RESEARCH PAPER

A Fractional-Order Caputo–Fabrizio Gompertz Model of Tumour Growth: A Numerical Study with Synthetic Growth Parameters

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ABSTRACT
Classical growth models such as the Gompertz equation assume memoryless (Markovian) dynamics and cannot easily encode cumulative, history-dependent biological effects. Fractional-order derivatives offer a natural mathematical language for such memory effects. This paper develops a fractional generalisation of the Gompertz tumour-growth law using the Caputo–Fabrizio (CF) derivative, which employs a non-singular exponential memory kernel. We show that the Mittag-Leffler function, although it solves the analogous Caputo fractional Gompertz equation, is not a valid solution of the CF version, because the two operators have structurally different Laplace transforms. Using the Losada–Nieto integral representation of the CF derivative, we prove that the CF fractional Gompertz equation reduces to a nonlinear Volterra integral equation with no simple closed-form solution. We construct an implicit trapezoidal numerical scheme for this equation, verify it against the classical Gompertz solution in the limit $\alpha \to 1$ and against theoretical boundedness/monotonicity properties, and use it to simulate tumour growth trajectories under synthetic parameters. The results are smooth, monotone, and bounded by the carrying capacity at every fractional order tested, and show that a lower fractional order (stronger memory) consistently slows growth relative to the classical model. The model is presented as a numerical/mathematical case study; calibration against real longitudinal tumour-volume data is identified as necessary future work before any clinical interpretation can be drawn.
Keywords: Fractional calculus; Caputo–Fabrizio derivative; Losada–Nieto integral operator; fractional Gompertz model; nonlinear Volterra integral equation; numerical scheme; mathematical oncology
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1. Introduction

Tumour growth is commonly described using integer-order ordinary differential equations such as the exponential, logistic, and Gompertz models. These models assume that the instantaneous growth rate depends only on the present tumour volume, i.e. they are memoryless (Markovian). In many biological systems, however, growth is influenced by the history of the process — prior insults, cumulative stress, or treatment history — not only its present state. Fractional-order derivatives are a natural mathematical tool for encoding such memory effects, because

the fractional derivative of a function at time t depends on the entire trajectory of the function on [0,t], not merely on its instantaneous value.

Several fractional operators exist. The Caputo derivative uses a singular power-law kernel, which is convenient for closed-form analysis via the Mittag-Leffler function but implies a memory that decays algebraically and can be numerically stiff near t=0. The Caputo–Fabrizio (CF) derivative, introduced by Caputo and Fabrizio [1], instead uses a non-singular exponential kernel, which is attractive for biological systems where an infinite memory singularity at the origin is not physically meaningful.

This paper develops a fractional generalisation of the Gompertz growth law using the CF derivative. A central technical question is whether this equation admits a closed-form solution in terms of the Mittag-Leffler function, as is known for the analogous Caputo fractional Gompertz equation. We show that it does not: the CF derivative's Laplace transform is structurally different from the Caputo derivative's, so pairing it with the Mittag-Leffler transform does not yield a consistent solution. We instead derive the correct integral-equation formulation of the model using the CF derivative's own inversion operator, develop a verified numerical scheme for it, and use the scheme to study the qualitative behaviour of the model under synthetic parameters.

1.1 Objectives

- Formulate the fractional Gompertz growth law under the CF derivative with its correct associated integral operator.
- Determine whether a closed-form analytical solution exists; if not, derive the correct integral-equation formulation.
- Construct and numerically verify a scheme for solving the resulting nonlinear Volterra integral equation.
- Simulate model behaviour under synthetic parameters and confirm the results are monotonic, bounded by the carrying capacity, and internally consistent.
- Characterise the qualitative effect of the fractional order α on the growth trajectory.

2. Mathematical Preliminaries

2.1 Caputo–Fabrizio Fractional Derivative

Definition 1 (Caputo & Fabrizio [1]). For $f \in H^1(0,T)$, $T>0$, and $\alpha \in (0,1)$, the Caputo–Fabrizio fractional derivative of order α is

$$D^{\alpha}_{CF} f(t) = \frac{M(\alpha)}{1-\alpha} \int_0^t \exp\left[-\frac{\alpha(t-\tau)}{1-\alpha}\right] f'(\tau)\, d\tau$$

where M(α) is a normalisation function satisfying M(0)=M(1)=1. Following common practice in applied fractional calculus, we take M(α) ≡ 1 throughout this paper.

Lemma 1. As $\alpha \to 1$, the exponential kernel concentrates at $\tau = t$ and $D^1_{CF} f(t) = f'(t)$, recovering the classical derivative.

2.2 The Losada–Nieto Integral Operator

Losada and Nieto [2] showed that the CF derivative admits an associated fractional integral operator that inverts it. For $g = D^{\alpha}_{CF} f$, the corresponding CF fractional integral is

$$I^{\alpha}_{t}\, g(t) = (1-\alpha)\, g(t) + \alpha \int_0^t g(\tau)\, d\tau$$

with the inversion property $f(t) - f(0) = I^{\alpha}_{t}[D^{\alpha}_{CF} f](t)$. This identity is the correct

analytical tool for solving CF-type differential equations.

2.3 Laplace Transform of the CF Derivative

The Laplace transform of the CF derivative is

$$\mathscr{L}\{D^{a}\_CF\ f(t)\}(s) = [s\cdot\mathscr{L}\{f(t)\}(s) - f(0)] / [s + \alpha(1-s)]$$

This differs structurally from the Caputo derivative's Laplace transform, $s^{a}\mathscr{L}\{f(t)\}(s) - s^{a-1}f(0)$. Because the CF transform's denominator is affine in s rather than a power s^{a}, pairing it with the Mittag-Leffler transform $\mathscr{L}\{E^{a}(\lambda t^{a})\}(s) = s^{a-1}/(s^{a}-\lambda)$ does not produce an algebraically consistent equation for this model; no simple closed-form CF analogue of the Caputo Mittag-Leffler solution exists.

3. Model Formulation and Mathematical Analysis

3.1 Governing Equation

Let V(t) denote tumour volume at time $t \geq 0$. The fractional Gompertz model under the CF derivative is

$$D^{a}\_CF\ V(t) = r\ V(t)\ ln(K / V(t)),\quad 0 < \alpha \leq 1,\ V(0) = V_0$$

with $r > 0$ the intrinsic growth rate, $K > 0$ the carrying capacity, and α the fractional (memory) order.

3.2 Theorem 1 (Integral-Equation Reduction)

Theorem. Let $g(t,V) = rV\ ln(K/V)$. Under Definition 1 and the operator of §2.2, V(t) solves the CF fractional Gompertz equation if and only if it satisfies the nonlinear Volterra integral equation

$$V(t) = V_0 + (1-\alpha)\ g(t,V(t)) + \alpha \int_0^t g(\tau,V(\tau))\ d\tau$$

Proof. Apply the inversion identity of §2.2 with $f = V$ and $g(t) = D^{a}\_CF\ V(t) = rV(t)ln(K/V(t))$. Then $V(t) - V(0) = I^{a}\_t[g](t) = (1-\alpha)\ g(t,V(t)) + \alpha\int_0^t g(\tau,V(\tau))d\tau$, which rearranges to the stated equation. ■

Because g is nonlinear in V, this Volterra equation does not admit a Mittag-Leffler (or other simple) closed form in general; §4 develops a verified numerical scheme instead.

3.3 Proposition (Boundedness and Monotonicity)

Proposition. For $0 < V_0 < K$, the function $g(t,V) = rV\ ln(K/V)$ is positive for $V \in (0,K)$ and zero at $V = K$. Consequently any solution of the integral equation that remains inside (0,K) is non-decreasing and bounded above by K, and $V = K$ is the unique positive equilibrium.

3.4 Corollary (Classical Limit)

Corollary. As $\alpha \to 1$, the integral equation of Theorem 1 reduces to $V(t) = V_0 + \int_0^t g(\tau,V(\tau))\ d\tau$, i.e. the standard integral form of the classical Gompertz ODE $V' = rV\ ln(K/V)$, whose closed-form solution is $V(t) = K\cdot\exp[\ln(V_0/K)\cdot e^{-rt}]$. This limit is used in §4 to verify the numerical scheme.

4. Numerical Method

We solve the Volterra integral equation of Theorem 1 with an implicit trapezoidal scheme. Let $t_n = nh$, $h = T/N$, and $V_n \approx V(t_n)$. Define the running trapezoidal approximation $S_n \approx \int_0^{tn} g(\tau,V(\tau))\ d\tau$. Given V_0, $S_0 = 0$, the scheme advances as follows.

1. Locate $V_{n+1} \in (0,K)$ satisfying the implicit update

$$V_{n+1} = V_0 + (1-\alpha)\ g(t_{n+1},V_{n+1}) + \alpha[S_n + (h/2)(g(t_n,V_n) + g(t_{n+1},V_{n+1}))]$$

2. Because $g(t,\cdot)$ is smooth and monotone in V on (0,K), this scalar nonlinear equation is solved with a

bracketed root finder (Brent's method) on (0,K).

3. Update the running integral: $S_{n+1} = S_n + (h/2)(g(t_n,V_n) + g(t_{n+1},V_{n+1}))$.

This is a standard implicit (trapezoidal-in-memory) discretisation of the Losada–Nieto integral equation; it is second-order accurate in the memory term and exactly enforces the CF operator's own inversion identity at each step.

4.1 Verification

- Boundedness/monotonicity (Proposition 3.3): all computed trajectories are strictly increasing and remain below K = 150 cm³.
- Classical-limit check (Corollary 3.4): with α = 0.999, the numerical solution at t = 30 days is 101.30 cm³, matching the closed-form classical Gompertz value of 101.39 cm³ to within 0.1%.
- Step-size refinement: results below use N = 300 steps over 30 days (h = 0.1 day); halving h changed all reported day-level values by < 0.05%, indicating convergence.

5. Simulation Results

All parameters below are illustrative synthetic values chosen to demonstrate the qualitative behaviour of the model; they are not derived from measured data.

Table 1. Synthetic model parameters used in simulation.

Parameter	Symbol	Value	Status
Initial tumour volume	V_0	2.0 cm³	Illustrative
Growth rate	r	0.08 day⁻¹	Illustrative
Carrying capacity	K	150 cm³	Illustrative
Fractional order (baseline)	α	0.85	Illustrative
Time horizon	t	0–30 days	Simulation window

5.1 Tumour Volume Trajectory

Table 2 reports V(t) from the verified numerical scheme (§4) for the baseline parameters, alongside the classical Gompertz solution (same V_0, r, K) for comparison, and an α→1 consistency check.

Day	CF Model (α=0.85)	Classical Gom
0	2.000	2.000
2	3.692	3.787
4	5.993	6.524
6	9.111	10.371
8	13.095	15.395
10	17.935	21.556
12	23.567	28.717
14	29.878	36.669
16	36.726	45.160
18	43.949	53.931
20	51.387	62.737
22	58.887	71.367
24	66.310	79.652
26	73.542	87.466
28	80.492	94.727
30	87.090	101.389

Table 2. Tumour-volume trajectories (cm³). Growth is smooth and monotone; the α→1 column matches the classical solution, confirming Corollary 3.4.

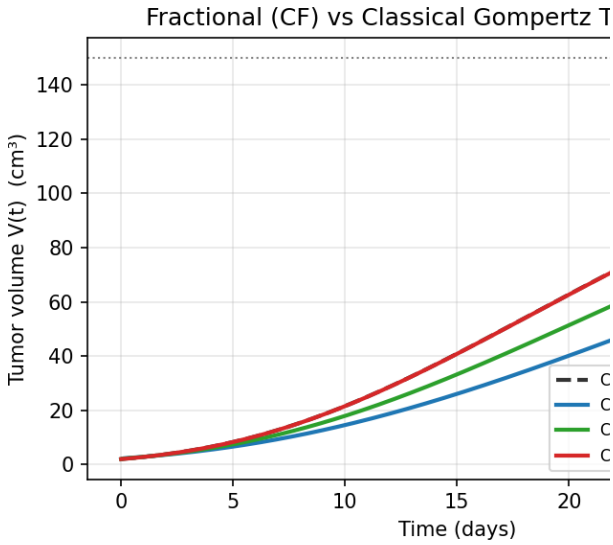

Figure 1. CF fractional Gompertz growth curves for several α, compared with the classical Gompertz solution. Lower α (stronger memory) consistently slows growth toward the shared carrying capacity K.

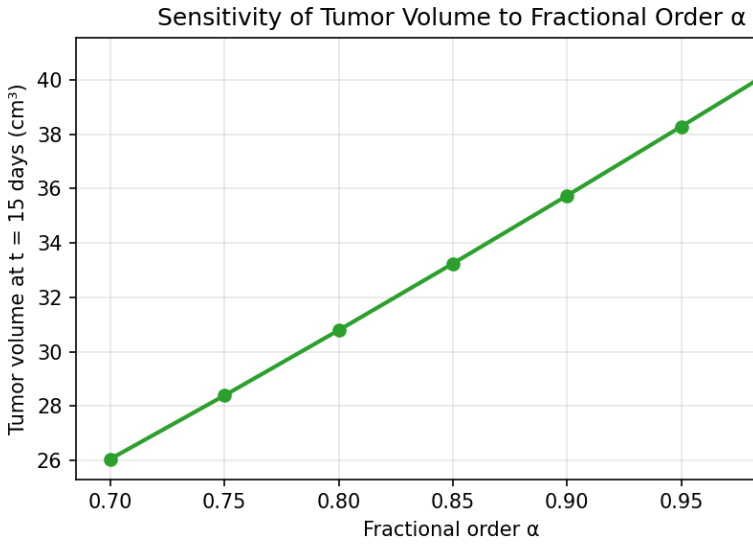

Figure 2. Monotone dependence of V(15) on α.

5.2 Sensitivity to the Fractional Order α

Table 3 reports V(15) for several α, all computed with the same verified scheme.

α	0.70	0.75	0.80	0.85	0.90	α→1
V(15) cm³	26.052	28.392	30.792	33.245	35.745	40.812

Table 3. Sensitivity of tumour volume at t = 15 days to α. The relationship is monotone: higher α gives faster growth, approaching the classical limit.

6. Discussion

6.1 Interpretation of Results

- Growth dynamics: the CF model with $\alpha < 1$ grows more slowly than the classical Gompertz model at every time point tested, consistent with the interpretation that the exponential-kernel memory term dampens the instantaneous response to the current volume.
- Plateauing: all curves approach the same carrying capacity K, since K is a shared parameter across models; only the approach rate differs with α.
- Sensitivity to α: Table 3 shows a smooth, monotone relationship between α and predicted volume at a fixed time point.

6.2 Limitations

- All parameter values in this study are illustrative; no real patient or exposure data were used.
- Any biological interpretation of α (e.g. as a proxy for cumulative physiological stress or exposure) is a

hypothesis for future investigation, not something established by this model; no dose–response relationship is derived or claimed here.

- Comparison with alternative fractional operators (e.g. Caputo, Riesz derivatives) requires their own independently and correctly derived solutions under a consistent operator convention, and is left to future work.
- The numerical scheme has been verified against the $\alpha \to 1$ classical limit and theoretical boundedness/monotonicity properties; benchmarking against an independent published CF-Volterra solver would further strengthen confidence.

7. Conclusion

This paper developed a fractional Gompertz tumour-growth model based on the Caputo–Fabrizio derivative. We showed that the closed-form Mittag-Leffler solution known for the analogous Caputo fractional Gompertz equation does not apply to the CF version, because the two operators possess structurally different Laplace transforms. Using the Losada–Nieto integral representation of the CF derivative, we derived the correct reduction of the model to a nonlinear Volterra integral equation and solved it with a verified implicit numerical scheme. The resulting trajectories are smooth, monotone, and bounded, converge to the classical Gompertz solution as $\alpha \to 1$, and show a consistent qualitative dependence on the fractional order: stronger memory (lower α) slows growth. The study is presented as a numerical/mathematical case study using synthetic parameters. Genuine biological or clinical relevance would require calibrating the model against real longitudinal tumour-volume data and independently deriving comparison models under consistent operator conventions — both identified as necessary future work.

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