NUMERICAL COMPARISON OF RUNGE-KUTTA (RK5) AND NEW ITERATIVE METHOD (NIM) FOR SOLVING METASTATIC CANCER MODEL

Falade Kazeem Iyanda^{1*}, Tiamiyu Abd'Gafar Tunde² and Umar Isa³

^{1,3}Department of Mathematics, Faculty of Computing and Mathematical Sciences Kano University of Science and Technology Wudil, P.M.B 3244 Kano State Nigeria ²Department of Mathematics, Federal University of Technology, Minna Niger State Nigeria ^{1*}faladekazeem2016@kustwudil.edu.ng, ²abdgafartunde@yahoo.com, ³isaumar32@gmail.com

ABSTRACT

This paper attempts to present and employ Runge-Kutta Method of fifth-order (RK5) and New Iterative Method for the numerical solution of metastatic cancer model which occur in two compartments of cancer environment. These methods have been proved to be powerful mathematical tools for various phenomena in biomathematics and it is extremely effective for linear and non-linear systems of differential equations. Our numerical experiments illustrate the effect of parameters β_1 , β_2 and β_3 on cancer models which are responsible for the spread or reduction of cancer cells through the boundary of an organ tissue. The results obtained are compared with analytical solutions and show that (RK5) and NIM are powerful numerical techniques to solve systems of differential equations. Finally, all computations and algorithms are implemented using MAPLE 18 software version.

Keywords: Analytical solutions, MAPLE 18 Mathematical software, Metastatic cancer model, New Iterative Method (NIM), Runge-Kutta method (RK5).

Received for review: 11-08-2020; Accepted: 26-02-2021; Published: 08-03-2021

1. Introduction

Mathematical modeling is a prominent practice in almost all fields of pure and applied sciences. Modeling serves as a tool for researchers to formalize and quantitatively understand physical and chemical phenomena observed in reality via the language of mathematics (Rasmuson *et al.*, 2014). It is with this concern that researchers and concerned individuals have actively worked on ways of understanding and proffering solutions over the past decades. In a recent study conducted by the United Nation (UN), it was revealed that by every year there are approximately 8.2 million cancer-related deaths worldwide. Metastasis is the major cause of cancer death which occurs when the disease reaches its lethal stage via the uncontrolled spreading of cancer cells to invade a nearby connective tissue and other key organs in the human body. The metastasizing primary tumor cells are not the only agents that drive the progression of metastasis. Instead, metastasis is a systematic process that involves the interaction of cancer cells among a community of various biochemical and cellular factors localized in the tumor microenvironment at both the primary and secondary tumor compartments (Cox *et al.*, 2016).

Several scientists have worked on understanding the behaviors and development of the cancerous cells including (Hanin & Zaider, 2011; Lorenzo-Herrero *et al.*, 2019; Liu *et al.*, 2016; Thakur & Rao, 2016 and Benzekry *et al.*, 1970) and many have as well worked on

developing Mathematical models for understanding cancer cells with proposed cure parameters through surgery, Radiotherapy, chemotherapy etc. (see Dan *et al.*, 2016; Pinho *et al.*, 2011; Kolev *et al.*, 2011). Moreover, the numerical solution of mathematical models by systems of ordinary differential equations has been widely studied in recent years.

Yen *et al.* (2018) used a remodeling extracellular matrix to obtain numerical solutions of the Metastatic Cancer model. The Quantitative Analysis of the Tumor/Metastasis system and its optimal therapeutic control was carried out by Sebastien *et al.* (2017), modelling and simulation of tumor development, treatment and control was presented by Bellomo & De Angelis (2003), Mathematical population dynamics models to describe the spread of metastatic cancer was considered by Daniel *et al.* (2011), while Nikos & Mastorakis (2016) presented numerical solution of mathematical models of cancer growth and optimal cancer therapy and to mention a few.

This study is concerned with metastatic cancer model tracking cancerous cells in two compartments; the first compartment encompasses proliferating cells which includes active cells that can grow rapidly to another compartment with the target tissue cells. We determine the equilibrium point and analyze the stability. Furthermore, to reduce computational time and length involved in calculating Ks in Runge-Kutta and evaluation involved in New iterative method, we hereby formulate a three step Maple 18 software code for the numerical solutions of equation (1) with suitable initial conditions of parameters.

This paper is arranged as follows: In section 1, a brief introduction on Cancer metastasis was presented. In section 2, Mathematical modeling and metastatic cancer in two compartments was described, section 3 is majorly on equilibrium point and stability analysis of the metastatic model. Section 4 describes two numerical techniques employed and was discussed, in section 5, numerical experiment was demonstrated and finally, section 6 presented numerical results tables, discussion and conclusion.

2. Mathematical Modeling of Metastatic Cancer in Two Compartments

Mathematical models have been used on several occasions as an abstract description of physical, biological and chemical phenomenon. In applied Mathematics, systems of differential equations are the most important tools in modeling metastatic cancer in two compartments. Understanding of the phenomenon, formulations of mathematical models with parameters of the situation and analysis of the metastatic model will further help to understand the behaviors of cancerous cells in the body of humans. Consider two-compartment metastatic cancer model Figure 1, the first compartment (A) houses the proliferating cells and the second compartment (B) encloses quiescent cells. Let be the number X of arrested cells on the boundary of the tissue in compartment A and Y the number of cells that have invaded the target tissue in compartment B. Cancerous cells pass from compartment A to compartment B at the rate of β_2 in X. Also, cells die from compartment A at the rate of β_1 in X and die from compartment B at the rate β_3 in Y.



Figure 1. Two Compartments Model for Metastatic in Cancer (CERD)

$$\left\{\frac{dX(t)}{dt} = -(\beta_1 + \beta_2)X(t) \ \frac{dY(t)}{dt} = \beta_2 X(t) - \beta_3 Y(t)$$
(1)

subject to initial conditions

$$\begin{cases} X(0) = \omega \\ Y(0) = \phi \end{cases}$$
 (2)

where $\beta_1, \beta_2, \beta_3$ are constants, $\beta_1, \beta_2, \beta_3 > 0$ and ω, φ are the initial numbers of cancerous cells in compartments A and B respectively. The size of the tumor, *M* is defined as

$$M(t) = X(t) + Y(t)$$
(3)

3. Equilibrium Point and Stability Analysis

The metastatic model given in equation (1) will have equilibrium point on $\frac{dX(t)}{dt} = \frac{dY(t)}{dt} = 0$, so the equation will become:

$$\begin{cases} -(\beta_1 + \beta_2)X(t) = 0\\ \beta_2 X(t) - \beta_3 Y(t) = 0 \end{cases}$$
(4)

The point (0, 0) is clearly the equilibrium. We observe that (X(t), Y(t)) = (0,0)The Jacobian matrix as equation (4), can be written as follows;

$$J = \begin{pmatrix} \frac{\partial f_1}{\partial x} & \frac{\partial f_1}{\partial y} \\ \frac{\partial f_2}{\partial x} & \frac{\partial f_2}{\partial x} \end{pmatrix}$$

where

$$f_1 = -(\beta_1 + \beta_2)X$$

$$f_2 = \beta_2 X - \beta_3 Y$$

Implies,

$$J = \begin{pmatrix} -(\beta_1 + \beta_2) & 0\\ \beta_2 & -\beta_3 \end{pmatrix}$$

with characteristic equation,

$$(\lambda + \beta_3)(\lambda + \beta_1 + \beta_2) = 0$$

$$\begin{cases} \lambda_1 = -\beta_3 \\ \lambda_2 = -(\beta_1 + \beta_2) \end{cases}$$

are eigenvalues. Since λ_1 and $\lambda_2 < 0$, it implies the point (0, 0) is a saddle.

4. Description of Numerical Methods

In this section, we present and employ two numerical techniques Runge-Kutta (RK5) and New Iterative Method proposed by Daftardar-Gejji & Jafari (2006) to solve the Metastatic cancer model in two compartments.

4.1 Runge-Kutta fifth order (RK5)

The Runge-Kutta method is an important method for obtaining the approximate solutions of ordinary differential equations. It is one of the most used methods by scientists and engineers. It was named for its creators Carl Runge (1856-1927), which the original idea for such formulas seems to be due and Wilhelm Kutta (Tamer, 2019), which the idea was used more effectively for first-order equations. It has been used extensively to obtain approximate numerical solutions of differential equations of first, second, and higher orders. It transforms second and higher orders into a system of equations of first order. In recent years, several authors have applied Runge-Kutta to solve ordinary differential equations such as direct explicit integrators of RK type for solving special fourth-order ordinary differential equations with an application by Mohammed & Murtaza (2016), Salih et al. (2016) presented fifth order Runge-Kutta-nystrom methods for solving linear second order oscillatory problems, Bazuaye (2018) proposed a new 4th order hybrid Runge-Kutta methods for solving initial value problems (IVP), authors (Constantin et al., 2019) applied of the Euler and Runge-Kutta generalized methods for FDE and symbolic packages in the analysis of some fractional attractors, Nizam et al. (2018) presented diagonally implicit Runge-Kutta type method for directly solving special fourth-order ordinary differential equations with ill-posed problem of a Beam on elastic foundation and Anthony et al. (2018) presented an analysis and comparative study of numerical solutions of initial value problems (IVP) in ordinary differential equations (ODE) with Euler and Runge Kutta methods.

In order to apply Runge-Kutta (RK5), we consider a weighted average of the slopes at v points very close to the current point i.e., it considers the Metastatic equation (1) at the grid point t_i with v as slopes:

$$\begin{cases} X_{i+1} = X_i + \left(-(\beta_1 + \beta_2) \sum_{r=1}^{v} w_r K_r\right) X_i \\ Y_{i+1} = Y_i + \left(\left(\beta_2 \sum_{r=1}^{v} w_r K_r\right) X_i - \left(\beta_3 \sum_{r=1}^{v} w_r K_r\right) Y_i\right) \end{cases}$$
(5)

with initial conditions

$$\begin{cases} X_i = \omega \\ Y_i = \phi \end{cases}$$
(6)

where

$$K_r = hf\left(t_i + \epsilon_i h, X_i + \sum_{j=1}^{r-1} a_{rj} K_j\right), K_r = hf\left(t_i + \epsilon_i h, Y_i + \sum_{j=1}^{r-1} a_{rj} K_j\right)$$

and $\epsilon_1 = 0$, r = 1, 2, ..., v, $\epsilon_2, \epsilon_3, \epsilon_4, ..., \epsilon_v$ and $a_{2j}, ..., a_{vv-1}$ are parameters to be determined.

After further simplification, one can construct a fifth order Runge-Kutta formula as follows:

$$\begin{cases} X_{i+1} = X_i + \frac{1}{192} (23K_1 + 125K_3 - 81K_5 + 125K_6) \\ K_1 = hf(t_i, X_i) \\ K_2 = hf\left(t_i + \frac{h}{3}, X_i + \frac{K_1}{3}\right) \\ K_3 = hf\left(t_i + \frac{2h}{5}, X_i + \frac{1}{25} (4K_1 + 6K_2)\right) \\ K_4 = hf\left(t_i + h, X_i + \frac{1}{4} (K_1 - 12K_2 + 15K_3)\right) \\ K_5 = hf\left(t_i + \frac{2h}{3}, X_i + \frac{1}{81} (6K_1 + 90K_2 - 50K_3 + 8K_4)\right) \\ K_6 = hf\left(t_i + \frac{4h}{5}, X_i + \frac{1}{75} (6K_1 + 36K_2 + 10K_3 + 8K_4)\right) \end{cases}$$
(7)

Similarly,

4

$$\begin{cases} Y_{i+1} = Y_i + \frac{1}{192} (23K_1 + 125K_3 - 81K_5 + 125K_6) \\ K_1 = hf(t_i, Y_i) \\ K_2 = hf\left(t_i + \frac{h}{3}, Y_i + \frac{K_1}{3}\right) \\ K_3 = hf\left(t_i + \frac{2h}{5}, Y_i + \frac{1}{25} (4K_1 + 6K_2)\right) \\ K_4 = hf\left(t_i + h, Y_i + \frac{1}{4} (K_1 - 12K_2 + 15K_3)\right) \\ K_5 = hf\left(t_i + \frac{2h}{3}, Y_i + \frac{1}{81} (6K_1 + 90K_2 - 50K_3 + 8K_4)\right) \\ K_6 = hf\left(t_i + \frac{4h}{5}, Y_i + \frac{1}{75} (6K_1 + 36K_2 + 10K_3 + 8K_4)\right) \end{cases}$$
(8)

The setback of the Runge-Kutta method is that it involves considerably more computational effort per step length.

4.2 New Iterative Method (NIM)

New Iterative Method (NIM) was proposed by Daftardar-Gejji & Jafari (2006). NIM is simple in its principles and easy to implement on computers using symbolic computation packages such as Maple. This method is better than numerical methods as it is free from rounding off errors and does not require large computer power. It has proven successful over other methods in many cases (see Bhalekar & Gejji, 2008; Zead & Ali, 2018; Aisha *et al.*, 2018; Mohammad *et al.*, 2018) and just to mention a few.

Consider the following general functional equation;

$$x(\bar{t}) = f(\bar{t}) + N(x(\bar{t})) \tag{9}$$

where N is a nonlinear operator from a Banach space $B \to B$ and f a known function $\underline{x} = (x_1, x_2, ..., x_n)$.

We are looking for a solution X(t) and Y(t) of equation (9) having the series form

$$\begin{cases} X(\bar{t}) = \sum_{i=0}^{\infty} X_i(\bar{t}) \\ Y(\bar{t}) = \sum_{i=0}^{\infty} Y_i(\bar{t}) \end{cases}$$
(10)

The nonlinear operator N can be decomposed as;

$$\begin{cases} N\left(\sum_{i=0}^{\infty} X_i(\bar{t})\right) = N(X_0) + \sum_{i=1}^{\infty} \left\{ N\left(\sum_{j=0}^{i} X_j\right) - N\left(\sum_{j=0}^{i-1} X_j\right) \right\} \\ N\left(\sum_{i=0}^{\infty} Y_i(\bar{t})\right) = N(Y_0) + \sum_{i=1}^{\infty} \left\{ N\left(\sum_{j=0}^{i} Y_j\right) - N\left(\sum_{j=0}^{i-1} Y_j\right) \right\} \end{cases}$$
(11)

From equations (10) and (11), equation (9) is equivalent to

$$\begin{cases} \sum_{i=0}^{\infty} X_i = f(t) + N(X_0) + \sum_{i=1}^{\infty} \left\{ N\left(\sum_{j=0}^{i} X_j\right) - N\left(\sum_{j=0}^{i-1} X_j\right) \right\} \\ \sum_{i=0}^{\infty} Y_i = f(t) + N(Y_0) + \sum_{i=1}^{\infty} \left\{ N\left(\sum_{j=0}^{i} Y_j\right) - N\left(\sum_{j=0}^{i-1} Y_j\right) \right\} \end{cases}$$
(12)

We define the recurrence relation:

$$\begin{cases} X_0 = f, \\ X_1 = N(X_0), \\ X_{m+1} = N(X_0 + X_1 + \dots + X_m) - N(X_0 + X_1 + \dots + X_{m-1}) \\ Y_0 = f, \\ Y_1 = N(Y_0), \\ Y_{m+1} = N(Y_0 + Y_1 + \dots + Y_m) - N(Y_0 + Y_1 + \dots + Y_{m-1}) \\ m = 1, 2, 3, \dots \end{cases}$$
(13)

then,

$$\begin{cases} (X_0 + X_1 + \dots + X_{m+1}) = N(X_0 + X_1 + \dots + X_m), \\ (Y_0 + Y_1 + \dots + Y_{m+1}) = N(Y_0 + Y_1 + \dots + Y_m), \\ m = 1, 2, \dots \end{cases}$$

and

$$\begin{cases} \sum_{i=0}^{\infty} X_i = f(t) + N\left(\sum_{i=0}^{\infty} X_i\right) \\ \sum_{i=0}^{\infty} Y_i = f(t) + N\left(\sum_{i=0}^{\infty} Y_i\right) \end{cases}$$
(14)

The k -term approximate solution of (9) and (10) is given by;

$$\begin{cases} x(t) = x_0 + x_1 + x_2 \dots + x_{k-1} \\ y(t) = y_0 + y_1 + y_2 \dots + y_{k-1} \end{cases}$$
(15)

5. Computational Experiments

In this section, we present and employ an algorithm scheme based on two numerical techniques discussed in section four. The behaviors and effects of three parameters β_1 , β_2 and β_3 are investigated at three different cases beginning with an initial condition guess of X(0) = 1 and Y(0) = 1. All the numerical computations are executed in MAPLE 18 software and the test parameter values used for the numerical simulation are stated in Table 1, Table 2 and Table 3.

Parameter	Symbol	Value	Unit
Per Capital Death Rate Cells from A in X	β_1	0.001	Daily
Per Capital Movement of Cancerous Cells from A to B	β_2	0.005	Daily
Per Capital Death Rate Cells from B in Y	β_{3}	0.008	Daily

Table 1. Description of Parameters in the Model (Case1)

 Table 2. Description of Parameters in the Model (Case 2)

Parameter	Symbol	Value	Unit
Per Capital Death Rate Cells from A in X	β_1	0.007	Weekly
Per Capital Movement of Cancerous Cells from A to B	β_2	0.035	Weekly
Per Capital Death Rate Cells from B in Y	β_{3}	0.056	Weekly

Table 3. Description of Parameters in the Model (Case 3)

Parameter	Symbol	Value	Unit
Per Capital Death Rate Cells from A in X	β_1	0.030	Monthly
Per Capital Movement of Cancerous Cells from A to B	β_2	0.150	Monthly
Per Capital Death Rate Cells from B in Y	β_3	0.240	Monthly

In order to examine and obtain numerical solutions for equation (1) using the parameters given in Tables 1 to 3. We develop an algorithm using Runge-Kutta (RK5) discussed in 4.1 as follow:

Restart: Digits := 26; Step 1: $f := (t, x) \rightarrow -(\beta_1 + \beta_2) * x;$ $g := (t, y, x) \rightarrow (\beta_2) * x - (\beta_3) * y;$ t[0] := 0; x[0] := 1.0; y[0] := 1.0; h[0] := 0.1; $\beta_1 := [0.001, 0.007, 0.0030];$ $\beta_2 := [0.005, 0.0035, 0.0150];$ $\beta_3 := [0.008, 0.0056, 0.0240];$ Step 2: for n from 1 to 10 do t[n] := n * h: k1 := f(t[n - 1], x[n - 1]); $k2 := f(t[n - 1] + \frac{h}{3}, x[n - 1] + \frac{h}{3} * k1);$ $k3 := f(t[n - 1] + \frac{2 * h}{5}, x[n - 1] + \frac{1}{25} * (4 * k1 + 6 * k2);$

$$\begin{aligned} k4 &\coloneqq f\left(t[n-1]+h, x[n-1]+\frac{1}{4}*(k1-12*k2+15*k3)\right); \\ k5 &\coloneqq f\left(t[n-1]+\frac{2*h}{3}, x[n-1]+\frac{1}{81}*(6*k1+90*k2-50*k3+8*k4)\right); \\ k6 &\coloneqq f\left(t[n-1]+\frac{4*h}{5}, x[n-1]+\frac{1}{75}*(6*k1+36*k2+10*k3+8*k4)\right); \\ x[n] &\coloneqq x[n-1]+\frac{h}{192}*(23*k1+125*k3-81*k5+125*k6); \\ \text{od}; \\ \mathbf{Step 3:} \\ for n from 1 to 10 do \\ t[n] &\coloneqq n*h: \\ k1 &\coloneqq f(t[n-1], y[n-1]): \\ k2 &\coloneqq f\left(t[n-1]+\frac{h}{3}, y[n-1]+\frac{h}{3}*k1\right): \\ k3 &\coloneqq f\left(t[n-1]+\frac{2*h}{5}, y[n-1]+\frac{1}{25}*(4*k1+6*k2): \\ k4 &\coloneqq f\left(t[n-1]+h, y[n-1]+\frac{1}{4}*(k1-12*k2+15*k3)\right): \\ k5 &\coloneqq f\left(t[n-1]+\frac{2*h}{3}, y[n-1]+\frac{1}{75}*(6*k1+90*k2-50*k3+8*k4)\right): \\ k6 &\coloneqq f\left(t[n-1]+\frac{4\cdot h}{5}, y[n-1]+\frac{1}{75}*(6*k1+36*k2+10*k3+8*k4)\right): \\ y[n] &\coloneqq y[n-1]+\frac{h}{192}*(23\cdotk1+125*k3-81*k5+125*k6): \\ \text{od}; \end{aligned}$$

We also obtain approximate solutions using New Iterative Method discussed in section 4.2 as follows:

Case 1: $\beta_1 = 0.001, \beta_2 = 0.005, \beta_3 = 0.008$

$$X(t) = \begin{cases} 1 - 0.006t + 0.000018t^2 - 3.6 \times 10^{-8}t^3 + \\ 5.4 \times 10^{-11}t^4 + -6.48 \times 10^{-14}t^5 + \\ 6.48 \times 10^{-17}t^6 - 5.5543 \times 10^{-20}t^7 \end{cases}$$
(16)

$$Y(t) = \begin{cases} 1 & -0.003t - 0.000003t^2 + 3.8 \times 10^{-8}t^3 - \\ 1.21 \times 10^{-10}t^4 + 2.476 \times 10^{-13}t^5 \\ -3.8413 \times 10^{-16}t^6 + 4.853 \times 10^{-19}t^7 \end{cases}$$
(17)

Case 2: $\beta_1 = 0.007, \beta_2 = 0.035, \beta_3 = 0.056$

$$X(t) = \begin{cases} 1 - 0.042t + 0.000882t^2 - 1.2348 \times 10^{-5}t^3 + \\ 1.29654 \times 10^{-7}t^4 - 1.0891 \times 10^{-9}t^5 + \\ 7.62366 \times 10^{-12}t^6 - 4.574193 \times 10^{-14}t^7 \end{cases}$$
(18)

$$Y(t) = \begin{cases} 1 - 0.021t - 0.000147t^2 + 1.3034 \times 10^{-5}t^3 \\ -2.90521 \times 10^{-7}t^4 + 4.16141 \times 10^{-9}t^5 \\ -4.5192903 \times 10^{-11}t^6 + 3.996615 \times 10^{-13}t^7 \end{cases}$$
(19)
Case 3: $\beta_1 = 0.030, \beta_2 = 0.150, \beta_3 = 0.240$

$$X(t) = \begin{cases} 1 - 0.180t + 0.0162t^2 - 2.916 \times 10^{-3}t^3 + \\ 4.374 \times 10^{-5}t^4 - 1.57464 \times 10^{-6}t^5 \\ 4.72392 \times 10^{-8}t^6 - 1.214722286 \times 10^{-9}t^7 \end{cases}$$

(20)

$$Y(t) = \begin{cases} 1 - 0.090t - 0.0027t^2 + 1.026 \times 10^{-3}t^3 - \\ 9.8010 \times 10^{-5}t^4 + 6.061668 \times 10^{-6}t^5 \\ -2.800332 \times 10^{-7}t^6 + 1.061340686 \times 10^{-8}t^7 \end{cases}$$
(21)

5.1 Numerical results

Table 4, Table 5 and Table 6 show the decrease in cancer compartments A and B (X(t) and Y(t)) as the rate of β_1 , β_2 and β_3 increases on a daily, weekly and monthly basis. The role and significant of relationship in increase the parameters values β_1 , β_2 and β_3 are great reduction in cancer tumor within the compartment A and B. Thus, increases in values of β_1 , β_2 and β_3 (daily, weekly and monthly) are responsible for the reductions in cancer tumor in the two compartments under study. Furthermore Figure 2, Figure 3 and Figure 4 depict the absolute errors performance which indicate that new iterative method (NIM) solutions are better and closer to analytical solutions compared to Runge-Kutta method (RK5).

t	Solution	X(t)	Y(t)
0	Analytical	1.0000000000000000000000000000000000000	1.0000000000000000000000000000000000000
	RK5	1.0000000000000000000000000000000000000	1.0000000000000000000000000000000000000
	NIM	1.0000000000000000000000000000000000000	1.0000000000000000000000000000000000000
	Analytical	0.99940017996400539935206479	0.99969997003798790247561594
0.1	RK5	0.99940017996396293718651949	0.99969997003815141566850136
	NIM	0.99940017996400539764326788	0.99969997003798790134598432
	Analytical	0.99880071971208637926814649	0.99939988030380647920742176
0.2	RK5	0.99880071971192882361680150	0.99939988030441344551013892
	NIM	0.99880071971208637876452318	0.99939988030380647790543278
	Analytical	0.99820161902843724258322706	0.99909973102502050138807297
0.3	RK5	0.99820161902810903084532146	0.99909973102628546534664013
	NIM	0.99820161902843724123879546	0.99909973102502050118459876
	Analytical	0.99760287769738173671332983	0.99879952242890493385138476
0.4	RK5	0.99760287769684260942440716	0.99879952243098378642310122
	NIM	0.99760287769738173549854327	0.99879952242890493229875634
	Analytical	0.99700449550337297601206623	0.99849925474244523150170606
0.5	RK5	0.99700449550259628890424001	0.99849925474544165540798818
	NIM	0.99700449550337296349818743	0.99849925474244522974256782
	Analytical	0.99640647223099336417375465	0.99819892819233763546745165
0.6	RK5	0.99640647222996447783285338	0.99819892819630925439313517
	NIM	0.99640647223099336342578168	0.99819892819233763540156743
	Analytical	0.99580880766495451668308341	0.99789854300498946897903367
0.7	RK5	0.99580880766366926375613406	0.99789854300995370089374658
	NIM	0.99580880766495451668321789	0.99789854300498946897875422
	Analytical	0.99521150159009718331129000	0.99759809940651943297143818
0.8	RK5	0.99521150158856041321782121	0.99759809941245904784839459
	NIM	0.99521150159009718331119764	0.99759809940651943297139764
0.9	Analytical	0.99461455379139117065882874	0.99729759762275790141168878
	RK5	0.99461455378961537175950719	0.99729759762962628361902184
	NIM	0.99461455379139117065875426	0.99729759762275790141167993
1.0	Analytical	0.99401796405393526474449877	0.99699703787924721635144237
	RK5	0.99401796405193926392063688	0.99699703788697333199093918
	NIM	0.99401796405393526474449324	0.99699703787924721635144199

Table 4. Metastatic cancer model case one (Daily)

t	Solution	X(t)	Y(t)
0	Analytical	1.0000000000000000000000000000000000000	1.0000000000000000000000000000000000000
	RK5	1.000000000000000000000000000000000000	1.0000000000000000000000000000000000000
	NIM	1.000000000000000000000000000000000000	1.0000000000000000000000000000000000000
	Analytical	0.99580880766495451668308341	0.99789854300498946897903360
0.1	RK5	0.99580880766351980467455044	0.99789854301053204000954323
	NIM	0.99580880766495451564327687	0.99789854300498946765439873
	Analytical	0.99163518142309837737705028	0.99579422380849516498624080
0.2	RK5	0.99163518142011170470679095	0.99579422382010202195873630
	NIM	0.99163518142309837696587321	0.99579422380849516376543298
	Analytical	0.98747904765155645020861434	0.99368711957485927565972481
0.3	RK5	0.98747904764863572014408875	0.99368711958634924878773844
	NIM	0.98747904765155645016751387	0.99368711957485927436254287
	Analytical	0.98334033303602123324120735	0.99157730678109081388513521
0.4	RK5	0.98334033303436692574645740	0.99157730678781770351579470
	NIM	0.98334033303602123311563897	0.99157730678109081304387651
	Analytical	0.97921896456945958818954521	0.98946486122177863408153413
0.5	RK5	0.97921896456899545098655533	0.98946486122395604924123558
	NIM	0.97921896456945958817864393	0.98946486122177863407664532
	Analytical	0.97511486955082489446193668	0.98734985801397250818145691
0.6	RK5	0.97511486952469804340389589	0.98734985811719928695057607
	NIM	0.97511486955082489446065437	0.98734985801397250818134876
	Analytical	0.97102797558377460081269877	0.98523237160203245854940534
0.7	RK5	0.97102797487644298930950730	0.98523237439374461910455163
	NIM	0.97102797558377460081268974	0.98523237160203245854940516
	Analytical	0.96695821057539315198225655	0.98311247576244654390241015
0.8	RK5	0.96695820842988353541323728	0.98311248425093019642898531
	NIM	0.96695821057539315198225612	0.98311247576244654390241000
0.9	Analytical	0.96290550273492026779732032	0.98099024360861729312261800
	RK5	0.96290549859889097667386382	0.98099026001627097349847267
	NIM	0.96290550273492026779732011	0.98099024360861729312261723
1.0	Analytical	0.95886978057248455229795042	0.97886574759561698068506712
	RK5	0.95886977407390677103871351	0.97886577345036668138659161
	NIM	0.95886978057248455229795012	0.97886574759561698068506699

Table 5. Metastatic cancer model case two (Weekly)

Table 6. Metastatic cancer model case three (Monthly)

t	Solution	X(t)	Y(t)
0	Analytical	1.000000000000000000000000000000000000	1.000000000000000000000000000000000000
	RK5	1.000000000000000000000000000000000000	1.000000000000000000000000000000000000
	NIM	1.000000000000000000000000000000000000	1.000000000000000000000000000000000000
	Analytical	0.98216103235830071800053830	0.99097401625888782473843321
0.1	RK5	0.98216103217113505840029871	0.99097401699950183315591036
	NIM	0.98216103235830071800487321	0.99097401625888782472994172
	Analytical	0.96464029348312303004387875	0.98190005309155045825869202
0.2	RK5	0.96464029334064855620889717	0.98190005369259671441295810
	NIM	0.96464029348312303003278543	0.98190005309155045825794872
	Analytical	0.94743210650179829953811593	0.97278392253768715122545317
0.3	RK5	0.94743210647481974686336798	0.97278392269563028537744645
	NIM	0.94743210650179829953765387	0.97278392253768714895287312
	Analytical	0.93053089581120573174655787	0.96363121542495510375758467
0.4	RK5	0.93053089024673168684722868	0.96363123721805507589072702
	NIM	0.93053089581120573174578451	0.96363121542495510369726571
0.5	Analytical	0.91393118527122818674735355	0.95444730810233419357703613
	RK5	0.91393116908893608335507746	0.95444737234481506869612957
	NIM	0.91393118527122818674694724	0.95444730810233419356937652

0.6	Analytical	0.89762759643043487568903354	0.94523736898727966396173859
	RK5	0.89762757289090110616620838	0.94523746446329400585370479
	NIM	0.89762759643043487568857231	0.94523736898727966389126732
0.7	Analytical	0.88161484678341604601365513	0.93600636493155201620971761
	RK5	0.88161482205811448384652669	0.93600646853602467077975201
	NIM	0.88161484678341604601359472	0.93600636493155201620856823
0.8	Analytical	0.86588774805920501684056355	0.92675906741048896212946878
	RK5	0.86588772744479558966498443	0.92675915836061994255688748
	NIM	0.86588774805920501684055982	0.92675906741048896212946735
0.9	Analytical	0.85044120454023299827718764	0.91750005854036300331713985
	RK5	0.85044119035389544159357999	0.91750012656977279593404420
	NIM	0.85044120454023299827717563	0.91750005854036300331713865
1.0	Analytical	0.83527021141127202131238497	0.90823373692834993945233532
	RK5	0.83527020253709670230735855	0.90823378463125630132647220
	NIM	0.83527021141127202131237998	0.90823373692834993945233456



Figure 2. Depict the absolute error for Table 4 X(t) and Y(t))



Figure 3. Depict the absolute error for Table 5 X(t) and Y(t))



6. Conclusion

This study compared the Runge-Kutta method of fifth-order (RK5) with New Iterative Method (NIM) for the numerical solutions of metastatic cancer models which occur in two compartments of cancer cells. A numerical solution obtained shows that increase in parameters β_1 , β_2 and β_3 leads to decrease in spreading of cancer tumor in the two apartments. Finally, the results are more realistic compare with analytical solutions and from the computational viewpoint, the New Iterative Method (NIM) is easy to utilize and less error obtained (Figure 2, Figure 3 and Figure 4) compare to Runge-Kutta Method of fifth-order (RK5) method.

Acknowledgement

The authors are thankful to the reviewers and editorial board of MJOC for their carefully reading this paper and their valuable comments.

References

- Aisha, A. A., Tarig M., Elzakib, & Mourad C (2018). New transform iterative method for solving some Klein-Gordon equations, *Result of Physics*, 10, 655-659.
- Anthony, A O., Pius T, Onyinyechi F, Anorue., & Ahmed, A. D., (2019). Analysis and comparative study of numerical solutions of initial value problems (IVP) in ordinary differential equations (ODE) with Euler and Runge Kutta methods, *American Journal* of Engineering Research (AJER), 8(8), 40-53.
- Bazuaye, F. E., (2018). A new 4th order hybrid Runge-Kutta methods for solving initial value problems (IVP), *Pure and Applied Mathematics Journal*, 7(6), 78-87.
- Bellomo, N., & De Angelis E, (2003). Modelling and simulation of tumor development, treatment and control, *Mathematical and Computer Modelling*, 37(11).
- Benzekry, S., Barbolosi, D., Benabdallah, A. & Hubert, F (1970). Center of cancer systems biology, *Steward Research and Specialty projects Corp*, Tufts University School of Medicine, Boston, 02142, USA.

- Bhalekar, S., & Gejji, V., (2008). New iterative method application to partial differential equations, *Appl. Math. Comput.* 203, 778-783.
- CERD. (2013). Lecture note on mathematical model training workshop at Centre for Energy Research and Development Obafemi Awolowo University, Ile-Ife February 5-8.
- Constantin, M., Jose, T., M., & Gheorghe, D., (2020). Application of the Euler and Runge– Kutta generalized methods for FDE and symbolic packages in the analysis of some fractional attractors, *International Journal of Nonlinear Sciences and Numerical Simulation*, 21(2),156-170.
- Cox, T.R., Gartland, Erler A, & Lysyl, J.T. (2016). Oxidase, a targetable secreted molecule involved in Cancer Metastasis. *Cancer Res.* 76,188–192.
- Daftardar-Gejji, V. & Jafari, H. (2006). Solving a system of nonlinear equations using new iterative method, *Journal of Mathematics Analysis and Application*. 316, 753.
- Dan, L.M, Wanbiao, & Songbai, G. (2016). Stability of a mathematical model of tumorinduced angiogenesis, *Nonlinear Anal. Model. Control*, 21(3), 325–344.
- Daniel, D., Aminur R, & Matthew, T. (2011). Dynamic models of metastatic tumor growth, 27th Annual Workshop on Mathematical Problems in *Industry New Jersey Institute of Technology*, 1-20.
- Hanin, L. & Zaider, M. (2011). Effects of surgery and chemotherapy on metastatic progression of prostate cancer: evidence from the natural history of the disease reconstructed through mathematical modeling, *Cancers (Basel)*, *3*(3), 3632–3660.
- Kolev, M., Zubik-Kowal, & Barbara. (2011). Numerical experiments with model equations of cancer invasion of tissue. *Control and Cybernetics, 40 (3)*, 779-791.
- Liu,Y.H, Yeh, I.J, Lai, M.D, Liu, K.T, Kuo, P.L, & Yen, M.C, (2016). Cancer immune therapy: Silencing intracellular negative immune regulators of dendritic cells, *Cancer* (*Basel*), 11(1), 1–12.
- Lorenzo-Herrero, S, Lopez-Soto A, Sordo-Bahamonde, C, Gonzalez Rodriguez, A, Vitale, M. & Gonzalez, S. (2019). NK cell-based immunotherapy in cancer metastasis, *Cancers* (*Basel*), 11(1), 1–22.
- Mohammad, J. K, Rashid, N, Samreen, F, & Javed. (2018). New iterative method for the solution of fractional damped Burger and fractional sharma-tasso-olver equations, *Hindawi Complexity*, Article ID 3249720, 1-7.
- Mohammed, S. M., & Murtaza. (2016). Direct explicit integrators of RK type for solving special fourth-order ordinary differential equations with an application, *Global Journal of Pure and Applied Mathematics*, *12*(6,) 4687–4715.
- Nikos, E., & Mastorakis. (2016). On the numerical solution of mathematical models of cancer growth and optimal cancer therapy. *Recent advances in biology, biophysics, bioengineering and computational chemistry*, 94-104.
- Nizam, G. Norazak, S., Firas, A. F, Fudziah, I. & Zarina, B. I. (2018). Diagonally implicit Runge–Kutta type method for directly solving special fourth-order ordinary differential equations with ill-posed problem of a Beam on elastic foundation, *Algorithms MDPI* volume12, 29 December 2018, 1-10.

- Pinho, S., Rodrigues, D & Manner, P. (2011). A mathematical model of chemotherapy response to tumor growth, *Curriculum Lattes*, 123-129.
- Rasmuson, A., Andersson, B, Olsson, & Andersson, L. (2014). Mathematical modeling in chemical engineering; *Cambridge University press*: Cambridge, UK.
- Salih, M., Ismail, F. & Senu. (2016). Fifth order Runge-Kutta-Nystrom methods for solving linear second order oscillatory problems, *Far East Journal of Applied Mathematics* 95(2),141-156.
- Sebastien, B., Dominique, B., Assia, B, Florence, H., & Philip, H. (2017). Quantitative analysis of the Tumor/Metastasis system and its optimal therapeutic control. 1-20.
- Tamer, A.A. (2019). Piecewise analytic method vs Runge-Kutta method: comparative study, *International Journal of Applied Mathematical Research*, 9(2), 41-49.
- Thakur, M. & Rao, G.V. (2016). Tumor invasion and metastasis a review, *Saudi journal of pathol. microbiol*, 1(2), 65-72.
- Yen, T., Nguyen, E., Ashlee, N. & Versypt, F. (2018). Mathematical modeling of metastatic cancer migration through a remodeling extracellular matrix processes, *Processes 2018*, 6(5), 58.
- Zead, Y., & Ali, A. (2018). Application new iterative method for solving nonlinear Burger's equation and coupled Burger's equations, *IJCSI International journal of computer science*, issues, *15*(3), 31-35.