Proceedings of the Pakistan Academy of Sciences:
A. Physical and Computational Sciences 55 (1): 71–79 (2018)

ISSN: 2518-4245 (print), 2518-4253 (online)

Pakistan Academy of Sciences

Research Article

Mathematical Modelling for Nonlinear Glycolytic Oscillator

Zain Ul Abadin Zafar

Faculty of Information and Technology, University of Central Punjab, Lahore, Pakistan

Abstract: Nowadays, numerical models have great importance in every field of science, especially for solving non-linear differential equations, partial differential equations, biochemical reactions, etc. The total time evolution of the reactant species which interacts with other species is simulated by the Runge-Kutta of order four (RK4) and by the Non-Standard finite difference (NSFD) method. A NSFD model has been constructed for the biochemical reaction problems and numerical experiments were performed for different values of discretization parameter 'h'. The results were compared with a well-known numerical scheme, i.e., RK4. The developed scheme NSFD gave better results than RK4

Keywords: Glycolytic oscillator, NSFD Method, RK4 method, chemical reaction

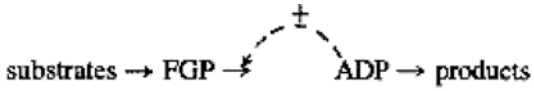
1. INTRODUCTION

In this article, we consider the well-known Glycolytic Oscillator model. A biochemical reaction that is universal in metabolic systems contains the following sequence of steps:

$$\text{glucose} \rightarrow \text{GGP} \rightarrow \text{FGP} \xrightarrow[\text{ATP}\ \ \text{ADP}]{\text{PFK}} \text{FDP} \rightarrow \text{products},$$

where glucose-6-phosphate is denoted by GGP, FGP is fructose-6-phosphate, FDP is fructose-1,6-diphosphate, ATP is adenosine triphosphate, ADT is adenosine diphosphate, and PFK is phosphofructokinase.

An assumption generally made is that the enzyme phosphofructokinase has two states, one of which has a higher activity. ADP stimulates this allosteric regulatory enzyme and produces the more active form. Thus a product of the reaction step mediated by PFK enhances the rate of reaction [1]. A schematic version of the kinetics is:



The equations for this system, where x stands for FGP and y stands for ADP, are as follows:

$$\begin{cases} \frac{dx}{dt} = \alpha - \beta x - xy^2 \\ \frac{dy}{dt} = \beta x + xy^2 - y \end{cases} \qquad (1)$$

subject to initial conditions; $x(0) = 1$ and $y(0) = 1$.

These equations, derived in many sources, are known to have stable oscillations as well as other interesting features. Note that α and β are positive constants and independent of time.

Received, October 2017; Accepted, March 2018
*Email: : Zain Ul Abadin Zafar: zainzafar2016@hotmail.com

First of all we will calculate the equilibrium points by equating both equations of system (1) equal to zero i.e,

$\alpha - \beta x - xy^2 = 0$ (2)

$\beta x + xy^2 - y = 0$ (3)

After solving the equations (2) & (3), we obtained one equilibrium point that is $(x^*, y^*) = \left(\frac{\alpha}{(\alpha^2+\beta)}, \alpha\right)$.

2. RK4 METHOD

In this section, we solve the systems (1) by RK4 Scheme as follows.

$$k_1 = h(\alpha - \beta x_n - x_n(y_n)^2)$$

$$m_1 = h(\beta x_n + x_n(y_n)^2 - y_n)$$

$$k_2 = h\left(\alpha - \beta\left(x_n + \frac{k_1}{2}\right) - \left(x_n + \frac{k_1}{2}\right)\left(y_n + \frac{m_1}{2}\right)^2\right)$$

$$m_2 = h\left(\beta\left(x_n + \frac{k_1}{2}\right) + \left(x_n + \frac{k_1}{2}\right)\left(y_n + \frac{m_1}{2}\right)^2 - \left(y_n + \frac{m_1}{2}\right)\right)$$

$$k_3 = h\left(\alpha - \beta\left(x_n + \frac{k_2}{2}\right) - \left(x_n + \frac{k_2}{2}\right)\left(y_n + \frac{m_2}{2}\right)^2\right)$$

$$m_3 = h\left(\beta\left(x_n + \frac{k_2}{2}\right) + \left(x_n + \frac{k_2}{2}\right)\left(y_n + \frac{m_2}{2}\right)^2 - \left(y_n + \frac{m_2}{2}\right)\right)$$

$$k_4 = h(\alpha - \beta(x_n + k_3) - (x_n + k_3)(y_n + m_3)^2)$$

$$m_4 = h\big(\beta(x_n + k_3) + (x_n + k_3)(y_n + m_3)^2 - (y_n + m_3)\big)$$

$$x_{n+1} = x_n + \frac{1}{6}[k_1 + 2k_2 + 2k_3 + k_4] \quad (4)$$

$$y_{n+1} = y_n + \frac{1}{6}[m_1 + 2m_2 + 2m_3 + m_4] \quad (5)$$

Table 1. Different values of α&β, with equilibrium points.

α	β	Equilibrium point (x^*, y^*)	Det J<1	1+Det(J)+ Trace (J)>0	1+Det(J) - Trace(j)>0
0.5	0.2	(1.111..,0.5)	0.970953554685612	3.937992363829684	0.003914745541540
1.0	0.2	(0.8333..,1.0)	0.963203463203463	3.916666666666666	0.009740259740260
0.6	0.8	(0.5172..,0.6)	0.871023921079538	3.732598510129098	0.009449332029977
2.0	2.0	(0.3333..,2.0)	0.689393939393939	3.344696969696969	0.034090909090909
2.5	3.0	(0.2702…,2.5)	0.595105140559686	3.146526691981237	0.043683589138135
1.0	1.0	(0.5,1.0)	0.848484848484849	3.681818181818182	0.015151515151515
3.0	0.5	(0.3157…,3.0)	0.638449270028217	3.232609495767390	0.044289044289044
0.7	0.35	(0.8333…,7.0)	0.944705356144470	3.882366096388236	0.007044615900704

Numerical Experiments

We have checked stability analysis for different values of parameter's and Numerical experiments are performed using the first entry of Table 1.

3. NON STANDARD FINITE DIFFERENCE METHOD

In this section we shall construct Non-Standard Finite Difference Scheme for the system (1). First order time derivatives are described by using forward difference approximation [4, 5]. f˙(t) can be approximated as

$$\frac{df(t)}{dt} = \frac{f(t+l)-f(t)}{l} + O(l) \text{ as } l \to 0$$

x^n and y^n are the approximations of *x(nl)* and *y(nl)*, for n=0,1,2,… and where *'l'* is step size of time. For satisfying biological nature of the continuous time model, it should be non-negative. The numerical method which has been developed to solve the system must hold Conservation law proposed by Mickens [6, 7]. To construct the NSFD scheme for system (1), we note the following statements

1. The linear and nonlinear terms on the right hand side of first equation of system (1) are in the form

$$-\beta x \approx -\beta x^{n+1}, \quad -xy^2 \approx -x^{n+1}(y^n)^2$$

2. The linear and nonlinear terms on the right hand side of second equation of system (1) are in the form

$$\beta x \approx \beta x^n, xy^2 \approx x^n(y^n)^2, -y \approx -y^{n+1}$$

So the system (1) can be written as

$$\frac{x^{n+1}-x^n}{h} = \alpha - \beta x^{n+1} - x^{n+1}(y^n)^2 \tag{6}$$

$$\frac{y^{n+1}-y^n}{h} = \beta x^n + x^n(y^n)^2 - y^{n+1} \tag{7}$$

Invoking some algebraic manipulations on Eqs. (6)-(7), the following relations are obtained:

$$x^{n+1} = \frac{\alpha h + x^n}{1+h\beta+h(y^n)^2} \tag{8}$$

$$y^{n+1} = \frac{y^n+\beta h x^n+h x^n(y^n)^2}{1+h} \tag{9}$$

3.1 Convergence Analysis

The stability and convergence of the proposed NSFD scheme about equilibrium point $\left(\frac{\alpha}{(\alpha^2+\beta)}, \alpha\right)$ are discussed here. Let

$$F = \frac{x + \alpha h}{(1 + \beta h + h y^2)}$$

And

$$G = \frac{y + h\beta x + h x y^2}{1 + h}$$

And the Jacobian matrix is

$$J(F^*) = \begin{bmatrix} \frac{\partial F}{\partial x} & \frac{\partial F}{\partial y} \\ \frac{\partial G}{\partial x} & \frac{\partial G}{\partial y} \end{bmatrix}$$

where as

$$\frac{\partial F}{\partial x}=\frac{1}{1+\beta h+hy^2},\quad \frac{\partial F}{\partial y}=-\frac{2(\alpha h+x)hy}{(1+\beta h+hy^2)^2},\quad \frac{\partial G}{\partial x}=\frac{h\boldsymbol{\beta}+hy^2}{1+h},\quad \frac{\partial G}{\partial y}=\frac{1+2hxy}{1+h}$$

At $(x^*,y^*)=\left(\frac{\alpha}{(\alpha^2+\beta)},\ \alpha\right)$ we have

$$\frac{\partial F}{\partial x}=\frac{1}{1+\beta h+h\alpha^2},\ \frac{\partial F}{\partial y}=-\frac{2\left(\alpha h+\frac{\alpha}{(\alpha^2+\beta)}\right)h\alpha}{(1+\beta h+h\alpha^2)^2},\ \frac{\partial G}{\partial x}=\frac{h\beta+h\alpha^2}{1+h},\ \frac{\partial G}{\partial y}=\frac{1+2h\frac{\alpha^2}{(\alpha^2+\beta)}}{1+h}$$

$$J=\begin{bmatrix}\dfrac{1}{1+\beta h+h\alpha^2} & -\dfrac{2\left(\alpha h+\frac{\alpha}{(\alpha^2+\beta)}\right)h\alpha}{(1+\beta h+h\alpha^2)^2}\\ \dfrac{h\beta+h\alpha^2}{1+h} & \dfrac{1+2h\frac{\alpha^2}{(\alpha^2+\beta)}}{1+h}\end{bmatrix}$$

From the basic theory of the stability analysis, we use the following lemma.

Lemma[10]: For the quadratic equation $\mu^2-\mu L+M=0$, both roots satisfy $|\mu_i|<1; i=1,2$ if and only if the following conditions are satisfied:

$1+M-L>0$

$1+L+M>0$

$M<1$

Let us define L = trace (J) and M = det (J)

$$J=\begin{bmatrix}\dfrac{1}{1+\beta h+h\boldsymbol{\alpha}^2} & -\dfrac{2\left(\alpha h+\frac{\boldsymbol{\alpha}}{(\boldsymbol{\alpha}^2+\boldsymbol{\beta})}\right)h\boldsymbol{\alpha}}{(1+\beta h+h\boldsymbol{\alpha}^2)^2}\\ \dfrac{h\boldsymbol{\beta}+h\boldsymbol{\alpha}^2}{1+h} & \dfrac{1+\frac{2h\boldsymbol{\alpha}^2}{(\boldsymbol{\alpha}^2+\boldsymbol{\beta})}}{1+h}\end{bmatrix}$$

where L = trace (J) $=\frac{1}{1+\beta h+h\boldsymbol{\alpha}^2}+\frac{1+\frac{2h\boldsymbol{\alpha}^2}{(\boldsymbol{\alpha}^2+\boldsymbol{\beta})}}{1+h}$

And M = det (J) $=\left(\frac{1}{1+\beta h+h\boldsymbol{\alpha}^2}\right)\left(\frac{1+\frac{2h\boldsymbol{\alpha}^2}{(\boldsymbol{\alpha}^2+\boldsymbol{\beta})}}{1+h}\right)+\left(\frac{2\left(\alpha h+\frac{\alpha}{(\alpha^2+\beta)}\right)h\boldsymbol{\alpha}}{(1+\beta h+h\boldsymbol{\alpha}^2)^2}\right)\left(\frac{h\boldsymbol{\beta}+h\boldsymbol{\alpha}^2}{1+h}\right)$

Now $1+M-L>0$ $\Longrightarrow \frac{h^2(\beta+\alpha^2)}{(1+\beta h+h\boldsymbol{\alpha}^2)(1+h)}>0$ (True $\forall$ $h$and $h\neq 0$)

Again $1+L+M>0$ $\Longrightarrow \frac{5h^2\alpha^4+6h^2\beta\alpha^2+2h\alpha^4+h^2\beta^2+4h\beta\alpha^2+2h\beta^2+6h\alpha^2+2h\beta+4\alpha^2+4\beta}{(\alpha^2+\beta)(1+\beta h+h\boldsymbol{\alpha}^2)(1+h)}>0,$

(True $\forall$ $h$and $h \neq 0$)

Again $M < 1 \Longrightarrow \frac{2h^2\alpha^4+2h^2\alpha^2\beta+2h\alpha^2+\alpha^2+\beta}{(\alpha^2+\beta)(1+\beta h+h\alpha^2)(1+h)} < 1$

(True $\forall$ $h$and $h \neq 0$)

Since $h > 0$ and $h \neq 0$, and all the conditions of the theorem are true, so the System is Stable for all values of h and converges to steady state.

Numerical Experiments

Numerical experiment is performed using first entry from the Table 1.

4. RESULTS AND DISCUSSION

The Numerical modelling of well-known Glycolytic Oscillator model has been analysed. The model has one unique equilibrium point. An unconditionally convergent non-standard finite difference numerical model has been constructed and numerical experiments are performed for different values of discretization parameter 'h'. Results are compared with the well-known numerical method i.e. Runge-Kutta method of order four (RK4). RK4 method and NSFD method converges for the time steps "h=0.001, 0.1, 1" (see Fig. 1-3,5-7) while RK4 method diverges and NSFD method converges for the time steps "h=2.243, 5, 10, 100" (For RK4, see Fig. 4 and for NSFD, Fig. 8). The comparison of both methods are shown in Fig. 9-10. Also the phase portrait of the given system is shown in Fig. 11.

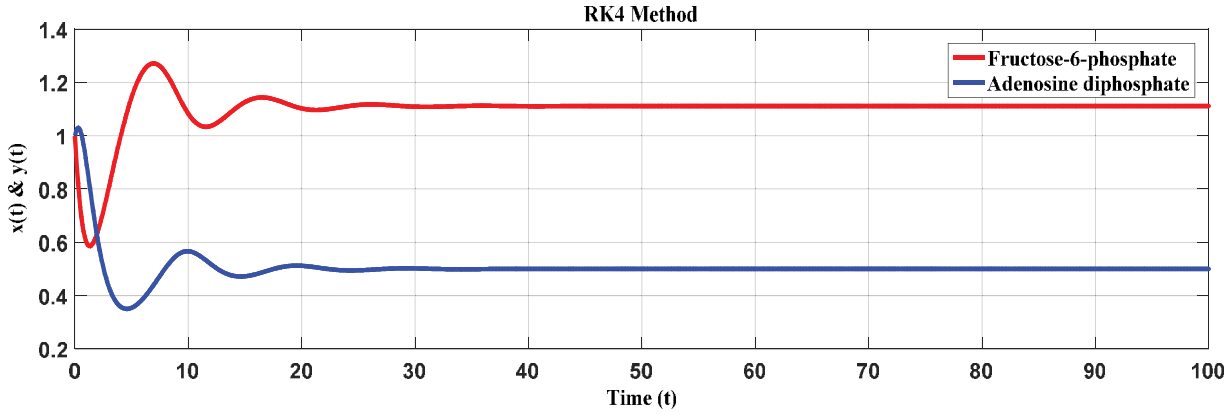


Fig. 1. The simulation with parameters α=0.5 and β=0.2 and step size 0.001.

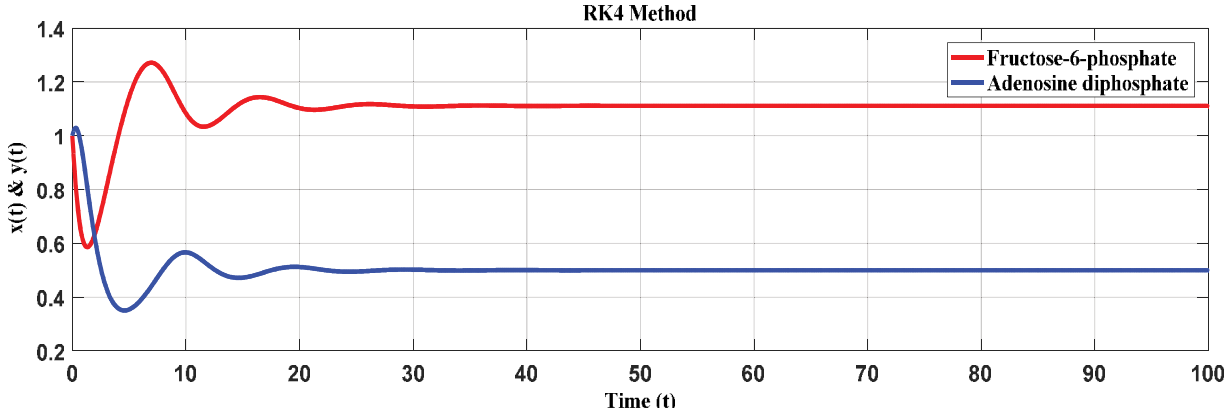


Fig. 2. The simulation with parameters α=0.5 and β=0.2 and step size 0.1.

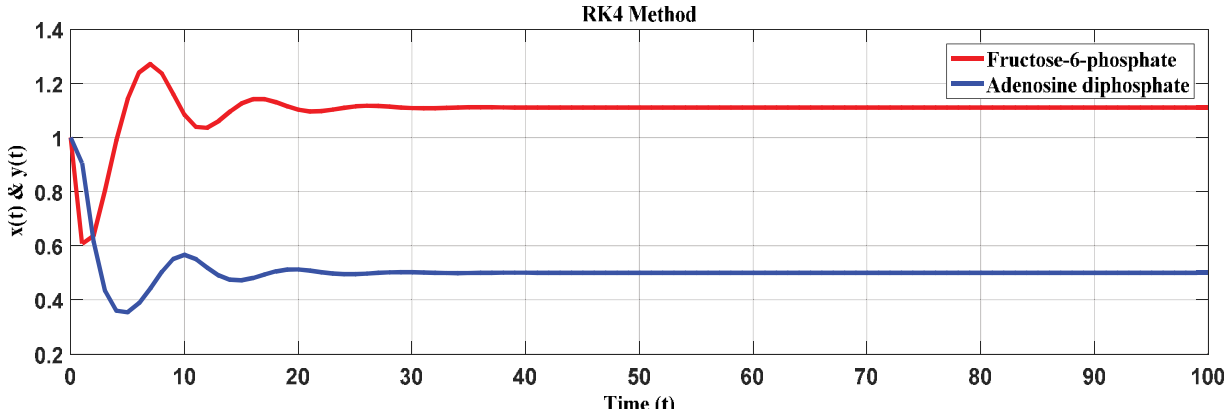


Fig. 3. The simulation with parameters α=0.5 and β=0.2 and step size 1.

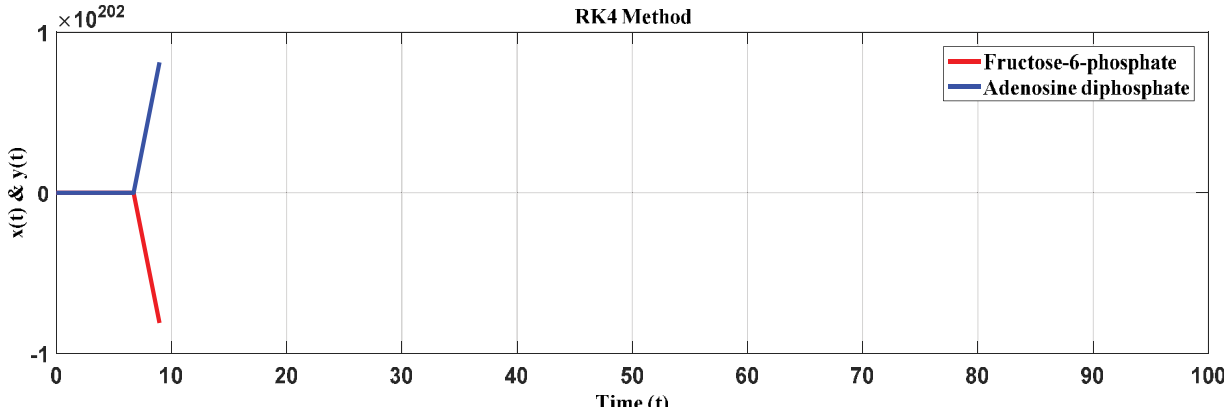


Fig. 4. The simulation with parameters α=0.5 and β=0.2 and step size 2.243.

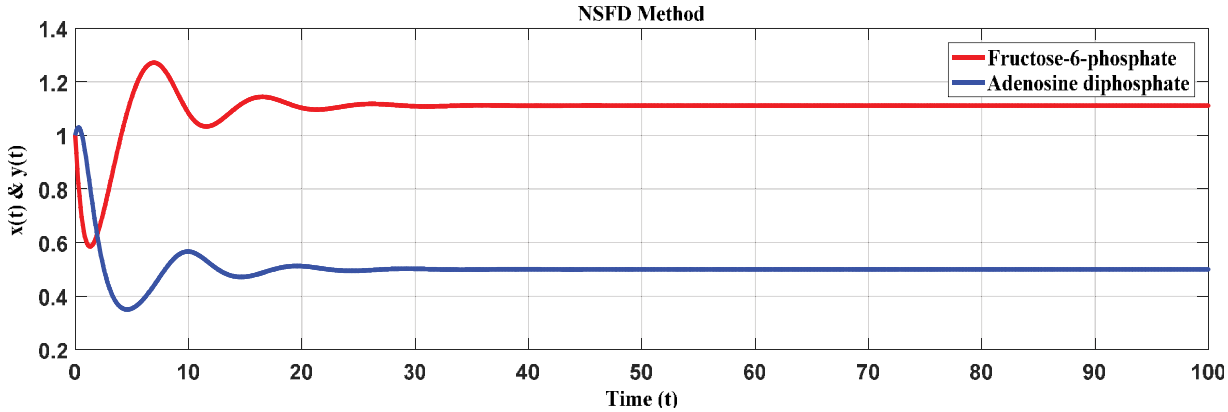


Fig. 5. The simulation with parameters α=0.5 and β=0.2 and step size 0.001.

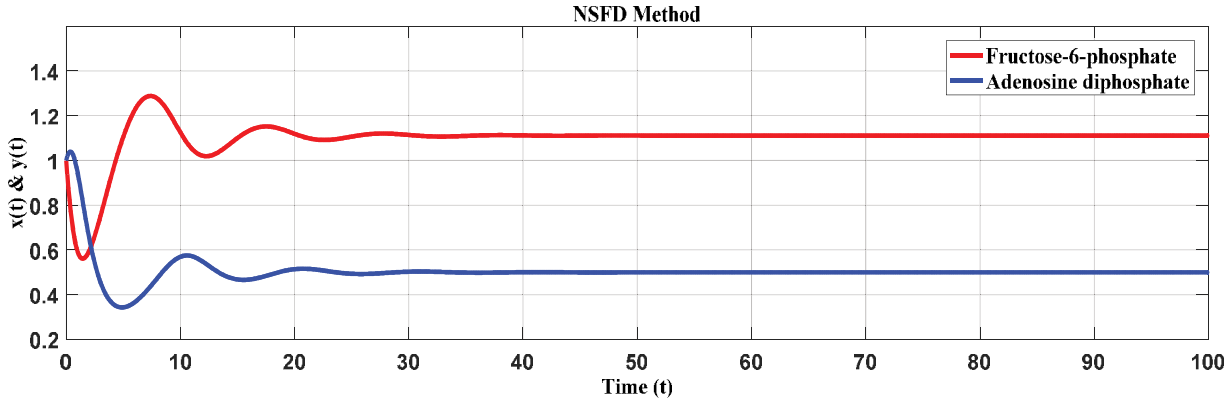


Fig. 6. The simulation with parameters α=0.5 and β=0.2 and step size 0.1.

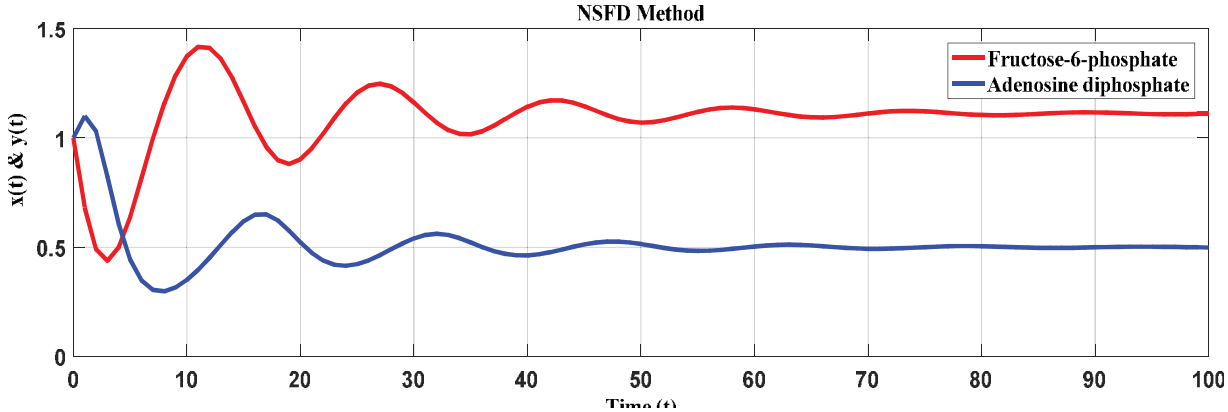


Fig. 7. The simulation with parameters α=0.5 and β=0.2 and step size 1.

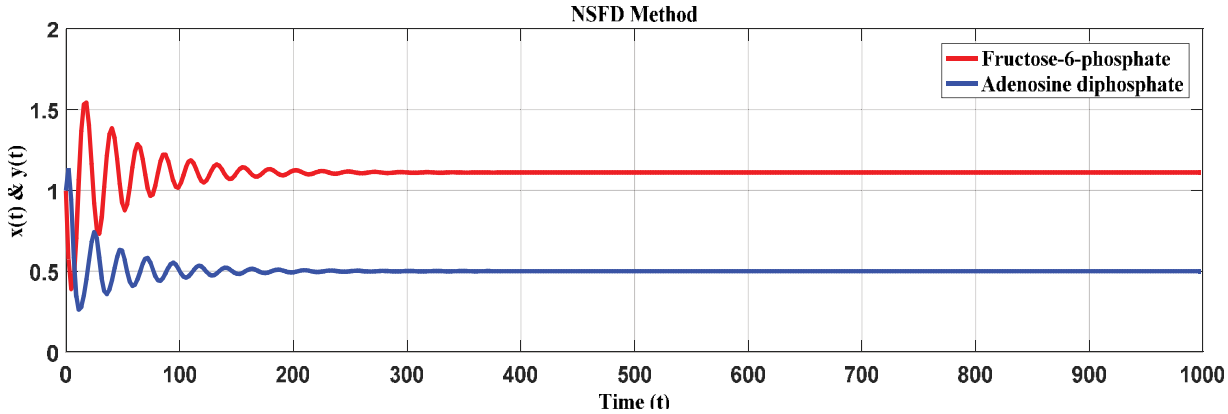


Fig. 8. The simulation with parameters α=0.5 and β=0.2 and step size 2.243.

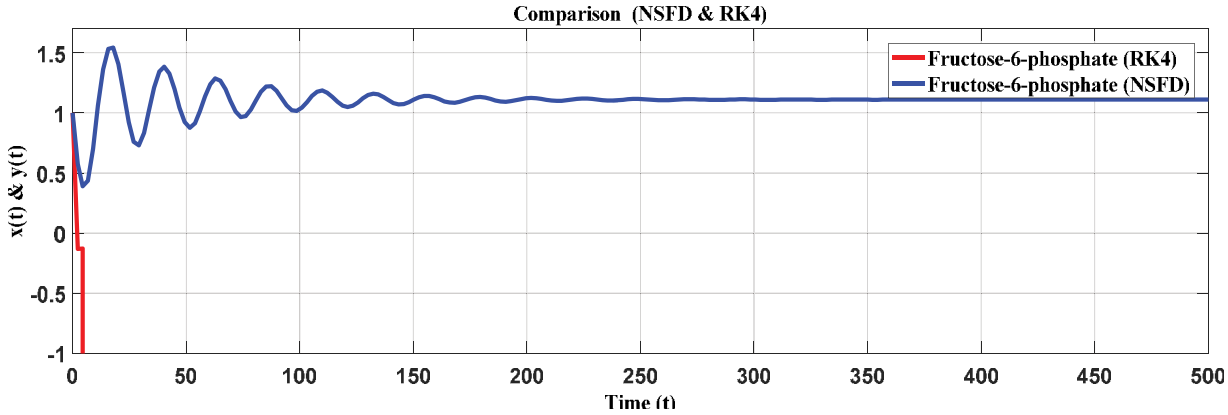


Fig. 9. The simulation with parameters α=0.5 and β=0.2 and step size 2.243

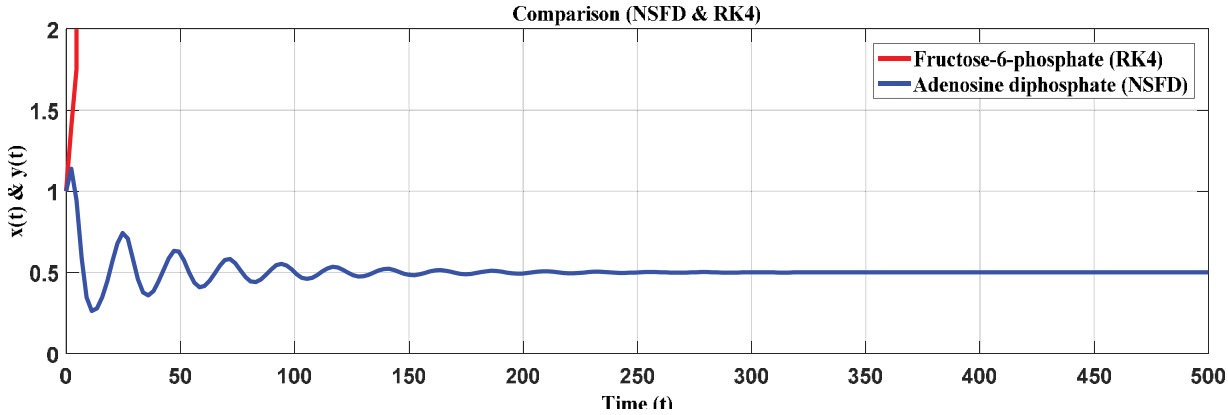


Fig. 10. The simulation with parameters α=0.5 and β=0.2 and step size 2.243.

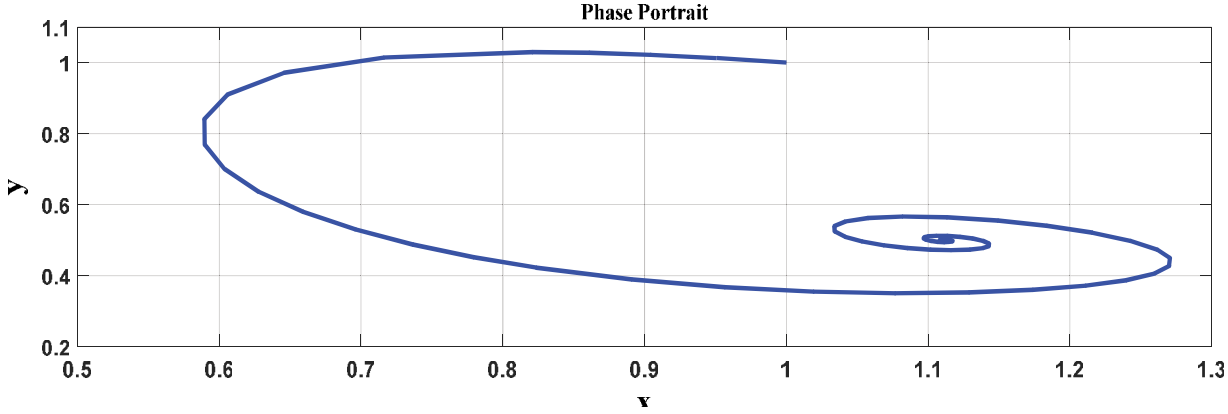


Fig. 11. The phase portrait with parameters α=0.5and β=0.2.

5. CONCLUSIONS

In this research, a non-standard finite difference scheme given by Mickens was successfully applied to find the numerical solution of the Glycolytic Oscillator model. It can be observed that when step size was increased up to 2.243 mm, the RK-4 scheme gave negative values of both GP & ADP, while the proposed Non-Standard Finite Difference (NSFD) scheme preserved positivity as well as convergence of the solution for these values of step size. Unlike RK-4, which fails for large time steps, the developed NSFD scheme gave results that converged to true steady states for any time step used. The proposed scheme is easy to implement and numerically stable.

6. REFERENCES

1. Keshat, L.E, *Mathematical Models in Biology.* Society for Industrial and Applied Mathematics, Philadelphia, PA, USA (2005).
2. Sen, A.K. An application of the Adomian decomposition method to the transient behavior of a model biochemical reaction. *Journal of Mathematical Analysis and Applications* 131: 232–245 (1988).
3. Pongsumpun, P. Mathematical model of Dengue disease with incubation period of virus. *International Journal of Mathematical, Computational, Physical, Electrical and Computer Engineering* 2(8): 535-539 (2008).
4. Zafar, Zain Ul Abadin, M. T. Hussain, A. Pervaiz, M. O. Ahmad & M. Kalim. A new fourth order compact difference scheme for one dimensional advection diffusion equation. *Pakistan Journal of Science.* 64: 359-362 (2012).
5. Zafar, Zain Ul Abadin, M.O. Ahmad, A. Pervaiz & M. Rafiq. Fourth Order Compact Method for One Dimensional Inhomogeneous Telegraph Equation with $O(h^4,k^3)$. *Pakistan Journal of Engineering and Applied Science* 14: 96-101 (2014).
6. Mickens, R.E. Numerical integration of population models satisfying conservation laws: NSFD Methods. *Biological Dynamics* 1(4):1751-1766 (2007).
7. Mickens, R.E. Dynamical consistency: a fundamental principle for constructing Non-standard finite difference schemes for differential equations. *Journal of Difference Equations and Applications,* 13(4): 645-653 (2005).
8. Arafa, A.A.M., S.Z. Rida & M. Hegagi, An Application of the homotopy analysis method to the transient behavior of a biochemical reaction model. *Information Science Letters* 3(1): 29-33 (2014).
9. Edeki, S.O., E.A. Owoloko, A.S. Osheku, A.A. Opanuga, H.I. Okagbue & G.O. Akinlabi. Numerical Solutions of Nonlinear Biochemical model using a Hybrid Technique, *International Journal of Mathematical Analysis* 9(8): 403-416 (2015).
10. Brauer, F. & C.C. Chavez. Mathematical models in population biology and epidemiology. *Springer-Verlag* (2001).
11. Hashim, I., M.S.H. Chowdhury & S. Mawa. On multistage homotopy perturbation method applied to non-linear biochemical reaction model. *Chaos Soltion and Fractals* 16: 823-827 (2008).
12. d'Onofrio, A., P. Manfredi & E. Salinelli. Dynamic behavior of a discrete-time SIR model with information dependent vaccine uptake. *Journal of Difference Equations and Applications* 22(3): 485-512 (2016).
13. Bairagi, N. & M. Biswas. A predator-prey model with Beddington-DeAngelis functional response: a non-standard finite differences method. *Journal of Difference Equations and Applications,* 22(4): 581-593 (2016).
14. Zafar, Zain Ul Abadin, K. Rehan, M. Mushtaq & M. Rafiq. Numerical treatment for nonlinear Brusselator chemical model. *Journal of Difference Equations and Applications* 23(3): 521-538 (2017).
15. Zafar, Zain Ul Abadin, K. Rehan, M. Mushtaq & M. Rafiq. Numerical modelling for nonlinear biochemical reaction networks. *Iranian Journal of Mathematical Chemistry* 8(4): 413-423 (2017).
16. Zafar, Zain Ul Abadin, K. Rehan & M. Mushtaq. Fractional-order scheme for bovine babesiosis disease and tick population. *Advances in Difference Equations* 86: 1-19 (2017).
17. Zafar, Zain Ul Abadin, M. Mushtaq & K. Rehan. A non-integer order dengue internal transmission model, *Advances in Difference Equations* 23: 1-23 (2018).
18. Zafar, Zain Ul Abadin, K. Rehan & M. Mushtaq. HIV/AIDS epidemic fractional-order model. *Journal of Difference Equations and Applications* 23(7): 1298-1315 (2017).
19. Zafar, Zain Ul Abadin, M. Mushtaq, K. Rehan & M. Rafiq. Numerical simulations of fractional order Dengue disease with incubation period of virus. *Proceedings of the Academy of Sciences: A. Physical and Computational Sciences* 54(3): 277-296 (2017).
20. Zafar, Zain Ul Abadin, K. Rehan, M. Mushtaq & M. Rafiq. Fractional numerical treatment for biochemical reaction networks. Proceedings of the Academy of Sciences: A. *Physical and Computational Sciences* 54(3): 297-304 (2017).