

Chaotic attractors in cancer and epidemic models: insights from predator-prey interactions

Abstract

The current study, in conjunction with an examination of existing literature, demonstrates that the emergence of chaotic behavior is predominantly attributed to interactions between predators and prey, as well as competitive dynamics. Similar patterns have been observed in the context of pandemics and cancer models, where deterministic chaos or chaotic dynamics result in complex oscillations and nonlinear interactions among cell populations. It is notable that the current pandemic exhibits key characteristics of a chaotic system and is recognized as one of the deadliest pandemics in contemporary history.

This study presents an analysis of a dynamical model of an ecosystem comprising one predator and three prey species, one of them is sick, one is healthy and one is immune. The findings indicate that variations in the reproduction rates of healthy prey and predator-prey interactions induce chaotic dynamic transients, which manifest as damped oscillations over extended periods. Upon monitoring the disease infectivity parameter (R) over time, a rapid decline in the healthy prey population is observed within days. In contrast, the infected prey population demonstrates a damped oscillatory growth and decay pattern, indicating that the predator consumes both healthy and infected prey. Over extended periods, all variables exhibit a tendency towards equilibrium. Phase portrait diagrams, generated using 3-D and 2-D representations with varied reproduction rates of healthy prey (parameter a) and disease infectivity (parameter R), reveal the existence of stable points, unstable points, saddle points, and bifurcation diagrams. The equilibrium points demonstrate characteristics of chaotic attractors. The chaotic propagation of a pandemic is highly sensitive to minor variations in the initial conditions (ICs) of physical factors. Mathematical models serve as crucial tools for devising strategic action plans to control epidemics and pandemics, offering real-time data for effective outbreak management. This research holds significant implications for ecological dynamics and disease modeling, with practical applications in public health and epidemiology.

Keywords: The chaotic dynamics, prey-predator interaction, time series, phase portraits diagrams, bifurcation diagram, Lyapunov exponents.

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Introduction

Borah et al.,¹ report extensively on the chaotic behavior of pandemics in low- to mid-income countries. Examples include the Plague epidemic in Bombay, India, chaotic epidemic crisis management in Mexico, Ebola Virus epidemic in Guinea, Liberia, and Sierra Leone, and Dengue in Pakistan. Additionally, the authors noted that certain cancer models exhibit deterministic chaos or chaotic dynamics, resulting in complex oscillations. Jones and Strigul² suggest that COVID-19 exhibits the qualitative characteristics of a chaotic system and is one of the deadliest pandemics in recent history due to its exponential spread. The Coronavirus disease, which emerged in 2019, has a high mortality rate.¹

The emergence of chaotic behavior can be attributed mostly to predator-prey and competition dynamics, as stated by Diekmann and Kretzschmar.³ Nonlinear interactions between cell populations, such as those found in cancer models and Parkinson's disease, also contribute to chaotic behavior, according to Gross et al.⁴ Stiefs et al.,⁵ have also observed chaotic long-term dynamics in models where the prey is infected.

Hesketh et al.,⁶ proposed that ecological models should consider the significance of human-environment interactions in comprehending and modifying human behavior. These models have been integrated at various levels of influence on behavior, including the policy,

community, organizational, social, and individual levels. However, fewer studies have explored correlates at the social, physical, and policy levels. In contrast to the behavior of oscillations, the effect of chaos on the stability of ecological models has been a topic of debate for a considerable period of time.⁵

Debbouche et al.,⁷ has presented that the conceived COVID-19 pandemic model that shows chaotic behaviors. The system dynamics are investigated via bifurcation diagrams, Lyapunov exponents, time series, and phase portraits. Besides that, which deterministic chaos is a common behavior in continuous time dynamical systems of differential equations with nonlinear terms, which show aperiodicity, ergodicity and sensitivity to initial conditions, which was argued by Allen et al.,⁸ This gives great importance to mathematical models as a possible tool for the development of strategies to plan for an anticipated epidemic or pandemic, and to deal with a disease outbreak in real time, Brauer et al.,⁹ pointed out. Mangiarotti et al.,¹⁰ presented an important study in the field of epidemiology. They developed several schemes to mathematically model infectious epidemics, with compartment models being the most used, these models divide in classes and determine interactions between them using mathematical formulation. Generally, it is difficult to formulate a complete model of an epidemic disease in equations within these formalisms due to the novelty of the disease and its rapidly changing shape and behavior. Volos¹¹ conducted research pointed out that a pandemic's propagation

is highly sensitive to slight variations in initial conditions of physical factors, such as the number of asymptomatic carriers, infected cases, and undetected cases. When studying an ongoing pandemic, chaos theory can be a powerful approach to define, model, and analyze the dynamics system. This involves taking into account relevant variables, equations that govern these variables, parameter values, constraints of the model, and reformulation of the equations based on existing observations are made, Mangiarotti et al.,¹⁰ have formulated this approach.

This work presents a study of a dynamical model of an ecosystem with one predator and three prey species, one of them is sick, one is healthy and other is immune. The study is based on the classical Lotka-Volterra model and the results show that the interaction between the predator and the prey species varying the reproduction rate of the healthy prey species. The time series results show a chaotic dynamic transient with damping oscillations for long times. This work demonstrates the potential usefulness of mathematical models that allows us to use strategies for planning for an anticipated epidemic or pandemic, as well as dealing with a disease outbreak in real time.

Materials and methods

Mathematical model

Eilersen et al.,¹² analyzed a dynamical model of an ecosystem consisting of one predator and three prey species, one of them is sick, one is healthy and other is immune. The authors assumed that healthy and infected animals are equally difficult to catch and equally nutritious for the predator. They found that the system exhibits chaotic behavior for a wide range of parameters. Gakkhar and Najji¹³ pointed out that the emergence of chaotic behavior is mainly due to predator-prey and competition dynamics.

The authors proposed the following model of the classical Lotka-Volterra equations,¹² which is represented by the system of equations (1).

$$\begin{cases} \frac{dx_s}{dt} = ax_s - Rx_s x_i - ax_s z \\ \frac{dx_i}{dt} = Rx_s x_i - ax_i z - x_i \\ \frac{dy}{dt} = by - acy z \\ \frac{dz}{dt} = d(x_s + x_i + y)z - dz \end{cases} \quad (1)$$

The given equation describes the populations of x_s and x_i as healthy and infected populations of the susceptible prey species, respectively. The population of the immune prey species is represented by y , and z represents the population of predators.

a = the reproduction rates of the healthy prey.

R = the disease basic reproduction number or disease infectivity. In real epidemics R varies from around 1;

b = the immune growth rates

c = the rate of the prey of species x and y eaten by predator

d = the rate at that predators starve in the absence of prey.

The Jacobian matrix for the system of equations (1) is presented in the following equation:

$$A = \begin{bmatrix} a - Rx_i - az & -Rx_s & 0 & ax_s \\ Rx_i & Rx_s - az - 1 & 0 & -ax_i \\ 0 & 0 & b - acz & -acy \\ dz & dz & dz & d(x_s + x_i + y) - d \end{bmatrix} \quad (2)$$

Numerical methods

The Scilab software¹⁴ was used to obtain an approximate solution for system (1), which is given by the following recurrence formula:

$$xp = x - inv(JF(x)) * (F(x)) \quad (3)$$

The solution, xp , is an approximation. $F(x)$ represents the matrix function of the system functions, and $JF(x)$ represents the Jacobian of the matrix function.

The parameters of the system (Eq. 1) have been proposed by Eilersen et al.,¹²

$$a = 7/400, b = 0.0208, c = 2, d = 0.3098, R = 1.025 \text{ and } R=1.5.$$

The parameters a , d , and R were varied between 0 and 2, and 1 and 5, respectively. The most relevant results were obtained for these parameter variations. Other ranges and parameters were tested, but the results were not satisfactory. The initial conditions for x_s , x_i , y , and z were 2.5, 0.001, 0.2, and 0.4, respectively. The time variation ranged from 0 to 450 days with a step of 0.04.

In this work, time series and phase portraits are presented in both 2D and 3D. The phase portraits display several stabilizations and/or critical points, each of which was analyzed to determine its stability. The eigenvalues of each point were calculated using the Jacobian matrix (2), and the Lyapunov exponents were also calculated to determine the behavior of the curves.

Results and discussions

A numerical simulation of the system (1) was carried out using the values of the parameters previously given. The system displays the critical points presented in Table 1 with their corresponding eigenvalues. The numerical values of the parameters and the initial values of the variables mentioned in the previous section were used to obtain the graphical results.

Table 1 The critical points and their corresponding eigenvalues in the phase portrait diagram

Point	Variables X_s - X_i - Z , varying a for $R=1.5$, Figure 4 (a)		
	Eigenvalues: $\lambda_1 : \lambda_2 : \lambda_3 : \lambda_4$	Lyapunov exponents	Point characteristic
1.1;0.01;0.2;1.5, for $a=0.8$ converge	-2.132, -0.210+0.619i, -0.210 - 0.619i, -0.508		Stable point
1.6;0.2;0.2;0.75, for $a=1.0$ No converge	0.174+1.010i, 0.174-1.01i, -1.241, +0.512	0.0248310 0.0248310 -0.669730	Unstable point

Table I Continued...

3.5;0.2;0.2;1.52, for a=1.7 no converge	-4.911, -0.133+1.805i, -0.133-1.805i, +1.597	Saddle point
Variables Xs-Y-Z, varying a for R=1.5, Figure 5 (a)		
0.01; 0.5; 0.2; 2.202, for a=0.5 converge	-0.166 -1.367 -2.069 -1.918	Stable point
1.442; 0.1 ;0.3; 1.242, for a=0.8 No converge.At the beginning of the branch	-1.698, -0.123+0.866i, -0.123-0.866i, 0.251	Unstable point
2.522 0.2 0.5 1.793, for a=1.6 No converge	-0.739+1.624i, -0.739- 1.624i, +0.366, -5.476	Saddle point
Variables Xs-Xi-Z, varying a for R=1.025, Figure 6 (a)		
1.057;0.1;0.2;2.447, for a=0.7 Converge	-0.642+ 0.380i, -0.642-0.380i, -1.411, -3.1580	Stable point
3.21;0.2;0.2;2.771, for a=1.7 Converge	-0.671 -2.11 + 1.295i -2.105 - 1.295i -9.159	Stable point
Variables Xs-Y-Z, varying a for R=1.025, Figure 7 (a)		
0.361;0.2;0.1;1.079, for a=0.4 Converge	-0.2485+0.196i, -0.248-0.196i, -0.948, -0.613	Stable point
2.572;0.2;0.1;1.597, for a=1.4 Not converge	-0.527+1.319i, -0.527-1.319i, -0.033, -4.238	Saddle point

The results of varying time up to 40 days with a step of 0.1 are shown in the following time series figures. Figure 1 illustrates the variables Xs, Xi, Y, and Z as a function of time, while varying the parameter *a*, which represents the reproduction rates of the prey’s healthy population.

Figure 1 displays the interaction between prey and predator at the initial instant for parameter *a* (approximately zero) in dotted line. While Xs (the prey’s health) rises and falls sharply, Z (the predator) rises only slightly. After 11 days, Xs begins to grow again but with an oscillatory shape that exhibits damping behavior. Similarly, Z also exhibits damped oscillatory behavior. Eilersen¹² also observed in the results of their work, which seemingly dampens oscillations and makes chaotic dynamics transient. However, after 30 days, the Xs and Z variables, along with other parameters, exhibit chaotic characteristics, while the other variables Xi and Y show no effect. For parameter *a* (approximately 2), shown with dashed lines, the variable Xs decreases after approximately 5 days. However, it has no further effect on the predator. Meanwhile, the predator Z grows until approximately 7 days and then slowly decreases due to a lack of food. The variable Xi, which represents infected prey, experiences slight growth and decline without any significant impact on the predator. Therefore, the variable Y, which represents immune prey, does not have any noticeable effect. The solid line represents the range of variation between the dotted and dashed lines.

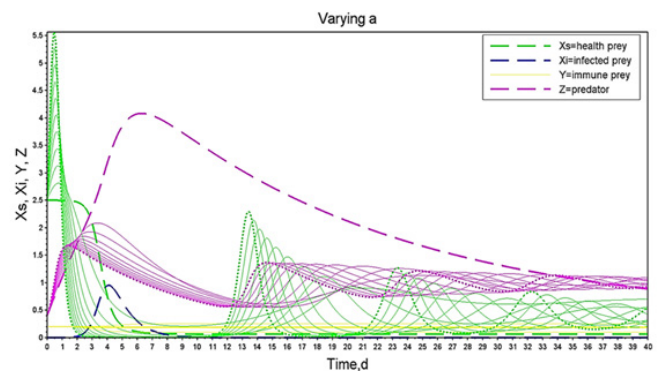


Figure 1 Time series showing the variation in reproductive rates of healthy prey (a).

Figure 2 shows the variables Xs, Xi, Y and Z as a function of time when the parameter *d* is varied from 0 to 2 and the time is increased up to 10 days. The variables Xs and Z, represented by dotted lines when *d* is around zero, exhibit an almost equilibrium interaction up to 3 days, after which they decay almost simultaneously. However, the Xi variable shows a slight increase until around 4 days, followed by a decrease, while the Y variable has no effect. For values of *d* close to 2 with the dashed lines, Xs decreases similarly to the dotted

lines, but the X_i variable increases until around 4 days and then decreases. Consequently, the Z variable increases, indicating that the predator feeds on infected prey. For long times, X_s , X_i , Y and Z reach equilibrium, except for d close to 2 for predator (dashed lines).

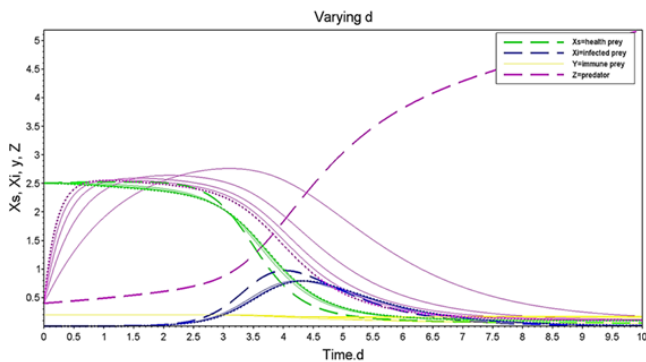


Figure 2 Time series in which the starvation rate of the predator in the absence of prey (d) varies.

In Figure 3, when the R parameter (which varies between 1-5), the X_s variable decreases rapidly within a few days. However, the variable X_i has a significant effect in the first few days as it grows and then decays in a damped oscillatory fashion. Meanwhile, Z grows and decays slowly as R increases, and it grows increasingly in an oscillatory way. From this we can deduce that Z feeds on X_s and X_i . Over long periods of time, all the variables tend to decrease and come into equilibrium.

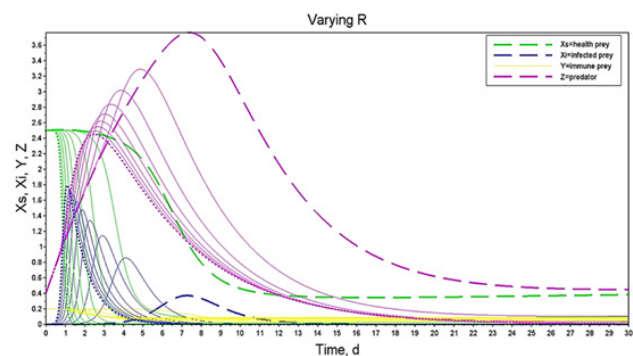


Figure 3 shows a time series of the disease basic reproduction number (R) as it varies over time.

Strogatz¹⁵ argued that deterministic chaos is a common behavior in continuous-time dynamical systems of differential equations with nonlinear terms. Such systems exhibit aperiodicity, ergodicity, and sensitivity to initial conditions. Momani et al.,¹⁶ presented numerical results and graphs showing the existence of chaos in the arbitrary order SIR epidemic system, by fractional order nonlinear system. Additionally, it is argued that this technique has significant potential for comprehending the intricate behaviors of diverse biological systems with chaotic characteristics. The time series outcomes of this study are highly consistent with those of the authors, despite not utilizing the fractional-order nonlinear system technique. Mangiarotti et al.,¹⁰ have employed time series plots and phase portraits to demonstrate that their proposed COVID-19 model displays chaos. The authors have identified the existence of chaos in their model by comparing their results with observed data. Chaotic behavior is mainly attributed to predator-prey and competition dynamics, as previously observed by Gakkhar and Naji.¹³ Deterministic chaos is a common behavior in continuous-time dynamical systems of differential equations with

nonlinear terms that exhibit aperiodicity, ergodicity, and sensitivity to initial conditions, this was confirmed by Strogatz.¹⁵ The parameter a was varied by setting R at 1.0 and 1.5, as suggested by Eilersen et al.¹² In each step of a that was 0.2, the time was varied from 0 to 450 days, as shown in Figures 4–7. Due to this variation, the figures presented different points of stability and non-stability, as shown in Table 1. At each critical point, we determined whether it was convergent or not by calculating the eigenvalues using the Jacobian matrix (2) and identifying the characteristics of each point. Figures 1–3 (time series), which were also analyzed by Borah et al.,¹ show the lack of significant effect of X_i and Y variables on Z .

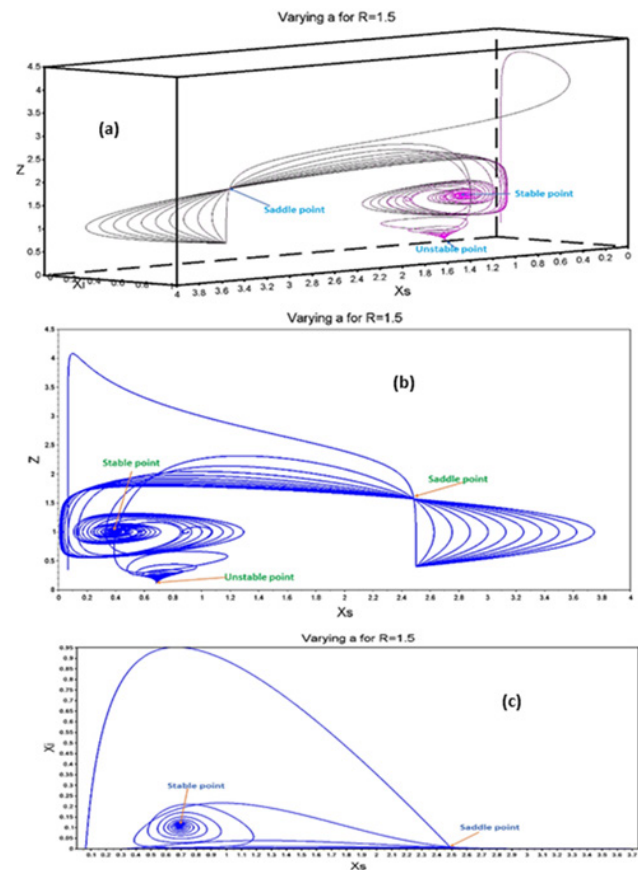


Figure 4 (a) shows the phase portraits of healthy prey (X_s), infected prey (X_i), and predator (Z). (b) The projections in the X_s - Z and (c) The projections in the X_s - X_i planes are presented varying a when $R=1.5$.

Figure 4 (a) in the Phase Portraits diagram shows the interaction of the variables X_s , X_i and Z in 3-D, varying the parameter a and fixing $R=1.5$, where three points of stability and non-stability appear (see Table 1), such as a stable point with chaos attractor characteristic, the other critical points are unstable point with chaos characteristic and saddle point. The interaction of X_s - Z and X_s - X_i variables in 2-D is also displayed. Figure 4 (b) represents the stable point with chaos attractor characteristics, the unstable point with chaos characteristics, and the other with saddle point. In Figure 4 (c), the interaction between X_s and X_i also shows a stable point with a chaos attractor characteristic and a saddle point. Borah et al.,¹ observed that the gradual evolution of chaos is distinctly visible through a period doubling pathway. Uthamacumaran's¹⁷ research showed that cancers are complex cybernetic systems that exhibit strange signaling attractors and a pattern gene expression like reaction-diffusion systems. The

author also argues that chaos, despite appearing random, may serve as a robust biomarker for tumor complexity and is bound to well-defined pattern structures in state space, known as strange attractors. The concept of “strange signaling attractors” refers to the idea that cancer cells can enter into stable yet abnormal states due to the altered dynamics of their signaling networks. These attractors can cause the cells to behave in ways that promote tumor growth and survival. This analogy is used to explain how cancer cells can create complex spatial patterns of growth and invasion, much like the patterns seen in certain chemical reactions.

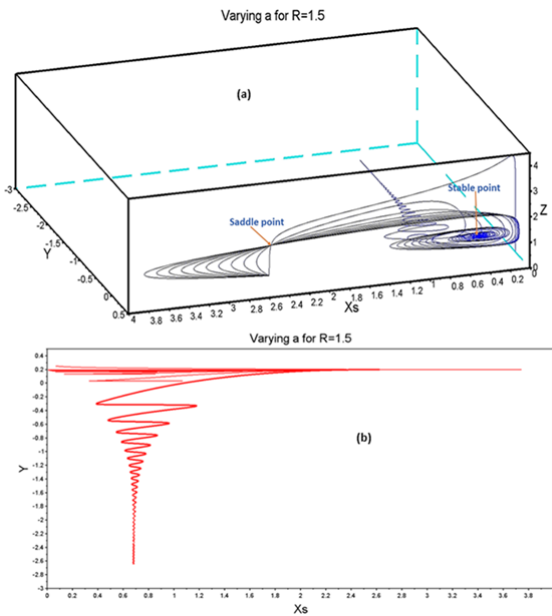


Figure 5 (a) Phase portraits of health prey (X_s), immune prey (Y) and predator (Z), (b) Projection in the X_s - Y . Showing a bifurcation diagram and varying a for $R=1.5$.

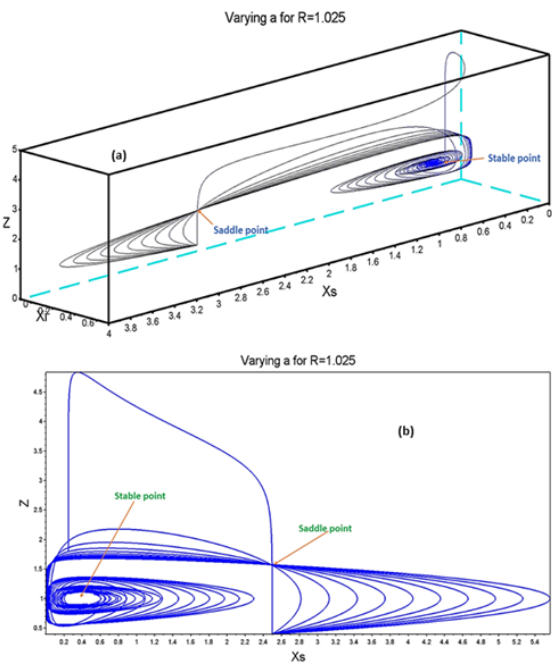


Figure 6 shows the phase portraits of healthy prey (X_s), infected prey (X_i), and predators (Z) in (a), and the projection in the X_s - Z plane with varying a for $R=1.025$ in (b).

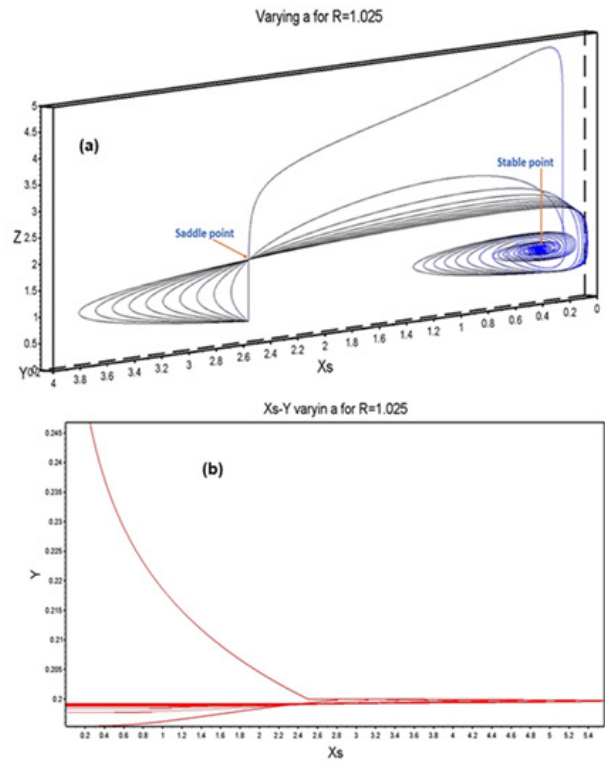


Figure 7(a) shows the phase portraits of healthy prey (X_s), immune prey (Y), and predator (Z). In (b), the projection in the X_s - Y plane displays a bifurcation diagram. The parameter a was varied for $R=1.025$.

In addition, Figure 5 (a) shows the iteration behavior of the X_s - Y - Z variables, varying the parameter a when $R=1.5$ is set. Where three critical points are observed, one stable with a chaos attractor characteristic, other showing the bifurcation diagram and the third with saddle point. However, Figure 5 (b) shows with more detail the bifurcation diagram on the projection X_s - Y . Elnawawy et al.,²⁰ stated that a bifurcation diagram reveals periodic windows and examines the robustness of the chaotic behavior versus parameter variations. And so, chaotic dynamics are efficient methods to control the gene expression, required for complex cellular processes involved in homeostasis.¹⁷

Chaotic dynamics in gene expression can play a role in regulating and controlling genes. Research suggests that chaotic behavior in transcription factors can modulate gene expression, up-regulating certain families of genes even amidst extrinsic and intrinsic noise. This modulation can lead to increased production of protein complexes and enhance the efficiency of their assembly, as proposed by Heltberg et al.¹⁸ Additionally, chaotic dynamics are associated with pluripotency in cells. According to Furusawa and Kaneko,¹⁹ cells that display irregular oscillations in gene expression have the ability to differentiate into multiple cell types. However, as differentiation proceeds, these irregular oscillations disappear, resulting in a reduction in pluripotency.

These findings suggest that chaotic dynamics have functional implications in cellular processes, including gene expression control, rather than being mere random fluctuations. They can contribute to the heterogeneity of cell states, which is beneficial in various biological contexts, such as multi-toxic environments.²⁰ However, it is important

to note that chaotic dynamics can be efficient under certain conditions. They are part of a larger and complex regulatory network that controls gene expression.

Next, the interaction of the Xs-Xi-Z variables varying the parameter a when $R=1.25$ is set, it is shown in Figure 6 (a). This shows two critical points, a stable point with attracting chaos behavior and a saddle point. Also was shown in Figure 6 (b) the projection in the Xs-Z, showing a stable point and a saddle point. Elnawawy et al.,²⁰ suggest that chaotic attractors could be indicative of therapy resistance, tumor recurrence, and cancer stemness. Although mathematical cancer models have shown that the emergence of chaotic attractors may indicate aggressive (adaptive) cancer states, their detection from empirical datasets is still underexplored.

Figure 7 (a) displays the interaction of the Xs-Y-Z variables, with the parameter a varying and R fixed at 1.025. The diagram shows two critical points: one stable with chaos attractor behavior and the other a saddle point. The bifurcation diagram behavior is shown in the Xs-Y projection, as seen in Figure 7 (b). The mathematical models used for the description of the complex dynamical processes in cancer have been shown to be a useful tool for the investigation of chaotic dynamics in cancer processes.²⁰

In their study, Hat et al.,²¹ analyzed the bifurcation diagram in the context of cancer research. This diagram is a visual representation used in mathematical and computational models to understand how changes in parameters within the system can lead to different states or behaviors of a tumor. It helps identify critical points where a small change in parameters can cause a significant shift in the system's dynamics, such as a transition from a stable state to uncontrolled growth (tumor development) or vice versa. In technical terms, a bifurcation diagram displays the potential steady states or equilibria of a system as a function of a parameter. It illustrates how the number and stability of these steady states change as the parameter varies. This tool is especially valuable in cancer research for comprehending how various genetic or environmental factors may impact the progression or treatment of the disease. Bifurcation diagrams can illustrate the concept of hysteresis in cancer, where the tumor's growth history affects its current behavior and potential treatment responses. This information is crucial for personalized medicine approaches as a tumor may react differently to the same treatment depending on its developmental path.

Borah et al.,¹ investigated eight fractional order (FO) models of the Bombay plague, cancer, and the COVID-19 pandemic through phase portraits, time series, Lyapunov exponents, and bifurcation analysis. The authors' results are similar to the present work in 2D, including phase portraits, time series, and bifurcation analysis. Debouche et al.,⁷ examined the nonlinear dynamic behavior of a COVID-19 pandemic model described by commensurate and incommensurate fractional-order derivatives. The stability of the equilibrium points was analyzed, and the results showed that the model exhibits chaotic behavior. The system dynamics were investigated via bifurcation diagrams, Lyapunov exponents, time series, and phase portraits. Thus, our results were like those presented in the article, both in 2-D and 3-D phase portraits, as well as in the time series results. Gupta and Dubey²² studied the dynamics of a prey-predator system in 2-D and 3-D, similar to our work. The authors posit that if an illness cannot be transmitted to offspring or predators that consume affected prey, then unaffected prey are assumed to be strong and will perform group defense against predators. The author's note that several animals, including buffalo, wildebeest, bees, ants, elephants, sardines, and tuna, exhibit this behavior.

After extensive simulations of the system (2), we found that some parameters correspond to chaotic behavior only in very narrow ranges of their values, such as, d . Therefore, the parameters a and R can generate chaos for wider ranges. Elnawawy et al.,²⁰ argued that the spread of epidemics and diseases exhibits chaotic dynamics, which have been modeled mathematically and confirmed by experimental results. Real-time control of these dynamics has also been presented. Eilersen et al.,¹² confirmed that the Lotka-Volterra equations, on which their work was based, present a highly simplified and slightly pathological picture of ecosystems. The authors argued that the pervasiveness of chaos depends on the validity of their assumptions. They also suggested that the Lotka-Volterra model can be used as a rough approximation of real ecosystem dynamics.

The applications of this work are numerous and include the understanding of complex ecological systems. The study analyzed the dynamics of a prey-predator system and provided insights into the behavior of interacting populations. This can assist in the understanding of the dynamics of real ecosystems and the design of effective conservation and management strategies. Additionally, the modeling of epidemics and diseases is another area where this work can be applied. The chaotic dynamics observed in the study can be applied to the modeling of the spread of epidemics and diseases. An understanding of the chaotic behavior of infectious diseases can assist in the prediction of their spread, the design of control measures, and the development of effective treatment strategies.

Conclusion

This study and the literature show that the emergence of chaotic behavior has been attributed mostly to predator-prey and competitive dynamics, therefore, the pandemics have a behave chaotic, as well as, cancer models have been found to display deterministic chaos or chaotic dynamics giving rise to complex oscillations, nonlinear interactions between cell populations occurs, in addition, it is worth emphasizing, COVID-19 manifests the main qualitative characteristics of a chaotic system and the most lethal of pandemics recently known.

The most relevant results of this work will be presented as follows.

The reproduction rates of prey affect the interaction between prey and predator. In the time series results, for a short period showed a chaotic dynamic transient with damping oscillations. For longer periods over 30 days, all parameters exhibited chaotic characteristics.

As the R parameter (which varies between 1 and 5) changes over time, the health of the prey declines rapidly within a few days, while the infected prey grows and decays in a damped oscillatory fashion. This leads us to deduce that the predator feeds on both healthy and infected prey. Over long periods of time, all variables tend to decrease and reach equilibrium.

A pandemic's chaotic propagation is highly sensitive to even minor variations in the initial conditions of physical factors.

The phase portrait diagrams were created using 3-D and 2-D geometry, varying a and R in only two values, and varying the Health, Infected, Immune, and Predator variables. Consequently, where are presented as stable point, unstable point, saddle point and bifurcation diagram appeared as in Table 1, these characteristics are shown in the results of the figures. It is worth noting that the equilibrium points exhibit the characteristics of chaotic attractors.

Mathematical models can be essential for developing strategies to plan for and deal with disease outbreaks in real-time. However, formulating a complete model of an epidemic disease in its equations

within these formalisms is a significant challenge due to the novelty of such diseases and their rapidly developing shape, behavior, and propagation.

This research has implications for ecological dynamics and disease modeling for practical applications.

Acknowledgments

None

Conflicts of interest

The author declares that they have no conflicts of interest.

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