Journal of Cancer Treatment and Research
2016; 4(4): 27-33
http://www.sciencepublishinggroup.com/j/jctr
doi: 10.11648/j.jctr.20160404.11
ISSN: 2376-7782 (Print); ISSN: 2376-7790 (Online)

Positivity Preserving Nonstandard Finite Difference Schemes Applied to Cancer Growth Model

M. Mehdizadeh Khalsaraei*, Sh. Heydari, L. Davari Algoo

Department of Mathematics, Faculty of Science, University of Maragheh, Maragheh, Iran

Email address:
Mehdizadeh@maragheh.ac.ir (M. M. Khalsaraei), Muhammad.mehdizadeh@gmail.com (M. M. Khalsaraei)
*Corresponding author

To cite this article:
M. Mehdizadeh Khalsaraei, Sh. Heydari, L. Davari Algoo. Positivity Preserving Nonstandard Finite Difference Schemes Applied to Cancer Growth Model. *Journal of Cancer Treatment and Research.* Vol. 4, No. 4, 2016, pp. 27-33. doi: 10.11648/j.jctr.20160404.11

Received: October 17, 2016; **Accepted**: January 4, 2017; **Published**: January 31, 2017

Abstract: When one solves differential equations, modeling biological or physical phenomena, it is of great importance to take physical constraints into account. More precisely, numerical schemes have to be designed such that discrete solutions satisfy the same constraints as exact solutions. In this work, we introduce explicit finite difference schemes based on the nonstandard discretization method to approximate solution of the cross-diffusion system from bioscience. The proposed schemes improve the accuracy and guarantee the positivity requirement, as is demanded for the solution of such system. We apply new methods for numerical integration of the cancer growth model for illustrating the performance of them.

Keywords: Partial Differential Equations, Cross-Diffusion Equations, Positivity, Nonstandard Finite Difference, Cancer Growth Model

1. Introduction

Partial differential equations (PDEs) appear in many physical, biological and economic applications [5, 13, 14, 26]. A major difficultly in the study of these equations is, in general, the lack of exact analytical solution or cannot be solved by a straight forward formula. One way to proceed is to use numerical methods to obtained useful approximations on the solutions. A popular and important is one based on the use of the finite differences (FDs) to construct discrete models of the PDEs of interest [25]. One shortcoming of standard FDs is that essential qualitative properties of the exact solution are not transferred to the numerical solution. One way to avoiding this disadvantage is to employ nonstandard finite difference (NSFD) schemes [1, 2, 7-10, 15, 19-23]. More precisely, NSFDs in addition to the usual properties of consistency, stability and hence convergency, produce numerical solutions which also exhibit essential properties of solutions [16, 17, 21]. A PDE that satisfies the condition of positivity of some of its solutions is the cross-diffusion equations from bioscience [3-6, 11- 14, 24].

In this paper we propose new positive NSFD schemes which enable us to solve accurately the cancer growth model.

The rest of the paper is organized as follows: In Section 2, we give some preliminaries and definitions including nonstandard finite difference methods for differential equations. In Section 3, we consider a mathematical model of cancer growth and show that approximations obtained from standard finite difference (SFD) scheme and existing NSFD scheme in [6] which produce negative values. In Section 4 we propose our new schemes and investigate the positivity requirement for them. Furthermore, to illustrate the advantages of new schemes we compare them with the results obtained from the SFD method and existing NSFD method in [6]. Finally we end the paper with some conclusions in Section 5.

2. Preliminaries and Definitions

We now give a brief summary of the NSFD methods for the numerical solution of

$$\frac{dy(t)}{dt} = f(y(t)), \quad (t \geq 0), \quad y(0)=y_0, \tag{1}$$

where $y(t)$ may be a single function or a vector of functions of length k mapping $[t_0, T) \to C^k$ and the corresponding f a single function or a vector of functions of length k mapping $([t_0, T), C^k) \to [t_0, T)$. Discretization of the continuous differential equation, or beginning instead with a difference equation, we define

$t_n = t_0 + n\Delta t$, where Δt is a positive step size, and say that the discretized version of the function y at time t_n is

$$y_n \approx y(t_n).$$

Then the discretized version of Eq. (1) becomes

$$D_{\Delta t} y_n = F_n(f, y_n), \tag{2}$$

where $D_{\Delta t} y_n$ represents the discretized version of $\frac{dy(t)}{dt}$ and $F_n(f, y_n)$ approximates $f(y(t))$ at time t_n.

We define the nonstandard finite-difference method based on a definition given by Anguelov and Lubuma [1,2].

Definition1. Method (2) is called a nonstandard finite-difference method if at least one of the following conditions is met:

- In the discrete derivatives $D_{\Delta t} y_n$ the traditional denominator Δt is replaced by a nonnegative function $\varphi(\Delta t)$ such that

$$\varphi(\Delta t) = \Delta t + O(\Delta t^2) \text{ as } 0 < \Delta t \to 0,$$

for example:

$$\varphi(\Delta t) = 1 - e(-\Delta t), \qquad \varphi(\Delta t) = \tanh(\Delta t).$$

- Nonlinear terms in $f(y(t))$ are approximated in a nonlocal way, i.e. by a suitable function of several points of the mesh. For instance, the non-linear terms y^2 and y^3 can be modeled as follows [2]:
- $y \approx a y_k + (1-a) y_{k+1}, \quad a \in R$
- $y^2 \approx a y_k^2 + b y_k y_{k+1}, \quad a+b=1, \ a,b \in R,$
- $y^3 \approx a y_k^3 + (1-a) y_k^2 y_{k+1}, \ a \in R.$

Definition 2. Any constant-vector $\tilde{y}$ satisfying

$$f(\tilde{y}) = 0$$

is called equilibrium point (fixed-point or critical point) of the differential equation in (1).

3. Solution of the Cancer Growth Model

3.1. Mathematical Model

As in [6], the relevant PDE system in this study is given by:

$$\begin{aligned} \frac{\partial u}{\partial t} &= u(1-u) - \frac{\partial}{\partial x}\left(u \frac{\partial c}{\partial x}\right), \\ \frac{\partial c}{\partial t} &= -pc, \\ \frac{\partial p}{\partial t} &= \varepsilon^{-1}(uc - p), \end{aligned} \tag{3}$$

where $u = u(x,t)$, $c = c(x,t)$ and $p = p(x,t)$ are concentrations of invasive cells, connective tissue and protease, respectively and invasive cells have an invasive flux of $u\frac{\partial C}{\partial x}$ into connective tissues and solution domain is $(x,t) \in [0, x_{\max}] \times [0,T]$. Take a partition of the interval $x_0 < x_1 <, \cdots, < x_N$ with $x_m = m\Delta x$, $m = 0,1,2,\cdots,N$, and $\Delta x = \frac{x_{\max}}{N}$ and divide the time interval of interest $[0,T]$ using equal time steps of size $\Delta t = \frac{T}{M}$ with $t_k = k\Delta t$, $k = 0,1,\cdots,M$. Let u_m^k be the approximation to $u(x_m, t_k)$.

Following Definition 2, system (3) has three types of constant steady-state solutions $E = (u, c, p)$:

- the trivial equilibrium $E_t = (0,0,0)$;
- the fully malignant equilibrium $E_m = (1,0,0)$;
- the normal healthy equilibrium $E_n = (0,c,0)$, where $c > 0$ is any constant.

3.2. SFD Scheme

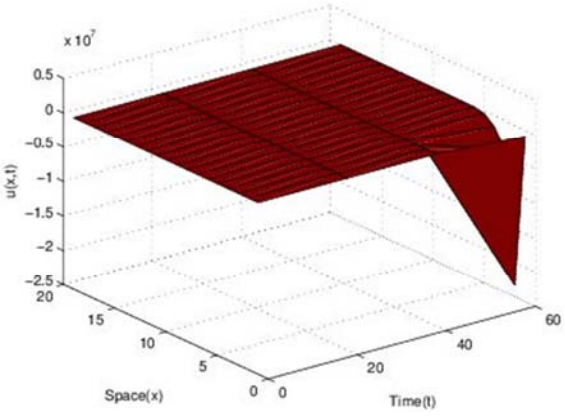
In this subsection, by using forward difference for $\frac{\partial u}{\partial t}$, $\frac{\partial c}{\partial t}$ and $\frac{\partial p}{\partial t}$, approximations $-p_m^k c_m^{k+1}$ for $-pc$, $\varepsilon^{-1}(u_m^k c_m^k - p_m^k)$ for $\varepsilon^{-1}(uc - p)$ and $u_m^k(1-u_m^k) - \frac{u_{m+1}^k - u_m^k}{\Delta x} \times \frac{c_m^k - c_{m-1}^k}{\Delta x} - u_m^k \frac{c_{m+1}^k - c_m^k + c_{m-1}^k}{(\Delta x)^2}$ for $u(1-u) - \frac{\partial}{\partial x}(u\frac{\partial c}{\partial x})$ at the grid points $(m\Delta x, k\Delta t)$, we consider a SFD scheme for solving the system (3) as:

$$\begin{aligned} &\frac{c_m^{k+1} - c_m^k}{\Delta t} = -p_m^k c_m^{k+1}, \\ &\frac{p_m^{k+1} - p_m^k}{\Delta t} = \varepsilon^{-1}(u_m^k c_m^k - p_m^k), \\ &\frac{u_m^{k+1} - u_m^k}{\Delta t} = u_m^k(1-u_m^k) - \frac{u_{m+1}^k - u_m^k}{\Delta x} \times \frac{c_m^k - c_{m-1}^k}{\Delta x} - u_m^k \frac{c_{m+1}^k - c_m^k + c_{m-1}^k}{(\Delta x)^2}. \end{aligned} \tag{4}$$

The explicit form of the scheme (4) can be written as follows:

$$\begin{aligned} c_m^{k+1} &= (1 + \Delta t p_m^k) c_m^k, \\ p_m^{k+1} &= p_m^k + \varepsilon^{-1}\Delta t(u_m^k c_m^{k+1} - p_m^k), \\ u_m^{k+1} &= (1 + \Delta t(1-u_m^k))u_m^k - (\frac{\Delta t}{\Delta x^2})(u_m^k(c_{m+1}^k - c_m^k) + u_{m-1}^k(c_{m-1}^k - c_m^k)). \end{aligned} \tag{5}$$

Figure 1 shows that the scheme (4) is unstable and produces negative values. More SFD schemes for solving (3) can be find in [6].



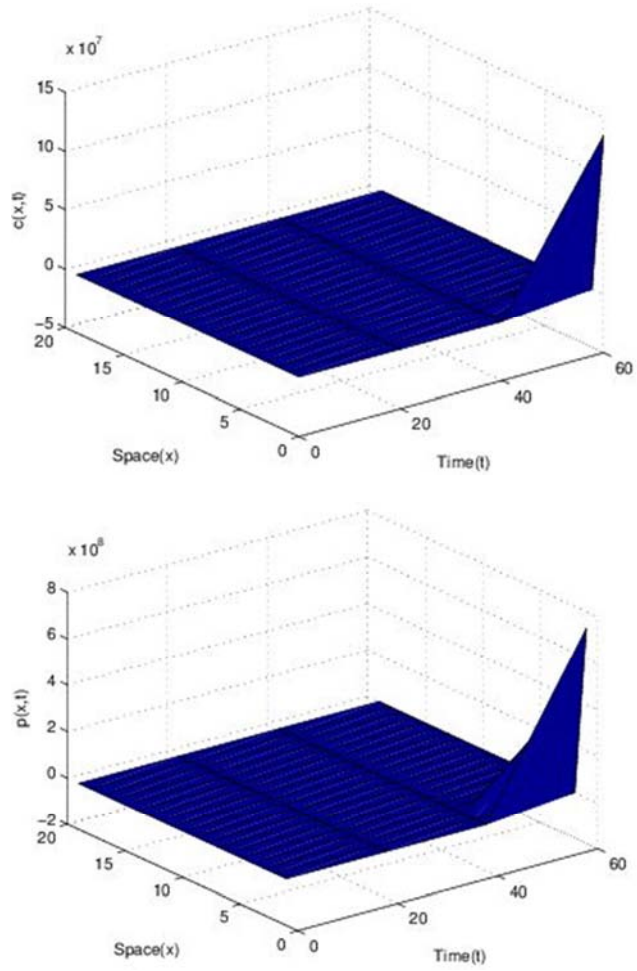


Figure 1. *Numerical results for (5) with* $\Delta x = 1,\ \Delta t = 1,\ \varepsilon = 0.2$.

3.3. A NSFD Scheme

To overcome the above defects some NSFD schemes have been proposed in [6], for example:

$$\begin{aligned}
&\frac{c_m^{k+1} - c_m^k}{\Delta t} = -p_m^k c_m^{k+1},\\
&\frac{p_m^{k+1} - p_m^k}{\varepsilon\varphi(\varepsilon^{-1}\Delta t)} = \varepsilon^{-1}(u_m^k c_m^{k+1} - p_m^{k+1}),\\
&\frac{u_m^{k+1} - u_m^k}{\varphi(\Delta t)} = u_m^k(1-u_m^{k+1}) - \frac{u_m^k c_{m+1}^k - (u_m^k + u_{m-1}^k)c_m^k + u_{m-1}^k c_{m-1}^k}{\psi^2(\Delta x)},
\end{aligned} \tag{6}$$

where $\varphi(\Delta t) = e^{\Delta t} - 1, \psi^2(\Delta x) = 2\varphi(\Delta t)$, and after simplifying we have

$$\begin{aligned}
&c_m^{k+1} = \frac{c_m^k}{1+\varphi(\Delta t)p_m^k},\\
&p_m^{k+1} = \frac{p_m^k + \varphi(\varepsilon^{-1}\Delta t)u_m^k c_m^{k+1}}{1+\varphi(\varepsilon^{-1}\Delta t)},\\
&u_m^{k+1} = \frac{2u_m^k[1+\varphi(\Delta t)] - [u_m^k c_{m+1}^k - (u_m^k + u_{m-1}^k)c_m^k + u_{m-1}^k c_{m-1}^k]}{2[1+\varphi(\Delta t)u_m^k]},
\end{aligned} \tag{7}$$

Figure 2, shows that the numerical results obtained from the scheme (7). We observe that method (7) has better behavior than the scheme (4) with the same value of the step-size, but still positivity is not guaranteed.

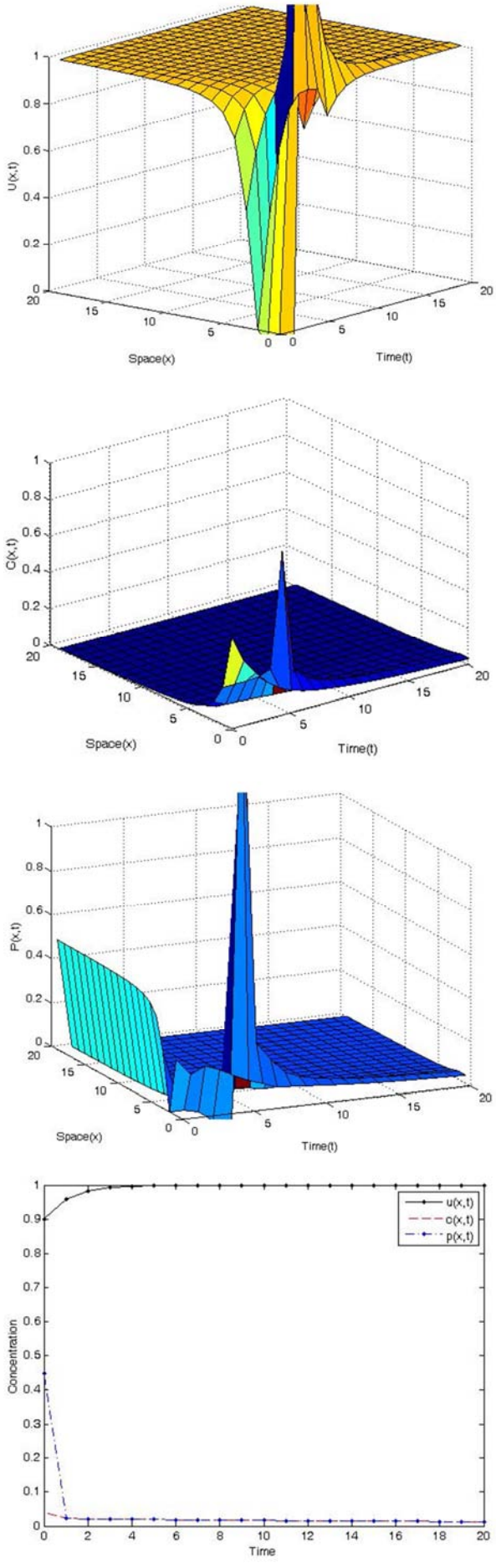


Figure 2. *Numerical results for (6) with* $\Delta x = 1,\ \Delta t = 1,\ \varepsilon = 0.2$.

4. Construction of the New NSFD Schemes

In this section, our main aim is to apply nonstandard discretization rules to construct two positive NSFDs for solving the system (3). Furthermore, we present the numerical results to confirm the properties of our new schemes and compare the performance of them with (4) and (6). What we shall be attempting to do, is to show the superior performance of new schemes for over (4) and (6). We do not claim that our numerical results demonstrate the superiority of our approach over any of the more nonstandard finite difference approaches. However, we do feel that our results indicate that a properly implemented version of our algorithm should be useful for the numerical integration of cancer growth model. We have programmed new schemes in MATLAB.

4.1. Scheme 1

Here by using the strategy of nonstandard discretization methods (using values at different time levels for discretization of $\frac{\partial u}{\partial t}$, $\frac{\partial c}{\partial t}$ and $\frac{\partial p}{\partial t}$, approximations $-p_m^k(2c_m^{k+1}-c_m^k)$ for $-pc$, $\varepsilon^{-1}(u_m^k c_m^{k+1}-\frac{3p_m^{k+1}-p_m^k}{2})$ for $\varepsilon^{-1}(uc-p)$ and

$$u_m^k(1-u_m^{k+1})-\frac{u_m^k-u_{m-1}^k}{\psi(\Delta x)}\times\frac{c_m^k-c_{m-1}^{k+1}}{\psi(\Delta x)}-u_m^k\frac{c_{m+1}^{k+1}-c_m^k+c_{m-1}^{k+1}}{\psi^2(\Delta x)}$$

for $u(1-u)-\frac{\partial}{\partial x}(u\frac{\partial c}{\partial x})$,
we propose our first scheme as:

$$\begin{aligned}
&\frac{c_m^{k+1}-c_m^k}{\varphi(\Delta t)}=-p_m^k(2c_m^{k+1}-c_m^k),\\
&\frac{p_m^{k+1}-p_m^k}{\varepsilon\varphi(\varepsilon^{-1}\Delta t)}=\varepsilon^{-1}(u_m^k c_m^{k+1}-\frac{3p_m^{k+1}-p_m^k}{2}),\\
&\frac{u_m^{k+1}-u_{m-1}^k}{\varphi(\Delta t)}=u_m^k(1-u_m^{k+1})-\frac{u_m^k-u_{m-1}^k}{\psi(\Delta x)}\times\frac{c_m^k-c_{m-1}^{k+1}}{\psi(\Delta x)}-u_m^k\frac{c_{m+1}^{k+1}-c_m^k+c_{m-1}^{k+1}}{\psi^2(\Delta x)},
\end{aligned}\tag{8}$$

by taking $\psi^2(\Delta x)=2(\Delta t)$ and after simplifying we have:

$$c_m^{k+1}=\frac{1+\varphi(\Delta t)p_m^k}{1+2\varphi(\Delta t)p_m^k}c_m^k,\tag{9}$$

$$p_m^{k+1}=\frac{2p_m^k+\varphi(\varepsilon^{-1}\Delta t)[2u_m^k c_m^{k+1}+p_m^k]}{2+3\varphi(\varepsilon^{-1}\Delta t)},\tag{10}$$

$$u_m^{k+1}=\frac{u_m^k(\varphi(\Delta t)-(1/2)c_{m+1}^{k+1})+u_{m-1}^k(1-(1/2)c_{m-1}^{k+1})+(1/2)(u_m^k+u_{m-1}^k)c_m^k}{(1+\varphi(\Delta t)u_m^k)},\tag{11}$$

Comparing with the method (5) the new proposed scheme performs well for larger time steps but the main advantage of this is that positive and stable(these results will be discussed in the following).

Theorem 1. For chosen $\varphi(\Delta t)$, sufficiency condition on Δt which scheme (8) to be positive is

$$\varphi(\Delta t)\geq\frac{1}{2},$$

Proof. Assume that $u_m^k>0,\ p_m^k>0$ and $0\leq c_m^k\leq 1$ according to (9) since

$$0\leq\frac{1+\varphi(\Delta t)p_m^k}{1+2\varphi(\Delta t)p_m^k}c_m^k\leq 1,$$

then $0\leq c_m^{k+1}\leq 1$, also from (10) we have $p_m^{k+1}>0$. Now for positivity of the u we have to put

$$\varphi(\Delta t)-\frac{1}{2}c_{m+1}^{k+1}\geq 0,$$

from which

$$\varphi(\Delta t)\geq\frac{1}{2}c_{m+1}^{k+1},$$

then the last inequality shows sufficiency of $\varphi(\Delta t)\geq\frac{1}{2}$ for positivity of proposed scheme, and this completes the proof.

In Figure 3 we observe that the solution of the new scheme for system (3) tend to (1,0,0), that is the same fully malignant equilibrium. Comparing the new proposed scheme with (4) and (6), we observe that the new scheme is positivity preserving, while approximations obtained by (4) and (6) gives negative values with initial conditions

$$u^0(x)=\exp(x^2),\quad c^0(x)=1-0.5u^0(x),\quad p^0(x)=0.5u^0(x)$$

and $\varphi(\Delta t)=e^{\Delta t}-1$.

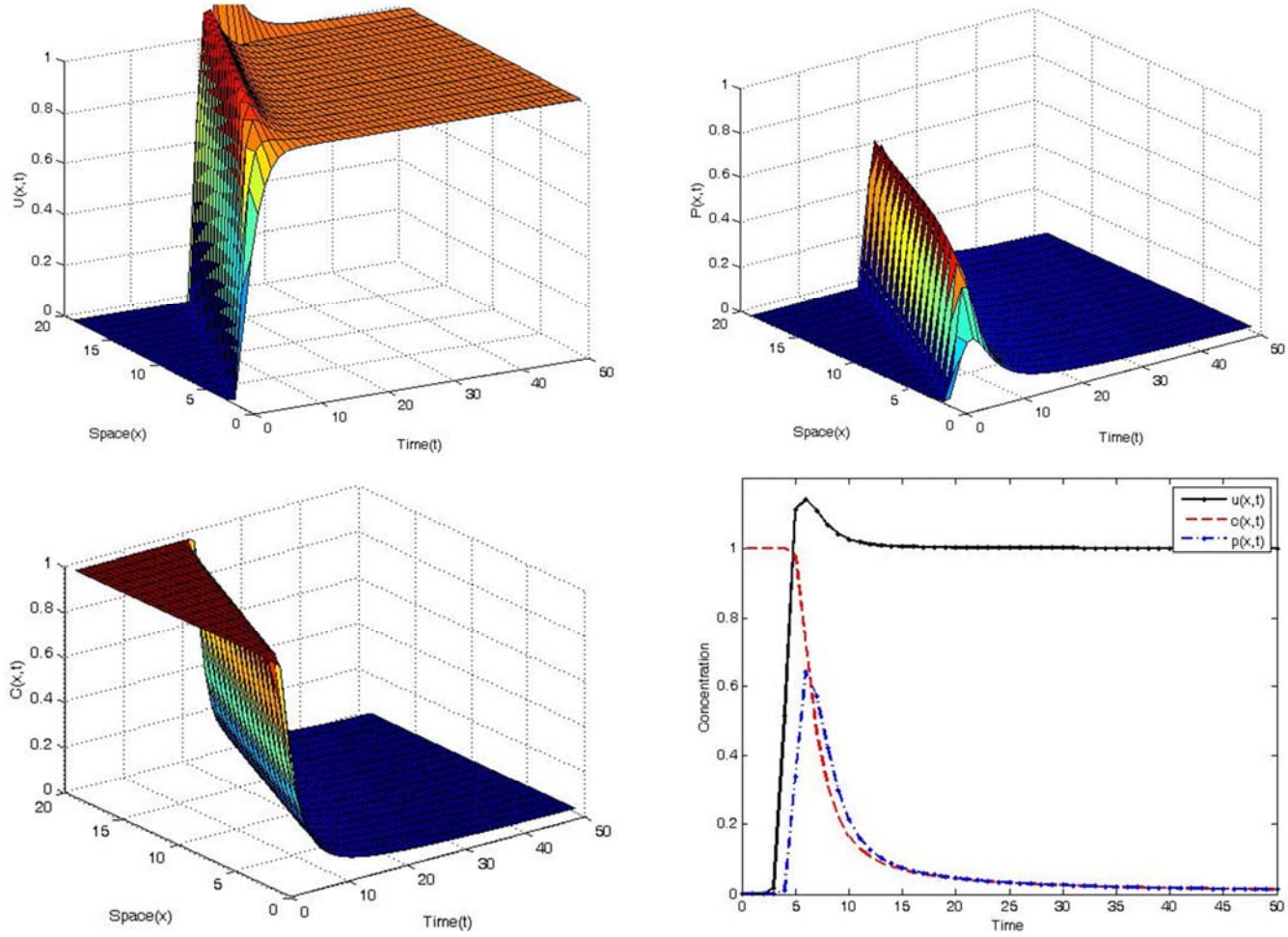


Figure 3. *Numerical results of the new scheme (6) with* $\Delta x = 1,\ \Delta t = 1,$ $\varepsilon = 0.2,\ \varphi(\Delta t) = e^{\Delta t} - 1$.

4.2. Scheme 2

We construct our second new NSFD method as:

$$\begin{aligned}
&\frac{c_m^{k+1} - c_m^k}{\varphi(\Delta t)} = -p_m^k c_m^{k+1}, \\
&\frac{p_m^{k+1} - p_m^k}{\varepsilon\varphi(\varepsilon^{-1}\Delta t)} = \varepsilon^{-1}(u_m^k c_m^{k+1} - 2p_m^{k+1} + p_m^k), \\
&\frac{u_m^{k+1} - u_{m-1}^k}{\varphi(\Delta t)} = 2u_m^k - u_m^{k+1} - u_m^k u_m^{k+1} - \frac{u_m^k - u_{m-1}^k}{\psi(\Delta x)} \times \frac{c_{m+1}^{k+1} - c_m^{k+1}}{\psi(\Delta x)} - u_{m-1}^k \frac{c_{m+1}^{k+1} - c_m^{k+1} + c_{m-1}^{k+1}}{\psi^2(\Delta x)}
\end{aligned} \tag{12}$$

after simplifying, the new NSFD scheme can be written as:

$$\begin{aligned}
&c_m^{k+1} = \frac{c_m^k}{1 + \varphi(\Delta t) p_m^k}, \\
&p_m^{k+1} = \frac{p_m^k + \varphi(\varepsilon^{-1}\Delta t)[u_m^k c_m^{k+1} + p_m^k]}{1 + 2\varphi(\varepsilon^{-1}\Delta t)}, \\
&u_m^{k+1} = \frac{u_m^k (1 + 2\varphi(\Delta t) + (1/2)(c_m^{k+1} + c_{m+1}^{k+1})) + (1/2)(c_m^{k+1} + c_{m-1}^{k+1}) u_{m-1}^k}{(1 + \varphi(\Delta t) + \varphi(\Delta t) u_m^k)}.
\end{aligned} \tag{13}$$

We have no formal proof for positivity of (13) (our interest for future) but, the numerical results obtained by the Math Toolbox software of MATLAB show that the new scheme is positivity preserving. It is evident that the new NSFD scheme improves the accuracy, giving better numerical results than the SFD scheme (4) and the NSFD scheme (6), see Figure 4.

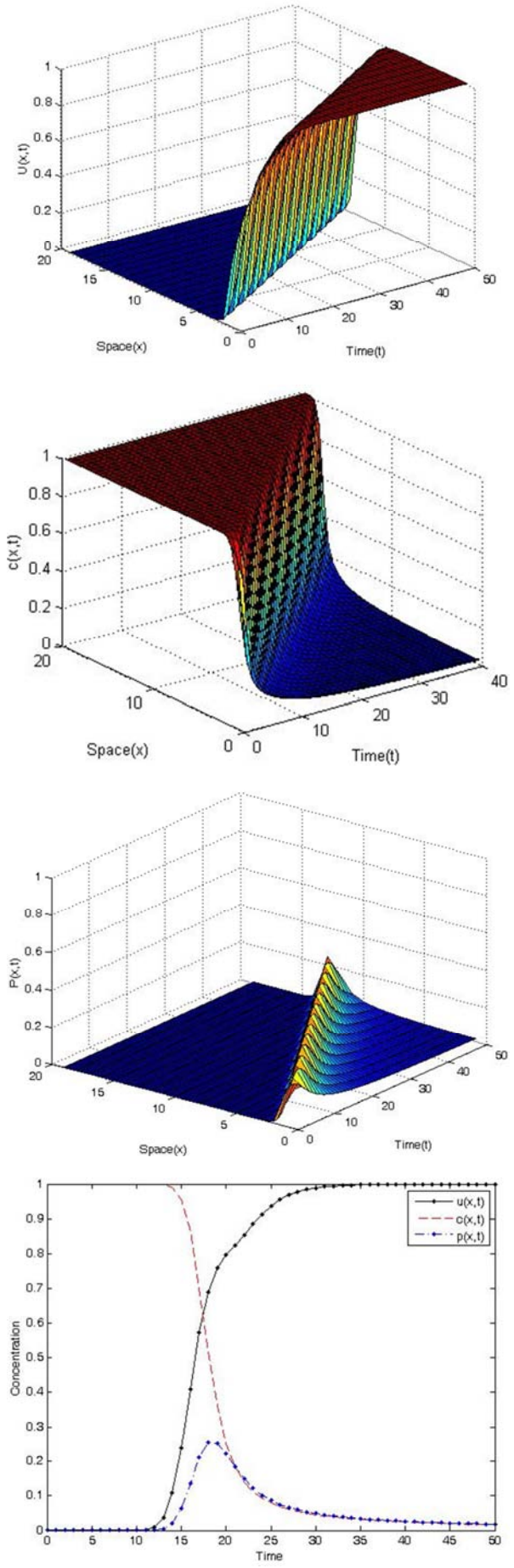


Figure 4. *Numerical results of the scheme (13) with* $\Delta x = 1,\ \Delta t = 1,\ \varepsilon = 0.2$, $\varphi(\Delta t) = e^{\Delta t} - 1$.

5. Conclusion

In this article, we proposed new NSFD schemes for solving the cancer growth model by renormalization of denominator of the discrete derivative and nonlocal approximation of the nonlinear terms. The power of our schemes over the standard ones is that they are reliable numerical simulations that preserve the stability and positivity properties of the exact solution. Solutions to the cancer growth model were presented to demonstrate the efficiency of the new scheme. Our interest, for future is to applying the proposed new positive nonstandard finite difference methods to other multi-dimensional dynamical systems. Also, construction of similar nonstandard schemes for the general case of biological systems and models with more nonlinear terms is our favorite. Here, all computations are performed by using MATLAB.

References

[1] Anguelov R., Lubuma J. M.-S.: Contributions to the mathematics of the nonstandard finite difference method and applications. Numerical Methods for Partial Differential Equations, 17, 518-543 (2001).

[2] Anguelov R., Kama P., Lubuma J. M.-S.: On non-standard finite difference models of reaction-diffusion equations. Journal of Computational and Applied Mathematics, 175, 11-29 (2005).

[3] Bellomo N., de Angelis E.: Selected topics in cancer modeling. genesis, Springer Science and Business Media, 255-276 (2008).

[4] Chen L., Jungel A.: Analysis of a parabolic cross-diffusion population model without self-diffusion. Journal of Differential Equations 224, 39-59 (2006).

[5] Chen-Charpentier B. M., Kojouharov H. V.: An unconditionally positivity preserving scheme for advection diffusion reaction equations. Mathematical and computer modelling, 57, 2177-2185 (2013).

[6] Chapwanya M., Lubuma J. M. S., R. E. Mickens.: Positivity-preserving nonstandard finite difference schemes for cross-diffusion equations in biosciences. Computers Mathematics with Applications, 68, 1071-1082 (2014).

[7] Dimitrov D. T., H. V. Kojouharov, Positive and elementary stable nonstandard numerical methods with applications to predator-prey models, J. Comput. Appl. Math. 189 (2006) 98–108.

[8] Dimitrov D. T., H. V. Kojouharov, Nonstandard numerical methods for a class of predator-prey models with predator interference, Electron. J. Diff. Equations 15 (2007) 67–75.

[9] Dimitrov D. T., H. V. Kojouharov, Nonstandard finite difference methods for predator-prey mpdels with general functional response, Math. Comput. Simulation 78 (2008) 1–11.

[10] Dimitrov D. T., H. V. Kojouharov, Stability-Preserving finite-difference methods for general multi-dimensional autonomous dynamical system, Int. J. Numer. Anal. Model. 4(2) (2007) 282–292.

[11] Jackson T. L., Byrne H. M.: A mechanical model of tumor encapsulation and trans-capsular spread. Mathematical Biosciences, 180, 307-328 (2002).

[12] Gucoglu A. K.: The Solution of Some Differential Equations by Nonstandard Finite Difference Method. Izmir Institute of Technology, Izmir (2005).

[13] Le D.: Coexistence with chemotaxis. SIAM Journal on Mathematical Analysis, 32, 504-521 (2000).

[14] Le D.: 'Cross-diffusion equations on n spatial dimensional domains'. Fifth Mississippi Conference on Differential Equations and Computational Simulations, Electronic Journal of Differential Equations, Conference 10, 193-210 (2003).

[15] Mickens R. E.: Nonstandard Finite Difference Models of Differential Equations. World Scientific, Singapore, (1994).

[16] Mehdizadeh Khalsaraei M.: An improvement on the positivity results for 2-stage explicit Runge-Kutta methods. Journal of Computatinal and Applied mathematics, 235, 137-143 (2010).

[17] Mehdizadeh Khalsaraei M., Khodadoosti F.: 2-stage explicit total variation diminishing preserving Runge-Kutta methods. Computational Methods for Differential Equations, 1, 30-38 (2013).

[18] Mehdizadeh Khalsaraei M., Khodadoosti F.: A new total variation diminishing implicit nonstandard finite difference scheme for conservation laws. Computational Methods for Differential Equations, 2, 85-92 (2014).

[19] Mehdizadeh Khalsaraei M., Khodadoosti F.: Nonstandard finite difference schemes for differential equations. Sahand Communications in Mathematical Analysis, 1, 47-54 (2014).

[20] Mehdizadeh Khalsaraei M., Khodadoosti F.: Qualitatively stability of nonstandard 2-stage explicit Runge- Kutta methods of order two. Computational Mathematics and Mathematical physics, 56, 235-242 (2016).

[21] Mehdizadeh Khalsaraei M.: Positivity of an explicit Runge-Kutta method. Ain Shams Engineering Journal, 6, 1217-1223 (2015).

[22] Mehdizadeh Khalsaraei M., Shokri Jahandizi R.: Positivity-preserving nonstandard finite difference schemes for simulation of advection-diffusion reaction equations. Computational Methods for Differential Equations, 2, 256-267 (2014).

[23] Murray J. D.: Mathematical biology I: an introduction. Springer, New York, (2002).

[24] Smith G. D: Numerical Solution of Partial Differential Equations: Finite Difference Methods. Oxford University Press, Oxford (1985).

[25] Shigesada N., Kawasaki K., Teramoto E.: Spatial segregation of interacting species. Journal of Theoretical Biology, 79, 83-99 (1979).