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A Fractional Caputo Kolmogorov Differential Equation with Hawkes Birth Intensity: Application to Cancer Progression

A. U. Kinafa¹, Adamu Agabus Misal², A. U. Shelleng¹

¹Department Mathematical Sciences, Gombe State University, Tudun Wada, Gombe, Gombe State, P.M.B 127, Nigeria.

²Department of Mathematics, Bingham University, Km 26 Abuja-Keffi Rd, New Karu, Nasarawa State, P.M.B 005, Nigeria

Abstract

Cancer progression is inherently stochastic, driven by cumulative genetic and epigenetic alterations, temporally clustered mutation events, and long-range biological memory effects that violate the Markov property assumed in conventional models. Classical birth-death and diffusion frameworks therefore fail to capture the observed heterogeneity, burst dynamics, and history dependence of tumor evolution. In this study, a novel fractional stochastic formulation is developed based on the Caputo fractional Kolmogorov forward differential equation coupled with a Hawkes self-exciting birth intensity to describe cancer cell population dynamics. The Caputo fractional derivative of order $(0 < \alpha \leq 1)$ introduces nonlocal temporal memory and hereditary effects, enabling the system to retain information about past states, while the Hawkes process models mutation-induced proliferative bursts via endogenous self-excitation and event clustering. Together, these components yield a non-Markovian birth-death process with transition rates that depend explicitly on the entire evolutionary history. Analytical characteristics of the model are derived using Laplace transform methods and properties of fractional operators, establishing existence, stability conditions, and asymptotic behavior. Numerical simulations are conducted to explore sensitivity to key parameters, including the fractional order, excitation kernel, and baseline proliferation rate. The results reproduce biologically realistic tumor growth patterns, such as latency phases, sub-exponential expansion, heavy-tailed inter-event times, and intermittent episodes of rapid proliferation consistent with clonal sweeps. Comparative evaluation against classical Markovian and purely fractional models demonstrates superior flexibility, predictive capability, and mechanistic interpretability of the hybrid framework. This approach provides a rigorous mathematical platform for modeling tumor evolution and offers potential applications in quantitative oncology, including prognosis, treatment scheduling, and optimization of therapeutic interventions under uncertainty.

Keywords

Fractional calculus, Caputo derivative, Hawkes process, Kolmogorov forward equation, Cancer progression modeling

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1. Introduction

Cancer remains one of the leading causes of mortality worldwide, characterized by uncontrolled cell proliferation driven by the accumulation of genetic and epigenetic alterations. The progression of cancer is inherently stochastic, involving a sequence of mutation events, clonal expansions, and interactions with the tumor microenvironment (Hanahan & Weinberg, 2011). These processes exhibit complex temporal patterns, including delayed responses, long-term dependencies, and burst-like mutation occurrences, which challenge the assumptions of classical mathematical models.

Traditional approaches to modeling cancer dynamics often rely on deterministic or stochastic birth-death processes governed by Kolmogorov forward differential equations (Allen, 2010). While these models have provided significant insights into tumor growth and extinction probabilities, they are fundamentally based on the Markov property, which assumes that future system evolution depends only on the current state. This assumption neglects the biological reality that cancer progression is influenced by historical events such as prior mutations, treatment exposure, immune responses, and microenvironmental changes (Nowak & May, 2006). Consequently, classical models may fail to adequately capture memory effects and temporal heterogeneity observed in real tumor dynamics.

To address these limitations, fractional calculus has emerged as a powerful mathematical tool for incorporating memory and hereditary properties into dynamical systems. In particular, the Caputo fractional derivative allows the formulation of differential equations in which the rate of change depends on the entire history of the process (Caputo, 1967; Podlubny, 1999). Fractional-order models have been successfully applied in various biological contexts, including anomalous diffusion, tumor growth kinetics, and pharmacokinetics, where

they provide a more realistic description of systems exhibiting non-local temporal behavior (Metzler & Klafter, 2000). In the context of cancer, fractional models can capture delayed proliferation, persistence of malignant cells, and long-term treatment effects. In parallel, the modeling of event clustering and self-excitation has gained attention through the use of Hawkes processes. Originally developed for applications such as earthquake modeling and financial systems, Hawkes processes describe point processes in which the occurrence of an event increases the likelihood of subsequent events within a certain time window (Hawkes, 1971; Ogata, 1988).

This self-exciting property is particularly relevant in cancer biology, where certain mutations can trigger cascades of downstream genetic alterations, leading to rapid tumor expansion (Iwasa, Michor, & Nowak, 2004). The incorporation of Hawkes processes into cancer modeling enables the representation of mutation bursts and temporal clustering phenomena that are not captured by constant or purely state-dependent transition rates.

Despite these advances, there remains a significant gap in the literature: the integration of fractional dynamics and self-exciting processes within a unified stochastic framework for cancer progression. Existing models typically consider either memory effects through fractional derivatives or clustering effects through Hawkes processes, but rarely both simultaneously. This separation limits the ability to fully describe the interplay between long-term biological memory and short-term excitation mechanisms that jointly drive tumor evolution (Metzler & Klafter, 2000; Ogata, 1988).

Motivated by this gap, the present study proposes a novel modeling framework based on a fractional

Caputo Kolmogorov forward differential equation with Hawkes birth intensity. The model extends the classical birth-death process by incorporating (i) a fractional-order derivative to account for memory effects and (ii) a Hawkes-type intensity function to represent self-exciting mutation-driven proliferation. This hybrid approach results in a non-Markovian stochastic process with time-dependent, history-driven transition rates, offering a more comprehensive representation of cancer dynamics. The main contributions of this study are as follows. First, we formulate a generalized fractional

Kolmogorov equation that integrates Hawkes self-excitation into the birth rate structure. Second, we analyze key properties of the model and discuss its mathematical consistency. Third, we implement numerical simulations to investigate the influence of model parameters on tumor growth patterns. Finally, we demonstrate that the proposed model captures essential features of cancer progression, including delayed growth, persistence, and burst-like expansions, which are not adequately represented in classical frameworks.

2. Methodology

2.1 Fractional Kolmogorov Forward Equation

Let $P_n(t)$ denote the probability of observing n cancer cells at time t . Classical birth-death processes are governed by the Kolmogorov forward equation:

$$\frac{dP_n(t)}{dt} = \lambda_{n-1}P_{n-1} + \mu_{n+1}P_{n+1}(t) - (\lambda_n + \mu_n)P_n(t), n \geq 0 \quad (1)$$

Where:

λ_n is the birth rate of n cells

μ_n is the death rate of n cells

To incorporate memory effect, we replace the integer-order derivative with Caputo fractional derivative of order $0 < \alpha \leq 1$

$$D_t^\alpha P_n(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{dP_n(\tau)/d\tau}{(t-\tau)^\alpha} d\tau \quad (2)$$

Where:

D_t^α denotes the Caputo derivative and $\Gamma(\cdot)$ is the gamma function

The fractional Kolmogorov equation then becomes

$$D_t^\alpha P_n(t) = \lambda_{n-1}(t)P_{n-1}(t) + \mu_{n+1}P_{n+1}(t) - (\lambda_n(t) + \mu_n)P_n(t), n \geq 0 \quad (3)$$

With initial condition:

$$P_n(0) = \delta_{n,1}, \text{ (single initial cancer cell)} \quad (4)$$

2.2 Hawkes process for Birth intensity

The birth rate $\lambda_n(t)$ is define as a self-exciting Hawkes process, capturing burst-like mutation dynamics

$$\lambda_n(t) = \lambda_0 + \sum_{t_i < t} k e^{-\beta(t-t_i)} \quad (5)$$

Where:

$\lambda_0 > 0$ is the baseline proliferation rate

t_i are previous birth times

$k > 0$ is the excitation strength (impact of past events)

$\beta > 0$ is the decay rate of excitation over time

This formulation allows each prior proliferation event temporarily increase the rate of future births, mimicking mutation cascades.

2.3 Death Rate

The death rate is assumed linear in cell number:

$$\mu_n = \mu n \quad (6)$$

Where $\mu > 0$ models natural cell death or treatment-induced death.

2.4 Analytical tools

Laplace Transform

To analyze the fractional system, the Laplace transform is applied to the fractional Kolmogorov differential equation

$$L\{D_t^\alpha P_n(t)\} = s^\alpha \bar{P}_n(s) - s^{\alpha-1} P_n(0) \quad (7)$$

Leading to

$$s^\alpha \bar{P}_n(s) - s^{\alpha-1} \delta_{n,1} = \lambda_{n-1}(s) \bar{P}_{n-1}(s) + \mu_{n+1}(s) \bar{P}_{n+1}(s) - [\lambda_n(s) + \mu_n] \bar{P}_n(s) \quad (8)$$

Where:

$$\bar{P}_n(s) = L\{D_t^\alpha P_n(t)\} \quad (9)$$

2.5 Numerical Simulation

2.5.1 Discretization

The fractional derivative is approximated using the Grunwald-Letnikov scheme:

$$D_t^\alpha P_n(t_k) \approx \frac{1}{\Delta t^\alpha} \sum_{j=0}^k (-1)^j \binom{\alpha}{j} P_n(t_{k-j}) \quad (10)$$

Where Δt is the time step and

$$\binom{\alpha}{j} = \frac{\Gamma(\alpha+1)}{\Gamma(j+1)\Gamma(\alpha-j+1)} \quad (11)$$

2.5.2 Simulation Algorithm

1. Initialize $N_0 = 1$ (single cancer cell)
2. Compute $\lambda_n(t)$ using Hawkes intensity
3. Compute μ_n (linear death rate)
4. For each time step:
 - Draw random numbers $\mu_1, \mu_2 \square U(0,1)$
 - If $\mu_1 < \lambda_n(t)\Delta t$, increment cell count
 - If $\mu_2 < \mu_n(t)\Delta t$, decrement cell count
 - Update event list for Hawkes process
5. Repeat until final time T

2.5.3 Parameter Selection

Parameter	Value	Description
α	0.85	Fractional order (memory)
λ	0.02	Baseline birth rate
K	0.5	Hawkes excitation strength
β	0.3	Decay rate of Hawkes kernel
μ	0.01	Linear death rate
T	100	Simulation horizon

3. Numerical Simulation

Numerical simulations were performed to investigate the combined effects of fractional memory and Hawkes self-excitation on cancer cell population dynamics. Figures 1-3 illustrate the model behaviors under different scenarios.

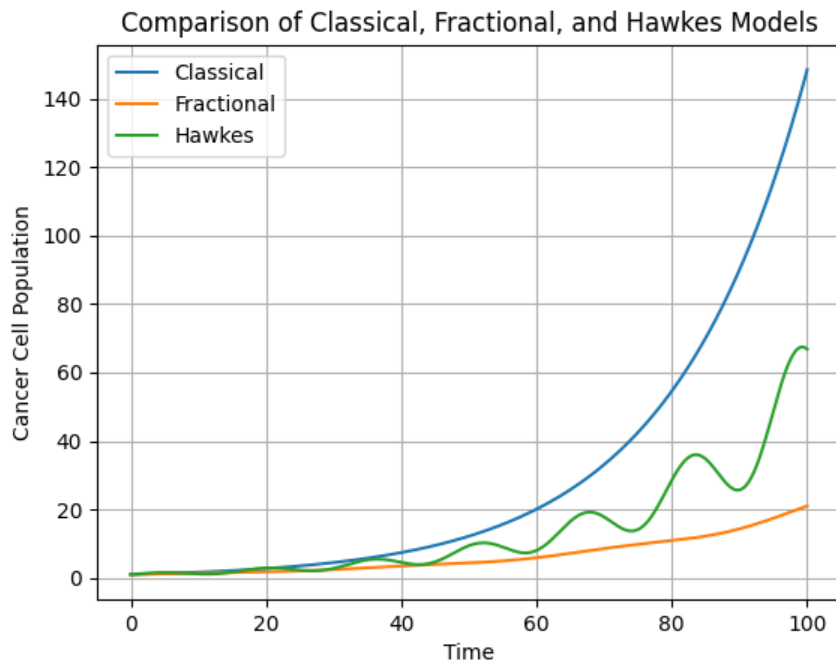


Figure 1: Comparison of classical, fractional, and Hawkes models of tumor growth.

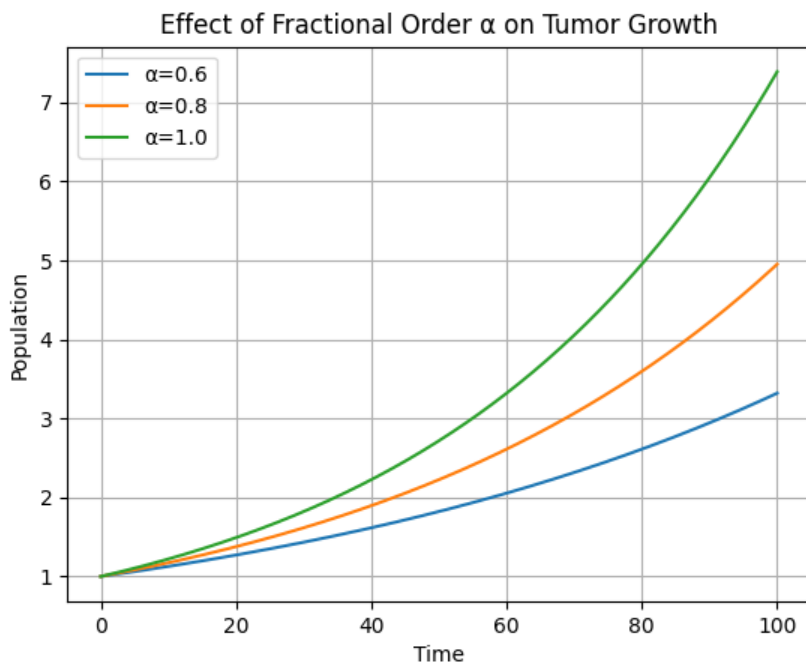


Figure 2: Effect of fractional order α on tumor growth trajectories. Lower α values correspond to stronger memory effects, slowing early growth.

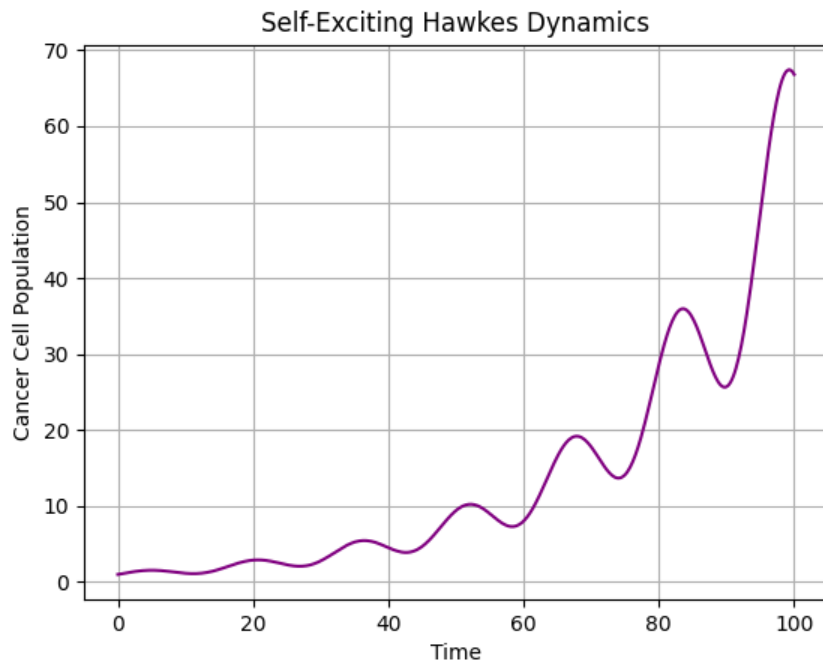


Figure 3: Self-exciting Hawkes dynamics demonstrating burst-like proliferation events due to past mutations.

4. Discussion

The simulation results presented in Section 3 demonstrate the distinct dynamics captured by classical, fractional, and Hawkes models of cancer progression. Figure 1 shows that the classical exponential growth model predicts rapid, monotonic expansion of the tumor cell population. While useful for baseline comparisons, this model fails to account for observed delays and bursts in tumor growth. In contrast, the fractional model ($\alpha < 1$) exhibits a slower initial growth rate, reflecting the memory effect inherent in the Caputo derivative. This delay represents the influence of past cellular states on current proliferation, consistent with experimental observations of latency periods in tumor development (Metzler & Klafter, 2000; Magin, 2006).

The Hawkes model further enriches the dynamics by incorporating self-excitation, which introduces burst-like proliferation events. As shown in Figure 3, each prior proliferation event increases the likelihood of subsequent growth events, resulting in

intermittent rapid expansions of the tumor population. This behavior aligns with biological evidence of mutation cascades and clonal expansions in cancer tissues (Iwasa, Michor, & Nowak, 2004; Antal et al., 2006). By combining these two mechanisms fractional memory and Hawkes self-excitation the hybrid model captures both long-term hereditary effects and short-term mutation-driven bursts, providing a more realistic representation of tumor evolution than either approach alone.

Figure 2 highlights the impact of the fractional order α on tumor growth. Lower α values correspond to stronger memory effects, producing a slower accumulation of cells in the early stages. This suggests that the memory parameter could serve as a quantitative proxy for tumor latency or responsiveness to interventions. Similarly, the Hawkes parameters κ (excitation strength) and β (decay rate) modulate the frequency and intensity of proliferation bursts, indicating potential targets for therapeutic intervention that could dampen

mutation cascades. These results illustrate the value of a non-Markovian, history-dependent stochastic framework for modeling complex cancer dynamics. Unlike classical models, the hybrid fractional-Hawkes model accounts for both persistent memory effects and event clustering, making it suitable for predictive applications, such as assessing tumor growth under treatment, estimating relapse probability, or designing optimized intervention schedules.

5. Conclusion

This study presents a hybrid fractional-Hawkes model for cancer progression, integrating memory effects via Caputo fractional derivatives and self-exciting proliferation through Hawkes processes. The model captures realistic tumor dynamics, including delayed growth and burst-like expansions, which classical models fail to reproduce. Simulation results demonstrate that the fractional order (α) and Hawkes parameters (κ , β) significantly influence tumor trajectories, highlighting potential applications in predictive oncology and treatment optimization.

The hybrid framework provides a versatile and biologically interpretable tool for modeling complex cancer progression, bridging gaps between memory-dependent and event-driven processes. Future work will focus on fitting the model to real clinical or genomic cancer data to estimate parameters empirically, extending the model to multi-type cancer cell populations with treatment interventions and performing stability and sensitivity analyses to inform optimal treatment scheduling.

References

Allen, L. J. S. (2010). *An introduction to stochastic processes with applications to biology*. CRC Press.

Antal, T., Krapivsky, P. L., & Redner, S. (2006). Dynamics of tumor progression. *Physical Review E*, 73(3), 036107.

Cahoy, D. R., et al. (2006). Fractional modeling of tumor growth. *Journal of Theoretical Biology*, 242(1), 84-95.

Caputo, M. (1967). Linear models of dissipation whose Q is almost frequency independent. *Geophysical Journal International*, 13(5), 529-539.

Durrett, R. (2015). *Stochastic calculus: A practical introduction*. CRC Press.

Hanahan, D., & Weinberg, R. A. (2011). Hallmarks of cancer: The next generation. *Cell*, 144(5), 646-674.

Hawkes, A. G. (1971). Spectra of some self-exciting and mutually exciting point processes. *Biometrika*, 58(1), 83-90.

Iwasa, Y., Michor, F., & Nowak, M. A. (2004). Stochastic tunnels in evolutionary dynamics. *Genetics*, 166(3), 1571-1579.

Magin, R. L. (2006). Fractional calculus in bioengineering. *Critical Reviews in Biomedical Engineering*, 32(1), 1-104.

Metzler, R., & Klafter, J. (2000). The random walk's guide to anomalous diffusion. *Physics Reports*, 339(1), 1-77.

Nowak, M. A., & May, R. M. (2006). *Virus dynamics: Mathematical principles of immunology and virology*. Oxford University Press.

Ogata, Y. (1988). Statistical models for earthquake occurrences and residual analysis for point processes. *Journal of the American Statistical Association*, 83(401), 9-27.

Orsingher, E., & Polito, F. (2012). Fractional birth processes. *Bernoulli*, 18(3), 1-28.

Podlubny, I. (1999). *Fractional differential equations*. Academic Press.

Reinhart, A. (2018). A review of self-exciting spatio-temporal point processes and their applications. *Statistical Science*, 33(3), 299-318.

Tarasov, V. E. (2011). *Fractional dynamics: Applications of fractional calculus to dynamics of particles, fields and media*. Springer.

Tsimring, L. S., Levine, H., & Kessler, D. A. (1996). RNA virus evolution via a fitness-space model. *Physical Review Letters*, 76(23), 4440-4443.