are the infected population I and the hospitalized population H. The scalar control signal u is the intensity of the NPIs.

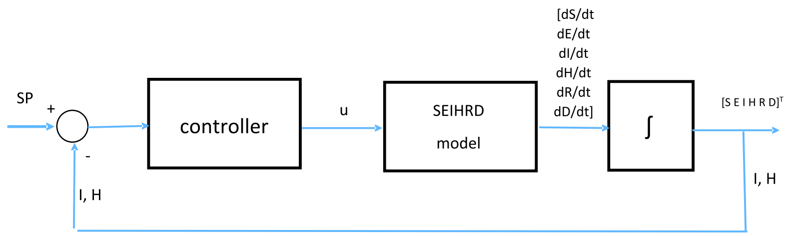

Figure 2. Block diagram of the closed-loop control system.

Of course, in practical situations it is necessary to determine which actions and at what level correspond to a certain intensity of NPIs, but this issue is outside the scope of this paper.

Next, we show the results of different strategies of NPIs applied on the SEIHRD model.

3.1 An Open-Loop Control System

In this first series of experiments, we apply a constant control action u; that is, the system shown in Figure 2 is an open-loop control one.

We consider as initial conditions $I = E = 0.001$, $H = R = D = 0$, so $S = 0.998$; that is, 0.1% of the population is diagnosed as positive on the first day and 0.1% of the population is asymptomatic infected.

During the first days of the epidemic, it was logical to consider that both exposed and infected people could spread the virus at the same rate because the contagion between humans was not known. Then, the disease was able to spread in a completely free scenario, in which no action was taken. This scenario has been called "*naif*" by several authors [5, 6].

Using equation (2) with R_0=2.8 as in [5, 6], and assuming that no actions are taken during the epidemic, then $\alpha = \beta = 0.1786$. The evolution of exposed, infected, hospitalized and dead people in this case is shown in Figure 3.

In this naif scenario, and using as initial condition 1 infected and 1 exposed person for different population quantities ($N > 1000$), the maximum values are always 17.75% for exposed people and 15.75% for infected people, and the times when these maximums are reached depend on the population value N as shown in Figure 4. The delay between both maximum values is a constant period of 9 days. Additionally, the number of dead people forecasted by this model is about 5.17% of the total population.

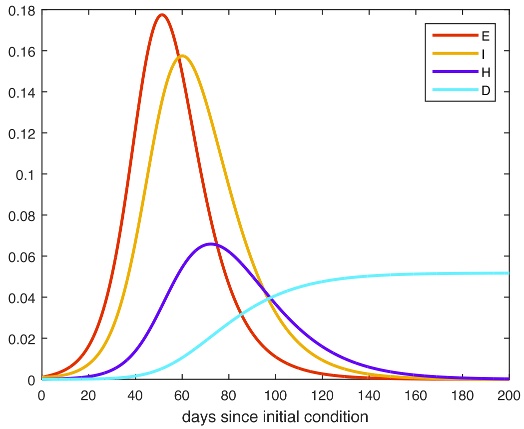

Figure 3. Population of exposed, infected, hospitalized and deaths group with no NPI. Naif scenario.

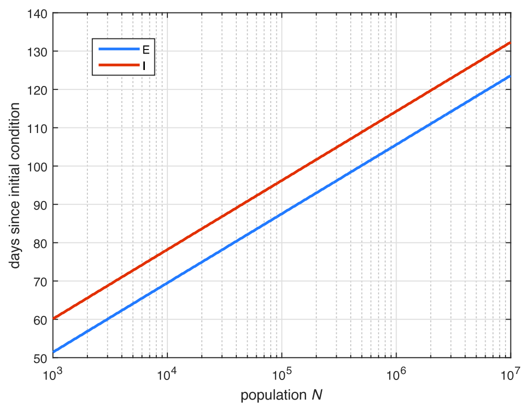

Figure 4. Times when exposed and infected groups reach the maximum values. Naif scenario.

Clearly, this naif scenario seems to be unrealistic since people tend to avoid contact with subjects showing symptoms or diagnosed as positive due to the severity of the COVID-19 disease. In consequence, as we stated before, in a more realistic scenario α is greater than β. In the rest of this paper, we consider $\beta = \alpha / 2$ to take into account this assumption.

Figure 5 is an area plot that shows the quantities of every group as time progresses with no NPIs being taken for illustrative purposes ($\beta = \alpha / 2$).

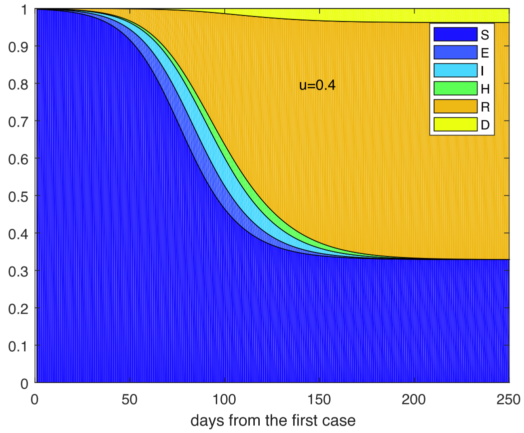

Figure 5. Population of each group with no NPI. $\beta = \alpha / 2$.

Figure 6 shows the evolution of the hospitalized group with different constant intensities of NPIs u and the proposed *SP*. Table 1 reports some results extracted from these simulations.

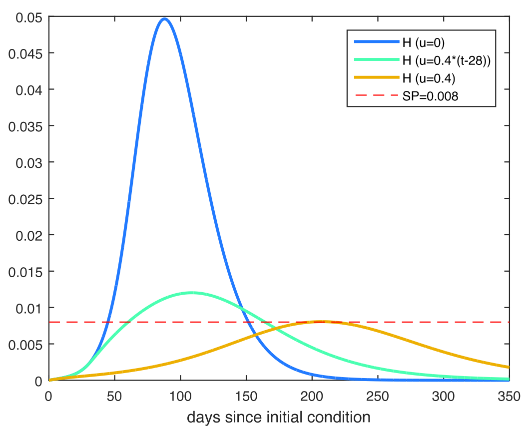

Figure 6. Population of the hospitalized group without NPI (blue), with an NPI of 40% intensity (yellow), with an intervention of 40% intensity applied four weeks after the appearance of the first case (light green) and *SP* (red). $\beta = \alpha / 2$.

	$u = 0$	$u = 0.4$	$u = 0.4$ step $(t - 28)$
final rate of deaths	0.0457	0.01425	0.022
maximum rate of hospitalized	0.0496	0.00801	0.0120
area under the curve u versus t	0	100	88.8

Table 1. Main results of several constant NPIs on the SEIHRD model after 250 days.

The results presented in Table 1 show that if no mitigation policy is adopted ($u = 0$), approximately 81% of the population will be infected and 4.57% will die. On the other hand, a minorly aggressive NPI, only 40% in intensity, is effective in reducing the final number of deaths as well as the maximum number of people hospitalized, which is a crucial issue in order not to collapse the health system (the maximum value of H reaches the SP). Moreover, a late application of this strategy, after more than four weeks since the first case arose, also significantly reduces these numbers.

3.2 A Proportional Controller

In this section, we simulate the behavior of the trajectories described by the normalized system equation (1) subject to a control action proportional to an adequate combination of the process variables. The objective of the control action is that the number of hospitalized people does not exceed the number of available beds. Of course, this number is highly variable in different countries, and can be increased during the duration of the epidemic with the construction of field hospitals, among other resources.

As noted in Section 3, adopting as a feedback variable only the number of hospitalized people H may lead to an overload of the health system in the next 10.6 days, for which a kind of predictive control that considers the number of infected people I must be used. Not all infected people need hospitalization. Most of the symptomatic cases are mild and remain mild in severity ($1 - p_2 = 81\%$) [20, 23]. So we consider that $p_2 = 19\%$ of infected people will need hospitalization in the following $\delta^{-1} = 5.5$ days. This number plus the number of people already hospitalized H must remain below the set point. We neglect the number of beds occupied by patients hospitalized for other diseases.

The proportional control variable proposed is

$$u = k_p\left(1 - \frac{SP - H - p_2 I}{SP - H}\right) \in [0, 1] \tag{5}$$

where k_p is a scalar gain with values between $[0, 1]$.

Note that if $I = 0$, then $u = 0$ and there is no need for public intervention because no one is going to require hospitalization for the next 5.5 days, and with $k_p = 1$, if a percentage of 19% of the infected people equals the number of available beds $SP - H$, then $u = 1$, which means that the public intervention must completely avoid the transmission of the virus because all these people will require hospitalization after $\delta^{-1} = 5.5$ days on average. Another point of view is to consider that this is a tracking trajectory problem, with a time-dependent reference signal equal to $r(t) = SP - H(t)$.

We consider the same initial conditions as those used in the former series of experiments, $I = E = 0.001$; that is, 0.1% of the population infected and presenting symptoms on the first day and 0.1% of the population infected and asymptomatic.

Figure 7 shows the trajectories of the state variables versus time with a gain $k_p = 1$. Note that the number of people hospitalized is always smaller than the set point. Figure 8 shows the control signal versus time.

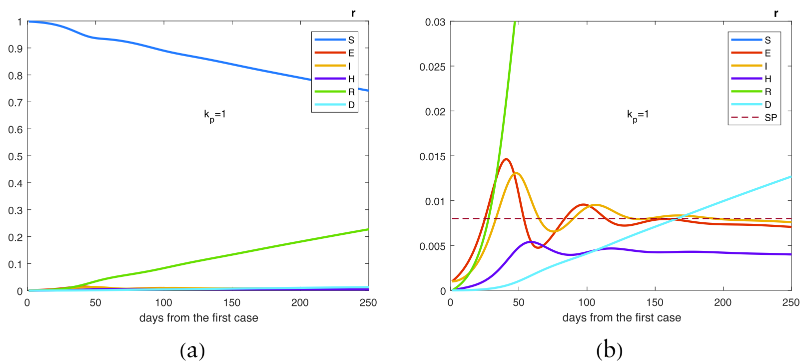

Figure 7. (a) Evolution of every group over time with a proportional control action with gain $k_p = 1$. (b) A zoom of (a). Set point equal to 0.008.

The control signal presents a maximum value of 0.8227, and the area under the curve of the control signal versus time is 98.8829. Notice that the smaller this action, the less the damage to the population and the economy. The constant control signal equal to 0.4 presents an area under the curve equal to 100 and equal to 88.8 when it is applied after four weeks (see Table 1).

We must bear in mind that NPIs are determined by government or popular decisions and hardly can change every day as the control signal calculated by the proportional controller does. Thus, we consider the application of NPIs with the intensity shown in Figure 9. The amplitudes and times of this control signal were obtained from that shown in Figure 8. The criterion used to generate this step-shaped control signal was as follows: when the control signal calculated in equation (5) reaches 80% of the next maximum value, the step-shaped control signal grows up to this maximum value, and when the control signal u decays to 120% of the next minimum value, the step-shaped control signal decreases to that minimum value. The detail of the trajectories of the states presented in Figure 10 shows that there are no significant differences in the results obtained by the controllers. The maximum number of hospitalized people is 0.0057, the final number of deaths is 0.0132, and the area under the curve u versus time is 87.38.

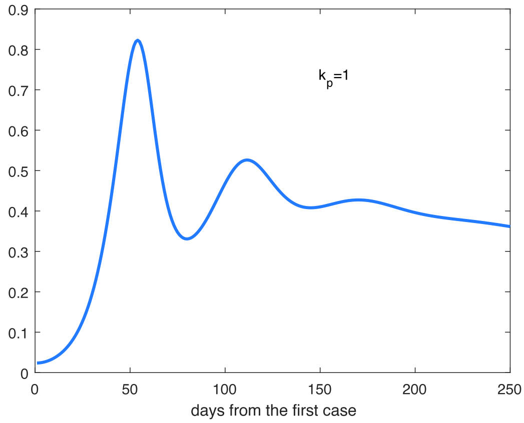

Figure 8. Control signal intensity over time using a proportional controller.

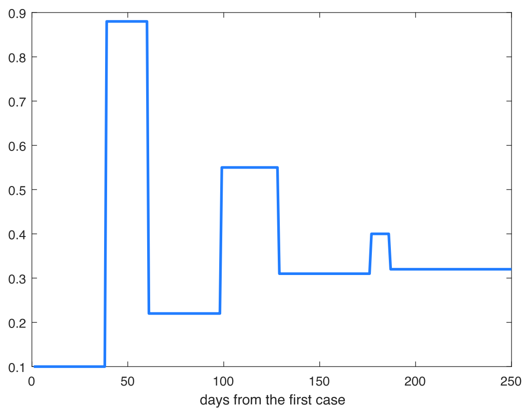

Figure 9. Step-shaped control signal over time using a proportional controller.

https://doi.org/10.25088/ComplexSystems.30.3.323

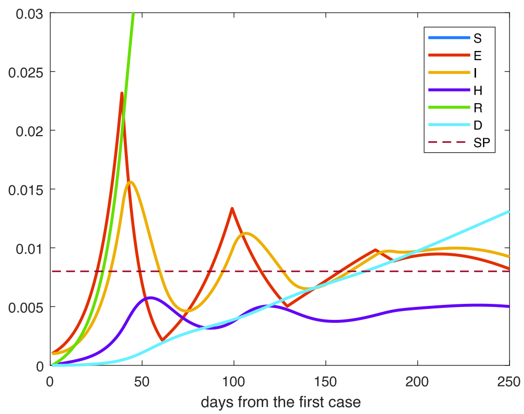

Figure 10. Detail of the trajectories of each state variable using a step-shaped control signal.

Table 2 shows the main results of the application of NPIs calculated using equation (5) with different values of the scalar gain k_p.

	$k_p = 1$	$k_p = 1$(step-shaped u)	$k_p = 0.7$	$k_p = 0.5$
final rate of deaths	0.0127	0.0132	0.0144	0.0157
maximum rate of hospitalized	0.0054	0.0057	0.0064	0.0074
area under the curve u versus t	98.8829	87.38	94.8331	91.2401

Table 2. Main results of several proportional NPIs on the SEIHRD model after 250 days, $SP = 0.008$.

3.3 Simulations with Uncertain Parameters and Considering Some Noncompliance with Nonpharmaceutical Interventions

In this section, we consider the more realistic situation in which the parameters are partially unknown. As mentioned in Section 2, there are large uncertainties in the parameters—they differ a lot according to the references researched and are very different according to the country studied.

In this series of experiments, the parameter α is randomly chosen between 0.15 and 0.6. The parameter β is also randomly chosen between 0.008 and 0.04. The incubation time γ^{-1} is between 2 and 6 days. The probability to present symptoms p_1 is between 40% and 80%. The recovery time is between 14 and 16 days, for both symptomatic and asymptomatic people. The probability to be hospitalized

p_2 is considered as a Gaussian distribution function of mean 0.19 and standard deviation of 0.1. The time to be hospitalized δ^{-1} is chosen to be between 3 and 7 days. The probability to die p_3 is between 10% and 16%. The time to die ϵ^{-1} is between 3 and 12 days. Finally, the recovery time from hospitalization μ^{-1} is randomly chosen to be between 10 and 20 days.

In addition, we also consider that there exists some noncompliance with NPIs. So we apply to equation (1) a control signal with Gaussian distribution of mean 80% of that calculated in equation (5) with standard deviation of 10%; that is, we assume that there is 20% on average noncompliance with the public measures adopted.

The initial conditions are also $I = E = 0.001$ and the gain is $k_p = 1$. Figure 11 shows the trajectories of the states of equation (1) during 250 days since the first symptomatic case arose. Figure 12 shows the control signal versus time. Table 3 reports some results extracted from this series of simulations.

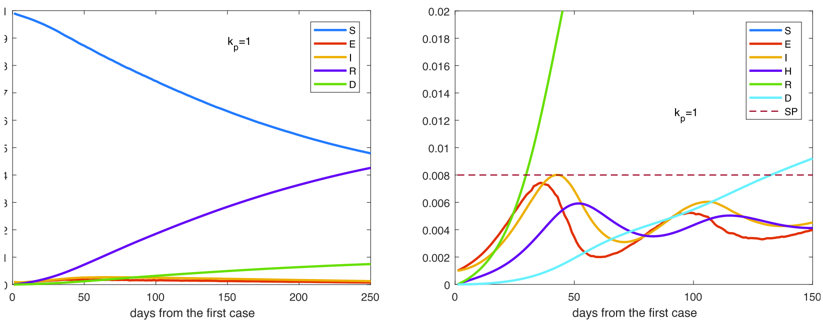

Figure 11. (a) Evolution of every group over time with a proportional control action with gain $k_p = 1$ and considering 20% of noncompliance of the NPIs policies on average. (b) A zoom of (a). Set point equal to 0.008.

	$k_p = 1$	$k_p = 0.7$	$k_p = 0.5$
final rate of deaths	0.0225	0.0248	0.0735
maximum rate of hospitalized	0.0067	0.0076	0.0508
area under the curve u versus t	73.7867	70.8435	77.4710

Table 3. Main results of several proportional NPIs on the SEIHRD model after 250 days considering 20% of noncompliance with the NPIs on average, $SP = 0.008$.

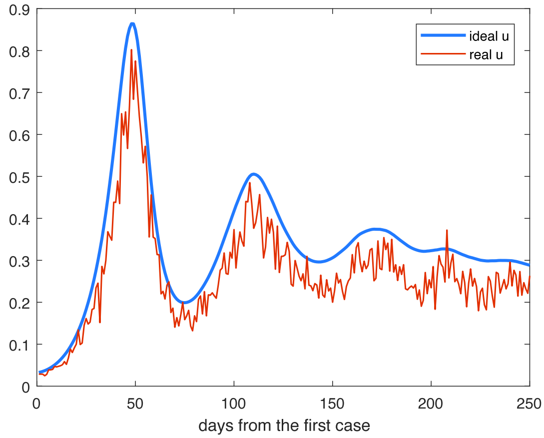

Figure 12. Control signal over time using a proportional controller and considering 20% of noncompliance of the NPIs policies on average. The blue curve is that calculated in equation (5), and the red curve is the control signal considering the random noncompliance.

The similarity of the results reported in Tables 2 and 3, as well as the trajectories shown in Figures 7 and 11, show that the proportional controller is robust to parameter uncertainties and to some noncompliance with the NPIs, which, of course, always occurs in practice.

3.4 Closed-Loop Analysis

In this section we analyze the nonlinear system equation (1) subject to the control action equation (5). Without loss of generality, we consider $k_p = 1$ for simplicity.

We assume as initial conditions $H(0) = R(0) = D(0) = 0$, $I(0) > 0$, $E(0) > 0$, which implies $S(0) = 1 - E(0) - I(0) < 1$. We also consider $p_2 I(0) \ll SP$, and hence $u(0)$ is slightly greater than 0.

All the state equations presented in equation (1) are continuous. If the number of infected people and of the hospitalized people increases until a level such that at a time t_1, $H(t_1) + p_2 I(t_1) = SP$, then $u(t_1) = 1$, which implies $\dot{S}(t_1) = 0$ (with $\nu = 0$) and $\dot{E}(t_1) = -(\gamma p_1 + \zeta(1 - p_1))E(t_1) < 0$.

From equation (3a), $\overline{u}(t_1) = 0$, and from equation (3b), $\dot{\mathbf{x}} = A\mathbf{x}$ at t_1, which is a globally exponentially stable linear system according to the analysis made in Section 2.1 (all its eigenvalues are strictly negative real numbers). As $\dot{E}(t_1) < 0$, due to the lower triangular structure of the matrix A, which has the entries on its main diagonal strictly negative and the entries on the lower subdiagonal non-negative, it yields that the other two components of the vector $\dot{\mathbf{x}}$, $\dot{I}(t_1)$ and $\dot{H}(t_1)$ are strictly negative. Hence, $H(t) + p_2 I(t)$ does not increase above SP for all $t > 0$.

With this result, we formulate the following lemma.

Lemma 1. In the nonlinear system equation (1) subject to the control action equation (5), with the initial conditions $H(0) = 0$, $p_2 I(0) \ll SP$, the signal $H(t) + p_2 I(t) \leq SP$ for all $t > 0$.

4. Conclusion

The proportional controller proposed to guide the adoption of non-pharmaceutical interventions (NPIs) showed its efficiency to keep the number of hospitalized people below a set point given by the health system capacity. Moreover, this very simple strategy is robust to uncertain parameters and to some level of noncompliance with public measures.

The control signal calculated by this method aims to guide the adoption of NPIs in order to minimize the social impact and the economic damages.

As an example, recently the Argentine government relaxed some restrictions adopted in the quarantine period, allowing more economic and recreational activities in some cities. The only criterion used to adopt this measure was the number of days in which the number of infected people doubled (the so-called doubling time). Even though this decision also can be considered as a closed-loop control action, the criterion adopted is a little improvised.

An open question is how to translate the rate of intensity of the NPIs calculated by the controller into concrete actions adopted by governments or public health authorities. Moreover, we must bear in mind that these measures cannot be continuously varied along the time parameter, as the control signal is, but they are decisions that should remain valid for at least a few days. However, although this issue is beyond the scope of this paper, some decisions can be adjusted every day, for example, the number of individuals with permission to leave their homes or the number of people allowed to enter a store, as suggested by the computed control effort equation (5).

Finally, as mentioned in Section 3, it is not possible to find an analytical solution of equation (4). However, the problem can be focused on a nonlinear programming one, where the objective function is subject to the dynamics of the nonlinear system, among other additional constraints such as $H < SP$, for example. The values of the state variables that minimize the objective function over the considered time horizon can be calculated by a suitable solver, as proposed in [25], in order to obtain the value of the control signal at each instant of time. This research is proposed as a future project.

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References

[1] Worldometer. "COVID-19 Coronavirus Pandemic." (May 6, 2021) www.worldometers.info/coronavirus.

[2] N. M. Ferguson, D. Laydon, G. Nedjati-Gilani, N. Imai, K. Ainslie, M. Baguelin, S. Bhatia, et al., "Report 9: Impact of Non-pharmaceutical Interventions (NPIs) to Reduce COVID19 Mortality and Healthcare Demand," Imperial College, London, UK, Technical Report, 2020. doi:10.25561/77482.

[3] W. O. Kermack and A. G. McKendrick, "A Contribution to the Mathematical Theory of Epidemics," *Proceedings of the Royal Society of London. Series A, Containing Papers of a Mathematical and Physical Character*, **115**(772), 1927 pp. 700–721. doi:10.1098/rspa.1927.0118.

[4] The World Bank. "Death Rate, Crude (per 1000 People) - Argentina. (May 18, 2021)
data.worldbank.org/indicator/SP.DYN.CDRT.IN?end=2019&locations=AR&start=1960&view=chart.

[5] Q. Lin, S. Zhao, D. Gao, Y. Lou, S. Yang, S. S. Musa, M. H. Wang, et al., "A Conceptual Model for the Coronavirus Disease 2019 (COVID-19) Outbreak in Wuhan, China with Individual Reaction and Governmental Action," *International Journal of Infectious Diseases*, **93**, 2020 pp. 211–216. doi:10.1016/j.ijid.2020.02.058.

[6] P. V. Savi, M. A. Savi and B. Borges, "A Mathematical Description of the Dynamic of Coronavirus Disease 2019 (COVID-19): A Case Study of Brazil," *Computational and Mathematical Methods in Medicine*, **2020**, 2020 9017157. doi:10.1155/2020/9017157.

[7] Z. Liu, P. Magal, O. Seydi and G. Webb, "A Model to Predict COVID-19 Epidemics with Applications to South Korea, Italy, and Spain," *Siam News*, May, 2020. sinews.siam.org/Details-Page/a-model-to-predict-covid-19-epidemics-with-applications-to-south-korea-italy-and-spain.

[8] J. Kantor, "Modeling and Control of a Campus COVID-19 Outbreak." (May 6, 2021).
github.com/jckantor/covid-19/blob/master/COVID-19.ipynb.

[9] J. M. Gutiérrez and J. L. Varona, "Análisis del COVID-19 por medio de un modelo SEIR," Universidad de Sevilla, Sevilla, Spain, Technical Report, Mar, 2020.
institucional.us.es/blogimus/2020/03/covid-19-analisis-por-medio-de-un-modelo-seir.

[10] G. Stewart, K. van Heusden and G. A. Dumont, "How Control Theory Can Help Us Control COVID-19," *IEEE Spectrum*, Jul 2020.
spectrum.ieee.org/biomedical/diagnostics/how-control-theory-can-help-control-covid19.

[11] I. Abdulrahman, "SimCOVID: An Open-Source Simulation Program for the COVID-19 Outbreak." medRxiv 2020.04.13.20063354.
doi:10.1101/2020.04.13.20063354.

[12] B. Tang, N. L. Bragazzi, Q. Li, S. Tang, Y. Xiao and J. Wu, "An Updated Estimation of the Risk of Transmission of the Novel Coronavirus (2019-nCov)," *Infectious Disease Modelling*, **5**, 2020 pp. 248–255. doi:10.1016/j.idm.2020.02.001.

[13] G. Giordano, F. Blanchini, R. Bruno, P. Colaneri, A. D. Filippo, A. D. Matteo and M. Colaneri, "Modelling the COVID-19 Epidemic and Implementation of Population-Wide Interventions in Italy," *Nature Medicine*, **26**, 2020 pp. 855–860. doi:10.1038/s41591-020-0883-7.

[14] M. Sadeghi, J. M. Greene and E. D. Sontag, "Universal Features of Epidemic Models under Social Distancing Guidelines." bioRxiv.
doi:10.1101/2020.06.21.163931.

[15] F. Pazos and F. E. Felicioni, "A Control Approach to the COVID-19 Disease Using a SEIHRD Dynamical Model," medRxiv
2020.05.27.20115295. doi:10.1101/2020.05.27.20115295.

[16] F. Pazos and F. E. Felicioni, "A Control Approach to the COVID-19 Disease Using a SEIHRD Dynamical Model," in *Proceedings of the 23rd Brazilian Conference on Automatic Control*, **2**(1), Santa Maria, RS, Brazil, 2020. Sociedade Brasileira de Automática, 2020.
doi:10.48011/asba.v2i1.1002.

[17] Y. Liu, A. A. Gayle, A. Wilder-Smith and J. Rocklöv, "The Reproductive Number of COVID-19 Is Higher Compared to SARS Coronavirus," *Journal of Travel Medicine*, **27**(2), 2020 taaa021.
doi:10.1093/jtm/taaa021.

[18] J. H. Jones, "Notes on $\mathcal{R}_0$," Earth Systems 214: Environmental Change and Emerging Infectious Disease, Stanford University, 2019. (May 18, 2021)
web.stanford.edu/class/earthsys214/notes/Jones_R0_notes2019.pdf.

[19] World Health Organization. "Coronavirus Disease 2019 (COVID-19) Situation Report–30." www.who.int/docs/default-source/coronaviruse/situation-reports/20200219-sitrep-30-covid-19.pdf?sfvrsn=3346b04f_2.

[20] S. Sanche, Y. T. Lin, C. Xu, E. Romero-Severson, N. Hengartner and R. Ke, "The Novel Coronavirus, 2019-nCov, Is Highly Contagious and More Infectious Than Initially Estimated." medRxiv 2020.02.07.20021154. doi:10.1101/2020.02.07.20021154.

[21] T. K. Tsang, P. Wu, Y. Lin, E. H. Y. Lau, G. M. Leung and B. J. Cowling, "Effect of Changing Case Definitions for COVID-19 on the Epidemic Curve and Transmission Parameters in Mainland China: A Modelling Study," *The Lancet Public Health*, **5**(5), 2020 pp. E289–E296. doi:10.1016/S2468-2667(20)30089-X.

[22] K. Mizumoto, K. Kagasha, A. Zarebski and G. Chowell, "Estimating the Asymptomatic Proportion of Coronavirus Disease 2019 (COVID-19) Cases on Board the Diamond Princess Cruise Ship, Yokohama, Japan, 2020," *Eurosurveillance*, **25**(10), 2020 pii=2000180. doi:10.2807/1560-7917.ES.2020.25.10.2000180.

[23] M. Lowth, "Coronavirus: What Are Asymptomatic and Mild COVID-19?" *Patient*, March 2020. patient.info/news-and-features/coronavirus-what-are-asymptomatic-and-mild-covid-19.

[24] C.-T. Chen, *Linear System Theory and Design*, 3rd ed., New York: Oxford University Press, 1999.

[25] M. D. Canon, C. D. Cullum Jr. and E. Polak, *Theory of Optimal Control and Mathematical Programming*, New York: McGraw-Hill, 1970.