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A review on applications of dynamical systems in biology and medicine

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Abstract: Dynamical systems theory offers a powerful framework for understanding complex, nonlinear interactions across various scientific disciplines. This review begins with a brief overview of the early development of dynamical systems to provide context for its theoretical foundations. The focus then shifts to applications in biology and medicine, summarizing the existing body of research on key topics such as smoking-related models, HIV infection, and tumor–immune interactions. The review highlights the scope and variety of studies conducted in each area, illustrating trends, methodological approaches, and the growing application of nonlinear modeling in understanding disease progression and treatment strategies. By emphasizing both historical context and contemporary research, the article underscores the relevance and impact of dynamical systems approaches in biomedical science.

Keywords: Dynamical Systems, Tumor–Immune Dynamics, Mathematical Modeling.

1. INTRODUCTION:

The study of nonlinear systems is a new branch and almost like a third revolution in physics, namely, nonlinear dynamics. In recent years, the consequences of nonlinear systems have had a considerable impact on variety of disciplines within physical, chemical and biological sciences as well as in the social sciences such as behaviour studies and economics. The focus has been both experimental and theoretical and in latter respect, a large part of research has dealt with numerical measures in addition to analytical results. The modern renaissance of nonlinear dynamics starts from the famous scientists, Henri Poincar´e and Birkhoff. One of the consequences of study of nonlinear system is the most fascinating concept, namely Chaos.

Dynamical systems theory (also known as nonlinear dynamics or chaos theory) comprises a broad range of analytical, geometrical, topological, and numerical methods for analysing differential equations and iterated mappings. As a mathematical theory, it should perhaps be viewed as a normal development within mathematics, rather than a scientific revolution or paradigm shift [1], as some popular accounts have claimed [2]. However, crucial motivations and ideas have entered this area of mathematics from the applied sciences, and a still-accelerating stream of applications driven by recent developments in dynamical systems theory began in the last third of the 20th century [3] for a sociohistorical analysis which discusses such extra-mathematical influences and describes the confluence of ideas and traditions that occurred in Western Europe and the US in the turbulent decade around 1970.

In this review, we provide a concise survey of dynamical systems theory with emphasis on its historical roots, its applications in biology and medicine, and its role in the study of tumor–immune interactions. The discussion begins with the early history of dynamical systems, tracing its foundations in analysis, geometry, and topology, and showing how it gradually extended beyond Newtonian mechanics to influence a wider scientific landscape. Attention then turns to applications in the life sciences, where mathematical models have been developed to describe population dynamics, epidemiological spread, neural processes, and physiological regulation, illustrating the versatility of dynamical methods in capturing biological complexity. A more focused exploration is devoted to tumor–immune dynamics, where nonlinear models play a critical role in understanding the interplay between cancerous cells and the immune system, offering insight into mechanisms of disease progression as well as potential therapeutic strategies.

2. EARLY HISTORY:

The modern theory of dynamical systems derives from the work of Poincaré (1854-1912) on the three-body problem of celestial mechanics and primarily from a single, massive and initially flawed paper [4]. In this paper, which won a prize celebrating the 60th birthday of King Oscar II of Sweden and Norway, Poincaré laid the foundations for qualitative analysis of nonlinear differential equations, and began to develop a coherent set of mathematical tools for their study. Following Poincaré’s work, Hadamard (1865-1963) considered the dynamics of geodesic flows, but the next major thrust was due to Birkhoff (1884-1944), who early in his career had proved Poincaré’s “last theorem” on fixed points of annulus maps [5]. In a book on two degree-of-freedom Hamiltonian systems [6] that still bears reading, Birkhoff showed that, close to any homoclinic point of a two-dimensional mapping, there is a sequence of periodic points with periods approaching infinity. He subsequently proved that annulus maps having points of two distinct periods contain complex limit sets separating their domains of attraction [7], thus providing a key clue for Cartwright and Littlewood in their studies of the van der Pol equation.

While Birkhoff was working in the U.S., Andronov, a student of Mandelstam established a strong group in dynamics in the U.S.S.R at Gorki (Nizhni-Novgorod), and he and Pontryagin introduced the key idea of structural stability under the name systems grossieres (coarse systems) [8]. This notion, now a central theme of the theory, asks what properties are necessary and sufficient for the qualitative behavior of the flow comprising all solutions of a given ODE to survive a small perturbation to the vector field defining it. Later, Peixoto generalized the Andronov Pontryagin results to flows on two-dimensional manifolds [9]. He proved that a flow on a compact two-dimensional manifold is structurally stable if and only if it has a finite number of fixed points and periodic orbits, all of which are hyperbolic, there are no orbits connecting saddle points, and the non-wandering set consists of fixed points and periodic orbits alone.

Smale [10] brought topological ideas to these problems in the late 1950s and began to generalize to $n > 2$ dimensions, defining gradient like flows that are now called Morse-Smale systems. Such a flow (or map) has a finite set of fixed points and periodic orbits, all of which are hyperbolic and all of whose stable and unstable manifolds intersect transversely, but no other nonwandering or recurrent points. Smale conjectured that a system is structurally stable if and only if it is Morse-Smale. Levinson subsequently drew Smales attention to a short paper on the periodically forced van der Pol equation. Levinson had worked on a simplified version of the problem and he suggested that it might provide a counterexample in the form of a structurally stable ODE with 5 infinitely many periodic orbits. This led to Smales creation of the horseshoe map in 1960, allegedly on the Leme beach of Rio de Janiero, while visiting Peixotos Institute of Pure and Applied Mathematics. Smales work appeared after a considerable delay [11], and became widely known only after an extensive survey article was published. Moser [12] subsequently gave a beautiful exposition of the horseshoe, providing explicitly-testable criteria to prove its presence in two-dimensional maps and explaining clearly how the presence of dense orbits precludes the existence of additional integrals of motion. This implies that the problem for which King Oscars prize was awarded is essentially insoluble.

Much of the work described above, including that of Peixoto and Smale, was topological in nature. Krylov and Bogoliubov developed analytical perturbation and averaging theories for nonlinear oscillation problems [13]; these were employed extensively in Andronovs group, 6 and generalized by [14] and others. Such methods were then used to prove the existence of transverse homoclinic orbits to periodic motions in periodically-forced oscillators [15] and in two- and three degree of-freedom Hamiltonian systems [16]. This provided the final link in a chain of methods and results that allows one to prove the existence of chaotic invariant sets in specific ODEs. The pioneering contributions of Poincaré, Birkhoff, Andronov, Pontryagin, Peixoto, Smale, and others laid the mathematical foundations of dynamical systems theory through topological and analytical insights into stability, structural properties, and the onset of complex behavior. These foundational contributions, culminating in methods to establish the existence of chaotic invariant sets, shaped the qualitative theory into a mature discipline by the mid-20th century. A decisive turning point came with Lorenz’s study of Rayleigh–Bénard convection, where his three-dimensional system revealed the striking phenomenon of sensitive dependence on initial conditions [17]. With these early contributions, the groundwork was firmly established, and more recent research continues to build on and extend these foundations in diverse directions.

3. APPLICATIONS IN THE FIELD OF BIOLOGY AND MEDICINE

Dynamical systems play an important role in determining the fate of many interacting systems. They are used to model a variety of phenomena found in the physical, financial, and biological realms.

3.1 Cigarette Smoking Model: Cigarette smoking is common in the World as a moral habit, although it having a strong junction with different types of dangerous diseases. No one of the smokers realized that smoking affects all the organs of our body specially inside means stomach, heart, lungs etc. The chemicals in cigarette damage the ability of our heart to function properly. Some mathematician’s effort to announce the people about awareness and control of smoking through mathematical models. For this goal, the first smoking model was presented by Castello et al, in which the compartments are potential smokers (the people which not become yet smokers and having the chance for starting the smoking), chain smokers (the people which are smoking daily five to ten cigarettes) and quit smokers (the people they were smokers in past and yet not smoking). Then Sharomi and

Gumel made their improvement in the form of including the chain smoker's class. After the start of Castello et al several mathematicians tried in different aspects to discussed the smoking model in integers order and fractional order. In 2018, Anwar Zeb and his three colleagues presented a paper [18] and discussed the dynamical behaviour of their proposed model in the form of Delayed Differential Equation (DDE) and show the conditions for asymptotic stability of the model in steady state. They also discussed the Hopf Bifurcation analysis and show the results graphically using the NSFD method with the help of MATLAB.

3.2 HIV Model: Over the past decade, a number of models have been developed to describe the immune system, its interaction with HIV and HCV, and the decline in $CD4^{+}T$ cells. Before 1995 both stochastic and deterministic models have been developed. Stochastic models can be used to account for the early events in the disease, when there are few infected cells and a small number of viruses or situations where the variability among individuals is of interest. One class of stochastic models has looked at the effects of increasing variability among viral strains, as a means of escaping control by the immune system, in the progression to AIDS, but this approach has been criticized. Deterministic model, which have been developed by many authors, examine the changes in mean cell numbers, and are more applicable to later stages of the process in which population sizes are large. These models typically consider the dynamics of the $CD4^{+}T$ cell and virus populations as well as the effects of drug therapy.

In 1989, Perelson [19] developed a simple model for the primary infection with HIV. Perelson et al. [20] extended the model and discussed some of the model's behaviour. They defined the model by considering four categories: uninfected $CD4^{+}T$ cells, latently infected $CD4^{+}T$ cells, productively infected $CD4^{+}T$ cells and virus population. Rong et al. [21] further modified the model by incorporating anti-retroviral effects to study the evolution of drug resistance. They considered three classes of $CD4^{+}T$ cells: uninfected cells, infected cells in eclipse phase and productively infected cells. The model depends on the observation that for a virus, when it enters a resting $CD4^{+}T$ cell, viral RNA may not be completely reverse transcribed into DNA. If the cell is activated shortly following infection, the reverse transcription can proceed to completion. However, the un-integrated virus harboured in the resting cell may decay with time and partial DNA transcripts are labile and degrade quickly. Hence a proportion of resting infected cells revert to the uninfected cells.

Following these models, in 2005, Xinyu Song and Shuhan Cheng [22] published a paper in which they discussed about the stability analysis of a delay differential equation model of HIV infection. They obtained the existence and local stability of boundary and positive equilibria, and determined conditions for which the system enters a Hopf-type bifurcation. Song and Cheng also discussed the global stability of boundary equilibria and permanence of the system and finally they obtain the condition for the existence of the periodic solution of system.

Meanwhile, at the same time, two Indian scholars Srivastava and Chandra [23] simplify the model for primary infection proposed by Rong et al. by considering only three categories: uninfected $CD4^{+}T$ cells, infected $CD4^{+}T$ cells and virus population. They studied the existence and local stability, global stability of the infected steady state. It was found that the delay has no effect on the dynamics of HIV in the proposed model. Following their work, in 2014, Qilin Sun and Lequan Min [24] slightly modified the above model proposed by

Srivastava and Chandra. They introduce a modified HIV infection differential equation model with a saturated infection rate and discussed the stability of the model.

Wang, Li and Wang [25] analysed the stochastic stability of internal HIV models driven by Gaussian white noise and Gaussian colored noise. They found that the intensities of noises influence greatly not only uninfected target cells, infected cell, and virus particles, but also their stationary marginal probability density functions. And compared with the internal HIV models with Gaussian white noises, systems driven by Gaussian white noise and Gaussian colored noise are more stable and more conform to reality.

Beyond these foundational frameworks, recent research has expanded HIV modeling to include features such as age structure, media influence, transcriptional latency, and immune escape dynamics [26-28].

3.3 Tumor-Immune Dynamics: It is well known that cancer is one of the greatest killer diseases in the world. Cancer, known medically as a malignant neoplasm, is characterized by an abnormal growth of cells. In cancer, cells divide and grow uncontrollably forming malignant tumors and invade nearby parts of the human body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream. Not all tumors are cancerous. The tumors which do not grow uncontrollably, do not invade neighbouring tissues, and do not spread throughout the body are not cancerous. There are over 200 different cancers including breast cancer, skin cancer, lung cancer, ovarian cancer, brain cancer, colon cancer, prostate cancer, and lymphoma and cancer. that afflict humans. Cancer symptoms vary widely based on the type of cancer.

A number of mathematical models of the interactions between the immune system and a growing tumor have been developed [29-31]. The kinetics of cell mediated cytotoxicity in vitro have also been described by mathematical [32,33]. With such models, numerical estimates of biologically significant parameters have been obtained, a number of phenomena interpreted, and predictions made.

Sharma and Samanta [34] worked on a paper to considered a tumor growth model with the effect of tumor-immune interaction and chemotherapeutic drug. In their model there are four compartments, namely, tumor cells, active CTL cells, helper T-cells, and chemotherapeutic drug. They have discussed the behaviour of the solutions of our system. The dynamical behaviour of our system by analysing the existence and stability of the system at various equilibrium points is discussed elaborately. They have set up an optimal control problem relative to the model so as to minimize the number of tumor cells and the chemotherapeutic drug administration. They used a quadratic control to quantify this goal and have considered the administration of chemotherapy drug as control to reduce the spread of the disease.

de Pillis, Savage and Radunskaya [35] proposed a new mathematical model of colorectal cancer growth and its response to monoclonal antibody (mAb) therapy. The model includes tumor cells, elements of the hosts immune response, and treatments. The model incorporates patient-specific parameters to account for individual variations in immune system strength and in medication efficacy against the tumor. They have simulated outcomes for groups of virtual patients on treatment protocols for which clinical trial data are available, using a range of biologically reasonable patient-specific parameter values. They also simulated experimental dosing schedules, and have found new schedules which, in their simulations, reduce tumor size more effectively than current treatment schedules. Additionally, they examined the systems equilibria and sensitivity to parameter values.

Beyond this foundational work, more recent studies have focused on refining tumor–immune interaction models by incorporating treatment strategies, stochastic effects, and optimal control approaches [36,37].

4. CONCLUSION:

Applications of dynamical systems theory in biology and medicine offer a powerful quantitative framework to analyze complex, nonlinear interactions within living systems. Such systems often involve feedback mechanisms, time delays, stochastic fluctuations, and multiscale interactions, which can significantly influence processes like disease progression, immune responses, and treatment outcomes. In this article, we first provide a brief overview of the early development of dynamical systems, setting the stage for understanding their theoretical underpinnings. We then focus on applications in biology and medicine, illustrating how these concepts have been implemented in specific mathematical models. Examples include models of HIV infection dynamics, which capture virus–host interactions and the effects of antiretroviral therapy; models exploring the physiological impact of smoking; and tumor–immune interaction models. These case studies highlight the ability of nonlinear dynamical modeling to bridge theory and practice, offering insights into system behavior, predicting outcomes, and guiding the design of effective interventions.

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