

THE EFFECTIVENESS OF RUNGE-KUTTA METHOD OF ORDER NINE TO SOLVE THE IMMUNITY MODEL FOR INFECTION OF MYCOBACTERIUM TUBERCULOSIS

Dewi Anggraeni¹⁵, Dafik¹⁶, Susi Setiawani¹⁷

Abstrak. Model sistem kekebalan tubuh terhadap infeksi *Mycobacterium tuberculosis* telah dikembangkan dan dikemas dalam bentuk sistem persamaan diferensial biasa non linier order satu. Model tersebut sangat kompleks sehingga memerlukan metode numerik untuk menyelesaikannya. Salah satu metode numerik yang efektif adalah metode Runge-Kutta. Penelitian ini akan merumuskan formula metode Runge-Kutta order sembilan, dan menentukan sifat dari metode tersebut sebelum merumuskannya, serta menganalisis konvergensi dan efektivitas dari metode Runge-Kutta order sembilan bila dibandingkan dengan metode Adam Bashforth-Moulton order sembilan. Metode dikatakan efektif dan efisien bila error yang terjadi pada metode dalam menyelesaikan model semakin kecil (menuju nol) dan waktu yang dibutuhkan metode untuk menyelesaikan model matematika semakin sedikit. Hasil penelitian menunjukkan bahwa metode Runge-Kutta order sembilan lebih efisien dan efektif dibandingkan metode Adam Bashforth-Moulton order sembilan dalam menyelesaikan model sistem kekebalan tubuh terhadap infeksi *Mycobacterium tuberculosis*.

Kata kunci : Metode Runge-Kutta order sembilan, konvergensi, efektivitas, model sistem kekebalan tubuh terhadap infeksi *Mycobacterium tuberculosis*.

INTRODUCTION

Most of problems in our life can be solved by mathematics. One example is in medical science. Mathematics is used to determine the spread of viruses, bacteria and the spread of infectious and non-infectious diseases. They are represented by mathematical models. One of infectious diseases caused by bacteria are tuberculosis. Based on the facts in the WHO (World Health Organization) report, the disease often attacks the old age human. This is caused by decreased the immunity in old age so that Avner Friedman, Joanne Turner, and Barbara Szomolay developed a model of the influence of age on immunity to infection with *Mycobacterium tuberculosis* [11].

The model is represented by a system of ordinary differential equations first order non-linier that is very complex. The model on the immunity to infection with *Mycobacterium tuberculosis* includes the relationships between the three populations of bacteria, two macrophage populations, four populations of cytokines, and two populations of T cells that is expressed by system of ordinary differential equation first order non-linier. The model are given by equation (1)-(11).

¹⁵Alumna of Mathematic Education, University of Jember

¹⁶Lecturer in Mathematic Education, University of Jember

¹⁷Lecturer in Mathematic Education, University of Jember

$$\begin{aligned} \frac{dB_I}{dt} = & \alpha_I B_I \left(1 - \frac{B_I^2}{B_I^2 + (NM_I)^2}\right) + k_1 n_3 M_R \frac{B_E}{B_E + c_1} - \\ & k_2 N M_I \frac{B_I^2}{B_I^2 + (NM_I)^2} - n_1 k_3 B_I \frac{I_\gamma}{I_\gamma + c_2} + \\ & n_2 k_4 B_A \frac{I_{10}}{I_{10} + c_3 I_\gamma + c_4}, \end{aligned} \quad (1)$$

$$\begin{aligned} \frac{dB_A}{dt} = & \alpha_A B_A - n_2 k_4 B_A \frac{I_{10}}{I_{10} + c_3 I_\gamma + c_4} + n_1 k_3 B_I \frac{I_\gamma}{I_\gamma + c_2} \\ & - n_2 \mu_{MA} B_A, \end{aligned} \quad (2)$$

$$\begin{aligned} \frac{dB_E}{dt} = & \alpha_E B_E - k_1 n_3 M_R \frac{B_E}{B_E + c_1} + k_2 N M_I \frac{B_I^2}{B_I^2 + (NM_I)^2} - \\ & k_5 M_A B_E + n_2 \mu_{MA} B_A, \end{aligned} \quad (3)$$

$$\begin{aligned} \frac{dM_I}{dt} = & k_1 M_R \frac{B_E}{B_E + c_1} - k_2 M_I \frac{B_I^2}{B_I^2 + (NM_I)^2} - k_3 M_I \frac{I_\gamma}{I_\gamma + c_2} + \\ & k_4 M_A \frac{I_{10}}{I_{10} + c_3 I_\gamma + c_4} - \mu_{MI} M_I, \end{aligned} \quad (4)$$

$$\begin{aligned} \frac{dM_A}{dt} = & -k_4 M_A \frac{I_{10}}{I_{10} + c_3 I_\gamma + c_4} + k_3 M_I \frac{I_\gamma}{I_\gamma + c_2} - \mu_{MA} M_A + \\ & k_6 M_R \frac{B_E}{B_E + c_5} \frac{I_\gamma}{I_\gamma + c_6}, \end{aligned} \quad (5)$$

$$\frac{dI_{10}}{dt} = k_7 M_I \frac{c_7}{I_{10} + c_7} - \mu_{10} I_{10}, \quad (6)$$

$$\frac{dI_{12}}{dt} = k_8 M_A \frac{c_8}{I_{10} + c_8} + k_9 M_R \frac{B_E}{B_E + c_9} - \mu_{12} I_{12}, \quad (7)$$

$$\frac{dI_2}{dt} = k_{10} T_4 - (k_{11} T_4 + k_{12} T_8) \frac{I_2}{I_2 + c_{10}} - \mu_2 I_2, \quad (8)$$

$$\frac{dI_\gamma}{dt} = (\lambda_u(t) + \lambda_y(t) T_8) \frac{I_{12}}{I_{12} + c_{11}} - \mu_\gamma I_\gamma, \quad (9)$$

$$\frac{dT_4}{dt} = \lambda_z(t) M_A I_{12} + k_1 3 T_4 \frac{I_2}{I_2 + c_{10}} - \mu_{T_4} T_4, \quad (10)$$

$$\frac{dT_8}{dt} = \lambda_x(t) (M_A + M_I) I_{12} + k_1 4 T_8 \frac{I_2}{I_2 + c + 10} - \mu_{T_8} T_8 \quad (11)$$

The estimation of initials values and parameters values of the model are gotten based on the result of research were done by Avner Friedman, Joanne Turner and Barbara Szomolary [11].

The model can't be solved by analytical method so that we must use the numerical method to solve it. One of the effective numerical method is the Runge-Kutta method. The level of this method is higher than Euler method, because this method has a high precision. The advantages of this method is the technique is more accurate because it has small truncation and integration errors [10]. Runge-Kutta method can be developed

to a higher order. Many previous research have developed Runge-Kutta method. Runge-Kutta method that has been found is third order Runge-Kutta (Asih, 2001), fourth order Runge-Kutta (Faisol, 2001), fifth order Runge-Kutta (Yustica, 2010), sixth order Runge-Kutta (Bukaryo, 2012), seventh order Runge-Kutta (shodiq, 2012) [15], and Eighth order Runge-Kutta (Ardhilia, 2013).

Runge-Kutta Method has three characteristics, that are:

1. Runge-Kutta method is one-step method, to obtain $y_{(m+1)}$ it need only the values at an earlier point, x_m, y_m ;
2. based on Taylor series, Runge-kutta method is up to h^p , where p is different for different methods and it is called order of method;
3. Runge-Kutta method does not require the evaluation of any derivative $f(x, y)$, but only function f itself.

Definition 1. Runge-Kutta method is defined by:

$$y_{n+1} = y_n + h \sum_{i=1}^m b_i k_i, \quad \text{where } k_i = f(x_n + c_i h, y_n + h \sum_{j=1}^{i-1} a_{ij} k_j),$$

with the assumption : $c_i = \sum_{j=1}^m a_{ij}$, dan $\sum_{i=1}^m b_i = 1$, $i = 1, 2, \dots$. The value of a, b, c can be expressed by Butcher Array table below.

0					
c_2	a_{21}				
c_3	a_{31}	a_{32}			
\vdots	\vdots	\vdots	\ddots		
c_m	a_{m1}	a_{m2}	\dots	a_{mm-1}	
	b_1	b_2	\dots	b_{m-1}	b_m

Based on previous studies, Runge-Kutta method with a higher order will be more effective if it was compared to the Runge-Kutta with a lower order. One such case, the Fifth Order Runge-Kutta method is more effective than the sixth order Runge-Kutta Method [19]. Runge-Kutta method with higher order is also more effective than other methods with lower order. One such case, the Seventh order Runge-Kutta Method is more effective than the sixth order Adam Bashforth-Moulton method [15].

Research to determine the effectiveness of the Runge-Kutta method if it is compared with other method and the same order has not been done. In this paper, we

will analyze the effectiveness of the ninth order Runge-Kutta method to solve a model on the immunity to infection with *Mycobaterium tuberculosis* and compare it with the ninth order Adam Bashforth-Moulton method.

RESEARCH METHOD

Research method of this research is deductive axiomatic and experiment. This research use the existed definitions and theorems to determine the characters of Ninth Order Runge-Kutta method and to formulate the formula of it. The existed definitions and theorems are taken form Lambert (1997) [12], Fausett (2008) [9], and Dafik (1999) [4]. Experiment method is used to analyze efficiency and effectiveness of Ninth Order Runge-Kutta method if it is compared with Ninth Orders Adam Bashforth-Moulton method.

THE RESULTS OF RESEARCH

Lemma 1. *Ninth Order Runge-Kutta Method has the following character :*

$$\sum_{i=1}^m b_i = 1, \quad \text{where } m = 9 \quad (12)$$

$$\sum_{i=2}^m b_i c_i^p = \frac{1}{p+1}, \quad \text{for } p = 1, 2, 3, \dots, m-1 \quad (13)$$

$$\sum_{i=3}^{m-1} b_i \left(\sum_{j=2}^{i-1} c_j^q a_{ij} \right) = \frac{1}{(q+1)(q+2)}, \quad \text{for } q = 1, 2, 3, \dots, m-3 \quad (14)$$

Proof. Based on definition (1), ninth order Runge-Kutta method is defined by :

$$y_{n+1} = y_n + h \sum_{i=1}^m b_i k_i, \quad \text{where } m = 9, \quad \text{then } y_{n+1} = y_n + h(b_1 k_1 + b_2 k_2 + b_3 k_3 + b_4 k_4 + b_5 k_5 + b_6 k_6 + b_7 k_7 + b_8 k_8 + b_9 k_9).$$

We use expansion of Taylor series to compare it with y_{n+1} and it is needed $y^{(1)}(x_n), \dots, y^{(9)}(x_n)$. To make easier, we suppose $J = f_x + f f_y$, $K = f_{xx} + 2f f_{xy} + f^2 f_{yy}$, $L = f_{xxx} + 3f f_{xxy} + 3f^2 f_{xyy} + f^3 f_{yyy}$, $M = f_{xxxx} + 4f f_{xxx} + 6f^2 f_{xxy} + 4f^3 f_{xyy} + f^4 f_{yyy}$, $N = f_{xxxxx} + 5f f_{xxxx} + 10f^2 f_{xxx} + 10f^3 f_{xxy} + 5f^4 f_{xyy} + f^5 f_{yyy}$, $O = f_{xxxxxx} + 6f f_{xxxxx} + 15f^2 f_{xxxx} + 20f^3 f_{xxx} + 15f^4 f_{xxy} + 6f^5 f_{xyy} + f^6 f_{yyy}$, $P = f_{xxxxxxx} + 7f f_{xxxxxx} + 21f^2 f_{xxxxx} + 35f^3 f_{xxxx} + 35f^4 f_{xxx} + 21f^5 f_{xxy} + 7f^6 f_{xyy} + f^7 f_{yyy}$, $Q = f_{xxxxxxxx} + 8f f_{xxxxxxx} + 28f^2 f_{xxxxxx} + 56f^3 f_{xxxxx} + 70f^4 f_{xxxx} + 56f^5 f_{xxx} + 28f^6 f_{xxy} + 8f^7 f_{xyy} + f^8 f_{yyy}$. And then we

get the derivate of $y(x_n)$ that are $y^{(1)} = f$, $y^{(2)} = J$, $y^{(3)} = K + Jf_y$, $y^{(4)} = L + Kf_y$, $y^{(5)} = M + Lf_y$, $y^{(6)} = N + Mf_y$, $y^{(7)} = O + Nf_y$, $y^{(8)} = P + Of_y$, $y^{(9)} = Q$.

The expansion of $y(x_{n+1})$ is done by substitute $y^{(1)}, y^{(2)}, \dots, y^{(9)}$ to Taylor series, that is:

$$\begin{aligned}
 y(x_{n+1}) = & y(x_n) + hf + \frac{1}{2!}h^2J + \frac{1}{3!}(K + Jf_y) + \frac{1}{4!}h^4(L + Kf_y) + \frac{1}{5!}h^5(M + Lf_y) \\
 & + \frac{1}{6!}h^6(N + Mf_y) + \frac{1}{7!}h^7(O + Nf_y) + \frac{1}{8!}h^8(P + Of_y) \\
 & + \frac{1}{9!}h^9Q + \frac{1}{10!}h^{10}y^{(10)}(x_n) + \dots
 \end{aligned} \tag{15}$$

The expansion of $k_1, k_2, k_3, k_4, \dots, k_9$ is done by rule of two variables Taylor series expansion [9] and substitute it to y_{n+1} . So, by compare $y(x_{n+1})$ with y_{n+1} we will get the characteristic of ninth order Runge-Kutta method.□

Corollary 1. *The formula of ninth order Runge-Kutta method (RK9A)*

$$\begin{aligned}
 y_{n+1} = & y_n + \frac{h}{105.000}(5062k_1 + 27.357k_2 + 1.260k_3 + 1.275k_4 + 35.050k_5 \\
 & - 16.800k_6 + 19.440k_7 + 27.273k_8 + 5.083k_9)
 \end{aligned}$$

where,

$$\begin{aligned}
 k_1 &= f(x_n, y_n) \\
 k_2 &= f(x_n + \frac{h}{6}, y_n + \frac{h}{6}k_1) \\
 k_3 &= f(x_n + \frac{h}{3}, y_n + \frac{h}{6}(k_1 + k_2)) \\
 k_4 &= f(x_n + \frac{h}{3}, y_n + \frac{h}{3}(-k_1 + k_2 + k_3)) \\
 k_5 &= f(x_n + \frac{h}{2}, y_n + \frac{h}{10}(k_1 + 2k_2 + k_3 + k_4)) \\
 k_6 &= f(x_n + \frac{2h}{2}, y_n + \frac{h}{48}(-10k_1 + 2k_2 + 25k_3 + 9k_4 + 6k_5)) \\
 k_7 &= f(x_n + \frac{2h}{3}, y_n + \frac{h}{240}(65k_1 + 27k_2 + 27k_3 - 8k_4 + 93k_5 - 44k_6)) \\
 k_8 &= f(x_n + \frac{5h}{6}, y_n + \frac{h}{5.4546}(-13.291k_1 + 24.768k_2 + 942k_3 + 3.336k_4 + \\
 & 22.542k_5 + 6.612k_6 + 546k_7)) \\
 k_9 &= f(x_n + h, y_n + \frac{h}{5.083}(-4.844k_1 + 984k_2 + 2.912k_3 + 125k_4 + 296k_5 \\
 & + 1.008k_6 + 102k_7 + 4.500k_8))
 \end{aligned}$$

Proof. To proof it, we must solve the Lemma (1), in order we get the value of matrix coefficient. It is solved by determine the value of $c_1, c_2, c_3, \dots, c_9$ such as we get the value

of b_1, b_2, \dots, b_9 that is satisfy with $c_i = \sum_{j=1}^9 a_{ij}$ and $\sum_{i=1}^9 b_i = 1$. the determination are $c_2 = \frac{1}{6}, c_3 = \frac{1}{3}, c_4 = \frac{1}{3}, c_5 = \frac{1}{2}, c_6 = \frac{2}{3}, c_7 = \frac{2}{3}, c_8 = \frac{5}{6}$, and $c_9 = 1$. To get the value of $a_{32}, a_{42}, a_{43}, \dots$, we must modified the Eq.(14) become $\sum_{i=2}^8 c_i^k (\sum_{j=i+1}^9 b_j a_{ji})$, $k = 1, 2, \dots, 6$ because Eq.(14) is very complex by suppose $\sum_{j=i+1}^9 b_j a_{ji} = A$ for $i = 2$, $\sum_{j=i+1}^9 b_j a_{ji} = B$ for $i = 3$ up to $\sum_{j=i+1}^9 b_j a_{ji} = G$ for $i = 8$. Then we get a new equation system by find the value of A, B, C, D, \dots, G to get the value of coefficient matrix that contain a_{32}, a_{42}, \dots . Based on the Runge-Kutta properties that are $c_i = \sum_{j=1}^9 a_{ij}$ dan $\sum_{i=1}^9 b_i = 1$, the coefficient matrix can be expressed by Butcher array at table (1). □

Table 1: Coefficient matrix Ninth Order Runge-Kutta Method (RK9A)

0	0								
$\frac{1}{6}$	$\frac{1}{6}$	0							
$\frac{1}{3}$	$\frac{1}{6}$	$\frac{1}{6}$	0						
$\frac{1}{3}$	$-\frac{1}{3}$	$\frac{1}{3}$	$\frac{1}{3}$	0					
$\frac{1}{2}$	$\frac{1}{10}$	$\frac{2}{10}$	$\frac{1}{10}$	$\frac{1}{10}$	0				
$\frac{2}{3}$	$-\frac{10}{48}$	$\frac{2}{48}$	$\frac{25}{48}$	$\frac{9}{48}$	$\frac{6}{48}$	0			
$\frac{2}{3}$	$\frac{65}{240}$	$\frac{27}{240}$	$\frac{27}{240}$	$-\frac{8}{240}$	$\frac{93}{240}$	$-\frac{44}{240}$	0		
$\frac{5}{6}$	$\frac{-13.291}{54.546}$	$\frac{24.768}{54.546}$	$\frac{942}{54.546}$	$\frac{3.336}{54.546}$	$\frac{22.542}{54.546}$	$\frac{6.612}{54.546}$	$\frac{546}{54.546}$	0	
1	$\frac{-4.844}{5.083}$	$\frac{984}{5.083}$	$\frac{2.912}{5.083}$	$\frac{125}{5.083}$	$\frac{296}{5.083}$	$\frac{1.008}{5.083}$	$\frac{102}{5.083}$	$\frac{4.500}{5.083}$	0
	$\frac{5.062}{105.000}$	$\frac{27.357}{105.000}$	$\frac{1.260}{105.000}$	$\frac{1.275}{105.000}$	$\frac{35.050}{105.000}$	$\frac{-16.800}{105.000}$	$\frac{19440}{105.000}$	$\frac{27.273}{105.000}$	$\frac{5.083}{105.000}$

The formula above is said RK9A method, because from the effect of Lemma (1), we can to get the new formula with the same c_1, c_2, \dots, c_9 but different a_{31}, a_{32}, a_{41} , and so on. The RK9A method is ninth order Runge-Kutta method with determination value $c_1 = 0, c_2 = \frac{1}{6}, c_3 = \frac{1}{3}, c_4 = \frac{1}{3}, c_5 = \frac{1}{2}, c_6 = \frac{2}{3}, c_7 = \frac{2}{3}, c_8 = \frac{5}{6}$, and $c_9 = 1$, and with maximal matrix coefficient. The other formula of ninth order Runge-Kutta method is called RK9B method that has the same c_1, c_2, \dots, c_9 but it has minimal matrix coefficient.

Corollary 2. *The formula of ninth order Runge-Kutta method (RK9B) is expressed by Butcher array at table (2)*

Table 2: Matriks koefisien Runge-Kutta Order Sembilan (RK9B)

0	0								
$\frac{1}{6}$	$\frac{1}{6}$	0							
$\frac{1}{3}$	$\frac{-368}{21}$	$\frac{125}{7}$	0						
$\frac{1}{3}$	$\frac{-13}{51}$	0	$\frac{10}{17}$	0					
$\frac{1}{2}$	$\frac{641}{1402}$	0	0	$\frac{30}{701}$	0				
$\frac{2}{3}$	$\frac{47}{28}$	0	0	0	$\frac{-85}{84}$	0			
$\frac{2}{3}$	$\frac{407}{648}$	0	0	0	0	$\frac{25}{648}$	0		
$\frac{5}{6}$	$\frac{44.705}{54.546}$	0	0	0	0	0	$\frac{125}{9.091}$	0	
1	$\frac{583}{5.083}$	0	0	0	0	0	0	$\frac{4.500}{5.083}$	0
	$\frac{5.062}{105.000}$	$\frac{27.357}{105.000}$	$\frac{1.260}{105.000}$	$\frac{1.275}{105.000}$	$\frac{35.050}{105.000}$	$\frac{-16.800}{105.000}$	$\frac{19440}{105.000}$	$\frac{27.273}{105.000}$	$\frac{5.083}{105.000}$

Theorem 1. *Ninth order Runge-Kutta method is convergent method because it satisfy*

$$\|e_n\| \leq \frac{h^9 M_{10}}{10! \check{L}} (e^{(x_n - x_0)\check{L}} - 1), \text{ where } \check{L} \text{ is Lipschitz constant.}$$

Proof. Global error is determined based on the definition of Global error [6],

$$e_n = y(x_n) - y_n \text{ such as } e_{n+1} = y(x_{n+1}) - y_{n+1},$$

$$e_{n+1} = e_n + h(y^{(1)}(x_n) - y_n^{(1)}) + \frac{1}{2!}h^2(y^{(2)}(x_n) - y_n^{(2)}) + \frac{1}{3!}h^3(y^{(3)}(x_n) - y_n^{(3)}) + \frac{1}{4!}h^4(y^{(4)}(x_n) - y_n^{(4)}) + \frac{1}{5!}h^5(y^{(5)}(x_n) - y_n^{(5)}) + \frac{1}{6!}h^6(y^{(6)}(x_n) - y_n^{(6)}) + \frac{1}{7!}h^7(y^{(7)}(x_n) - y_n^{(7)}) + \frac{1}{8!}h^8(y^{(8)}(x_n) - y_n^{(8)}) + \frac{1}{9!}h^9(y^{(9)}(x_n) - y_n^{(9)}) + \frac{h^{10}}{10!}y^{(10)}(\eta)$$

Based on Lipschitz condition [3] and assume $|y^{(10)}(\eta)| < M_{10}$, then we get $\|e_{n+1}\| \leq$

$$\|e_n + hL_1e_n + \frac{1}{2!}h^2L_2e_n + \frac{1}{3!}h^3L_3e_n + \frac{1}{4!}h^4L_4e_n + \frac{1}{5!}h^5L_5e_n + \frac{1}{6!}h^6L_6e_n + \frac{1}{7!}h^7L_7e_n + \frac{1}{8!}h^8L_8e_n + \frac{1}{9!}h^9L_9e_n + \frac{h^{10}}{10!}M_{10}\|. \text{ Based on norm vector definition [3], we get } \|e_{n+1}\| \leq (1 + h\check{L})\|e_n\| + \frac{h^{10}}{10!}M_{10}, \check{L} = \text{konstanta Lipschitz. in fact, } \|e_0\| = 0, \|e_1\| \leq \frac{h^{10}}{10!}M_{10}, \|e_2\| \leq (1 + h\check{L})\frac{h^{10}}{10!}M_{10} + \frac{h^{10}}{10!}M_{10}, \|e_3\| \leq (1 + h\check{L})(1 + h\check{L})\frac{h^{10}}{10!}M_{10} + (1 + h\check{L})\frac{h^{10}}{10!}M_{10} + \frac{h^{10}}{10!}M_{10}, \dots, \|e_n\| \leq (1 + (1 + h\check{L}) + (1 + h\check{L})^2 + \dots + (1 + h\check{L})^{n-1})\frac{h^{10}}{10!}M_{10}. \text{ So, we get } \|e_n\| \leq \frac{h^9 M_{10}}{10! \check{L}} (1 + h\check{L})^n - 1.$$

Because of $h, (1 + h\check{L})^n \leq e^{nh\check{L}}, h = \frac{x_n - x_0}{n}, \check{L} > 0, (1 + h\check{L})^n \leq e^{nh\check{L}}, h = \frac{x_n - x_0}{n}$, then

$\lim_{h \rightarrow 0} \|e_n\| \leq \lim_{h \rightarrow 0} \frac{h^9 M_{10}}{10! L} (e^{(x_n - x_0)L} - 1) = 0$. So, ninth order Runge-Kutta method is convergence method. \square

Simulation Result

In this section we describe simulation result based on the gotten solution by ninth order Runge-Kutta method to solve model on the immunity to infection with *Mycobacterium tuberculosis*.

The models include the interaction between 3 populations of bacteria, 2 populations of macrophages, 4 concentrations of cytokines, and 2 population of T lymphocytes, that are T CD4+ and T CD8+. On the graph BI population, population of intracellular bacteria in young mice and old mice since the beginning infected increase drastically, but in young mice, it decreases after nearly 15×10^5 cell/ml and old mice continue to rise until it reaches $2,3 \times 10^6$ cell/ml. The population of extracellular bacteria in young mice and old mice increase up to $1,8 \times 10^5$, but extracellular bacteria load of young mice decrease up to 7×10^4 , and in old mice, it decrease up to $1,5 \times 10^5$. the both of extracellular bacteria stabilize after 40 days. Populations of activated bacteria in young mice and old mice increased drastically since 15 days of infection, and young mice faster than old mice in stabilize. This fact caused the old age human easily attacked tuberculosis.

The concentrate of IL-10 in old mice is more than young mice. The increased of IL-10 can decrease the immunity to activate bacteria so that it increase activated macrophage. This fact caused the old age human easily attacked tuberculosis. The function of $IFN - \gamma$ is to disable infected macrophage so that it is become activated macrophage that is active to disable *Mycobacterium tuberculosis*. The concentrate of $IFN - \gamma$ in old mice is less than young mice. This fact also caused the old age human easily attacked tuberculosis.

Efficiency of Ninth Order Runge-Kutta Method

Ninth Order Runge-Kutta and Adams Bashforth-Moulton method are convergent because the error of both method are close to zero. In addition to the graph convergence, it also produced the number of iterations and time are presented in Table 3.

Table 3 shows that any value specified tolerance, RK9B method requires more iterations than the methods RK9A, and the method most require iterations to reach

Table 3: Table of Efisiensi

Indikator	Tol (ϵ)	young mice			old mice		
		RK9A	RK9B	ABM9	RK9A	RRK9B	ABM9
Iteration	10^{-1}	92.820	92.816	93.848	91.247	91.267	91.310
	10^{-3}	133.477	133.482	133.517	123.179	123.212	123.265
	10^{-5}	174.115	174.128	174.165	154.930	154.978	155.036
time (secon)	10^{-1}	181,459	45,3339	126,440	167,529	42,9780	108,9810
	10^{-3}	241,0210	71,3069	184,8760	217,4330	63,1020	152,9460
	10^{-5}	315,7600	110,9940	284,7000	280,9410	90,5720	213,2840

the tolerance is ABM9 method. So that we can say that Runge-Kutta method with matrix coefficient value minimal requires more iterations than Runge-Kutta method with matrix coefficient value maximal. However, based on Table 5, RK9B method takes less time than the RK9A method. This is because the ninth order Runge-Kutta relies on a previous step, ie k_1 affect k_2 , k_2 influence k_3 , and so on. In Methods RK9A value of k_2 is affected k_1 , k_3 if influenced k_1 and k_2 , k_4 is influenced k_1 , k_2 , and k_3 , and so on, each worth k_i is affected all values of k in advance ($k_{i-1}, k_{i-2}, \dots, k_1$). While, because the coefficient matrix of the RK9B method is minimal then the value of k_4 is only influenced k_1 and k_3 , k_5 is only affected k_1 and k_4 , the value of k_i is only affected by two k ie k_1 and k_{i-1} , so that ABM9 method needs more time than the RK9B method.

Then, ninth order Runge-Kutta metode which be compared with ABM9 is RK9B method. Table 5 shows that RK9B method needs the least amount of time than the ABM9 method. so, we can conclude that Ninth Order Runge-Kutta method is more effective than ninth order Adam Bahforth-Moulton.

Effectiveness of Ninth Order Runge-Kutta Method

The data generated from the execution of the effectiveness of such errors are presented in Table 6. Based on the table, iterations that are used to analyze the effectiveness of the ninth order Runge-Kutta method than Ninth Order Adam Bashforth-Moulton is 10.000, 50.000, 100.000, 115.000, 125.000, 150.000, 175.000, and 200.000. At iteration 10.000 to 100.000, it can not be determined the most effective method, because at the 10.000 iterations, ABM9 method has the smallest error, whereas at 50.000 and 100.000 iterations the smallest error occurs in the method RK9B. But at iteration 115.000, and so on indicate that the method RK9A has the smallest error. It can be concluded that the ninth order Runge-Kutta more effective than Ninth Order Adam

Bashforth-Moulton methods to solve a model on the immunity to infection with *Mycobacterium tuberculosis*.

Table 4: Effectiveness in young mice

Iteration (n)	<i>Error</i>		
	RK9A	RK9B	ABM9
10.000	76,171886	76,183000	76,169763
50.000	12,412641	12,411799	12,447050
100.000	$4,436146 \times 10^{-2}$	$4,434942 \times 10^{-2}$	$4,451410 \times 10^{-2}$
115.000	$8,113087 \times 10^{-3}$	$8,113704 \times 10^{-3}$	$1,530210 \times 10^{-2}$
125.000	$2,613003 \times 10^{-3}$	$2,613837 \times 10^{-3}$	$2,624033 \times 10^{-3}$
150.000	$1,537487 \times 10^{-4}$	$1,538936 \times 10^{-4}$	$1,545185 \times 10^{-4}$
175.000	$9,044539 \times 10^{-6}$	$9,058975 \times 10^{-6}$	$9,097000 \times 10^{-6}$
200.000	$5,322508 \times 10^{-7}$	$5,331821 \times 10^{-7}$	$5,355000 \times 10^{-7}$

Table 5: Effectiveness in old mice

Iteration (n)	<i>Error</i>		
	RK9A	RK9B	ABM9
10.000	41,216065	41,188425	41,189464
50.000	27,851661	27,869678	27,935266
100.000	$2,846000 \times 10^{-2}$	$2,856079 \times 10^{-2}$	$2,875000 \times 10^{-2}$
115.000	$5,213087 \times 10^{-3}$	$5,214104 \times 10^{-3}$	$6,730210 \times 10^{-3}$
125.000	$7,680794 \times 10^{-4}$	$7,718964 \times 10^{-4}$	$7,778736 \times 10^{-4}$
150.000	$2,045277 \times 10^{-5}$	$2,058641 \times 10^{-5}$	$2,075871 \times 10^{-5}$
175.000	$5,424954 \times 10^{-7}$	$5,471520 \times 10^{-7}$	$5,518000 \times 10^{-7}$
200.000	$1,443548 \times 10^{-8}$	$1,443549 \times 10^{-8}$	$1,444000 \times 10^{-7}$

CONCLUSION

Based on the results of the discussion, we can conclude that:

1. Ninth Order Runge-Kutta method has the following character:

$$\sum_{i=1}^m b_i = 1, \quad \text{where } m = 9$$

$$\sum_{i=2}^m b_i c_i^p = \frac{1}{p+1}, \quad \text{for } p = 1, 2, 3, \dots, m-1$$

$$\sum_{i=3}^{m-1} b_i \left(\sum_{j=2}^{i-1} c_j^q a_{ij} \right) = \frac{1}{(q+1)(q+2)}, \quad \text{for } q = 1, 2, 3, \dots, m-3$$

2. The formula of Ninth Order Runge-Kutta method (RK9A) is:

$$y_{n+1} = y_n + \frac{h}{105.000} (5062k_1 + 27.357k_2 + 1.260k_3 + 1.275k_4 + 35.050k_5 - 16.800k_6 + 19.440k_7 + 27.273k_8 + 5.083k_9)$$

where,

$$k_1 = f(x_n, y_n)$$

$$k_2 = f\left(x_n + \frac{h}{6}, y_n + \frac{h}{6}k_1\right)$$

$$k_3 = f\left(x_n + \frac{h}{3}, y_n + \frac{h}{6}(k_1 + k_2)\right)$$

$$k_4 = f\left(x_n + \frac{h}{3}, y_n + \frac{h}{3}(-k_1 + k_2 + k_3)\right)$$

$$k_5 = f\left(x_n + \frac{h}{2}, y_n + \frac{h}{10}(k_1 + 2k_2 + k_3 + k_4)\right)$$

$$k_6 = f\left(x_n + \frac{2h}{3}, y_n + \frac{h}{48}(-10k_1 + 2k_2 + 25k_3 + 9k_4 + 6k_5)\right)$$

$$k_7 = f\left(x_n + \frac{2h}{3}, y_n + \frac{h}{240}(65k_1 + 27k_2 + 27k_3 - 8k_4 + 93k_5 - 44k_6)\right)$$

$$k_8 = f\left(x_n + \frac{5h}{6}, y_n + \frac{h}{5.4546}(-13.291k_1 + 24.768k_2 + 942k_3 + 3.336k_4 + 22.542k_5 + 6.612k_6 + 546k_7)\right)$$

$$k_9 = f\left(x_n + h, y_n + \frac{h}{5.083}(-4.844k_1 + 984k_2 + 2.912k_3 + 125k_4 + 296k_5 + 1.008k_6 + 102k_7 + 4.500k_8)\right)$$

3. Ninth order Runge-Kutta is convergent method because it satisfy : $\|e_n\| \leq$

$$\frac{h^9 M_{10}}{10! \check{L}} (e^{(x_n - x_0)\check{L}} - 1), \text{ where } \check{L} \text{ is Lipschitz constant.}$$

4. Ninth Order Runge-Kutta is more efficient and more effective than Ninth Order Adam Bashforth-Moulton to solve a model on the immunity to infection with *Mycobacterium tuberculosis*

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