International Journal of Scientific Research & Engineering Trends
Volume 12, Issue 3, May-Jun-2026, ISSN (Online): 2395-566X

Advances in Fractional-Order Modeling: A Review of Applications in Medicine, Epidemiology and System Optimization

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Abstract- — Traditional integer-order differential equations are increasingly recognized for their limitations in capturing the non-local, memory-dependent and hereditary properties inherent in complex biological and physical systems. This review provides a comprehensive synthesis of recent research into the application of fractional-order derivatives—including the standard Caputo, Caputo-Fabrizio, Atangana-Baleanu and generalized ψ-Caputo operators—across diverse scientific domains. In epidemiology, these models have proven superior to classical approaches for analyzing the transmission dynamics of diseases such as Tuberculosis, COVID-19 and Dengue fever with some models achieving a 28.6% reduction in predictive error by accounting for specific population behaviors and environmental factors. In oncology, fractional modeling has refined the simulation of radiotherapy and chemotherapy by integrating vital radiobiological factors like cell repair and repopulation, leading to more precise treatment protocols. Beyond medicine, the sources demonstrate the utility of fractional calculus in modeling ecological food chain interactions, world population growth and USA GDP rates as well as optimizing multi-agent systems and gradient descent algorithms. By employing rigorous qualitative analyses (e.g.fixed-point theory) and advanced numerical schemes (e.g.Adams-Bash forth-Moulton method), these studies establish that fractional-order derivatives provide a more flexible and realistic framework for capturing the complexities of real-world phenomena. This review underscores the transformative potential of fractional calculus in enhancing predictive accuracy for public health management and socio-economic forecasting.

Keywords: Caputo, Epidemiology, Cancer, Covid-19, Fractional Derivative.

I. INTRODUCTION

Traditional integer-order differential equations are often limited in their ability to capture the complexities of biological and physical systems because they do not account for memory and hereditary effects. Fractional calculus addresses these limitations by providing non-local operators where the future state of a system depends on its entire history. This review examines how various fractional derivatives offer superior accuracy and flexibility in modeling real-world phenomena.

Gamma Function:
The Gamma function is denoted by

$$\Gamma(z) = \int_0^\infty e^{-t} t^{z-1} dz \qquad \ldots (1)$$

Which converges in right half of the complex plane $R(z) > 0$.
Caputo Derivative:
Caputo's definition can be written as

$${}_a^C D_t^\alpha f(t) = \frac{1}{\Gamma(\alpha - n)} \int_a^t \frac{f^n(\tau)\, d\tau}{(t-\tau)^{\alpha+1-n}} \qquad \ldots (2)$$

Where, n-1<α<n
Liouville-Caputo operator (C):
Liouville-Caputo operator (C) is defined as follows,

$${}_0^C D_t^\alpha u(x,t) = \frac{1}{\Gamma(n-\alpha)} \int_0^t \frac{u^n(x,\tau)\, d\tau}{(t-\tau)^{\alpha+1-n}} \qquad \ldots (3)$$

Where, n-1<α<n
Where u^n is the derivative of integer nth order of $u(x,t), n = 1,2,\ldots \in N$ and $n-1 < \alpha \le n$
Caputo Fabrizio Operator (CFC):
Caputo Fabrizio operator (CFC) is expressed as follows,

$${}_0^{CFC} D_t^\alpha u(x,t) = \frac{(2-\alpha)M(\alpha)}{2(n-\alpha)} \int_0^t \exp\left(-\alpha \frac{(t-\theta)}{n-\alpha}\right) u^n(x,\tau)\, d\tau \qquad \ldots (4)$$

Where
M(α) is normalized function M(0)=M(1)=1
This operator has non singular kernel so it uses exponential law.

Atangana-Baleanu Fractional Derivative (ABC):
Atangana –Balenau fractional derivative in Liouville- Caputo sense (ABC) with order (α>0) is given as follows

$$ {}^{ABC}_{0}D^{\alpha}_{\tau}(.) = \frac{M(\alpha)}{1-\alpha}\int_0^{\tau} E_{\alpha}\left(\frac{-\alpha(\tau - t)}{1-\alpha}\right) D(.)dt \quad \dots(5) $$

Where,

$E_{\alpha}(z) = \sum_{k=0}^{\infty} \frac{z^k}{\Gamma(\alpha k+1)}$ Is Mittag-Leffler function

$M(\alpha)$ is normalized function $M(0) = M(1) = 1$

II. LITERATURE REVIEW

Epidemiological Dynamics
Fractional-order models have been extensively applied to analyze the transmission of infectious diseases, yielding more precise predictions than classical models.

- **Tuberculosis (TB):** Research focusing on TB transmission in Pakistan and China demonstrates that fractional models better align with real incidence data. For instance, a Caputo fractional-order model of TB in China achieved a 28.6% reduction in error (RMSE) compared to integer-order models, identifying an optimal fractional order of 0.93. These studies highlight that contact rates, treatment failure rates and age-structured susceptibility are critical factors in disease control [4][13].

The study created a fractional-order model to understand how tuberculosis spreads using real data from Khyber Pakhtunkhwa. The results showed that the disease decreases when the reproduction number is below one and treatment plays a major role in controlling TB. The model gives more accurate and realistic results than traditional methods and shows that proper treatment and public health efforts can effectively reduce TB spread.

In the future, this model can be improved by adding vaccination, relapse cases and TB data from the whole country. It can also include real-life factors like drug resistance, age groups, co-infections and public awareness. Researchers can use better mathematical methods and numerical techniques to make the model more accurate. These improvements will help in better planning and control of tuberculosis in the long term. [4]

- **COVID-19:** Multiple studies utilized fractional derivatives to understand COVID-19 propagation in Thailand and Wuhan. These models show that combining precautionary measures with home remedies (such as nutritional supplements and herbal infusions) significantly bolsters recovery rates and mitigates pandemic spread [5][6].

The study created a mathematical model to understand how COVID-19 spreads. It shows that if each infected person spreads the disease to less than one person on average, the outbreak will stop. The model also shows that quarantine, precautions and supportive care help reduce infections and increase recovery. Using real data from Thailand, the results prove the model works well and can help governments plan better strategies to control pandemics. [5]

The study uses a new fractional calculus method to solve a COVID-19 spread model. It proves the model has a stable and reliable solution and shows that the method can describe real epidemic data more accurately than traditional methods. The results and graphs help understand and predict the spread of COVID-19, so the approach is useful for real-world disease analysis and modelling. [6]

- **Dengue Fever:** Using the Caputo-Fabrizio derivative, researchers found that environmental factors like temperature and biting rates are pivotal in transmission. Reducing the "memory index" of a population through intervention can effectively lower the prevalence of the virus [3].

III. MEDICAL SCIENCE AND ONCOLOGY

The sources provide a comprehensive look at optimizing cancer treatments through fractional modeling.

Radiotherapy: Cancer Models using the Caputo derivative account for vital radiobiological factors like cell repair and repopulation. The mathematical models used Simulations of six patients is revealed that the fractional derivative value and the cancer cells proliferation coefficient are the most sensitive predictors of final tumour volume.

Researchers have created new mathematical tools that use a memory-based approach to better understand complex systems like breast cancer growth and how groups of agents (like robots or cells) coordinate. They found that these models are very reliable and can accurately predict tipping points where cancer might suddenly grow or stay at a safe, low level. In the future, scientists plan to use these tools to find the best timing and doses for medical treatments and to develop more advanced ways to manage and prevent diseases. [7]

Chemotherapy and Optimal Control: The use of Atangana-Baleanu and Caputo-Fabrizio derivatives allows for a non-singular description of drug diffusion and tumor-immune interaction. Optimal control models incorporating immunotherapy and anti-angiogenic therapy have proven effective in minimizing cancer cell counts by utilizing nonstandard numerical techniques like the N2LIM [8][9][12].

The researchers created a new math model to study how breast cancer cells and immune cells (the body's defenders) interact. They found that this model is a practical and easy-to-use tool for predicting how the disease behaves over time. A major finding was that the model can represent "cancer without disease," a situation where cancer cells stay at a very low level and do not grow into a dangerous tumor. By using special fractal math, the model is able to remember the history and memory of how the cancer has grown, which makes it more accurate than older, simpler models.

In the future, the team plans to improve the model by adding time delays to see how the timing of the body's reactions affects cancer growth. They also want to use the model to test different treatments, like chemotherapy and immunotherapy, to figure out the best doses and schedules to stop the cancer from spreading. The ultimate goal is to use this math to create better strategies for managing and preventing breast cancer in real patients. [12]

IV. ECOLOGICAL AND POPULATION DYNAMICS

Fractional calculus is increasingly used to model complex species interactions and socio-economic trends.

Food Chain Interactions: A three-species food chain model under the fractal-fractional Caputo (FFC) derivative explored the impact of cannibalism and stage-structured behavior (mature vs. immature predators) on ecosystem stability [10].

In this study, researchers used an advanced mathematical model to look at how a food chain of three different species—prey, middle predators, and top predators—interact in nature. They discovered that their math tool is very reliable for showing how these populations can stay stable even when their numbers seem to jump around unpredictably. This helps us better understand the balance of ecosystems and how different animals depend on one another. Moving forward, the team plans to use even more complex math methods to study "crossover" behaviours, which will help explain how animal groups react to sudden shifts or changes in their environment

Economic and Growth Models: The generalized ψ-Caputo derivative, which differentiates with respect to a kernel function, provides a "trial" function that can be calibrated to fit real data. This framework has successfully modeled world population growth in Lithuania and Qatar, as well as USA GDP growth rates, offering higher flexibility than classical exponential models [1][2].

V. COMPUTATIONAL METHODS AND OPTIMIZATION

Beyond modeling, the sources introduce novel algorithms for system optimization.

Caputo Fractional Gradient Descent (CFGD): A new optimization algorithm, CFGD, was proposed to find stationary points more efficiently than standard Gradient Descent (GD). By utilizing adaptive terminals, this method mitigates the dependence on the condition number of the objective function, resulting in significant acceleration toward the optimal solution [11].

Multi-Agent Systems: Fractional derivatives are used to solve leader-follower consensus problems. These models ensure that tracking errors between multiple agents and a virtual leader asymptotically converge to zero, provided the system matrix eigenvalues satisfy specific fractional-order stability conditions[10][11].

Future Scope

Researchers plan to make these mathematical tools even more powerful by adding "time delays" to see how the timing of the body's reaction affects a disease like breast cancer. They intend to use Artificial Intelligence (AI) and deep learning to make complex calculations much faster and explore more advanced math formulas to find hidden patterns in how diseases spread. Scientists also aim to test these models with real-life patient data from clinics to figure out the perfect timing and doses for treatments like chemotherapy and radiation. Finally, they want to expand their work to a national level to help governments better plan for vaccinations and manage outbreaks of diseases like COVID-19 and Tuberculosis.

VI. CONCLUSION

The reviewed research underscores that fractional-order modeling is no longer just a theoretical mathematical tool but a vital instrument for practical problem-solving in science and engineering. By capturing the non-local and memory-dependent nature of real-life processes, these models provide more reliable insights for healthcare policy, disease management and economic forecasting.

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