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Solving Tumor Growth Dynamic Using Runge-Kutta and Backward Euler Method

Nur Azmina Mohd Suhaimi[1], Norzuria Ibrahim[1*]

[1] *Department of Mathematics and Statistics, Faculty of Applied Sciences and Technology, UTHM Kampus Cawangan Pagoh, Hab Pendidikan Tinggi Pagoh, KM 1, Jalan Panchor, 84600 Pagoh, Muar, Johor, MALAYSIA.*

*Corresponding Author: norzuria@uthm.edu.my
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Abstract

The use of a model of tumor growth was a significant means of improving our understanding of cancer. The Gompertz model is the most common form of nonlinear growth behaviour of tumours that occurs with cancer growth. This study presented the author's analysis of the numerical solution of the Gompertz model for malignant cancers using two numerical methods: the fourth-order Runge-Kutta (RK4) and the Backward Euler methods. The author conducted numerical simulations of the Gompertz model using predetermined initial conditions and parameters, and the numerical solutions were compared to the true analytical solution in order to assess their accuracy. The author performed an error analysis with a variety of different step sizes in order to assess the accuracy of the numerical methods. The analysis of these two methods done using Python with the initial condition data take from Kaggle. The results of the study demonstrated that both numerical methods can be used to approximate the growth behaviour of tumours; however, the RK4 method consistently produces more accurate results as a result of its ability to produce higher-order elapsed time convergence, while the Backward Euler method produces larger amounts of numerical error, especially for larger step sizes. The author concluded that the RK4 method is more appropriate for the accurate simulation of the Gompertz tumour model and that this highlights the importance of selecting appropriate numerical methods and step sizes in order to produce reliable simulations of tumour growth.

1. Introduction

Tumor development is a complicated biological phenomenon caused by irregular cell growth, potentially resulting in benign or malignant tumors and profoundly affecting human health [1],[2]. Grasping tumor development is crucial for enhancing diagnosis, treatment strategies, and clinical decision-making. Mathematical modelling has emerged as a vital method for illustrating the dynamics of tumor growth, enabling researchers to anticipate tumor behaviour over time when experimental or clinical information is scarce. Among different models, the Gompertz growth model is commonly utilized because it effectively represents the sigmoidal growth trend seen in tumors, marked by swift initial expansion followed by stabilization as environmental factors like nutrient supply and space gain prominence [3],[4]. As first-order differential equation along with parameters, it allows the Gompertz model to describe the tumor that grow rapidly at early stages and slowing down when it maximum size in another word called carrying capacity [4],[5]. Although it is effective, the nonlinear characteristic of the Gompertz equation frequently hinders the derivation of analytical solutions, necessitating the use of numerical methods. Numerical analysis is essential for addressing these models, especially in grasping tumor development and assessing treatment effectiveness. Nonetheless, choosing a suitable numerical method continues to be difficult because of the compromises between accuracy, stability, and computational efficiency.

The development of the Gompertz tumor growth model is calculated using two numerical methods: the fourth-order Runge-Kutta (RK4) technique and Backward Euler. Ultimately, the goal of this paper is to determine if one of these two methods produces better results than the other based on accuracy when modelling tumor growth. This paper focuses on the development of a basic ordinary differential equation (ODE) tumor model. Consequently, this study did not involve any tumor progression from host of immune system response, nor does it relate to any human clinical or preclinical data. RK4 is applied directly to the equation as it is an explicit scheme while for Backward Euler is implemented using Newton's method as rootfinder method to solve the nonlinear equations for each time step [6]. All calculations and simulations were conducted using Python programming language, which allowed for the numerical calculation and visualization of various tumor growth dynamics. Numpy and Matplotlib libraries in Python is used to efficiently provided numerical computation and graphical presentation. This makes it suitable for showing the tumor growth simulations [7]. This study offered an understanding of how numerical methods affect modelling of tumor progression, benefits and limitations of using explicit and implicit methods and provides a deeper understanding of how numerical methods can be used to model complex biological systems [2],[7].

2. Methodology

2.1 Mathematical Model for Tumor Growth

Mathematical model often used to test hypothesis, prove and help understand the mechanism system but in term of tumor growth, it can explain the change tumor cell population over time. This help in capture key biological processes such as cell proliferation, death, and resource limitations. In this research, it focusses more on one of tumor growth model which is Gompertz model.

Gompertz model is preferable regression approach that also will show the volume growth of tumor over time [4]. In this model, it involves carrying capacity (K) that means maximum tumor size follow environmental constraints like nutrients and space. It can be shown in the form of:

$$\frac{dy}{dt} = ry\ ln\left(\frac{K}{y}\right) \tag{1}$$

where:

$\frac{dy}{dt}$ = growth rate

y = tumor size

r = relative growth rate

K = carrying capacity

2.2 Step Sizes

In this research, the different step sizes are used for both method RK4 and Backward Euler to resolve tumor growth based on Gompertz model. RK4 method requires moderate step sizes as it has greater accuracy. Meanwhile for Backward Euler method, as it is implicit method and more stable to approach as the tumor growth close to carrying capacity, it allows larger step sizes without risking instability though it introduces numerical damping. Step sizes are chosen to balance computational efficiency with accuracy solution for both methods [6].

2.3 Runge-Kutta Method

This method always used for solving initial-value of differential equations that also important to study explicit and implicit method solving ODEs through time discretization. First-order ordinary differential equations general form is:

$$\frac{dy}{dt} = f(t, y) \quad , y(t) = y_0 \tag{2}$$

It is to determine unknown function of $y(x)$ that satisfies the first order differential equation and corresponding initial values [8]. The unknown function can be solved using RK4 as defined by:

$$y_{i+1}=y_i+\frac{k_1+2k_2+2k_3+k_4}{6}\ ,\ i=0,1,\ldots,n \tag{3}$$

where :

$$k_1 = hf(x_i, y_i) \tag{4}$$

$$k_2 = hf(x_i + \frac{h}{2}, y_i + \frac{k_1}{2}) \tag{5}$$

$$k_3 = hf\left(x_i + \frac{h}{2}, y_i + \frac{k_2}{2}\right) \tag{6}$$

$$k_4 = hf(x_i + h, y_i + k_3) \tag{7}$$

2.4 Backward Euler method

This method stimulates tumor growth model as differential equation system. The benefits are its stability properties and it allow rapid changes in growth behaviour [6]. The equation is:

$$y_{k+1} = y_k + h(f(t_{k+1}, y_{k+1})) \tag{8}$$

where:

h = step sizes

y_k = tumor size at time step k

y_{k+1} = tumor size at next time step $k+1$

$f(t, y)$ = tumor growth dynamics

This equation contains nonlinear algebraic equations. That is when rootfinder is used which is Newton's method. It can find the root of the function in the form of $G(Y) = 0$.

$$Y^{(k+1)} = Y^{(k)} - \frac{G(Y^k)}{G'(Y^k)} \tag{9}$$

where:

$$G(Y^k) = Y - y_n - hf(t_{n+1}, Y)$$

$$G'(Y^k) = 1 - h\frac{\partial f}{\partial y}(t_{n+1}, Y)$$

2.5 Python Application

Python is a programming language that was created by Guido van Rossum in 1991 and is still popular programming and widely used by everyone. It is a general-propose language that can create many multiple programmes not only limited to specific problem. Python has been used by many non-programmers for variety everyday task such as accountants want to organise their finances report. In this research, libraries like Numpy and Matplotlib will be used to compare the result between the two method and plot the graph to see the result clearer [9].

3. Result and Discussion

3.1 Numerical Simulation for Tumor Growth Model

The numerical result that can be obtained demonstrates typical characteristic of tumor growth by Gompertz model with the time interval every 5 minutes for 2 hours. The value from these two methods also compared with the exact solution of the Gompertz model which is:

$$y(t) = Ke(-\left(ln\frac{K}{y_0}\right)e^{-rt}) \tag{10}$$

Evaluate numerical solution against its exact solution help in confirming convergence of numerical methods. As step sizes smaller using both of the method, numerical solution is expected to becomes closer towards the exact solution [10]. This verifies that numerical method is accurately applied.

3.2 Approximation method under different step sizes, h

This section discusses the comparison of different step sizes on accuracy between the two method which are RK4 and Backward Euler method. It involves initial conditions using tumor size, y_0= 5.37561155, growth rate, r = 0.111875621 and carrying capacity, K = 100. The results will show how well they can accurately perform tasks at different step sizes which are h = 0.01 and h = 0.05 (11).

Table 1 Value tumor sizes when h = 0.01

Time (minutes)	Runge-kutta fourth method (cm)	Backward euler method (cm)	Exact value Tumor model
0.0	5.3756	5.3756	5.3756
10.0	5.6800	5.6803	5.6800
20.0	5.9765	5.9771	5.9765
30.0	6.3022	6.3032	6.3022
40.0	6.6391	6.6405	6.6391
50.0	6.9664	6.9681	6.9664
60.0	7.3250	7.3271	7.3250
70.0	7.6947	7.6972	7.6947
80.0	8.0529	8.0558	8.0529
90.0	8.4443	8.4476	8.4443
100.0	8.8468	8.8505	8.8468
110.0	9.2357	9.2398	9.2357
120.0	9.6596	9.6642	9.6596

From the values in Table 1, it can be concluded that both methods are closely overlap with the exact value when h=0.01 is used throughout the time interval. RK4 almost achieves perfect alignment with the exact value which means it has a high accuracy value. Backward Euler that also follows the same trend with exact however it has slightly different values that were barely noticeable and the differences can be seen by the value in the Table 1. Even though both method approximate with the exact value, it still shows that RK4 gives out identical value with the exact value which indicates higher accuracy than the Backward Euler that shows small differences to the exact value which indicates lower accuracy.

Table 2 Value tumor sizes when h = 0.05

Time (minutes)	Runge-kutta fourth method (cm)	Backward euler method (cm)	Exact value Tumor model
0.0	5.3756	5.3756	5.3756
10.0	5.6436	5.6450	5.6436
20.0	6.0142	6.0177	6.0142
30.0	6.3022	6.3073	6.3022
40.0	6.5989	6.6056	6.5989
50.0	7.0080	7.0169	7.0080
60.0	7.3250	7.3356	7.3250
70.0	7.6506	7.6630	7.6506
80.0	8.0983	8.1132	8.0983
90.0	8.4443	8.4609	8.4443

100.0	8.7988	8.8174	8.7988
110.0	9.2850	9.3061	9.2850
120.0	9.6596	9.6826	9.6596

When the step sizes changed into h = 0.05, the difference between two methods becomes more apparent like stated in the Table 2. RK4 method still produce result that are close to the exact value showing higher accuracy even with the bigger step sizes. Nonetheless, Backward Euler method shows much bigger differences from the exact value. This suggests that the accuracy of Backward Euler decreases quickly as a larger step sizes is used. The table indicates that larger step sizes reduce numerical accuracy and it confirms that RK4 method is more dependable than the Backward Euler method for estimating tumor size using the Gompertz tumor growth model.

3.3 Error Analysis

After calculating the difference between the step sizes, this section presented error analysis as shown in Fig. 1to measure accuracy of RK4 and Backward Euler method. This is calculated by finding difference between numerical solution and accurate analytical solution of Gompertz model.

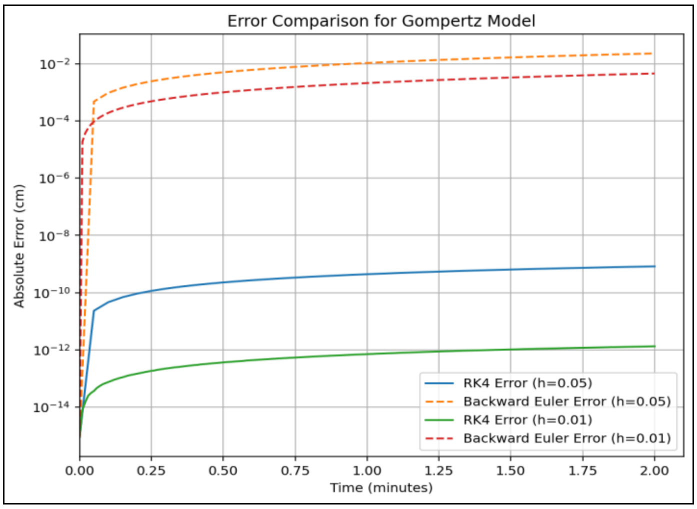

Fig. 1 Error analysis

Table 3 Error values of RK4 and Backward Euler

Time (minutes)	Runge-kutta fourth method h = 0.01 (cm)	Runge-kutta fourth method h = 0.05 (cm)	Backward euler method h = 0.01 (cm)	Backward euler method h = 0.05 (cm)
0.0	$8.8818e-16$	$8.8818e-16$	$8.8818e-16$	$8.8818e-16$
10.0	$1.2701e-13$	$6.9305e-11$	$3.2893e-04$	$1.4542e-03$
20.0	$2.4336e-13$	$1.6006e-10$	$6.5097e-04$	$3.4757e-03$
30.0	$3.6415e-13$	$2.2682e-10$	$1.0058e-03$	$5.0509e-03$
40.0	$4.8217e-13$	$2.9241e-10$	$1.3729e-03$	$6.6740e-03$
50.0	$5.9242e-13$	$3.7797e-10$	$1.7290e-03$	$8.9083e-03$
60.0	$7.0699e-13$	$4.4068e-10$	$2.1179e-03$	$1.0633e-02$
70.0	$8.2245e-13$	$5.0212e-10$	$2.5168e-03$	$1.2397e-02$
80.0	$9.2903e-13$	$5.8201e-10$	$2.9006e-03$	$1.4804e-02$
90.0	$1.0285e-12$	$6.4038e-10$	$3.3166e-03$	$1.6647e-02$
100.0	$1.1333e-12$	$6.9741e-10$	$3.7400e-03$	$1.8519e-02$
110.0	$1.2275e-12$	$7.7136e-10$	$4.1446e-03$	$2.1054e-02$
120.0	$1.3287e-12$	$8.2524e-10$	$4.5799e-03$	$2.2981e-02$

The RK4 method solutions were very close to the exact analytical solution when using h = 0.01, and the reason is that the method is more accurate and converge at a higher order of accuracy than the Backward Euler solutions. The Backward Euler method had the largest errors visually and numerically, especially for h = 0.05, indicating that first-order methods are less accurate [12]. Although all of the computed errors very small, the error analysis showed that the RK4 method produced a much better estimate of the Gompertz tumor growth model due to its higher-order explicit formulation that gave it a closer match to the exact solution [13].

4. Conclusion

This research examined the numerical resolution of the Gompertz tumor growth model through the RK4 method and the Backward Euler method, with the objective of assessing their accuracy in estimating the exact analytical solution. Numerical simulations showed that both approaches were able to replicate the typical sigmoidal growth pattern of tumor development; nonetheless, the RK4 method consistently yielded results that were more in line with the precise solution, especially for smaller step sizes, owing to its superior convergence characteristics [14]. The Backward Euler method, though yielding acceptable approximations, showed noticeably larger errors with increasing step sizes, highlighting the constraints of first-order methods in effectively representing nonlinear tumor dynamics [12]. These results validate that decreasing the step sizes enhances numerical precision for both techniques, with RK4 continuing to be the more dependable method when accurate tumor growth estimation is needed [13]. Subsequent studies could build on this research by integrating adaptive step-sizes techniques, different tumor growth models, parameters that vary over time, and more intricate frameworks like spatial or multi-dimensional models to boost realism and predictive accuracy [7].

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Conflict of Interest

Authors declare that there is no conflict of interests regarding the publication of the paper.

Author Contribution

The authors confirm contribution to the paper as follows: ***study conception and design****: Nur Azmina Mohd Suhaimi, Norzuria Ibrahim;* ***data collection****: Nur Azmina Mohd Suhaimi;* ***analysis and interpretation of results*** *Nur Azmina Mohd Suhaimi, Norzuria Ibrahim;* ***draft manuscript preparation****: Nur Azmina Mohd Suhaimi, Norzuria Ibrahim. All authors reviewed the results and approved the final version of the manuscript.*

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