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PROTOTYPE GLIOMAS: INVARIANT SOLUTIONS AND EXPECTED SURVIVAL TIMES

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Abstract. In this paper, we consider invariant solutions to a partial differential equation with arbitrary coefficients describing the proliferation and diffusion of gliomas or human brain tumors. We consider four grades of tumors that are underpinned by growth characteristics of the tumor into the brain. The equation describing the concentration of glioma cells is solved by the application of Lie point symmetries in two ways. Firstly, the standard approach of applying the invariants admitted by symmetries, and secondly by solving a Cauchy problem with the aid of symmetry invariant surface conditions. The solutions are analysed under realistic parameter values to provide biological implications in the prediction of tumor cell densities and survival times after diagnosis.

1. **Introduction.** Gliomas are highly invasive tumors of the human brain. Such tumors account for almost 50% of all human brain tumors [1], and feature aggressive growth rates that imply short life expectancies of about 6 to 12 months. In the literature pertaining to the mathematical modelling of gliomas, the Burgess equation [4] is a highly effective model of interest.

This particular equation is driven by two properties, invasiveness and proliferation of the tumor. There are many facets to tumor modelling, but in this study, similar to [4], we concentrate on the spread of untreated gliomas. A tumour has billions of cells and treatment varies greatly to kill the tumor cells. Popular treatments include a diagnostic magnetic resonance image followed by biopsy or surgical resection. Other therapies to destroy tumors include chemotherapy and radiotherapy. In considering treated gliomas, the medium of mathematical analysis would need to include specific boundary or initial conditions that represent the treatment.

Most mathematical models of gliomas are limited in some way. For instance, many models ignore factors such as age, gender, anatomic boundaries etc., and often include necessary assumptions, such as the uniform expansion of tumors or that individual tumor cells are all equal in size. However, despite some of these perceived problems, mathematical equations provide experimental benchmarks and open many doorways to study complicated phenomenon. For this reason,

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the mathematical analysis of gliomas is an active study with varying perspectives [24, 19, 23, 8, 21].

The Burgess equation as a tumor growth model imbibes that the rate of change of tumor cell density is equal to the diffusion plus growth of tumor cells. The dynamics of the invasive and diffusive brain tumor is modelled by the parabolic equation

$$\frac{\partial u(x,t)}{\partial t} - b\frac{\partial^2}{\partial x\,\partial x}u(x,t) - \frac{2b}{x}\frac{\partial}{\partial x}u(x,t) - pu(x,t) = 0, \tag{1}$$

where $u(x,t)$ is the concentration of tumour cells at location x at time t, b is the diffusion coefficient which measures the invasiveness of the tumor cells, p is the net rate of growth of cells (proliferation rate of the tumour less cell loss) and x measures the distance from the centre (i.e. the origin of glioma). This model may assume the initial condition (IC),

$$u(x,0) = \zeta(x), \tag{2}$$

in a three dimensional unbounded domain.

In [4] an exact solution for the above equation (without any details) is given as

$$u(x,t) = \frac{N_0\,\mathrm{e}^{pt}}{8}\mathrm{e}^{-\frac{x^2}{4\,bt}}\,(\pi\,bt)^{-\frac{3}{2}}, \tag{3}$$

where N_0 is a constant related to the initial number of tumor cells. This is a solution for an untreated glioma and as mentioned previously, we too will consider untreated gliomas.

In the nineteenth century, Sophus Lie [15] described a technique to classify certain equations that are reducible to simple equations. However, this particular application of his work is certainly not trivial. This is our approach in the present paper.

In the recent past, Mahomed [17] had discussed transformations of parabolic equations to simple equations, like the heat equation. In his work, complicated transformation formulae are presented, but simple transformations can easily be found by inspection and by understanding Lie's classification work. We require simple transformations that can incorporate initial values.

Transformations to simple models like the heat equation are not new. In fact, in mathematical financial modelling, Black and Scholes [2] were the first to reduce a financial equation named after them, to the classical heat equation. Notably in [3], Kolmogorov related equations, transformed to the backward heat model were under investigation. The solution of equations such as (1) can be found via fundamental solutions [12, 7] (a particular solution with specific singularities), which in fact is an invariant solution [13].

We present exact solutions of the Burgess equation based on an optimal one dimensional subalgebra. However, in this paper we also manipulate point symmetries in a technique that ensures the initial condition is satisfied. We note that group invariant solutions are usually considered free of initial or boundary values. As a consequence of this study, we offer a mathematical treatment of simplifying an important equation in medical biology. We remark that there are direct methods for symmetry reductions without using group theory in the literature, see the CK method [6] or a modified version [16].

The organization of the study is as follows. In Section 2, we transform the Burgess equation into the one dimensional heat transfer equation, followed by the construction of invariant solutions in two comprehensive ways. The first approach is a classical one that makes use of the optimal system of one dimensional subalgebras, and secondly, an initial-value problem. Section 3 describes the primary results of this investigation where we establish certain characteristics of the obtained solutions of (1). We conclude our results in Section 4.

2. Transformations and solutions.

It is possible to transform (1) to the classical heat equation by a simple change of variables. This idea provides a mathematical tool to solve (1) via group invariant properties of the heat equation and a Cauchy problem that satisfies an initial condition (2).

Therefore we establish the following theorem.

Theorem 2.1. *Eq. (1) is converted to*

$$\omega_\tau - \omega_{xx} = 0, \tag{4}$$

which is the 1+1 heat equation, under the transformations

$$\tau = bt, \tag{5}$$

followed by

$$u(x,t) = \omega(x,\tau)\exp\left(-\ln x + \frac{p}{b}\tau\right). \tag{6}$$

Proof. A straightforward application of (5)-(6), renders Eq. (1) to the form (4). The same invertible transformations give us that the initial condition (2) becomes

$$\omega(x,0) = x\zeta(x). \tag{7}$$

□

Next, we divide our approach into two parts. In the first approach, we use the standard symmetry based method to find exact solutions, and in the second approach, we apply symmetries in conjunction with an initial-value problem. Both approaches yield valuable solutions that provide detailed insights into the mathematical modelling of gliomas.

2.1. The classical symmetry invariant method.

The symmetry generators of the heat equation (4), are given in the most general form as

$$X = \xi(x,\tau,\omega)\frac{\partial}{\partial x} + \eta(x,\tau,\omega)\frac{\partial}{\partial \tau} + \phi(x,\tau\omega)\frac{\partial}{\partial \omega}, \tag{8}$$

or, equivalently

$$\begin{aligned} X \quad = \quad & \left(4c_1\tau^2 + 2c_2\tau + c_6\right)\frac{\partial}{\partial \tau} + \left(4c_1 x\tau + c_2 x + 2c_3\tau + c_4\right)\frac{\partial}{\partial x} \\ & \times \left(\left(c_1(-2\tau - x^2) - c_3 x + c_5\right)\omega + \alpha(x,\tau)\right)\frac{\partial}{\partial \omega}. \end{aligned} \tag{9}$$

In the above expression, the function $\alpha(x,\tau)$ is an arbitrary solution that satisfies the heat equation, i.e. $\alpha_\tau = \alpha_{xx}$.

The Lie point symmetries of (4) are well-known, they are:

$$\begin{aligned} X_1 = \frac{\partial}{\partial x}, \quad X_2 = \frac{\partial}{\partial \tau}, \quad X_3 = \omega\frac{\partial}{\partial \omega}, \\ X_4 = x\frac{\partial}{\partial x} + 2\tau\frac{\partial}{\partial \tau}, \quad X_5 = 2\tau\frac{\partial}{\partial x} - x\omega\frac{\partial}{\partial \omega}, \\ X_6 = 4\tau x\frac{\partial}{\partial x} + 4\tau^2\frac{\partial}{\partial \tau} - (x^2+2\tau)\omega\frac{\partial}{\partial \omega}, \\ X_\alpha = \alpha(x,\tau)\frac{\partial}{\partial \omega}. \end{aligned} \tag{10}$$

The optimal one dimensional subalgebra [20] based on the above generators are

$$X_1,\ X_2 + cX_3,\ X_2 - X_5,\ X_2 + X_6 + cX_3,\ X_4 + 2cX_3,$$

where $c \in \mathbb{R}$. The invariant solutions based on these subalgebras are divided into the following five cases:

Case (i) X_1**.** An exact solution of (4) is

$$\omega(x, \tau) = C_1, \tag{11}$$

where C_1 denotes an arbitrary constant hereunder. A reversal of the transformations (5) and (6) from Theorem 2.1, gives the exact solution for (1), viz.

$$u(x, t) = C_1 \exp\left(-\ln x + pt\right). \tag{12}$$

Case (ii) $X_2 + cX_3$**.** An exact solution of (4) is

$$\omega(x, \tau) = \left(C_1\, \mathrm{e}^{\sqrt{c}x} + C_2\, \mathrm{e}^{-\sqrt{c}x}\right) \mathrm{e}^{c\tau}, \tag{13}$$

C_2 is an arbitrary constant hereunder, so that from Theorem 2.1, we have the exact solution for (1), viz.

$$u(x, t) = \frac{1}{x}\left(C_1\, \mathrm{e}^{2\sqrt{c}x} + C_2\right) \mathrm{e}^{-\sqrt{c}x+(cb+p)t}. \tag{14}$$

For $c = 0$, we have

$$\omega(x) = C_1 x + C_2, \tag{15}$$

and a reversal of the transformations (5) and (6) from Theorem 2.1, gives the exact solution for (1), viz.

$$u(x, t) = (C_1\, x + C_2)\, \mathrm{e}^{-\ln(x)+pt}. \tag{16}$$

Case (iii) $X_2 - X_5$**.** An application of the invariants of this subalgebra produces the exact solution of (4) as

$$\omega(x, \tau) = \left(C_1 \operatorname{Ai}\left(\tau^2 + x\right) + C_2 \operatorname{Bi}\left(\tau^2 + x\right)\right) \mathrm{e}^{x\tau + \frac{2\,\tau^3}{3}}, \tag{17}$$

where $Ai(x)$ and $Bi(x)$ are the *Airy Ai* and *Airy Bi* functions, respectively. A reversal of the transformations (5) and (6) from Theorem 2.1, gives the exact solution for (1), namely

$$u(x, t) = \frac{C_1 \operatorname{Ai}\left(b^2t^2 + x\right) + C_2 \operatorname{Bi}\left(b^2t^2 + x\right)}{x} \mathrm{e}^{\frac{2\,b^3t^3}{3} + \frac{(3\,xb+3\,p)t}{3}}. \tag{18}$$

Case (iv) $X_2 + X_6 + cX_3$**.** This subalgebra gives us the exact solution of (4), that is

$$\omega(x, \tau) = \frac{\left(C_1\, M_{\frac{i}{4}c,\,\frac{1}{4}}\left(\frac{ix^2}{4\,\tau^2+1}\right) + C_2\, W_{\frac{i}{4}c,\,\frac{1}{4}}\left(\frac{ix^2}{4\,\tau^2+1}\right)\right)}{\sqrt{x}} \times \mathrm{e}^{\frac{1}{8\,\tau^2+2}\left(\left(-4\,\tau^2-1\right)c \arctan\left(\frac{1}{2\,\tau}\right)-2\,\tau x^2\right)}, \tag{19}$$

where $W(\mu, \nu, z)$ and $M(\mu, \nu, z)$ are Whittaker functions.

In this case, a reversal of the transformations from Theorem 2.1, gives the exact solution for (1), viz.

$$u(x, t) = \left(C_1\, M_{\frac{i}{4}c,\,\frac{1}{4}}\left(\frac{ix^2}{4\,b^2t^2+1}\right) + C_2\, W_{\frac{i}{4}c,\,\frac{1}{4}}\left(\frac{ix^2}{4\,b^2t^2+1}\right)\right) \times \mathrm{e}^{\frac{1}{8\,b^2t^2+2}\left(\left(-4\,b^2ct^2-c\right) \arctan\left(\frac{1}{2\,bt}\right)+8\,b^2pt^3+\left(-2\,bx^2+2\,p\right)t\right)} x^{-\frac{3}{2}}. \tag{20}$$

Case (v) X_4+2cX_3**.** The symmetry invariants of the subalgebra produce the exact solution of (4) as

$$\omega(x,\tau)=\mathrm{e}^{-\frac{x^2}{4\tau}}\left(\frac{\tau}{x^2}\right)^{c-\frac{1}{2}}\left(U\left(c+1,\,\frac{3}{2},\,\frac{x^2}{4\,\tau}\right)C_2+M\left(c+1,\,\frac{3}{2},\,\frac{x^2}{4\,\tau}\right)C_1\right)x^{2\,c},\tag{21}$$

where $U(\mu,\nu,z)$ and $M(\mu,\nu,z)$ are Kummer functions.

Finally, a reversal of the transformations (5) and (6) from Theorem 2.1, gives the exact solution for (1), viz.

$$u(x,t)\\=\mathrm{e}^{\frac{4\,pt^2b-x^2}{4\,bt}}\left(\frac{bt}{x^2}\right)^{c-\frac{1}{2}}\left(U\left(c+1,\,\frac{3}{2},\,\frac{x^2}{4\,bt}\right)C_2+M\left(c+1,\,\frac{3}{2},\,\frac{x^2}{4\,bt}\right)C_1\right)x^{2\,c-1}.\tag{22}$$

2.2. **The Cauchy problem via symmetries.** In addition to the above invaraint solutions, it is of great interest to explore exact solutions subject to an initial-value problem. In this regard, the 1+1 heat equation is a fascinating model that admits a remarkable fundamental solution. In this subsection, we illustrate how symmetry generators plus the fundamental solution, solves a Cauchy problem for the heat equation. This process, once the transformations of Theorem 2.1 are reversed, leads to the solution of (1) subject to the IC. This process has been successfully applied to other models, particularly in the mathematics of finance [5, 14, 18, 10].

We recall that the fundamental solution of (4) is

$$A(x,\tau):=\begin{cases}\frac{1}{\sqrt{4\pi\tau}}e^{-\frac{x^2}{4\tau}}, & (x\in\mathbb{R},\tau>0),\\ 0, & (x\in\mathbb{R},\tau<0)\end{cases}\tag{23}$$

which is singular at (0,0). The function $A(x-\theta,\tau)$ is also a solution of (4) for each fixed $x\in\mathbb{R}$, then consequently the convolution [9]

$$\omega(x,\tau)=\int_{\mathbb{R}}A(x-\theta,\tau)\omega(\theta,0)d\theta\quad(x\in\mathbb{R},\tau>0),\tag{24}$$

is another solution to the heat model (4). For a discussion on the uniqueness of this solution, we refer the reader to [22].

We recall (9) and apply the invariant surface condition (ISC) [20]

$$\xi\omega_x+\eta\omega_\tau-\phi=0,\tag{25}$$

where it is imposed that $\tau=0$. Hence, for $F(x)=\omega(x,0)$, this leads to the condition [11]

$$\frac{\phi(x,0,F(x))-\xi(x,0,F(x))F'(x)}{\eta(x,0,F(x))}=\omega_{xx}.\tag{26}$$

Therefore (26) translates to an IC,

$$\alpha(x,0)=\left(c_1x^2+c_3x-c_5\right)F(x)+\left(c_2x+c_4\right)F'(x)+c_6F''(x).\tag{27}$$

Equation (27) is a general initial condition and it provides less restrictive criteria on the initial values so that they may be obtained by a symmetry. We now demonstrate some selective solutions, but more exist and can be found by the same process.

We emphasise that the function $\alpha(x,\tau)$ is also a solution to (4), so we may design an initial problem for the heat equation, viz.

$$\begin{cases} \alpha_\tau - \alpha_{xx} = 0, & \text{in } \mathbb{R}\times(0,\infty), \\ \alpha(x,0), & \text{on } \mathbb{R}\times\{\tau=0\}. \end{cases} \tag{28}$$

If one can solve (28), we will find $\alpha(x,\tau)$, which would give us a new symmetry that solves the original model (1) subject to its IC.

A description of the steps in performing this calculation follows. Suppose we let $c_4 = 1, c_1 = c_2 = c_3 = c_5 = c_6 = 0$, where more solutions can be found from other choices of c_i. Hence

$$\alpha(x,0) = F'(x),$$

and

$$X = \frac{\partial}{\partial x} + \alpha(x,\tau)\frac{\partial}{\partial \omega}. \tag{29}$$

Thus, via the ISC (25), we obtain that the solution to (4) is

$$\omega(x,\tau) = \int \alpha(x,\tau)dx + H(\tau). \tag{30}$$

We let $H(\tau)=0$ for simplicty and use Theorem 2.1 to obtain an exact solution of (1) subject to its IC.

Let us consider two further cases, not from subalgebras as before, but from different IC's.

Case (vi). Take the Gaussian pulse as the IC, $\zeta(x) = \frac{N_0 e^{-x^2}}{\sqrt{\pi}}$, and by convolution,

$$\alpha(x,\tau) = \frac{\left(-2\,x^2+4\,\tau+1\right)N_0}{\sqrt{\pi}} \mathrm{e}^{\frac{x^2}{4\,\tau(4\,\tau+1)}}\mathrm{e}^{-\frac{x^2}{4\,\tau}}\left(4\,\tau+1\right)^{-\frac{5}{2}}. \tag{31}$$

By the application of (30), the solution to the heat equation is

$$\omega(x,\tau) = \frac{xN_0}{\sqrt{\pi}}\mathrm{e}^{\frac{x^2}{4\,\tau(4\,\tau+1)}-\frac{x^2}{4\,\tau}}\left(4\,\tau+1\right)^{-\frac{3}{2}}, \tag{32}$$

and by Theorem 2.1, the Burgess equation has solution, subject to (2), as

$$u(x,t) = \frac{N_0\mathrm{e}^{pt}}{\sqrt{\pi}}\mathrm{e}^{-\frac{x^2}{4\,bt+1}}\left(4\,bt+1\right)^{-\frac{3}{2}}. \tag{33}$$

This solution is a similar version of the exact solution (3), presented in [4] by Burgess et al. A simple check that this solution is subject to (2) can be seen if we let $t=0$ in (33).

Case (vii). Consider another IC, for example, the exponential $\zeta(x) = N_0 e^x$. By the same procedure, we find

$$\alpha(x,\tau) = \mathrm{e}^{-\frac{x^2}{4\,\tau}}N_0\mathrm{e}^{\frac{(2\,\tau+x)^2}{4\,\tau}}\left(2\,\tau+x+1\right), \tag{34}$$

and the heat equation's solution is then

$$\omega(x,\tau) = \left(2\,\tau+x\right)\mathrm{e}^{-\frac{x^2}{4\,\tau}+\frac{(2\,\tau+x)^2}{4\,\tau}}N_0. \tag{35}$$

Finally, Burgess' equation for gliomas has solution, subject to (2), as

$$u(x,t) = \frac{\left(2\,bt+x\right)\mathrm{e}^{(b+p)t+x}N_0}{x}. \tag{36}$$

Once again, if we let $t=0$, we see that (36) is subject to the IC.

3. **Mathematical results.** A natural progression of the above Lie point symmetry analysis is to contextualise the results implied by the exact solutions. For our analysis, we adopt the following parameter assumptions from [4]: the tumor grows from a point cell value $N_0 = 1.2 \times 10^6$, the radius $x = 1.5$ cm is equivalent to the time of diagnosis of the tumor, defined as t_i, a radius of $x = 3$ cm is equivalent to the time of death, defined as t_d and a critical cell density value is 8.0×10^6 cells/cm^3. Above the critical cell density, the glioma is detectable by scans, hence its importance. We note that the highest concentration of cells is at the centre $x = 0$.

By convention, there are four prototype (untreated) gliomas, described by the size of proliferation p and diffusion b, that is, 10 fold variations in diffusion and proliferation may be considered, with high proliferation at the value $p = 0.012$, while high diffusion is set as $b = 0.0013$ [4]. The diffusion rate in cm^2/day is estimated by observed rates in CT scans [4].

We differentiate between the following growth characteristics or four prototypes:
A: High Grade (high proliferation/diffusion),
B: Intermediate (high proliferation),
C: Intermediate (high diffusion),
D: Low Grade (low proliferation/diffusion).

We present some interesting results from our cases in the figures and tables that follow. In Table 1, we consider cases (i)-(iii) in relation to the four prototypes, in order to calculate the survival years between diagnosis and death. Case (i) and (ii) when $c = 0$, is independent of diffusion, so we omit the B and C prototypes, due to redundancy.

Table 1. Growth characteristics of four prototypic tumors

Case	Growth Characteristic	Proliferation p	Diffusion b	t_i	t_d	Survival (years)
(i)	A	0.012	-	0.53	0.68	0.15
	D	0.0012	-	5.26	6.84	1.58
(ii)	A	0.012	0.0013	0.78	1.24	0.46
$c \neq 0$	B	0.012	0.00013	0.86	1.35	0.49
	C	0.0012	0.0013	4.17	6.57	2.40
	D	0.0012	0.00013	7.83	12.35	4.52
$c = 0$	A	0.012	-	0.33	0.39	0.06
	D	0.0012	-	3.32	3.77	0.45
(iii)	A	0.012	0.0013	1.02	1.50	0.48
	B	0.012	0.00013	1.11	1.78	0.67
	C	0.0012	0.0013	10.24	12.67	2.43
	D	0.0012	0.00013	10.12	14.49	4.37

In Table 2, we report on the tumor cell density under the four types of gliomas, using cases (vi) and (vii). For these results, we adopt the data in [23] and [4], where time of diagnosis is $t_i = 1.35$ and time of death is $t_d = 1.84$.

In contrast, Figures 1-3, examines the behaviour of cell density per increasing radius, where again, time of diagnosis is $t_i = 1.35$ and time of death is $t_d = 1.84$. Some high grade tumors A and intermediate grade tumors B are considered for cases (i), (ii), (iii), (v), (vi) and (vii).

TABLE 2. Cell density under time of diagnosis t_i and time of death t_d

Evolution of an untreated glioma - four prototypes

	(vi)		**(vii)**	
Stage	$\mathbf{t_i}$	$\mathbf{t_d}$	$\mathbf{t_i}$	$\mathbf{t_d}$
Number of cells under A	1.99×10^7	3.05×10^7	7.0×10^9	2.9×10^{11}
Number of cells under B	2.97×10^7	1.74×10^8	2.31×10^9	8.85×10^{10}
Number of cells under C	0.97×10^5	0.21×10^6	3.42×10^7	2.05×10^8
Number of cells under D	1.44×10^5	1.01×10^6	1.12×10^7	6.23×10^7

Primary Observations:

a) We observe from Figs. 1-3, which provides the spatial profile of tumor cells at the time of diagnosis and death, that the cell densities around the centre, approach between 100 and 100 000 times the critical cell density.

b) In Table 1, as expected, high grade gliomas have the shortest survival time, with low grade gliomas having the longest life expectancy.

c) The survival years reported in [23] and also applied in [4], for high grade gliomas is 0.49. From table 1, we note that our survival expectations for high grade gliomas in (*ii*) and (*iii*) are close to this value, even though the time of diagnosis and death differ markedly. The exact value of 0.49 years is observed for an intermediate tumor in (*ii*). Hence, both (*ii*) and (*iii*) are good candidate solutions for further insight.

d) From Table 2, we remark that diffusion and proliferation rates have a significant impact on cell densities.

e) Under the survival estimate of 0.49 years, we note that in Table 2, the number of cells under glioma prototype A (and B) exceed the critical cell density for time of death and diagnosis, for the solutions (vi) and (vii) found under initial conditions.

f) We already know that the solution of case (vi) is very similar to Burgess' solution, and hence this case encompasses all the insights offered by Burgess et al. [4].

4. **Conclusion.** Although highly simple, the Burgess equation is a remarkable and fundamental illustration of tumors and their invasive and growth properties. Thus, the equation was analysed by Lie symmetry generators to find exact solutions, either subject to an initial condition or governed by one of its one dimensional subalgebras. Such models are often characterised by difficult solution methods, however we have illustrated a simple and effective transformation to deal with this equation.

In the present paper, under the solutions obtained, we have discussed the expected survival time of a diagnosed patient and examined the growth of the untreated glioma. The proliferation and diffusion rate of the tumor in the above mentioned problem proved to be significant as shown by the survival results of four prototype gliomas.

Avenues for further investigation via symmetries are substantial, and include simulations with treatment therapies, the incorporation of tumor cell size dynamics, and other factors such as age-group, gender etc. The development and extension of symmetry analysis to such models will shed light into tumor modelling, and as shown here, symmetry invariant solutions are able to contribute to the understanding of the dynamics of tumor cells. From a mathematical point of view, symmetry properties

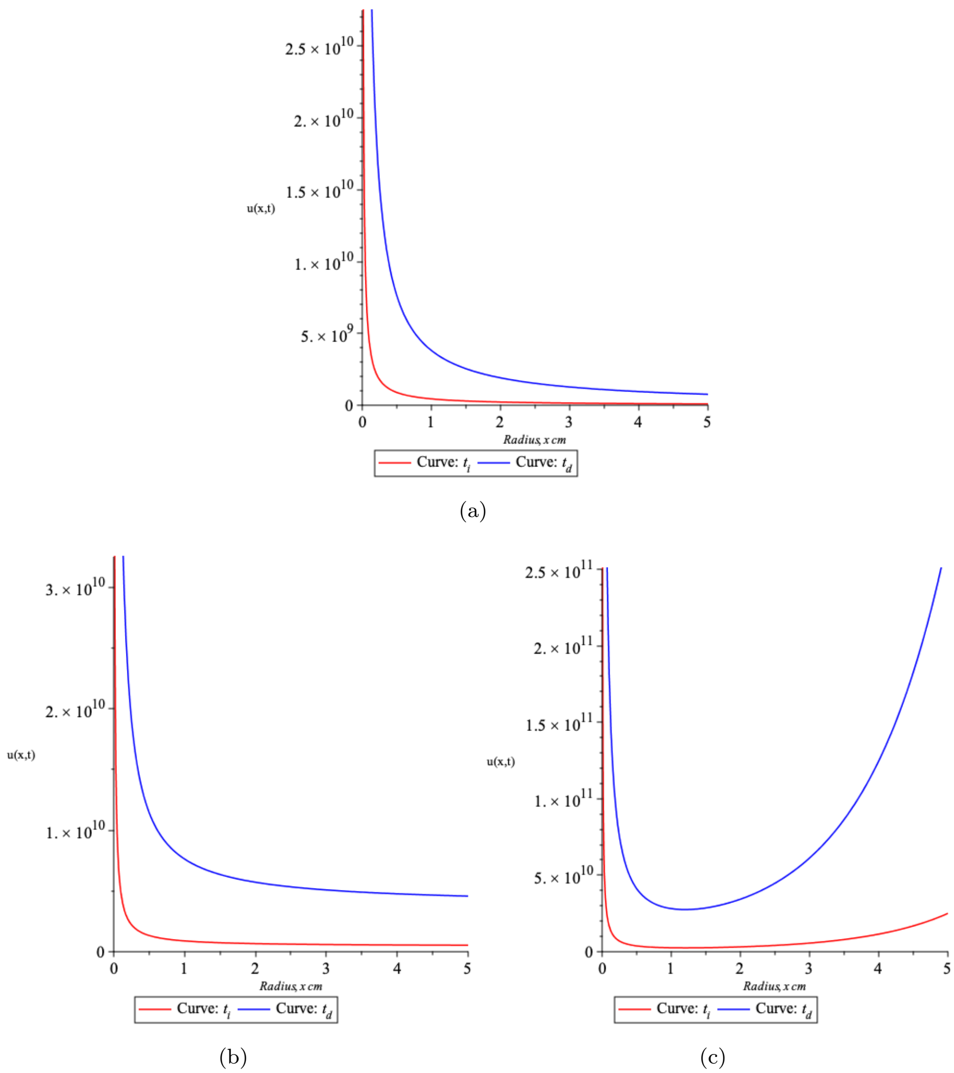

FIGURE 1. Graphical illustration of the tumor cell density versus radius under parameter selection $C_1 = C_2 = 1.2 \times 10^6$ and $c = 1$: (a) of a high grade tumor A of Eq. (12); (b) of a high grade tumor A of Eq. (14); (c) of a high grade tumor A of Eq. (16).

have always been at the forefront in analysis, and initial-data problems should not be avoided by any perceived symmetry method limitations. Indeed, the enhanced applications of symmetries in biological and medical fields, are far-reaching.

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Competing interests. None.

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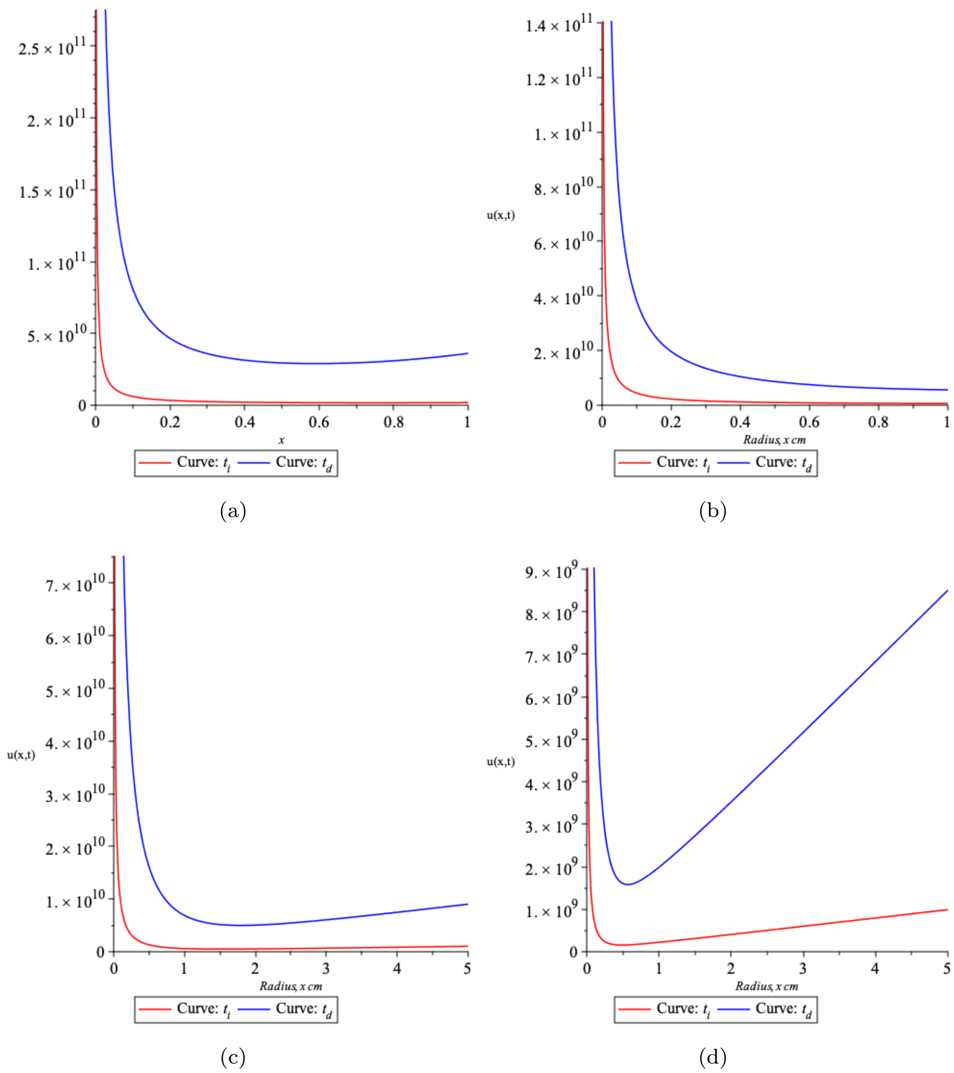

FIGURE 2. Graphical illustration of the tumor cell density versus radius under parameter selection $C_1 = C_2 = 1.2 \times 10^6$ and $c = 1$: (a) of a high grade tumor A of Eq. (18); (b) intermediate tumor B of Eq. (18) (c) of a high grade tumor A of Eq. (22); (d) intermediate tumor B of Eq. (22)

Data availability. Not Applicable.

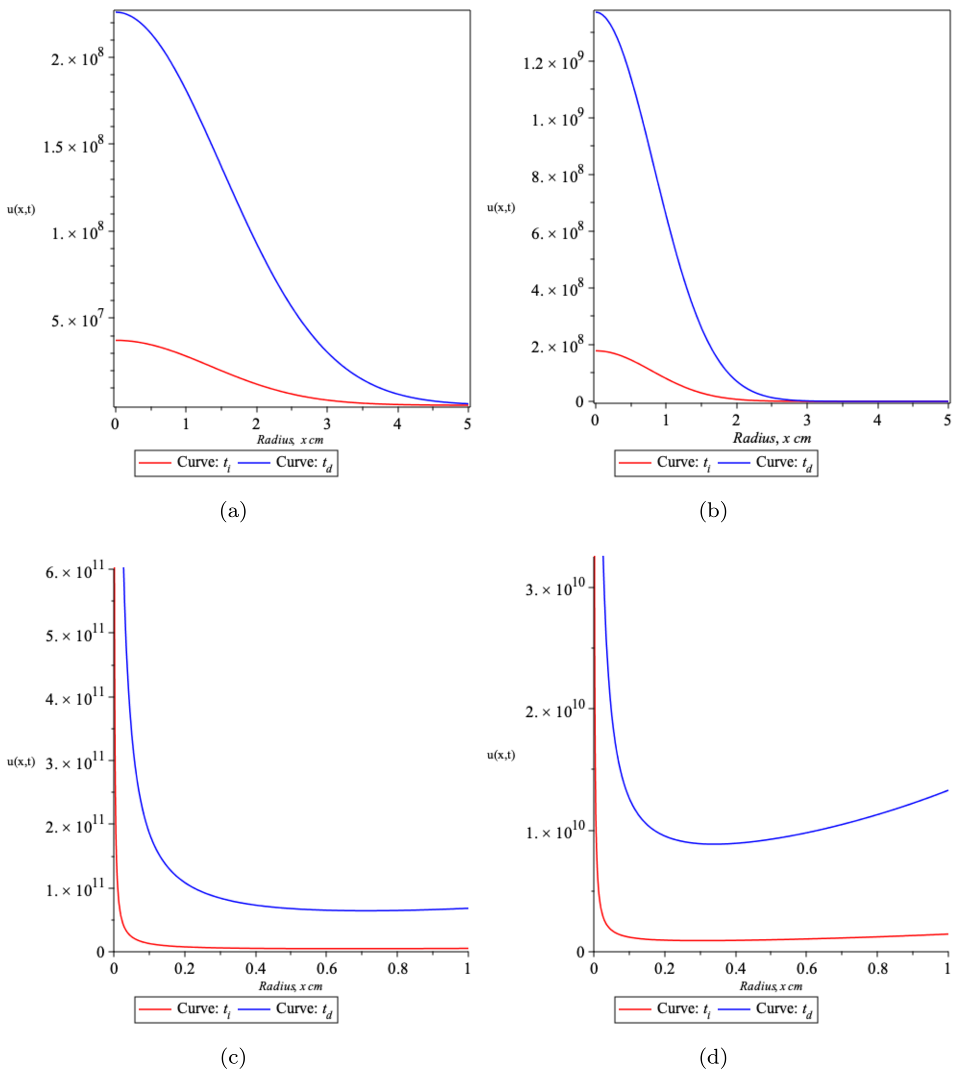

FIGURE 3. Graphical illustration of the tumor cell density versus radius under N_0: (a) of a high grade tumor A of Eq. (33); (b) intermediate tumor B of Eq. (33); (c) of a high grade tumor A of Eq. (36); (d) intermediate tumor B of Eq. (36).

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