Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Research article

Non-pharmaceutical intervention to reduce COVID-19 impact in Argentina

Demián García-Violiña, Ricardo Sánchez-Peña b,d,*, Marcela Moscoso-Vásquez b,d, Fabricio Garellic

a Departamento de Ciencia y Tecnología, Universidad Nacional de Quilmes, Roque Sáenz Peña 352, B1876BXD, Bernal, Buenos Aires, Argentina
b Centro de Sistemas y Control, Instituto Tecnológico de Buenos Aires, Av. Eduardo Madero 399, C1106, CABA, Argentina
c Group of Control Applications, LEICI, Universidad Nacional de La Plata, Calle 48 y 116, CC 91 (1900), La Plata, Buenos Aires, Argentina
d CONICET, Argentina

A B S T R A C T

This work is focused on the multilevel control of the population confinement in the city of Buenos Aires and its surroundings due to the pandemic generated by the COVID-19 outbreak. The model used here is known as SEIRD and two objectives are sought: a time-varying identification of the infection rate and the inclusion of a controller. A control differential equation has been added to regulate the transitions between confinement and normal life, according to five different levels. The plasma treatment from recovered patients has also been considered in the control algorithm. Using the proposed strategy the ICU occupancy is reduced, and as a consequence, the number of deaths is also decreased.

© 2021 ISA. Published by Elsevier Ltd. All rights reserved.

1. Introduction

The epidemiological outbreak of the novel coronavirus disease 2019 (COVID-19), as named by the World Health Organization on 11 February 2020 [1], has arisen during December 2019 in Wuhan, the Chinese city located in the province of Hubei, of 11 million people. Thus, since the detection of the first COVID-19 cases, the outbreak has turned into a global health crisis with more than 12 million infected and half a million deaths worldwide to date [1]. Within this context, considering that vaccines or other pharmaceutical interventions have not yet been developed to mitigate the disease expansion, the majority of countries have considered social distancing as the unique response to contain and positively deal with the pandemic growth. Essentially, social distancing prevents the saturation of the health systems due to a large amount of COVID-19 patients simultaneously requiring medical care. The first global experience of social distancing implementation, through lockdown policies was on January 23, when residents of Wuhan were ordered to stay indoors for an indefinite time. After that day, each country has applied lockdown policies with different characteristics depending on several local and political factors.

Within the literature, several mathematical models have been considered to study the dynamics, causes, and key factors of pandemic outbreaks, and also used to forecast the spreading trend of diseases [3]. Thus, with the aim of efficiently administrate lockdown interventions, widely studied classical epidemiological models [4,5], have been immediately considered and adapted to the COVID-19 case to obtain reliable estimates of its epidemiological characteristics, such as the transmission dynamics. Thus, as soon as the COVID-19 outbreak appeared, some mathematical models have been proposed to describe its dynamics from different points of view. For example, the epidemiological description for the Chinese case has been addressed by Tang et al. [6] and He et al. [7] using classical discrete compartmental models, essentially based on Binomial and Poisson probability distributions, which appeared as extensions of the well-known SIR model [3]. In addition, the Chinese case has been also studied by Lin et al. [8], using a deterministic SIR-based approach. Similarly, the Japanese case has been also addressed by Kuniya [9] using a SEIR model, which is fitted using a recursive least mean square approach. Using the estimation approach presented by Kuniya [9], the case of the Metropolitan Area of Buenos Aires (AMBA), depicted in Fig. 1, which includes the city of Buenos Aires and 40 neighboring cities, has been addressed using mobility information to daily adapt the model by Tagliazucchiet al. [10], using a SEIR-based model considering mild, moderate, and hospitalized individuals. In addition, a detailed discussion about epidemiological models...
and their main features (stochastic or deterministic, discrete or continuous-time, etc.) has been provided by Tagliazucchi et al. [10] for the AMBA case, from a precise mathematical perspective.

The first infected case in Argentina, was reported on March 3, imported by a passenger traveling to Buenos Aires from Milan, Italy [11], one of the main European epicenters of the pandemic [1], while the first death was on March 7. Considering the Chinese and European experiences, to prepare the health system before a local outbreak, Argentina applied a hard lockdown on March 20. During the following months, even though the lockdown intervention was extended, five different phases were used to adapt this measure to the evolution and requirements of each region across the country. However, despite the efforts made by the government to anticipate the events, to date (mid-July) Argentina has reported more than 1,700 deaths and 90,000 infected cases [1]. The AMBA region is presently the local epicenter of the pandemic, containing more than 91% of the cases of the country in an area that represents only 0.14% of Argentina's surface [11].

Within this framework, using the possibility provided by mathematical models, control systems and dynamic strategies play a decisive role in defining efficient lockdown policies. The management of these interventions together with strategies that aid in reducing, for example, the disease growth, social fatigue, and the negative economical impact of the lockdown protocols, can be efficiently improved using control theory. Considering the recent literature of control theory applied to the COVID-19 case, Casella [12] challenges the applicability of control strategies based on daily reports, from a theoretical control perspective, and, at the same time, proposes a control methodology. Based on the dynamical features of the COVID-19 problem, optimization based control strategies, such as model predictive control (MPC), have been presented for the Brazilian [13], French [14], and German [15] cases. Particularly, Köhler et al. [15], considering model uncertainty, tackles the problem from a robust control point of view [16,17] to extend the applicability of the control strategy to a more realistic case. Optimal control strategies are beginning to be explored for the Argentinian case [18]. However, there is no application of an automatic control methodology that addresses the COVID-19 problem for Argentina.

Based on the work presented by Morato et al. [13], in this study a control algorithm is proposed for the AMBA case, while a SEIRD model is fitted using actual Argentine data to design a realistic control strategy. Particularly, the control law presented here has the purpose of minimizing the intensive care unit (ICU) occupancy and is based on two control actions: alternation between different lockdown levels and the reduction of critically infected patients using plasma donation from recovered ones. The reduction of the ICU occupancy is the main performance objective, although as a consequence, a significant reduction in the number of deceased is also achieved. It is important to note that, in terms of the real applicability of control strategies for the COVID-19 problem, the control methodology presented in this work considers the already implemented lockdown phases. Consequently, the control law proposed in this study is based upon several discrete levels of actuation, which are intrinsically linked to the severity of the different phases considered in lockdown interventions. Within this context, the inclusion of the ICU occupancy as a control objective, the consideration of the effect of plasma donation therapy, the discrete levels of actuation, as well as the adaptive estimation of the main epidemic model parameter, are worth highlighting. Additionally, a precise stability analysis for the control strategy presented in this study is provided using classical results from polytopic linear parameter varying (LPV) systems.

This work has been submitted on July 21st, 2020, and the data from which the model and controller have been designed was updated to July 7th. In all cases, as mentioned before, the data considered in this study has been taken from the reports provided by the corresponding official health authorities. The model estimation and control methodology presented here, even though constrained to the AMBA case, can be adapted to diverse dynamical epidemiological situations and different countries, as shown for AMBA-Argentina and Spain. Additionally, to date, it is worth noting that the epidemiological situation for the AMBA case has not been studied in detail, beyond the results presented by Tagliazucchi et al. [10]. Here, an innovative approach is presented in terms of parameter estimation, system identification, and control methodologies, which aims to efficiently regulate the policies adopted by the Argentinian government to mitigate the pandemic spread. In addition, it should be noted that this methodology can be straightforwardly extrapolated to other regions with even different periods.
The remainder of this work is organized as follows. Section 2 articulates the basics of epidemiological models most commonly used in the literature to describe the COVID-19 phenomenon. The model identification approach is described in Section 3. Additionally, in Section 3, using real data the identified model is validated. Section 4 analyzes the impact of urban mobility changes on the pandemic spread in the AMBA region. The main core of the control strategy proposed in this study is contained in Section 5. In Section 6 the application of the proposed controller is assessed and validated using empirical data. Finally, conclusions on the overall application of the proposed controller are provided in Section 7.

2. Epidemiological models

As evidenced from recent literature [8,12,13], the evolutionary dynamics of the COVID-19 pandemic can be adequately described using well-known SIR models that account for susceptible (S), infected (I), and recovered (R) individuals [4]. In this work, two SIR-model extensions are used, considering exposed (SEIR) and deceased (SEIRD) individuals.

2.1. Parameter definitions

\( N \) Total population

\( N_{ICU} \) Number of intensive care units

\( S \) Individuals susceptible to becoming infected

\( E \) Exposed individuals, infected without symptoms yet

\( I \) Infected individuals

\( R \) Removed in SEIR and Recovered individuals in SEIRD.

\( D \) Deceased individuals

\( \beta \) likelihood of infection per unit time (1/day)

\( \gamma \) inverse of the average time infectious individuals can infect others

\( \epsilon \) inverse of the average latency time

\( \rho \) probability of an infected individual to die before recovery

\( \psi \) control signal

\( \mu \) proportion of ICU occupancy

\( \alpha_{off} \) settling-time to leave lockdown

\( \alpha_{on} \) settling-time to start lockdown

\( \sigma_p \) fraction of plasma donation that recovers near-to-critical patients and reduces ICU occupation

\( \sigma_{ICU} \) fraction of infected patients that need medical attention in the ICU

\( 1 \) In SEIR, \( R \) stands for Removed.

2.2. SEIR and SEIRD models

The first SIR model extension is the SEIR model, which includes the group of Exposed individuals as an additional state. In this case, the population balance should be maintained as \( S(t) + E(t) + I(t) + R(t) = N \forall t \geq 0 \), hence \( R \) stands for Removed. The model equations are:

\[
\begin{align*}
\dot{S}(t) &= -\frac{\beta I(t)S(t)}{N} \\
\dot{E}(t) &= -\epsilon E(t)\\
\dot{I}(t) &= \epsilon E(t) - \gamma I(t)\\
\dot{R}(t) &= \gamma I(t)
\end{align*}
\]

Next, following the inclusion of the variable \( D(t) \) of deceased individuals as made by Morato et al. [13], the SEIRD model is expressed as:

\[
\begin{align*}
\dot{S}(t) &= -\frac{\beta I(t)S(t)}{N} \\
\dot{E}(t) &= -\epsilon E(t)\\
\dot{I}(t) &= \epsilon E(t) - \frac{\gamma}{1-\rho} I(t)\\
\dot{R}(t) &= \gamma I(t)\\
\dot{D}(t) &= \frac{\rho}{1-\rho} \gamma I(t).
\end{align*}
\]

with \( N = S(t) + E(t) + I(t) + R(t) + D(t) \forall t \geq 0 \), and here \( R \) stands for Recovered.

Particularly, considering the number of patients in hospitals \( H \), the mild infected \( J \), and the incoming travelers \( F \), the SEJIHR model has been proposed and validated by Tagliazucchi et al. [10] for the AMBA case using official data. In the approach used by Tagliazucchi et al. [10], the parameter \( \beta \) is adapted using cell phone mobility data to account for population interaction. However, given the observed difference between the number of cell phones and the total population, additional information besides the mobility data is required to analytically adapt the SEJIHR model [10].

Regarding the SIR and SEIRD model features, some advantages and disadvantages of each model can be discussed. On one hand, the main advantage of the SEIRD model is its capability of describing infections where there is a significant incubation period during which individuals have been infected but have not been officially detected as infected individuals yet. During this period, the individual is in compartment \( E \) and could be capable of transmitting the infection. Thus, the inclusion of the compartment \( E \) essentially distinguishes the SEIRD from the SIR model. Furthermore, the added compartment \( D \) allows the model to differentiate between recovered and deceased individuals, in contrast to the SIR model where recovered and dead individuals are considered as removed. On the other hand, some features of the SEIRD model that can be mentioned as disadvantages can also be discussed. Firstly, the addition of compartments, i.e. \( E \) and \( D \), requires knowledge of additional system parameters. However, throughout the epidemiology literature [5], model parameters are generally considered constant, except for the contagion rate, \( \beta(t) \), which simplifies the use of the model. In addition, the model parameters have been consistently estimated by Qin et al. [19], for example. Secondly, accurate modeling on, for example, hospitalization conditions, death situation, or intensity of infection, cannot be achieved with the SEIRD model. For those situations where a more precise epidemiology description is required, an
extended class of compartmental epidemiology models is available, as the ones considered by He et al. [7] or Tagliazucchi et al. [10], more focused on modeling rather than control. However, the purpose of this study is widely covered by the considered SEIRD model, since an accurate estimate of infected and hospitalized in intensive care units (ICUs) individuals are obtained using only the available official data provided by the local health authority. Thus, the model allows for a control-oriented epidemiology estimation and, consequently, forecasting. Therefore, from a control perspective, the high fidelity estimation achieved with the SEIRD model can be mentioned as an additional advantage.

Finally, it should be taken into account that, beyond the particular model, this study essentially provides a methodological procedure for system identification and control of epidemiological problems. Thus, this procedure does not strictly depend on the model nor the particular epidemiological case. Consequently, the model could be replaced by another one according to a specific epidemiological situation, while the proposed methodology can be applied straightforwardly following the sequence presented in the following sections.

## 3. Identification and validation

The epidemiology models are shown in Eqs. (1) and (2) can be well described considering mostly constant parameters which are determined from particular disease features, such as the average latency or recovery times. Nevertheless, parameter $\beta$ in Eqs. (1) and (2) depends on several time-dependent factors, although based on certain assumptions it can be considered constant. The approaches considering $\beta$ constant are useful for short-term descriptions, but as a time-dependent coefficient, the model has a better fit of the empirical data (as evidenced in the works of Podduck et al. [11]). Moreover, in Eq. (2) (second line), the fixed optimization domain $(1 - \delta)\beta_{k-1} \leq \beta \leq (1 + \delta)\beta_{k-1}$ is defined to reduce the computational effort using the variation rate of $\beta(t)$ to empirically determine $\delta$. Particularly in this study, $\delta = 0.2$ is used for $k \geq 1$, while the fixed optimization range $\beta \in [0, 5]$ is considered for $k = 0$ to search over an extended range and avoid the use of an initial condition $\beta_0$. Note that, if an initial $\beta_0$ is used, for example, $\beta_0 = 0.22$ as considered by Tagliazucchi et al. [10], the optimizer in Eq. (3) would develop a trajectory for $\beta(t)$ which intersects the optimal paths (depending on $w_i$) shown in Fig. 3.

The estimation of $\beta(t)$ is carried out considering the period between March 3, when the first infected case was detected, and July 7. Real data of active infected, $I(t)$, totally removed (total recoveries plus deaths), $R(t)$, and accumulated infected cases, $I(t) + R(t)$, reported by MINSAL [11] are used for validation. The results of the estimation of $\beta(t)$, for $w_i = 5$, 10, and 20, are shown using solid, dashed, and dotted black lines, respectively, in Fig. 3. It is worth highlighting that all the key government interventions, for example, the first lockdown implementation on March 19, can be noted in Fig. 3.

The results shown in Fig. 3 were obtained using a $\gamma = 1/36$, which was empirically tuned focusing on the estimation-matching between real and estimated data ($\hat{I}(t)$ and $\hat{R}(t)$). Note that, even though the strict meaning of the $\gamma$ coefficient represents the transition rate from infected to recovery or removed (depending on the model), the value can be tuned using experimental data to represent a realistic case. It is important to highlight that, although different values for $\gamma$ have been considered in the literature [8,9], $\gamma$ is generally deemed constant and, to obtain a model which describes the experimental measurements, $\beta(t)$ is estimated as a time-dependent coefficient in different ways.

In addition, Figs. 4(a)–(c) show the comparison between real cases ($I(t)$ and $R(t)$, dashed lines) and, estimated cases ($\hat{I}(t)$ and $\hat{R}(t)$, solid lines) considering Eq. (1) for $w_i = 5$, 10, and 20, respectively. The active infected cases ($I(t)$ and $\hat{I}(t)$), the total removed cases ($R(t)$ and $\hat{R}(t)$) and the total accumulative cases ($I(t) + R(t)$ and $\hat{I}(t) + \hat{R}(t)$) are depicted with triangular, square, and circular markers, respectively. The obtained matching between real and estimated data is worth highlighting, for all $w_i$ considered. It can be noted that, in Fig. 3, the use of a wider moving window, $w_i = 20$, acts as a low-pass filter in the estimation of $\beta(t)$. Conversely, the utilization of $w_i = 5$ allows for achieving higher fidelity estimations (Fig. 4(a)), while the obtained $\beta(t)$, in Fig. 3, shows a higher frequency-changing rate.

Finally, for the sake of validation and comparison between cases of different countries, the $\beta(t)$ estimation results for the AMBA and Spanish cases using a $w_i = 5$ are shown in Fig. 5. It is important to highlight that, even though the results in Fig. 5 are obtained considering the first infected case for both AMBA and
Fig. 3. $\beta(t)$ estimation results for $w_L = 5$ (solid), $w_L = 10$ (dashed), and $w_L = 20$ (dotted) for the AMBA case between March 3 and July 7.

Fig. 4. Estimation of active infected, removed and accumulative infected cases for (a) $w_L = 5$, (b) 10, and (c) 20, for the AMBA case between March 3 and July 7. The active infected, removed, and accumulative cases are depicted with triangular, square, and circular markers, respectively. The real ($I(t)$ and $R(t)$) and estimated ($\hat{I}(t)$ and $\hat{R}(t)$) data are depicted with dashed and solid lines, respectively.

Spain, the estimation analysis is performed within the period in which the Spanish recovery cases were available (until May 18 when the Ministry of Health of Spain has stopped providing the recovery cases [21]). In Figs. 5(a) and (b), with the same reference code used in Fig. 4, active infected ($I(t)$ and $\hat{I}(t)$), removed ($R(t)$ and $\hat{R}(t)$), and accumulative cases ($I(t) + R(t)$ and $\hat{I}(t) + \hat{R}(t)$) are depicted with triangular, square, and circular markers, respectively. In addition, in Figs. 5(a) and (b), the real ($I(t)$ and $R(t)$) and estimated ($\hat{I}(t)$ and $\hat{R}(t)$) data are depicted with dashed and solid lines, respectively. Additionally, in Fig. 5(c) the results of the estimation of $\beta(t)$ for the AMBA and Spanish cases are depicted using black-dashed and black-solid lines, respectively.

Fig. 5(a) shows that the initial increase experienced by Spain is significantly higher than the one for the AMBA, shown in Fig. 5(b). From the comparison of Figs. 5(a) and (b), it is important to note the order of magnitudes of the AMBA and Spanish cases ($10^3$ for
In increasing mobility after the implementation of Phase-2, and the reduction in mobility is not as drastic as on March 19. A lockdown was reinstated and is effectively followed by an increasing trend on infected individuals (Fig. 5), the hard Phase-2 social lockdown relief measures increasing the number of activities excepted from the lockdown are indicated by the vertical dashed lines.

4. Impact of mobility on COVID-19 dynamics

To further validate the relation observed on the estimation of $\beta(t)$ and the lockdown measures, Fig. 6 presents the relative variations of mobility on AMBA region, $m(t)$, from mid-February to July 7th and the estimation of $\beta(t)$ obtained using $w_l = 5$. Furthermore, for the sake of comparison and clarification, $m(t)$ and the estimation of $\beta(t)$ are depicted in Fig. 6 using dotted-purple and solid-black lines, respectively. Relative mobility data were obtained from Google LLC [22] for Buenos Aires city (CABA) and Buenos Aires province (PBA) since there is not an available specific set of mobility data for the AMBA region. However, considering that the AMBA is the industrial and financial area of the PBA and contains 80% of its population, mobility data for PBA and CABA can be considered as a good approach to the mobility data corresponding to the AMBA region, mainly for this study.

Fig. 6 shows the impact on the mobility of the government measures. Firstly, a reduction of the citizen’s mobility is observed as an immediate consequence of the lockdown initial date on March 19, which represented the first phase of the Argentinian lockdown. A gradual decline is observed before this date as a response to the “Quedate en casa” (“Stay at home”) campaign, promoted by the government on March 11 as cases began to rise in the country. Circulation begins to recover as the lockdown phase changes (Phase 2 from early April, and Phase 3 from early May). This trend continues after AMBA remains in Phase 3, but more sectors return to activity with the government’s approval after mid-May as social lockdown relief measures. However, given the rising trend on infected individuals (Fig. 5), the hard Phase-1 lockdown was reinstated and is effectively followed by an attenuation on the previous increasing mobility. Here, regardless of being deemed by the government as a return to Phase-1, more exceptions are still applicable concerning the original Phase-1, and the reduction in mobility is not as drastic as on March 19. This same drastic reduction is observed in $\beta(t)$ after Phase-1, which supports the previous observation on its correlation with the lockdown measures. This decay is then slowed down by increasing mobility after the implementation of Phase-2.

It is important to note that, even though the increasing trend of mobility throughout the different phases of the lockdown applied in AMBA, social awareness and knowledge related to the COVID-19 contagion and prevention have also been increased. Then, as long as the mobility has increased the application of new measures as, for example, the use of face masks, hand sanitizer, or even social distancing have been adopted, which positively compensate the negative impact of the mobility.

However, even though the time-varying coefficient $\beta(t)$, which depends on many factors, globally represents the general contagion rate of the total population, mobility can be considered as one of the main drivers directly affecting it. Thus, to provide a better insight into the existing link between the resulting estimation of $\beta(t)$ shown in Fig. 3, and the global relative mobility $m(t)$ depicted for the AMBA case in Fig. 6 with a dotted-purple line, a cross-correlation analysis is provided in this study. To this end, the estimation of $\beta(t)$ is obtained using a $w_l = 5$, while the analysis is performed in the period contained between days 30 and 110. Note that, within the mentioned analysis period, both $\beta(t)$ and $m(t)$ describe a steady-state behavior, given that the transient response, generated by the first lockdown intervention, vanished before the thirteenth day, as can be noted in Fig. 6. For the analysis, the following function is considered:

$$\bar{x}(t) = \frac{x(t) - x_i(t)}{\max \{x(t) - x_i(t)\}}, \quad (4)$$

where $t \in [30, 110]$, $x(t)$ represents $\beta(t)$ or $m(t)$, $x_i(t)$ represents the linear trend of $x(t)$, which is obtained using standard curve fitting techniques based on least-mean squares, and finally, to compensate the different variation ranges of $\beta(t)$ and $m(t)$, a maximum value normalization is applied to define $\bar{x}(t)$. Note that, considering Eq. (4), $\max \{x(t)\} = 1$, and the maximum is always reached in the domain. Additionally, it is worth highlighting that the increasing linear trend $m_i(t)$ can be seen in Fig. 6, where $m(t)$ is indicated with a purple-dotted line. Then, a cross-correlation analysis between $\beta(t)$ and $m(t)$, which is computed as:

$$R(m(t), \beta(t)) = \int_{-\infty}^{\infty} m(t)\beta(t + \tau)d\tau, \quad (5)$$

is performed. In Fig. 7(a) and (b), the results of the cross-correlation (5) and the normalized variables $\bar{m}(t)$ and $\bar{\beta}(t)$ in (4) are shown, respectively. In Fig. 7(a), the cross-correlation result is depicted with a solid-black line. Here, the null hypothesis
of no correlation between $\bar{m}(t)$ and $\beta(t)$ was tested, obtaining a $p$-value of $p = 0.002$, thus meaning that both signals are significantly correlated with a confidence level of 95%. In addition, from the cross-correlation analysis the obtained lag ($\tau = d_2 - d_1$) between these two variables, and consequently between $\beta(t)$ and $m(t)$, is approximately between 5 and 7 days, which is marked in Fig. 7(a) with a shadowed blue area.

It is important to highlight that the obtained lag between $\beta(t)$ and $m(t)$ matches the latency period of the disease $1/\epsilon$, i.e., the time between the infection and its detection as considered for the model identified in Section 3. In addition, in Fig. 7(b), the normalized mobility $\bar{m}(t)$, the normalized $\beta(t)$, and a shifted version of the normalized $\beta(t)$, $\beta(t - 6)$, are depicted using dotted-purple, dashed-gray, and solid-black lines, respectively. Furthermore, in Fig. 7(b) using the same reference code as in Fig. 6, the application of the second and third lockdown phases are indicated using orange and yellow lines with star markers. Note that all the lockdown and lockdown-like interventions applied by the Argentinian government have been precisely detailed in Fig. 6. Finally, from the overall behavior shown in Fig. 7(b), the existing link between the estimation of $\beta(t)$ and the mobility $m(t)$ has been quantified.

The results shown in Fig. 7(b) indicate the presented high correlation and causal relationship between mobility and the contagion rate. Thus, the mobility, using the results in Fig. 7(b), is proven to be an effective social intervention to control the contagion rate and, consequently, the number of infected cases, which generally represents one of the main control objectives. By way of example, from the comparison of the events considered by the Argentinian government to affect social mobility, indicated in both Figs. 6 and 7, it can be seen that these actions, like the one indicated on day 63, directly impact the contagion rate $\beta$ with a lag of 6 days, which is in the order of the incubation time [19].

5. Control algorithm

The proposed control algorithm seeks the minimization of the ICU occupancy and is based on two control actions: alternating between different lockdown levels and the reduction of critically infected patients employing plasma donation from recovered ones. Following this main performance objective, a significant reduction in the number of deceased people can be achieved. It is important to take into account that there is already a control procedure carried out by the government. It is far better than continuing with normal living conditions, but it can also be improved. Here, the control algorithm proposed acts over the present situation, which can be sensed through the time-varying $\beta(t)$ computed in Section 3. Therefore, the open-loop (OL) definition refers to the actual governmental control, and the SEIRD variables in OL with varying $\beta(t)$ should closely follow the official values reported for AMBA. Hence, the closed-loop (CL) regulation of the lockdown levels should be applied over the actual lockdown situation.

The following equation is a modification of the one used by Morato et al. [13], in the context of this pandemic in Brazil. Here the controller produces an output $\psi(t)$ that regulates the lockdown in five different levels. These are applied over the already implemented phases defined by the government authorities.

$$\psi(t) = \alpha_{\text{off}} \left[ 1 - \psi(t) \right] \left[ 1 - u(t) \right] + \alpha_{\text{on}} \left[ \psi_t - \psi(t) \right] u(t)$$

The controller input $u(t)$ switches between 1 and 0 according to the increase or decrease of the ICU occupation, respectively. This input commands the strengthening or loosening of the lockdown. Parameter $\psi_t$ regulates the different levels, and is also a function of the fraction of ICU occupation concerning the total number of ICU places:

$$\psi(t) = \frac{\sigma_{\text{ICU}}(t) - \sigma_{\text{R}}(t)}{N_{\text{ICU}}}$$

It is computed as the rate $\sigma_{\text{ICU}}$ of infected ($I$) patients requiring an ICU minus the rate $\sigma_{\text{R}}$ of the recovered patients ($R$) that have donated plasma to the first group, divided by $N_{\text{ICU}}$. The latter is used to recover some of the hospitalized infected patients that would otherwise need an ICU.

The control levels go from 1 ($\psi_t = 0$) with stricter lockdown to 5 ($\psi_t = 0.9$) that allows more relaxed living conditions, depending on the $\beta(t)$ value which is being considered. The command to move from a relaxed to a lockdown situation and vice versa is $u(t)$. Note that $u = 1$ represents moving to a more strict lockdown level, and $\psi \rightarrow \psi_t$, with a settling time $\alpha_{\text{on}}$. Instead, $u = 0$ represents a transition to a more relaxed situation and $\psi \rightarrow 1$ with a settling time $\alpha_{\text{off}}$. Both time constants are determined from the analysis in Section 4.

Therefore, the occupancy of ICUs is benefited by an experimental treatment that is being implemented in Argentina and other countries around the world which includes plasma donation from recovered patients\(^2\) [23–26]. In most cases, this donation is applied to patients in near-critical situations, possibly hospitalized, before they are admitted to the ICU. Approximately half the recovered patients that donate plasma have the necessary antibody count or levels of Immune-globulin G (IgG) that benefit an infected patient [27]. Also, donations are voluntary, and here a very conservative assumption is made that only 3% of R donate plasma to critical patients. It has not been considered here, but could also decrease the ICU occupancy.
plasma. Finally, this is an experimental procedure that recovers near-critical patients, and the literature [23] refers to an 80% effectiveness of patients receiving convalescent plasma. Therefore in this simulation, a proportion of $\sigma_{p} = 0.5 \times 0.03 \times 0.8 = 0.012$ is considered, which is approximated to 1% effectiveness of the recovered patients’ plasma donations. Concerning the infected patients requiring an ICU, a $\sigma_{icu}(t)$ is applied, based on the official occupation reports provided by MINSAL [11].

Therefore, in this dynamical system, the index that regulates the propagation of this virus is the product $\psi(t)\beta(t)$. The first parameter $\psi(t)$ is the one commanded by the controller. The second parameter $\beta(t)$ represents the actual situation of the population in terms of contagion, under government control. Therefore this product modulates the mean transmission rate according to the different lockdown levels, in this case in five levels. Here we have considered two different cases for $\beta$, one constant and the other time-varying. The former is an average value, used for instance in the work presented by Tagliazucchi et al. [10]. The latter has been validated with the official data, as indicated in Fig. 4, and reflects the actual pandemic evolution dynamics produced by the government decisions.

For social and political reasons, the transitions between phases cannot be frequent. Therefore this controller can also regulate the minimum time in lockdown, which in this work, will be considered as 7 days. Further variations of this minimum lockdown duration will not be explored here. A diagram of the controller is illustrated in Fig. 8.

Finally, we may describe the model and controller as follows, for example in the SEIRD case. For practical purposes, and particularly in Argentina, we assume $N \approx S$ (see Fig. 9) then:

$$
\begin{bmatrix}
S(t) \\
E(t) \\
I(t) \\
R(t) \\
D(t)
\end{bmatrix} =
\begin{bmatrix}
0 & 0 & \psi(t)\beta(t) & 0 & 0 \\
0 & -\epsilon & \psi(t)\beta(t) & 0 & 0 \\
0 & 0 & \epsilon & -1/\tau & 0 \\
0 & 0 & \gamma & -1/\tau & 0 \\
0 & 0 & \gamma & -1/\tau & 0
\end{bmatrix}
\begin{bmatrix}
S(t) \\
E(t) \\
I(t) \\
R(t) \\
D(t)
\end{bmatrix},
$$

and,

$$
\dot{\psi}(t) = \alpha_{ef} (1 - \psi(t)) [1 - u] + \alpha_{on} |\psi_1 - \psi(t)| u
$$

$$
\dot{\psi}_1 = f(\mu).
$$

The model in (8) has a (quasi) Linear Parameter Varying (LPV)3 dynamics assuming $\psi(t)\beta(t)$ can be computed in real-time. The latter is true considering the slow dynamics of this model and that $\psi(t)\beta(t)$ can be updated daily or even faster. Eqs. (7) and (9) solve the 5 levels described previously depending on the ICU bed occupancy $\mu$. The quadratic stability of the model in Eq. (8) can be assessed by an LMI computed for all possible trajectories [28] of $\psi(t)\beta(t)$. Since $\psi(t)\beta(t) \in \mathbb{R}$, this region is a real interval and only 2 LMIs need to be computed. Also, in this case, $\dot{X}_{SEIRD} + A_{SEIRD}^T X < 0$ for $X > 0$ is equivalent to $\text{Re}(\text{eig}(A_{SEIRD})) < 0$ in both bounds of the interval (Theorem 4.3, [28]), being $\text{Re}()$ and $\text{eig}()$ the real part and eigenvalue operators, respectively. The interested reader is referred to the work by Becker and Packard [28] for a detailed discussion on the stability of LPV systems using, as in the case of this study, single Lyapunov functions. A comprehensible discussion on the stability of LPV systems is beyond the scope of this study.

This system is clearly unstable, or in the best situation, it is marginally stable. Nevertheless, the controller objective is not to completely stabilize it but only to attenuate the unstable growth so that the ICU occupancy is below 100%. From matrix $A_{SEIRD}$ in Eq. (8), as will be seen in the example, it becomes clear that the $\text{eig}(A_{SEIRD})$ for the upper bound of $\psi(t)\beta(t)$ is marginally stable (3 poles in $s = 0$) up to $\beta(t)\psi(t) < 0.071$. Above this value, a positive eigenvalue appears. This is reasonable because the objective is to decrease the value of $\psi(t)\beta(t)$ as much as possible. If naturally, the contagion rate $\beta(t)$ does not decrease, the control based on $\psi(t)$ will decrease the product by other means, i.e. $\psi(t) \rightarrow 0$ represents a stricter lockdown (level-1).

6. Example

In this section, considering the AMBA area, a case study is presented. The total population is $N = 17.5$ million and a 45-day simulation is initiated starting from May 28th. The SEIRD model has been considered in two cases for $\beta$: constant and time-varying. The initial values are obtained from daily official information: $I = 8,063, F = 3,000, R = 3,460$ and $D = 395$. It starts with 2,600 available ICUs, and 20% of them are already occupied. Some parameters have been obtained from the model proposed by Tagliazucchi et al. [10] that have been validated with official data: $\beta = 0.22$ (in the constant case), $\epsilon = 0.196, \gamma = 0.028$. For time-varying $\beta(t)$, the estimate obtained in 3 with $w_t = 5$ has been considered. This choice was made to agree with the minimum lockdown duration of 1 week, to fully capture the effect of such lockdown on the disease spreading dynamics.

In addition, the settling times to restrict or release the lockdown are $\sigma_{on} = 4$ and $\sigma_{ef} = 1$, respectively. These values were selected according to the response times observed in Fig. 6 due to the government’s measure. Releasing the lockdown was almost immediately reflected in mobility, while in both restrictive cases (March 19th and July 14th) a 4-day delay was observed. A conservative value has been chosen for $\sigma_{on} = 0.01$ as explained in Section 5. As previously mentioned, a time-varying $\sigma_{on}$ was considered. An identification procedure was performed based on least-squares, obtaining the evolution for this parameter through-out the considered dates. For this, the objective was to match the available data for ICU occupancy as released by MINSAL [11] with the one predicted by the SEIRD model on (2) for the open-loop case with time-varying $\beta$, using moving time windows of two days and a 5-day estimate for $\beta$. This scenario corresponds to the present lockdown regulations adopted by the government so far, reflected by the open-loop variable $\beta(t)$ identified with day-by-day data from the start of the pandemic in Argentina. According to the communications of PBA government officials, a decreasing trend in the rate of ICU admissions was found with the identification procedure. Moreover, $\rho$ was also fitted to match the official decease rate, obtaining $\rho = 0.04$.

In terms of stability analysis, the bounds on both time-varying parameters are $\psi(t) \in [0, 1]$ and $\beta(t) \in [0.1587, 0.826]$, therefore the interval of this product is $\beta(t)\psi(t) \in [0, 0.826]$. As a consequence the stability of the LPV matrix $A_{SEIRD}(\beta, \psi)$ is established by its eigenvalues on both limits: $\text{eig}(A_{SEIRD}(0)) = (0, 0, 0, -0.977, -0.2, -0.547, 0.275)$, clearly quadratically unstable due to the last positive eigenvalue. Even in the constant case, i.e. $\beta = 0.22$, the upper bound of $[A_{SEIRD}(0.22)]$ produces an unstable pole at $s = 0.1128$.3

---

3 The quasi terms refer to the fact that the time-varying parameter $\psi(t)$ is not measured but estimated in real-time, and it depends on two states of the model, I and R.
Fig. 9. Comparison of the number of susceptible, exposed, infected and removed individuals for closed-loop control with constant (dashed, round markers) and time-varying (solid, square markers) $\beta$, open-loop with time-varying $\beta$ (dashed–dotted) and the official AMBA records (solid with cross markers).

Fig. 10. (a) Controller modulations of lockdowns in 5 levels for $\beta$ constant (dashed) and time-varying (solid), considering a minimum of 1-week lockdown. (b) ICU occupation for constant and time-varying $\beta$ in both the controlled and uncontrolled cases. AMBA is the official data for this region.

The results obtained for both closed-loop constant and time-varying $\beta$ are shown in Figs. 9 and 10(a). In the former, the improvement achieved by considering the time-varying dynamics is observed. The closed-loop with constant $\beta$ leads to more infected subjects than the policy applied by the government, which corresponds to the case with open-loop and time-varying $\beta(t)$. The match between this last case and the government’s policy for AMBA is shown in Fig. 9, where the number of active infected and recovered subjects is the same for both. This situation is further improved by the closed-loop with $\beta(t)$ scenario. In the latter, as explained previously, the control strategy is applied over the present lockdown adopted by the government so far, reflected in the variable $\beta(t)$ identified with day-by-day data, which represents a real-time photograph of the present situation. This official policy would correspond to $\psi = 1$ (no extra-regulation). It is understandably, less restrictive than the closed-loop cases, due to political, social, and economic factors, as discussed in Section 3. The modulation of lockdowns in levels proposed here is a consequence of the control algorithm through parameter $\psi(t)$ and would have had consequences over the real-time identification of $\beta(t)$. In Fig. 10(a), the constant $\beta$ case requires a stronger modulation than the time-varying case, but even then it leads to a greater number of infected people. In addition, the
modulation intervals using the time-varying $\beta$ are longer, which is better from a social (and political) point of view. Again, the levels indicated by the controller are applied above the lockdown phases defined by the government that correlates with the official mobility, as indicated in Section 4.

In Fig. 10(b) the main objective of the controller results in a percentage of ICU occupancy that reaches values over 91% for constant $\beta$, and then decreasing after a much stricter lockdown (see Fig. 10(a)) to 60%, which is also the value for the ICU occupation under the government’s policy. This indicator is greatly reduced when considering the closed-loop for time-varying $\beta$, obtaining less than 25% of used ICU places. Here, it is worth highlighting that the measures taken by the government helped in alleviating the demand for ICU units in comparison with the uncontrolled situation (which reaches 100% occupation in around 22 days) and the controlled scenario, both with constant $\beta$. This last scenario, despite having reached a higher occupancy level as a consequence of less restrictive initial measures, can avoid the saturation of ICU units. Then, by adopting a stricter policy as shown in Fig. 10(a), it can reduce ICU occupancy. However, as it is shown in the same figure, by considering the closed-loop varying dynamics of the pandemic spread, better outcomes on ICU occupation would have been achieved and could be improved upon if this strategy is applied to future lockdown modulations.

A comparison is made with different levels of plasma donation with time-varying $\beta(t)$, including the case where no plasma is applied to infected patients. The results are shown in Fig. 11(a). It is clear that the more recovered patients donate, the less demand for ICU will take place. This improvement represents a very useful delay in reaching the peak of the pandemic, which buys precious time to be prepared, e.g. increasing ICU places and/or promoting plasma donation. In addition, a lower occupation of ICU places represents also the possibility to relax the lockdown, which in turn could activate the economy. Take into account that in this example, the utilization of plasma represented by coefficient $\sigma$ has been selected very conservatively (1%). With a higher percentage of effective donation as defined in Section 5, the transition between levels could be even better than the one obtained in Fig. 10(a), and even a complete liberation of ICU units would be achieved.

In addition, the number of deaths is also lower when using this controller combined with the time-varying $\beta$, as illustrated in Fig. 11(b). In the same figure, a comparison with simulations without a controller (open-loop) is also made, which verify that this controller reduces both, ICU occupancy and the number of deaths. This example is based on official data and some assumptions concerning the plasma donation procedure. Presently, the actual value of ICU occupation is 59.7% with over 1600 deaths. They are above the ones presented here with a time-varying $\beta(t)$ in closed-loop, and well below the open-loop case (with constant $\beta$). Once again, the efforts of the government by taking the necessary steps in terms of lockdown to preserve lives are evidenced. Nevertheless, our results show that an even better strategy could be considered that would have decreased both values significantly, to 22.4% and 1,309 respectively.

7. Conclusions

A time-varying $\beta(t)$ estimation, based on official data reflects the actual mobility situation among the population. This is combined with a controller designed to reduce the percentage of ICU occupation, which also decreases the number of deceased. These two results are the main core of this work. As a consequence, valuable time can be gained by delaying the peak of this pandemic by reducing the use of ICU’s, with the contribution also of plasma donation from recovered patients. A strong effort should be made to encourage this donation because it could be of paramount importance to handle this disease.

The identification, analysis and design procedures performed in this work can be extended to any other region, by using reliable data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

The authors appreciate the valuable conversations with Dr. Ernesto Kofman and Dr. Rodrigo Castro. Moreover, the guidance of Dra. Laura Bover and Dra. Andrea Gamarnik regarding the plasma therapy currently under clinical research is very much appreciated.
Funding sources

This work was supported by Consejo Federal de Ciencia y Técnica of Argentina [COFECY COVID19 (2020)]. Demián García-Viollini is supported by Universidad Nacional de Quilmes, Argentina. Ricardo Sánchez-Peña, Marcela Moscoso-Vásquez are supported by CONICET, Argentina and Instituto Tecnológico de Buenos Aires, Argentina. Fabricio Garelli is supported by Universidad Nacional de La Plata, Argentina and CONICET, Argentina.

References

[1] World Health Organization, Coronavirus Disease (COVID-19) Dashboard. Available online: https://covid19.who.int/ (accessed on 10 February, 2021), 2020.
[2] Miraglia M. La historiografía ambiental en la provincia de Buenos Aires, Región Metropolitana y Ciudad Autónoma de Buenos Aires, Universidad Nacional de General Sarmiento, Buenos Aires, Argentina, 2018.
[3] Keeling MJ, Rohani P. Modeling Infectious Diseases in Humans and Animals. Princeton University Press; 2011.
[4] Kermack Wo, McKendrick AG. A contribution to the mathematical theory of epidemics. Proc. R. Soc. Lond. Ser. A 1927;115(772):700–21.
[5] Daley DJ, Gani J. Epidemic Modelling: An Introduction. 15, Cambridge University Press; 2001.
[6] Tang S, Tang B, Bragazzi NL, Xia F, Li T, He S, Ren P, Wang X, Peng Z, Xiao Y, Wu J. Stochastic discrete epidemic modeling of COVID-19 transmission in the Province of Shaanxi incorporating public health intervention and case importation, medRxiv (2020).
[7] He S, Tang S, Kong L. A discrete stochastic model of the COVID-19 outbreak: Forecast and control. Math Biosci Eng 2020;17(4):2792–804.
[8] Lin Q, Zhao S, Gao D, Lou Y, Yang S, Musa SS, Wang MH, Cai Y, Wang W, Yang L, et al. A conceptual model for the outbreak of coronavirus disease 2019 (COVID-19) in Wuhan, China with individual reaction and governmental action, Int. J. Infect. Dis. 2020.
[9] Kuniya T. Prediction of the epidemic peak of coronavirus disease in Japan, 2020a. J. Clin. Med. 2020;9:789.
[10] Tagliazucchi E, Balenzuela P, Travizano M, Mindlin G, Mininni P. Lessons from being challenged by COVID-19. Chaos Solitons Fractals 2020:137.
[11] Ministerio de Salud de la Nación Argentina. 2020. Informe Diario. Available online: https://www.argentina.gob.ar/coronavirus/informe-diario (accessed on 10 February, 2021), 2020.
[12] Casella F. 2020. Can the COVID-19 epidemic be controlled on the basis of daily test reports?, 2020. arXiv:2003.06967v3.
[13] Morato MM, Bastos SB, Cajufero DO, Nornay-Rico JE. An optimal predictive control strategy for COVID-19 (SARS-CoV-2) social distancing policies in Brazil. Annu Rev Control 2020;50:417–31.
[14] Djidjou-Demassea R, Michalakisia Y, Choiyaa M, Sofoneaa MT, Alizon S. Optimal COVID-19 epidemic control until vaccine deployment, 2020. https://doi.org/10.1101/2020.04.02.20049189.
[15] Köhler J, Schwenkel L, Koch A, Berberich J, Pauli P, Allgöwer F. Robust and optimal predictive control of the COVID-19 outbreak. May 2020. arXiv:2005.03580v1.
[16] Zhou K, Doyle JC, Glover K. Robust and Optimal Control, vol. 40. Prentice hall New Jersey, 1996.
[17] Sánchez-Peña RS, Snaezer M. Robust Systems Theory and Applications. Wiley New York; 1998.
[18] Lotito P, Gianatti J, Parette L. COVID-19: Herramientas de optimización y control, Conference. Available online: https://www.youtube.com/watch?v=sFETHcFcLPc (accessed on 10 February, 2021), 2020.
[19] Qin J, You C, Lin Q, Hu T, Yu S, Zhou X-H. Estimation of incubation period distribution of COVID-19 using disease onset forward time: a novel cross-sectional and forward follow-up study. Sci Adv 2020;6(33):eabc1202.
[20] Kuniya T. Prediction of the epidemic peak of coronavirus disease in Japan, 2020. J. Clin. Med. 2020b;9(3):789.
[21] Grupo Correo, Hoy Extremadura Newspaper, Available online: https://www.hoy.es/sociedad/salud/diario-coronavirus-espana-20200319134410-ntrc.html (accessed on 10 February, 2021), 2020.
[22] Google LLC, Google COVID-19 community mobility reports, https://www.google.com/covid19/mobility/ (accessed on 10 February, 2021), 2020.
[23] Duan K, Liu B, Li C, Zhang H, Yu T, Qu J, Zhou M, Chen L, Meng S, Hu Y, et al. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. Proc Natl Acad Sci 2020;117(17):9490–6.
[24] Convalescent plasma COVID-19, https://www.groupepc-19.com/ (accessed on 10 February, 2021), 2020.
[25] Banwait RS, Salabei JK, Fishman TJ, Iyer UG. Convalescent plasma in COVID-19. HCA Healthc. J. Med. 2020;1(1):3.
[26] Rajendran K, Narayanasamy K, Rangarajan J, Rathinam J, Natarajan M, Ramachandran A. Convalescent plasma transfusion for the treatment of COVID-19: Systematic review. J Med Virol 2020.
[27] Gamarnik A. Conversations of the authors with Dr. A. Gamarnik, Head of the Instituto de Investigaciones Bioquímicas in Buenos Aires, 2020. Fundación Instituto Leloir, July 2020.
[28] Becker G, Packard A. Robust performance of linear parametrically varying systems using parametrically-dependent linear feedback. Systems Control Lett 1994;23(3):205–15.