



Review

Chaos theory in the understanding of COVID-19 pandemic dynamics

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ARTICLE INFO

Keywords:

Chaos Theory
epidemiology
emerging viruses
SARS-CoV-2
coronaviruses
pandemic
epidemic

ABSTRACT

The chaos theory, a field of study in mathematics and physics, offers a unique lens through which to understand the dynamics of the COVID-19 pandemic. This theory, which deals with complex systems whose behavior is highly sensitive to initial conditions, can provide insights into the unpredictable and seemingly random nature of the pandemic's spread. In this review, we will discuss some literature data with the aim of showing how chaos theory could provide valuable perspectives in understanding the complex and dynamic nature of the COVID-19 pandemic. In particular, we will emphasize how the chaos theory can help in dissecting the unpredictable, non-linear progression of the disease, the importance of initial conditions, and the complex interactions between various factors influencing its spread. These insights are crucial for developing effective strategies to manage and mitigate the impact of the pandemic.

1. Introduction

The Coronavirus disease 2019 (COVID-19), caused by the novel coronavirus Severe Acute Respiratory Syndrome- CoronaVirus-2 (SARS-CoV-2), emerged in late 2019 and swiftly escalated into a global pandemic (Huang et al., 2020). Its impact has been profound and multifaceted, affecting nearly every aspect of life worldwide. The disease, characterized by respiratory symptoms, led to significant morbidity and mortality, straining healthcare systems globally (Shroff et al., 2021). Due to the rapid spread of SARS-CoV-2, COVID-19 necessitated unprecedented Public Health measures, such as lockdowns and social distancing, which resulted in wide-ranging economic and social repercussions (Mofijur et al., 2020). On the other hand, COVID-19 crisis contributed to a rapid progress of the scientific research in different fields, including the development/implementation of tools to predict disease spreading and evolution as well as the impact of Public Health interventions (Excler et al., 2023).

Mathematical models play a central role in the management of an infectious disease (Grassly and Fraser (2008)), as they can help in predicting epidemiological aspects (e.g. number of individuals expected to be infected, number of fatalities, time of the epidemic peak) (Glasser et al., 2004; Huppert and Katriel (2013)) crucial for planning and implementing effective Public Health measures (Glasser et al., 2004).

During the past few decades, different scientific methods were adopted/developed to predict the epidemiological burden of infectious diseases (Schaffer, 1985; Schaffer and Kot, 1985; Olsen et al., 1988; Hethcote et al., 1989; Grenfell et al., 1995; Earn et al., 2000; Mandal and Banerjee (2012); Kumar, et al., 2019; Machado et al., 2020), including the one caused by a coronavirus emerged in the human population earlier than SARS-CoV-2, i.e. SARS-CoV-1 (Lipsitch et al., 2003; Gumel et al., 2004; Masuda et al., 2004; Bauch et al., 2005).

If forecasting the behavior of an epidemic is difficult, making useful predictions on the course of a pandemic caused by a novel infectious agent is even more complicated. Despite this challenge, several mathematical models have been developed, especially trying to model the dynamics of the COVID-19 spread as well as the potential impact of adopted countermeasures (Giordano et al., 2020; Adak et al., 2021; Sivakumar and Deepthi, 2021; Lee et al., 2023). As most of the biological and social parameters taken into account by mathematical models are often unknown or affected by variations and uncertainty (Bandt et al., 2020), some stochastic models were also developed in the case of the SARS-CoV-2 pandemic (Chinazzi et al., 2020; Giordano et al., 2020; Jia et al., 2020; Li et al., 2020; Lee et al., 2023).

The chaos theory, in its most basic form, is a branch of mathematics focusing on systems that are highly sensitive to initial conditions (Fernández-Díaz, 2024). The chaos theory, when applied to

Abbreviations: SARS-CoV-1, Severe Acute Respiratory Syndrome Coronavirus 1; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; MERS-CoV, Middle East Respiratory Syndrome Coronavirus; COVID-19, Coronavirus disease 2019.

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<https://doi.org/10.1016/j.gene.2024.148334>

Received 16 January 2024; Accepted 28 February 2024

Available online 7 March 2024

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epidemiology, brings several important principles that are highly relevant for understanding and managing disease spread (Mangiarotti et al., 2020): i) the “butterfly effect,” i.e. how small changes in initial conditions can lead to vastly different outcomes of dynamic systems. In epidemiology, this principle exemplify the concept that minor variations at the start of an outbreak (such as the number of initial cases, location, or timing) can significantly influence the epidemic course; ii) the non-linearity of dynamic systems. Biological and Public Health systems are inherently non-linear. This non-linearity can result in unexpected behaviors like sudden outbreaks or rapid declines in case numbers without obvious causes; iii) the chaos theory indicates that, under certain conditions, even the more apparently unpredictable system presents patterns that can be identified with the correct tools. Epidemiological systems are complex, involving interactions between human behavior, environmental factors, pathogen characteristics, and healthcare interventions. The chaos theory should help in understanding how these dynamic components interact and influence each other, allowing, for instance, predictions of epidemic trajectory; iv) the concept that patterns can be similar at different scales is a central concept of the chaos theory. In epidemiology, this means that the patterns of the disease spread might be similar in small communities as well as in larger populations, allowing for scalable models and interventions; finally v) the principle of the feedback mechanisms, where the output of a system feeds back into its input. In epidemiology, feedback loops can be seen in how public health measures affect the disease course, which in turn influences further Public Health decisions.

In this review, we will discuss literature data addressing how chaos theory can enable a deeper understanding of the complexity underlying infectious disease spread and control, resulting in effective strategies for managing Public Health crises. In particular, we will focus on how the chaos theory principles have been adopted to model the COVID-19 pandemic. We will also discuss how the same principles could be applied to an emerging pathogen with the aim of predicting its chance to establish a long-lasting relationship with the new host, as in the case of recently emerged coronaviruses and the human population.

2. The chaos theory applied to the analysis of epidemic/pandemic behavior

Different mathematical models have been adopted in the last decades to predict the course of infectious disease epidemics, while advanced computational methodologies can be used to analyze and predict the impact of Public Health interventions, such as pharmacological treatments and vaccination. The birth of the modern mathematical epidemiology can be set in 1927 when Kermack and coworkers published a seminal work describing the first mathematical model known as “susceptible-infected-recovered” (SIR) model (Kermack et al., 1927). SIR represents one of the earliest models based on the classification of the population exposed to the infectious agents in well-defined classes, whose interactions are studied by adopting pre-established mathematical rules. To better mirror the complexity of the epidemic dynamics, these approaches have been implemented over times (Mata and Dourado, 2021).

The main current models adopted to infer the course of infectious diseases can be summarized in: deterministic, stochastic, agent-based, or a combination of these approaches. Most of these are methods are based on compartment models where the probability of the transition of the population from one compartment to the other is differently modelled in stochastic and/or in deterministic frameworks (Tolles and Luong, 2020). In general, all of these models try to capture the complexity of the real world, such as mobility patterns, social contacts, age stratification and spatial distribution of the population. Overall, these advanced models meant to account for the intrinsic complexity of the analyzed phenomenon, are very useful to predict some aspects of the epidemic course, such as the number of people that will be affected, what percentage of a population should undergo vaccination, the potential impact of certain

containment measures. However, one of the main limitations of these methods is linked to the fact that most of the mechanisms driving/influencing the progress of an epidemic are unknown, thus negatively affecting the prediction power of the mathematical formulation. This restraint is particularly true in the case of outbreaks caused by new pathogens (Sapkota et al., 2021; Afzal et al., 2022).

In nature, several complex systems do exist that, while displaying an apparent random and unpredictable behavior, present underlying patterns and can be described by deterministic laws. Falling in the definition we found, for instance, weather and climate. These dynamical systems are highly sensitive to initial conditions, meaning that a tiny change in the initial conditions can have a significant effect at later stages of their development (Fernández-Díaz, 2024). The apparent chaos inherent in these systems is defined “deterministic chaos”. The chaos theory is an interdisciplinary area of mathematics that focuses on the study of structures characterized by deterministic chaos. Based on these premises, the chaos theory finds applications in a variety of disciplines, including meteorology, anthropology, environmental science, economics, and ecology. Interestingly, the spread of an infectious disease met most of the criteria that define a chaotic behavior. First, disease spread can be non-linear and highly sensitive to initial conditions; indeed even small changes in the initial conditions can have a significant impact on the evolution of an outbreak. Small changes in factors such as population density, mobility, or social behavior can lead to vastly different outcomes. Furthermore, epidemics are characterized by unpredictability and pattern sensitivity. Public health systems are complex, with numerous interacting components like healthcare infrastructure, human behavior, environmental factors, and pathogen characteristics. In line with these observations studies have described chaotic behavior in different epidemics (Speakman and Sharpley (2012); Mangiarotti, 2015; Mangiarotti et al., 2016; Augusto and Khan, 2018) as well as in the recent COVID-19 pandemic (Mangiarotti et al., 2020). Evidence has brought to light some limitations of the traditional compartmental epidemiological models, stressing the need to apply methods more suitable to catch the chaotic dynamic nature of infectious diseases (May, 1976; Viboud et al., 2003; Schaffer, 1985; Schaffer and Kot, 1985; Olsen et al., 1988; Hethcote et al., 1989; Sugihara and May, 1990; Grenfell et al., 1995; Casagrandi et al., 2006). This limitation is particularly evident in the case of outbreaks caused by emerging pathogens such as Ebola virus and SARS-CoV-2 (Machado et al., 2020; Mangiarotti et al., 2016; Mangiarotti et al., 2020; Afzal et al., 2022). In a very interesting work Borah and coworkers, by evaluating infectious and non-infectious pandemics, show that their behavior is indeed chaotic with features that are not entirely captured by integer-order models, such as the compartmental ones (Borah et al., 2022). The Authors, then, propose fractional-order methods based on the chaos theory, as more accurate and realistic tools to model the dynamics and progression of pandemics. This conclusion is supported by the data obtained with these tools in modelling of Bombay plague, cancer and COVID-19 pandemics (Borah et al., 2022).

3. The chaos theory applied to the analysis of COVID-19 pandemic behavior

In the case of COVID-19, different works underlined the chaotic nature of the pandemic urging for the adoption of chaos theory based models to predict its course and the potential impact of Public Health countermeasures (Machado et al., 2020; Giordano et al., 2020; Jones and Strigul, 2021; Necesito et al., 2022; Postavaru et al., 2021; Sapkota et al., 2021; Sivakumar and Deepthi, 2021). Interestingly Matouk by comparing a compartmental model to a fractional order one based on chaos theory principles, demonstrated that the latter was more powerful in explaining the pandemic data and its complex dynamics (Matouk, 2020).

Indeed, several features of the COVID-19 worldwide spread and the effect of interventions clearly meet some of the main principles of chaos

theory (Table 1), thus supporting the application of this model to study/ infer various aspects of this pandemics.

Based on this premise, Sivakumar and Deepthi applied the chaos theory to investigate the complexity and unpredictable nature of the COVID-19 dynamics, by using data from several Countries/Regions worldwide (Sivakumar and Deepthi, 2021). On the other hand, Mangiarotti and co-workers, adopted a chaos theory based method suitable for the detection of deterministic patterns underling dynamical behaviors, named global modelling technique (Gouesbet and Letellier, 1994; Lainscsek et al., 2001; Letellier et al., 2009; Mangiarotti et al., 2012; Mangiarotti et al., 2020). This approach allows the analyses of systems that are highly sensitive to the initial conditions, working even when relevant variants are unknown, a condition that, as mentioned above, is frequent in epidemiology. Finally, its application leads to compact and better interpretable mathematical equations (Mangiarotti and Huc, 2019). This approach was previously applied to the 1896–1911 Bombay bubonic plague (Mangiarotti, 2015) as well as to the West Africa epidemic of Ebolavirus (2013-2016) (Mangiarotti et al., 2016)

Mangiarotti and coworkers used this modelling method to analyze the COVID-19 pandemic in Asia and Italy and to foresee its behavior in additional countries where the disease arrived later on. The scenarios predicted by the model were confirmed, providing evidence that this approach could be adopt to manage rapidly evolving contexts (Mangiarotti et al., 2020).

Debbouche and coworkers (Debbouche et al., 2022) further extended these findings by using among other chaos theory tools the Lyapunov exponent (LE). The LE is a measure of the rate at which nearby trajectories in a dynamic system diverge. In studying COVID-19, a high LE

would suggest a high degree of unpredictability in the spread of the virus. This method can help identify periods or locations where the pandemic behaves more chaotically. Debbouche’s results, not only confirmed the conclusions of Mangiarotti’s work, but also indicated that the numbers of new cases, severe cases, and fatality cases show a chaotic behavior in the absense of interventions aimed at controlling the spread of the disease. Another research group adopted LE to study the rise and decay of SARS-CoV-2, coming up with a two-step model and predicting the number of fatalities in the absence of social and other Public Health measures (Zheng and Bonasera, 2020). In their elegant work, Necesito and coworkers described the chaotic behavior of COVID-19 by adopting state space plots and convergent cross mapping (CCM) (Necesito et al., 2022). State space plots are used to visualize the trajectory of a dynamic system in a multidimensional space. In the context of COVID-19, these plots can depict changes in the number of cases over time, illustrating how the disease trajectory changes in response to various factors like public health interventions or changes in public behavior. CCM is a technique used to detect causal relationships in complex systems. It can be applied to COVID-19 data to understand how different variables, such as government policies or social behaviors, influence the spread of the virus. In the study by Necesito et al., state space plots and CCM were used to analyze the effect of non-pharmaceutical interventions on the number of cases and the changes in asymptotic behavior. The conclusion was that, overall, the adopted measures were effective, but their efficacy was reduced by the increased density of the population (Necesito et al., 2022).

4. The logistic map as a tool to model COVID-19 spread and viral evolution

The logistic map is a mathematical model that exhibits chaotic behavior under certain conditions (May, 1976). Taking into account the non-linear and sensitive nature of disease transmission, the logistic map can be used, for instance, to predict the spread of a pandemic/epidemic by modeling the growth of case numbers over time (Sugihara and May, 1990). Mathematically the logistic map is expressed by the equation:

$$x(n+1) = r \cdot x(n) \cdot [1 - (n)]$$

This nonlinear difference equation represents a recurrence relation meaning that each element of the sequence at the step “n + 1” is a function of the same elements at the step “n”. It reflects the notion that, given certain starting conditions, after a sufficiently long period of time dynamic systems tend to evolve towards a set of states that are defined attractors. The logistic map can be applied to the study of driven-damped systems that incorporate both positive and negative feed-backs, as is the case of a population growth (Storch et al., 2017). In this context, the variable x(n) is a percentage measure of the population size at the time “n” while x(n+1) is the value at the time “n+1” (e.g. after 1 year of observation). Thus, the x value ranges between 0 (i.e. 0 % = population extinction) and 1 (i.e. 100 % = maximum possible population). The growth rate “r”, on the other hand, reflects the combined effect of reproduction and density-dependent mortality (starvation) on the population size. If r falls in the interval [0,4], the variable x(n) remains in the range [0,1], displaying, during the logistic map iteration, the following behavior:

r<1: x(n) goes to 0 leading to the population extinction (grey part of the logistic map in Fig. 1)

1<r<3 a linear growth of the population is observed and x(n) settles down to a specific value, expressed by the ratio r-1/r (light green part of the logistic map in Fig. 1). This value will be reached rapidly when 1 < r < 2, and after some fluctuations in the interval 2< r <3.

3<r< 3.56995 is the period-doubling cascade in which the population grows with permanent oscillations among fixed numbers of values (yellow part of the logistic map in Fig. 1)

r ≈ 3.56995 (hereafter referred as 3.57 for simplicity) represents the onset of chaos. Within the interval 3.57< r<4, slight variations in the initial population yield dramatically different results over time. As

Table 1
Features of COVID-19 pandemic that meet principles of the chaos theory.

Sensitivity to Initial Conditions	The trajectory of COVID-19 in different regions showed how initial conditions, such as the timing of the first case, public health responses, population density, and mobility patterns, could significantly influence the spread and severity of the outbreak
Non-Linearity and Unpredictability	The spread of COVID-19 did not always follow a linear pattern. Instead, it exhibited non-linear dynamics, with sudden spikes in cases and varying rates of transmission over time and across locations. This unpredictability made it challenging to forecast the course of the pandemic precisely
Complex System Dynamics	The spread of COVID-19 involved multiple interacting factors, including biological characteristics of the virus, human behavior, environmental factors, and socio- economic conditions. These elements created a complex system with emergent properties that were difficult to predict or control.
Feedback Loops	Responses to the pandemic, such as lockdowns, social distancing measures, and mask mandates, acted as feedback mechanisms. The effectiveness of these measures influenced the course of the pandemic, which in turn affected public health policies and individual behaviors
Fractal Patterns and Scaling	The patterns of COVID-19 spread showed self-similarity across different scales. For example, the virus transmission dynamics within a small community could reflect broader patterns observed at a national or global level.
Edge of Chaos and Phase Transitions	The concept of being on the “edge of chaos” is where systems operate between order and disorder. COVID-19 demonstrated this with sudden shifts or phase transitions, like the emergence of new variants or unexpected outbreak clusters, changing the dynamics of the pandemic.

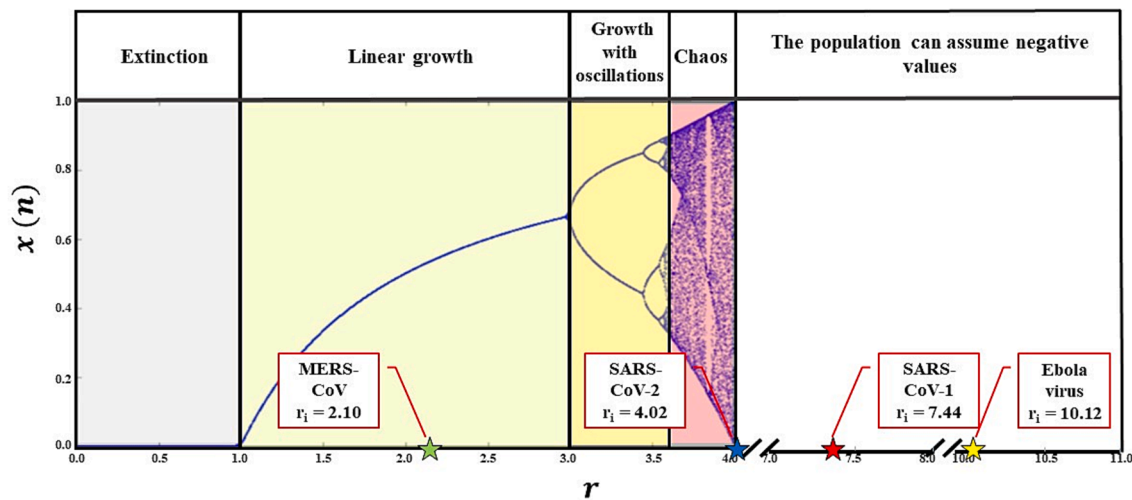


Fig. 1. Bifurcation diagram of the logistic map. The bifurcation diagram depicts the graphical representation of the logistic map applied to the population size. In the interval $[0 < r < 4]$ for which $0 < x < 1$, the graph can be divided into 4 zones: i) a grey zone characterized by the r values linked to extinction of the population; ii) a light green zone depicting a linear growth; iii) the yellow zone defining a growth with oscillations; iv) the pink one representing the chaos zone. Stars indicate the initial r values (r_i) calculated for the different emerging viruses under study, as reported in (Roggero et al., 2023). In the graph is also reported the white zone corresponding to r values above 4 for which the population size can achieve negative results. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Adapted from Roggero et al., 2023

already discussed this is a main feature of the “deterministic chaos”, that is then well expressed by this part of the logistic map. In this case, we do not observe oscillations of finite period but the system is governed by so called “chaotic attractors” (pink part of the logistic map in Fig. 1).

$r > 4$ the sequence diverges for almost all the initial population size and $x(n)$ leaves the interval $[0, 1]$, eventually reaching negative values.

If we graphically represent all the values hit (fixed points) or asymptotically approached (periodic orbits or chaotic attractors) by $x(n)$ given a certain r we generate a bifurcation diagram, as reported in Fig. 1.

Application of chaos concepts to ecology and to population growth date back to the seminal work of Robert May who propose their application to model the behavior of biological populations with discrete, non-overlapping generations (May, 1976). The logistic map is, at least partially, analogous to the logistic equation first formulated by Verhulst (Verhulst, 1847). In this context, different research groups have adopted and implemented logistic growth models to predict the trend of the pandemic (Pelinovsky et al., 2020; Shen, 2020; Wu et al. (2020); Wang et al., 2020; Zou et al., 2020; Triambak et al., 2021; Pelinovsky et al., 2022). Interestingly some research groups also applied the bifurcation analysis to the study of COVID-19 spread and behavior, also in the context of Public Health interventions, such as vaccination (Shen, 2020; Idisi et al., 2023)

On the other hand, we recently took advantage of the logistic map to support our proposition that emerging viruses undergo an evolution that is conditioned by the rules of chaos (Roggero et al., 2023). By taking into account the three coronaviruses recently emerged in the human population (i.e. SARS-CoV-1, MERSV-CoV, SARS-CoV-2) as well as the Ebola virus causing the 2014 West Africa epidemic (Lawrence et al., 2017) we calculated among other parameters, the initial r value for each pathogens by adopting the formula:

$$r = \frac{\ln \frac{P_t}{P_0}}{t}$$

where P_t represents the total number of infections at time t , P_0 is the initial number of infections, while t is the time frame of data collection under evaluation. If t is the time expressed in days requested for doubling the initial number of infected individuals, P_t becomes $2 P_0$ and the formula can be simplified into:

$$T = \frac{\ln 2 \times 365}{r}$$

or

$$r = \frac{\ln 2 \times 365}{T}$$

In this way, we could use publically available data (Roggero et al., 2023) to calculate T and thus r . If we define the initial r (r_i) as the value obtained for the first T , we find for the emerging viruses under evaluation the following r_i :

SARS-CoV-1 = 7.44
MERS-CoV = 2.10
SARS-CoV-2 = 4.02
Ebola virus = 10.12

Overall, our data indicate that r_i is correlated with the chances of the virus to establish a long-lasting relationship with the new host: an emerging virus is able to spread/adapt only when it displays an r_i falling in an interval of values frankly associated with the chaotic growth, as it is the case of SARS-CoV-2 (Fig. 1). Indeed, among the viruses under evaluation, SARS-CoV-2 was the only one giving rise to a pandemic and still circulating in the human population. By contrast, neither emerging viruses with an r_i above 4 (SARS-CoV-1 and Ebola virus), a condition, as mentioned above associated with population size negative values, nor a pathogen with an r_i falling with the linear growth part of the logistic map (MERS-CoV) were capable of becoming pandemic. While SARS-CoV-1 and Ebola virus were eradicated by the human population, MERS-CoV is still occasional transmitted through zoonotic events. In conclusion, we believe that the r_i value reflects intrinsic biological features of the emerging virus, affecting the type of pathogen initial growth/spreading in the population and, as a consequence, its chances to establish a long-lasting relationship with the new host. As this adaptation is linked to specific mutations of the viral genome that are maintained, it is possible to speculate that an initial chaotic growth enables the acquisitions of this favorable genomic changes, while different types of growth do not. In this context, the r_i could provide useful information about the possibility that an emerging virus could adapt to the human species, becoming a threat to humankind.

Although we applied the chaos theory directly to the viral spread in the population, it is tempting to speculate that the same rules could drive the emergence of those favorable mutations within the viral genome. Interestingly, the different SARS-CoV-2 variants of concerns (VOCs) that appeared during the pandemic (Markov et al., 2023), although they

emerged in different parts of the world and independently from each other, share sets of mutations, indicating possible convergent evolution (Starr et al., 2022; Telenti et al. (2022)). In particular, looking at the Spike protein of the virus, where, given its functions, most of the mutations map, changes appear to localize in topically clustered hot spots (Starr et al., 2022; Telenti et al. (2022)). This observation would suggest that in emerging viruses prone to establish a long-lasting relationship with the new host, mutations that allow this adaptation converge in specific genomic regions, that would function as attractor elements. In this application of chaos theory to viral evolution, the initial conditions would be represented by the specific features of the founder virus genome. This founder genome would mutate following the attractor elements that inherently drive its evolution towards virus survival and fitness.

5. Conclusive remarks and still open challenges

In conclusion, insights from chaos theory can significantly inform public health policies and strategies for responding to the COVID-19 pandemic by highlighting the importance of flexibility, adaptability, and a nuanced understanding of the complex dynamics at play. Not only, chaos theory might even help in predicting emerging virus evolution and adaptation to the new host. However, it has to be underlined that applying chaos theory to real-world scenarios like the COVID-19 pandemic still presents several challenges. First chaos theory requires extensive and high-quality data to accurately model complex systems. In the context of COVID-19, consistent, detailed, and real-time data collection was challenging due to varying testing rates, differences in reporting standards, and the asymptomatic nature of many cases. Chaos theory highlights the need for continuous monitoring of epidemiological data. Rapid adjustments to strategies based on real-time data can be more effective than rigid, long-term plans. Since chaos theory suggests that small-scale dynamics can significantly influence larger systems, it supports the idea of localized, targeted interventions that consider specific demographic, geographic, and social factors. Policies can be seen as part of a feedback loop where the outcome of an intervention informs the next step. For example, the impact of social distancing measures on infection rates should guide subsequent decisions on tightening or easing these measures. While chaos theory provides a framework for understanding complex systems, there is still a lot that is unknown about how chaotic dynamics play out in real-world scenarios, especially in a situation as unprecedented as the COVID-19 pandemic. The constantly evolving nature of the COVID-19 virus, with new variants emerging, adds another layer of complexity. Models need to be continuously updated to account for these changes, which can be a significant challenge. While chaos theory models can provide detailed insights, they can also become so complex that they are difficult to use in practical decision-making. Finding the right balance between model precision and usability is a key challenge.

Despite these limitations, chaos theory remains a valuable tool in understanding and managing the complexities of the COVID-19 pandemic, offering insights that traditional models may not capture. Addressing these challenges requires ongoing research, interdisciplinary collaboration, and a commitment to refining and adapting models as new data and insights become available.

CRedit authorship contribution statement

Arianna Calistri: Conceptualization, Writing – review & editing.
Pier Francesco Roggero: Conceptualization, Writing – review & editing.
Giorgio Palù: Conceptualization, Supervision, Writing – original draft.

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.

Data availability

No data was used for the research described in the article.

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