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Juxtaposition across Mathematical Modeling, Stochastic Processes along with the Lenses of Philosophy of Science and AI integration in Medicine and Biology: An Overview

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ABSTRACT The ultimate reason for the ubiquity of mathematics in modern science entails the essence of mathematical thinking and processes so that complex phenomena including those emerging in medical and biological systems can be understood, and thus, scientific models at their crux can be generated. The consequent complexities and uncertainties require the applications of stochastic processes in mathematical modeling with Artificial Intelligence (AI) techniques used in realms of medicine and biology. Within these conditions, clinical evaluation evidence and model explainability are considered to ensure accountable, effective and safe uses of AI in clinical settings, along with robust, reliable as well as accurate understanding of various complex processes that manifest huge numbers of heterogeneous temporospatial scales. The role of philosophy within science can be expounded by its juxtaposition with models and empirical data explicated by philosophy whose pillars are driven into semantic, pragmatic and syntactic structures of scientific theory that also make up the foundational tenets of algorithmic thinking and patterns. While philosophy of science examines and reflects on the concepts, theories, arguments and methods of science, it should also be borne in mind that scientific theory, by its definition, relates to applications validated by its predictions as units of analyses. Concerning mathematical models, their structure and behavior in target systems are also to be addressed so that explicit common patterns that are implicit in scientific practice can be included in this complex influx. On the other hand, critical functions of mathematical modeling from the pragmatic aspect include the unification of models and data, model fitting to the data, identification of mechanisms depending on observations as well as predictions of future observations. Given these, philosophy of science in medical and biological fields is stated to prompt a comprehensive understanding to construct holistic mathematical models particularly in complex sciences including different attributes of complexity, evolution and adaptation. Regarding the position of AI, its algorithms and mathematical modeling, the methods of neural networks, statistics, operations research, fractional calculus, fractals, and so forth can be employed with AI being capable of uncovering hidden insights embedded in big data concerning medical and biological issues in view of contemporary scientific thinking and processes. In addition, the treatment and handling of uncertainty in clinical medicine and biological problems over their processes may disclose compelling challenges due the fact that uncertainties are one of the intrinsic features of nearly all mathematical models which are formed based on three basic types of uncertainty: interval, Bayesian and stochastic. Accordingly, the current overview aims at providing answers built on sophisticated models considering the explanation and interpretation of design and formulation considering that the extant research literature could have some fragmented points in terms of original and application-oriented works. To these ends, the opportunities, challenges, limitations and conjunctures with respect to mathematical modeling in medicine and biology are addressed while role of philosophy of science is discussed within the context of mathematical modeling and applications in medicine and biology. In addition to these points, the delineation of forecasting, prediction, estimation and approximation concerning different mathematical modeling with the integration of AI in medicine and biology is explained. Thereby, an overview is inclusively presented by comprising the principles underpinning the medical and biological systems within a framework in relation to the diagnostic and disease-related treatment processes and follow-up, which can provide new directions in novel formulations, designs and interpretations based on mathematical modeling processes to be constructed and solved through practicality as well as to-the-point specific means.

KEYWORDS
Mathematical modeling
AI-based mathematical modeling
Differential equations
Philosophy of science
Fractional calculus
Fractals
Applied Mathematics
Computational fractal-based methodologies in medicine and biology
Engineering applications in medicine and biology
Biomedical decision-making
Probabilistic clinical reasoning
Stochastic processes
Brownian motion
Data analytics-based models
Data distribution
Dynamic precision medicine
Public health challenges
Predictive bias
Complexity
Computational complexity
Complex systems
Algorithmic thinking and processes

INTRODUCTION

Mathematical modeling in medicine and biology is not only the implication of the development of advanced computer capabilities but also the increasing access to the simulations of complex systems. The sampling of clinical data leading to the experiments generated has paved the way for novel and profound outlooks regarding the dynamics and complex patterns of medical and biological systems which do not always manifest steady attributes. Another input of mathematical modeling employed in medicine and biology is its emphasis placed on accurate and precise definitions of medical notions so that misunderstanding and overlooking instances and / or observations can be prevented, which can also preclude the waste of time and efforts. Against this backdrop, mathematics is stated to provide the means for the structuring of thoughts, models, computations, simulations, schemes and ultimately applications.

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The adoption of systemic properties and addressing them by unveiling the spontaneous processes in a dynamical system further from the equilibria without any existence of an external force acting on the system are among the pivotal tenets of modern scientific thinking which reveals a challenge posed against the dichotomy between the natural world and social world by considering the notions revolving around evolution, order and complexity. Even though simplicity may be thought as the direct dichotomy of complexity, as Leonardo da Vinci put: "Simplicity is the ultimate sophistication.", simplicity embodies certainty, coherence and intelligibility. To illustrate, clarity of water reveals transparency and purity, and simplicity on these surfaces is retained thoroughly unpretentious and effortless, which implies the fundamental ground of consolidation of inherent peace.

The ultimate reason for the ubiquity of mathematics in modern science is the necessity of mathematical thinking to understand complex phenomena. The mathematical approach includes quantification of observations, modelling, classification, optimization, data processing, analysis, prediction and validation. Correspondingly, computational technologies in different complex systems depending on mathematical-driven informed frameworks are able to allow for the generation of more realistic and applicable adaptive models under transient, dynamic and ever-evolving circumstances of different complex systems (Karaca 2022b).

AI and applications thereof as well as related digital technologies and their tools can enable the mimicking of human intelligence, generating ample ideas based on personalized needs and functions with better precision and less time consumption in medicine and biology. The employment of different machine learning methods can provide significant affordances in healthcare systems through the extraction of the relevant patterns and determination of correlations as well as associations among the multiple features concerning big datasets. Regarding mathematics, a value to convert empirical data into applicable models can be found based on mathematical operations, which may reduce the human toll in processes such as disease identification to a large extent.

Machine learning's predictive models, on the other hand, can demonstrate enhanced rules in medical and clinical practices for critical decision-making concerning individuals' care. Among the related studies, the work (Chen *et al.* 2023) uses custom machine learning algorithm for large-scale disease screening handling heart disease as an example. For this aim, the authors introduce a novel algorithm to train a patient-specific machine learning model with customization attained on neural network architecture, data processing as well as loss function. The results show the powerfulness of the algorithm proposed for the screening of disease to save lives and lessen the economic burdens of heart diseases. The adoption of AI by a stream of machine learning with extraordinary performance is handled in (Ge *et al.* 2023) where the impact of inflationary effects on healthcare tasks concerning medical datasets are investigated. The study's experiments show that removal of each inflationary impact can correspond with a decrease in classification accuracy, yet removal of all the inflationary effects produce a reduction of the evaluated performance by 30 %. Another study (Wang *et al.* 2023) provides a novel model named MLFL-NET with high accuracy for the fine-grained classification of bone marrow cells using multi-level features.

The study shows the significance of AI-assisted diagnosis support system of morphological examination depending on bone marrow smears, ie. classification, prediction and cells detection of leukemia types. Last but not least, clinical evaluation evidence and model explainability are considered for ensuring accountable, effective and safe uses of AI in clinical settings. A related study (Jin *et al.* 2024) conducts a clinical user-centered evaluation to make the assessment of AI assistance utility. The evaluation obtained by the study shows the clinical utility of AI in terms of providing assistance to physicians on the glioma grading task while identifying clinical usage gaps as well as the limitations related to existing explainable AI techniques for future improvement.

Fractals, as intriguing forms of infinitely complicated shapes in mathematics, display peculiar patterns of their own with their inherent properties, repeating in continuum. Fractals provide a unified perspective concerning varied trajectories of complexities in the natural world as well as medicine and biology by opening up novel dimensions with multiple layers. Fractals, fractal theory and analysis are directed toward the assessment of data's fractal characteristics with multiple methods assigning fractal dimensions to the datasets. Moreover, it is possible to model dynamical processes and systems of fractional order with respect to both natural and artificial phenomena by ordinary or partial differential equations with integer order, which can be described fittingly by ordinary and partial differential equations. Furthermore, fractional, or non-integer order, calculus can provide a concise model to describe the dynamic events occurring in medical and biological elements.

Concerning non-integer (or fractional) power model, it can be noted that a unit with a non-integer exponent is stated to represent a fractional power, whereas a unit with an integer exponent is said to represent a whole number power, which suggests that a unit with a non-integer exponent is a more precise measurement compared to a unit with an integer exponent. To illustrate, analytical results of linear integer-order differential equations are signified by the exponential functions' combination. The Mittag-Leffler function displays a power-law asymptotic behavior, representing the analytical results pertaining to linear fractional-order differential equations. Owing to this inherent quality, the results of linear fractional-order differential equations often manifest the properties related to power-law (Karaca and Baleanu 2022).

Expanding on these aspects, the use of artificial intelligence and machine learning ensure the maximization of model accuracy and minimization of functions such as computational burden, which can provide one with mathematical-informed frameworks that can allow for robust, reliable and accurate understanding of various complex processes manifesting huge numbers of heterogeneous temporal and spatial scales. Such a degree of complexity entails a holistic understanding of different processes through multi-stage integrative models able to capture significant attributes to explain complex systems' confounding behavior in terms of prediction and control. Accordingly, a study (Havlin *et al.* 1995) provides a review of biological systems which are marked by fractal geometry focusing on long range power law correlations in DNA sequences. The study also provides the discussion of applying fractal scaling analysis to different medical aspects like the dynamics of heartbeat regulation.

Another paper (Grizzi *et al.* 2019) aims at reviewing complexity and fractal geometry concerning the nuclear medicine images in biomedical imaging, addressing the identification of pathognomonic patterns of shape in anatomical entities as well as their changes from natural states to pathological states. The use of fractional calculus models related to complex dynamics in biological tissues is handled in (Magin 2010) where several bioengineering research-related areas with the application of fractional calculus to build new mathematical models are explained. The contribution of fractional calculus is provided in the study (Vosika *et al.* 2013) which shows that fractional calculus gives a new dimension for understanding and describing complex systems' behaviors and basic nature. Using fractional calculus to model biological systems' electrical properties, the authors derive a new class of generalized models for electrical impedance and apply those to human skin based on experimental data fitting.

Mathematical modeling in medicine and biology demonstrates the significance of mathematical models as a result of the development and spread of efficient and time-saving computers, which can facilitate the access to simulations of complex systems characterized by uncertainty, nonlinearity, irregularity, randomness, and so forth. Another important point in this emergence and spread is due to the precise continuous samplings of new clinical data generating experiments which can provide insights into biological and medical systems' dynamics, behaviors and patterns.

In addition, mathematics provides a tool to structure thoughts which can help with the answering of new important questions brought about by the application of mathematical models. Consequently, used as a part of mathematical models, differential equations lend a vast diversity of their applications to describe various phenomena, patterns and processes, and yet, the need to develop more universal and efficient methods to solve differential equations has been satisfied with the emergence of computer science and also scientific computing, namely ANNs, as being one of those methods (Evans 2022). This attribute becomes more critical particularly in complex dynamic problems including disease identification, classification, diagnosis, prognosis, treatment, control and management as well as other issues emerging in biological and medical systems. The study (Yang *et al.* 2023) is concerned with the development of a neural ordinary differential equation (ODE) model to visualize deep neural network behaviors when multiparametric MRI-based glioma segmentation is done, which is a method to improve the capability of deep learning explainability.

The results of the study show that all neural ODE models illustrated image dynamics successfully. By addressing equation-based modeling and showing its complementary quality, the study (Daun *et al.* 2008) states the importance of differential equations as a simulation tool in biological and clinical sciences. Another work (Ning *et al.* 2023) shows the power of differential equations in epidemic models as well as deep neural networks with AI models as reliable tools to analyze and treat COVID-19 transmission, demonstrating that the inferred parameters from the proposed epidemiological deep neural networks (Epi-DNNs) method can provide a predictive compartmental model, which can serve to forecast future dynamics. Subsequently, the paper concerned with a fractional recurrent neural network (RNN) proposes a novel approach for the aim of achieving the synchronization of a cancer cell model based on observer scheme.

Considering the importance of recurrent neural networks, the framework proposed by the study is stated to serve as a method for prediction into the fractional-order chaotic cancer systems with uncertain orders' behavior (Behinfaraz *et al.* 2023). All these findings and points point to the significance of mathematical medicine and biology along with the tools they offer in cases of diagnosis, model building, classification, differentiation, uncertainty management and complexity quantification, among many others.

The juxtaposition of mathematical modeling with stochastic processes can be handled within the framework of AI integration in medical and biological systems while keeping philosophy of science in mind. Correspondingly, mathematical models are formulated and solved systematically based on the particular type of the problem at hand arising in medicine and biology. Inter- and multidisciplinary-driven research includes mathematical modeling being exposed to evolving in diverse areas. In view of the fact that the extant research literature may have some incomplete and fragmented points in terms of original and application-based works, the current overview aims to address the following relevant questions:

What could make up the opportunities, challenges, limitations and conjunctures with respect to mathematical modeling in medicine and biology?

How can the role of philosophy of science be interpreted within the context of mathematical modeling and applications in medicine and biology?

What demarcates the distinctions of forecasting, prediction, estimation and approximation concerning different mathematical modeling with the integration of AI in medicine and biology?

How could an overview be presented encompassing principles which underpin medical and biological systems that consider a framework to be provided with regard to the diagnostic and disease-related as well as follow-up processes?

In line with the responses to the questions set above, the remainder of the present review is as follows. Section 2 provides an overview of mathematical modeling in medicine and biology in relation to the questions forwarded herein. Section 3 provides Conclusion, Contemporary Mathematical Medicine and Biology Thoughts, and Future Directions.

OVERVIEW OF MATHEMATICAL MODELING IN MEDICINE AND BIOLOGY

Mathematical Modeling in Medicine and Biology: Opportunities, Challenges, Limitations and Conjunctures

Mathematical modeling is to establish a mathematical model according to the actual- veritas problems, while generating new ways of solving and calculating the model so that the actual problems in real life can be solved in line with the results calculated. Henceforth, the essence of a mathematical model is noted to be a dynamic simulation, rather than being directed by a fixed way of thinking. More precisely, mathematical modeling involves the converting of problems from application realm into manageable mathematical formulations bearing arithmetical and hypothetical analyses to ensure answers, solutions, perception and guidance that will benefit for the relevant configuration of peculiar application. Along these lines, the value of mathematical modeling lies in precision and strategy geared towards problem solution, which could be the schemes allowing a systematic understanding of the system modeled besides more optimal designs as well as efficient employment of modern computing capabilities from the lenses of novel perspectives.

Having a robust grasp of inputs and outputs concerning mathematical modeling can be considered to be a noteworthy stage from theoretical mathematical domain to application-oriented mathematical expertise, which can pave the way for tackling challenges in current modern technological landscape so that mastering and excelling can be realized by making most of the opportunities and mitigating the risks.

The essence of mathematical modeling as a process is derived from understanding, analyzing and forecasting behavior concerning real-world phenomena through the creation of mathematical representations of them. Regarding the relevance of machine learning and AI, mathematical modeling can allow for the description and analysis of big datasets through the use of mathematical equations and algorithms, which can make one gain profound insights into the latent and underlying correlations as well as patterns within the data. Machine learning, as a technique of data analytics, can teach computers to do what comes naturally to humans and animals, which is to say, learning based on experience. Accordingly, machine learning algorithms make use of computational methods to directly learn from the data with no reliance on a predetermined equation as a model. It is possible to represent mathematical models as systems of differential equations which describe the way different variables in the model may change over time or as depending on other independent variables. Partial differential equations involve an unknown function with several variables or one or several of its partial derivatives. If one is solved, it means one may determine the unknown function satisfying the partial differential equation (Karlsson Faronius 2023; Pinchover and Rubinstein 2005). Ordinary differential equations (ODEs) and partial differential equations (PDEs) are ubiquitous in applied mathematics due to their description of time-depending phenomena. In specific cases, the supplementing of differential equations is conducted to tackle memory effects (integro-differential equations or time-delay differential equations) as well as noise (stochastic differential equations) (Amigó and Small 2017).

Differential equations are generally employed in medicine, biology, physics, engineering, and so forth for expressing a relation between the function and its derivatives. In exact sciences, they are used as a technique for the determination of the functions over their domain if the functions and some of the derivatives are known. A differential equation includes one or more functions along with its derivatives. The rate of change of a function at a point is defined by the derivatives of the function. Overall, the aim of a differential equation is the examination of the solutions which satisfy the equations and the solutions' properties. Some types of differential equations are ODEs, PDEs, linear differential equations, nonlinear differential equations, homogeneous differential equations, nonhomogeneous differential equations, among others. Accordingly, a first-order differential equation is defined by an equation: $dy/(dx=f(x,y))$ of two variables x and y with its function $f(x,y)$ which are defined on a region in the xy-plane. Having only the first derivative dy/dx, the equation is of the first order, and higher-order derivatives do not exist. The differential equation in first-order can also be denoted according to Equation 1 as follows (Daun *et al.* 2008):

$$y' = f(x,y) \text{ or } (d/dx)y = f(x,y) \tag{1}$$

The five basic types of differential equations in the first order are linear differential equations, homogeneous equations, exact equations, separable equations and integrating factor. The second order differential equation is a specific type of differential equation involving a derivative of a function of order 2 without other higher-order derivative of the function which may appear in the equation. The equation with the second-order derivative is the second-order differential equation denoted according to Equation 2 as follows:

$$d/dx(dy/dx) = d^2y/dx^2 = f''(x) = y'' \tag{2}$$

The five basic types of differential equations in the second order are linear second ODE, homogeneous second ODE, nonhomogeneous second ODE, Second ODE with constant coefficients, and so forth. A second order differential equation is defined as a differential equation that includes a function and its second-order derivative and no other higher-order derivative of the function can appear in the equation. It can be of different types depending upon the power of the derivative and the functions involved. Fractional order differential equations are generalized and noninteger order differential equations that can obtained in space and time through a power law memory kernel of nonlocal relationships by taking into account the properties of fractional-order calculus and he use of non-local information of the image for reconstruction (Li and Zhao 2024). Since they are robust in terms of describing memory-related aspects of different substances, theoretical analyses and numerical methods are significant with viable applications in various fields of research. One relevant study aims to understand tumor growth in human liver, and thus, the authors used a temporal fractional-order parabolic partial differential equation, carrying out the analysis by numerical methods. They employed the Caputo derivative to explore the impact of medication therapy on tumor growth (Takale *et al.* 2024). A fractional order total variation model for additive noise removal employing a different fractional order of the regularization term of the objective function is the content of another study which deals with the denoising model for medical images based on space and time fractional derivatives on a finite domain as discretized with effective applications of Grünwald-Letnikov and Caputo derivatives. The study shows the benefits of the model in terms of smoothing the homogeneous regions, which in turn improved edge information by showing further details of the image (Abirami *et al.* 2023).

Treatment and handling of uncertainty in clinical medicine and biological problems over their due processes pose compelling challenges due the fact that uncertainties are known to be one of the intrinsic features of nearly all mathematical models which are constructed based on three basic types of uncertainty involving interval, Bayesian and stochastic (Karaca and Cattani 2018; Karaca and Moonis 2022). The application of these models is for the description of measurements in unmonitored fluctuations that may bring about ambiguities in the results. There are also other reasons why uncertainties appear. The most significant reasons include the factors that impact the behavior of the system that is modeled being unknown to the modeler, some factors being overlooked during the modeling process as they may have little effect on the model behavior and relationships among the impactful factors being simplified because of the complexity concerning the mathematical description.

Besides these reasons, model uncertainty has two main sources, which are the model's mathematical structure and the parameter values (Koen-Alonso and Yodzis 2005). While modeling a predictive model, the major aim would be to replicate a certain phenomenon as closely as possible, so uncertainty may be deemed to be undesirable at this level which needs to be eliminated or reduced as much as possible (Brugnach *et al.* 2008). In that regard, uncertainty is considered to be an attribute which must be understood and associated with the quality of the information employed for building or running a model (Zimmermann 2000). Regarding uncertainty in data, numerical computations can be conducted to deliver an output which has uncertainty formulated in terms. Furthermore, uncertainty models need their corresponding rules themselves within well-defined semantics (Oberguggenberger 2005).

Uncertainties can be divided into three broad categories: complete uncertainty (obscurity), inauthenticity and ambiguity. Some methods are typically used to account for the uncertainty in mathematical models. Regarding the types of uncertainty, Aleatoric uncertainty signifies inherent uncertainty in a given system, which is more difficulty to tackle by more data collection or experimentation. It is known to be a stochastic type of variation which his possible to be represented via a probability distribution. On the other hand, epistemic uncertainty is due to the actual model, which can be followed up towards a lack of knowledge about the latter one in terms of shortcoming. It is stated that this specific uncertainty can be managed if more information can be obtained regarding the system as a whole (Heid *et al.* 2023). Accordingly, the term stochastic derived is from the word originally meaning random or chance, which is the opposite of sure, certain or deterministic (Arthur 1985). While a deterministic model makes the prediction of a single outcome based on a particular set of circumstances, a stochastic model makes the prediction of a set of possible results that are weighted by their probabilities. In fact, stochastic models are mathematical models for random phenomena that evolve in space or indexed by time in a random way. A stochastic model's specification with the techniques may change in four likely combinations of discrete or continuous time and discrete or continuous state space. A stochastic process involves the representation of a family of random variables which are denoted by a function on a variable $f(x)$, which approximates a number with the result of the related experiments (Fortier and Michel 2003).

Some advanced topics handled in stochastic processes include but are not limited to stopping theorems, filtration, theoretic probability Brownian motion, Itô calculus, functional limit theorems and stochastic integration. Stochastic processes, as mathematical approaches, are beneficial for understanding and analyzing dynamical systems which random components evolving over time. A stochastic model or process signifies an equation with a random variable. Stochastic models are known to be complex in terms of analyzing in computational and analytical ways, so in-depth probability and statistical theories are required along with the advance techniques (Mubayi *et al.* 2019).

Fractal method, namely box-counting dimension with the least square regression, besides multifractal method (Wavelet transform modulus maxima with Gaussian wavelet analysis) were applied to the stroke subtypes' dataset for identifying efficient and significant attributes in the stroke subtypes which were classified with the Feedforward Backpropagation (FFBP) algorithm (Karaca *et al.* 2020b). The values of the Hurst exponent may range from 0 to 1, which is considered to be an important feature with its range being considerably appropriate for serving as the domain of images. When the sub-images of an original image are converted into estimates of Hurst exponent, the estimates of 0-1 can be saved as a characteristic image or feature belonging to another input source image.

With the application of ML and DL models on certain images, it becomes possible to supply the characteristic image for another input so that the general classification rate can be enhanced through the two inputs. Consequently, the effectiveness is concerned with the accuracy of the estimation as based on the Hurst exponent, which indicates that the higher the accuracy of estimation is the better the classification rate will be (Chang 2024). Regarding Brownian motion, it can be noted that its mathematical theory and related stochastic processes have indications of the way this theory is connected with other branches of mathematics (Karaca 2022a). Multifractional Brownian Motion (mBm), one of the stochastic multifractal models, is used for analyzing and extracting dissimilar images, signals or patterns. In addition, fractal Brownian Motion (fBm) provides important models for a broad range of phenomena that emerge in the natural world.

Multifractal analysis is known to handle the singularity structure of functions or signals both locally and globally. Hölder exponent at each point, on the other hand, provides the local information with the global information achieved by a characterization of the statistical or geometrical distribution of the Hölder exponents, referred to as multifractal spectrum (Karaca *et al.* 2020a). With respect to nonlinear phenomena which requires the intricate systems' representation on space and time variables, Itô calculus, as the stochastic calculus version of the change belonging to the variables formula and chain rules, involves the second derivative of f, resulting from the property that Brownian motion has non-zero quadratic variation (Karaca *et al.* 2023b).

As a mathematical model of time-dependent random phenomena, stochastic processes being broad and interdisciplinary combine mathematics, computer intensive methods, applied probability and statistical inference. Therefore, they have diverse fields of application and conjunctures such as medicine, biology, neurophysiology, physics, chemistry, computer science, finance, and so forth by addressing Markov chains, random walks as well as branching processes to name some. Derived from these, a related challenge could be put forth as such: mathematical models in medicine are a reality in all the applications whose impact is for the betterment of patient care provided that the medical community in general undertakes a foundational understanding, directing the application of findings based on reasonable confidence following critical reviews. In that regard, it will be possible for modeling to respond to otherwise unanswerable questions and significantly expand our knowledge base from actual study data. Furthermore, reasonable and mathematical components of a model need to be based on valid research concerning actual patients (Chambers 2000).

In view of the diverse related domains of application and conjunctures, mathematical models are instrumental in providing insights into the complex processes also concerning biological systems by retrieving the essential meaning of hypotheses, which allows the true understanding of the system (Torres and Santos 2015). The study of complex systems has experienced an exponential increase since it focuses on large systems which are constituted by different living entities, which makes them difficult to be understood and modeled depending only on the interactions and dynamics of some individual entities localized in time and space. What is needed would be the accurate and precise mathematical description of collectively emerging behaviors (Coscia 2011; Karaca *et al.* 2019; Wang *et al.* 2022). Comprehension of the role of nonlinear interactions happens to be one of the compelling challenges and limitations in some cases while studying complex systems due to the emergence of qualitatively different states, which is to say new collective states, which cannot be regarded as mere combinations of the individual units' states within the system. This complexity suggests one cannot determine the dynamics of each entity by the dynamics of all other entities. Such determination can rather be possible by their action as a whole.

It is widely acknowledged that AI-based mathematical modeling and its means have had transformative robustness in several domains, including medicine and biology owing to high dimensionality and complexity. Along with the opportunities brought, a substantial number of unique attributes, signals and features contained within the data has, on the other hand, led to some challenges in the development and validation of solutions that can be applied to diverse populations, as well as to medical and biological systems. Figure 1 depicts the intricate reciprocal relations and interactions in a network configuration of inherent opportunities and data complexities.

Philosophy of Science within Comprehensive Mathematical Modeling and Related Applications in Medical and Biological Environments

Philosophy can elucidate mathematical modeling and its juxtaposition along with models and empirical data can be explicated, and

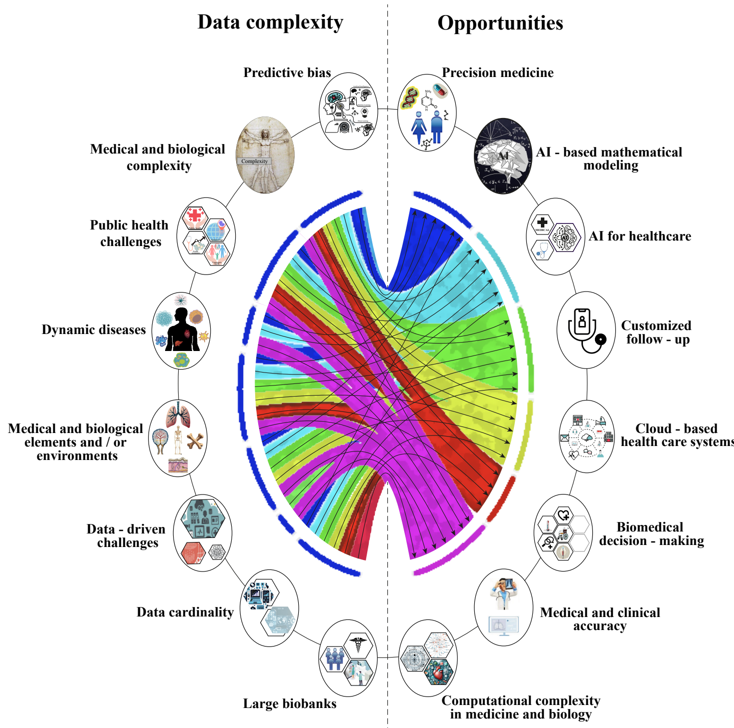

Figure 1 Opportunities and data complexities within the intricate medical and biological systems through their reciprocal interactions

within this context, the main philosophical pillars, namely semantic, pragmatic and syntactic structures of scientific theory, which also constitute core patterns of algorithmic thinking and patterns. Critical functions of mathematical modeling from the pragmatic aspect include the unification of models and data, model fitting to the data, identification of mechanisms relying on observation as well as prediction of future observations (Winther 2012).

The philosophy of science, on the other hand, addresses particular issues that emerge in particular sciences as well as the general issues related to the nature and validity of science. With respect to medicine and biology, one question is posed, which is: if medicine is distinctive, in what ways can one see this distinctiveness? Since a broad array of health and health care practitioners including physicians is involved, it becomes important to analyze the mathematical statements concerning the medical and biological problems. The reason why medicine needs philosophy within new models based on mathematics-informed schemes can be clarified as such: a broad definition of philosophy of medicine is the systematic set of ways to articulate, clarify and address the philosophical issues arising in medicine (Chin-Yee 2017). To give one example, the phenomenological approach focusing on an individual's experiences and the impact of the disease can make one think about a more person-centered approach versus disease-centered approach.

In broad terms, philosophy of science examines and reflects on the concepts, theories, arguments, assumptions, aims and methods of science. In this respect, scientific theory, its definition, applications and those validated by its predictions are units of analyses. With relation to mathematical models, their structure and behavior in target systems are at stake so that explicit common patterns which are implicit in scientific practice are put under scope and analyzed. With target system, it is meant an effectively isolated part of the universe, whether they are physical, biological or empirical, made to function by internal or external causes with their interactions in the universe delineated through a fixed, namely input and output, interface. In virtue of these, mathematical modeling has the constituents of behavior, mechanism and structure. Changes which are generated in the target system are supposed to be detectable in an external way by means of measurements of the system's characterizing quantitative properties.

The application of mathematics to medicine is a research area within the scope of applied mathematics, aiming to create mathematical models of various disease processes which consider the interactions between the complex biological system's various complex components. When integrated with philosophy of thought, this kind of approach can increase understanding into the onset of the diseases and the way they progress. Another benefit of this mode of thinking based on mathematical analysis has to do with the examination of available treatment strategies that can allow the identification of the most optimal one for each medical and / or clinical case. Some of the extensive application areas include but are not limited to cancer treatments and mathematical modeling of them, sequencing of surgical operations, implications of different modes of therapies and their effects on tumors. On neuron level, theoretical neuroscience with the use of mathematical equations aims to understand the way neurons process information which means the way brain coordinates the entire activity of a particular organism, which is related to the behaviors and functions of neurons.

The mathematical description of medicine-related phenomena can be approached in two ways. The first is related to finding the regularities in quantitative analysis of medical data. The mathematical models recommended through this approach is said to have a descriptive design to be implemented for deducing the mechanisms of phenomena under consideration of research. The second approach is related to predicting the system behavior by using the data on mechanisms which lie under the described processes. This sort of mathematical models could have a generalized character describing biological processes on any levels of complexity. In that regard, mathematical models provide a compromise between the two experiments to describe the problem adequately (Karpov 2009). Notwithstanding, the examination of evolutionary many-body and multi-level self-organized complex systems, including medical and biological systems, require the analysis of the following aspects: they own an entangled hierarchy concerning components which may change in time, having the likelihood of their process and components' loss along with their emergence of ever-increasing complexity. To cope with such challenges, it is essential to develop robust and flexible memory which can ensure better adaptation through learning. To sum up, philosophy of science in the medical and biological fields prompt a comprehensive understanding to form holistic mathematical models including simulation, optimization, operationalization, and so forth as experimental and empirical systems with important implications in medicine and biology, particularly complex sciences with the inclusion of complexity, evolution and adaptation so that reassessments in modeling and applications can be conceived and put into practice.

Delineation of Mathematical modeling with Artificial Intelligence in Medicine and Biology: Forecasting, Prediction, Estimation and Approximation

The generation and extensive utilization of modern technologies have prompted the reliance of forecasting and prediction as the principal means for the guiding of critical decision-making processes. Forecasting and prediction are used interchangeable, yet they have certain differences. Forecasting refers to the process of estimating future events or trends based on statistical methods and historical data, involving the analyses of patterns and trends in past or historical data so that informed guesses can be made about the outcomes. As for time frame, forecasting, as a time-based prediction, focuses typically on the prediction of such outcomes over a longer time frame, like months, years or decades, and the aim of forecasting is to provide more accurate estimates of future outcomes. For these reasons, forecasting would be more appropriate to be used while dealing with time series data.

On the other hand, prediction refers to the making of an educated projection or guess regarding a specific outcome without reliance on statistical methods and historical data, which is one difference between forecasting. Another difference is related to the aspect of time frames with prediction not having the need to be time based merely, as it can also be based on multiple causal factors that have impact on the target variable. With this aspect, it is stated that predictions can be short-term and immediate, so they can be employed for the estimation of outcomes for near future up until one year, for example. In addition, predictions are said to be less accurate for their reliance on assumptions and judgement. To sum up, forecasting and prediction are used as methods for the future outcomes' estimation with certain differences. The reliance on historical data and statistical methods characterizes forecasting, whereas prediction is marked by the making of educated projections or guesses with no dependence on the factors mentioned above. Another element is estimation which suggests the finding of the optimal parameter with the use of historical data. Prediction, on the other hand, makes use of the data for the computation of the unseen data's random value. Historical data are what is needed for learning the dependencies for machine learning and modeling.

Multiple observations may be the case with the data with each observation having multiple variables, with this aspect, estimation is known to be the process of optimizing the true state of nature. This aspect of estimation makes it relevant to model building so that it becomes possible to find the most appropriate parameter to best describe the historical data's multivariate distribution. While prediction makes the leveraging of the model that is already built. Mathematical models include equations that have variables and constants, and while estimating with models four steps can be followed for the related process: a priori bounds (limit to the number of solutions regarding the problem), existence and uniqueness (the proving that there is one solution exactly), convergence (an iterative method rather than a closed form) and approximations (the level of goodness an approximation has to the ideal solution for the converged solution to be provided) (Saaty and Alexander 1981).

Estimation is following the event's occurrence, namely posterior probability, while prediction is a type of estimation prior to the event's occurrence, which is to say apriori probability. In summary, forecasting is oriented towards process by following a particular methodology and assuming the past behavior deemed to be an adequate indicator of what will happen in the future. Forecasting encompasses the projection of future developments with a certain level of uncertainty as a result of external factors which may influence the outcome. Prediction, by considering all the historical processes, influences variables and interactions so that future can be revealed. Although all forecasts are predictions, all predictions are not estimations.

Mathematics can provide the language and means for modeling and analyzing structures, including networks, and for profound understanding of the inner workings of Artificial Neural Networks (ANNs), it is of utmost importance to capture the underlying mathematical principles. Artificial neural networks (ANNs), which are known to be intricate networks of interconnected nodes namely neurons are capable of learning from data, recognizing patterns and thus making predictions (Baleanu *et al.* 2023; Karaca *et al.* 2022b). Owing to these aspects, ANNs which adopt the basic model of neuron analogues have had a groundbreaking impact in AI through the emulation of the way human brain operates. In these regards, mathematical principles enable one to gain insights and generate informed decisions, and hence, the crucial role of mathematics becomes evident from the very beginning of initial design until the optimization processes. The connection of mathematical and ANNs is also worthy of mentioning since mathematical modeling constructs the foundation of ANNS by the representation of the relationships between input data and output predictions. Therefore, it becomes possible to create a framework for learning and inference through mathematical models and to formulate the ANNs' behaviors and structures through mathematical techniques so that algorithms and predictions can be rendered efficient and accurate. It should also be noted that mathematical models should be continuously refined, and new mathematical techniques should be generated so that advancements in computational power can be achieved exceeding the boundaries of what neural networks can realize, which can be possible by understanding and optimizing these networks.

At the core of AI, algorithms are placed, and mathematical modeling is regarded to be placed as the core thinking of algorithms. By making use of the methods of neural networks, statistics, operations research, AI is capable of uncovering hidden insights embedded in big data concerning medical and biological issues owing to its judgment abilities and automatic perception properties. The expression of practical problems mathematically is done through ODEs, PDEs, calculus of variations, stochastic processes, nonlinear analyses, and so forth. The contributions of mathematics to the development of AI have been groundbreaking owing to mathematics' laying the theoretical foundations of the AI systems so that the algorithms could be created, modeled and methodologies to enable machines to learn, do reasoning and make informed decisions could be provided. To give one example, linear algebra can enable the data representation and manipulation, which has paved the way for facilitating high dimensional data handling, natural language processing, recommendation systems and signal / image processing and/or recognition. Optimization theory has also witnessed advancements to form the foundation of training and fine-training of the AI-related models. The use of AI has provided numerous opportunities in different areas including the healthcare domain since the integration of mathematical principles with AI can solve the problems related to the enabling of innovative applications. As for the challenges, it is possible that AI may encounter difficulties in the mathematical modeling of problems in medical and biological systems because of the challenge arising in modeling representations of complex cases, incidents and representations whose highly dynamic and heterogenous characteristics cause the exacerbation of the reciprocal interactions and interrelated phenomena.

Nevertheless, AI enables a collaborative environment encompassing the skills, expertise, knowledge and abilities of different individuals from different areas while making it possible that mathematical theories are translated into practical and feasible solutions that can have tangible real-world impacts. In healthcare particularly, mathematics has contributed to the medical imaging techniques which are powered by AI while providing advancements in the disease diagnosis models. The integration of mathematics and AI has also provided contributions to the personalized treatment optimization algorithms, which has had substantial impact on the development of precision medicine which is a form of medicine using information regarding an individual's genes or proteins so that a disease can be prevented and / or diagnosed. Mathematical modeling, AI and datasets for the prediction and management of COVID-19 are reviewed in a study (Mohamadou *et al.* 2020) in regards to the dynamics and early detection of COVID-19 through mathematical modeling and AI so that a comprehensive overview of the methods used the relevant literature and COVID-19 open source datasets could be provided. Another study proposes an integrated approach with multi-source complex spatial data concerning the accurate prediction, diagnosis and prognosis of Multiple Sclerosis (MS) subgroups for their accurate prediction, diagnosis and prognosis by Hidden Markov Model, Viterbi algorithm and Forward-Backward algorithm, being among the dynamic and efficient products of AI-based and knowledge-based systems under the principles of precision medicine (Karaca *et al.* 2022a).

The use of specific information about a person's particular problem can help more precise and accurate diagnosis, plan effective working treatments and make prognosis accordingly. All these pave the way for improved patient outcomes as well as more efficient delivery of healthcare services. Fractional calculus is demonstrated to be a powerful tool for system identification including the ability of approximating nonlinear functions as a result of nonlinear activation functions and diverse inputs as well as outputs' employment. This enhances the processing and control of complex, chaotic and heterogeneous elements in complex and dynamic systems (Karaca 2023a). To put differently, the idea of fractional-order integration and differentiation besides the inverse relationship between them allows fractional calculus applications span across different domains including science, medicine and engineering, to name some. Within the mathematics-informed framework, the approach of fractional calculus can ensure reliable insights into complex processes that comprise a range of temporal-spatial gauges, which can pave the way for developing and implementing novel applicable models through fractional-order calculus.

In these regards, computational science and modeling are geared toward simulating and investigating complex systems via computers by employing different dimensions of mathematics such as entropy, wavelets, differential equations, fractional calculus, fractals, multifractals, fractional methods, quantum means, machine learning techniques, deep learning, AI applications, and so on. A well-constructed computational model, therefore, would consist of numerous variables that characterize the medical and biological system, which can make the performing of many simulated experiments via computerized means possible. Consequently, AI techniques with their combination of fractal, fractional analysis besides mathematical models have provided various applications which may also constitute the prediction of mechanisms that extensively range from living organisms to their intricate reciprocal interactions across spectra. Besides providing solutions to real-world complex problems both on local and global scale.

Across these lines, a neural network is regarded as a black box which approximates a function based on some exemplary computations, so when the complexity of the neural network increases, the functions it can approximate also become further complicated (Karaca *et al.* 2023a). To cite relevant works in these overlapping scopes, one paper (Joshi *et al.* 2023) reviews the use of fractional calculus in different ANN architectures known as fractional-order artificial neural networks (FANNs), which are important. Another paper is related to the review in fractional calculus in image processing (Yang *et al.* 2016) which shows the possibility that fractional-order, as fundamental mathematical tool, can be used to accurately model many systems in science and engineering.

The methods developed are used to solve the fractional systems' problem. Some of the techniques handled in the review are image segmentation, image denoising, image recognition, and so forth. The application of fractional calculus is handled by putting emphasis on signal processing, electromagnetics, continuum mechanics and physics as well. Accordingly, the study (Magin 2010) addresses the fractional derivative's accurate description of natural phenomena that are encountered in common engineering problems. It is further suggested that if the range of mathematical operations is expanded, it will be possible to develop novel and potentially beneficial functional relationships to model complex biological systems rigorously and directly. Last but not least, the study (Karaca 2023b) uses fractional calculus operators and Bloch-Torrey PDE for signal processing and neuronal multi-components to enable to the estimation and prediction of brain microstructure with Diffusion Magnetic Resonance Imaging (DMRI) and SpinDoctor. The study provides contributions to show the way how to tackle the complex structures inherent in the brain composition through sophisticated, integrative and multi-staged mathematical models to be employed effectively as part of healthcare services to maintain the life quality of the patients while providing facilitation in the clinical, medical and other related processes.

CONCLUSION, CONTEMPORARY MATHEMATICAL MEDICINE AND BIOLOGY THOUGHTS, AND FUTURE DIRECTIONS

Mathematical modeling in medicine and biology does not only comprise the implication of the development of advanced computer capabilities but also the ever-increasing access to the processes of complex systems. Mathematics being at the core of AI is capable of providing the means to structure thoughts, models, computations, simulations, schemes and eventually applications. Medical and biological applications of mathematical models situated at each relevant model considered should be profoundly measured, with each model brimming with biology. The ultimate reason for the ubiquity of mathematics in modern scientific and processes is the requirement of mathematical thinking embracing emerging frontiers of scientific inquiry so that complex phenomena can be understood and interpreted. In that regard, mathematical approaches include quantification of observations, modelling, classification, optimization, data processing, analysis, prediction and validation.

Upon the building of higher-level modeling tools and construction of larger modeling knowledge bases, critical processes like integration, cooperative developments and customization have become indispensable. Furthermore, the integration of mathematical modeling including stochastic processes and uncertainty quantization in machine learning and AI has transfigured the capabilities of these technologies, which allow for empowering thereof towards the aim of extracting useful insights and making accurate predictions, estimations and forecasting from the voluminous datasets. The leveraging of powerful computing resources and their integration with advanced image analysis techniques have also enabled the predictions to be manageable by demonstrating how complex systems will be behaving under particular conditions.

It is oft-cited that multiple paths should be directed at and linked with a common end stated towards the overarching aim of unifying sciences. In computational medicine and biology, this point becomes even more critical as it lies at the interface of individualization and personalization of medical decision-making processes so that short-term, medium-term and long-term health outcomes can be enhanced. This opportunity reduces the burden on healthcare and enables timesaving, which shows the aim of precision medicine that includes the tailoring of treatment to suit each patient's specific needs and characteristics. These processes also indicate the significance of prediction and estimation along with anticipation, control and management of the complexity of unexpected events which can be achieved depending on the detailed information retrieved from different biological elements, genetic cues, biomarkers, phenotypic factors, and so forth.

The consideration of these points is pivotal in terms of unraveling the complexities of the related models built, which can offer impactful insights into equilibria, adaptive systems and qualitative transformations underpinning disease dynamics. Aside from these intricate opportunities including the mathematical principles with AI capable of solving the problems related to the enabling of innovative applications, challenges are also at stake. In some instances, it is possible to encounter some difficulties concerning AI, deep learning or machine learning methods in the mathematical modeling of problems in medical and biological systems due to the hardships emerging in the modeling representations of complex cases, incidents and representations which manifest highly dynamic and heterogenous characteristics leading to the exacerbation of the reciprocal interactions and interrelated phenomena. Yet, these challenges can be overcome with the collaborative environment that includes the expertise, knowledge and abilities of individuals from different areas so that mathematical theories can be translated into practical and feasible solutions with tangible real-world impacts.

Based on these opportunities and ways of tackling complexities as well as challenges, some of the following future directions can be succinctly considered:

- Novel and adaptive techniques can be developed to be utilized for the diagnosis of molecular level diseases,
- The subtleties of disorders including genetic, epidemiological, infectious and biological ones,
- Advanced clinical and medical applications with regard to dynamic diseases can be constructed and implemented to deal with a variety of disorders and diseases,
- Mathematical models including stochastic and statistical models, population-dynamics models and complex-network models can be conceived and applied,
- New directions with novel formulations, designs and interpretations based on mathematical modeling processes can be constructed and solved through practicality as well as to-the-point specific means in fields of medicine and biology, among the other related ones,
- The description of major threads concerning mathematical modeling in medicine and biology in science dynamics can be expanded so that the impact of mathematical modeling can be enhanced with improved performance, increased problem-solving capabilities and augmented real-time decision-making processes.

Based on these considerations at the pillars of scientific perspective and holistic vision, the handling of uncertainty and complexity in clinical medicine and biological problems over their processes need the analysis of intrinsic features of almost all mathematical models which are formed based on three basic types of uncertainty: interval, Bayesian and stochastic. Consequently, the present overview has aimed at providing answers built on sophisticated models that encompass the explanation and interpretation of design and formulation. Within this framework, mathematical modeling in medicine and biology has been addressed while elaborating on the important role of philosophy of science as discussed under the context of mathematical modeling, theories as well as applications in medicine and biology.

Availability of data and material

Not applicable.

Conflicts of interest

The author declares that there is no conflict of interest regarding the publication of this paper.

LITERATURE CITED

Abirami, A., P. Prakash, *et al.*, 2023 Fractional diffusion equation for medical image denoising using adi scheme. Journal of Population Therapeutics and Clinical Pharmacology **30**: 52–63.

Amigó, J. M. and M. Small, 2017 Mathematical methods in medicine: neuroscience, cardiology and pathology. Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences **375**: 20170016.

Arthur, J. L., 1985 An introduction to stochastic modeling (howard m. taylor and samuel karlin). SIAM Review **27**: 581.

Baleanu, D., Y. Karaca, L. Vázquez, and J. E. Macías-Díaz, 2023 Advanced fractional calculus, differential equations and neural networks: Analysis, modeling and numerical computations. Physica Scripta **98**: 110201.

Behinfaraz, R., A. A. Ghavifekr, R. De Fazio, and P. Visconti, 2023 Utilizing fractional artificial neural networks for modeling cancer cell behavior. Electronics **12**: 4245.

Brugnach, M., C. Pahl-Wostl, K.-E. Lindenschmidt, J. Janssen, T. Filatova, *et al.*, 2008 Chapter four complexity and uncertainty:

Rethinking the modelling activity. Developments in Integrated Environmental Assessment **3**: 49–68.

Chambers, R. B., 2000 The role of mathematical modeling in medical research:"research without patients?". Ochsner Journal **2**: 218–223.

Chang, Y.-C., 2024 Deep-learning estimators for the hurst exponent of two-dimensional fractional brownian motion. Fractal and Fractional **8**: 50.

Chen, L., P. Ji, Y. Ma, Y. Rong, and J. Ren, 2023 Custom machine learning algorithm for large-scale disease screening-taking heart disease data as an example. Artificial Intelligence in Medicine **146**: 102688.

Chin-Yee, B., 2017 The new medical model: why medicine needs philosophy. Canadian Medical Association. Journal **189**: E896.

Coscia, V., 2011 On the mathematical theory of living systems, i: Complexity analysis and representation. Mathematical and computer modelling **54**: 1919–1929.

Daun, S., J. Rubin, Y. Vodovotz, and G. Clermont, 2008 Equation-based models of dynamic biological systems. Journal of critical care **23**: 585–594.

Evans, L. C., 2022 *Partial differential equations*, volume 19. American Mathematical Society.

Fortier, P. J. and H. Michel, 2003 *Computer systems performance evaluation and prediction*. Digital Press.

Ge, W., C. Lueck, H. Suominen, and D. Apthorp, 2023 Has machine learning over-promised in healthcare?: A critical analysis and a proposal for improved evaluation, with evidence from parkinson's disease. Artificial Intelligence in Medicine **139**: 102524.

Grizzi, F., A. Castello, D. Qehajaj, C. Russo, and E. Lopci, 2019 The complexity and fractal geometry of nuclear medicine images. Molecular Imaging and Biology **21**: 401–409.

Havlin, S., S. Buldyrev, A. Goldberger, R. Mantegna, S. Ossadnik, *et al.*, 1995 Fractals in biology and medicine. Chaos, Solitons & Fractals **6**: 171–201.

Heid, E., C. J. McGill, F. H. Vermeire, and W. H. Green, 2023 Characterizing uncertainty in machine learning for chemistry. Journal of Chemical Information and Modeling **63**: 4012–4029.

Jin, W., M. Fatehi, R. Guo, and G. Hamarneh, 2024 Evaluating the clinical utility of artificial intelligence assistance and its explanation on the glioma grading task. Artificial Intelligence in Medicine **148**: 102751.

Joshi, M., S. Bhosale, and V. A. Vyawahare, 2023 A survey of fractional calculus applications in artificial neural networks. Artificial Intelligence Review **56**: 13897–13950.

Karaca, Y., 2022a Multi-chaos, fractal and multi-fractional AI in different complex systems. In *Multi-Chaos, Fractal and Multi-Fractional Artificial Intelligence of Different Complex Systems*, pp. 21–54, Elsevier.

Karaca, Y., 2022b Theory of complexity, origin and complex systems. In *Multi-Chaos, Fractal and Multi-fractional Artificial Intelligence of Different Complex Systems*, pp. 9–20, Elsevier.

Karaca, Y., 2023a Computational complexity-based fractional-order neural network models for the diagnostic treatments and predictive transdifferentiability of heterogeneous cancer cell propensity. Chaos Theory and Applications **5**: 34–51.

Karaca, Y., 2023b Fractional calculus operators-bloch partial differential equation-artificial neural networks-computational complexity modeling of the micro-macrostructural brain tissues with diffusion mri signal processing and neuronal multi-components. Fractals **31**: 2340204–547.

Karaca, Y. and D. Baleanu, 2022 Computational fractional-order calculus and classical calculus ai for comparative differentiability prediction analyses of complex-systems-grounded paradigm. In *Multi-Chaos, Fractal and Multi-fractional Artificial Intelligence of Different Complex Systems*, pp. 149–168, Elsevier.

Karaca, Y., D. Baleanu, and R. Karabudak, 2022a Hidden markov model and multifractal method-based predictive quantization complexity models vis-á-vis the differential prognosis and differentiation of multiple sclerosis' subgroups. Knowledge-Based Systems **246**: 108694.

Karaca, Y., D. Baleanu, M. Moonis, and Y.-D. Zhang, 2020a Theory, analyses and predictions of multifractal formalism and multifractal modelling for stroke subtypes' classification. In *Computational Science and Its Applications–ICCSA 2020: 20th International Conference, Cagliari, Italy, July 1–4, 2020, Proceedings, Part II 20*, pp. 410–425, Springer.

Karaca, Y., D. Baleanu, M. Moonis, Y. D. Zhang, and O. Gervasi, 2023a Editorial special issue: Part IV-III-II-I series: Fractals-fractional AI-based analyses and applications to complex systems.

Karaca, Y., D. Baleanu, Y. D. Zhang, O. Gervasi, and M. Moonis, 2022b *Multi-Chaos, Fractal and Multi-Fractional Artificial Intelligence of Different Complex Systems*. Academic Press.

Karaca, Y. and C. Cattani, 2018 Naive bayesian classifier. Comput. Methods Data Anal pp. 229–250.

Karaca, Y. and M. Moonis, 2022 Shannon entropy-based complexity quantification of nonlinear stochastic process: diagnostic and predictive spatiotemporal uncertainty of multiple sclerosis subgroups. In *Multi-Chaos, Fractal and Multi-Fractional Artificial Intelligence of Different Complex Systems*, pp. 231–245, Elsevier.

Karaca, Y., M. Moonis, and D. Baleanu, 2020b Fractal and multifractional-based predictive optimization model for stroke subtypes' classification. Chaos, Solitons & Fractals **136**: 109820.

Karaca, Y., M. Moonis, Y.-D. Zhang, and C. Gezgez, 2019 Mobile cloud computing based stroke healthcare system. International Journal of Information Management **45**: 250–261.

Karaca, Y., M. Ur Rahman, M. A. El-Shorbagy, and D. Baleanu, 2023b Multiple solitons, bifurcations, chaotic patterns and fission/fusion, rogue waves solutions of two-component extended (2+ 1)-d itô calculus system. Fractals **31**: 2350135.

Karlsson Faronius, H., 2023 Solving partial differential equations with neural networks.

Karpov, A. V., 2009 Mathematical modeling in medicine. Mathematical Models of Life Support Systems **2**: 312.

Koen-Alonso, M. and P. Yodzis, 2005 7.3| dealing with model uncertainty in trophodynamic models: A patagonian example. DYNAMIC FOOD WEBS: MULTISPECIES p. 381.

Li, C. and D. Zhao, 2024 A non-convex fractional-order differential equation for medical image restoration. Symmetry **16**: 258.

Magin, R. L., 2010 Fractional calculus models of complex dynamics in biological tissues. Computers & Mathematics with Applications **59**: 1586–1593.

Mohamadou, Y., A. Halidou, and P. T. Kapen, 2020 A review of mathematical modeling, artificial intelligence and datasets used in the study, prediction and management of covid-19. Applied Intelligence **50**: 3913–3925.

Mubayi, A., C. Kribs, V. Arunachalam, and C. Castillo-Chavez, 2019 Studying complexity and risk through stochastic population dynamics: Persistence, resonance, and extinction in ecosystems. In *Handbook of Statistics*, volume 40, pp. 157–193, Elsevier.

Ning, X., L. Jia, Y. Wei, X.-A. Li, and F. Chen, 2023 Epi-dnns: Epidemiological priors informed deep neural networks for modeling covid-19 dynamics. Computers in biology and medicine **158**: 106693.

Oberguggenberger, M., 2005 The mathematics of uncertainty: models, methods and interpretations. In *Analyzing uncertainty in civil engineering*, pp. 51–72, Springer.

Pinchover, Y. and J. Rubinstein, 2005 *An introduction to partial differential equations*, volume 10. Cambridge university press.

Saaty, T. L. and J. M. Alexander, 1981 *Thinking with models: mathematical models in the physical, biological, and social sciences*. RWS Publications.

Takale, K., U. Kharde, and S. Gaikwad, 2024 Investigation of fractional order tumor cell concentration equation using finite difference method. Baghdad Science Journal .

Torres, N. V. and G. Santos, 2015 The (mathematical) modeling process in biosciences. Frontiers in genetics **6**: 169934.

Vosika, Z. B., G. M. Lazovic, G. N. Misevic, and J. B. Simic-Krstic, 2013 Fractional calculus model of electrical impedance applied to human skin. PloS one **8**: e59483.

Wang, S.-H., Y. Karaca, X. Zhang, and Y.-D. Zhang, 2022 Secondary pulmonary tuberculosis recognition by rotation angle vector grid-based fractional fourier entropy. Fractals **30**: 2240047.

Wang, W., M. Luo, P. Guo, Y. Wei, Y. Tan, *et al.*, 2023 Artificial intelligence-assisted diagnosis of hematologic diseases based on bone marrow smears using deep neural networks. Computer Methods and Programs in Biomedicine **231**: 107343.

Winther, R. G., 2012 Mathematical modeling in biology: philosophy and pragmatics. Frontiers in Plant Science **3**: 102.

Yang, Q., D. Chen, T. Zhao, and Y. Chen, 2016 Fractional calculus in image processing: a review. Fractional Calculus and Applied Analysis **19**: 1222–1249.

Yang, Z., Z. Hu, H. Ji, K. Lafata, E. Vaios, *et al.*, 2023 A neural ordinary differential equation model for visualizing deep neural network behaviors in multi-parametric mri-based glioma segmentation. Medical Physics **50**: 4825–4838.

Zimmermann, H.-J., 2000 An application-oriented view of modeling uncertainty. European Journal of operational research **122**: 190–198.

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