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# Nonlinear science against the COVID-19 pandemic

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## ABSTRACT

This special issue showcases recent uses of mathematical and nonlinear science methods in the study of different problems arising in the context of the COVID-19 pandemic. The sixteen original research papers included in this collection span a wide spectrum of studies including classical epidemiological models, new models accounting for COVID-19 specificities, non-pharmaceutical control measures, network models and other problems related to the pandemic.

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## 1. Introduction

In late December 2019 the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infecting humans was identified in Wuhan, China. This virus was the cause of a pulmonary disease known as CoronaVirus Disease-19 (COVID-19) [1,2]. The virus was found to be genetically very similar to the SARS-CoV-1 that produced the 2003 outbreak. Various viral outbreaks have occurred in the last few years, such as those caused by MERS-CoV, SARS-CoV, Ebola, Zika, swine flu H1N1, but all of them were controlled before spreading globally. Due to its ease of transmission [2–4], SARS-CoV-2 led to the worst global pandemic since the 1918 flu. In fact, by April 2021, more than 140,000,000 people had been infected and 3,000,000 died officially from the disease, with real numbers expected to be larger.

It was soon clear that the only weapon that could defend us from this global threat was science, and indeed the scientific race to understand and mitigate the disease has been unprecedented. In only a few weeks the pulmonary disease was attributed to the novel coronavirus. By January 13, 2020, the PCR protocol used to detect the virus was available and a few months later there were hundreds of diagnostic tests available. In a few months, almost 100,000 viral genomes were sequenced, allowing for a better understanding of the pathogen. In six months there were tens of thousands of scientific papers available on SARS-CoV-2. By the end of 2020, four vaccines were already available and more than 100 candidates under study.

Applied mathematicians, epidemiologists, physicists and many other scientists with a modeling background also joined the battle. Many tried using their knowledge to help in any way they could. The tools in the nonlinear scientist's toolbox turned out

to be useful for providing a better understanding of some aspects of the disease, its propagation dynamics and its control. Beyond the simpler statistical models used for diagnosis and prognosis of COVID-19 patients [5], more sophisticated modeling tools were used, such as deterministic, data-driven, stochastic, agent-based models and their combinations, frequently used to forecast the progression of the epidemic, as well as the effects of non-pharmaceutical interventions. Modeling is also playing an important role in helping to find cures for the disease and in the design of new vaccines [6].

In March 2020, there were many preprints of different levels of quality exploring the use of those mathematical tools that would not fit well either in medical or in applied mathematics journals. This motivated us to start this COVID-19 collection. Although Physica D is not in general a mathematical modeling journal, we wanted to offer a vehicle for the fast publication of selected works of quality dealing with (nonlinear) mathematical models shedding light on different aspects of the pandemic. Different types of papers are included in this collection. In what follows I briefly summarize their content, grouping them by similarity of subject.

## 2. New results for classical epidemiological models

Some of the studies contained in this special collection provide important breakthroughs in the understanding of classical epidemiological models that had been available for almost a century. In Ref. [7], the authors studied the classical Susceptible–Infected–Recovered (SIR) model. This classic model does not allow for exact analytic solutions and the authors constructed accurate closed-form solutions through the use of Asymptotic Approximants. The solution was constructed by analytically continuing a divergent power-series solution so that it matched the long-time asymptotic behavior of the epidemic model. A related study for

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the Susceptible–Exposed–Infected–Recovered (SEIR) model was developed in Ref. [8]. Explicit solutions were created by constructing a single second-order nonlinear differential equation and analytically continuing its divergent power-series solution in such a way that it matched the correct long-time exponential damping of the epidemic model. This was achieved through an asymptotic expansion in the form of a modified symmetric Padé approximant that incorporated the damping.

In Ref. [9] a simple explicit approximate formula was obtained giving the peak time of the outbreak in the context of the SIR model. This fundamental problem had been unaddressed for a very long time. Interestingly, the methodology can be extended to analyze other more complex types of epidemiological models.

In a fourth study dealing with general epidemiological models, Ballesteros et al. [10] proved that any epidemiological compartmental model with constant population is a Hamiltonian dynamical system, the total population playing the role of the Hamiltonian function. They also showed that some particular cases of those models are bi-Hamiltonian. New interacting compartmental models among different populations, endowed with a Hamiltonian structure, were described. The Poisson structures underlying their Hamiltonian description were presented, and their Casimir functions shown to provide a tool allowing exact analytical solutions to be found for epidemiological models, such as those describing the dynamics of the COVID-19 pandemic.

Liu and Li [11] derived an epidemic model in which infected individuals had a discrete set of states of infectivity, and could switch between different states. The model also incorporated a general incidence form in which new infections were distributed over different disease states. The authors discussed the role of the transmission–transfer network for infectious diseases. Under the assumption that the transmission–transfer network was strongly connected, they established that the basic reproduction number was a sharp threshold parameter: if  $R_0 \leq 1$ , the disease-free equilibrium was found to be globally asymptotically stable and the disease always died out; however if  $R_0 > 1$ , the disease-free equilibrium was unstable, the system was uniformly persistent and initial outbreaks led to persistent disease infection. For a restricted class of incidence functions, they proved that there was a unique endemic equilibrium that was globally asymptotically stable when  $R_0 > 1$ . Furthermore, the impact of different state structures on  $R_0$ , on the distribution of the disease states at the unique endemic equilibrium, and on disease control and prevention was discussed, as well as the implications for the COVID-19 pandemic.

Another fundamental problem is the correct fitting of epidemiological model parameters from data. Calibration of SIR-type models provides a good example of the difficulties inherent in the solution of inverse problems, especially in the context of data with uncertainties. Comunian, Gaburro and Giudici [12] used a SIRD (including a compartment of deceased patients) model and set up in a framework of discrete inverse problems, explicitly considering the role and the relevance of data. Together with a physical vision of the model, their work addressed the issue of parameter calibration in SIR models numerically, and discussed how the uncertainties in the data affected the reliability of calibrated model parameters, and ultimately, of model predictions.

### 3. Extending SEIR models to describe the COVID-19 pandemic and non-pharmaceutical control measures

Several studies in the special collection deal with the construction of epidemiological models suited to the particularities of the COVID-19. Although SIR and SEIR models provide a simple way to capture the essentials of transmissible disease dynamics, they miss key ingredients present in COVID-19. These include

the presence of asymptomatic infectious individuals, or the fact that immunity acquired after the disease is transient. Moreover, standard models do not distinguish between those who have recovered and deaths due to the disease, the existence of different degrees of severity of the disease, with a fraction of the patients requiring hospitalization or even admission to intensive care units. Finally, they must be extended to account for the description of non-pharmaceutical interventions.

In that regard, Ng and Gui [13] studied a modified SEIRS model with additional exit conditions in the form of death rates and resusceptibility. In their model they could tune the exit conditions to extend prediction on the current projections of the pandemic into three possible outcomes; death, recovery, and recovery with a possibility of resusceptibility. Their study also considered specific information, such as population aging, a possible time delay in the development of the pandemic due to control action measures, as well as resusceptibility with temporary immune response. The proposed mathematical model intended to better reflect the dynamics of the COVID-19 epidemic, and provide a test bench to describe the spread of the disease and discuss different control actions. The model was verified using real-world data from South Korea and Northern Ireland.

Vyasarayani and Chatterjee [14] studied a SEIQR (for Susceptible–Exposed–Infectious–Quarantined–Recovered) model for an infectious disease, with time delays for latency and an asymptomatic phase. For fast pandemics, where no individuals have immunity initially, and all individuals acquire immunity after recovery, the SEIQR model decoupled into two nonlinear delay differential equations (DDEs). The particular case of perfect quarantining and no self-recovery before quarantine was studied using the method of multiple scales and led to a first order ordinary differential equation (ODE). With imperfect quarantining and nonzero self-recovery, the long-wave approximation allowed the system to transform into a second order ODE. These three approximations captured the full time dynamics of the outbreak, from initiation to final saturation. Their analysis showed the effect of a temporary phase of social distancing on the reduction of the total number of infected individuals. An explicit equation for the reduction was obtained.

Other extensions of SIR-type models were studied by Cadoni and Gaeta [15], Neves and Guerrero [16], and Ramos et al. [17]. In the first of these studies, the authors discussed an extension of the SIR model including a large set of asymptomatic infectious individuals, the A-SIR model [15]. They discussed how the presence of an undetected pool of patients could influence the size and timescale of the epidemic substantially. The model described Italian epidemiological data for the first wave of contagions quite well, when accounting for the effect of the restrictive measures put in place by the Government. Using the available data for Italy, the researchers compared the efficiency of different containment strategies such as social distancing, lockdown, tracing, early detection and isolation, on the epidemic dynamics.

A slightly generalized version of the same model was studied in [16]. The authors discussed how to fit the model parameters using only time series of deceased individuals, due to the large uncertainties in the numbers of asymptomatic infectious individuals. The scheme was applied to the time series data for Lombardy in Italy and São Paulo state in Brazil. The researchers found strong evidences that the adoption of social distancing measures contributed to a slower increase in the number of deceased individuals when compared to the baseline of no reduction in the infection rates. They discussed a key element of SIR-type models, namely the fact that it is possible for them to describe accurately the datasets but projections to the future are quite uncertain. In their case, this was motivated by the uncertainty in the value of a key parameter: the probability that

an infected individual is fully symptomatic, and in the intensity of the social distancing measures adopted. This fact led them to the conclusion that making predictions would require accurate data for the real number of infected individuals, either symptomatic or asymptomatic.

Ramos et al. [17] studied the minimal extension of SIR-type models allowing social distancing, contact tracing and health system measures to be implemented in a simple way in order to study the effect of these measures and estimate the need for hospital beds, which has been one of the major problems for policy makers during the successive peaks of the outbreaks of the disease. They constructed the so-called  $\theta$ -SEIQRD model, showed its good performance for Italian data and studied different scenarios.

Finally, Gandolfi [18] performed a very interesting study of the optimal strategies to minimize the propagation of the disease in schools. In his study he modeled the transmission dynamics of the epidemic within a single school using a SEAIR model with an external source of infection and a suitable loss function, and then evaluated the best opening plans. It turned out that blended models, with almost periodic alternations of in-class and remote teaching days or weeks, were generally close to optimal. In a prototypical example, the optimal strategy prescribed a school opening of 90 days out of 200 with the number of COVID-19 cases among the individuals related to the school increasing by about 67% with respect to no opening, instead of the around 200% increase that would have been a consequence of full opening. As clinical fraction is low in children, these solutions could lead to very few or no symptomatic cases within the school during the whole school year. An interesting implication of the study is that full opening of schools without measures to reduce the daily infection rate governing contagion (face masks, social distancing, etc.) would substantially increase the number of cases unless the spread of the virus is completely under control in the surrounding region (e.g. with fewer than 5 active cases for every million people).

#### 4. Beyond SEIR-type epidemiological models

As discussed before, SEIR-type models provide a simple conceptual framework allowing the interplay of different subpopulations over the course of an epidemic to be understood. They allow for the description of datasets and may allow for the qualitative discussion of the effect of control measures. However, its predictive power is limited, since they miss essential aspects of the dynamics of epidemics, such as spatial aspects. Interactions leading to transmission of the disease require contacts in space, which adds an element of complexity that is accounted for in more sophisticated models.

Vivas Miranda et al. [19] constructed a hybrid model for COVID-19 epidemics accounting for spatial aspects. Their model was based on a network of nodes corresponding to cities. Local epidemic dynamics was based on local SIR models on network nodes and population flow across these networks of cities was responsible for a complex lag dynamic in the contagion curves. The epidemic evolution at each location depended both on the local SIR parameters and on the transport flow. When heterogeneity of local contagion rates and flow across the network were included, forecasts for the epidemic were found to differ from those of the homogeneous ODE model. This effect was more relevant when more cities were considered. Mitigation scenarios were studied to evaluate the effect of early interventions reducing contacts through the network. Restricting the flow between cities in the initial stages of the epidemic was found to be a key control measure for flattening the contagion curve.

#### 5. Other COVID-19 related problems

Nonlinear science and applied mathematics methods have been used to shed light on many other problems arising in the context of the COVID-19 pandemic beyond epidemiological questions. Our special collection contains several such papers.

Firstly, Padhy and Dimri [20] studied the scaling of the surface roughness of coronaviruses, including the SARS-CoV-2, using fractal and spectral analyses of electron microscopy images. In that paper, fractal dimensions (FD) were obtained and subjected to ANOVA tests for statistical significance. SARS-CoV-2 particles could not statistically be resolved by their shape on the basis of the FD values, but they could be distinguished from SARS-CoV particles. The topological entropies measured for images of varying size showed correlation with the fractal dimensions. Spectral analyses showed a departure from power-law self-similarity, suggesting an apparent scaling of surface roughness over a band of at most an order of magnitude. The spectral crossover that corresponds to characteristic length scale may represent average viral size. These results may be useful in inferring the nature of the surface of contact between viral particles and human cells, causing infection and also in providing clues for new drugs.

Beare and Toda [21] studied the distribution of confirmed cases of COVID-19 across US counties and found empirically a power law at the right tail of the distribution. They studied whether the combination of Gibrat's law and a suitable age distribution could explain this power-law behavior. Using daily county-level data from the onset of COVID-19 in the US in January 2020 until the end of March 2020, they estimated the distributions of growth rates and ages, using a gamma parametrization of the former and a truncated logistic parametrization of the latter. Their main result was that the power-law exponent implied by the estimated growth rate and age distributions, matched the exponent obtained from the distribution of cases across counties at the end of March very well. This was an indication that the combination of Gibrat's law with a suitable age distribution could explain the decay of the right tail of the distribution of COVID-19 cases across US counties.

Finally, James and Menzies [22] studied the impact of COVID-19 on the populations and equity markets of 92 countries. They compared country-by-country equity market dynamics to cumulative COVID-19 case and death counts and new case trajectories. They examined the multivariate time series of cumulative cases and deaths, particularly regarding their changing structure over time, revealed similarities between the case and death time series, and found key dates at which the structure of the time series changed. They next classified new case time series, obtained five characteristic classes of trajectories, and quantified the discrepancies between them with respect to the behavior of waves of the disease. Finally, they showed there were no relationships between countries' equity market performances and their success in managing COVID-19. Thus, countries' equity indexes were found to be unresponsive to the pandemic, with most changes happening in March 2020.

#### 6. Conclusion

The Physica D article collection on COVID-19 shows the variety of theoretical approaches that can help in understanding and managing the COVID-19 pandemic. It contains several papers on general classical epidemiological problems whose interest goes beyond the immediate relevance to the current pandemic. Several papers deal with epidemiological models specific to COVID-19, describing different aspects of the dynamics of the pandemics. Some of these papers also discuss the effectiveness (or otherwise) of non-pharmaceutical interventions such as quarantining part

of the population, school closures, the use of social distancing, contact tracing and measures related to the health system. Other topics studied include the scaling of surface roughness of coronaviruses, power laws in the numbers of cases, and the impact of the disease on the countries' populations and equity markets. All in all, this highlights the role of data and model-based approaches in the COVID-19 pandemic and brings out the relevance of scientific approaches in addressing one of the largest global crises that has affected our societies in the XXIst century.

### 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.

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