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Modelling the spreading of the SARS-CoV-2 in presence of the lockdown and quarantine measures by a *kinetic-type reactions* approach

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We propose a realistic model for the evolution of the COVID-19 pandemic subject to the lockdown and quarantine measures, which takes into account the timedelay for recovery or death processes. The dynamic equations for the entire process are derived by adopting a *kinetic-type reactions* approach. More specifically, the lockdown and the quarantine measures are modelled by some kind of inhibitor reactions where susceptible and infected individuals can be *trapped* into inactive states. The dynamics for the recovered people is obtained by accounting people who are only traced back to hospitalized infected people. To get the evolution equation we take inspiration from the Michaelis Menten's enzyme-substrate reaction model (the so-called *MM reaction*) where the *enzyme* is associated to the *available hospital beds*, the *substrate* to the *infected people*, and the *product* to the *recovered people*, respectively. In other words, everything happens as if the hospitals beds act as a *catalyzer* in the hospital recovery process. Of course, in our case, the reverse *MM reaction* has no sense in our case and, consequently, the kinetic constant is equal to zero. Finally, the ordinary differential equations (ODEs) for people tested positive to COVID-19 is simply modelled by the following kinetic scheme $S + I \Rightarrow 2I$ with $I \Rightarrow R$ or $I \Rightarrow D$, with S, I, R and D denoting the compartments susceptible, infected, recovered and deceased people, respectively. The resulting *kinetic-type equations* provide the ODEs, for elementary *reaction steps*, describing the number of the infected people, the total number of the recovered people previously hospitalized, subject to the lockdown and the quarantine measure and the total number of deaths. The model foresees also the second wave of infection by coronavirus. The tests carried out on real data for Belgium, France and Germany confirmed the correctness of our model.

Keywords: mathematical model; COVID-19; dynamics of population.

1. Introduction

Coronavirus disease 2019 (COVID-19) is caused by a new coronavirus (SARS-CoV-2) that has spread rapidly around the world. Most infected people have no symptoms or suffer from mild, flu-like symptoms, but some become seriously ill and can die. In recent weeks coronavirus has had too many opportunities to spread again. After successfully tamping down the first surge of infection and death, Europe is now in the middle of a second coronavirus wave as it moves into winter (Cacciapaglia *et al.*, 2020; Bailey, 1975; Sonia & Nunn, 2006; Vynnycky & White, 2010; Gleick, 1987). Even though several vaccines for COVID-19 are actually been produced other ways of slowing its spread have to continue to be explored. One way of controlling the disease is the lockdown and the quarantine measures. The lockdown measures are emergency measures or conditions imposed by governmental authorities, as during the outbreak of an epidemic disease, that intervene in situations where the risk of transmitting the virus is greatest. Under these measures, people are required to stay in their homes and

to limit travel movements and opportunities for individuals to come into contact with each other such as dining out or attending large gatherings. The lockdown measures are more effective when combined with other measures such as the quarantine. Quarantine means separating healthy people from other healthy people, who may have the virus after being in close contact with an infected person, or because they have returned from an area with high infection rates. Similar recommendations include isolation (like quarantine, but for people who tested positive for COVID-19) and physical distancing (people without symptoms keep a distance from each other). Several governments have then decided that stricter lockdown and quarantine measures are needed to bring down the number of infections. In this work we shall propose interventions that are as targeted as possible. Unfortunately, the greater the number of infections, the more sweeping the measures have to be. Tightening the measures will have an impact on our society and the economy but this step is needed for getting the coronavirus under control.

Several models have been developed to describe the pandemic dynamics, which are based on the classic compartmental epidemiological models (Coullet, 2020; Brauer & Castillo-Chavez, 2012) and adapting them to the specific case of COVID-19. Epidemiological models, describing disease transmission within a population, provide important insights to understand which control mechanisms can lead, under what circumstances, to remove, or at least reduce, the infection. In the case COVID-19 it is necessary to consider particularly detailed models to accurately predict the dynamics of the epidemic (Nowzari *et al.*, 2016b). One commonly used model is the *SIR model* (Kermack & Mc Kendrick, 1927) for human-to-human transmission, which describes the flow of individuals through three mutually exclusive stages of infection: *susceptible*, *infected* and *recovered*. Putra and Khozin Mu'tamar (Putra & Khozin, 2019) used the particle swarm optimization algorithm to estimate parameters in the SIR model. The results indicate that the suggested method is precise and has low enough error compared to other analytical methods. Mbuvha and Marwala (Mbuvha & Marwala, 2020) calibrated the SIR model to South Africa's reported cases after considering different scenarios of the reproduction number (R_0) for reporting infections and healthcare resource estimations. Qi *et al*. (Qi *et al.*, 2020) proposed that both daily temperature and relative humidity can influence the occurrence of COVID-19 in Hubei and other provinces. Salgotra and Gandomi (Salgotra *et al.*, 2020) developed two COVID-19 prediction models based on genetic programming and applied these models in India. They found that genetic evolutionary programming models have proven to be highly reliable for COVID-19 cases in India. Other models may accurately portray the dynamic spread of specific epidemics. For the COVID-19 pandemic, several models have been developed. Lin and colleagues extended a SEIR (*susceptible*, *exposed*, *infectious*, *removed*) model considering risk perception and the cumulative number of cases (Lin *et al.*, 2020), Anastassopoulou and colleagues proposed a discrete-time SIR model including dead individuals (Anastassopoulou *et al.*, 2020b), Casella developed a control-oriented SIR model that stresses the effects of delays and compares the outcomes of different containment policies (Casella, 2021) and Wu and colleagues (Wu *et al.*, 2020) used transmission dynamics to estimate the clinical severity of COVID-19. A SUQC model (that is, with *susceptible*, *un-quarantined infected*, *quarantined infected* and *confirmed infected* classes) is proposed in Zhao and Chen (Zhao & Chen, 2020) to describe the COVID-19 dynamics in China and analyse the effects of some control measures. Also, some researchers (Al-qaness *et al.*, 2020) and (Singh *et al.*, 2020) preferred to use hybrid algorithms to enhance the power of forecasting algorithms. Naudé (Naudé, 2020) and Rahimi *et al*. (Rahimi *et al.*, 2021) provided a review and brief analysis of the most important machine learning forecasting models against COVID-19. *Auto regressive integrated moving average* (ARIMA) method is also used to forecast short-term confirmed cases of COVID-19. Ahmar and del Val used the SutteARIMA method to predict cases of COVID-19 and Spain Market Index (IBEX 35) (Ahmar & Del Val, 2020). Chakraborty and Ghosh (Chakraborty & Ghosh, 2020) presented a real-time forecast of confirmed COVID-19 cases for multiple countries as well as a risk assessment of the novel

COVID-19 for some profoundly affected countries using the regression tree algorithm. A simple moving average approach was used by Chaudhry *et al.* (2020) to predict COVID-19 confirmed cases in Pakistan. Chen *et al.* (2020) used a five-parameter logistic growth model to reconstruct and forecast the COVID-19 epidemic in the USA; however, the authors claimed the accuracy of their model depends on federal- and state-level policy decisions. Zhao *et al*. (Zhao *et al.*, 2020) introduced a platform, icumonitoring.ch, to provide hospital-level projections for intensive care unit (ICU) occupancy based on SEIR models. The proposed platform could help ICU managers to estimate the need for additional resources and is updated every 3–4 days. Chimmula and Zhang (Chimmula & Zhang, 2020) applied *long short-term memory* networks as a deep learning technique for predicting COVID-19 outbreaks in Canada. Their approach identified the key features for estimating the trends of the pandemic in Canada. A simple ARIMA model was proposed by Chintalapudi *et al.* (2020) to estimate registered and recovered cases after a lockdown in Italy. A SIDARTHE model is proposed by Giordano and colleagues (Giordano *et al.*, 2020) where the population is divided into eight classes: S (*susceptible*), I (*infected*), D (*diagnosed*, that is, detected asymptomatic infected); A (*ailing*, that is, undetected symptomatic infected), R (*recognized*, that is, detected symptomatic infected), T (*threatened*, that is, detected infected with life-threatening symptoms), H (*healed*, i.e., recovered) and E (*extinct*, i.e., dead). The final goal of the contribution in Giordano et al. (2020) is to estimate the impact of different actions to contain the contagion in Italy. To this aim, the authors evaluate different possible scenarios by suitably modifying some model parameters. Mahalle and Kalamkar (Mahalle *et al.*, 2020) categorized forecasting models as mathematical models and machine learning techniques, using WHO and social media communications as datasets.

We have illustrated this long list of works in the field in order to highlight that, while facing the same problem, albeit with different methods, they are all united by a single 'common thread': the overall objective of these works is to obtain the dynamics describing realistic situations of the spread of SARS-CoV2 infection by means of macroscopic descriptions. It should immediately be said that we can consider this task as achieved if we are able to

1. model the distribution of hospitals in a country;
2. model the distribution of the poles of attraction of susceptible people (e.g., shopping centers, workplaces, etc.);
3. identify a mechanism that allows to establish when a pole of attraction becomes *saturated* with infected people by proposing alternative poles of attraction;
4. modelling the lockdown and the quarantine measures adopted by the government of the country;
5. determine the nature of the intrinsic (ie spontaneous) fluctuations to which a macroscopic system is subjected, determining the correlation function by statistical mechanics.

To our knowledge, the current techniques mentioned above are unable to resolve the issues listed above. As evident from a comparison between the theoretical results and experimental data, although these models give a trend of the features exhibited by the time-series data, it hardly represents the actual trends. For instance, as the effect of latent time has not been considered, growth in active cases of infections, as predicted by the susceptible-infectious-recovered-deceased model (SIRD model), remains very steep. Further, as quarantine effects have not been considered, the decay predicted by the SIRD model is much slower than reality. The predicted value of total number of deaths is also much higher than actual. Hence, this model needs proper modifications to corroborate all the three data sets—infected, recovered and dead—simultaneously. Lockdown and quarantine measures and the role of the time delay play a significant role in the way the infection spreads over time. Hence, we need to incorporate these factors

into the model. When several factors are involved simultaneously in a process, how should we proceed then? A suggestion comes to us from how physicists approached the study of the science of *Nonlinear Phenomena and Complex Systems*:

- First of all we must realize that it is unrealistic to think to be able to describe a complex phenomenon, only by using *macroscopic models* that, in addition, are *over-simplified*;
- Secondly, we must accept the idea that it is not possible to take into consideration, with a single model, all the factors involved in a complex phenomenon;
- As physicists currently do to study the dynamics of thermodynamic systems (i.e., *macroscopic systems*) far from equilibrium, the macroscopic model that describes the dynamics of the system must be derived from fundamental processes i.e., by a *microscopic description* and not directly by a *macroscopic* approach (as it is the case, for instance, for the SIRD model).

In this work we introduce a *kinetic-type reactions* (KTR) approach (Sonnino *et al.*, 2020; Sonnino *et al.*, 2021), calibrated on the COVID-19 outbreak data in Belgium, France and Germany. Here, by analogy, we are authorized to introduce the following *microscopic postulates*:

1. *The microscopic detailed balance principle is respected*. The overall COVID-19 spreading process may be decomposed into elementary processes (contacts among individuals, or steps, or *elementary reactions*). It states that at equilibrium, each elementary process is in equilibrium with its reverse process. It should be noted that this principle has important repercussions at the macroscopic level such as, for example, the validity of the reciprocity relations of the coefficients that appear in the macroscopic model.
2. *The law of mass action is satisfied*. The rate at which an elementary step proceeds is directly proportional to the product of the concentrations of the *reactants* (in our case the 'populations'). It explains and predicts behaviours of populations in dynamic equilibrium. Specifically, it implies that for a system in equilibrium, the ratio between the 'reacting' populations density and the produced populations density is constant.
3. Finally, *the Th. De Donder principle is satisfied* (Prigogine, 1947; Prigogine, 1954). The Th. De Donder principle establishes that a chemical reaction, however complex, can always be reduced to a finite series of elementary chemical steps. In this principle lies all the real potential power of the KTR approach. It is easily checked that several current models applied to a different data set violate the Th. De Donder principle.

It is worth remembering that, as can be easily understood, the three above axioms provide strict constraints to the coefficients appearing in the macroscopic model, which, contrarily to the models described in the works illustrated above, can no longer be chosen arbitrarily. We shall see that the KTR approach is very promising and allows to achieve this goal in a relatively simple way. Indeed, the KRT approach

- models each actor by a dedicated 'chemical species' that can only be created or destroyed as the result of one, or several, elementary steps,
- allows to determine the dynamics of the system starting from this set of elementary steps;
- thanks to its flexibility, allows to analyse complex situations where several variables are involved, such as R, Q, R_h, I_h, etc.

To the best of our knowledge, this approach, at fundamental level, has never been proposed in the literature. Concretely, as is customary in the study of complex phenomena, we face the problem of the spread of the SARS-CoV 2 virus by proceeding step-by-step. In this work we shall limit ourselves to analyse the dynamics of the infectious, recovered and deceased people by taking into account also the findings reported in Sonnino & Nardone (2020) and Sonnino (2020). The lockdown and quarantine measures imposed by governments to population as well as the role of the hospitals and health institutes are also herein modelled. In this framework, the dynamics of the health institutes is obtained by taking inspiration from the Michaelis–Menten's enzyme-substrate reaction model (the so-called *MM reaction*; Michaelis & Menten, 1913; Srinivasan, 2020a; Srinivasan, 2020b) where the *enzyme* is associated to the *available hospital beds*, the *substrate* to the *infected people* and the *product* to the *recovered people*, respectively. In other words, everything happens as if the hospital beds act as a *catalyser* in the hospital recovery process (Sonnino *et al.*, 2020). We shall see that the combined effect of the restrictions measures with the action of the health institutes is able to contain and even dampen the spread of the SARS-CoV-2 epidemic. In addition, the time delay for recovery or death processes are duly taken into account. More specifically, in our model, we have the following 11 compartments:

S = Number of susceptible people. This number concerns individuals not yet infected with the disease at time t, but they are susceptible to the disease of the population;

S_L = Number of susceptible people subject to the lockdown measures;

I_h = Number of hospitalized infected people;

I_Q = Number of people in quarantine. This number concerns individuals who may have the virus after being in close contact with an infected person;

I = Number of people who have been infected and are able of spreading the disease to those in the susceptible category (in this compartment, I_h and I_Q are not accounted);

r_h = Cumulative recovered people previously hospitalized;

R = Cumulative number of recovered people (by excluding people previously hospitalized) meaning specifically individuals having survived the disease and now immune. Those in this category are not able to be infected again or to transmit the infection to others;

d_h = Cumulative number of people previously hospitalized dead for COVID-19;

D = Cumulative number of dead people (by excluding the compartment d_h), for COVID-19;

L = Number of *inhibitor sites* mimicking lockdown measures:

Q = Number of *inhibitor sites* mimicking quarantine measures.

In addition, N, defined in Eq. (18), denotes the number of total cases.

The manuscript is organized as follows. In Section 2 we derive the deterministic ordinary differential equations (ODEs) governing the dynamics of the infectious, recovered and deceased people. The lockdown and quarantine measures are modelled in Subsection 2.2. The dynamics of the hospitalized individuals (i.e., the infectious, recovered and deceased people) can be found in Subsection 2.4. As mentioned above, the corresponding ODEs are obtained by considering the *MM reaction model*. The equations governing the dynamics of the full process and the related *basic reproduction number* are reported in Section 3 and Section 4, respectively. It is worth mentioning that our model foresees also the second wave of infection by coronavirus. As shown in Section 5, in absence of the restrictive measures and by neglecting the role of the hospitals and the delay in the reactions steps, our model reduces to the classical SIRD model (Kermack & McKendrick, 1927). Finally, Section 6 shows the good agreement between the theoretical predictions with real data for Belgium, France and Germany. The last section, Section 7, presents the conclusions and perspectives of this manuscript.

2. Model for COVID-19 in the presence of the lockdown and quarantine measures

The population is assigned to compartments with labels S, I, R, D, etc. The dynamics of these compartments is generally governed by deterministic ODEs, even though stochastic differential equations should be used to describe more realistic situations (Sonnino *et al.*, 2021). In this Section, we shall derive the deterministic ODEs obeyed by compartments. This task will be carried out by taking into account the theoretical results recently appeared in the literature (Sonnino, 2020; Sonnino *et al.*, 2020) and without neglecting the delay in the reactions steps.

2.1 *Modelling the susceptible people*

If a susceptible person encounters an infected person, the susceptible person will be infected as well. So, the scheme simply reads

$$S + I \xrightarrow{\mu} 2I \tag{1}$$

2.2 *Modelling the lockdown and quarantine measures*

The lockdown measures are mainly based on the isolation of the susceptible people, (eventually with the removal of infected people by hospitalization), but above all on the removal of susceptible people. It is assumed the lockdown and quarantine measures are modelled by some kind of inhibitor reaction where the susceptible people and the infected can be *trapped* into inactive states S_L and I_Q, respectively. Indicating with L and Q the inhibitor sites mimicking the lockdown and the quarantine measures respectively, we get

$$\begin{aligned} &S + L \underset{k_{LMax}-k_L}{\overset{k_L}{\rightleftharpoons}} S_L \\ &I \xrightarrow{k_Q} I_Q \xrightarrow{k_{QR},\, t_{QR}} R \end{aligned} \tag{2}$$

In the scheme (2), symbol $\Longrightarrow$ stands for a *delayed reaction* just like *enzyme degradation processes* for instance. Here, $L_{max} = S_L + L$ hence, if $L \simeq L_{Max}$, an almost perfect lockdown measure would totally inhibit virus propagation by inhibiting all the susceptible people S and the infected people I. A not so perfect lockdown measure would leave a fraction of I free to spread the virus. The number of inhibitor sites may be a fraction of the number of the infected people. Figure 1 shows the behaviour of the lockdown efficiency parameter adopted in our model. For simplicity, we have chosen a parameter that is constant $k_{LMax} \neq 0$ inside the time interval $t_1 \leqslant t \leqslant t_2$ and vanishes outside it. The *inverse lockdown efficiency parameter* is $k_L^{-1} = k_{LMax} - k_L$, which is equal to k_{LMax} outside the door and vanishes inside the the interval $t_1 \leqslant t \leqslant t_2$.

Finally, from Schemes (1) and (2), we get the ODEs for S, L, Q and I_Q:

$$\begin{aligned} \dot{S} &= -\mu SI - k_L S(L_{Max} - S_L) + (1 - k_L)(L_{Max} - L) \\ \dot{S}_L &= k_L SL - k_L^{-1} S_L \\ \dot{I}_Q &= k_Q I - \chi I_{Q_{(t-t_R)}} \end{aligned} \tag{3}$$

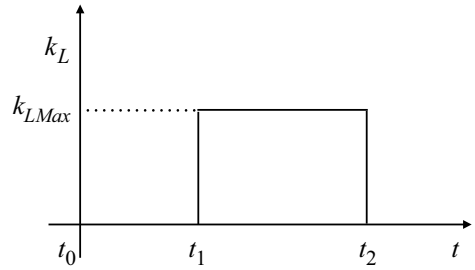

FIG. 1. ***Lockdown efficiency parameter.*** *For simplicity, in our model, the lockdown efficiency parameter k_L is a door-step function. This function is constant, $K_{LMax} \neq 0$, within the range $t_1 \leqslant t \leqslant t_2$ and zero outside it.*

with the *dot* above the variables denoting the *time derivative*.

2.3 *ODE for the total recovered people*

At the first approximation, the ODE for the *total recovered people R* (i.e. the total individuals having survived the disease) is trivially obtained by considering the following *kinetic scheme*:

$$I \xrightarrow{\chi,\, t_R} R \qquad (4)$$

$$I_Q \xrightarrow{k_{QR},\, t_{QR}} R$$

That is, the rate of R_t is approximatively proportional to the number of the infected people I at time t i.e.[1]

$$\dot{R} = \chi I_{(t-t_R)} + \chi R_{(t-t_R)} \qquad (5)$$

where we have introduced the time-delay t_R (the number of the recovered people at time time t is proportional to the infected people at time $t - t_R$). However, it is useful to clarify the following. In Eqs (4), R stands for the *total number of the recovered people* (i.e. the number of the recovered people previously hospitalized, plus the number of the asymptomatic people, plus the infected people who have been recovered without being previously hospitalized). The natural question is: *how can we count R and compare this variable with the real data?* The current statistics, produced by the ministries of health of various countries, concern the people released from the hospitals. Apart from Luxembourg (where the entire population has been subject to the COVID-19-test), no other countries are in a condition to provide statistics regarding the total people recovered by COVID-19. Hence, it is our opinion that the equation for R is not useful since it is practically impossible to compare R with the experimental data. We then proceed by adopting approximations and to establish the differential equation whose solution can realistically be subject to experimental verification. More specifically:

[1] Notice that the first *reaction* in the scheme Eq. (4) is the dynamic equation for the total recovered people adopted in the SIRD model (Kermack & McKendrick, 1927).

Firstly, we assume that R is given by three contributions:

$$R = r_h + r_A + r_I \tag{6}$$

with r_h, r_A and r_I denoting the *total number of the recovered people previously hospitalized*, *the total number of asymptomatic people* and the *total number of people immune to SARS-CoV-2*, respectively. Secondly, we assume that the two contributions r_A and r_I are negligible i.e. we set $r_A \approx 0$ and $r_I \approx 0$.[2]

2.4 *ODE for the recovered people in the hospitals*

Now, let us determine the dynamics for the recovered people in the hospitals. So, we account people who are only traced back to hospitalized infected people. We propose the following model:

$$I + b_h \xrightarrow{k_1} I_h \xrightarrow{k_r,\, t_r} r_h + b_h \tag{7}$$

$$I_h \xrightarrow{k_d,\, t_d} d_h + b_h$$

with b_h denoting the number of available *hospital beds*, I the number of *infected people*, I_h the number of *infected people blocking an hospital bed*, r_h the number of *recovered people previously hospitalized* and d_h the number of *people deceased in the hospital*. Of course,

$$I_h + b_h = C_h = const. \qquad \text{where} \quad C_h = \text{Total hospital}'\text{s capacity} \tag{8}$$

The dynamic equations for the processes are then:

$$\dot{I}_h = k_1 I(C_h - I_h) - k_r I_{h(t-t_r)} - k_d I_{h(t-t_d)} \tag{9}$$

$$\dot{r}_h = k_r I_{h(t-t_r)}$$

$$\dot{d}_h = k_d I_{h(t-t_d)}$$

where t_r and t_d are the *average recovery time delay* and the *average death time delay*, respectively, and we have taken into account Eq. (8) i.e., $b_h = C_h - I_h$. In general $t_r \neq t_d \neq 0$. Of course, the variation of $r(t)$ over a period Δt is:

$$\Delta r_{ht} = r_{ht} - r_{h(t-\Delta t)} \tag{10}$$

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[2] We consider that the SARS-CoV-12 has just appeared for the first time. So, we do not consider the asymptomatic people who are immune to the virus without any medical treatment.

2.5 *ODE for people tested positive to COVID-19*

The number of the infected people may be modelled by the following *kinetic scheme*

$$\begin{aligned} S + I &\xrightarrow{\mu} 2I \\ I &\xrightarrow{\chi,\, t_R} R \\ I &\xrightarrow{\alpha,\, t_D} D \\ I + b &\xrightarrow{k_1} I_h \\ I &\xrightarrow{k_Q} I_Q \end{aligned} \tag{11}$$

The scheme (11) stems from the following considerations

1. **a)** If a susceptible person encounters an infected person, the susceptible person will be infected;
2. **b)** The infected people can either survive and, therefore, be recovered after an average time-delay t_R, or die after an average time-delay t_D;
3. **c)** The schemes (2) and (7), respectively, have been taken into account.

The differential equation for the infected people is reads then

$$\dot{I} = \mu SI - k_Q IQ - k_1 I(C_h - I_h) - \chi I_{(t-t_R)} - \alpha I_{(t-t_D)} \tag{12}$$

2.6 *ODE for deaths*

In this model, we assume that the rate of death is proportional to the infected people, according to the scheme (11). By also taking into account the scheme (2), we get

$$I \xrightarrow{\alpha,\, t_D} D \tag{13}$$

and the corresponding ODE for deaths reads

$$\dot{D} = \alpha I_{(t-t_D)} \tag{14}$$

3. Set of ODEs for the spread of SARS-CoV-2 when the lockdown and the quarantine measures are adopted

By collecting the above ODEs, we get the full system of differential equations governing the dynamics of the number of the infected people, the total number of the recovered people previously hospitalized

and the total number of deceased peopled, when the lockdown and the quarantine measures are adopted

$$\begin{aligned}
\dot{S} &= -\mu SI - k_L S(L_{Max} - S_L) + k_L^{-1} S_L \qquad \text{with} \quad k_L^{-1} = k_{Max} - k_L \\
\dot{S}_L &= -k_L S(L_{Max} - S_L) + k_L^{-1} S_L \\
\dot{I} &= \mu SI - k_Q I - k_1 I(C_h - I_h) - \chi I_{(t-t_R)} - \alpha I_{(t-t_D)} \\
\dot{I}_h &= k_1 I(C_h - I_h) - k_r I_{h(t-t_r)} - k_d I_{h(t-t_d)} \\
\dot{I}_Q &= k_Q I_t - \chi I_{Q(t-t_R)} \\
\dot{r}_h &= k_r I_{h(t-t_r)} \\
\dot{R} &= \chi I_{(t-t_R)} + \chi I_{Q(t-t_R)} \\
\dot{d}_h &= k_d I_{h(t-t_d)} \\
\dot{D} &= \alpha I_{(t-t_D)}
\end{aligned} \tag{15}$$

From Eqs (15) we get

$$S + S_L + I + I_Q + I_h + R + r_h + D + d_h = const. \tag{16}$$

or, by taking into account that $S + S_L = S_{Tot.}$, $R + r_h = R_{Tot.}$, $D + d_h = D_{Tot.}$ and $I + I_Q + I_h = I_{Tot.}$ we get

$$S_{Tot.} + I_{Tot.} + R_{Tot.} + D_{Tot.} = const. \tag{17}$$

The number of total cases N is defined as

$$N_{Tot.} = I_{Tot.} + r_h + D_{Tot.} \tag{18}$$

4. The basic reproduction number

We note that, in absence of the lockdown and the quarantine measures, the dynamics of the infectious class depends on the following ratio:

$$R_0 = \frac{\mu}{\chi + \alpha} \frac{S}{N_{Tot.}} \tag{19}$$

with $N_{Tot.}$ denoting the *total population*. R_0 is the *basic reproduction number*. This parameter provides the expected number of new infections from a single infection in a population by assuming that all subjects are susceptible (Bailey, 1975; Sonia & Nunn, 2006). The epidemic only starts if R_0 is greater than 1, otherwise the spread of the disease stops right from the start.

5. Comparison with the SIRD model

The SIRD model is one of the simplest compartmental models, and many models may be derived from this basic form. According to the SIRD model, the dynamic equations governing the above compartments read (Kermack & McKendrick, 1927)

$$\begin{aligned} \dot{S} &= -\mu SI \\ \dot{I} &= \mu SI - \chi I - \alpha I \\ \dot{R} &= \chi I \\ \dot{D} &= \alpha I \end{aligned} \tag{20}$$

It is easily checked that Eqs (15) reduce to Eqs (20) by adopting some assumptions. In particular:
1) The system is not subject to the lockdown and quarantine measures;
2) The average time delay may be neglected;
3) Hospitals do not enter in the dynamics.
Under these assumptions, Eqs (15) reduce to the SIRD equations:

$$\begin{aligned} \dot{S} &\simeq -\mu SI \\ \dot{I} &\simeq \mu SI - \chi I - \alpha I \\ \dot{R} &= \chi I \\ \dot{D} &= \alpha I \end{aligned} \tag{21}$$

6. Application of the model and appearance of the second wave of SARS-CoV-2 infection

Let us now apply our model to the case of a small country, Belgium, and to other two big countries, France and Germany. Real data are provided by the various National Health agencies (Belgium—*Sciensano*, Sciensano, 2021A; France—*Santé Publique France*, France, 2021B; Germany—*Robert Koch Institut. Country data from Worldbank.org*, Koch Institute, 2021C) and compiled, among others, by the European Centre for Disease Prevention and Control (ECDC). It should be noted that this measures do not generally provide the true new cases rate but reflect the overall trend since most of the infected will not be tested (Our World in Data, 2021D). It should also be specified that real data provided by ECDC refer to the *new cases per day*, which we denote by $\Delta I_{new}(t)$. By definition, $\Delta I_{new}(t)$ corresponds to the new infected people generated from step $I + S \xrightarrow{\mu} 2I$ solely during 1 day, and *not* to the compartment I. Hence, the ECDC data have to be confronted vs the theoretical predictions provided by the solutions for $S(t)$ and $S_L(t)$ of our model, according to the relation $\Delta I_{new}(t) = -\Delta S(t) - \Delta S_L(t)$. The values of the parameters used to perform these comparisons are shown in Table 1.

Initial μ and k_1 values have been estimated (fitted) from the measurements using the short period at the start of the pandemic using simple exponential solution valid during that period. $I(60)$ is the initial value of infected from 1 March 2020 (day 60) obtained from the respective measurements. Hospital capacity is evaluated from the different countries' published capacity. Lockdown starting dates and duration are retrieved from each country's Covid policies (ECDC, 2021E). Other parameters have been estimated by best fit of new cases during the first wave. We draw attention to the fact that the constants

TABLE 1 *List of the parameters*

Parameters	Belgium	France	Germany
Density $[km^{-2}]$	377	119	240
Surface $[km^2]$	30530	547557	348560
μ $[d^{-1}km^2]$	0.00072	0.002	0.00093
μ after L_1	0.000288	0.00087	0.000387
χ $[d^{-1}]$	0.062	0.062	0.0608
α $[d^{-1}]$	0.05 χ	0.05 χ	0.02 χ
k_L $[d^{-1}]$	0.07	0.06	0.06
k_Q $[d^{-1}]$	0.02	0.01	0.01
L_m $[km^{-2}]$	377.0	119	240
k_1 $[d^{-1}km^2]$	0.01	0.01	0.01
$k_d + k_r$ $[d^{-1}]$	0.2	0.2	0.21
$\frac{k_d}{k_r}$	0.5	0.5	0.1
t_r $[d]$	7	7	7
t_d $[d]$	7	7	7
t_R $[d]$	8	8	8
t_D $[d]$	8	8	8
C $[km^{-2}]$	0.0655	0.0091	0.023
$I(60)$ $[km^{-2}]$	0.0023	0.0018	0.0014
Start L_1 $[d]$	77	71	76
End L_1 $[d]$	124	131	125
Start L_2 $[d]$	306	303	306

μ, L_m, k_1, C and $I(60)$ have been normalized with respect to the surface of the country. As it can be seen, the values of the re-normalized constants are the same values, at least in terms of orders of magnitude, irrespective of the magnitude of the country in question (Belgium, France and Germany). However, we are aware that the interpretation may vary from one country to another. Finally, numerical solutions to the time delayed ODEs have been obtained by making use of the MATLAB `dde23` module with a constant time delay. Discontinuities have been avoided for the historical values and a Runge–Kutta implicit scheme is used (Shampine & Thompson, 2001).

During the first lockdown, countries have taken various actions to limit coronavirus spreading (social distancing, wearing masks, reducing high density hotspots, etc.). In order to include these measures in a simple way, we assumed that the net effect is to reduce the actual infection kinetic rate μ by some constant factor. This is given in the table as μ after L_1. Note that the transition occurs instantaneously in our model; this leads to the sharp drop in the total infected at that time shown in the figures. Other parameters are tuned to account for the actual variability of ΔI_{new} (but not its absolute value) and official number of deaths ($D_{Tot.}(t) = D(t) + d_h(t)$). The delay for recovery and death processes has been estimated from the measurements of hospitalization recovery in a country. For instance, Fig. 2 shows the estimation of the recovery time-delay for Belgium: it corresponds to the *time interval* between the peak of the new admission and the peak of the recovered people from hospitals. A similar procedure has been adopted for estimating the recovery and death time-delays also for France and Germany.

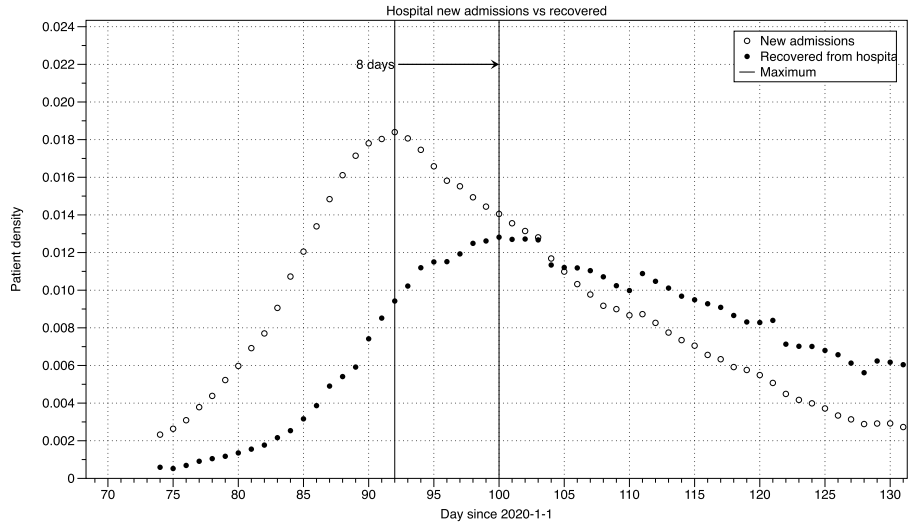

FIG. 2. *Estimation of the time delay. The time delays have been estimated by considering the time interval between the peak of the new admission and the peak of the recovered people from hospitals. This figure corresponds to the Belgian case.*

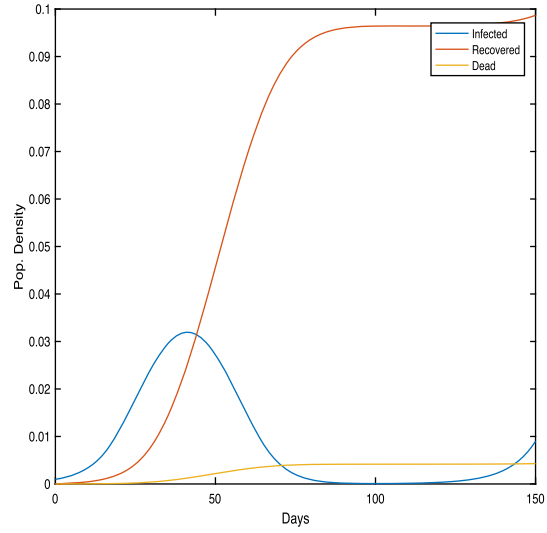

FIG. 3. *Theoretical solutions for infectious (I), cumulative number of recovered people (R) and deaths (D) for Belgium.*

• **Belgian case**.
Figure (3) refer to the Belgian case. In particular, Fig. (3) shows the solutions of our model for the infectious (I), total recovered (R) and total deceased (D) people. Figure (4) illustrates the theoretical solutions for hospitalized infectious (I_h), the total recovered (r_h) and total deceased (d_h) people previously hospitalized.

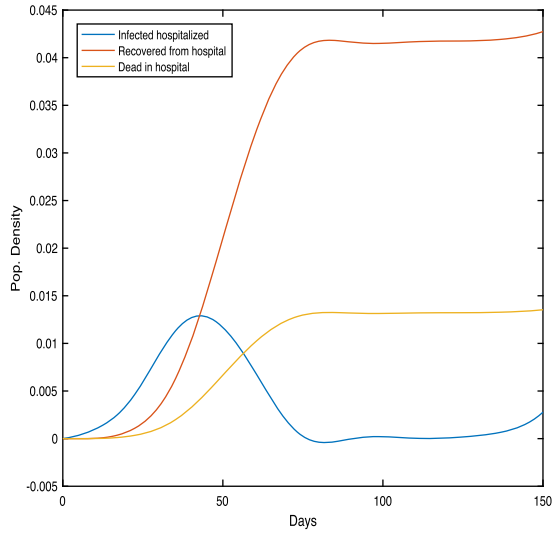

FIG. 4. *Theoretical solutions for hospitalized infectious (I_h), total recovered (r_h) and total deceased (d_h) people, previously hospitalized, for Belgium.*

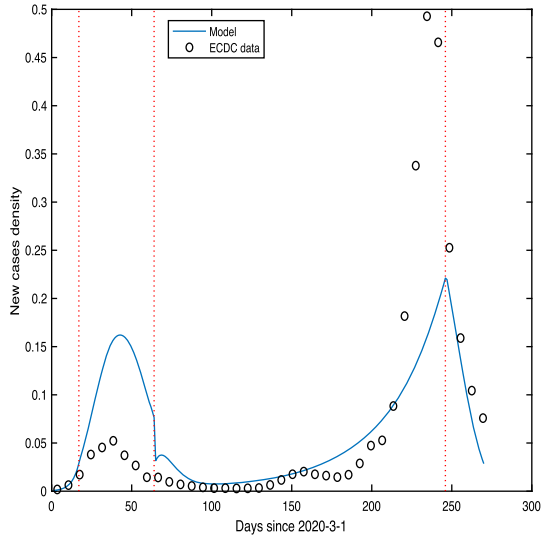

FIG. 5. *Comparison between the theoretical prediction for ΔI_{New} with real data provided by the data base Sciensano, for Belgium.*

Figures (5) and (6) show the comparison between the theoretical predictions for $\Delta I_{new}(t)$ and deaths and real data for Belgium (according to the database *Sciensano*). Notice in Fig. 5 the prediction of the *second wave of infection by SARS-CoV-2*

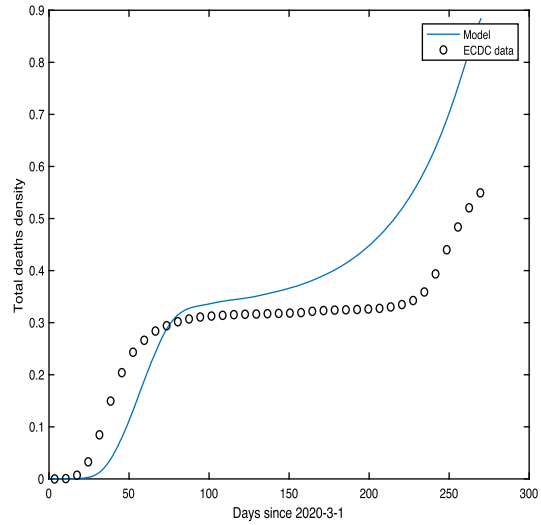

FIG. 6. *Comparison between the theoretical solution of our model for deaths with real data provided by the database Sciensano, for Belgium.*

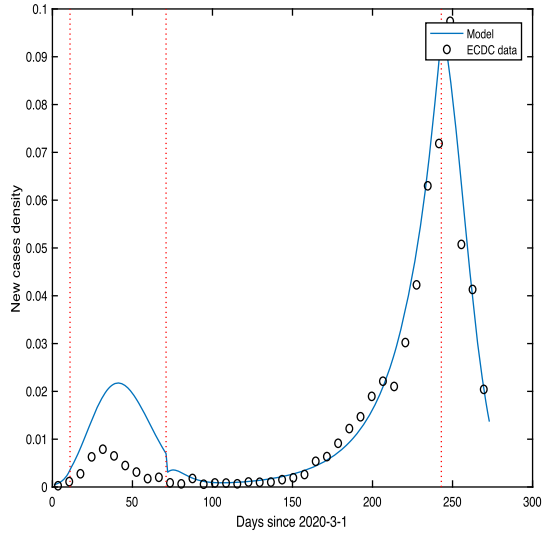

FIG. 7. *Comparison between the theoretical prediction for ΔI_{New} with real data provided by the data base Santé Publique France, for France.*

• **French case**.

Figures (7) and (8) show the comparison between the theoretical predictions for $\Delta I_{new}(t)$ and deaths and real data for Belgium (according to the database *Santé Publique France*). Notice in Fig. 7 the prediction of the *second wave of infection by SARS-CoV-2*

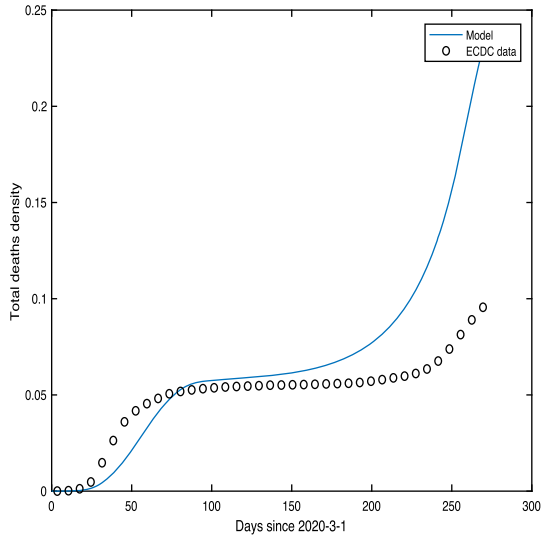

FIG. 8. *Comparison between the theoretical solution of our model for deaths with real data provided by the database Santé Publique France, for France.*

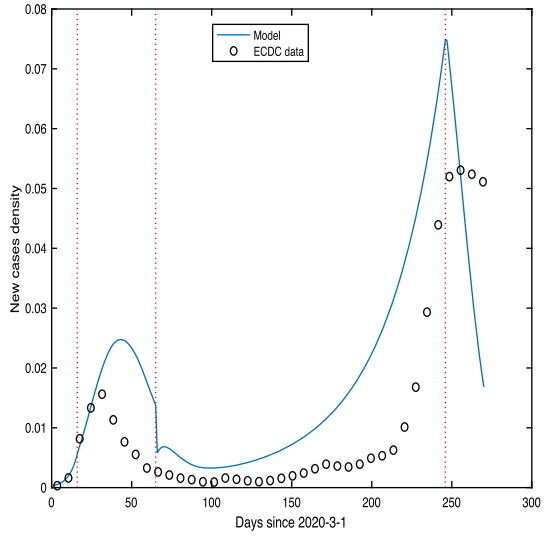

FIG. 9. *Comparison between the theoretical prediction for ΔI_{New} with real data provided by the data base (Robert Koch Institut. Country data from Worldbank.org), for Germany.*

• **German case**.
Figures (9) and (10) show the comparison between the theoretical predictions for $\Delta I_{new}(t)$ and deaths and real data for Belgium (according to the database *(Robert Koch Institut). Country data from Worldbank.org*). Notice in Fig. 9 the prediction of the *second wave of infection by SARS-CoV-2*.

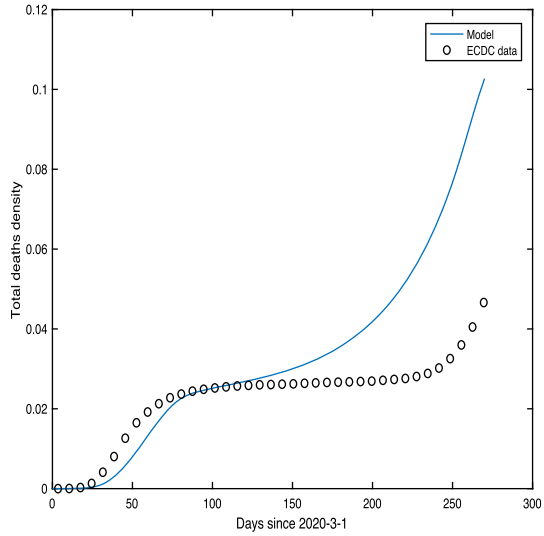

FIG. 10. *Comparison between the theoretical solution of our model for deaths with real data provided by the database (Robert Koch Institut. Country data from Worldbank.org*), for Germany.

7. Perspectives

It is worth noting the *degree of the flexibility* of our model. For example, let us suppose that we need to set up a model able to distinguish old population (over 65 year old) from the young one (with age not exceeding 35 years), by assuming that the older population is twice as likely to get infected by coronavirus with respect to the younger one. In this case, it is just sufficient to replace the scheme $I + S \xrightarrow{\mu} 2I$ with the scheme

$$\begin{aligned} &I + S_Y \xrightarrow{\mu_y} 2I \\ &I + 2S_O \xrightarrow{\mu_o} 3I \\ &S = S_Y + S_O \end{aligned} \tag{22}$$

with S_Y and S_o denoting the *susceptible young people* and the *susceptible old people*, respectively. Another example could be the following. Let us suppose that we need to distinguish two class of infected individuals:
1) Infected people (denoted by I_1) able to transmit the coronavirus to susceptible according to the (standard) scheme $I_1 + S \to 2I$;
2) Infected people (denoted by I_2) having the capacity to transmit the virus, say, seven times higher with respect to the category **1)**. In this case, the corresponding scheme reads:

$$\begin{aligned} &I_1 + S \xrightarrow{\mu_1} 2I \\ &I_2 + 7S \xrightarrow{\mu_2} 8I \\ &I = I_1 + I_2 \end{aligned} \tag{23}$$

It is then easy to write the ODEs associated to schemes (22) and (23).
Let us now consider another aspect of the model. In Subsection (2.2), we have introduced scheme (2) that models the lockdown measures. As mentioned, such measures are imposed by national governments to all susceptible population. However, we can also take into consideration the hypothesis that these measures are not rigorously respected by the population and this for various reasons: neglect of the problem, depression due to prolonged isolation, lack of confidence in the measures adopted by the government, desire to attend parties with friends and relatives, refusal to wear masks in crowded environments, etc. These actions invalidate the effectiveness of lockdown measures significantly. Scheme (2) still adapts to describe these kind of situations with the trick of replacing Fig. 1 with another one that models the *emotional behaviour* of susceptible people (or with an analytic expression that may be obtained by using the *mathematical basis* introduced in Sonnino *et al.*, 2021). The ODEs read

$$\begin{aligned} \dot{S} &= -\mu SI - k_E S(E_{Max} - S_E) + (1 - k_E)(E_{Max} - E) \\ \dot{S}_E &= k_E SE - k_E^{-1} S_E \end{aligned} \tag{24}$$

where E stands for *emotional*.
This paper, together with Sonnino *et al.* (2021), are the first contributions to the overall objectives aiming to obtain the correct space-time stochastic differential equations able to describe realistic situations of spread of SARS-CoV2 infection in large countries. This goal can only be achieved if we are able to

1. model the distribution of hospitals in a country;
2. model the distribution of the poles of attraction of susceptible people (e.g., shopping centers, workplaces, etc.);
3. identify a mechanism that allows to establish when a pole of attraction becomes 'saturated' with infected people by proposing alternative poles of attraction;
4. modelling the lockdown and the quarantine measures adopted by the government of the country;
5. determine the nature of the intrinsic (ie spontaneous) fluctuations to which a macroscopic system is subjected, determining the correlation function by statistical mechanics.

At first glance, such a work program would appear to be too ambitious and, to our knowledge, the state-of-the-art of the current alternative techniques are unable to resolve the issues listed above. The approach KTR proposed by us is very promising and allows to achieve this goal in a relatively simple way. With the axioms enunciated in the Introduction, the "kinetic-type reactions" approach

- models each actor by a dedicated 'chemical species' that can only be created or destroyed as the result of one, or several, elementary steps,
- allows to determine the dynamics of the system starting from this set of elementary steps;
- thanks to its flexibility allows to analyse complex situations where several variables are involved, such as R, Q, R_h, I_h, etc.

8. Conclusions

We showed that our model is able to produce predictions not only on the first but also on the second or even the third waves of SARS-CoV2 infections. The theoretical predictions are in line with the official number of cases with minimal parameter fitting. We discussed the strengths and limitations of the proposed model regarding the long-term predictions and, above all, the duration of how long the lockdown and the quarantine measures should be taken in force in order to limit as much as possible the intensities of subsequent SARS-CoV-2 infection waves. This task has been carried out by taking into account the theoretical results recently appeared in the literature (Sonnino & Nardone, 2020) and without neglecting the delay in the reactions steps. Our model has been applied in two different situations: the spreading of the coronavirus in a small country (Belgium) and in big countries (France and Germany). Finally, we mention that in Sonnino *et al.* (2021), we have incorporated real data into a stochastic model. The goal is to obtain a comparative analysis against the deterministic one, in order to use the new theoretical results to predict the number of new cases of infected people and to propose possible changes to the measures of isolation.

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