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AN ACCURATE FIFTH-ORDER METHOD FOR SOLVING STIFF PHARMACOKINETICSS MODELS

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ABSTRACT. This paper presents a linear multistep interpolation and collocation block hybrid method that is zero stable and convergent. The method is formulated to approximate the solution of stiff pharmacokinetics models. By implementing the method, the maximum absolute errors are compared with a few existing methods and known stiff solvers. Results show that the new method performs better than the existing methods it was compared with.

1. INTRODUCTION

A system of equations is said to be stiff if there are large differences in the scales of the independent variable (time) and dependent variable (solution). They commonly arise in areas like chemical kinetics, physical and biological systems. Due to the nature of these systems they require specialized numerical methods to solve them. In recent times, researchers have come up with a variety of methods to tackle the challenges associated with stiff system of ODEs.

In more concise terms this paper considers finding numerical approximations to first–order stiff pharmacokinetic initial valued ordinary differential equations of the form;

$$\frac{\mathrm{d}y}{\mathrm{d}x} = f(x,y), \qquad x \in \mathbb{R}, \tag{1}$$

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on the interval $[c,d]$ subject to $y(c) = y_0$, with $f : \mathbb{R}^r \to \mathbb{R}^r$, and $r > 0$.

Milne & Reynolds [1] presented a class of numerical methods for solving ODEs with high accuracy and efficiency. They developed a fifth–order methods which were more accurate than a fourth–order method and demonstrated the superiority of their method via numerical experiments. The methods used 'four point' formulae in contrast to three point formulae derived by Hull & Newbery [2]. The stability for the case was investigated and the accuracy compared with the case of two substitutions per step. It is better to use one substitution per step than to double the step length and retain two substitutions per step. However, the methods developed by Milne & Reynolds [1] were not tested on stiff systems.

Suleiman et al [3] developed a super class of block Backward Differentiation Formula (BBDF) for solving stiff ODEs. The method is of order 3 with smaller error constant than the conventional BBDF. It is A-stable and generates two points at each step on integration.This method out performed the 1BDF (1-point backward differentiation formula) in terms of accuracy and has a reduced integration step when compared with the 1BDF method. In a related development, Babangida et al [4] proposed a numerical method that computes 2-points simultaneously at each step of integration. The scheme is a modification of an already existing DI2BBDF (Diagonally implicit 2block backward differentiation formula) method.

Based on recent reviews of diagonally Implicit Runge–Kutta methods applied to stiff ODEs by same authors, several DIRK (Diagonally implicit Runge–Kutta) type methods were presented in the paper. Their characteristics and applications were also provided. The methods given, ranges from third–to–sixth order in four–to–nine stages and L-stable. Three L-stable diagonally implicit Runge–Kutta methods were compared with various direct time integration algorithms. The optimal order of embedded pairs of DIRK methods were examined and the stability properties investigated. Five new explicit first stage singly diagonally implicit Runge–Kutta (ESDIRK) methods were presented based on lessons learned from the works of other authors. Due to their relative ease of execution, the sub class of diagonally implicit Runge–Kutta (DIRK) methods has became one of the most commonly used in solving stiff first–order ODEs (see, Kennedy & Carpenter [5]).

Ijam & Ibrahim [6] proposed a p–Dagonally Implicit Block Backward Differentiation Formula (p-DIBBDF) to accurately solve stiff ODEs. By choosing the best value for the parameter p they developed a method

that possesses a smaller error constant and a larger stability region compared to other methods. The selection of p for optimal stability properties in terms of zero stability, absolute stability, error constant and convergence were also discussed. Numerical results showed that the p-DIBBDF method performs better than the existing fully and diagonally block backward differentiation formula (BBDF) methods.

Ijam et al [7] also proposed a diagonally implicit scheme of block backward differentiation formula for solving stiff Pharmacokinetics models. An efficient two–point block method based on backward differentiation formula which is A-stable and converged was constructed. By implementing the algorithm, the numerical solution to the models was compared with some existing methods. Their method proved efficient when compared to other methods and known stiff solvers like `ode15s`. Nevertheless, we show in the present paper with numerical experiments that our method gives better approximations to the same problem considered.

Yakubu et al [8] developed a continuous block implicit hybrid one–step collocation method which combined the advantages of both implicit and explicit methods, using a continuous block approach to handle stiffness. They demonstrated the method's ability to handle complex Pharmacokinetics models with multiple compartments. In this paper, we present an accurate Fifth–order block hybrid method for the numerical approximation of two and three stiff pharmacokinetic models. The method developed is based on a collocation and interpolation approach is zero stable, convergent with a large region of absolute stability.

2. THE HEART OF THE MATTER

In this section, we show how the new method is derived. We also find the order, order of convergence, error constant and investigate the stability, convergence of the method. We used the following continuous formulation

$$y(x) = \alpha_0(x)y_n + h[\beta_0(x)f_n + \beta_1(x)f_{n+1} + \beta_{\frac{3}{2}}(x)f_{n+\frac{3}{2}} + \beta_{\frac{17}{9}}(x)f_{n+\frac{17}{9}} + \beta_2(x)f_{n+2}],$$

where $\alpha_0^2 + \beta_0^2 > 0$ and the other β's are the remaining continuous coefficients which are obtained by inverting the matrix

$$D=\begin{bmatrix} 1 & x_n & x_n^2 & x_n^3 & x_n^4 & x_n^5 \\ 0 & 1 & 2x_n & 3x_n^2 & 4x_n^3 & 5x_n^4 \\ 0 & 1 & 2x_{n+1} & 3x_{n+1}^2 & 4x_{n+1}^3 & 5x_{n+1}^4 \\ 0 & 1 & 2x_{n+\frac{3}{2}} & 3x_{n+\frac{3}{2}}^2 & 4x_{n+\frac{3}{2}}^3 & 5x_{n+\frac{3}{2}}^4 \\ 0 & 1 & 2x_{n+\frac{17}{9}} & 3x_{n+\frac{17}{9}}^2 & 4x_{n+\frac{17}{9}}^3 & 5x_{n+\frac{17}{9}}^4 \\ 0 & 1 & 2x_{n+2} & 3x_{n+2}^2 & 4x_{n+2}^3 & 5x_{n+2}^4 \end{bmatrix}.$$

By replacing x_n with $x_{n+1}-h, x_{n+\frac{3}{2}}=x_{n+1}+\frac{h}{2}, x_{n+\frac{17}{9}}=x_{n+1}+\frac{8h}{9}$, and $x_{n+2}=x_{n+1}+h$, the D matrix becomes:

$$D=\begin{bmatrix} 1 & x_{n+1}-h & (x_{n+1}-h)^2 & (x_{n+1}-h)^3 & (x_{n+1}-h)^4 & (x_{n+1}-h)^5 \\ 0 & 1 & 2(x_{n+1}-h) & 3(x_{n+1}-h)^2 & 4(x_{n+1}-h)^3 & 5(x_{n+1}-h)^4 \\ 0 & 1 & 2x_{n+1} & 3x_{n+1}^2 & 4x_{n+1}^3 & 5x_{n+1}^4 \\ 0 & 1 & 2(x_{n+1}+\frac{1}{2}h) & 3(x_{n+1}+\frac{1}{2}h)^2 & 4(x_{n+1}+\frac{1}{2}h)^3 & 5(x_{n+1}+\frac{1}{2}h)^4 \\ 0 & 1 & 2(x_{n+1}+\frac{8}{9}h) & 3(x_{n+1}+\frac{8}{9}h)^2 & 4(x_{n+1}+\frac{8}{9}h)^3 & 5(x_{n+1}+\frac{8}{9}h)^4 \\ 0 & 1 & 2(x_{n+1}+h) & 3(x_{n+1}+h)^2 & 4(x_{n+1}+h)^3 & 5(x_{n+1}+h)^4 \end{bmatrix}. \quad (2)$$

Now, we obtain the determinant of (2) as:

$$\det(D)=\frac{4760}{729}h^{10}. \quad (3)$$

2.1. **Theorem.** Given that $\varepsilon>0$, then

$$h>\left[\frac{729\varepsilon}{4760}\right]^{\frac{1}{10}},$$

if in addition $\varepsilon=2^{-52}$ (`macheps` which is machine epsilon), $h>0.01992$, then the D matrix is non–singular.

Proof: Since by assumption $\varepsilon>0$, then let

$$\frac{4760h^{10}}{729}>\varepsilon.$$

This implies that

$$h^{10} > \left[\frac{729\varepsilon}{4760}\right],$$

and

$$h > \left[\frac{729\varepsilon}{4760}\right]^{\frac{1}{10}}.$$

Now, substituting $\varepsilon = 2^{-52}$ yields

$$h > \left[\frac{729}{4760}\right]^{\frac{1}{10}} = \left[\frac{729 \times 2^{-52}}{4760}\right]^{\frac{1}{10}} = 0.01992.$$

Therefore, if $h > 0.01992$ then the determinant of D will be nonzero, ensuring the non–singularity of D.

The determinant of D is non–zero if and only if $\frac{4760}{729}h^{10}$ is non–zero. Now, we can find the inverse C from $DC = I$ where I is a square matrix of size six by six. The entries on the first row of the C matrix makes up the continuous coefficients used to obtain the continuous formulation with $w = x_{n+1} - x$:

$$y(x) = y_n - \frac{(72w^5 + 215hw^4 + 220h^2w^3 + 80h^3w^2 - 587h^5)}{2040h^4} f_n$$

$$+ \frac{(216w^5 + 375hw^4 - 200h^2w^3 - 750h^3w^2 - 480h^4w + 839h^5)}{480h^4} f_{n+1}$$

$$- \frac{(144w^5 + 160hw^4 - 240h^2w^3 - 320h^3w^2 + 256h^5)}{105h^4} f_{n+\frac{3}{2}}$$

$$+ \frac{(52488w^5 + 32805hw^4 - 87480h^2w^3 - 65610h^3w^2 + 67797h^5)}{19040h^4} f_{n+\frac{17}{9}}$$

$$- \frac{(216w^5 + 105hw^4 - 340h^2w^3 - 240h^3w^2 + 259h^5)}{120h^4} f_{n+2}.$$

We evaluated the continuous scheme at $w = \{0, -\frac{h}{2}, -\frac{8}{9}, -h\}$. In essence, for $w = 0$, using $w = x_{n+1} - x$, $x = x_{n+1} + 0 = x_{n+1}$ which is same as $y(x) = y(x_{n+1}) = y_{n+1}$, and for $w = -\frac{h}{2}$, using $w = x_{n+1} - x, x = x_{n+1} + \frac{h}{2} = x_{n+\frac{3}{2}}$. Hence,

$$y(x) = y(x_{n+\frac{3}{2}}) = y_{n+\frac{3}{2}}.$$

If $w = -\frac{8h}{9}$, -$\frac{8h}{9} = x_{n+1} - x$, and $x = x_{n+1} + \frac{8h}{9} = x_{n+\frac{16}{9}}$ and for $w = -h$, using $w = x_{n+1} - x$, $x = x_{n+1} + h = x_{n+2}$. Finally,

$$y(x) = y(x_{n+2}) = y_{n+2}.$$

We used the above to obtain the following four discrete schemes which makes the new block method

$$y_{n+1} = y_n + \frac{587h}{2040} f_n + \frac{839h}{480} f_{n+1} - \frac{256h}{105} f_{n+\frac{3}{2}} + \frac{67797h}{19040} f_{n+\frac{17}{9}} - \frac{259h}{120} f_{n+2} \tag{4}$$

$$y_{n+\frac{3}{2}} = y_n + \frac{183h}{640} f_n + \frac{4977h}{2560} f_{n+1} - \frac{141h}{70} f_{n+\frac{3}{2}} + \frac{59049h}{17920} f_{n+\frac{17}{9}} - \frac{1287h}{640} f_{n+2} \tag{5}$$

$$y_{n+\frac{17}{9}} = y_n + \frac{225403h}{787320} f_n + \frac{2029069h}{1049760} f_{n+1} - \frac{1257728h}{688905} f_{n+\frac{3}{2}} + \frac{36397h}{10080} f_{n+\frac{17}{9}} - \frac{555169h}{262440} f_{n+2} \tag{6}$$

$$y_{n+2} = y_n + \frac{73h}{255} f_n + \frac{29h}{15} f_{n+1} - \frac{64h}{35} f_{n+\frac{3}{2}} + \frac{2187h}{595} f_{n+\frac{17}{9}} - \frac{31h}{15} f_{n+2}. \tag{7}$$

2.2. **Order and Consistency of the Method.** In this section, we summarize the order, error constant, zero stability, consistency and convergence of the block hybrid method under discussion: Let

$$\alpha_0 = -\begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \end{bmatrix}, \alpha_1 = \begin{bmatrix} 1 \\ 0 \\ 0 \\ 0 \end{bmatrix}, \alpha_{\frac{3}{2}} = \begin{bmatrix} 0 \\ 1 \\ 0 \\ 0 \end{bmatrix}, \alpha_{\frac{17}{9}} = \begin{bmatrix} 0 \\ 0 \\ 1 \\ 0 \end{bmatrix}, \alpha_2 = \begin{bmatrix} 0 \\ 0 \\ 0 \\ 1 \end{bmatrix}.$$

In the same vein,

$$\beta_0 = \begin{bmatrix} \frac{587}{2040} \\ \frac{183}{640} \\ \frac{225403}{787320} \\ \frac{75}{255} \end{bmatrix}, \beta_1 = \begin{bmatrix} \frac{839}{480} \\ \frac{4977}{2560} \\ \frac{2029069}{1049760} \\ \frac{29}{15} \end{bmatrix}, \beta_{\frac{3}{2}} = \begin{bmatrix} -\frac{256}{105} \\ -\frac{141}{70} \\ -\frac{1257728}{688905} \\ -\frac{64}{35} \end{bmatrix},$$

$$\beta_{\frac{17}{9}} = \begin{bmatrix} \frac{67797}{19040} \\ \\ \frac{59049}{17920} \\ \\ \frac{36397}{10080} \\ \\ \frac{2187}{595} \end{bmatrix}, \beta_2 = \begin{bmatrix} -\frac{259}{120} \\ \\ -\frac{1287}{640} \\ \\ -\frac{555169}{262440} \\ \\ -\frac{31}{15} \end{bmatrix}.$$

In finding the order and error constant, we substituted the above vectors in the following formulas:

$$C_0 = \alpha_0 + \alpha_1 + \alpha_{\frac{3}{2}} + \alpha_{\frac{17}{9}} + \alpha_2 = 0,$$

$$C_1 = \left[\alpha_1 + \left(\frac{3}{2}\right)^1 \alpha_{\frac{3}{2}} + \left(\frac{17}{9}\right)^1 \alpha_{\frac{17}{9}} + 2^1\alpha_2\right] - \left[\beta_0 + \beta_1 + \beta_{\frac{3}{2}} + \beta_{\frac{17}{9}} + \beta_2\right] = 0,$$

$$C_2 = \frac{1}{2!}\left[\alpha_1 + \left(\frac{3}{2}\right)^2 \alpha_{\frac{3}{2}} + \left(\frac{17}{9}\right)^2 \alpha_{\frac{17}{9}} + 2^2\alpha_2\right] - \left[\beta_1 + \left(\frac{3}{2}\right)\beta_{\frac{3}{2}} + \left(\frac{17}{9}\right)\beta_{\frac{17}{9}} + 2\beta_2\right] = 0,$$

$$C_3 = \frac{1}{3!}\left[\alpha_1 + \left(\frac{3}{2}\right)^3 \alpha_{\frac{3}{2}} + \left(\frac{17}{9}\right)^3 \alpha_{\frac{17}{9}} + 2^3\alpha_2\right] - \frac{1}{2!}\left[\beta_1 + \left(\frac{3}{2}\right)^2 \beta_{\frac{3}{2}} + \left(\frac{17}{9}\right)^2 \beta_{\frac{17}{9}} + 2^2\beta_2\right] = 0,$$

$$C_4 = \frac{1}{4!}\left[\alpha_1 + \left(\frac{3}{2}\right)^4 \alpha_{\frac{3}{2}} + \left(\frac{17}{9}\right)^4 \alpha_{\frac{17}{9}} + 2^4\alpha_2\right] - \frac{1}{3!}\left[\beta_1 + \left(\frac{3}{2}\right)^3 \beta_{\frac{3}{2}} + \left(\frac{17}{9}\right)^3 \beta_{\frac{17}{9}} + 2^3\beta_2\right] = 0,$$

$$C_5 = \frac{1}{5!}\left[\alpha_1 + \left(\frac{3}{2}\right)^5 \alpha_{\frac{3}{2}} + \left(\frac{17}{9}\right)^5 \alpha_{\frac{17}{9}} + 2^5\alpha_2\right] - \frac{1}{4!}\left[\beta_1 + \left(\frac{3}{2}\right)^4 \beta_{\frac{3}{2}} + \left(\frac{17}{9}\right)^4 \beta_{\frac{17}{9}} + 2^4\beta_2\right] = 0$$

$$C_6 = \frac{1}{6!}\left[\alpha_1 + \left(\frac{3}{2}\right)^6 \alpha_{\frac{3}{2}} + \left(\frac{17}{9}\right)^6 \alpha_{\frac{17}{9}} + 2^6\alpha_2\right] - \frac{1}{5!}\left[\beta_1 + \left(\frac{3}{2}\right)^5 \beta_{\frac{3}{2}} + \left(\frac{17}{9}\right)^5 \beta_{\frac{17}{5}} + 2^5\beta_2\right] \neq 0.$$

The above demonstrates that:

$$C_0 = C_1 = C_2 = C_3 = C_4 = C_5 = 0, \text{ and } C_6 \neq 0.$$

Since C_6 is non–zero, this shows that the error constant is

$$\text{Error Constant} = C_6 = \begin{bmatrix} \frac{41}{12960} \\ \\ \frac{47}{15360} \\ \\ \frac{2363153}{765275040} \\ \\ \frac{1}{324} \end{bmatrix}.$$

This is summarized in Table 1.

Table 1. Table showing the Error Constants of the discrete schemes.

$\mathbf{y_i}$	**Order**	**Error Constant $\mathbf{C_6 \neq 0}$**
y_{n+1}	5	$3.16358024691358 \times 10^{-3}$
$y_{n+\frac{3}{2}}$	5	$3.059895833333333 \times 10^{-3}$
$y_{n+\frac{17}{9}}$	5	$3.087978669734217 \times 10^{-3}$
y_{n+2}	5	$3.08641975308642 \times 10^{-3}$

2.3. **Order of Convergence.** In this section, we examine the order of convergence of the newly derived block hybrid method. We begin by presenting this well known definition of Lipschitz condition which will be used shortly.

Definition 1. [11] A function $f(x,y)$ satisfies the Lipschitz condition on a domain $D \subseteq \mathbb{R}^2$, if there exists a constant $L > 0$ such that:

$$|f(x,y) - f(x,y^*)| \leq L|y - y^*|,$$

for all $(x,y),(x,y^*) \in D$.

In the same vein, we define the convergence as used above.

Definition 2. [11] A LMM is said to be convergent if, for all initial value problems subject to the above Lipschitz condition:

$$\lim_{h \to 0} y_n = y^*(x_n),$$

for all solutions $\{y_n\}$ of the method.

Lemma 1. The order of convergence of each of the discrete schemes in (4) is $p+2$.

Proof. Assuming the exact solution of y_{n+1} is :

$$y^*_{n+1} = y^*_n + \frac{587hf_n}{2040} + \frac{839hf_{n+1}}{480} - \frac{356hf_{n+\frac{3}{2}}}{105} + \frac{67797hf_{n+\frac{17}{9}}}{19040} - \frac{259hf_{n+2}}{120} + \frac{41}{12960}h^6 y^{*(6)}(\xi_n) + R_7,$$

where R_7 is the remainder term. Assuming the exact solution of y_{n+2} is:

$$y^*_{n+2} = y^*_n + \frac{73hf_n}{255} + \frac{29hf_{n+1}}{15} - \frac{64hf_{n+\frac{3}{2}}}{35} + \frac{2187hf_{n+\frac{17}{9}}}{595} - \frac{31hf_{n+2}}{15} + \frac{1}{324}h^6y^{*(6)}(\xi_n) + R_7,$$

and so on and so forth.

Subtract y_{n+1} from y^*_{n+1} to obtain:

$$\begin{aligned} y^*_{n+1} - y_{n+1} = y^*_n &+ \left[\frac{587hf_n}{2040} + \frac{839hf_{n+1}}{480} - \frac{356hf_{n+\frac{3}{2}}}{105} + \frac{67797hf_{n+\frac{17}{9}}}{19040} - \frac{259hf_{n+2}}{140}\right] \\ &- y_n - \left[\frac{587hf_n}{2040} + \frac{839hf_{n+1}}{480} - \frac{356hf_{n+\frac{3}{2}}}{105} + \frac{67797hf_{n+\frac{17}{9}}}{19040} - \frac{259hf_{n+2}}{140}\right] \\ &+ \frac{41}{12960}h^6y^{*(6)}(\xi_n) + R_7. \end{aligned}$$

Expanding the above,

$$\begin{aligned} y^*_{n+1} - y_{n+1} = y^*_n - y_n &+ \frac{587}{2040}\left[f(x_n, y^*_n) - f(x_n, y_n)\right] \\ &+ \frac{839h}{480}\left[f(x_{n+1}, y^*_{n+1}) - f(x_{n+1}, y_{n+1})\right] \\ &- \frac{356h}{105}\left[f(x_{n+\frac{3}{2}}, y^*_{n+\frac{3}{2}}) - f(x_{n+\frac{3}{2}}, y_{n+\frac{3}{2}})\right] \\ &+ \frac{67797h}{19040}\left[f(x_{n+\frac{16}{9}}, y^*_{n+\frac{17}{9}}) - f(x_{n+\frac{17}{9}}, y_{n+\frac{17}{9}})\right] \\ &- \frac{259h}{140}\left[f(x_{n+2}, y^*_{n+2}) - f(x_{n+2}, y_{n+2})\right] \\ &+ \frac{41}{12960}h^6y^{*(6)}(\xi_n) + R_7. \end{aligned}$$

Let $d_n = y^*_n - y_n, d_{n+\frac{3}{2}} = y^*_{n+\frac{3}{2}} - y_{n+\frac{3}{2}}, d_{n+1} = y^*_{n+1} - y_{n+1}$, etc. After taking the absolute values of both left and right side, imposing the triangular inequality and with Lipschitz conditions yields:

$$\begin{aligned} |d_{n+1}| \leq \left(1 + \frac{587}{2040}L\right)|d_n| &+ \frac{839h}{480}L|d_{n+1}| \\ &+ \frac{356h}{105}L|d_{n+\frac{3}{2}}| + \frac{67797h}{19040}L|d_{n+\frac{17}{9}}| \\ &+ \frac{259h}{140}L|d_{n+2}| + \frac{41h^6}{12960}|y^{*6}_n(\xi_n)|. \end{aligned}$$

This simplifies to:

$$\begin{aligned}\left(1-\frac{839h}{480}L\right)|d_{n+1}| \leq \left(1+\frac{587h}{2040}L\right)|d_n| \\ &+\frac{356h}{105}L|d_{n+\frac{3}{2}}| \\ &+\frac{67797h}{19060}L|d_{n+\frac{17}{9}}|+\frac{259h}{140}L|d_{n+2}| \\ &+\frac{41h^6}{12960}|y_n^{*6}(\xi_n)|+\mathscr{O}(h^7).\end{aligned}$$

As $h\to 0$, with the exception of $|d_n|$ every other term on the right hand side tends to zero while on the left hand side we are left with $|d_{n+1}|$ and by the definition of convergence,

$$\lim_{h\to 0} y_{n+1} = y^*_{n+1}.$$

Subtract y_{n+2} from y^*_{n+2} to obtain:

$$\begin{aligned}y^*_{n+2}-y_{n+2} = y^*_n+\frac{73hf_n}{255}+\frac{29hf_{n+1}}{15}-\frac{64hf_{n+\frac{3}{2}}}{35}+\frac{2187hf_{n+\frac{17}{9}}}{595}-\frac{31hf_{n+2}}{15} \\ -y_n-\left[\frac{73hf_n}{255}+\frac{29hf_{n+1}}{15}-\frac{64hf_{n+\frac{3}{2}}}{35}+\frac{2187hf_{n+\frac{17}{9}}}{595dd}-\frac{31hf_{n+2}}{15}\right] \\ +\frac{1}{324}h^6y^{*(6)}(\xi_n)+R_7.\end{aligned}$$

Expanding the above,

$$\begin{aligned}y^*_{n+2}-y_{n+2} = y^*_n-y_n+\frac{73}{255}\left[f(x_n,y^*_n)-f(x_n,y_n)\right] \\ +\frac{29h}{15}\left[f(x_{n+1},y^*_{n+1})-f(x_{n+1},y_{n+1})\right] \\ -\frac{64h}{35}\left[f(x_{n+\frac{3}{2}},y^*_{n+\frac{3}{2}})-f(x_{n+\frac{3}{2}},y_{n+\frac{3}{2}})\right] \\ +\frac{2187h}{595}\left[f(x_{n+\frac{17}{9}},y^*_{n+\frac{17}{9}})-f(x_{n+\frac{17}{9}},y_{n+\frac{17}{9}})\right] \\ -\frac{31h}{15}\left[f(x_{n+2},y^*_{n+2})-f(x_{n+2},y_{n+2})\right]+\frac{1}{324}h^6y^{*(6)}(\xi_n)+R_7.\end{aligned}$$

Let $d_n = y^*_n-y_n, d_{n+\frac{3}{2}} = y^*_{n+\frac{3}{2}}-y_{n+\frac{3}{2}}, d_{n+2} = y^*_{n+2}-y_{n+2}$ etc. Taking the absolute values of both sides, using the triangular inequality and imposing appropriate Lipschitz conditions yields:

$$\begin{aligned}|d_{n+2}| \leq \left(1+\frac{73}{255}L\right)|d_n|+\frac{29h}{15}L|d_{n+1}| \\ +\frac{64h}{35}L|d_{n+\frac{3}{2}}|+\frac{2187h}{595}L|d_{n+\frac{17}{9}}| \\ -\frac{31h}{15}L|d_{n+2}|+\frac{h^6}{324}|y_n^{*6}(\xi_n)|.\end{aligned}$$

This simplifies to:

$$\left(1+\frac{31h}{15}L\right)|d_{n+2}| \leq \left(1+\frac{73h}{255}L\right)|d_n| + \frac{29h}{15}L|d_{n+1}| + \frac{64h}{35}L|d_{n+\frac{3}{2}}| + \frac{2187h}{595}L|d_{n+\frac{17}{9}}| + \frac{h^6}{324}|y_n^{*6}(\xi_n)| + \mathscr{O}(h^7).$$

As $h \to 0$, with the exception of $|d_n|$ every other term on the right hand side tends to zero while on the left hand side we are left with $|d_{n+2}|$ and by the definition of convergence,

$$\lim_{h\to 0} y_{n+2} = y^*_{n+2}.$$

Thus, $|d_{n+2}| \leq |d_n|$ and $y^*_{n+2} - y^*_n \leq y_{n+2} - y_n$ holds. The convergence of y_{n+2} is established in agreement with [13, 14].

In the same vein, it can be shown that the other y_{n+i}'s for $i \in \left\{\frac{3}{2}, \frac{17}{9}\right\}$ converge. Hence, we have shown that the new block hybrid method is convergent, the remainder term R_7 which is

$$R_{p+1} = C_{p+2}h^{p+2}y^{*(p+2)}(\xi) = \mathscr{O}(h^7).$$

Therefore, the order of convergence of the new method is $p+2$ which is seven [13]. □.

2.4. **Region of Absolute Stability.** In this section, we plotted the region of absolute stability of the new method using the stability polynomial. To get the stability polynomial which will be used in plotting the region of absolute stability of the new method, we re–write the new block hybrid method in Linear Multistep form as follows:

$$\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} y_{n+1} \\ y_{n+\frac{3}{2}} \\ y_{n+\frac{17}{9}} \\ y_{n+2} \end{bmatrix} = \begin{bmatrix} 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{bmatrix} \begin{bmatrix} y_{n-1} \\ y_{n-\frac{3}{2}} \\ y_{n-\frac{17}{9}} \\ y_n \end{bmatrix} + h \begin{bmatrix} \frac{839}{480} & -\frac{256}{105} & \frac{67797}{19040} & -\frac{259}{120} \\ \frac{4977}{2560} & -\frac{141}{70} & \frac{59049}{17920} & -\frac{1287}{640} \\ \frac{2029069}{1049760} & -\frac{1257728}{688905} & \frac{36397}{10080} & -\frac{555169}{262440} \\ \frac{29}{15} & -\frac{64}{35} & \frac{2187}{595} & -\frac{31}{15} \end{bmatrix} \begin{bmatrix} f_{n+1} \\ f_{n+\frac{3}{2}} \\ f_{n+\frac{17}{9}} \\ f_{n+2} \end{bmatrix}$$

$$+h\begin{bmatrix} 0 & 0 & 0 & \frac{587}{2040} \\ 0 & 0 & 0 & \frac{183}{640} \\ 0 & 0 & 0 & \frac{335403}{787320} \\ 0 & 0 & 0 & \frac{73}{255} \end{bmatrix}\begin{bmatrix} f_{n-1} \\ f_{n-\frac{3}{2}} \\ f_{n-\frac{17}{9}} \\ f_n \end{bmatrix}.$$

In addition, we used the following to analyze the zero stability of the block method, where the matrices are respectively

$$A=\begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}, B=\begin{bmatrix} 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 \end{bmatrix},$$

$$G=\begin{bmatrix} \frac{839}{480} & -\frac{256}{105} & \frac{67797}{19040} & -\frac{259}{120} \\ \frac{4977}{2560} & -\frac{141}{70} & \frac{59049}{17920} & -\frac{1287}{640} \\ \frac{2029069}{1049760} & -\frac{1257728}{688905} & \frac{36397}{10080} & -\frac{555169}{262440} \\ \frac{29}{15} & -\frac{64}{35} & \frac{2187}{595} & -\frac{31}{15} \end{bmatrix}, R=\begin{bmatrix} 0 & 0 & 0 & \frac{587}{2040} \\ 0 & 0 & 0 & \frac{183}{640} \\ 0 & 0 & 0 & \frac{225403}{787320} \\ 0 & 0 & 0 & \frac{73}{255} \end{bmatrix},$$

We used the matrices above to find the determinant

$$\rho(w,z)=\det\left[Aw-B-Rz-Gzw\right],$$

where $y'=\lambda y$, $z=\lambda h$ is the usual test equation, $w=e^{i\theta}, i^2=-1$ and $\theta\in[0,2\pi]$. This results in the following stability polynomial:

$$\rho(w,z)=\frac{((51w^4-w^3)z^4+(-(275w^4)-25w^3)z^3+(810w^4-210w^3)z^2}{1080}+\frac{(-(1380w^4)-780w^3)z+1080w^4-1080w^3}{1080}.$$

We used the above stability polynomial to plot the region of absolute stability in octave and this results is in Figure 1.

Figure 1, shows that the interval of absolute stability of our method above is $(0,5.32)$.

In order to study the zero-stability of the method, we solved

$$\det[rA-B]=r^4-r^3=r^3(r-1)=0.$$

Therefore, the roots are $r=0$ of multiplicity 3 and $r=1$ (simple). Hence, our method is zero stable from [11].

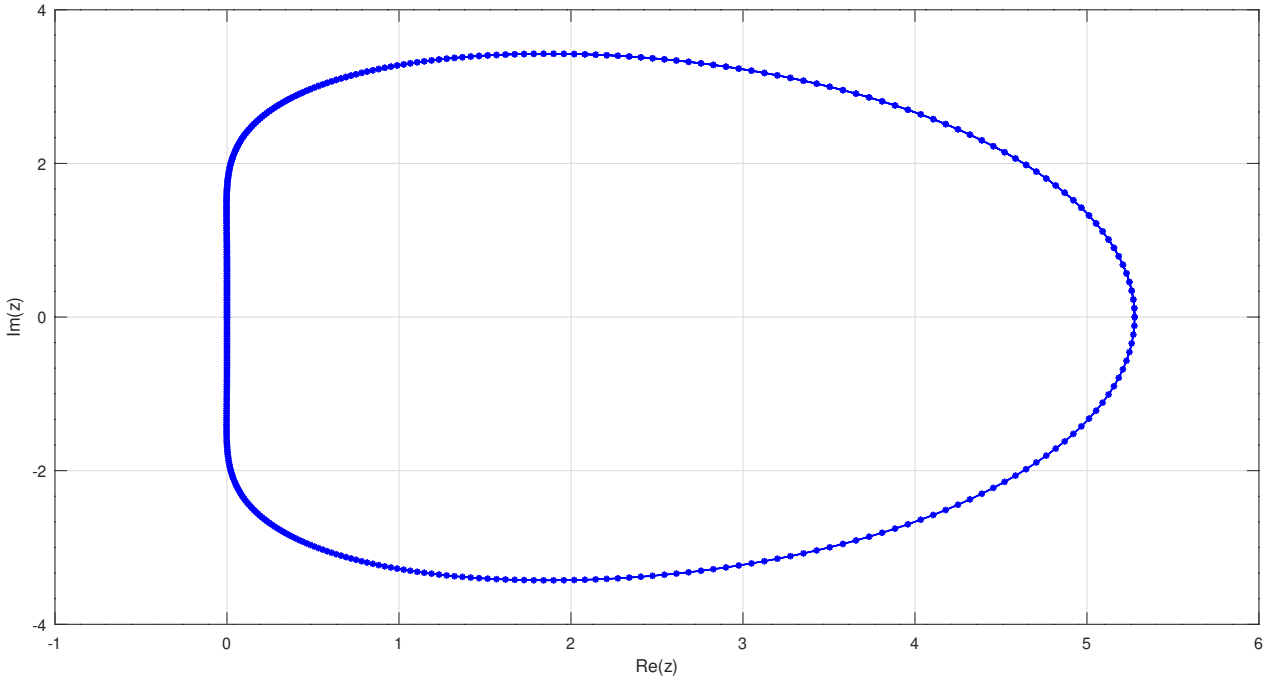

FIGURE 1. Region of absolute stability of our method.

2.5. **Numerical Experiments.** The goal in this section is to show the strength of our method over those in the literature. This is achieved by comparing the maximum absolute error of our method with those of [7]: p-DIBBDF, NDIBBDF and the well known stiff solver ode15s. The models: A, B and C and corresponding parameters used for the examples in this section are presented in Ijam et al [7]. Results are presented by tables and figures. We used a 64–bit DELL Latitude laptop running on Intel(R) Core(TM) i5-5200U CPU @ 2.20GHz, manufactured in the USA in computing the `cputimes`. Besides, the Number of Function Evaluations (NFEs) of the new method is 20 per block.

Before we present the three models, we give the following examples which supports our method.

Example 2.1. *Consider the following differential equations which models influenza disease [15]*

$$\frac{dS}{dt} = rI - cSI$$
$$\frac{dI}{dt} = cSI - rI,$$

where S represents the size of the susceptible population, I the size of the infected population. If a susceptible person interacts with an infected person, there is a probability c that the susceptible person will become infected. Each infected person recovers from the infection at a rate r and becomes susceptible

again. Here c is the contact rate and r, the recovery rate. Furthermore the total population size is constant ($S+I=N$). After reducing the above system to a single differential equation in I, then we arrived at the differential equation

$$\frac{dS}{dt} = c(N-I)I - rI.$$

Besides, it was assummed that the parameters are $c = 0.5, N = 5$, *and* $r = 0.5$. *The differential equation becomes*

$$\frac{dS}{dt} = 0.5(5-I)I - 0.5I, \quad \textit{subject to } I(0) = 1,$$

the exact solution is

$$I(t) = \frac{-4\exp(2t)}{1-5\exp(2t)},$$

and a fixed step size of $h = 0.125$ *results in Table 2.*

Table 2. Comparison table for Example 2.1.

t	Exact	Approximate	Absolute Error
3.0	0.8003967970605821	0.8004013613245774	$4.5642639953102915\times10^{-06}$
6.0	0.8000009830751846	0.8000009943888220	$1.1313637360288453\times10^{-08}$
9.0	0.8000000024367968	0.8000000024648036	$2.8006819086101586\times10^{-11}$
12.0	0.8000000000060402	0.8000000000061095	$6.9277916736609768\times10^{-14}$
15.0	0.8000000000000150	0.8000000000000150	$0.0000000000000000\times10^{00}$

We present the next example with a large step size of $h = 0.1$ and the results are presented in Table 3.

Example 2.2. *The IVPs defined as*

$$\begin{bmatrix} y_1'(x) \\ y_2'(x) \end{bmatrix} = \begin{bmatrix} 998 & 1998 \\ -999 & -1999 \end{bmatrix} \begin{bmatrix} y_1(x) \\ y_2(x) \end{bmatrix}$$

subject to $y_1(0) = 1$, $y_2(0) = 0$ and a fixed step size of $h = 0.1$. The exact solution is $y_1(x) = 4\exp(-x) - 3\exp(-1000x)$ and $y_2(x) = -2\exp(-x) + 3\exp(-1000x)$.

Table 3. Results of our method on Example 2.2 versus [16] and [17].

x	y_i	Absolute Error in our method	Absolute Error in [16]	Absolute Error in [17]
5	y_1	3.9039×10^{-09}	4.9294×10^{-14}	1.3920×10^{-11}
	y_2	1.9519×10^{-09}	2.4647×10^{-14}	6.9700×10^{-11}
40	y_1	1.9691×10^{-23}	3.6082×10^{-15}	3.3628×10^{-12}
	y_2	9.8457×10^{-24}	1.7972×10^{-15}	1.6818×10^{-12}
70	y_1	3.2246×10^{-36}	1.9732×10^{-16}	2.9325×10^{-13}
	y_2	1.6123×10^{-36}	9.8662×10^{-17}	1.4664×10^{-13}

Table 3 shows that our method though of order 5, outperformed methods of order 6 [17] and order 7 [16] in the literature for $x = 40$ and $x = 70$.

Example 2.3. *The Kaps problem*

$$\begin{aligned} y_1 &= -1002y_1(x) + 1000y_2^2(x), \\ y_2 &= y_1(x) - y_2(x)^2 - y_2(x), \ \textit{with}\ y_1(0) = 1,\ y_2(0) = 1. \end{aligned}$$

The exact solution is $y_1(x) = \exp(-2x)$, $y_2(x) = \exp(-x)$, our method was compared with the works of [18] as shown in Table 4.

Table 4. Absolute error (Error) of our method on Example 2.3.

h	N	Error y_1	Error y_2	Error in y_1[18]	Error in y_2 [18]
2.500	4	3.914×10^{-04}	2.294×10^{-06}	2.167×10^{-09}	1.350×10^{-05}
1.250	8	1.760×10^{-09}	1.600×10^{-06}	2.332×10^{-09}	2.891×10^{-05}
0.833	12	2.460×10^{-09}	2.690×10^{-07}	2.307×10^{-09}	2.969×10^{-05}
0.625	16	1.221×10^{-09}	6.806×10^{-08}	2.298×10^{-09}	2.998×10^{-05}
0.500	20	7.152×10^{-10}	2.094×10^{-08}	2.294×10^{-09}	3.011×10^{-05}

2.6. **Model A.**

Example 2.4. *The differential equations which consist of the concentration in the GI tract $y_A(t)$ and $y_B(t)$ the concentration in the bloodstream*

$$f(x,y) = \begin{bmatrix} y'_A(t) \\ y'_B(t) \end{bmatrix} = \begin{bmatrix} -2\ln(2)y_A(t) \\ 2\ln(2)y_A(t) - \frac{\ln(2)}{5}y_B(t) \end{bmatrix},$$

on the interval $t \in [0,6]$. The exact solution is $y_A(t) = \exp(-2\ln(2)t)$ and $y_B(t) = -\frac{10}{9}(\exp(-2\ln(2)t) - \exp(-\frac{\ln(2)}{5}t))$.

Result of Example 2.4 are shown in Table 5 and Figure 3.

Table 5. Drug concentration in Model A.

h	Methods	Maximum Error	`cputime`
10^{-2}	New Method	6.541×10^{-13}	1.549×10^{-1}
	ρBIDDF	3.097×10^{-4}	1.489×10^{-5}
	NDIBBDF	3.561×10^{-4}	3.976×10^{-5}
	ode15s	7.750×10^{-3}	3.406×10^{-2}
10^{-4}	New Method	1.221×10^{-15}	4.358×10^{-1}
	ρBIDDF	3.266×10^{-8}	4.809×10^{-4}
	NDIBBDF	3.817×10^{-8}	5.656×10^{-3}
	ode15s	1.532×10^{-4}	6.093×10^{-2}
10^{-6}	New Method	9.992×10^{-16}	9.294×10^{-1}
	ρBIDDF	5.299×10^{-11}	2.348×10^{-2}
	NDIBBDF	3.249×10^{-10}	4.978×10^{-1}
	ode15s	2.441×10^{-6}	9.375×10^{-1}

2.7. **Model B.** The results for Model B(i) are presented by Table 6 and Figure 4, those of Model B(ii) and B(iii) are presented in Tables 7, 8 and Figures 5 and 6 respectively. The improved accuracy of our method is well documented.

Example 2.5. *The formulation of drugs with different drug carrier materials is applied widely in the pharmaceutical sciences field to control drug delivery*

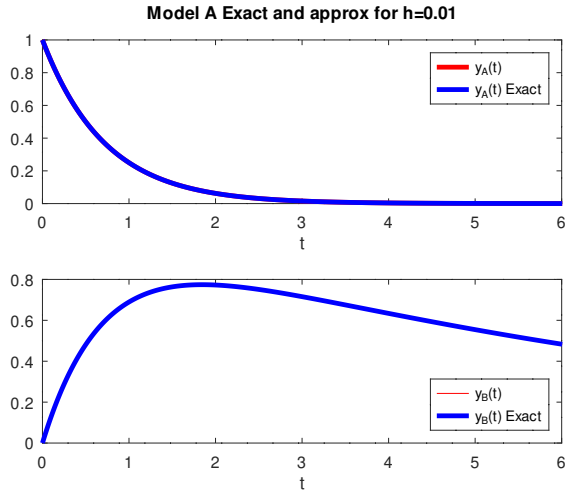

FIGURE 2. Solution of our method and the exact solution on Example 2.4.

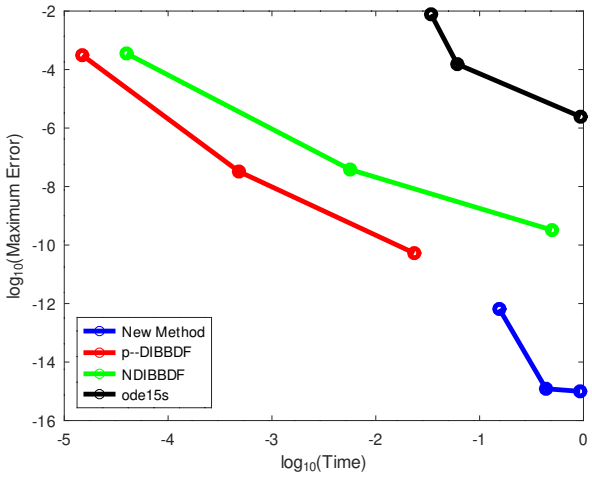

FIGURE 3. Absolute error of our method on Example 2.4.

and improve drug release where a_{GI} and a_{Plasma} are the rate constants in the GI tract and plasma, respectively

$$f(x,y) = \begin{bmatrix} y'_A(t) \\ y'_B(t) \end{bmatrix} = \begin{bmatrix} -a_{GI}y_A(t) \\ a_{GI}y_A(t) - a_{Plasma}y_B(t) \end{bmatrix},$$

such that $y_A(0) = 1.0ng/mL$ and $y_B(0) = 0$.

$$y_A(t) = \exp(-a_{GI}t),$$

$$y_B(t) = -\frac{a_{GI}}{a_{GI} - a_{Plasma}}[\exp(-a_{GI}t) - \exp(-a_{Plasma}t)], \quad a_{GI} \neq a_{Plasma}.$$

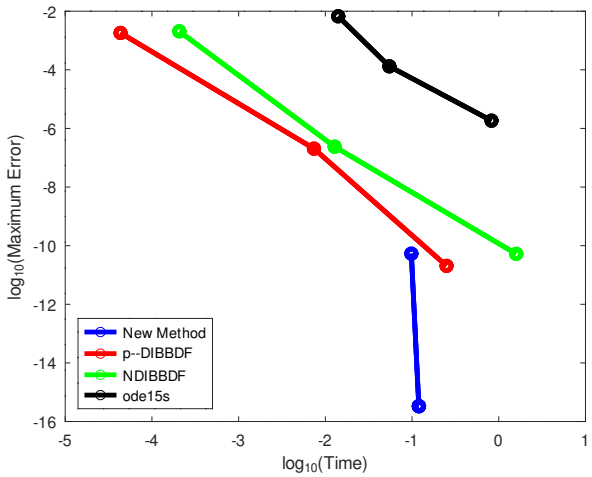

FIGURE 4. Graph of $\log_{10}$ Maximum Error against $\log_{10}$ Time of Model B(i)

Table 6. Drug concentration in Model B–Compound (i)

h	Methods	Maximum Error	`cputime`
10^{-2}	New Method	5.332×10^{-11}	9.811×10^{-2}
	ρBIDDF	1.819×10^{-3}	4.340×10^{-5}
	NDIBBDF	2.059×10^{-3}	2.068×10^{-4}
	ode15s	6.711×10^{-3}	1.406×10^{-2}
10^{-4}	New Method	3.330×10^{-16}	1.197×10^{-1}
	ρBIDDF	2.046×10^{-7}	7.385×10^{-3}
	NDIBBDF	2.390×10^{-7}	1.278×10^{-2}
	ode15s	1.313×10^{-4}	5.468×10^{-2}
10^{-6}	New Method	3.330×10^{-16}	1.200×10^{-1}
	ρBIDDF	2.050×10^{-11}	2.497×10^{-1}
	NDIBBDF	5.259×10^{-11}	1.587×10^{-0}
	ode15s	1.845×10^{-6}	8.250×10^{-1}

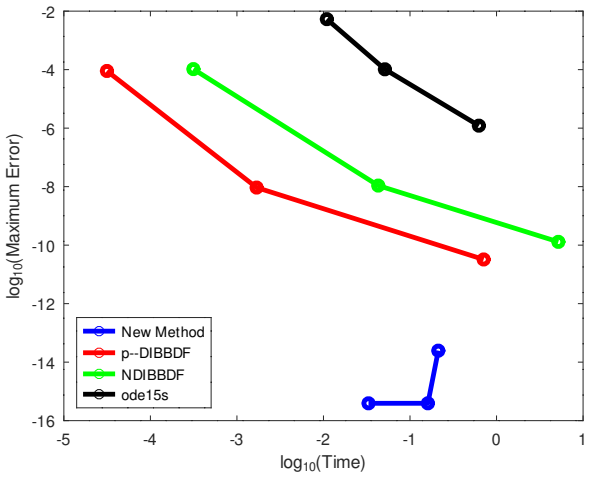

FIGURE 5. Graph of $\log_{10}$ Maximum Error against $\log_{10}$ Time of Model B(ii)

Table 7. Drug concentration in Model B–Compound (ii)

h	Methods	Maximum Error	`cputime`
10^{-2}	New Method	2.470×10^{-14}	2.122×10^{-1}
	ρBIDDF	9.008×10^{-5}	3.146×10^{-5}
	NDIBBDF	1.043×10^{-4}	3.139×10^{-4}
	ode15s	5.325×10^{-3}	1.093×10^{-2}
10^{-4}	New Method	3.920×10^{-16}	1.609×10^{-1}
	ρBIDDF	9.302×10^{-9}	1.688×10^{-3}
	NDIBBDF	1.087×10^{-8}	$4\ .295\times10^{-2}$
	ode15s	1.027×10^{-4}	5.125×10^{-2}
10^{-6}	New Method	3.915×10^{-16}	3.314×10^{-2}
	ρBIDDF	3.238×10^{-11}	7.096×10^{-1}
	NDIBBDF	1.294×10^{-10}	5.179×10^{0}
	ode15s	1.215×10^{-6}	6.250×10^{-1}

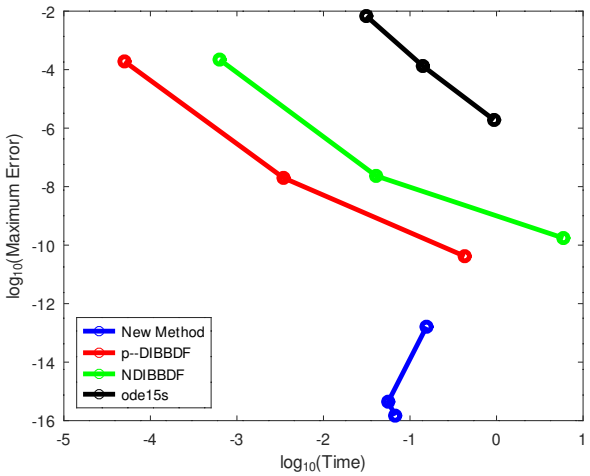

FIGURE 6. Graph of $\log_{10}$ Maximum Error against $\log_{10}$ Time of Model B(iii)

Table 8. Drug concentration in Model B–Compound (iii)

h	Methods	Maximum Error	cputime
10^{-2}	New Method	1.624×10^{-13}	1.550×10^{-1}
	ρBIDDF	1.910×10^{-4}	5.017×10^{-5}
	NDIBBDF	2.207×10^{-4}	6.301×10^{-4}
	ode15s	6.803×10^{-3}	3.125×10^{-1}
10^{-4}	New Method	4.440×10^{-16}	5.602×10^{-2}
	ρBIDDF	1.993×10^{-8}	3.453×10^{-3}
	NDIBBDF	2.330×10^{-8}	4.057×10^{-2}
	ode15s	1.332×10^{-4}	1.406×10^{-1}
10^{-6}	New Method	1.484×10^{-16}	6.732×10^{-2}
	ρBIDDF	4.190×10^{-11}	4.284×10^{-1}
	NDIBBDF	1.749×10^{-10}	5.917×10^{-1}
	ode15s	1.904×10^{-6}	9.370×10^{-1}

2.8. **Model C(i).**

Example 2.6. *The two–compartment mathematical model is presented in a linear ODEs approach as follows:*

$$f(x,y) = \begin{bmatrix} -y_a'(t) \\ y_b'(t) \end{bmatrix} = \begin{bmatrix} -ay_a(t) \\ ay_a(t) - cy_b(t) \end{bmatrix},$$

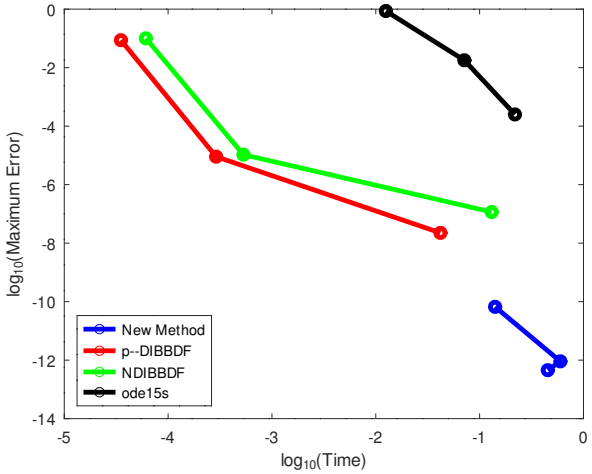

FIGURE 7. Graph of $\log_{10}$ Maximum Error against $\log_{10}$ Time of Model C(i)

with $y_a(0) = c_0$ *and* $y_b(0) = 0$. *The exact solution is given as*

$$y_a = c_0 \exp(-at),$$
$$y_b = \frac{c_0 a}{a-c}[\exp(-ct) - \exp(-at)], \quad a \neq c.$$

Results of this example are represented by Table 9 and Figure 7. Both the figure and table shows that the new method had the smallest maximum error.

Table 9. Drug concentration in Model C–Compound (i)

h	Methods	Maximum Error	`cputime`
10^{-2}	New Method	6.656×10^{-11}	1.408×10^{-1}
	ρBIDDF	8.694×10^{-2}	3.514×10^{-5}
	NDIBBDF	1.004×10^{-1}	6.108×10^{-5}
	ode15s	8.620×10^{-1}	1.250×10^{-2}
10^{-4}	New Method	9.094×10^{-13}	5.989×10^{-1}
	ρBIDDF	9.057×10^{-6}	2.897×10^{-4}
	NDIBBDF	1.058×10^{-5}	5.312×10^{-4}
	ode15s	1.786×10^{-2}	7.100×10^{-2}
10^{-6}	New Method	4.547×10^{-13}	4.529×10^{-1}
	ρBIDDF	2.246×10^{-8}	4.189×10^{-2}
	NDIBBDF	1.160×10^{-7}	1.305×10^{-1}
	ode15s	2.510×10^{-4}	2.187×10^{-1}

2.9. **Model C(ii).**

Example 2.7. *The differential equation arises from the intravenous blood and tissue drug model*

$$\frac{dy_A(t)}{dt} = -(b+c)y_A(t) + ay_B(t); \quad y_A(0) = D$$
$$\frac{dy_B(t)}{dt} = by_A(t) - ay_B(t); \quad y_B(0) = 0,$$

where

$$D = \textit{Initial drug usage concentration} = 500$$
$$a = \textit{Rate of Drug in tissue medium constant} = 0.3293/\textit{hour}$$
$$b = \textit{Rate of drug in bloodstream constant} = 0.9776/\textit{hour}$$
$$c = \textit{Clearance constant} = 0.2213/\textit{hour}.$$

The exact solution is given by

$$y_A(t) = \exp(-0.7641t)(500\cosh(0.7148249575945149t) - \frac{271750\sinh(0.7148249575945149t)}{\sqrt{798398}},$$
$$y_B(t) = 683.8037687504362\exp(-0.7641t)\sinh(0.7148249575945149t).$$

See Table 10 and Figure 8 for the results of Example 2.7.

Table 10. Drug concentration in Model C–Compound (ii).

h	Methods	Maximum Error	`cputime`
10^{-2}	New Method	3.266×10^{-10}	7.275×10^{-1}
	ρBIDDF	1.285×10^{-1}	2.627×10^{-5}
	NDIBBDF	1.476×10^{-1}	5.039×10^{-5}
	ode15s	8.070×10^{-1}	2.375×10^{-2}
10^{-4}	New Method	6.252×10^{-13}	7.527×10^{-1}
	ρBIDDF	1.359×10^{-5}	2.718×10^{-4}
	NDIBBDF	1.588×10^{-5}	7.831×10^{-4}
	ode15s	1.915×10^{-2}	9.812×10^{-2}
10^{-6}	New Method	5.115×10^{-13}	7.620×10^{-1}
	ρBIDDF	2.216×10^{-8}	1.893×10^{-2}
	NDIBBDF	1.709×10^{-7}	3.698×10^{-2}
	ode15s	2.941×10^{-4}	7.812×10^{-1}

2.10. **Model C(iii).**

Example 2.8. *The delivery mechanism of Model C(iii) is a one-directional model which is presented in terms of drug concentrations in the following compartments: arterial blood $y_A(t)$; tissue $y_B(t)$; and venous blood $y_C(t)$. The*

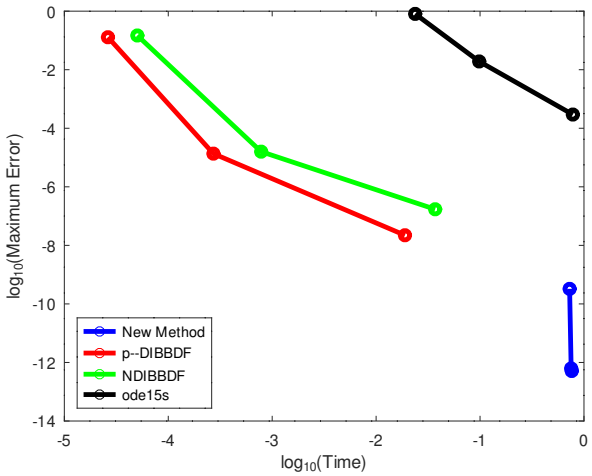

FIGURE 8. Graph of $\log_{10}$ Maximum Error against $\log_{10}$ Time of Model C(ii)

differential equations representing the three compartment model is represented by:

$$\begin{aligned} y'_A(t) &= -ay_A(t); \qquad y_A(0) = c_0, \\ y'_B(t) &= ay_A(t) - by_B(t); \qquad y_B = 0, \\ y'_C(t) &= by_B(t) - cy_C; \qquad y_C(0) = 0. \end{aligned}$$

We write the above as: $f(x,y) = \begin{bmatrix} y'_A(t) \\ y'_B(t) \\ y'_C(t) \end{bmatrix} = \begin{bmatrix} -ay_A(t) \\ ay_A(t) - by_B(t) \\ by_B(t) - cy_C(t) \end{bmatrix}$.

The exact solution as provided by `maxima` is

$$y_A(t) = c_0 e^{-at},$$

$$y_B(t) = \frac{ac_0(e^{bt} - e^{at})e^{-bt-at}}{b-a},$$

$$y_C(t) = \frac{\left[(ab^2 - a^2b)c_0e^{bt+at} + \left[(abc - ab^2)c_0e^{bt} + (a^2b - abc)c_0e^{at}\right]e^{ct}\right]e^{-ct-bt-at}}{(b-a)c^2 + (a^2 - b^2)c + ab^2 - a^2b}.$$

The result of our method as it compares to the exact solution is shown in Figure 9. Table 11 and Figure 10 show the results of Example 2.8 as it compares with those in the literature.

Table 11. Drug concentration in Model C–Compound (iii)

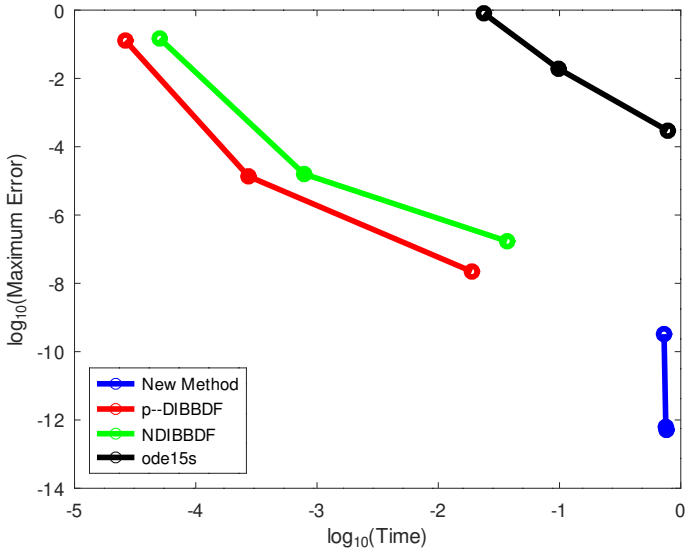

FIGURE 9. Solution versus exact on Example 2.8.

h	Methods	Maximum Error	cputime
10^{-2}	New Method	7.736×10^{-11}	1.563×10^{-1}
	ρBIDDF	9.464×10^{-2}	1.049×10^{-5}
	NDIBBDF	1.093×10^{-1}	8.061×10^{-5}
	ode15s	2.820×10^{-1}	2.250×10^{-2}
10^{-4}	New Method	1.070×10^{-12}	2.266×10^{-1}
	ρBIDDF	9.873×10^{-6}	4.154×10^{-4}
	NDIBBDF	1.153×10^{-5}	1.925×10^{-3}
	ode15s	8.642×10^{-3}	9.375×10^{-2}
10^{-6}	New Method	1.056×10^{-12}	7.950×10^{-1}
	ρBIDDF	2.018×10^{-8}	8.808×10^{-2}
	NDIBBDF	1.363×10^{-7}	1.247×10^{-1}
	ode15s	1.592×10^{-4}	3.125×10^{-1}

Tables 5–11 displays the numerical results of the new method in comparison with, p-DIBBDF, NDIBBDF and the stiff solver ode15s using different step sizes of $10^{-2}, 10^{-4}, 10^{-6}$. Based on the results, we observed that the new method resulted in a smaller maximum error than the other methods for all test problems although with a slightly higher CPU Time.

To illustrate the performances of the suggested methods and other compared methods, graphical representations are shown in Figures 2–10. It follows that the graphs of $\log_{10}$ Maximum Error against $\log_{10}$ Time showed the superiority of the new method over the other methods p-DIBBDF, NDIBBDF, ode15s in

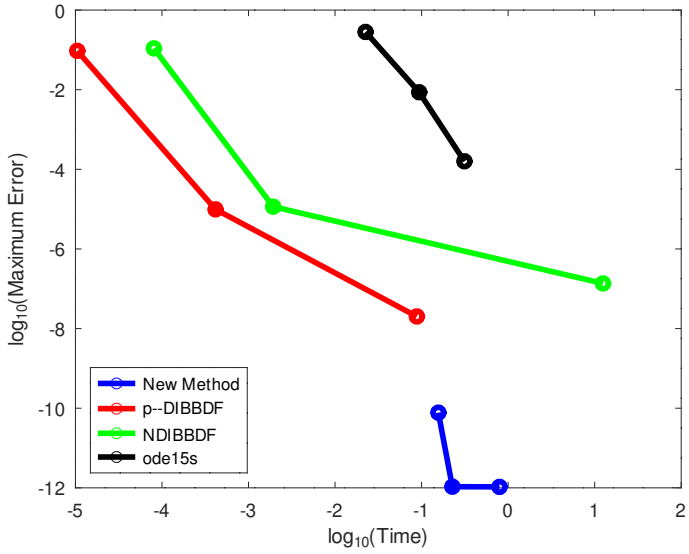

FIGURE 10. Graph of $\log_{10}$ Maximum Error against $\log_{10}$ Time of Model C(iii)

terms of accuracy. Overall, we observed that the new method outperforms the other methods in the existing literature.

On a final note, we computed the Rate by using the following formula from [19] and [20]:

$$\text{Rate} = \log_2\left(\frac{\max_{1\le j\le N}|y_j(x)-y_{j,h}|}{\max_{1\le j\le N}|y_j(x)-y_{j,h/2}|}\right),$$

which gave rise to Table 12 for Model A and Table 13 for Model C(iii). Both tables showed that the Rate is matched with the theoretical order of accuracy.

Table 12. Rate is matched for Model A.

N	Max Err	Rate
2	5.8604×10^{-08}	–
4	1.9453×10^{-09}	4.91
8	6.2701×10^{-11}	4.95
16	1.9894×10^{-12}	4.97
32	6.2284×10^{-14}	4.99
64	2.2204×10^{-15}	4.81

Table 13. Rate is matched for Model C(iii).

N	Max Err	Rate
2	7.4630×10^{-07}	–
4	3.4771×10^{-08}	4.42
8	1.2641×10^{-09}	4.78
16	4.2322×10^{-11}	4.90
32	1.3882×10^{-12}	4.93

3. CONCLUDING REMARKS

In this article, we developed a fifth–order block hybrid method for solving two and three compartmental pharmacokinetics models. The method proved to be zero stable, with a large region of absolute stability and convergent. Our results were compared with other methods as reported in Ijam et al [7]. Solution curves were also presented for selected problem considered. Our method showed better accuracy than the other methods it was compared with in [7].

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