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# Computational Complexity-based Fractional-Order Neural Network Models for the Diagnostic Treatments and Predictive Transdifferentiability of Heterogeneous Cancer Cell Propensity

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**ABSTRACT** Neural networks and fractional order calculus are powerful tools for system identification through which there exists the capability of approximating nonlinear functions owing to the use of nonlinear activation functions and of processing diverse inputs and outputs as well as the automatic adaptation of synaptic elements through a specified learning algorithm. Fractional-order calculus, concerning the differentiation and integration of non-integer orders, is reliant on fractional-order thinking which allows better understanding of complex and dynamic systems, enhancing the processing and control of complex, chaotic and heterogeneous elements. One of the most characteristic features of biological systems is their different levels of complexity; thus, chaos theory seems to be one of the most applicable areas of life sciences along with nonlinear dynamic and complex systems of living and non-living environment. Biocomplexity, with multiple scales ranging from molecules to cells and organisms, addresses complex structures and behaviors which emerge from nonlinear interactions of active biological agents. This sort of emergent complexity is concerned with the organization of molecules into cellular machinery by that of cells into tissues as well as that of individuals to communities. Healthy systems sustain complexity in their lifetime and are chaotic, so complexity loss or chaos loss results in diseases. Within the mathematics-informed frameworks, fractional-order calculus based Artificial Neural Networks (ANNs) can be employed for accurate understanding of complex biological processes. This approach aims at achieving optimized solutions through the maximization of the model's accuracy and minimization of computational burden and exhaustive methods. Relying on a transdifferentiable mathematics-informed framework and multifarious integrative methods concerning computational complexity, this study aims at establishing an accurate and robust model based upon integration of fractional-order derivative and ANN for the diagnosis and prediction purposes for cancer cell whose propensity exhibits various transient and dynamic biological properties. The other aim is concerned with showing the significance of computational complexity for obtaining the fractional-order derivative with the least complexity in order that optimized solution could be achieved. The multifarious scheme of the study, by applying fractional-order calculus to optimization methods, the advantageous aspect concerning model accuracy maximization has been demonstrated through the proposed method's applicability and predictability aspect in various domains manifested by dynamic and nonlinear nature displaying different levels of chaos and complexity.

**KEYWORDS**
Computational complexity
Complex systems
Artificial Intelligence (AI)
Chaos theory
Fractional calculus
Fractional-order derivatives
Mittag-Leffler functions
Heavy-tailed distributions
Computational biocomplexity
Nonlinearity and uncertainty
Multilayer perceptron algorithm (MLP)
Neural networks
Transdifferentiable mathematics-informed framework
Complex order optimization
Mathematical biology
Data-driven fractional-order biological modeling
Cancer cell propensity.

## INTRODUCTION

Universal order and complex universe, correspondingly, require solutions and models to address the complexity challenge by self-organization, harmonization and synchronization. Complex-fractional models in complex dynamical processes, therefore, have extensive schemes made up of hierarchical, spatial as well as topological structures that have assorted likely granularities of the particular system by differential equations. On the other hand, complex order fractional derivatives govern complex-fractional systems in which memory and nonlinearity are seen as the two aspects of complex-fractional systems with complex variables, which point out the significance of the modeling of memory-intense systems. Complex-order systems which functions within a universal order manifests multiple dynamical interactive components grounded on multiscale spatial and temporal fields, which points towards the integration for the construction of an operational whole on a holistic spectrum. Fractional calculus (FC), owing to its ability of reflecting the systems' actual state properties, exhibiting unforeseeable variations, makes the generalization of integration and differentiation possible. In that regard, it can provide a new added value for the enhanced description of the characteristics concerning different complex systems. When it is necessary to summon solutions for the complex models, simulations, technological advances have enabled the integration of fractional calculus and Artificial Intelligence (AI) applications particularly for the managing

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of uncertainty and making critical multi-stage and multi-criteria decisions within the framework of mathematical modeling. Formation and validation of hypothesis can, hence, be minimized in terms of time, with the acceleration of experiments and numerical simulations along with the substantial volume of data analyses, which have become precise, reliable and trustworthy.

Fractional-order calculus (FOC), being based on fractional-order thinking, concerns the differentiation and integration of non-integer orders, which enables improved understanding of complex and dynamic systems with or without time delays. Certain complex systems in nature may not always be likely to be characterized by classical integer-order calculus models; therefore, a fractional-order system-based model is capable of describing the system performance in a more accurate manner. The processing as well as control of complex elements are also enhanced whilst making the performance more optimal owing to FOC. The fractal processes' discontinuous nature necessitates a reinvestigation of equations of motion including fractional operators. In this regard, fractional calculus paves the way for modeling the impact of an erratic background in a system with its description merging with nonlinear dynamics.

Fractional thinking as a sort of in-between thinking is situated between the integer-order moments, and there, fractional moments are needed as empirical integer moments cannot converge. Between the integer dimensions, there exist fractal dimensions whose significance is seen when data possess no characteristic scale length. The non-integer operators that are required to define dynamics with long-time memory and spatial heterogeneity are at stake between the integer value operators local in time and space. Taking all these into account, it can be said that the modern inclination of science requires the understanding and even embracing of complexity where complex phenomena oblige us to find new ways of thinking. Fractional calculus is one way to provide framework towards such thinking (West 2016; West *et al.* 2003). Fractional differential equations are also beneficial means to characterize and show the dynamics of complex phenomena with spatial heterogeneous characteristics and long memory. The fractional derivative of real order is seen as the degree of structural heterogeneity between the homogeneous and also in homogeneous spheres in which complexity usually arise with respect to systems made up of elements interacting with one another which may be intrinsically hard in terms of modeling (Lopes and Tenreiro Machado 2019).

Fractional-order differential and integral equations enable the conventional integral and differential equations' generalization by extending the related conceptions with respect to different biological phenomena. Correspondingly, adeptness in computational complexity ensures an interconnected, integrative and multifarious angle towards problems; which is the cause of applicable sets of ideas and implementations to be implemented for the identification of the subtle features of complex dynamic systems. One significant point to bear in mind is to acknowledge the varying degrees of problems in order that the models can be established in a way that can be adjustable and fitting the matter into the right data, as handled in various disciplines like neuroscience (Singhal *et al.* 2010), biology (Magin 2010) and so on.

Mathematical-informed frameworks with computer-assisted proofs are used so that it becomes possible to be equipped with reliable and accurate understanding in complex heterogeneity and dynamic structure of temporally and spatially multiple transient states. There still exist means in mathematics awaiting to construct their way in theoretical biology as is in the case of fractional, or non-integer order calculus whose application emerges as a powerful and strategic approach of modeling in the light of forthcoming opportunities and challenges in mathematical medicine. Fractional mathematical oncology, in this regard, deals with memory effects, heterogeneous scales and dormant periods with respect to the onset and development of tumors in a straightforward way (Valentim *et al.* 2021). Biological phenomena and problems, inherently characterized by nonlinearity and uncertainty, modeled by ordinary or partial differential equations with integer order, are possible to be described well through the employing of ordinary and partial differential equations. The variables, attributes, parameters, initial conditions as well as observation states in the model are to be considered for computational purposes. At each instance of time, it is possible to measure the correct information by a non-integer order derivative.

One relevant study on that subject matter is (Ziane *et al.* 2020) aims at applying the local fractional homotopy analysis method (LEHAM) in order to get the non-differentiable solution of two non-linear partial differential equations (PDEs) concerning the Cantor sets' biological population model. The proposed method is demonstrated to be effective and powerful in terms of solving those PDEs with LFHAM being applied for the solution of other nonlinear PDEs with local fractional derivative. Another study is on biomathematical modeling (Carletti and Banerjee 2019), distinguishing demographic noise and environmental noise. The authors present a technique for simulating and modeling demographic noise that goes in backward direction. Neurological phenomena, on the other hand, have layered, multi-phase and multi-functional materials like those of brain tissue with interconnected networks.

In order to enhance the comprehension how the brain provides its functions, robust mathematical-informed as well as feedback engineering frameworks which use basic scientific concepts to interpret and direct the experiments investigating brain's responses to different stimuli, diseases and treatment courses thereof are required. In neuroscience, one of the related studies (Lewis *et al.* 2016) is concerned with the ratio processing system (RPS) tuned to the holistic magnitudes suited for grounding fraction learning difficulties about symbolic fractions. The proposed premise is the capability to represent ratio/fraction magnitudes stated by the RPS could upkeep a more profound grasping of fractions as relative magnitudes, which shows the critical importance of RPS about learning with regard to fractions. In short, fractional dynamics could be applicable both for the oculomotor system and for the motor control systems.

A fractional derivative's physical meaning is said to be an open problem and for the modeling of various memory related phenomena, a memory process is made up of two stages: short has permanent retention and the second one is ruled by a simple model of fractional derivative. The fractional model is shown to fit the test data of memory related phenomena in different fields like mechanics and biology perfectly though the numerical least square model. Thus, the physical meaning concerning fractional order is found to be an index of memory based on that scheme (Du *et al.* 2013). Fractional Calculus (FC), refers to the calculus of derivatives and integrals of arbitrary complex order or real order has wide-ranging domains of application. Different studies are available in the literature addressing the solution of varying fractional order biological disease models in environments displaying uncertainty. The application of Caputo operator to convey non-integer derivative of fractional order can be found in (Khan *et al.* 2020), handling of chaos control and synchronization of a biological snap oscillator through a new fractional model is addressed with regard to bio-

engineering in (Sommacal *et al.* 2008), biology (Toledo-Hernandez *et al.* 2014), (Tokhmpash 2021), signal processing (Gutierrez *et al.* 2010), image processing (Debnath 2003), electronics (Krishna and Reddy 2008) robotics (Singh *et al.* 2021), control theory (Panda and Dash 2006), (Garrappa 2015). Numerical parameters, variables and radiation elements are used for the treatment model's simulation. It has been concluded that the model is capable of simulating the treatment process of cancer and make the prediction of the results of other protocols related to radiation.

Regarding the broad class of functions, the Riemann–Liouville definition is employed in the process of the problem formulation, with the Grünwald-Letnikov definition being referred to for achieving some numerical solutions. The use of Riemann-Liouville fractional calculus' operators is considered in (Rodríguez-Germá *et al.* 2008) for the reduction of linear ordinary or PDEs with variable coefficients to more simple problems through certain commutative differential relations. Thus, it has been aimed to avoid the singularities in the original equations and the case of Bessel differential equations is used as the related example. The efficiency of the technique employing Riemann-Liouville operators of fractional calculus has been shown by (Rodríguez-Germá *et al.* 2008). Regarding the derivatives of Riemann-Liouville and Caputo derivatives, Riemann-Liouville derivative as one of mostly employed fractional derivatives and some important features of the Caputo derivative are discussed in (Li *et al.* 2011) which provides benefits for the understanding of fractional calculus as well as modeling of fractional equations in the fields of science and engineering.

Mittag-Leffler (ML) functions, with their various properties and one to five and more parameters, are inclined towards modification on a complex plane with the extension of particular fractional-calculus operators owing to their use in the various direct applications and involvements in fractional calculus and fractional differential equations concerning biology, physics, applied sciences and engineering. Among the studies in the literature, the following work can be referred to: (Fernandez and Husain 2020), (Pang *et al.* 2018).

Fractional order calculus theory, employed for addressing varying orders of derivatives and integrals, lends itself to diverse kinds of definitions for fractional order derivatives with Riemann–Liouville, Caputo and Grünwald–Letnikov being the most frequently used ones. On the other hand, fractional calculus affords tools that can describe and deal with complex phenomena as well as its connection to the inherent properties that are nonlinear complex considering the memory effects and apparently chaotic behavior. In view of that, the fractional order derivative notion is ubiquitous in different areas, offering diverse and varying methods concerning fractional order derivative (FOD) (KARCI *et al.* 2014).

It is noted that fractional derivatives have the capability of improving the machine learning algorithms' accuracy, with computing power, if and when utilized for spectral data, signals and images. Given these, fractional derivatives and, successively, fractional calculus have proved to provide a framework to be able to enhance optimization tasks. One example of work handled within that view is by (Raubitzek *et al.* 2022) providing exemplary applications to segment MRI brain scans, for stroke, to be applied as input for a machine learning algorithm. Another work addresses practical software optimization methods to implement fractional-order backward difference, sum, and differintegral operator, which are dependent on the Grünwald–Letnikov definition regarding the evaluation of fractional-order differential equations in embedded systems owing to their more convenient form in contrast with Caputo and Riemann–Liouville definitions (Matusiak 2020).

The work of (Viola and Chen 2022) provides an evaluation of a fractional-order self-optimizing control architecture for the purpose of process control. As a consequence, the related controller is stated to enhance the system closed-loop response under different operating conditions while reducing convergence time of the real-time derivative-free optimization algorithm through fractional-order stochasticity. Furthermore, another paper is related to the optimization techniques of image analysis algorithms. The authors optimize the Grünvald - Letnikov fractional - order backward difference for the estimation of the position of the marker in a sequence of images, and through the mathematical foundation of the fractional order derivative optimization tool of the study, it is observed that process or load linked with the optimized algorithm was reduced by 35% and more (Jachowicz *et al.* 2022).

Conducting predictions reliant on mathematical models with regard to processes and datasets related to biology requires the parameters concerning machine learning. Moreover, the fitting of the parameters to experimental data is challenging as it is important and essential to find the model parameters' optimal values during when the model parameters' different values may exhibit consistent aspects with the data, called the identifiability. For ANNs, learning is a noteworthy stage concerning convergence rate, as obtained potentially by the use of fractional-order gradient in data science.

One respective study, (Gomolka 2018), utilizes a model of a neural network with a new backpropagation rule by making use of a fractional order derivative mechanism. Another study, (Kadam *et al.* 2019) addresses the ANN approximation of fractional derivative operators. The study (Mall and Chakraverty 2018) develops an ANN technique to find solution of FDEs and shows the advantage of them in terms of describing various real-world application problems of physical systems. A MLP architecture and error back propagation algorithm are used to minimize the error function and modify the weights and biases as parameters. ANN output is said to yield a suitable approximate solution of FDE and the accuracy of the method is put forth as such. (Wu *et al.* 2017) investigates in depth the ML stability of a class of fractional-order neural networks in the field of neurodynamics. The results established are dependent on the FDE theories of FDE and differential equation with generalized piecewise constant arguments with the derived criteria improving and extending the respective results. Finally, (Niu *et al.* 2021) provides the discussion of an optimal randomness case study for a stochastic configuration network (SCN) machine-learning method having heavy-tailed distributions along with the discussion of the employment of fractional dynamics in analytics concerning big data to quantify variability due to the complex systems' generation.

Complex systems are marked by order and homogeneity as well as the hierarchy of subsystems and different levels in space and time. Therefore, the observation of the interconnection with respect to different biological elements such as cells, molecules and tissues, with a focus on their qualitative properties, is required. Considering this intricate complexity, it would not be adequate to characterize and identify only the discrete biological components of the system. Thus, mathematical models play a noteworthy role for the complex problems' solution and the viable applications to biological data so that it can be possible to attain a thorough understanding of the emergent interactions between heterogeneous biological components and their related pathways. In this way, it can be ensured to reveal the correlations between different observable phenomena characterized by heterogeneity and dynamic properties in an accurate and robust way.

Life is endowed with many diverse and peculiar attributes, which invokes the investigation of its origin that is not possible to obtained from scratch, referring to its molecular constituents. These complex systems in life do not only evolve through time, they also have a past which is jointly responsible for the present behaviors. On the other hand, the evolution of its forms cannot be predicted; in that sense, evolution, as a universal process and dynamics, brings about diverse phenomenology of life with its related theory leading to rich phenomenology of life on earth for modern biology and mathematical bioengineering which has been subject to modifications due to its nature over the years. The complexity of living systems can be expressed in cells and tissues' structures and functions, which means biological functions of each element are embedded in a three-dimensional alignment of the cells of each tissue, extracellular matrices and anatomical organization. Biocomplexity, alternatively, with multiple scales ranging from molecules to cells and organisms addresses complex structures and behaviors that emerge from nonlinear interactions of active biological agents. Due to this complexity of biological systems and elements, chaos theory seems to be one of the most applicable areas of life sciences in view of nonlinear dynamic and complex systems of living and non-living environment.

Biocomplexity, with multiple scales that range from molecules to cells and organisms, is concerned with complex structures and behaviors emerging from nonlinear interactions of active biological agents. This alignment of emergent complexity deals with the organization of molecules into cellular machinery through that of cells into tissues as well as that of individuals to communities. As healthy systems keep up their complexity in their lifetime and are chaotic, disease is seen as an outcome when the loss of complexity or the loss of chaos occurs. Furthermore, mathematical models enable researchers to dig into the degree of complexity concerning processes, routes and the way these are interconnected. One of the related studies in this domain is (Tzoumas *et al.* 2018) on the sensor selection to determine the minimum number of state variables which are required to be measured for the monitoring of the evolution of the biological system. The authors focus on the solution of different problems of sensor selection and consider biologically motivated discrete-time fractional-order systems. The work (Blazewicz and Kasprzak 2012) addresses the progress of research in computational biology based on computer science and operational research, presenting the different issues around complexity as inspired by computational biology.

Algorithms and complexity along with their conceptual aspects become significant on the condition that their definition is done vis-*á*-vis formal computational models (Du and Ko 2011). Since computing is proven to be critical to be able to deal with exhaustive data tasks and achieve scalable solutions to complex problems, researchers and developers should be familiar with impacts of computational complexity to better grasp and design efficient algorithms in computational biology. Algorithmic (computational) complexity, known as running time, is a way of comparing the efficiency of an algorithm. For a given task, an algorithm doing the completion of a task is considered to be more complex if more steps are the case.

It is possible to express the algorithmic complexity with the *Big O* notation varying in relation to the size of the input. The measurement of complexity is considered based on the duration it takes for a program to run in relation to the size of the input (time complexity) or to the memory it is to take up (space complexity). One related work (Sidelnikov *et al.* 2018) investigates the application of dynamic deep neural networks for non-linear equalization in long haul transmission systems. The optimum dimensions are identified by extensive numerical analysis and computational complexity of the systems are calculated as a function of system length. The authors demonstrate performance at a considerably lower cost of computation.

Neural networks and fractional order calculus are known to be efficient to identify systems, which concerns the capability to approximate nonlinear functions. One of the relevant studies (Aguilar *et al.* 2020) is concerned with a fractional gradient descent method. By using the Caputo derivative, the authors made the evaluation of the fractional-order gradient of the error. The performance of the proposed fractional-order backpropagation algorithm was shown on certain datasets. The study (Boroomand and Menhaj 2009) on neural networks for the identification of the problem proposes a new approach to the neural networks. In another relevant study (Xue *et al.* 2020), a fractional order gradient descent with momentum method was used for updating the weights of neural network for the purpose of data classification. The error analysis of the study put forth the effectiveness of the algorithm in accelerating the convergence speed of gradient descent method, which also improves the performance with validity and accuracy.

Different computing techniques have been developed for optimized solutions regarding fractional order systems. Computational complexity, accordingly, proves to be significant to analyze problems as their complexity increases in size. Measuring the extent of the work required for the different problems' solution, computational complexity can provide a practical classification tool from the powerful lenses where the patterns can be observed both on a distinctive level and as a whole. In line with a novel mathematics-informed framework and multi-staged integrative method regarding computational complexity, there is no existing previous work as this work in the literature, obtained from such an interconnected and inclusive perspective with the methods proposed. With its novel mathematics-informed framework and multifarious integrative methods concerning computational complexity, this study has the aim of establishing a robust, reliable as well as accurate model depending upon the integration of fractional-order derivative and ANN for the purposes of diagnosis and differentiability prediction purposes for heterogeneous cancer cell that displays various transient and dynamic biological properties.

The other aim of the present work is to reveal the importance of computational complexity so that the fractional-order derivative with the least complexity could be obtained to be able to attain the optimized solution. Accordingly, the subsequent steps were integrated and applied: first of all, the Caputo fractional-order derivative with three-parametric Mittag-Leffler function (MLF) $(\alpha, \beta, \gamma)$ was applied to the cancer cell dataset. Hence, the new fractional models with changeable degrees were formed by enabling data fitting with the fitting algorithm MLF which has three parameters, depending upon the heavy-tailed distributions. Afterwards, the new datasets (mfc_cancer cell and the mfr_cancer cell dataset) were generated. As the following step, classical derivative (calculus) was applied to the cancer cell dataset, and from this application, the cd_ cancer cell datasets were generated. After that, the performance of the new dataset, obtained from the application of the first step and the performance of the dataset obtained from the application of the second step as well as of the cancer cell dataset was compared by the multilayer perceptron (MLP) algorithm application. As the following step, the fractional order derivatives models that could be the most optimal for the disease were produced. Last but not least, computational complexity was

employed to achieve the Caputo fractional-order derivative (FOD) that has the least complexity, for the purpose of obtaining the optimized solution as a result.

This multifarious scheme, by the application of fractional-order calculus (FOC) to optimization methods and the experimental results, have allowed us to highlight the advantage of the maximization of the model's accuracy and the minimization of the cost functions. This corroborates the applicability of the proposed method in different domains which are characterized by nonlinear and dynamic nature with varying levels of complexity. Multistage integrative models can capture the regular and significant attributes on temporal and spatial scales, besides fractional-order differential and integral equations demonstrate the generalization of classical calculus by the extension of the conceptions concerned with biological processes and systems.

The rest of the study is structured in the following manner. Section 2 is on Biocomplexity, Biological Dataset, Related Method and Methodology with the subheading, 2.1 Complex Heterogenous Cancer Cell Dataset of the Study and 2.2 Method and Methodology. Subsequently, Section 3 addresses Experimental Results and Discussion: Computation- related Application of Caputo Fractional-Order Derivatives with Three-Parametric Mittag-Leffler Functions, ANN algorithm and Computational Complexity. Finally, Section 4, provides the Concluding Remarks and Future Directions of this work.

## BIOCOMPLEXITY, BIOLOGICAL DATASET, RELATED METHOD AND METHODOLOGY

### Complex Heterogenous Cancer Cell Dataset of the Study

Biocomplexity addresses the complex interactions within and among different systems are evident; and thus, biocomplexity necessitates an integrated exploration of coupled human-natural systems by looking into the reasons for and consequences of biological dynamics so that it can provide the related mathematical models of complex biological phenomena to comprehend them, and to interpret and guide quantitative experimental processes. Accordingly, an accurate interpretation of the data entails the grasping of many emergent and dynamic properties that are due to the interchange of various varying biological elements in complex heterogeneous biological systems. Given such complexity, only identifying and characterizing the individual biological components in the system would not be sufficient. To address these challenges, mathematical modeling, which enables researchers to look into the degree of complexity, along with statistical techniques are important to investigate problems. If the disruptions concerning the processes and the way the interaction occurs is understood well, then it will also be possible to identify the factors that have impact on the disease. Consequently, the present study handles a complex biological dataset concerned with cancer cell, which manifests complex, heterogeneous and dynamic properties, with an undeniable effect on health and life quality, being one of the most frequent reasons for mortality.

Regarding the aims of diagnosis and differentiability prediction concerning the heterogeneous cancer cell, 30 different columns were employed. The other related details with respect to the heterogenous biocomplex cancer cell dataset with attributes computed unit-wise can be found in the following reference (Murphy 1994). Biocomplexity with a quantitative and integrative approach refers to the study of the emergence of complex and self-organized behaviors based on the interacting of numerous simple agents. This kind of an emergent complexity is representative of the different levels of organization concerning molecules and tissues. Biocomplexity, arises from biological, environmental, chemical, behavioral, physical and social interactions, encompassing the presence of multiple scales (Michener *et al.* 2001).

If one is to have a thorough understanding of the correct interpretation of data, knowing the dynamic and emerging characteristics is important. Robust, accurate and appropriate mathematical modeling serves the investigation of problems due to the fact that mathematical models allow the exploration of the way complexity processes and disruptions regarding these processes affecting the course of the disease, which also has critical impact on its prediction. This study deals with biological dataset, namely cancer cell, which shows heterogeneous, dynamic as well as complex characteristics which need to be taken under careful control in order to prevent possible detrimental effects for the future.

### Method and Methodology

#### *Algorithm based on Heavy-tailed distribution for Data Fitting with the ML Functions*

***Three-parametric ML functions*** $(\alpha,\ \beta,\ \gamma)$ Being among the domains of mathematical analysis, special function is linked with different topics (Garrappa 2015). MLF is also one of the important classes of special functions with its extensions [46]. For benefits of fractional calculus and fractional exponential functions, (Karaca and Baleanu 2022a), (Camargo *et al.* 2012) and (Fernandez and Husain 2020) can be referred to. (Baleanu and Karaca 2022) can be referred to for the details concerning the original function of ML relying on different parameters with different extensions.

### The Basic Theory Behind Heavy- tailed Distributions

#### *Pareto distribution: a power-law probability distribution*

The Pareto distribution is known as a power-law probability distribution which is employed to describe different observable phenomena concerning science, social life, control and so forth (Newman 2005). Pareto distribution $(P_D)$ as a random variable (Arnold 2014) is followed by the Pareto distribution provided it owns the tail's array as such according to Eq. (1):

$$P_D(V) = \begin{cases} 1 - \frac{(b)}{V} & V \leq b \\ 0. & V < b \end{cases} \tag{1}$$

$a$ and $b$ respectively show the scale and shape parameters with 1 and 1 values.

#### *Weibull distribution: a continuous probability distribution*

The Weibull distribution is employed to describe a particle size distribution (Almalki and Nadarajah 2014). The Weibull $W_D$ as a random variable (Baleanu and Karaca 2022) follows the Weibull along with the tail formula as obtained in line with Eq. 2 (Kharazmi 2016)

$$W_D(V) = exp^{(\frac{V}{k})^{\zeta}} \tag{2}$$

$k$ and $\zeta$ refer for shaping and scaling the parameters (Gorenflo *et al.* 2020).

#### *Cauchy distribution: a continuous probability distribution*

The Cauchy distribution refers to the spread of the ratio of normally distributed two independent random variables with a mean of zero (Steck 1958). The Cauchy distribution $(C_D)$ as a random variable (Arnold and Beaver 2000) is followed with the tail formula whose formulation can be provided according to Eq. 3:

$$C_D(V) = \frac{1}{\pi} arctan\left(\frac{2(V-\mu)}{\beta}\right) + \frac{1}{2} \tag{3}$$

$b$ and $u$ respectively with 1 and 0 values represent the scale and location parameters. Mittag-Leffler (ML) distribution: probability distributions on the half line $[0, \infty)$.

Shown as $E_\alpha(y)$, the ML distribution states its reliance upon the cumulative density function (cdf) or distribution function, given based on Eq. 4 (Chakraborty and Ong 2017).

$$f(x;\ \alpha) = 1 - E_\alpha(-y^\alpha) = \sum_{k=1}^{\infty}(1)^{k-1}(k\,\alpha).x^{k\,\alpha-1} \Big/ \{\Gamma(\alpha k+1),$$
$$x > 0,\ \ 0 < \alpha \leq 1 \tag{4}$$

The ML distribution has different shapes and distributional properties (see (Mainardi and Gorenflo 2000), (Mittag-Leffler 1903), (Pillai and Functions 1990), (Karaca and Baleanu 2022a) for further related details.

The comparison of these four distributions is conducted in relation with their performances, by using log likelihood value (MLE) and the Akaike Information Criterion (AIC). The respective definitions can be presented in the following manner:

$AIC = -21nL + 2k$, and $k$ shows the number of parameter(s) and $L$ shows the maximum log-likelihood with regard to a particular dataset. Moreover, the other related applications of the were done as well. (please see ref. ((D'Agostino 2017), (Fan and Gijbels 2018)) for further details). Relatively high (small) values of log likelihood (AIC) may hint better fittings, as overviewed in Table 1 for different relevant distributions, which clearly yield the best of the fit. In addition, the performance of the likelihood ratio test is also provided in order that different distributions can be differentiated (see Table 1).

Figure 3 shows the functions along with the four related heavy tailed distributions. The computations were conducted by Matlab with the pattern of $[\ ] = gml\_fun(\ )$, made for the evaluation pertaining to the MLF (Petrás 2011), (Karaca and Baleanu 2022a).

The biological datasets handled in this study were fit as per the three-parametric MLF $(\alpha,\ \beta,\ \gamma)$. Algorithm 1 (see Section 3.1) is based on heavy-detailed distributions, having been applied on the cancer cell dataset to identify the optimized three-parametric MLF, found with heavy-tailed distributions. As a result, the optimized MLF $(\alpha,\ \beta,\ \gamma)$ were obtained, which is an important stage to explore the complex attributes.

### The Basic Theory Behind the Fractional Calculus

Fractional calculus (FC) may be considered to be a natural extension of traditional integer order calculus because this area of mathematics is concerned with the investigation and application of the concepts of integral and non-integer differential calculus (Karaca and Baleanu 2022c). The main publications on the subject matter were seen in the early 20th centur (Tenreiro Machado *et al.* 2010).

The basic notions can be seen in classical materials by (Oldham and Spanier 1974), (Ross 1977). More recent ones can be found in the works of (David *et al.* 2011), (De Oliveira and Tenreiro Machado 2014), (Kochubei *et al.* 2019), (Valentim *et al.* 2021). Mathematical biology, with an interdisciplinary approach, looks into cancer-related phenomena via mathematical models in an inclusive way. Encompassing wide-ranging domains from biology to materials science, mathematical biological enables the comprehension of biological systems that cause disease.

By this virtue, fractional-order models can enable a better understanding related to oncological biological particularities, which contributes potentially to critical multi-stage decision-making including early diagnosis techniques, tumor evolution and treatment procedures as well as therapies tailored depending on the patient.

FC regarded as a generalization of integer order calculus, with the related core notions are presented by depending on more basic conjectures. Factorials, for example, make up only natural numbers, so this has constricting factors for its domains of applications (Herrmann 2011). Gamma function is introduced for any as factorial generalization, indicated as in (Karaca and Baleanu 2022a) can be generalized as well through the replacement of its factorial component with a gamma function, producing the following in accordance with Eq. (5).

$$e^z = \sum_{n=0}^{\infty}\frac{z^n}{\Gamma(1+n)} \tag{5}$$

and hence, the MLF for $\Re(z) > 0$ is introduced as follows, (Mittag-Leffler 1903) based on Eq (6).

$$E_\alpha(z) = \sum_{n=0}^{\infty}\frac{z^n}{\Gamma(1+n\alpha)'} \tag{6}$$

as extended to concede the three parameters for $\Re(z) > 0$ (Wiman 1905) according to Eq (7).

$$E_{\alpha,\beta}(z) = \sum_{n=0}^{\infty}\frac{z^n}{\Gamma(n\alpha+\beta)} \tag{7}$$

For the purpose of representing the solution of several fractional problems related to mathematics and physics, the MLF is critical, as the exponential functions are for integer calculus. This is because numerous simple functions are the specific cases of this generalization, so a number ofstudies have investigated the related particularities along with its uses (Camargo *et al.* 2012); (Gorenflo *et al.* 2020).

### Fractional-Order Derivatives

Fractional-order derivative models are employed for the accurate modeling of the systems that require different analytical and numerical methods along with their related their applications to new and complex problems. Being a critical function with extensive domains of application, MLF is employed as a fractional differential method. The following power series are usedto define the MLF in line with the following references (Karaca and Baleanu 2022a), (Gutierrez *et al.* 2010) Eq. (8).

It, as an entire function, ensures a simple generalization of the exponential function whose reduction and convergence can be found in more detail in (Mainardi and Gorenflo 2000). The complex plane denotations and approaches related to the MLF, can be found in (Baleanu and Karaca 2022), (Mainardi 2020).

### Caputo Fractional-Order Derivatives

The Caputo Fractional-order derivative is employed to model phenomena, considering the significant interactions of past and problems that have nonlocal properties based on equations having memory. The related definition is addressed as per Eq. 9 (Gutierrez *et al.* 2010), which is used to solve the differential equations:

$$D_\alpha^m\ f(t) = \frac{1}{\Gamma(m\alpha)}\int_0^t \frac{f^{(m)}(\tau)}{(t-\tau)^{\alpha+1-m}}d\tau, \tag{8}$$

Being similar to Caputo fractional derivative (CFD), Grünwald-Letnikov fractional derivative is related to most of the analytic functions, and there is a insignificantly different aspect identified when the constant function is addressed. For a constant, the Caputo fractional derivative equals to 0. However, the Riemann–Liouville counterpart does not equal to 0. Caputo fractional derivative is generally used to address the initial value FODE (Gutierrez *et al.* 2010).

The important implications about fractional integral and derivatives of the power function $(t-t_0)^{\beta}$ for, $\beta > -1$ are the case and for the Caputo's derivative, Eq. 16 is employed in the following way:

$$D_{t_0}^{\alpha}(t-t_0)^{\beta} = \begin{cases} 0 & \beta \in 0, 1, ..., m-1 \\ \frac{\Gamma(\beta+1)}{\Gamma(\beta-\alpha+1)}(t-t_0)^{\beta-\alpha} & \beta > m-1 \\ non\ existing & otherwise \end{cases}$$

$D^m$ and $f^{(m)}$ signify the integer-order derivatives (Garrappa *et al.* 2019).

When compared with the Riemann–Liouville, the Laplace transform for the Caputo's derivative is initialized with the standard initial values shown in terms of integer-order derivatives (Ouyang and Wang 2016).

### Artificial Neural Networks Algorithm

As a series of algorithms attempting to recognize the underlying patterns in a set of data, neural networks, systems of neurons, whether they be organic or artificial in nature, mimic the way the human brain operations through different processes. Since neural networks, rooted in artificial intelligence, can be adaptive in changing input, the network generates the best possible result without the need of redesigning the output criteria. As a special type of machine learning algorithms, Artificial Neural Networks (ANNs) are modeled by mimicking the human brain, and they enjoy predictive and solution abilities.

ANNs can learn from the data of the past, just like the neurons in the human nervous system learn from the past data, and can provide responses in prediction or classification forms. ANN is a self-learning network, conducts the learning from sample data sets and signals; and as nonlinear models, they manifest a complex relationship between the inputs and outputs to discover a new pattern. Accordingly, Multi-layered perceptron (MLP) is a type of network in which multiple layers of a group of perceptron are together loaded in order to make a model. In a multi-layered perceptron, the arrangement of the perceptrons is seen in interconnected layers (Karaca 2016).

The use of the MLP networks, with at least three layers, signifies there is a training set of input-output pairs (for further details on the weight coefficients, please refer to (Karaca and Cattani 2018), (Karaca *et al.* 2020), (Karaca and Baleanu 2022b)). For its related steps and architecture, please see (Mia *et al.* 2015), (Alsmadi *et al.* 2009) and (Abdul Hamid *et al.* 2011). The input signal propagates via the network layer by layer. The signal-flow of the network with two hidden layer is provided in Figure 1. Multilayer feed forward back propagation algorithm is utilized for network training and network performance testing.

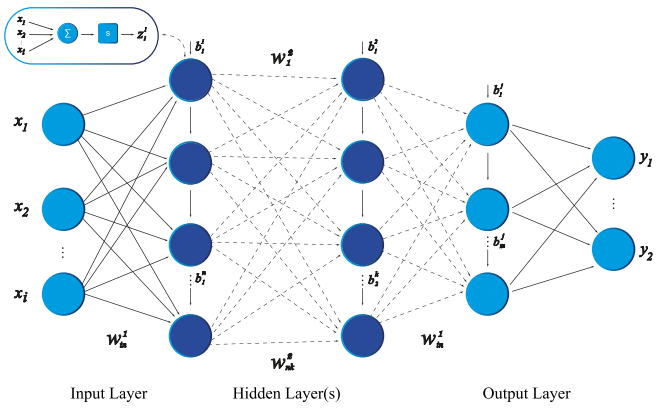



**Figure 1** The configuration depiction of the MLP algorithm

The back-propagation algorithm involves the subsequent steps (Karaca and Baleanu 2020), (Karaca and Cattani 2018) and (Zhang and Wu 2008).

**Step 1.** Initialization: The algorithm at first is to be initialized regarding that one does not know any previous information. The thresholds and synaptic weights are picked among a uniform distribution. Sigmoid shows the activation function.

**Step 2.** The network should be presented by epochs of training examples to conduct computations of forward and backward.

**Step 3.** The preferred response vector is $d(n)$ in the output layer of computation nodes, which is a forward computation, if the input vector to the layer of sensory nodes is $x(n)$. The computation of the network's local fields and signals related to function is done by proceeding forward via the network through each of the layers. If the sigmoid function is employed, then equation provided below is considered to obtain the output signal:

$$y_j^{(l)} = \varphi_j(v_j(n))$$

If $l$=1, meaning that the j neuron is in the first hidden layer, then this is obtained:

$$y_j^{(0)} = x_j(n)$$

Here, $x_j(n)$ refers to the $jth$ element of the input vector $x(n)$.

Let, $L$ refers to the depth of network. If the neuron $j$ is in the output layer, that is to say, $l = L$ then

$$y_j^{(L)} = o_j(n)$$

Hence, the error signal will be:

$$e(n) = d_j(n) - o_j(n)$$

$d_j(n)$ refers to the $jth$ element of the vector of preferred response $d(n)$.

**Step 4.** The following equation in backward computation shows the local gradients of the network (Haykin 2009).

$$\delta_j^l(n) = \begin{cases} e_j^L(n)\varphi_j'(n)(v_j^L(n)) & output\ layer\ L \\ \\ \theta_j'(v_j^i(n))\sum_k \delta_k^{(i+1)}(n) w_{kj}^{(i+1)}(n) & hidden\ layer\ L \end{cases}$$

$\varphi_j'(\bullet)$ refers to differentiation concerning the argument. The network's synaptic weights in layer l need to be adapted to as per the generalized data rule. If $\eta$ is the training-rate parameter and $\alpha$ signifies the momentum constant, the following is to be obtained:

$$w_{ji}^l(n+1) = w_{ji}^{(l)}(n) + \infty[w_{ji}^{(l)}(n-1)] + \eta\ \delta_i^{(l)}(n) y_i^{(l-1)}(n)$$

**Step 5.** Last but not least, the computations regarding the forward and backward need to be iterated till the stopping criterion chosen can be fulfilled. The learning-rate parameters and momentum are adjusted through reducing the related values as the number of iterations goes up.

In the current study, MLP algorithm was applied to the cancer cell dataset $(768 \times 9)$ for the purposes of diagnosis and differentiability concerning the disease classification and prediction.

### Computational Complexity

Computational complexity serves the goal of classifying and comparing the practical aspect of problem solutions regarding finite combinatorial objects (Stockmeyer 1987). Technically, *Big-O notation*, used to describe the complexity of algorithms, presents the approximation or placing of an upper bound on the *resource requirements* for an algorithm. The *complexity* of the algorithm signifies the computational complexity and technically speaking, computational (algorithmic) complexity can be applied both to *space* and *time* (storage and memory) resource necessities. As a matter of fact, many individuals focus their attention on the *running time* of an algorithm (Arora and Barak 2009), (Chivers *et al.* 2015). Algorithmic complexity is denoted by the term of "*on the order of*", which indicates the approximate cost of the algorithm considering the aforementioned resource requirements. "*on the order of*" is written in an abbreviated form in capital "*O*". This gives us the more recognized term, that is to say the *Big-O notation* (Karaca *et al.* 2022).

Computational complexity measures how much work is required for the solution of different problems and providing a practical classification tool beside dealing with complex problems through the powerful lenses from which the patterns can be observed both on a distinctive level and as a whole, considering the resource usage. Concerning the temporal aspect, computational time complexity denotes the change in an algorithm's runtime, and this process is dependent on the variation in the size of the input data. When it comes to spatial properties, space complexity is the description of the amount of additional memory a related algorithm needs to have, which is dependent on the input data's size.

#### *Big-O notation is: O (formula)*

*Big-O* notation depends on the input parameters for whose details (Karaca *et al.* 2022) can be referred to. Figure 2 depicts the order of growth concerning the algorithms stated in *Big-O* notation.

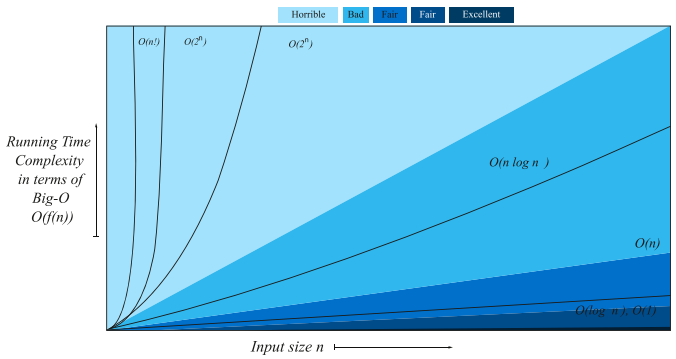



**Figure 2** The order of growth pertaining to algorithms stated in *Big-O* notation

*Big-O* notation is a notation which is utilized to represent algorithmic complexity. It is expedient to contrast with various algorithms because the notation actually yields the conveying of the algorithm scales. That is to say, the input size becomes larger, and this is often referred to as the *order of growth* (see Figure 2) (Chivers *et al.* 2015).

#### *Complexity of the Fast Fourier Transform (FFT) Computation*

The problem related to the Fourier transform (FT) is because of its sine/cosine its complex exponential form or regression model form, necessitating $O(n^2)$ operations to compute all the Fourier coefficients. This does not apply for the short time series, though. Notwithstanding, for quite long time series, this situation may be an exhaustive computational process although performed on developed computers of the current era.

FFT is known to be an important improvement for the reduction of the complexity of the FT computation from $O(n^2)$ to $O(n\ log\ n)$, (Al Na'mneh and Pan 2007). The core notion behind this is that: assume that there is a time series $y_1, ..., y_n$ and one would like to calculate the complex Fourier coefficient $z_1$. It requires the following computation with the formula:

$$z_0 = \sum_{t=0}^{n-1} y_t,$$

Which is proportional to the data mean. In the case that data are de-trended or de-meaned, then this value will be 0. The next Fourier coefficient will be:

$$z_1 = \sum_{t=0}^{n-1} y_1 exp(-2\pi i.1.t/n)$$

$$= y_0 exp(-2\pi i.1.0/n) + y_1 exp(-2\pi i.1.1/n) + ...$$

Let us suppose that one would like to calculate the new coefficient . Then, this shall necessitate the computation as such:

$$z_2 = y_0\ exp(-2\pi i.2.0/n) + y_1\ exp(-2\pi i.2.1/n) + ...$$

In the $2^{nd}$ term, the exponential in the sum for $z_2$ is the same that in the $3^{rd}$ term in the sum for $z_1$, equaling to $exp(-2\pi i.1.2/n)$. There exists no need to calculate this exponential quantity two times, so one may calculate it for the first time when we assume recovering from memory is speedier compared to computing that from the very beginning. The FFT algorithm, therefore, can be regarded as an intricate bookkeeping algorithm being able to monitor such symmetries in the Fourier coefficients' computational processes.

## EXPERIMENTAL RESULTS AND DISCUSSION: COMPUTATION-RELATED APPLICATION OF CAPUTO FODS WITH THREE-PARAMETRIC ML FUNCTIONS $(\alpha,\ \beta,\ \gamma)$, ANN ALGORITHM AND COMPUTATIONAL COMPLEXITY

Mathematics-informed modeling of complex systems by FODs relying upon FC plays a critical role for one to achieve the related syntheses robustly and effectively. Correspondingly, the current study has aimed at establishing an accurate model depending upon the integration of FOD and ANN for the diagnosis and differentiability pertaining to the prediction of disease which exhibits transient biological features. One other goal has been to illustrate the benefit of computational complexity to obtain the FOD that has the least complexity to be able to obtain the solution which is optimized. For this particular purpose, the proposed integrative multifarious approach has followed the below stated stages:
i) Caputo fractional derivative along with MLF that had three parameters $(\alpha,\ \beta,\ \gamma)$ was applied to the cancer cell dataset. In this way, it was possible to establish the new fractional models which had distinct degrees through the conducting of data fitting with the fitting algorithm MLF with three parameters $(\alpha,\ \beta,\ \gamma)$ dependent on Heavy-tailed distributions (see Algorithm 1). Through the algorithm, it was possible to obtain the optimized ML $(\alpha,\ \beta,\ \gamma)$ functions, which enabled us to find the best fitting MLF with three parameters $(\alpha,\ \beta,\ \gamma)$ in the cancer cell dataset. As a result, the new datasets, namely the mfc_cancer cell dataset and mfr_cancer cell dataset were obtained.
ii) The classical derivatives were applied to the cancer cell dataset (the raw dataset); and obtained the cd_cancer cell datasets.
iii) The performances of the new dataset (in line with step i), the dataset obtained from the classical derivative (calculus) application (in line with step ii) and the cancer cell dataset were compared by the MLP algorithm application. Consequently, the most optimal fractional order derivative model for the disease was engendered.
iv) In order to attain the Caputo FOD with the optimized solution and the least complexity, computational complexity was addressed. Computational complexity with the Caputo FOD (ML with three functions) and classical derivative (calculus) was calculated comparatively through the identification of the complexity concerning the cancer cell dataset. *Big O* was used to identify the derivatives which had the maximum and minimum level of complexity. The experimental results obtained from the multifarious approach with an integrative scheme corroborate and reveal the applicability of the proposed scheme. It is, consequently, shown that the Caputo FOD with the least complexity produced the most successful end result as per the output derived from that MLP algorithm.

MATLAB (MATLAB 2022) and Phyton (Van Rossum and Drake Jr 1995) were used for the obtaining of all the analyses, results and visual depictions of the study.

### Computation-related Application of ML Functions with Heavy-tailed distributions' Algorithm for Optimized Cancer Cell Data Fitting

Algorithm 1 was applied to the cancer cell dataset so that it could be possible to make the identification of the optimized MLF with three parameters $(\alpha,\ \beta,\ \gamma)$ to fit the data possible. Hence, it was possible to obtain the optimized ML $(\alpha,\ \beta,\ \gamma)$ functions. To put it differently, this application enabled the finding of the best fitting MLF with three parameters in the cancer cell dataset.

Algorithm 1 has been benefited from for the fitting with three parameters related to MLF based on heavy-tailed distributions. The related steps for Algorithm 1 can be referred to in (Karaca and Baleanu 2022a).

Algorithm 1 was applied to the cancer cell dataset ($569 \times 25$) for the nine attributes in units (see the details related to the dataset in the following reference (Murphy 1994)).

For the analyses, negative log likelihood: -log L was taken for the log likelihood value. The best fit distribution was generated (retrieved from the AIC, SD, MAE, MAPE, SSE, MSE and RMSE calculations). The lowest of the two values was taken and the best fitting distribution was achieved in order that the ML functions representing the data most in the most suitable way were obtained (Step 4 carried out based on Algorithm 1). The lowest value for each distribution was taken; and conducted computations for all the nine attributes. As an exemplary view, the presentations for one attribute, which is the Smoothness, are shown in Table 1). Hence, the lowest value obtained is marked bold in the respective tables. The illustrations of the figures based on the computations gained from the above mentioned attribute provided in the table indicating the distribution beside the related peak points (see Figure 3).

Table 1 depicts the smoothness attribute showing the lowest value taken for each of the heavy-tailed distributions.

The depictions regarding the calculations gained from the attributes provided in Table 1 for the Smoothness attribute the four related heavy-tailed distributions and its peak points are indicated in Figure 3. Two approaches are applicable to handle each of the cancer cell data set attribute to perform the aforementioned analysis. The former one is as such: based on the results which are obtained from each distribution as per Algorithm 1, the most accurate distribution is obtained based on the results as attained with the lowest value. The latter one has to do with the addressing of the results based on $\alpha$, $\beta$ and $\gamma$ values depending on the results produced by the 4 heavy-tailed distributions together with the eight statistical values while performing the comparison of the connected attributes inherently (for further details Table 1 can be referred to); and in addition, the most accurate distribution is achieved based on the outcomes gained with the minimum value. Should there be extreme points within the distribution, those extreme values would not be considered for the analyses conducted in the current work.

The best outcome for ML function with three parameters was found to be MLF (10, 2, 2) for the cancer cell dataset.

### Computation-related Application of Caputo FODs to Cancer Cell Dataset

Algorithm 2 provides the steps of fractional derivatives with non-integer orders for the cancer cell dataset, concerned with the identification of the order degree to find the most significant attribute.
Algorithm 2: Application of the Caputo FODs on cancer cell dataset that has non-integer orders.
**Step 1:** Establish non-integer orders $(y = orders = [0.1,\ 0.2,\ 0.3,\ ...,\ 0.9])$.
**Step 2:** All of the orders are applied to the attributes specifically in the dataset, as a result of which values were obtained for the $y$ order fractional derivatives, identified in Step 1.
**Step3:** Obtain 3D graphs of 3 types of derivatives as grid and surface $(x,\ y,\ z) = (for\ each\ attribute\ of\ the\ data\ u,\ alpha,\ derivative\ of\ all\ the\ data)$.

Figure 4 presents the application steps of CFOD on the cancer cell dataset. The most significant orders were obtained based on the application of the procedures indicated in Figure 3, and for the related orders, CFOD models were identified, as detailed with the outcomes derived accordingly.

**Table 1 Smoothness attribute computation concerning the cancer cell dataset for MLF depending upon Heavy-tailed distributions**

| Distributions | $\alpha$ | $\beta$ | $\gamma$ | -log L | AİC | SD | MAE | MAPE | SSE | MSE | RMSE |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Mittag-Leffler | 0.5 | 0.5 | 0.5 | 631.09718 | 1264.1944 | 0.008366 | 0.329849 | 0.534995 | 61.909033 | 0.108803 | 0.329853 |
| Cauchy dist. | 0.5 | 0.5 | 0.5 | 834.76194 | 1671.5239 | 0.008366 | 0.230607 | 0.374042 | 30.260861 | 0.053183 | 0.230613 |
| Pareto dist. | 0.5 | 0.5 | 0.5 Inf | Inf | 0.008366 | 0 | 0 | 0 | 0 | 0 | |
| Weibull dist. | 0.5 | 0.5 | 0.5 | 350.9032 | 703.8064 | 0.008366 | 0.539741 | 0.875463 | 165.77254 | 0.29134 | 0.539759 |
| Mittag-Leffler | 3 | 1 | 1 | 816.59675 | 1635.1935 | 0.002348 | 0.238082 | 0.234318 | 32.252786 | 0.056683 | 0.238083 |
| Cauchy dist. | 3 | 1 | 1 | 1054.8973 | 2111.7946 | 0.002348 | 0.156618 | 0.154142 | 13.957155 | 0.024529 | 0.156618 |
| Pareto dist. | 3 | 1 | 1 | 18.14285 | 38.285699 | 0.002348 | 0.968628 | 0.95332 | 533.86979 | 0.93826 | 0.968638 |
| Weibull dist. | 3 | 1 | 1 | 578.14566 | 1158.2913 | 0.002348 | 0.362015 | 0.356292 | 74.5705 | 0.131055 | 0.362016 |
| Mittag-Leffler | 5 | 1 | 3 | 808.74844 | 1619.4969 | 0.000352 | 0.241388 | 0.240808 | 33.154539 | 0.058268 | 0.241388 |
| Cauchy dist. | 5 | 1 | 3 | 1047.1228 | 2096.2456 | 0.000352 | 0.158772 | 0.15839 | 14.343667 | 0.025209 | 0.158772 |
| Pareto dist. | 5 | 1 | 3 | 2.738101 | 7.476202 | 0.000352 | 0.9952 | 0.992808 | 563.55062 | 0.990423 | 0.9952 |
| Weibull dist. | 5 | 1 | 3 | 570.37073 | 1142.7415 | 0.000352 | 0.366994 | 0.366112 | 76.63567 | 0.134685 | 0.366994 |
| Mittag-Leffler | 5 | 1 | 7 | 810.58361 | 1623.1672 | 0.00082 | 0.240611 | 0.239266 | 32.941402 | 0.057894 | 0.240611 |
| Cauchy dist. | 5 | 1 | 7 | 1048.9504 | 2099.9009 | 0.00082 | 0.158263 | 0.157378 | 14.251833 | 0.025047 | 0.158263 |
| Pareto dist. | 5 | 1 | 7 | 6.378511 | 14.757021 | 0.00082 | 0.988854 | 0.983328 | 556.38788 | 0.977835 | 0.988855 |
| Weibull dist. | 5 | 1 | 7 | 572.1984 | 1146.3968 | 0.00082 | 0.365817 | 0.363773 | 76.145014 | 0.133823 | 0.365818 |
| Mittag-Leffler | 7 | 2 | 1 | 807.37739 | 1616.7548 | 0 | 0.24197 | 0.24197 | 33.314695 | 0.05855 | 0.24197 |
| Cauchy dist. | 7 | 2 | 1 | 1045.7534 | 2093.5068 | 0 | 0.159155 | 0.159154 | 14.412869 | 0.02533 | 0.159155 |
| Pareto dist. | 7 | 2 | 1 | 0.00272 | 2.005439 | 0 | 0.999995 | 0.999993 | 568.99456 | 0.99999 | 0.999995 |
| Weibull dist. | 7 | 2 | 1 | 569.00136 | 1140.0027 | 0 | 0.367879 | 0.367878 | 77.005408 | 0.135335 | 0.367879 |
| Mittag-Lefflerr | 7 | 2 | 2 | 807.37874 | 1616.7575 | 1e-06 | 0.24197 | 0.241968 | 33.314536 | 0.058549 | 0.24197 |
| Cauchy dist. | 7 | 2 | 2 | 1045.7548 | 2093.5095 | 1e-06 | 0.159154 | 0.159153 | 14.412801 | 0.02533 | 0.159154 |
| Pareto dist. | 7 | 2 | 2 | 0.005439 | 2.010879 | 1e-06 | 0.99999 | 0.999986 | 568.98912 | 0.999981 | 0.99999 |
| Weibull dist. | 7 | 2 | 2 | 569.00272 | 1140.0054 | 1e-06 | 0.367878 | 0.367876 | 77.00504 | 0.135334 | 0.367878 |
| Mittag-Lefflerr | 7 | 2 | 4 | 807.38147 | 1616.7629 | 1e-06 | 0.241968 | 0.241966 | 33.314217 | 0.058549 | 0.241968 |
| Cauchy dist. | 7 | 2 | 4 | 1045.7575 | 2093.515 | 1e-06 | 0.159153 | 0.159152 | 14.412663 | 0.02533 | 0.159153 |
| Pareto dist. | 7 | 2 | 4 | 0.010879 | 2.021757 | 1e-06 | 0.999981 | 0.999971 | 568.97824 | 0.999962 | 0.999981 |
| Weibull dist. | 7 | 2 | 4 | 569.00544 | 1140.0109 | 1e-06 | 0.367876 | 0.367872 | 77.004304 | 0.135333 | 0.367876 |
| Mittag-Leffler | 7 | 2 | 8 | 807.3869 | 1616.7738 | 3e-06 | 0.241966 | 0.241961 | 33.31358 | 0.058548 | 0.241966 |
| Cauchy dist. | 7 | 2 | 8 | 1045.7629 | 2093.5259 | 3e-06 | 0.159152 | 0.159149 | 14.412387 | 0.025329 | 0.159152 |
| Pareto dist. | 7 | 2 | 8 | 0.021757 | 2.043515 | 3e-06 | 0.999962 | 0.999943 | 568.95649 | 0.999924 | 0.999962 |
| Weibull dist. | 7 | 2 | 8 | 569.01088 | 1140.0218 | 3e-06 | 0.367872 | 0.367865 | 77.002832 | 0.13533 | 0.367872 |
| Mittag-Leffler | 10 | 2 | 2 | 807.37603 | 1616.7521 | 0 | 0.241971 | 0.241971 | 33.314854 | 0.05855 | 0.241971 |
| Cauchy dist. | 10 | 2 | 2 | 1045.7521 | 2093.5041 | 0 | 0.159155 | 0.159155 | 14.412938 | 0.02533 | 0.159155 |
| Pareto dist. | 10 | 2 | 2 | 5e-06 | 2.000011 | 0 | 1 | 1 | 568.99999 | 1 | 1 |
| Weibull dist. | 10 | 2 | 2 | 569 | 1140 | 0 | 0.367879 | 0.367879 | 77.005775 | 0.135335 | 0.367879 |
| Mittag-Leffler | 10 | 2 | 5 | 807.37603 | 1616.7521 | 0 | 0.241971 | 0.241971 | 33.314853 | 0.05855 | 0.241971 |
| Cauchy dist. | 10 | 2 | 5 | 1045.7521 | 2093.5041 | 0 | 0.159155 | 0.159155 | 14.412938 | 0.02533 | 0.159155 |
| Pareto dist. | 10 | 2 | 5 | 1.4e-05 | 2.000027 | 0 | 1 | 1 | 568.99997 | 1 | 1 |
| Weibull dist. | 10 | 2 | 5 | 569.00001 | 1140 | 0 | 0.367879 | 0.367879 | 77.005774 | 0.135335 | 0.367879 |
| Mittag-Leffler | 10 | 2 | 7 | 807.37604 | 1616.7521 | 0 | 0.241971 | 0.241971 | 33.314853 | 0.05855 | 0.241971 |
| Cauchy dist. | 10 | 2 | 7 | 1045.7521 | 2093.5041 | 0 | 0.159155 | 0.159155 | 14.412938 | 0.02533 | 0.159155 |
| Pareto dist. | 10 | 2 | 7 | 1.9e-05 | 2.000038 | 0 | 1 | 1 | 568.99996 1 | 1 | |
| Weibull dist. | 10 | 2 | 7 | 569.00001 | 1140 | 0 | 0.367879 | 0.367879 | 77.005774 | 0.135335 | 0.367879 |

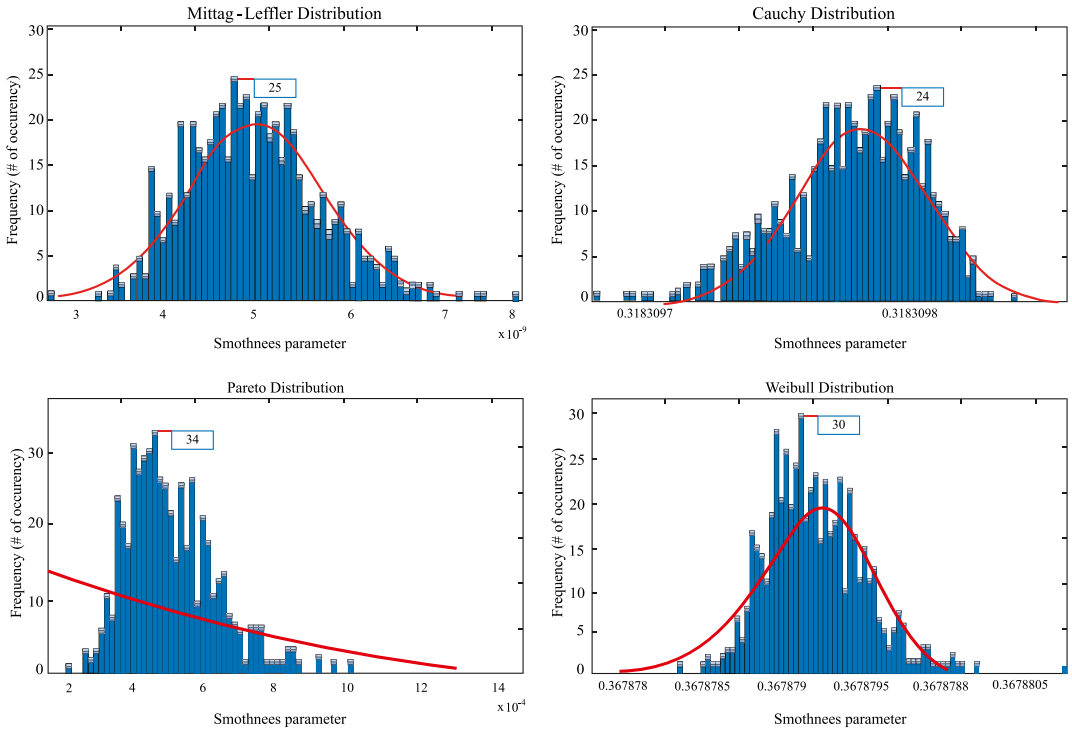



**Figure 3** Smoothness attribute computation based on cancer cell dataset for MLF depending upon Heavy-tailed distributions.

The computation-related application of CFODs and classical derivative, both with $(y = orders = [0.1,\ 0.2,\ 0.3, ...,\ 0.9])$, for all of the related parameters were conducted for the cancer cell dataset. As an example to depict the computations in a clear way, Figure 4 is presented for three parameters (the radius parameter, the symmetry parameter and the smoothness parameter). Figure 4 shows the computational application of CFODs and classical derivative, both with $y(= orders)$, for 3 parameters for the cancer cell dataset. CFOD and classical derivative models were identified for the related orders. The computation-related application of CFODs and classical derivative, for all the parameters were carried out concerning the cancer cell dataset. To illustrate, for depicting the computations in a evident manner, Figure 4 provides the three parameters including radius, symmetry and smoothness). Figure 4 shows the computation-related application of CFODs and classical derivative, both with $y(= orders)$, for the cancer cell dataset. CFOD and classical derivative models were identified for these orders.

### Computation-related Application of ANN Algorithm to Cancer Cell Dataset and Optimized Results Diagnostic Treatments and Predictive Transdifferentiability

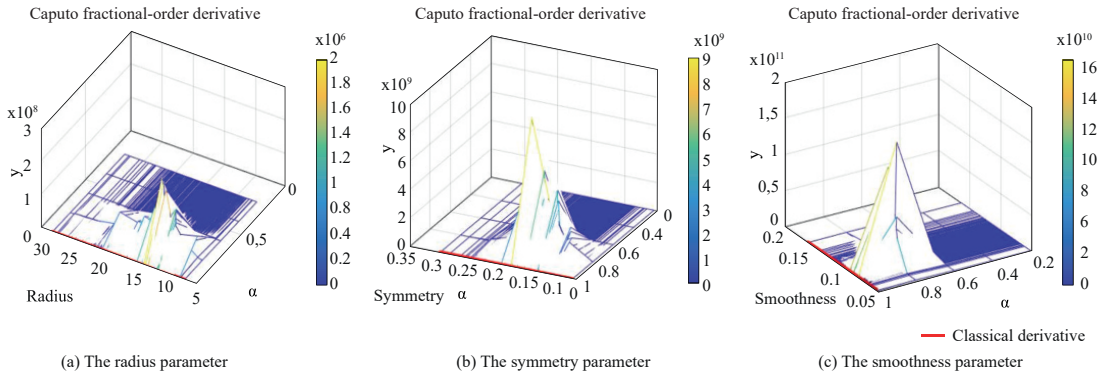
The computation-related application of CFODs and classical derivative obtained in Figure 4 for all the parameters for the cancer cell dataset generates the significant attributes in newly obtained datasets. CFOD and classical derivative models were found and determined for the related orders depending upon the model. Table 2 shows the parameters of that MLP algorithm, employed in the present study.

Figure 5 presents the application of CFODs with MLF parameters MLF (10, 2, 2) to the cancer cell dataset, besides the new datasets (mfc_cancer cell dataset and mfr_cancer cell dataset), as taken from the significant attributes from the related application, with MLP algorithm application, to the new dataset ensuring performance of the orders with respect to the disease diagnosis as well as differentiability.

Figure 6 presents the application of classical derivative to the cancer cell dataset, besides that of the MLP algorithm application to the new dataset (cd_cancer cell dataset), which provides the orders' performance with respect to the disease diagnosis and differentiability.

CFODs indicate the condition of higher conditions concerning regularity in terms of differentiability. The related derivative needs to be calculated initially for the fractional derivative of a function in the sense of Caputo.

Table 3 presents the outcomes generated by CFODs; and the classical derivative application is contrasted with the outcomes of classical derivative showing that CFOD (with order 0.8) provides us with better results. The result that MLP algorithm application cancer cell dataset based on CFOD and classical calculus yielding the respective highest accuracy results is presented for the related orders: for order 0.2 (79.4376%); for order 0.5 (80.1406%); for order 0.8 (83.4798%) and for order 1 (79.9649%) in Table 3. It is observed that the results obtained by CFOD application with changing orders produces more accurate outcomes. As a consequence, the CFOD for differentiable functions generated accuracy rates with more robustness. Hence, the definition for CFODs is performed for differentiable functions while functions without any first-order derivative may own fractional derivatives with all orders which equal to lower than 1.




(a) The radius parameter (b) The symmetry parameter (c) The smoothness parameter

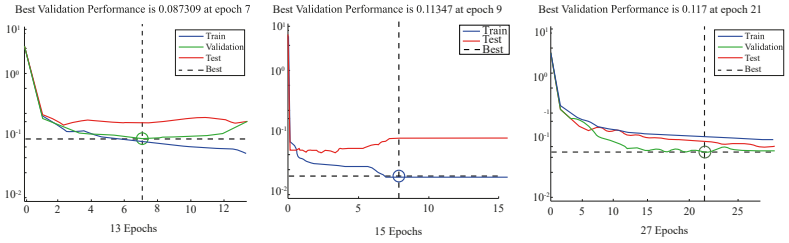
**Figure 4** Computation-related application of CFODs and Classical derivative for the three parameters (a) The radius (b) The symmetry and (c) The smoothness for the cancer cell dataset.

**Table 2 MLP algorithm's Network Parameters**

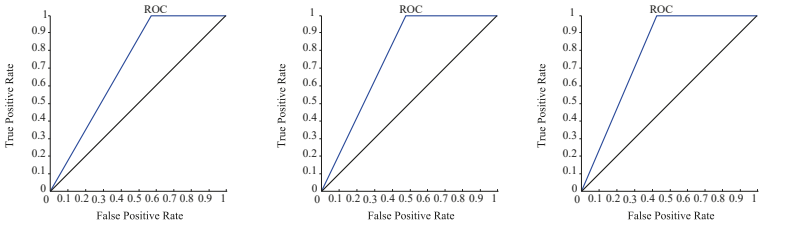
| Network Properties | Values |
|---|---|
| Adoption learning function | Learngdm |
| Training Properties | Levenberg- Marquart ('trainlm') |
| Transfer function | Tansig |
| Performance | Mean squared error (MSE) |
| Epoch number | 1000 |
| Hidden layer number | 3 |
| Test dataset | (85x1) |
| Training dataset | (399x1) |
| Validation dataset | (85x1) |
| Output | Cancer |

**Table 3 The optimized outcomes derived from CFODs with three-parametric MLF and classical derivatives for the mfc_cancer cell dataset with MLP algorithm**

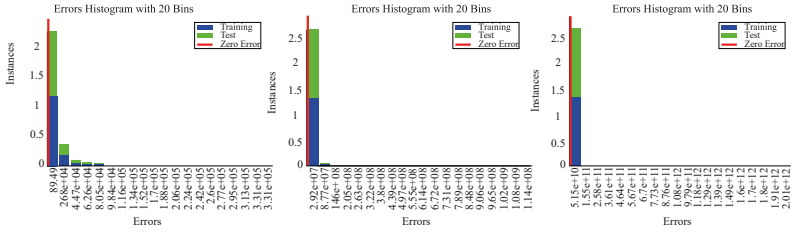
| Fractional Differential Type/Order | Percentage of Correct Classification (Accuracy) | Sensitivity | Precision | Specificity | F1-score | Multiclass Classification (MCC) | Area Under ROC Curve the (AUC) |
|---|---|---|---|---|---|---|---|
| Caputo/0.2 | 79.4376 | 100 | 75.3165 | 44.8113 | 85.9206 | 0.58095 | 0.72406 |
| Caputo/0.5 | 80.1406 | 96.9188 | 77.2321 | 51.8868 | 85.9627 | 0.57669 | 0.76685 |
| Caputo/0.8 | 83.4798 | 98.0392 | 80.0915 | 58.9623 | 88.1612 | 0.65292 | 0.79883 |
| Caputo/1 | 79.9649 | 99.1597 | 76.1290 | 47.6415 | 86.1314 | 0.58548 | 0.74041 |
| Dataset | 80.6678 | 96.9188 | 77.7528 | 53.3019 | 86.2843 | 0.58816 | 0.77370 |



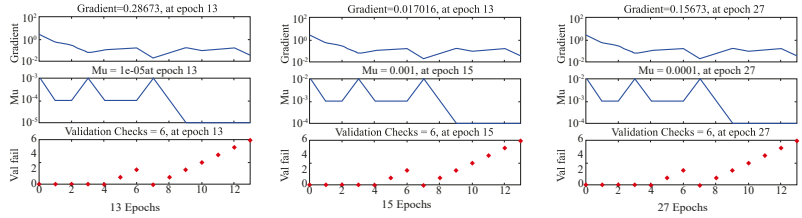

(a) Best validation performance (MSE) for mfc_cancer cell dataset



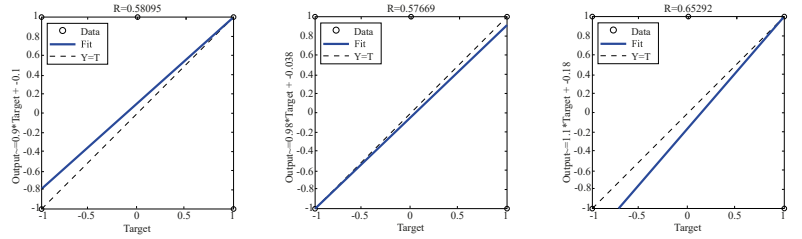

(b) ROC analyses for mfc_cancer cell dataset



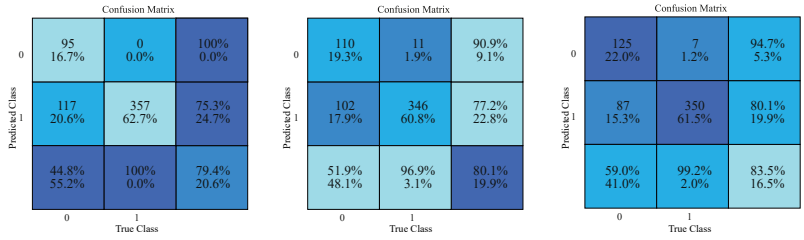

(c) Error histogram for mfc_cancer cell dataset




(d) Training state for mfc_cancer cell dataset

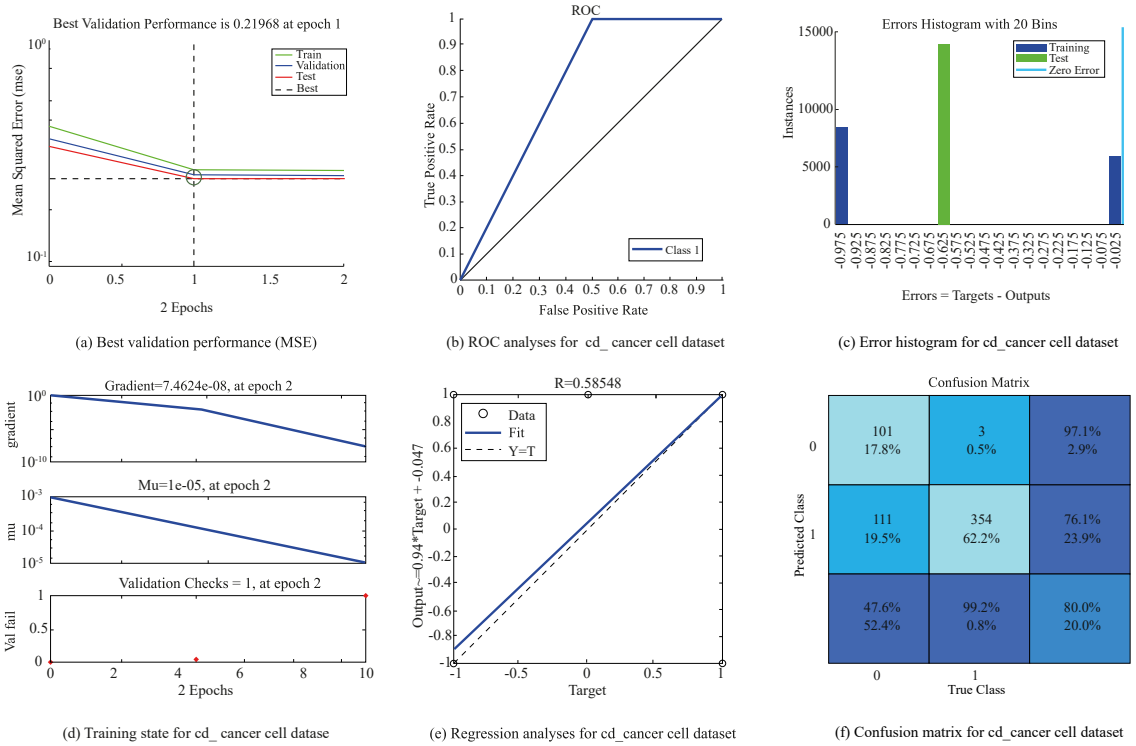



(e) Linear regression graphs for mfc_cancer cell dataset




(f) Confusion matrix for mfc_cancer cell dataset

**Figure 5** The MLP algorithm application to the mfc_cancer cell dataset (a) Best validation performance analyses (b) ROC analyses (c) Error Histograms with 20 Bins (d) Training state analyses (e) Linear regression graphs and (f) Confusion matrices




(a) Best validation performance (MSE)

(b) ROC analyses for cd_ cancer cell dataset

(c) Error histogram for cd_cancer cell dataset

(d) Training state for cd_ cancer cell datase

(e) Regression analyses for cd_cancer cell dataset

(f) Confusion matrix for cd_cancer cell dataset

**Figure 6** The MLP algorithm application to the cd_cancer cell dataset (a) Best validation performance analyses (b) ROC analyses (c) Error Histograms with 20 Bins (d) Training state analyses (e) Linear regression graphs and (f) Confusion matrices

### The Application of Computational Complexity based on Caputo FOD to the cancer cell dataset

Computational complexity, is utilized to classify the computational problems. As it is not possible to address some matters in computational biology in a computational sense, it could be limiting to search for the optimal solution for some practical reasons. Consequently, those kinds of matters are addressed through heuristics and approximations to be able to overcome the computational requirements that bring about solutions which are suboptimal. Yet, when essential complexity of an algorithm is investigated, it can also be possible to identify the algorithm's efficiency.

Bearing that in mind, during the conducting of the complexity computations for the three-parametric ML function, CFOD and classical derivative, FFT, integration, gamma function and $m^{th}$ derivative were shown in *Big O* form.

The computational complexity application for the MLF with three parameters is as per Eq. 10.

$$E^{\gamma}_{\alpha,\beta}(x) = \sum_{n=0}^{\infty} \frac{\Gamma(\gamma+n)}{\Gamma(\gamma)\Gamma(n\alpha+\beta)} \cdot \frac{x^n}{n!} \quad \alpha, \beta, \delta > 0, \; x \in \mathbb{R}^N \tag{9}$$

$$O(E^{\gamma}_{\alpha,\beta}(x)) = O\left(\frac{\Gamma(\gamma+n)}{\Gamma(\gamma)\Gamma(n\alpha+\beta)} \cdot \frac{x^n}{n!}\right) \tag{10}$$

The application of the computational complexity for CFOD based on the 3 parametric ML function can be seen according to Eq.11.

$$\begin{aligned} O(D^{\alpha} f(t)) &= O\left( \frac{1}{\Gamma(m-\alpha)} \int_0^t \frac{f^{(m)}(\tau)}{(t-\tau)^{(\alpha+1-m)}} d\tau \right) \\ O(D^{\alpha} f(t)) &= O(log(m\alpha)^{-2}.N^2.O_{ML}(N)^m) \\ O(D^{\alpha} f(t)) &= O(log(1\alpha)^{-2}.N^2.O_{ML}(N)) \end{aligned} \tag{11}$$

The outcomes of the computational complexity application depending on the CFOD and classical derivatives to the cancer cell dataset are presented in Table 4.

While carrying out the complexity computations with regard to three-parametric MLF $(\alpha,\ \beta,\ \gamma)$, CFOD, classical derivative, FFT, integration, gamma function and $m^{th}$ derivative are handled in the form of *Big O*.

The outcomes regarding the application of computational complexity based on Caputo FOD and classical derivatives to the cancer cell dataset are presented in Table 4.

CFOD is $\alpha \leq 1$, then $\alpha$ the value goes down. The complexity, in the meantime, goes up logarithmically. When this condition is at stake, $\alpha = 1$, then it belongs to the category of trivial.

As per the complexity outcomes obtained for CFOD related to the computational complexity as obtained (presented in Table 4), as it can be observed, the lowest complexity order is for 0.8 and the highest complexity is the case for order 0.2.

The lowest order, namely 0.8, with the least complexity of CFOD, provides the most successful outcome as 83.80% in the diagnostic and classification purpose of disease related to cancer cell by the ANN algorithm.

**Table 4 Outcomes of the computational complexity application depending on theCaputo FOD and classical derivativeto the cancer cell dataset.**

| | Order | Cancer cell dataset (N=24) | |
|---|---|---|---|
| **Caputo FOC** (for Eq.11) | $(\alpha)$**= 0.2** | (N/log(0.8))2*(log(-18*N-4)/N) | = 2.9294e+03+1.5142e+03i |
| | $(\alpha)$**= 0.5** | (N/log(0.5))2*(log(-18*N-4)/N) | = 3.0360e+02+1.5693e+02i |
| | $(\alpha)$**= 0.8** | (N/log(0.2))2*(log(-18*N-4)/N) | = 56.3116+29.1080i |
| | $(\alpha)$**= 1** | (N/log(0))2*(log(-18*N-4)/N) | = 0 |

## CONCLUDING REMARKS AND FUTURE DIRECTIONS

Computational complexity which concerns the way needed resources are employed for the answer and solution of the problem is important to address the computational problems in complex and nonlinear systems. Since it could not be to address some of the problems in computational biology in a computational perspective, it could be restricting to seek the optimal solution due to practical reasons. As a result, sometimes those problems are addressed by heuristics and approximations so that one can overcome the computational requirements; yet, such an approach may result in solutions which are suboptimal. When the essential complexity of an algorithm is explored, the efficiency of the algorithm is able to be assessed through computational complexity. As uncertainties in the complex processes bring about computational complexity, fractional-order models are employed in a widespread way to describe the real processes and phenomena. Fractional-order calculus concerns the integration and differentiation of non-integer orders and it is dependent on fractional-order thinking. The aim is to enable a better grasp of complex and dynamic systems, to improve the processing and control of complex elements and to make the optimization performance more optimal.

Dynamic complexity arises from the latent factors and the interactions between factors which may have a significant influence on the systems' performance. It is not possible to characterize some particular complex systems in nature by classical integer-order calculus models; so a fractional-order system based model which is capable of describing the system performance more accurately is needed. Different levels of complexity are one of the most characteristic features of biological systems; therefore, the rules of how complex behaviors and patterns emerge and the novel physical as well as chemical properties and functions with relation to biological entities need to be holistically understood. The behavior of high-level structures is also more than the whole of the direct interactions between one single component. Biocomplexity, as an integrative approach and philosophy, addresses the emergence of complex and self-organized behaviors which are based on the interaction of many simple agents. This sort of an emergent complexity represents the organization of molecules into cellular machinery, including the organization of cells into tissues and to the organization of individuals into communities.

It should also be noted that biocomplexity arises from many different interactions including biological, environmental, chemical, behavioral, physical and social ones, with the presence of multiple scales. Within the mathematics-informed framework based on FOC and ANNs, the integrative approaches can be employed for reliable and accurate comprehension of different complex biological processes that make up spatio-temporal scales. This line of methods has the aim of achieving optimized solutions through maximizing the accuracy of the model and minimizing the computational cost. In this way, capturing the significant and regular attributes on those spatio-temporal scales can provide the generalization of classical calculus by the extension of the conceptions related to biological processes and systems. Computational complexity also comes to the foreground since it is used to measure the extent of work required for the solution of different problems while providing us with a practical classification tool when one deals with complex problems. Accordingly, the present study has aimed at constructing a robust as well as an accurate model reliant upon the integration of FOD as well as ANN for the diagnostic and predictive differentiability aims for cancer cell propensity.

We have also attempted to show the importance of computational complexity to obtain the FOD with the lowest complexity so that it could be possible to obtain the optimized solution. Based on the experimental results obtained from this study, the CFOD has yielded the most accurate results for order 0.8 in terms of diagnosis and differentiability of the disease, which also has shown its critical role, suggesting the selection of the appropriate alternative mathematical models can be established in advance so that we can take uncertain situations under control and conduct the management effectively. The results also highlight the advantages of CFOD since it allows the conventional initial and boundary conditions to be encompassed in the formulation of the problem as well as its derivative for the constant as zero. On the flipside, the functions that lack differentiable properties do not have fractional derivative, that is to say, Caputo derivative's application areas remain has to be decreased. Furthermore, other fractional order derivatives (Riemann–Liouville, Grünwald-Letnikov and so forth) can be applied and compared with the machine learning methods with respect to different datasets. In view of these, the multifarious scheme with the related integrative steps, based on the application of FOC to the optimization means and the experimental results, have enabled us to emphasize the benefits of model accuracy maximization and cost function minimization.

Considering these elements and approach addressed in this study, the below directions can be stated for future investigation:

- The integrated method of fractional-order calculus and Artificial Intelligence (AI) methods can have a facilitating role for the prediction of future occurrence of manifold phenomena while comparing the predicted data with the actual data to validate with high-performance computing.
- Fractional order and fractional derivatives along with the generalization of integer calculus order, addressing the varying orders of derivatives and integrals as used in this study, can provide a viable framework to enhance optimization tasks focusing on complex order optimization.
- The increased capability of machine learning algorithms with computing power and accuracy for spectral data, signals, images and so forth in connection with the inherent properties

help the managing of memory effects and apparently chaotic behavior in critical multi-stage decision-making processes.
- The promoting of new methods to enhance performance outcomes can be suggested to take strategic actions to yield optimal results for accurate prediction of future in areas characterized by dynamic complexity where "know-why" research activities are required to develop models that merge phenomenological and data-oriented approaches in other applicable domains.
- The sophisticated integrative and multi scale approach used with computer-assisted proofs focusing on computational bio complexity fosters inter- and trans disciplinary work through the employment of computational power and combined expertise of different complex realms.

All in all, the experimental results obtained enable the diagnosis and differentiability in cancer cell prediction based on computational complexity, fractional order derivatives and ANN. Taken together, the scheme proposed with a multi-stage approach and/or novel methods in this study has demonstrated the proposed method's applicability and satisfactory predictive aspect in different domains characterized by dynamic, chaotic, heterogeneous and nonlinear nature displaying varying levels of complexity, which is of crucial value in terms of timely detection and taking action toward appropriate and tailored treatments.

#### Conflicts of interest

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

#### Availability of data and material

Not applicable.

## LITERATURE CITED


Abdul Hamid, N., N. Mohd Nawi, R. Ghazali, and M. N. Mohd Salleh, 2011 Accelerating learning performance of back propagation algorithm by using adaptive gain together with adaptive momentum and adaptive learning rate on classification problems. In *Ubiquitous Computing and Multimedia Applications: Second International Conference, UCMA 2011, Daejeon, Korea, April 13-15, 2011. Proceedings, Part II 2*, pp. 559–570, Springer.

Aguilar, C. Z., J. Gómez-Aguilar, V. Alvarado-Martínez, and H. Romero-Ugalde, 2020 Fractional order neural networks for system identification. Chaos, Solitons & Fractals **130**: 109444.

Al Na'mneh, R. and W. D. Pan, 2007 Five-step fft algorithm with reduced computational complexity. Information processing letters **101**: 262–267.

Almalki, S. J. and S. Nadarajah, 2014 Modifications of the weibull distribution: A review. Reliability Engineering & System Safety **124**: 32–55.

Alsmadi, M., K. B. Omar, and S. A. Noah, 2009 Back propagation algorithm: the best algorithm among the multi-layer perceptron algorithm .

Arnold, B. C., 2014 Pareto distribution. Wiley StatsRef: Statistics Reference Online pp. 1–10.

Arnold, B. C. and R. J. Beaver, 2000 The skew-cauchy distribution. Statistics & probability letters **49**: 285–290.

Arora, S. and B. Barak, 2009 *Computational complexity: a modern approach*. Cambridge University Press.

Baleanu, D. and Y. Karaca, 2022 Mittag-leffler functions with heavy-tailed distributions' algorithm based on different biology datasets to be fit for optimum mathematical models' strategies. In *Multi-Chaos, Fractal and Multi-fractional Artificial Intelligence of Different Complex Systems*, pp. 117–132, Elsevier.

Blazewicz, J. and M. Kasprzak, 2012 Complexity issues in computational biology. Fundamenta Informaticae **118**: 385–401.

Boroomand, A. and M. B. Menhaj, 2009 Fractional-based approach in neural networks for identification problem. In *2009 Chinese Control and Decision Conference*, pp. 2319–2322, IEEE.

Camargo, R. F., E. C. de Oliveira, and J. Vaz, 2012 On the generalized mittag-leffler function and its application in a fractional telegraph equation. Mathematical Physics, Analysis and Geometry **15**: 1–16.

Carletti, M. and M. Banerjee, 2019 A backward technique for demographic noise in biological ordinary differential equation models. Mathematics **7**: 1204.

Chakraborty, S. and S. Ong, 2017 Mittag-leffler function distribution-a new generalization of hyper-poisson distribution. Journal of Statistical distributions and applications **4**: 1–17.

Chivers, I., J. Sleightholme, I. Chivers, and J. Sleightholme, 2015 An introduction to algorithms and the big o notation. Introduction to Programming with Fortran: With Coverage of Fortran 90, 95, 2003, 2008 and 77 pp. 359–364.

D'Agostino, R., 2017 *Goodness-of-fit-techniques*. Routledge.

David, S., J. Linares, and E. Pallone, 2011 Cálculo de ordem fracionária: apologia histórica, conceitos básicos e algumas aplicações. Revista Brasileira de Ensino de Física **33**: 4302–4302.

De Oliveira, E. C. and J. A. Tenreiro Machado, 2014 A review of definitions for fractional derivatives and integral. Mathematical Problems in Engineering **2014**.

Debnath, L., 2003 Recent applications of fractional calculus to science and engineering. International Journal of Mathematics and Mathematical Sciences **2003**: 3413–3442.

Du, D.-Z. and K.-I. Ko, 2011 *Theory of computational complexity*, volume 58. John Wiley & Sons.

Du, M., Z. Wang, and H. Hu, 2013 Measuring memory with the order of fractional derivative. Scientific reports **3**: 3431.

Fan, J. and I. Gijbels, 2018 *Local polynomial modelling and its applications*. Routledge.

Fernandez, A. and I. Husain, 2020 Modified mittag-leffler functions with applications in complex formulae for fractional calculus. Fractal and Fractional **4**: 45.

Garrappa, R., 2015 Numerical evaluation of two and three parameter mittag-leffler functions. SIAM Journal on Numerical Analysis **53**: 1350–1369.

Garrappa, R., E. Kaslik, and M. Popolizio, 2019 Evaluation of fractional integrals and derivatives of elementary functions: Overview and tutorial. Mathematics **7**: 407.

Gomolka, Z., 2018 Backpropagation algorithm with fractional derivatives. In *ITM web of conferences*, volume 21, p. 00004, EDP Sciences.

Gorenflo, R., A. A. Kilbas, F. Mainardi, S. V. Rogosin, *et al.*, 2020 *Mittag-Leffler functions, related topics and applications*. Springer.

Gutierrez, R. E., J. M. Rosário, and J. Tenreiro Machado, 2010 Fractional order calculus: basic concepts and engineering applications. Mathematical problems in engineering **2010**.

Haykin, S., 2009 *Neural networks and learning machines, 3/E*. Pearson Education India.

Herrmann, R., 2011 *Fractional calculus: an introduction for physicists*. World Scientific.

Jachowicz, R. E., P. Duch, P. W. Ostalczyk, and D. J. Sankowski, 2022 Fractional order derivatives as an optimization tool for object detection and tracking algorithms. IEEE Access **10**: 18619–

18630.
Kadam, P., G. Datkhile, and V. A. Vyawahare, 2019 Artificial neural network approximation of fractional-order derivative operators: analysis and dsp implementation. In *Fractional Calculus and Fractional Differential Equations*, pp. 93–126, Springer.
Karaca, Y., 2016 Case study on artificial neural networks and applications. Applied Mathematical Sciences **10**: 2225–2237.
Karaca, Y. and D. Baleanu, 2020 A novel r/s fractal analysis and wavelet entropy characterization approach for robust forecasting based on self-similar time series modeling. Fractals **28**: 2040032.
Karaca, Y. and D. Baleanu, 2022a Algorithmic complexity-based fractional-order derivatives in computational biology. In *Advances in Mathematical Modelling, Applied Analysis and Computation: Proceedings of ICMMAAC 2021*, pp. 55–89, Springer.
Karaca, Y. and D. Baleanu, 2022b Artificial neural network modeling of systems biology datasets fit based on mittag-leffler functions with heavy-tailed distributions for diagnostic and predictive precision medicine. In *Multi-Chaos, Fractal and Multi-fractional Artificial Intelligence of Different Complex Systems*, pp. 133–148, Elsevier.
Karaca, Y. and D. Baleanu, 2022c 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, 2022 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. and C. Cattani, 2018 Computational methods for data analysis. In *Computational Methods for Data Analysis*, De Gruyter.
Karaca, Y., M. Moonis, and D. Baleanu, 2020 Fractal and multifractional-based predictive optimization model for stroke subtypes' classification. Chaos, Solitons & Fractals **136**: 109820.
KARCI, A. *et al.*, 2014 Fractional order derivative and relationship between derivative and complex functions. Mathematical Sciences and Applications E-Notes **2**: 44–54.
Khan, H., A. Khan, M. Al Qurashi, D. Baleanu, and R. Shah, 2020 An analytical investigation of fractional-order biological model using an innovative technique. Complexity **2020**: 1–13.
Kharazmi, O., 2016 Generalized weighted weibull distribution. Journal of Mathematical Extension **10**: 89–118.
Kochubei, A., Y. Luchko, V. E. Tarasov, and I. Petráš, 2019 *Handbook of fractional calculus with applications*, volume 1. de Gruyter Berlin, Germany.
Krishna, B. and K. Reddy, 2008 Active and passive realization of fractance device of order 1/2. Active and passive electronic components **2008**.
Lewis, M. R., P. G. Matthews, and E. M. Hubbard, 2016 Neurocognitive architectures and the nonsymbolic foundations of fractions understanding. In *Development of mathematical cognition*, pp. 141–164, Elsevier.
Li, C., D. Qian, Y. Chen, *et al.*, 2011 On riemann-liouville and caputo derivatives. Discrete Dynamics in Nature and Society **2011**.
Lopes, A. M. and J. Tenreiro Machado, 2019 The fractional view of complexity.
Magin, R. L., 2010 Fractional calculus models of complex dynamics in biological tissues. Computers & Mathematics with Applications **59**: 1586–1593.
Mainardi, F., 2020 Why the mittag-leffler function can be considered the queen function of the fractional calculus? Entropy **22**: 1359.
Mainardi, F. and R. Gorenflo, 2000 On mittag-leffler-type functions in fractional evolution processes. Journal of Computational and Applied mathematics **118**: 283–299.
Mall, S. and S. Chakraverty, 2018 Artificial neural network approach for solving fractional order initial value problems. arXiv preprint arXiv:1810.04992 .
MATLAB, 2022 *version 9.12.0 (R2022a)*. The MathWorks Inc., Natick, Massachusetts.
Matusiak, M., 2020 Optimization for software implementation of fractional calculus numerical methods in an embedded system. Entropy **22**: 566.
Mia, M. M. A., S. K. Biswas, M. C. Urmi, and A. Siddique, 2015 An algorithm for training multilayer perceptron (mlp) for image reconstruction using neural network without overfitting. International Journal of Scientific & Technology Research **4**: 271–275.
Michener, W. K., T. J. Baerwald, P. Firth, M. A. Palmer, J. L. Rosenberger, *et al.*, 2001 Defining and unraveling biocomplexity. BioScience **51**: 1018–1023.
Mittag-Leffler, G., 1903 Sur la nouvelle fonction ea (x). Comptes rendus de l'Académie des Sciences **137**: 554–558.
Murphy, P. M., 1994 Uci repository of machine learning databases. http://www. ics. uci. edu/˜ mlearn/MLRepository. html .
Newman, M. E., 2005 Power laws, pareto distributions and zipf's law. Contemporary physics **46**: 323–351.
Niu, H., Y. Chen, and B. J. West, 2021 Why do big data and machine learning entail the fractional dynamics? Entropy **23**: 297.
Oldham, K. and J. Spanier, 1974 *The fractional calculus theory and applications of differentiation and integration to arbitrary order*. Elsevier.
Ouyang, Y. and W. Wang, 2016 Comparison of definition of several fractional derivatives. In *2016 International Conference on Education, Management and Computer Science*, pp. 553–557, Atlantis Press.
Panda, R. and M. Dash, 2006 Fractional generalized splines and signal processing. Signal Processing **86**: 2340–2350.
Pang, D., W. Jiang, and A. U. Niazi, 2018 Fractional derivatives of the generalized mittag-leffler functions. Advances in Difference Equations **2018**: 1–9.
Petrás, I., 2011 *Fractional derivatives, fractional integrals, and fractional differential equations in Matlab*. IntechOpen.
Pillai, R. and O. M.-L. Functions, 1990 Related distributions. Ann. Inst. Statist. Math **42**: 157–161.
Raubitzek, S., K. Mallinger, and T. Neubauer, 2022 Combining fractional derivatives and machine learning: A review. Entropy **25**: 35.
Rodríguez-Germá, L., J. J. Trujillo, and M. Velasco, 2008 Fractional calculus framework to avoid singularities of differential equations. Fract. Cal. Appl. Anal **11**: 431–441.
Ross, B., 1977 Fractional calculus. Mathematics Magazine **50**: 115–122.
Sidelnikov, O., A. Redyuk, and S. Sygletos, 2018 Equalization performance and complexity analysis of dynamic deep neural networks in long haul transmission systems. Optics express **26**: 32765–32776.
Singh, A. P., D. Deb, H. Agrawal, K. Bingi, and S. Ozana, 2021 Modeling and control of robotic manipulators: A fractional calculus point of view. Arabian Journal for Science and Engineering **46**: 9541–9552.
Singhal, G., V. Aggarwal, S. Acharya, J. Aguayo, J. He, *et al.*, 2010 Ensemble fractional sensitivity: a quantitative approach to neuron selection for decoding motor tasks. Computational intelli-

gence and neuroscience **2010**: 1–10.
Sommacal, L., P. Melchior, A. Oustaloup, J.-M. Cabelguen, and A. J. Ijspeert, 2008 Fractional multi-models of the frog gastrocnemius muscle. Journal of Vibration and Control **14**: 1415–1430.
Steck, G. P., 1958 *A uniqueness property not enjoyed by the normal distribution*. Sandia Corporation.
Stockmeyer, L., 1987 Classifying the computational complexity of problems. The journal of symbolic logic **52**: 1–43.
Tenreiro Machado, J., V. Kiryakova, and F. Mainardi, 2010 A poster about the old history of fractional calculus. Fractional Calculus and Applied Analysis **13**: 447–454.
Tokhmpash, A., 2021 *Fractional Order Derivative in Circuits, Systems, and Signal Processing with Specific Application to Seizure Detection*. Ph.D. thesis, Northeastern University.
Toledo-Hernandez, R., V. Rico-Ramirez, G. A. Iglesias-Silva, and U. M. Diwekar, 2014 A fractional calculus approach to the dynamic optimization of biological reactive systems. part i: Fractional models for biological reactions. Chemical Engineering Science **117**: 217–228.
Tzoumas, V., Y. Xue, S. Pequito, P. Bogdan, and G. J. Pappas, 2018 Selecting sensors in biological fractional-order systems. IEEE Transactions on Control of Network Systems **5**: 709–721.
Valentim, C. A., J. A. Rabi, and S. A. David, 2021 Fractional mathematical oncology: On the potential of non-integer order calculus applied to interdisciplinary models. Biosystems **204**: 104377.
Van Rossum, G. and F. L. Drake Jr, 1995 *Python tutorial*, volume 620. Centrum voor Wiskunde en Informatica Amsterdam, The Netherlands.
Viola, J. and Y. Chen, 2022 A fractional-order on-line self optimizing control framework and a benchmark control system accelerated using fractional-order stochasticity. Fractal and Fractional **6**: 549.
West, B. J., 2016 *Fractional calculus view of complexity: tomorrow's science*. CRC Press.
West, B. J., M. Bologna, and P. Grigolini, 2003 *Physics of fractal operators*, volume 10. Springer.
Wiman, A., 1905 Über den fundamentalsatz in der teorie der funktionen e a (x) .
Wu, A., L. Liu, T. Huang, and Z. Zeng, 2017 Mittag-leffler stability of fractional-order neural networks in the presence of generalized piecewise constant arguments. Neural Networks **85**: 118–127.
Xue, H., Z. Shao, and H. Sun, 2020 Data classification based on fractional order gradient descent with momentum for rbf neural network. Network: Computation in Neural Systems **31**: 166–185.
Zhang, Y.-D. and L. Wu, 2008 Weights optimization of neural network via improved bco approach. Progress In Electromagnetics Research **83**: 185–198.
Ziane, D., M. Hamdi Cherif, D. Baleanu, and K. Belghaba, 2020 Non-differentiable solution of nonlinear biological population model on cantor sets. Fractal and Fractional **4**: 5.

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