International Journal of
Science and Engineering Investigations vol. 7, issue 83, December 2018

ISSN: 2251-8843

Numerical Analysis on Finite Differences of Fisher-Kolmogorov Equation with Positivity Constraints

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Abstract-Given that tumor growth can be modeled by a mathematical equation, we carried out in this work an important observation about the computational solution of the Fisher-Kolmogorov equation, when considering conditions related to the problem of tumor growth. We apply three numerical methods of finite differences, and we note the results always considering the characteristics of the biological problem. We compare the numerical results using two- or three-dimensional graphs. We performed a computational confirmation of what was stated mathematically.

Keywords- *Tumors, Fisher-Kolmogorov, Finite Differences*

I. INTRODUCTION

The tumor growth in the brain show some important characteristics. One of them is that the cancerous cells spread yourselves mainly in the white and gray substances in the cerebral cortex; another characteristic is the density cells always presents smaller positive values that certain maximum load capacity [1]. The treatment planning for this growth can be enhanced from the observation in an efficient modeling [1]. In this area, a very used model for represents the tumor growth is the Fisher-Kolmogorov Equation [2].

Some works has been done in order to apply and solve the Fisher-Kolmogorov Equation. For example, in [1] we found the equation application as an aid in the treatment through the Radiology. Still, in [3] the equation solutions are used to modeling the growth and, in this way, delineate the target of Radiotherapy. Also observed of equation that in [4] the Fisher-Kolmogorov model is used to determinate and to observe the extrapolation margins of tumors. In [5] the Fisher-Kolmogorov Equation tensor it is applied to growth modeling and design of radiological target. Is important to say that no one of the cases mentioned exist a preoccupation of investigating the mechanism used to solve the equation and nor assess other mechanism solution. The Fisher-Kolmogorov Equation is a Partial Differential Equation and is common to apply the Classic Method of Finite Differences in the solutions of this kind of equation [6]. But, in this specific case is not possible to find a relation between the parameters that guarantee the positivity of solutions yet, because as already mentioned, the cells density and the equation solution, just have positive values. For solve positivity problems, others mechanisms about Finite Differences has been studied [7].

In this work we'll show one comparison between three schemes from Finite Differences for the Fisher-Kolmogorov Equation solution that mold the brain tumors growth. The first scheme we'll call Classic Scheme or Usual comes to the approximation to the first temporal derivate and second space derivate by Taylor series [8] and the no linear term approximation is made in a localized way [9]. The second scheme, denominated Non-standard, is different to the first in the no linear discretization term, because here is done a discretization no local in a computer domain [10]. The third scheme, Non-standard too, differs in subtle ways from the second scheme, and this difference will be presented throughout the text.

II. METHODS

The following is the mathematical model of Fisher-Kolmogorov and three finite difference schemes used to solve approximate manner the model. We emphasized in each schema some relevant points regarding the relationship between the model and the requirement of having a cell density that is positive and less than a maximum load

A. Fisher-Kolmogorov Model

Then we show the mathematic model used in the tumor model growth [11,12].

$$\frac{\partial u(x,t)}{\partial t} = \nabla.\left(D(x)\nabla u(x,t)\right) + \rho\, u(x,t)\left(1 - \frac{u(x,t)}{c}\right), \quad (1)$$

with $u(x,t)$ like the density function of the cell, ρ represents the rate of proliferation which is assumed to be spatially constant, c is the maximum, and D capacity (x) is the diffusion tensor that depends on the position, such that

$$D(x) = \begin{cases} D_w\,.\,I \;\; x \in \text{white substance;} \\ D_{g\,.}\; I \;\; x \in \text{gray substance}, \end{cases}$$

the number one dimension of identity matrix 3 [15,16].

Without loss of generality we can reduce the problem to a particular case involving only the scalar D_w, and for the other cases proceeded analogously. Therefore, the particular case to be taken is:

$$u_t = D_w u_{xx} + \rho\, u \left(1 - \frac{u}{c}\right), \tag{2}$$

u_t is the is the first derivative of $u(x,t)$ from ate u_{xx} is the second derivative of $u(x,t)$ with respect to x.

B. Finite Difference Usual Scheme

Seeing the solution $u(x,t)$, finite set of points of the discrete domain, we have that $u(x,t) \cong u_j^n$, with u_j^n as a computational numerical solution. Expanding $u(x,t)$ in a Taylor series [8] and approximating by finite differences we obtain the following expressions [9].

$$u_t \cong \frac{u_j^{n+1} - u_j^n}{\Delta t}, \tag{3}$$

$$u_{xx} \cong \frac{u_{j+1}^n - 2u_j^n + u_{j-1}^n}{\Delta x^2} \quad . \tag{4}$$

Taking into account expressions (3) and (4) and approach $u(x,t) \cong u_j^n$, the Fisher-Kolmogorov equation approximated by Usual Scheme of Finite Difference is

$$\frac{u_j^{n+1} - u_j^n}{\Delta t} = D_w \frac{u_{j+1}^n - 2u_j^n + u_{j-1}^n}{\Delta x^2} + \rho\, u_j^n \left(1 - \frac{u_j^n}{c}\right). \tag{5}$$

The Finite Differences Scheme, showed in the (5) equation don't represents one relation between the Δt e Δx^2 parameters such that positive initial data gave rise to positive solutions [10]. In order to overcome this positivity problem, we'll show two Finite Non-usual Difference Non-usual Scheme. The scheme in Finite Differences more famous by (Non-standard Finite Difference Methods) are defined to R. E. Mickens [13,17].

C. Finite Difference Non-standard Scheme 1

With the objective in increase the comprehension for the two differences Finite Difference Schemes, that will be show soon, we rewrite the equation (2) in this way:

$$u_t = D_w u_{xx} + \rho\, u \left(1 - \frac{\bar{u}}{c}\right). \tag{6}$$

The Finite Difference Non-standard Scheme 1 is different to the usual scheme just about the u and $\bar{u}$ approximation, because u is approximate for one media of three values in a fix time step, equation (7). But the $\bar{u}$ approximation is done according to the equation (8), take the values with step ahead of time [10].

$$u \cong \frac{u_{j+1}^n + u_j^n + u_{j-1}^n}{3} \tag{7}$$

$$\bar{u} \cong u_j^{n+1} \tag{8}$$

For to guarantee the scheme positivity [9] it's just taken Δt and Δx like it:

$$\frac{\rho}{3} - \frac{2D_w}{\Delta x^2} + \frac{1}{\Delta t} \geq 0 \,. \tag{10}$$

But the Finite Difference Non-standard Scheme 1 allows a relation between his parameters for to guarantee that the cells density by this method, always be positive. Besides, this scheme doesn't work when we see the fate that the density always be minor or the same to maximum charge and for this reason, we present a Second Finite Difference Non-standard Scheme.

D. Finite Difference Non-standard Scheme 2

The equation (2) can be rewrite in this way:

$$u_t = D_w u_{xx} + \rho\, u - \rho\, \frac{u^2}{c}. \tag{11}$$

The difference between the non-standard scheme 2 and the non-usual scheme is in the no linear time approximation u^2, because here the same is approximated according to the expressing (12)

$$u^2 \cong \frac{u_{j+1}^n + u_j^n + u_{j-1}^n}{3} u_j^{n+1} \,. \tag{12}$$

So, the Finite Difference Non-standard Scheme 2 in the explicit way, that approximate the Fisher-Kolmogorov Equation is [14]

$$u_j^{n+1} = \frac{D_w R\left(u_{j+1}^n + u_{j-1}^n\right) + (\rho\, \Delta t + 1 - 2D_w R) u_j^n}{\left[1 + \frac{\rho\, \Delta t}{3c}\left(u_{j+1}^n + u_j^n + u_{j-1}^n\right)\right]} \,. \tag{13}$$

For to guarantee the positivity of the scheme (13), just take:

$$\rho\, \Delta t + 1 - 2D_w R \geq 0 \,. \tag{14}$$

The Finite Difference Non-standard Scheme 2in the equation (14), allows a relation between her parameters that guarantee the positivity solutions, the cells density. But one another factor have an important emphasis in this method analysis that the fate the same allows a relation between the parameters the density always be minor or the same to maximum charge, in the scheme (5) and (9) doesn't presents. Is important to say that Mickens et al show [14]:

$$\frac{u_{j+1}^n + u_j^n + u_{j-1}^n}{3} \leq 1 \tag{15}$$

and

$$\rho\, \Delta t + 1 - 2D_w R = D_w R \tag{16}$$

so

$$u_j^{n+1} \leq 1 \tag{17}$$

to $n = 0, 1, 2, 3, \dots, N$.

Following, we done in the same way about what Mickens et al [14] done for to generalize the result and show that:

$$\frac{u_{j+1}^n + u_j^n + u_{j-1}^n}{3} \leq c \tag{15}$$

and

$$\rho\, \Delta t + 1 - 2D_w R = D_w R \tag{16}$$

so

$$u_j^{n+1} \leq c \tag{17}$$

para $n = 0, 1, 2, 3, \dots, N$ and c equal the maximum charge.

First, we multiply and divide the expression (15) for

$$3D_w - \rho \Delta x^2 \tag{18}$$

and we obtain

$$\frac{(3D_w-\rho\Delta x^2)(u^n_{j+1}+u^n_j+u^n_{j-1})}{3(3D_w-\rho\Delta x^2)} \le c\ . \tag{19}$$

Expression (16) we finally come to the follow equality

$$\Delta t = \frac{\Delta x^2}{3D_w-\rho\Delta x^2}\ . \tag{20}$$

Substituting the expression. (20) in (19) and realizing a little algebraic manipulation we come the following inequality:

$$D_wR\left(u^n_{j+1}+u^n_j+u^n_{j-1}\right) \le c + \frac{\rho\,\Delta t}{3}\left(u^n_{j+1}+u^n_j+u^n_{j-1}\right) \tag{21}$$

And with consequence,

$$\frac{D_wR\left(u^n_{j+1}+u^n_{j-1}\right)+(\rho\,\Delta t+1-2D_wR)u^n_j}{\left[1+\frac{\rho\,\Delta t}{3c}\left(u^n_{j+1}+u^n_j+u^n_{j-1}\right)\right]} \le c\ . \tag{22}$$

So:

$$u_j^{n+1} \le c. \tag{23}$$

We verify that the scheme (13) guarantee the positivity solutions and maintain the cells density always minor or like to maximum charge, since that the conditions into the text be considerate.

III. RESULT

A. Computer simulations

For to do the present simulations in the figures (1)-(4) we use the Matlab software and the following parameters: $\Delta x = 0.19$, $c = 2$, $\rho = 25$, initial condition $f(x) = 0.5c + 0.5c\sin 2x$, Δt we use the equation (20).

IV. DISCUSSION

After the observing the presented simulations in the figures (1) – (4) we realize that the computational results confirm that the presentation of the methods described in topics (2.1) and (2.2), namely, the usual finite difference scheme doesn't guarantee positive and solutions showing some negative solutions this kind of solution isn't interest to the Fisher-Kolmogorov model in regard to the problem of the tumours growth (figure 1 an figure 4), the no standard scheme 1 preserves the positivity however, we noticed in Figures 2 and 4 that the cell density reaches equal values to 15 which contradicts the condition imposed in the simulations that the maximum load should be less than or equal to 2. Already the figure 3 show that the no standard scheme 2 in addition to preserving the positivity still show values for cell density as expected, less than or equal to 2, this information is confirmed in a local manner in a figure [4] when you see that the solution graphic in the indicated times do not exceed the value of the maximum load.

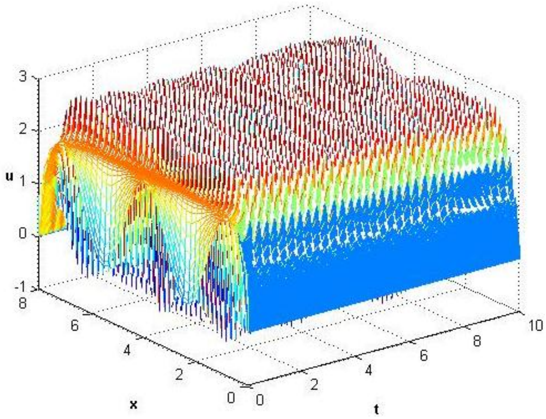

Figure 1. Solution obtained through the Usual

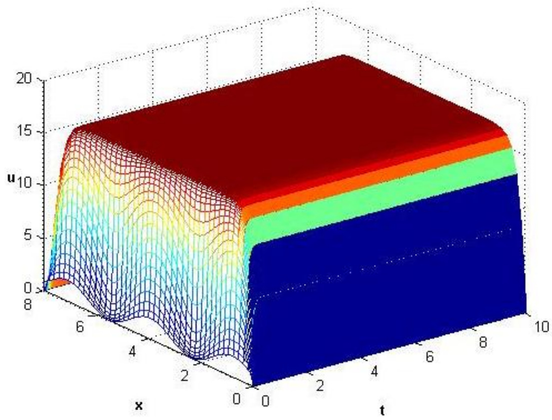

Figure 2. Solution obtained through the first No-standard Scheme 1

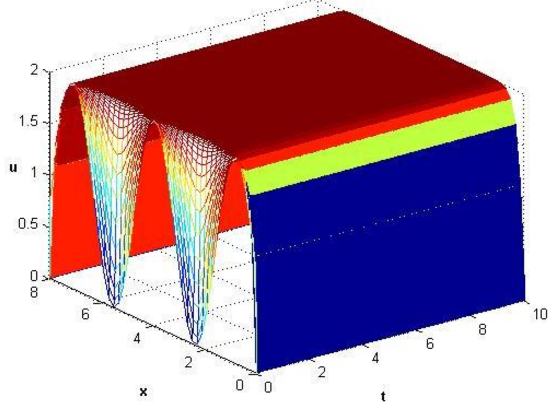

Figure 3. Solution obtained through the first No-standard Scheme 2

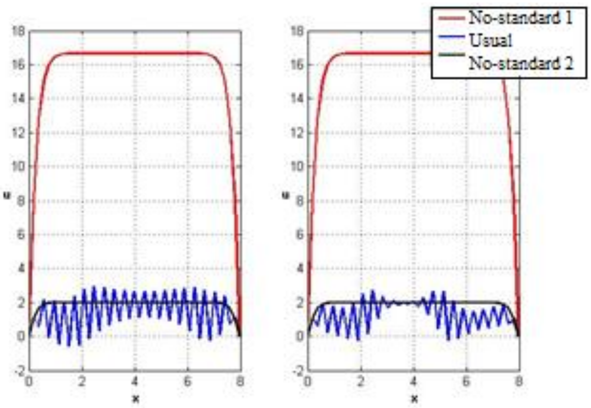

Figure 4. Solutions of the three schemes with $t = 100\Delta t$ and $t = 230\Delta t$

V. CONCLUSION

The Finite Differences Schemes showed in this work although possess little differences in terms of the modeling they show significant differences as regards the computational solution of mathematical model used in the tumor growth study and these differences permeates primarily on the discretization choice parameters which in turn can lead to method error. Its important point that the simulations have been done just for conditions tests presented in each one description and this way, prove computationally what have been showed mathematically. We hope that our results can add further the study problem addressed.

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