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NUMERICAL SOLUTION OF DRUG DIFFUSION MODEL USING THE CLASSIC RUNGE KUTTA METHOD

AROLOYE SOLUADE JOSEPH[1] AND OWA DAVID OLUWAROTIMI[2]

[1,2]Department of Mathematics, Faculty of Science, University of Lagos.

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ABSTRACT

This research investigates the workability approach of the Fourth-order Runge-Kutta method (RK4), to tackle the drug diffusion in the two-compartment model which are the blood and Gastrointestinal tract (GI tract). The theoretical importance of the system of first-order ODEs is considered with initial conditions which served as the drug diffusion into the human body model. The exact solution was calculated using a matrix form of eigenvalues and eigenvectors. The ordinary differential equations describing the problem are solved by the RK4 method on PYTHON. Graphs plots and tables of absolute error analyses are used to show the efficiency of the RK4 method. Our results and finding revealed that RK4 results have approximately the same as exact solution. The analysis of computational error obtained is carried out. At every stage, the numerical result obtained is compared with that of exact solution. The result is also compared with some related result in literature and there is excellent agreement

1. Introduction

Ordinary differential equations (ODEs) are important in solving model or equations in Applied Mathematics., Engineering and Sciences. Drug diffusion into the system can be modeled by differential equations that modeled the rate of change of drug concentration over time and space. These equations account for various factors such as drug properties, the medium through which the drug diffuses (e.g., blood, tissues), and the physiological conditions of the body. Systems of ODEs play vital roles not just in Mathematics, Sciences and Engineering but also in other profession.

*Corresponding author: AROLOYE SOLUADE JOSEPH
E-mail address: saroloye@unilag.edu.ng
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Differential equations provide mathematical expressions that relate the relationship between the current value of a quantity and its rate of change. Runge-Kutta is the type of numerical approach systematically used to calculate an estimated value at each step of the sequences. Mimi and Syahirbanum [1] used Runge-Kutta approach to Solve System of First-Order Ordinary Differential Equations. The classic Runge-Kutta method was employed in this research work to solve drug diffusion model. Runge-Kutta Method "explores the efficacy of the Fourth-order Runge-Kutta (RK4) method in solving practical problems modeled by a system of First-order Ordinary differential equations (ODE). The Runge-Kutta is the numerical method adopted to compute an solution at each step of the sequences. Ahmad et al. [2] investigated adopted second, third and fourth order approach to tackle the numerical accuracy of classical Runge-Kutta. Comparison of their results indicates that the fourth classical Runge approach is better in all scenario. RK methods is very good and reliable to handle implicit and explicit approach for solving ODEs through time discretization by Chauhan and Srivastava [3]. RK4 approach is efficient, good, accurate and reliable and numerical solution derived by this approach attain converges at faster rate. The numerical solution of the model ODEs is calculated quickly and efficiently using the RK4 approach than by the forward Euler apporach [3]. Meanwhile, Islam [4] showed classical fifth and eight Runge Kutta are less inaccurate and less efficient than RK4 since RK4 involves fewer simulation time to compute truncation local and global error in the numeric

This research paper focus on use and model implication of ODEs by solving required mathematical models which capturing drug diffusion into human body system and the second part of the objective is to solve the required models by using closed form method and classical Runge Kutta method. Then, the result of first order ODEs with classical approach approach is validated by comparing with its closed form solution. Kayode [5] examined the analysis of Zero-Stable Numerical approach for Fourth-Order ordinary. Differential Equations. Onkar and Rastogi [6] studied Zhou's Differential Transformation kind for Study of Arm Race Richardson Model. Roslan et al. [7] used classical-order of Runge-Kutta approach to solving Zhou chaotic system.

The main focus of this noble research is to carry out thorough investigations of the numerical solution of drug diffusion into the human system body which used a system of first-order ODE and solved it numerically. Therefore, in this subsection, we will introduce a real life situation of the described problem. In this case, we study diffusion drug into the blood and gastrointestinal tract (GI tract). A two-reserved model for drug assimilation and movement through the GI tract and blood was studied. Pharmacokinetics was adopted to examine biomathematical modeling and goals of the equations model are to obtain the expected impact of medication and the duration it takes to reach the desired destination, Koch-Noble [8].

2. Problem Formulation

The classical Runge Kutta approach is used to tackle the challenging regarding the use of system of ODE which is diffusion drug into human system body model. Diffusion Drug into human body system model capture relationship between drug in flow and mass concentration of drug at the expected site through various department in the system. Pharmacokinetics is the branch of pharmacology concerned with movement of drugs within the body, Kaim et al, [9]. Pharmacokinetics is a good and reliable way to introduce biomathematical modeling. Awonuiyi [10] examined algorithmic collocation method for indirect solution of fifth-order initial-value model of ordinary differential equations.

Let $c_1(t)$ denote the mass concentration of the drug in the stomach and $c_2(t)$ bloodstream department respectively. Let c_0 be the initial mass concentration of drug in the system

The general form of the two-partition model capturing the level of change in oral drug administration is indicated as

$\frac{dc_1(t)}{dt} = -k_1c_1(t); \quad c_1(0) = c_0\ \}$ (1)

$\frac{dc_2(t)}{dt} = k_1c_1(t) - k_2c_2(t); \ c_2(0) = 0\ \}$ (2)

Assume the initial mass concentration of the drug is co. The general formula of the equation is given as with initial conditions $c_1(0) = c_0$ and $c_2(0) = 0$.

Each equation relates the change in drug mass concentration in their respective partitions over A specify period

3. Numerical Method

The RK4 method is based on (Roslan et al, 2013) and described as the following

$$\left.\begin{aligned} y_{n+1} = y_n + \tfrac{1}{6}h(k_1 + 2k_2 + 2k_3 + k_4) \\ k_1 = f(t_n, c_n) \\ k_2 = f\left(t_n + \tfrac{1}{2}h, c_n + \tfrac{1}{2}hk_1\right) \\ k_3 = f\left(t_n + \tfrac{1}{2}h, c_n + \tfrac{1}{2}hk_2\right) \\ k_4 = f(t_n + h, c_n + hk_3) \end{aligned}\right\} \quad 3$$

Classical Runge Kutta is a four-stage reliable Runge-Kutta method, which means that four function evaluations are required to proceed the numerical approach in a one-time direction.

4. Exact solution

A general system of ODEs can be written as follows

$c'_1(t) = k_{11}c_1 + k_{12}c_2$ (4)

$c'_2(t) = k_{21}c_1 + k_{22}c_2$ (5)

Where x_n, n =1,2 is a component of t.

To evalute homogeneous systems of ODEs, it can be expressed in a matrix form $x' = Ax$.

Where $\begin{pmatrix} c_1' \\ c_2' \end{pmatrix} = \begin{pmatrix} k_{11} & k_{12} \\ k_{21} & k_{22} \end{pmatrix}\begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$ (6)

A is known as the matrix of coefficient. Then, the eigenvalues are determined using

$|A - \lambda I| = 0$ (7)

where I is an identity matrix. The roots of the characteristic's polynomial, $\lambda_1\ and\ \lambda_2$ are the eigenvalues of A.

From the drug diffusion equations;

$\frac{dc_1}{dt} = -k_1c_1$ (8)

$\frac{dc_2}{dt} = k_1c_1 - k_2c_2$ (9)

We represent the equation in a matrix form $\frac{dc}{dt} = AC$

$A = \begin{pmatrix} -k_{12} & 0 \\ k_{12} & -k_{20} \end{pmatrix}$ (10)

To find the eigenvalues and the corresponding eigenvectors,

We solve for Det (A – λI) = 0

$Det\ A = \begin{pmatrix} -k_{12}-\lambda & 0 \\ k_{12} & -k_{20}-\lambda \end{pmatrix} = 0$ (11)

This gives

$$(-k_{12} - \lambda)(-k_{20} - \lambda) = 0$$

Therefore $\lambda_1 = -k_{12}\ and\ \lambda_2 = -k_{20}$

we put each eigenvalue above into

(A – λI) $V = 0$

$(A - -k_{12}I)V = 0$
For $\lambda_1 = -k_{12}$
$(A + k_{12}I)V = 0$
$\begin{pmatrix} 0 & 0 \\ k_{12} & -k_{20} + k_{12} \end{pmatrix}\begin{pmatrix} v_{11} \\ v_{12} \end{pmatrix} = 0$
Solving this we get $v_{11} = 1 \; and \; v_{12} = 0$
$v_1 = \begin{pmatrix} 1 \\ 0 \end{pmatrix}$
For $\lambda_2 = -k_{20}$
$(A + k_{20}I)V = 0$
$\begin{pmatrix} -k_{20} + k_{12} & 0 \\ k_{12} & 0 \end{pmatrix}\begin{pmatrix} v_{21} \\ v_{22} \end{pmatrix} = 0$
Solving this we get $v_{21} = 0 \; and \; v_{22} = 1$
$v_2 = \begin{pmatrix} 0 \\ 1 \end{pmatrix}$
Let $\begin{pmatrix} v_{11} \\ v_{12} \end{pmatrix} \; and \; \begin{pmatrix} v_{21} \\ v_{22} \end{pmatrix}$ be eigen vectors. The general solution to the system is a linear combination of the eigenvectors multiplied by exponential functions of their corresponding eigenvalues. Therefore, the general solutions become

$$c(t) = c_1 \begin{pmatrix} v_{11} \\ v_{12} \end{pmatrix} e^{\lambda_1 t} + c_2 \begin{pmatrix} v_{21} \\ v_{22} \end{pmatrix} e^{\lambda_2 t} \quad (12)$$

$$c(t) = c_1 \begin{pmatrix} 1 \\ 0 \end{pmatrix} e^{-k_{12}t} + c_2 \begin{pmatrix} 0 \\ 1 \end{pmatrix} e^{-k_{20}t} \quad (13)$$

This gives the solutions for $c_1(t) \; and \; c_2(t)$

$$c_1(t) = c_1 e^{-k_{12}t} \quad (14)$$

$$c_2(t) = c_2 e^{-k_{20}t} \quad (15)$$

4. Results and Discussions

The initial conditions are carefully selected to solve the equations describing the problem. Diffusing Drug into human body system model is noted as problem testing which is prescribed homogeneous of equation. The closed form results of problem is obtained through classical Runge Kutta approach as clearly stated above. The obtained result for classical Rung Kutta approach is validated using various step length, h which are *h=0.01, 0.001* to determine the accurate step length to obtain the accuracy of classical Runge Kutta apporach.

4.1. Test problem

Consider the homogeneous system

$$\frac{dc_1}{dt} = -k_1 c_1$$

$$\frac{dc_2}{dt} = k_1 c_1 - k_2 c_2$$

With initial conditions $c_1(0) = 500$ and $c_2(0) = 0$
Take $k_1 = 1 \; and \; k_2 = 0.5$

4.1.2 Numerical results

The classical Rungen Kutta approach is used to find the numerical results of the test problem. The results are calculated using the python software. The performance is presented in the table 1 for

step size 0.01 and table 2for the step size 0.001 and was also graphically depicted in figure 1 and 2,

4.1.3 Exact solution

For the Exact Solution

We First write the system in matrix form as follow

$$\begin{pmatrix} c_1' \\ c_2' \end{pmatrix} = \begin{pmatrix} -k_1 & 0 \\ k_1 & k_e \end{pmatrix} \begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$$

Obtain the eigen values we get $(\lambda + k_1)(\lambda + k_e) = 0 \; where \; \lambda_1 = -k_1 \; and \; \lambda_2 = -k_e$

For case $\lambda_1 = -k_1$ the system is

$$\begin{pmatrix} 0 & 0 \\ k_1 & -k_e + k_1 \end{pmatrix} \begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

Solving the equation $(k_1 v_1 + (-k_e + k_1)v_2 = 0 \; and \; let \; v_2 = 1 \; we \; get \; v_1 = \frac{k_e - k_1}{k_1}$

For case $\lambda_2 = -k_e, the \; system \; is$

$$\begin{pmatrix} -k_1 + k_e & 0 \\ k_1 & 0 \end{pmatrix} \begin{pmatrix} v_1 \\ v_2 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

Solving the bottom equation $(k_1 + k_e)v_1 + 0v_2 = 0, and \; let \; v_2 = 1 \; we \; get \; v_1 = 0.$
The general solution is

$$\begin{pmatrix} c_1(t) \\ c_2(t) \end{pmatrix} = \begin{pmatrix} \frac{k_e - k_1}{k_1} \\ 1 \end{pmatrix} e^{-k_1 t} + c_b \begin{pmatrix} 0 \\ 1 \end{pmatrix} e^{-k_e t}$$

We find that $c_1 = 500 \frac{k_e - k_1}{k_1} \; and \; c_2 = 500 \frac{-k_1}{k_e - k_1} \; hence \; the \; particular \; solution \; is$

$$\begin{pmatrix} c_1(t) \\ c_2(t) \end{pmatrix} = \begin{pmatrix} 500e^{(-k_1 t)} k_1 \\ \frac{k_1}{k_1 - k_e} 500(e^{(-k_e t)} - e^{(-k_1(t))}) \end{pmatrix}$$

$$where \; k_1 = 1 \; and \; k_2 = \; 0.5$$

$$we \; can \; assume \; \; k_e = \; k_2 = \; 0.5$$

$$\begin{pmatrix} c_1(t) \\ c_2(t) \end{pmatrix} = \begin{pmatrix} 500e^{(-1t)} k_1 \\ \frac{1}{1 - 0.5} 500(e^{(-0.5t)} - e^{(-1t)}) \end{pmatrix}$$

$$\begin{matrix} c_1(t) \\ c_2(t) \end{matrix} = \begin{pmatrix} 500e^{(-1t)} k_1 \\ 1000(e^{(-0.5t)} - e^{(-1t)}) \end{pmatrix}$$

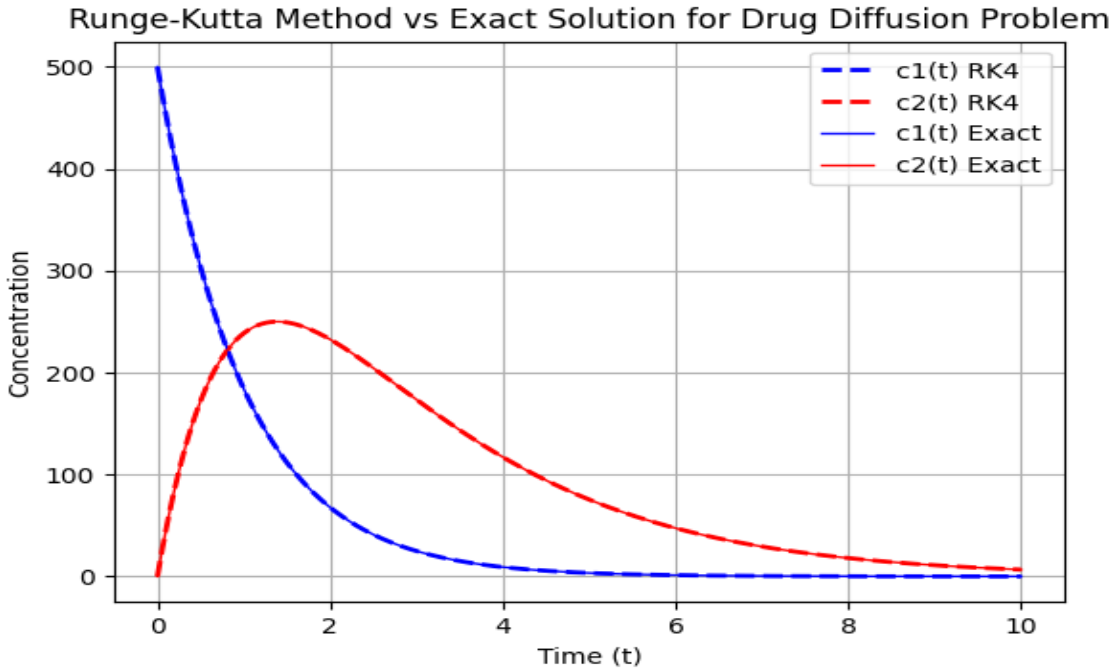

Figure 1 shows The Result Of The closed form Solution And th classical Runge Kutta Method Over A Time Frame Of 10 hours and The Step Size of 0.001

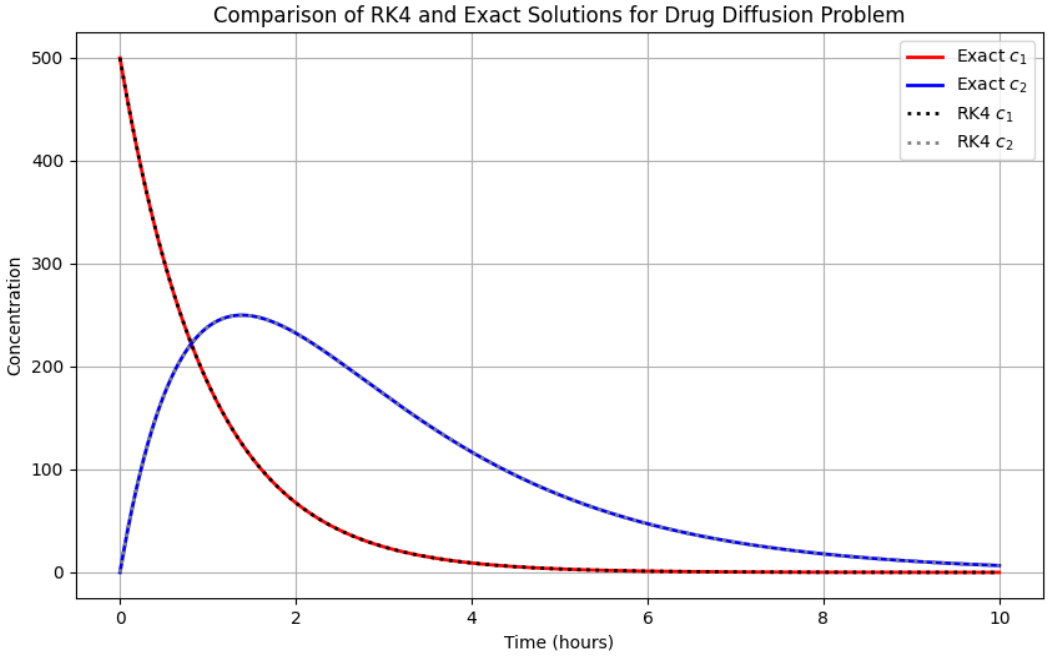

Figure 2 shows the graph of the exact solution and classical Runge Kutta fourth order method with a step size of 0.01

Table 1 shows The Result Of The clos form Solution And The classical Runge Kutta Method Over A Time Frame Of 10 hours and The Step Size of 0.01

Time (hours)	RK4 C1(t)	RK4 C2(t)	Exact C1(t)	Exact C2(t)
0	500	0	500	0
1	183.939720601177	238.651218511864	183.93972058572	238.651218541191 04
2	67.667641629678	232.544157914009	67.667641618306	232.544157934 82
3	24.8935341902074	173.343091769765 52	24.893534183931	173.343091780565
4	9.15781944744523 6	117.019644343137	9.157819444367 089	117.019644347 87
5	3.36897350095821	75.347051623055	3.368973499542 7334	75.347051624813 33
6	1.23937608895805	47.30831619072904	1.239376088333 1792	47.308316191197584
7	0.45594098304544 944	29.2855014567803	0.455940982777 25814	29.285501456763985
8	0.16773131406401 257	17.980176260989	0.167731313951 2559	17.980176260831666
9	0.06170490209000 575	10.985586734323748	0.061704902043 33978	10.985586734155628
10	0.02269996490031 738	6.692547069461033	0.022699964881 242426	6.692547069322982

Table 2 shows The Absolute Error of the close form Solution and The classical Runge Kutta Method Over a Time Frame Of 10 hours and The Step Size of 0.01.

Time (hours)	Absolute Error C1(t)	Absolute Error C2(t)
0	0.0	0.0
1	1.545654981782718e-08	2.9326969297471805e-08
2	1.1372321750968695e-08	2.082066430375562e-08
3	6.275463704241702e-09	1.0800363270391244e-08
4	3.0781475146568482e-09	4.740613235298952e-09
5	1.4154832861379418e-09	1.7576979871591902e-09
6	6.248739303771345e-10	4.685460908149253e-10
7	2.681913024993321e-10	1.6402879055021913e-11
8	1.1275666511600946e-10	1.5766588035148743e-10
9	4.6665969699599685e-11	1.681197403513579e-10
10	1.9074953422348884e-11	1.3805045995241016e-10

Table 3: Numerical results of classical Runge kutta method for solving test problem (a) h = 0.001

Time (hours)	RK4 C1(t)	RK4 C2(t)	Exact C1(t)	Exact C2(t)
0	500	0	500	0
1	183.939720601177 5	238.651218511864 07	183.9397205857212	238.651218541 19104
2	67.6676416296786 6	232.544157914009 05	67.66764161830633	232.544157934 8297
3	24.8935341902074 33	173.343091769765 52	24.89353418393197	173.343091780 56589
4	9.1578194474452 36	117.019644343137 88	9.157819444367089	117.019644347 8785
5	3.3689735009582 167	75.34705162305563	3.368973499542733 4	75.3470516248 1333
6	1.2393760889580 532	47.30831619072904	1.239376088333179 2	47.3083161911 97584
7	0.4559409830454 4944	29.285501456780388	0.455940982777258 14	29.2855014567 63985
8	0.1677313140640 1257	17.98017626098933	0.167731313951255 9	17.9801762608 31666
9	0.0617049020900 0575	10.985586734323748	0.061704902043339 78	10.9855867341 55628
10	0.0226999649003 1738	6.692547069461033	0.022699964881242 426	6.69254706932 2982

Table 4 shows The Absolute Error of the close form Solution And classical Runge Kutta Method Over A Time Frame Of 10 hours and The Step Size of 0.001

Time (hours)	Absolute Error C1(t)	Absolute Error C2(t)
0	0.0	0.0
1	1.545629e-08	2.9327e-08
2	1.137232e-08	2.0821e-08
3	6.275e-09	1.080e-08
4	3.078e-09	4.741e-09
5	1.4155e-09	1.75779e-09
6	6.2649e-10	4.685e-10
7	1.553196e-07	1.6403e-11
8	4.667e-11	1.5766e-10
9	4.6667e-11	1.6812e-10
10	1.9075e-11	1.3805e-10

The drug initial usage are given as 600 and the duration for the drug to be completely vanished from GI tract is calculated 11 hours. The tables and graphs in each level of the scenarios shows that the drug assimilates into GI tract that denoted as c_1, we noted the graph decreasing over time of duration. Along the line, the drug vanished from GI tract and went to bloodstream which is denoted as c_2 , we also observed that graph decreases and at some point, it increases and extend to zero. Finally, the amount of drug is completely vanished from the body system when the graphs of c_1 and c_2 is equivalent to zero. The table 1 and Table 2 showed the result of close form solution and classical Run Kutta method. In comparing the two solutions, we can see clearly that Classical Runge Kutta approach is more reliable and preferable by using smaller step length.

CONCLUSION

Pharmacokinetics is an important aspect of pharmacology because it studies the movement of drug molecules in the body. The drug diffusion is an important part of pharmacokinetics that introduces biomathematical modeling. The classical Runge Kutta approach has very efficient and effective approach for many practical applications in various profession, field of science and engineering. One of which was studied in this research is the application of the approach in solving the numerical solution of diffusion drug into the human body system which is a system of ODE. By comparing close form solution and classical Runge Kutta approach for the applications of system of ODEs, RK4 method is approximately accurate since its approaching to exact solution.

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