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AN OPTIMAL IMPLICIT BLOCK METHOD FOR SOLUTIONS OF THE TUMOR-IMMUNE INTERACTION MODEL OF ODEs

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Abstract

Due to the widespread use of differential equations, numerical methods are being developed in order to solve numerous difficult initial value problems (IVPs) when an analytical solution would seem to be impractical. The goal of this study was to employ Taylor series expansion to construct a 2-point fully implicit block backward differentiation formula (2IBBDF), examine its stability characteristics and then apply the suggested approach to one of the models for tumor-immune interaction that are already in existence. Regarding the resolution of the tumor-immune interaction model, the research has compared the numerical outcomes of the suggested method with some of the current

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methodologies. The proposed technique outperforms the Ode15s and 2-point block backward differentiation formula (BBDF) in relation to accuracy in the scale error and in most of computational time.

1. Introduction

The majority of real-world issues we face, particularly in the physical, social, and life sciences, may be described by using differential equations. Most of differential equations can be used to describe issues involving kinetics, chemical reactions, electrical circuits, vibrations, and population growth, for instance. Such differential equations come in two kinds: non-stiff and stiff. In order to create numerical schemes that are advantageous in terms of accuracy, scale error, and computation time, researchers developed a variety of numerical methods. Some of these include the early work of (Curtiss & Hirschfelder [11]), the extended BDF (Cash [9]), and the modified extended BDF (Cash [10]). With the work of (Ibrahim et al. [12]), a new 5th order IBM for 1st order stiff ODEs (Musa et al. [20]), a new superclass of BBDF for stiff ODEs (Suleiman et al. [35]), and numerical treatment of the block method for the solution of ODEs (Sagir [29]), the block method was given priority. The tumor-immune interaction model was resolved by (Nasir et al. [22]) using the block technique. Numerous studies by (Ibrahim et al. [13]; Aksah et al. [7]; Ibrahim & Zawawi [14]; Nasir et al. [23]; Majid et al. [16]; Rani et al. [27]; Zawawi et al. [38]; Nasarudin et al. [21]; Ibrahim et al. [13]; Muangchoo [17]; Saudi & Sulaiman [32]; Shafiq et al. [33]; Abd Rasid et al. [5]; Musa et al. [19]; Abdullahi & Musa [1]; Abdullahi et al. [3]; Abdullahi et al. [2]; Abdullahi et al. [4]; Sagir [30]; Yahaya & Sagir [37]; Sagir [28]; Sagir & Abdullahi [31]; Rahim et al. [26]; Rahim et al. [25]; Yaacob et al. [36]; Sujatono [34]) have at one point or another established numerical algorithms with excellent stability qualities.

This study uses a technique known as implicit BBD for solving a set of first-order IVPs involving ODEs of the type

$$y' = f(x, \widehat{Y}), \qquad \widehat{Y}(a) = \rho\eta, \qquad a \le x \le b, \tag{1}$$

where $\widehat{Y} = (y_1, y_2, y_3, \ldots, y_n)$ and $\eta\overline{\rho} = (\rho\eta_1, \rho\eta_2, \rho\eta_3, \ldots, \rho\eta_n)$.

The suggested strategy will be used to solve the model of tumor-immune interaction using ordinary differential equations (Kirschner & Panetta [15]).

2. Method Formulation

Consider

$$\sum_{j=0}^{3} \alpha_{j,i} y_{n+j-1} = h\beta_{k,i}(f_{n+k} + f_{n+k-1}), \quad k = i = 1, 2. \tag{2}$$

Definition 2.1.

The linear difference operator L connected with the linear multi-step method is defined as

$$L\{y(x), h\} = \sum_{j=0}^{k} [\alpha_j y(x + jh) - h\beta_j y'(x + jh)], \tag{3}$$

where $y(x)$ is considered as test function and it is repeatedly differentiable on the interval $[a, b]$. Expanding $y(x + jh)$ as well as $y'(x + jh)$ by the Taylor series about x, and similarly expanding the conventional conditions produces:

$$L\{y(x), h\} = c_0 y(x_n) + c_1 h y'(x_n) + c_2 h^2 y''(x_n) + \cdots + c_q h^q y^q(x_n) + \cdots.$$

The implicit method of Equation (2) is constructed by using a linear operator L_i. To obtain the first and second points, define the linear operator L_1 and L_2 associated with (2) as

$$L_1[y(x_n), h)] : \alpha_{0,i} y_{n-1} + \alpha_{1,i} y_n + \alpha_{2,i} y_{n+1} + \alpha_{3,i} y_{n+2} - h\beta_{k,i}[f_{n+k} + f_{n+k-1}] = 0, \tag{4}$$

$$L_2[y(x_n), h)] : \alpha_{0,i} y_{n-1} + \alpha_{1,i} y_n + \alpha_{2,i} y_{n+1} + \alpha_{3,i} y_{n+2} - h\beta_{k,i}[f_{n+k} + f_{n+k-1}] = 0. \tag{5}$$

The formula that is found when $k = i = 1$ relates to the 1st point, whereas $k = i = 2$ relates to the 2nd point. Apply the Taylor's series to expand (4) and (5) results in an equation set that can be handled at once. The coefficient $\alpha_{2,1}$ is standardized to 1 for the 1st point, while $\alpha_{3,2}$ is standardized to 1 for the 2nd. Inferred the proposed method (2IBBDF) is as follows:

$$y_{n+1} = \frac{1}{9} y_{n-1} + y_n - \frac{1}{9} y_{n+2} + \frac{2}{3} hf_{n+1} + \frac{2}{3} hf_n, \tag{6}$$

$$y_{n+2} = \frac{1}{13} y_{n-1} - \frac{3}{13} y_n + \frac{15}{13} y_{n+2} + \frac{6}{13} hf_{n+2} + \frac{6}{13} hf_{n+1}. \tag{7}$$

3. Stability Analysis of the Method

Definition 3.1.

The linear multi-step technique is considered to be zero-stable if no root of the first characteristic polynomial has a modulus greater than one and all roots with a modulus of one are simple.

The stability of the method (6)-(7) can be obtains utilizing the standard test equation of the form:

$$y' = \lambda y, \qquad \mathrm{Re}(\lambda) < 0, \tag{8}$$

where λ is a complex number.

The matrix form of the previous Equations (6)-(7) is

$$A_0 Y_m = A_1 Y_{m-1} + h[B_0 F_{m-1} + B_1 F_m], \tag{9}$$

$$\begin{bmatrix} 1 & \frac{1}{9} \\ -\frac{15}{13} & 1 \end{bmatrix} \begin{bmatrix} y_{n+1} \\ y_{n+2} \end{bmatrix} = \begin{bmatrix} \frac{1}{9} & 1 \\ \frac{1}{13} & -\frac{3}{13} \end{bmatrix} \begin{bmatrix} y_{n-1} \\ y_n \end{bmatrix} + h \begin{bmatrix} 0 & \frac{2}{3} \\ 0 & 0 \end{bmatrix} \begin{bmatrix} f_{n-1} \\ f_n \end{bmatrix} + h \begin{bmatrix} \frac{2}{3} & 0 \\ \frac{6}{13} & \frac{6}{13} \end{bmatrix} \begin{bmatrix} f_{n+1} \\ f_{n+2} \end{bmatrix}. \tag{10}$$

(10) can be written as

$$\begin{bmatrix} 1-\frac{2}{3}h\lambda & \frac{1}{9} \\ -\frac{15}{13}-\frac{6}{13}h\lambda & 1-\frac{6}{13}h\lambda \end{bmatrix}\begin{bmatrix} y_{n+1} \\ y_{n+2} \end{bmatrix} = \begin{bmatrix} \frac{1}{9} & 1+\frac{2}{3}h\lambda \\ \frac{1}{13} & -\frac{3}{13} \end{bmatrix}\begin{bmatrix} y_{n-1} \\ y_n \end{bmatrix}, \quad (11)$$

where

$$A = \begin{bmatrix} 1-\frac{2}{3}h\lambda & \frac{1}{9} \\ -\frac{15}{13}-\frac{6}{13}h\lambda & 1-\frac{6}{13}h\lambda \end{bmatrix}, \quad B = \begin{bmatrix} \frac{1}{9} & 1+\frac{2}{3}h\lambda \\ \frac{1}{13} & -\frac{3}{13} \end{bmatrix}. \quad (12)$$

To find the first characteristic polynomial for (6)-(7), we use

$$\det[At - B] = 0.$$

To get the polynomial as follows:

$$R(h, t) = \frac{44}{39}t^2 - \frac{14}{13}t^2h\lambda - \frac{40}{39}t + \frac{4}{13}t^2(h\lambda)^2 - \frac{4}{13}th\lambda - \frac{4}{39} - \frac{4}{13}t(h\lambda)^2 - \frac{2}{39}h\lambda. \quad (13)$$

Put $\bar{h} = \lambda h$ implies, the first characteristic polynomial will emerge

$$R(\bar{h}, t) = \frac{44}{39}t^2 - \frac{14}{13}t^2\bar{h} - \frac{40}{39}t + \frac{4}{13}t^2\bar{h}^2 - \frac{4}{13}t\bar{h} - \frac{4}{39} - \frac{4}{13}t\bar{h}^2 - \frac{2}{39}\bar{h}. \quad (14)$$

Put $\bar{h} = 0$ and get the stability polynomial as

$$R(0, t) = \frac{44}{39}t^2 - \frac{4}{39} - \frac{40}{39}t, \quad (15)$$

$$t = 1, \; t = -\frac{1}{11}. \quad (16)$$

As a result, the technique (6)-(7) is zero stable according to Definition 3.1 above.

Definition 3.2.

A linear multistep approach is referred to as A-stable if its stability region fully encloses the negative half-plane.

The region for the stability of the proposed method is drawn, by considering the stability polynomial in (14). The boundary of the stability region is described by the cluster of points as $t = e^{i\theta}$, $0 \leq \theta \leq 2\pi$. The following stability region was the complex plot of the suggested approach using the Maple software. The suggested approach (2IBBDF) is, by Definition 3.2, an A-stable method.

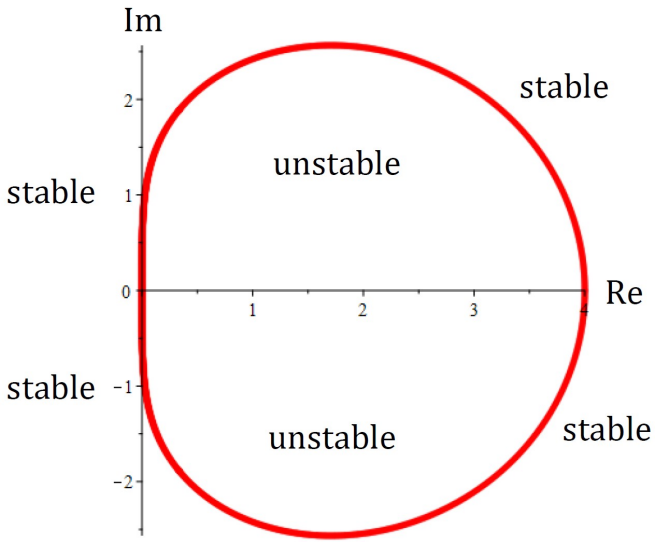

Figure 3.1. A-stability region of the proposed method according to Definition 3.2.

4. Tumor-Immune Interaction Model

Many scientists are putting a lot of effort into creating models of the tumor-immune interaction, some of which include: mathematical simulation of the immune-tumor relationship (Qamar Din & Jameel [24]),

concerning tumor evolution and the immune system's interaction, modelling and mathematical issues (Bellamo & Preziosi [8]), and a review of tumor-immune system dynamics models (Adam & Bellamo [6]). This paper examines a model of tumor-immune interaction created (Kirschner & Panetta [15]) that takes the form of

$$\frac{dE}{dt} = cT - u_2E + \frac{P_1EI_L}{g_1 + I_L} + s_1, \tag{17}$$

$$\frac{dT}{dt} = r_2(T)T - \frac{aET}{g_2 + T}, \tag{18}$$

$$\frac{dI_L}{dt} = \frac{P_2ET}{g_3 + T} - u_3L + s_2, \tag{19}$$

with initial conditions as

$$E(0) = E_0 \quad T(0) = T_0 \quad I_L(0) = I_{L_0}, \tag{20}$$

where $E(t)$ is the effector cells, $T(t)$ is the tumor cell and cytokine $I_L(t)$.

5. Numerical Results and Discussions

In this section, the tumor-immune interaction model (17)-(20) will be solved by using the developed schemes in (6)-(7). The error and parameter ideas from (Nasir et al. [22]) were retained.

Table 5.1. Notation and descriptions used in the paper

Acronyms	Descriptions
2IBBDF	2-point implicit block backward differentiation formula
Ode15s	A variable order solver base on numerical differentiation formula
BBDF	Block backward differentiation formula with fixed step size
c	The tumor's antigenicity in the model
h	Step size
t	Computing time in microseconds

Table 5.2. Approximated numerical solutions for the model (17)-(20) with the proposed method (6)-(7) considering the antigenicity value as 0 (i.e., $c = 0.000$)

Antigenicity	h	Method	Error	Comp-time
		Ode15s	9.75492e-4	125000
	10^{-3}	BBDF	9.27010e-5	7526
		2IBBDF	9.16321e-6	59217
		Ode15s	7.97585e-5	218750
$\boldsymbol{c}$ = **0**.000	10^{-4}	BBDF	4.68400e-6	48667
		2IBBDF	4.42161e-6	46103
		Ode15s	5.12100e-6	4484375
	10^{-5}	BBDF	970000e-7	464695
		2IBBDF	9.13064e-7	458864

Table 5.3. Approximated numerical solutions for the model (17)-(20) with the proposed method (6)-(7) considering the antigenicity value as 0.025 (i.e., $c = 0.025$)

Antigenicity	h	Method	Error	Comp-time
		Ode15s	9.82605e-4	29690
	10^{-3}	BBDF	9.30660e-5	7798
		2IBBDF	9.26732e-5	6963
		Ode15s	982372e-5	234375
$\boldsymbol{c}$ = **0**.025	10^{-4}	BBDF	3.87500e-6	49331
		2IBBDF	3.63366e-6	32392
		Ode15s	7.75505e-6	4046875
	10^{-5}	BBDF	970000e-7	467225
		2IBBDF	9.60006e-7	499721

Table 5.4. Approximated numerical solutions for the model (17)-(20) with the proposed method (6)-(7) considering the antigenicity value as 0.050 (i.e., c = 0.050)

Antigenicity	h	Method	Error	Comp-time
		Ode15s	1.01073e-3	15625
	10^{-3}	BBDF	1.01065e-4	7438
		2IBBDF	9.90432e-5	8446
		Ode15s	6.32461e-4	250000
$\boldsymbol{c}$ = **0**.050	10^{-4}	BBDF	1.48890e -5	49016
		2IBBDF	1.13901e-6	48178
		Ode15s	4.22429e-6	4656250
	10^{-5}	BBDF	9.85000e-7	470719
		2IBBDF	8.90020e-7	459641

The figures of $\text{Log}_{10}(\text{error})$ vs the step size h for the modelled problem are produced to be able to provide a stronger visual influence on the effectiveness of the 2IBBDF technique in comparison to the Ode15s and BBDF methods.

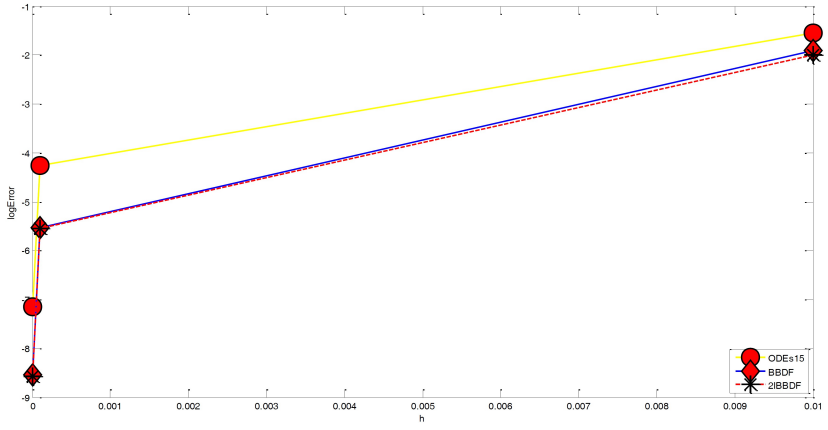

Figure 5.1. Graph of $\text{Log}_{10}(\text{error})$ against h for Table 5.2.

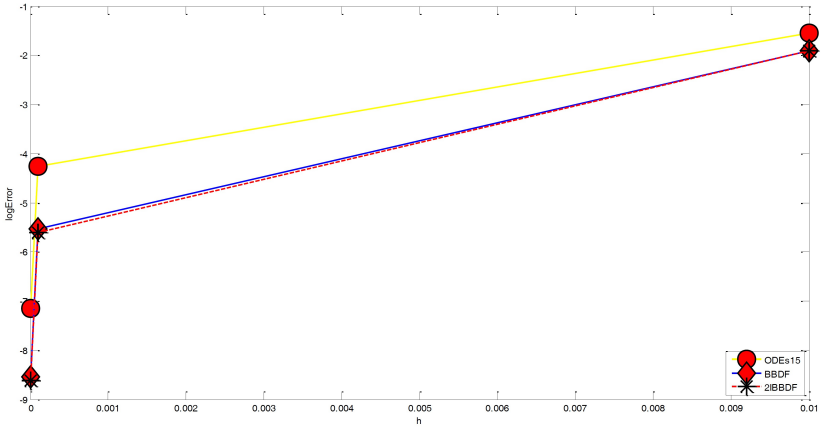

Figure 5.2. Graph of $\text{Log}_{10}(\text{error})$ against h for Table 5.3.

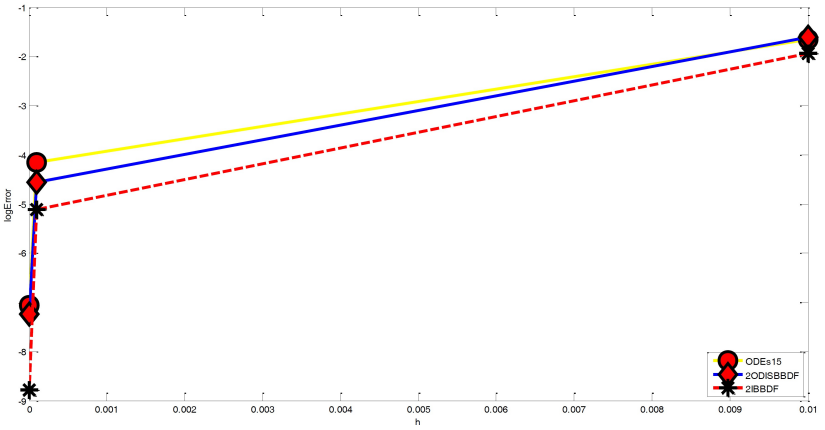

Figure 5.3. Graph of $\text{Log}_{10}(\text{error})$ vs h for Table 5.4.

From Tables 5.2, 5.3, and 5.4 demonstrate that the scaled errors for the suggested technique, 2IBBDF, are lower when compared to those of the Ode15s and BBDF methods based on the problem under consideration, the tumor-immune interaction model. The BBDF, as compared to the Ode15s, is more accurate. The scale error of the suggested technique is reduced in comparison to the other two ways, as shown more clearly by the plot of the $\text{Log}_{10}(\text{error})$ against the step size h. The outcomes have demonstrated that the initial value problem of the proposed model of ordinary differential equations could well be solved by using the 2IBBDF.

6. Conclusion

The established method can roughly estimate the values of two solutions, $y_n + 1$ and $y_n + 2$, at spot point, respectively. It is determined that the proposed technique (2IBBDF), which can solve both stiff and non-stiff IVPs, has zero and A-stable stability qualities. The findings that were tabulated and the graphs that were displayed show how well the proposed technique performed in relation to accuracy of the scale error when compared to the other methods that were taken into consideration for the study. In terms of executional time, the 2IBBDF scheme requires minimum executional time as compared to Ode15s and BBDF. While, BBDF has more of error and produced minimum execution time compared to Ode15s. The newly proposed block scheme, 2IBBDF generate more solution values then the MATLAB solver Ode15s, obtained two solution values simultaneously at each iteration while Ode15s obtained one solution value at a spot point. As a result, the suggested approaches can be used to handle a model of tumor-immune interaction of first-order initial value problems of ODEs.

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Appendix A

Used parameters and their descriptions

Parameters	Descriptions
$\frac{dE}{dt}$	The population of effector-cells' rate of change
$\frac{dT}{dt}$	The tumor cell's rate of change
$\frac{dI_L}{dt}$	The rate of IL-2 concentration change
c	Measurement of the tumor's antigenicity
u_2	An effector cells' normal life span
P_1	Every day, IL-2 stimulates effector cells
g_1	The stimulated effector cell's concentration
s_1	Effector cells' exterior source (treatment)
$r_2(T)$	The model of logistic growth
a	The effectiveness of the immunological reaction
g_2	The tumor cells' loss of volume
u_3	The rate of degraded of the IL-2
s_2	The IL-2 (treatment) as an external input
P_2	The tumor's interaction with the activated effector cells
g_3	The amount of activated effector cells by contact with tumor

Appendix B

Values of the parameters

$0 \leq c \leq 0.05$	$u_2 = 0.03$	$P_1 = 0.1245$	$g_1 = 2 \times 10^7$
$g_2 = 1 \times 10^5$	$r_2 = 0.18$	$b = 1 \times 10^{-9}$	$a = 1$
$u_3 = 10$	$P_2 = 5$	$g_3 = 1 \times 10^3$	