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NUMERICAL SOLUTION FOR IMMUNOLOGY TUBERCULOSIS MODEL USING RUNGE KUTTA FEHLBERG AND ADAMS BASHFORTH MOULTON METHOD

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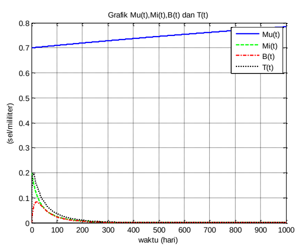
Graphical abstract



Abstract

The Immunology tuberculosis model that has been formulated by (Ibarguen, E., Esteva, L., & Chavez, L, 2011) in the form of a system of nonlinear differential equations first order. In this study, we used to Runge Kutta Fehlberg method and Adams Bashforth Moulton method. This study has been obtained numerical solution of the model. The results showed that the relative error obtained from the Adams Bashforth Moulton method is smaller when compared with the Runge Kutta Fehlber method. There are two methods has a high accuracy in solving systems of nonlinear differential equations.

Keywords: Runge Kutta Fehlberg, Adams Bashforth Moulton, Immunology of Tuberculosis Models

1.0 INTRODUCTION

The immunology celluler of tuberculosis models shaped system of nonlinear differential equations, thus requiring a special method to determine the solution. Settlement system of nonlinear differential equations is generally difficult to solved [1]. In this study, we used to Runge Kutta Fehlberg (RKF) method and Adams Bashforth Moulton (ABM) method for solving systems of nonlinear differential equations.

RKF method is a one-step numerical methods with high accuracy while ABM method is a numerical method-shaped two-step predictor corrector with good accuracy.

This study aims to determine how the numerical solution of the model of Tuberculosis immunology with RKF method and ABM method, as well as how to compare the two methods.

The mathematical models used to understand Mycobacterium Tuberculosis (Mtb) interaction with the immune system in the lung include: bacterial, T lymphocytes and macrophages.

2.0 LITERATURE REVIEW

In a scientific paper titled *A Mathematical for Celluler Immunology of Tuberculosis* obtained mathematical models of cellular immunology at the tuberculosis, which consists of four dependent variables. The fourth variable is the population of uninfected macrophages, macrophage population is infected, the bacteria population Mtb and *T* cell *populations.* Let Mu (t), Mi (t), B (t) and T (t) of each state the number of population at the time t, then the mathematical model of the cellular immunology of tuberculosis can be described as follows:

$$\frac{dMu(t)}{dt} = \mu_U - \mu_U Mu(t) - \beta B(t) Mu(t)$$

$$\frac{dMi(t)}{dt} = \beta B(t) Mu(t) - \alpha_T Mi(t) T(t) - \mu_I Mi(t)$$

$$\frac{dB(t)}{dt} = rMi(t) - \gamma_U Mu(t) B(t) - \mu_B B(t)$$

$$\frac{dT(t)}{dt} = k_1 Mi(t) - k_1 Mi(t) T(t) - \mu_T T(t) \qquad (1)$$

Where $\beta, \alpha_T, \mu_U, \mu_I, \mu_B, \gamma_U, r,$ and k_1 everything is a positive coefficient. β shows the rate of bacterial infection, α_T indicating the growth rate *T* cell of the infected macrophages, μ_U is uninfected macrophage death rate, μ_I as the death of infected macrophages, μ_B showing the natural death rate of bacteria, γ_U as the rate of death due to bacteria-infected macrophages, r average number production of bacteria in infected macrophages and k_1 are the growth rate T cells [2].

3.0 METHODOLOGY

Research methods used by the author in this study are the study of literature or *library research* is to examine and study the books, journals and other references that support the research. Runge-Kutta method is a numerical method one-step, because this method requires only one previous point to compute the new value. Runge-Kutta method is often used Runge-Kutta method of order four. There are several types of Runge-Kutta methods that depend on the value *of n* is used. For *n = 1* is called the Runge Kutta method of order one, while the authors used a method Fehlberg Runge Kutta order 4 and 5 (RKF 45). The RKF 45 method belonging to the family of Runge-Kutta method of order 4, but has an accuracy up to order 5. Accuracy This is possible because of the high RKF 45 method has 6 pieces of calculation constants whose role is to update the solution to order 5 [3].

Formulations of the Runge Kutta Fehlberg method (RKF 45) are as follows:

4th Order Formula:

$$y_{i+1} = y_i + \frac{25}{216}k_1 + \frac{1408}{256}k_3 + \frac{2197}{4104}k_4 + \frac{1}{5}k_5 \quad (2)$$

5th Order Formula:

$$\hat{y}_{i+1} = y_i + \frac{16}{135}k_1 + \frac{6656}{12825}k_3 + \frac{28561}{56437}k_4 - \frac{9}{50}k_5 + \frac{2}{55}k_6 \quad (3)$$

Where $k_1 = hf(x_i, y_i)$, $k_2 = hf(x_i + \frac{1}{4}h, y_i + \frac{1}{4}k_1)$,

$k_3 = hf(x_i + \frac{3}{8}h, y_i + \frac{3}{32}k_1 + \frac{9}{32}k_2)$,

$k_4 = hf\left(x_i + \frac{12}{13}h, y_i + \frac{1932}{2197}k_1 - \frac{7200}{2197}k_2 + \frac{7296}{2197}k_3\right)$,

$k_5 = hf(x_i + h, y_i + \frac{439}{216}k_1 - 8k_2 + \frac{3860}{513}k_3 - \frac{845}{4104}k_4)$,

$k_6 = hf(x_i + \frac{1}{2}h, y_i - \frac{8}{27}k_1 + 2k_2 - \frac{3544}{2565}k_3 + \frac{1859}{4104}k_4 - \frac{11}{40}k_5 h)$

.

RKF 45 relative error is the difference y_i *in the order of 4th and 5th order, so* formulated:

$$\hat{y}_{i+1} - y_{i+1} = \frac{1}{360}k_1 - \frac{128}{4275}k_3 - \frac{2197}{75240}k_4 + \frac{1}{50}k_5 + \frac{2}{55}k_6 \quad (4)$$

Settlement of ordinary differential equations using Adams Bashforth Moulton method is the process of looking for value function *y (x)* at point *x* certain of nonlinear ordinary differential equations of first order $y' = f(x, y)$ and the initial value $y(x_0) = y_0$ that are known to predict the predictor equation and make corrections to the equation corrector. Initial values required in Adams Bashforth Moulton method fourth order can be obtained from one-step method *(one-step method)*. So as to obtain a combination of good results, Runge-Kutta method of order-4 can be used together Adams Bashforth Moulton method of 4th order.

Formulation ABM Method 4th order is as follows:

Predictor ABM Formula:

$$py_{i+1} = y_i + \frac{h}{24}(55y'_n - 59y'_{n-1} + 37y'_{n-2} - 9y'_{n-3}) \quad (5)$$

Corrector ABM Formula:

$$y_{i+1} = y_i + \frac{h}{24}(9py'_{n+1} + 19y'_n - 5y'_{n-1} + y'_{n-2}) \quad (6)$$

With $y'_i = f(x_i, y_i), \forall_i = 3,4, \ldots$

The relative error ABM method 4th order has been formulated as follows:

$E_{ABM} = -\frac{19}{270}(y_{i+1} - py_{i+1}) = D_{i+1}$ (Bronson, R. dan Costa, G.B, 2007).

4.0 RESULTS AND DISCUSSION

Parameters and initial values are used as in Table 1. Completion of the system of equations (1) above by using RKF 45 can be performed with the following steps:

Identification parameter values and initial values of the system of differential equations (1) *Mu* variable *Mu(0), Mi(0), B(0)* and *T(0).*

Determining the value of *t* (time), which will be determined along with the completion magnitude *h* (step size)

Determining the method formulation R KF 45 for the system of equations (1)

Calculate the variables contained in the formula RKF 45 by using a predetermined formula, the variable k_1 - k_6, m_1 -m_6, n_1 -n_6 and p_1 -p_6.

Calculating Mu_{i+1}, Mi_{i+1}, B_{i+1} and T_{i+1} by substituting the variables that have been obtained in step 4 into the formulation methods of RKF 45 in step 3

Based on the above steps, in this study the authors determine the amount of *t* (time) to be resolved is *t* = 1000 *h* (step size) = 0.1 and *i* starts from 0 to 1000. Then, as the value of k_1 - k_6, m_1 -m_6, n_1 -n_6 and p_1 - p_6 are known, then substituted into the equation (2) and (3) so that the first iteration calculations can be performed as follows:

RKF 4th Order calculation:

$$Mu_{0+1} = Mu_0 + \frac{25}{216}k_1 + \frac{1408}{256}k_3 + \frac{2197}{4102}k_4 - \frac{1}{5}k_5$$

$$Mu_1 = 0.7 + \frac{25}{216}(0.0000099) + \frac{1408}{256}(0.0000989987725) + \frac{2197}{4102}(0.000009899697851) - \frac{1}{5}(0.000009899672671)$$

$$Mu_1 = 0.7000098998$$

RKF 5th Order calculation:

$$\hat{M}u_{0+1} = Mu_0 + \frac{16}{135}k_1 + \frac{6656}{12825}k_3 + \frac{28561}{56437}k_4 - \frac{9}{50}k_5 + \frac{2}{55}k_6$$

$$\hat{M}u_1 = Mu_0 + \frac{16}{135}(0.0000099) + \frac{6656}{12825}(0.0000989987725) + \frac{28561}{56437}(0.000009899697851) - \frac{9}{50}(0.000009899672671) + \frac{2}{55}(0.000009899836334)$$

$$\hat{M}u_{0+1} = 7000098992$$

Solutions Mi (t), B (t) and Q (t) can be solved in the same manner as above, after for the 2nd iteration until the 1000 calculation is done with the help of matlab program in order to obtain a system solution with RKF 45 as per shown in Table 1.

Table 1 Solution system of equations (1) with the RKF 45 method

i	t	Variabel	Solution RKF	
			Orde-4	Orde-5
0	0.1	Mu_i	0.7000098998	0.000098992
		Mi_i	0.1997705748	0.1997705898
		B_i	0.0010953448	0.0010952763
		T_i	0.0094874849	0.0094869002
1000	100	Mu_i	0.70973890785489	0.70098835331038
		Mi_i	0.02534013996889	0.15219300148588
		B_i	0.02387361413303	0.06859884960258
		T_i	0.03746338277466	0.19141029376893
10000	1000	Mu_i	0.78432660796594	0.78432193451241
		Mi_i	0.00000092745234	0.00000092929546
		B_i	0.00000073025277	0.00000073170851
		T_i	0.00000140963308	0.00000141243443

Completion of the system of equations (1) by using the ABM can be done with the following steps:

1. Identification parameter valuesand initial values of the system of differential equations (1) *Mu* variable *Mu(0), Mi(0), B(0)* and *T(0)*.
2. Determining the value of *t* (time), which will be determined along with the completion magnitude *h* (step size)
3. Calculating four initial solution $Mu_{0...3}$, $Mi_{0...3}$, $B_{0...3}$ and $T_{0...3}$ using Runge Kutta 4th Order method.
4. Determining the value of f_n, f_{n-1}, f_{n-2} and f_{n-3} with *n*=3,4,… defined as follows:

   $$f_{n-3} = f_0 = f(t_0, Mu_0, Mi_0, B_0, T_0)$$
   $$f_{n-2} = f_1 = f(t_1, Mu_1, Mi_1, B_1, T_1)$$
   $$f_{n-1} = f_2 = f(t_2, Mu_2, Mi_2, B_2, T_2)$$
   $$f_n = f_3 = f(t_3, Mu_3, Mi_3, B_3, T_3)$$

   For value g_n, j_n and k_0 do the same steps as in f_n
5. Determine the numerical solution with an predictors used ABM method 4th Order.
6. Calculating the value of $f_{n+1}, g_{n+1}, j_{n+1}$ dan k_{n+1}.
7. From the calculation of step 6 further calculates a numerical solution using the method corrector ABM- 4th order.
8. Corrector ABM method iterated on *n* to meet,

$\frac{19}{270}\frac{|y_{n+1} - py_{n+1}|}{y_{n+1}} < \varepsilon$ for *n* = 3,4,5,… and ε is the dismissal of the desired criteria, namely $\varepsilon = 5x10^{-8}$.

Based on the above steps, in this study the authors determine the amount of *t* (time) to be resolved is *t* = 1000 *h* (step size) = 0.1 and *i* starts from 0 to 1000. Furthermore, after the four initial solution and value f_n, g_n, j_n and k_n with *n* = *1,2,3* known, then substituted into the equation (5) and (6) so that the first iteration calculations can be performed as follows:

Calculation of predictor ABM 4th Order:

$$pMu_{n+1} = Mu_n + \frac{h}{24}(55f_n - 59f_{n-1} + 37f_{n-2} - 9f_{n-3})$$

$$pMu_{3+1} = Mu_3 + \frac{h}{24}(55f_3 - 59f_2 + 37f_1 - 9f_0)$$

Calculation of correcctor ABM 4th Order:

$$Mu_{n+1} = Mu_n + \frac{h}{24}(9f_{n+1} + 19f_n - 5f_{n-1} + f_{n-2})$$

$$Mu_{3+1} = Mu_3 + \frac{h}{24}(9f_4 + 19f_3 - 5f_2 + f_1)$$

Solutions Mi(t), B(t) and T(t) can be solved in the same manner as above, after for the 2nd iteration until the 1000 calculation is done with the help of matlab program in order to obtain a system solution equation (1) with ABM method as shown in Table 2.

Table 2 Solution system of equations (1) using ABM method

I	*t*	Vari bel	**Solution** ABM	
			predictor	corrector
4	0.5	Mu_i	0.7000049524	0.7000049520
		Mi_i	0.1989761780	0.1989761783
		B_i	0.00432527462	0.004325274544
		T_i	0.03556886560	0.03556887438
100 0	100	Mu_i	0.70973840206275	0.70973840206275
		Mi_i	0.02551775753494	0.02551775753494
		B_i	0.02405045835086	0.02405045835086
		T_i	0.03771836083017	0.03771836083016
100 00	100 0	Mu_i	0.78432284958716	0.78432284958716
		Mi_i	0.00000094967835	0.00000094967835
		B_i	0.00000074775997	0.00000074775997
		T_i	0.00000144341432	0.00000144341432

Figure 1 shows the population (Mu), (Mi), (B) and (T) *starting on day 0 with* parameter values and initial values that have been presented in Table 1. The initial value $(Mu(0) = 0.7)$, $(Mi(0) = 0.2)$, $(B(0) = 0)$, and $(T(0) = 0)$, *constantly* moving up the growth charts (Mu) is beginning on day 1 until day 100, which reached 0.8 cells / ml, while the chart growth (Mi) *continuous* that started moving down on day 1 until day 1000 reached 0002 cells / ml. The movement of growth charts (B) and (T) has increased to 15 the next day to a continuous decline until today to 1000 which reached 0.002 cells / ml. This graph according to the results obtained Ibarguen, E., Esteva, L., & Chavez, L, 2011.

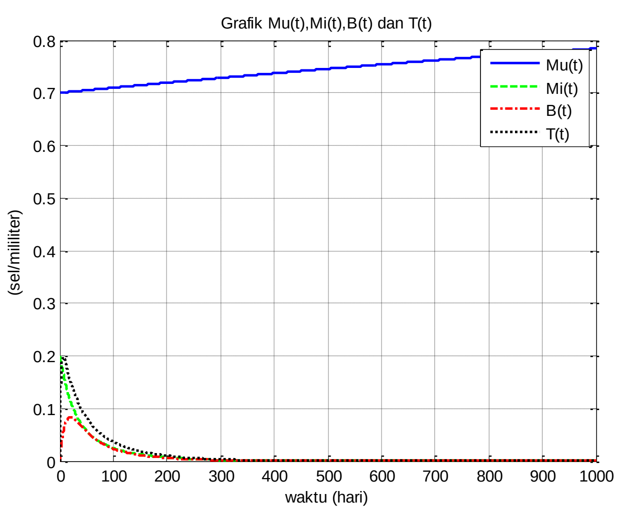


Figure 1 Graph *Mu(t),Mi(t),B(t)* and *T(t)* at *t*=1000

5.0 CONCLUSION

Based on the results of the discussion, it can be concluded that in solving the system of nonlinear differential equations in the model of the cellular immunology of tuberculosis with Runge Kutta Fehlberg method can be done in several stages as in the description above discussion. Completion of numerical of cellular immunology of tuberculosis with Adams Bashforth Moulton method can be done by several stages as in the description above discussion.

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