

UDC 004

Information Technology. Computer Engineering

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## NUMERICAL SIMULATIONS FOR ONE CANCER MODEL

One particular cancer model is solved and analyzed computationally using Over-Relaxation method. Results are compared for Runge-Kutta 4 (RK4), Finite Difference methods, using different computational aspects.

*Keywords:* cancer model, over-relaxation method

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## ЧИСЛОВОЕ МОДЕЛИРОВАНИЕ ДЛЯ ОДНОЙ МОДЕЛИ РАКА

В работе одна конкретная модель рака решается и численно анализируется с использованием метода верхней релаксации. Результаты сравниваются для методов Рунге-Кутты и конечных разностей, с использованием различных вычислительных аспектов.

**Ключевые слова:** модель рака, метод верхней релаксации.

Գ. Դալլաքյան

## ԹՎԱՅԻՆ ՄՈՂԵԼԱՎՈՐՈՒՄ ՔԱՂՑԿԵՂԻ ՄԵԿ ՄՈՂԵԼԻ ՀԱՄԱՐ

Աշխատանքում քաղցկեղի որոշակի մոդելի համար վերին ռելակսացիայի մեթոդով ստացվում են լուծումներ և կատարվում է դրանց թվային վերլուծություն: Արդյունքները համեմատվում են Ռունգե-Կուտտի և վերջավոր տարբերությունների մեթոդների արդյունքների հետ, օգտագործելով տարբեր հաշվողական ասպեկտներ:

**Keywords:** քաղցկեղի մոդել, վերին ռելակսացիայի մեթոդ:

### Introduction to the proble

As we mentioned earlier, cancer is killer disease that has become a major cause of death in the worldwide. World Health Organization (WHO) estimated about six million deaths annually due to cancer [1]. Cancer, as an uncontrolled growth of abnormal cells, is just like a wound that never heals. Excessive alcohol intake, sunlight exposure, nuclear fusion and genetic mutations are some of the causes for cancer.

Cancer treatment is influenced by a number of factors such as severity of disease, treatment techniques and strength of a patient's immune system [2]. In previous decades, efforts have been diverted towards controlling the growth of cancer by studying its dynamical properties with an aim to predict how the tumor will grow in order to divert medicine to the part of tumor where most growth is expected. The model, governing cancer growth, is chaotic where small changes in initial condition

may results in huge changes in the final results. Therefore, correct parameter analysis is very important to tackle this disease and treatment. For the cancer models, mathematicians can measure how much the disease will spread at a given time, or threshold values necessary for certain conditions such as eradication to be achieved. In [3] a dynamical system is derived in form of nonlinear differential equations in order to analyze dynamics of cancer that are proved to be chaotic and the exact solution of model cannot be obtained using the known techniques. Thus, one has to rely on approximate solutions. The most well-known technique to approximate solution of system of nonlinear equations is Newton's method which is known to be plagued by its dependence on the initial guess. Recently third and fourth order of convergence techniques have been proposed and analyzed to get efficient results [4].

### Numerical methods

We will use Over-Relaxation (OR) for Finite-Difference (FD) to approximate the solution of one cancer growth model. FD discretization of chaotic cancer model results into a system of nonlinear equations that are well-known to be hard to approximate. Over-Relaxation is efficient and advanced numerical tool to find the approximate solutions of differential equations. This technique has vast range of applications, for instance, to analyze sensitive and chaotic systems, to check vibration responses of dynamical systems of high frequencies, to predict structural behavior of plates, in observing the sound radiation from resonating bodies and many others. OR method is one of the better techniques to get excellent results and to save computational time [5].

#### *Mathematical algorithm*

In this section we describe the model along with a brief introduction to finite difference and OR technique. Over-Relaxation is an iterative method and solves matrix equations iteratively.

Back substitutions give zeros on all of lower elements where back substitutions through Jacobi's algorithm are

$$x_i^{k+1} = \frac{\sum_{j=1}^n a_{ij} x_j^k + b_i}{a_{ii}}$$

But there is another method called Gauss-Seidel method which is more efficient than Jacobi method. The Gauss-Seidel method is based on Jacobi method and given as;

$$x_i^{k+1} = \frac{-\sum_{j=1}^n a_{ij} x_j^{k+1} - \sum_{j=i+1}^n a_{ij}^k x_j^k + b_i}{a_{ii}}$$

Gauss-Seidel method is an iterative method based on Jacobi's method and uses all the previous values of  $x$  and already computed values. Over-Relaxation method is based on Gauss-Seidel method. This method moves towards the relaxation or make the solution converge faster  $x_i^{k+1} = x_i^k + \omega R_i$ , where  $\omega$  is the relaxation factor and  $R_i$  is the residual vector.

The aim of using OR method is that we want to minimize the residual or to minimize error. The residual value in Gauss-Seidel method is given as

$$R_i = \sum_{j=1}^{ni-1} \frac{a_{ij}x_j^{k+1}}{a_{ii}} - \frac{-\sum_{j=1}^n a_{ij}x_j^k + b_i}{a_{ii}}$$

Hence Gauss-Seidel to Over-Relaxation becomes

$$x_i^{k+1} = x_i^k - \omega \left[ \sum_{j=1}^{ni-1} \frac{a_{ij}x_j^{k+1}}{a_{ii}} - \frac{-\sum_{j=1}^n a_{ij}x_j^k + b_i}{a_{ii}} \right]$$

From the same logic, OR-Newton’s method is derived as

$$x_i^{k+1} = x_i^k - \omega \frac{G_i(x^{k,i-1})}{G_{ii}(x^{k,i-1})}, \quad i = 1, 2, \dots, n \text{ and } k = 0, 1, 2, \dots \quad (1)$$

Where  $G_{ii} = \frac{\partial G_i}{\partial x_i}$ , plays the role of residual vector in which  $G_i$  is the vector representing system of nonlinear equations and

$$x^{(k,0)} = (x_1^{(k,0)}, x_2^{(k,0)}, \dots, x_n^{(k,0)}) = x^{(k)},$$

$$x^{(k,l)} = (x_1^{(k,l)}, x_2^{(k,l)}, \dots, x_n^{(k,l)})^t = (x_1^{(k+1)}, x_2^{(k+1)}, \dots, x_n^{(k+1)})^t, \quad \text{for } j = 1, 2, \dots, n$$

It gives

$$x_l^{(k,l)} = x_l^{(k,j-1)}, \quad i \neq j, \quad l = 1, 2, \dots, n.$$

Consider a nonlinear system of equations

$$\vec{X} = \vec{F}(x_1, x_2, \dots, x_n) \text{ where } \vec{X} = [\dot{x}_1, \dot{x}_2, \dots, \dot{x}_n]^t$$

and

$$\vec{F} = [f_1(x_1, \dots, x_n), f_2(x_1, \dots, x_n), \dots, f_n(x_1, \dots, x_n)]^t$$

The first order forward difference approximation of  $f$  with respect to  $t$  using Taylor series expansion is

$$\frac{df}{dt} = \frac{f_{i+1} - f_i}{h} + O(h), \quad (2)$$

where  $h$  represents the step size.

Using (2) into (1), we get

$$x_{1,i+1} = x_{1(i)} + h f_1(x_1, x_2, \dots, x_{n-1}),$$

$$x_{2,i+1} = x_{2(i)} + h f_2(x_1, x_2, \dots, x_{n-1}),$$

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$$x_{n,i+1} = x_{n(i)} + h f_n(x_1, x_2, \dots, x_{n-1}).$$

(3)

Applying OR-Newton method to the system (3), we obtain the following system of nonlinear equations after simplification as;

$$\begin{aligned}x_{1,i+1} &= (1 - \omega)x_{1(i)} + \omega \{x_{1(i)} + h f_1(x_1, x_2, \dots, x_{n-1})\}, \\x_{2,i+1} &= (1 - \omega)x_{2(i)} + \omega \{x_{2(i)} + h f_2(x_1, x_2, \dots, x_{n-1})\}, \\&\cdot \\&\cdot \\&\cdot \\x_{n,i+1} &= (1 - \omega)x_{n(i)} + \omega \{x_{n(i)} + h f_n(x_1, x_2, \dots, x_{n-1})\}.\end{aligned}$$

The above is a general strategy to apply finite difference OR technique to solve any nonlinear system.

### **The state of the problem**

Now we apply this technique to the cancer growth model given in [4] for particular values of coefficients:

$$\begin{aligned}\dot{x} &= x(1 - x) - a_{12}xy - a_{13}xz, \\ \dot{y} &= r_2y(1 - y) - a_{21}xy, \\ \dot{z} &= \frac{r_3xz}{x + k_3} - a_{31}xz - d_3z\end{aligned}$$

No. of iterations x10 <sup>5</sup>	Time Elapsed-RK4(Sec)	Time Elapsed-FD(Sec)	Time Elapsed-RK4(Sec)
13	13.0916	0.0847	0.0841
4	3.8070	0.3402	0.3361
2	1.9834	0.1671	0.1663
0.5	0.6133	0.0418	0.0413
0.25	0.3786	0.0211	0.0211

where  $x(t)$  represents the tumor cells at time  $t$ ,  $y(t)$  shows the number of healthy host cells at time  $t$ , and  $z(t)$  is the number of effector immune cells at time  $t$ , in the single tumor-site compartment. Moreover,  $a_{12}, a_{21}, a_{13}, a_{31}, r_2, r_3, k_3, d_3$  are parameters [6] defined as:

$$\begin{aligned}a_{12} &= 1, \quad a_{21} = 1.5, \quad a_{13} = 2.5, \quad a_{31} = 0.2, \\ r_2 &= 0.6, \quad r_3 = 4.5, \quad k_3 = 1, \quad d_3 = 0.5\end{aligned}$$

By using first order Finite Difference approximation, above system takes the following form;

$$\begin{aligned} x_{i+1} &= x_i + h \{x_i (1 - x_i) - a_{12}x_i y_i - a_{13}x_i z_i\}, \\ y_{i+1} &= y_i + h \{r_2 x_i (1 - y_i) - a_{21}x_i y_i\}, \\ z_{i+1} &= z_i + h \left\{ \frac{r_3 x_i z_i}{x_i + k_3} - a_{31}x_i z_i - d_3 z_i \right\}. \end{aligned}$$

Now by applying OR technique our system reduces into

$$\begin{aligned} x_{i+1} &= (1 - \omega) x_i + \omega \left[ x_i + h \{x_i (1 - x_i) - a_{12}x_i y_i - a_{13}x_i z_i\} \right], \\ y_{i+1} &= (1 - \omega) y_i + \omega \left\{ y_i + h \{r_2 x_i (1 - y_i) - a_{21}x_i y_i\} \right\}, \\ z_{i+1} &= (1 - \omega) z_i + \omega \left[ z_i + h \left\{ \frac{r_3 x_i z_i}{x_i + k_3} - a_{31}x_i z_i - d_3 z_i \right\} \right]. \end{aligned}$$

Above nonlinear system is approximated using Newton’s method for different values to control the convergence of the method.

**Numerical simulation**

Tolerance	Finite Difference	OR-Method
10 <sup>-11</sup>	220297	269730
10 <sup>-10</sup>	29670	26973
10 <sup>-9</sup>	29661	26965
10 <sup>-8</sup>	6576	5979
10 <sup>-7</sup>	6571	5975

Below a cancer chaotic model [7], after discretization and approximation through OR-method, is analyzed. The comparison is made with its well-known competitor numerical schemes, RK4 and Finite Difference.

Table below gives the time elapsed by the computational scheme for the prescribed number of iterations. For this purpose, x(0) = y(0) = z(0) = 0.1 is taken as initial condition and step size is taken as h = 0.0005. We can see that the OR method in these three schemes requires less time to calculate the results compared to the Finite Difference and the RK4 method. Since the estimated time plays a key role in numerical approaches, it does not take much time to obtain effective results. The table checks the leading and improved OR behavior compared to the other schemes used.

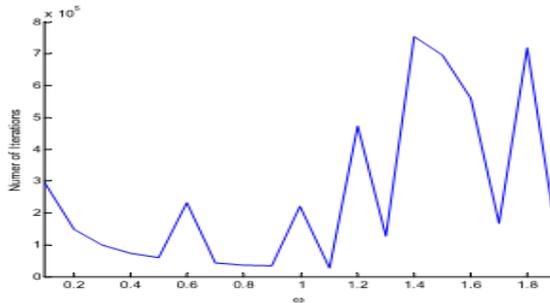
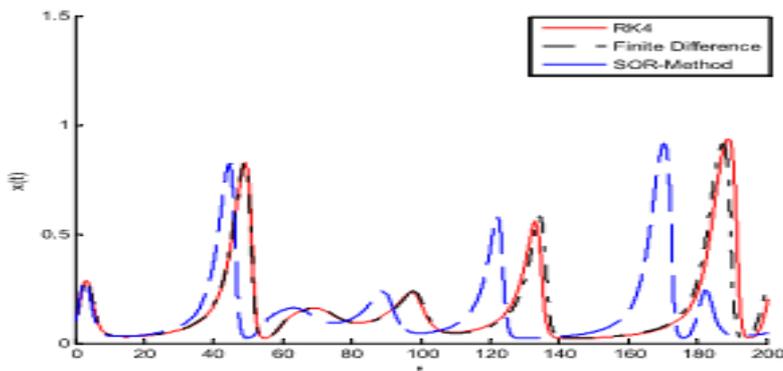


Figure 1. Variations of iterations with Relaxations parameter

To understand the effect of tolerance, Table 2 gives count of number of iterations for the finite difference and OR method. We can observe, from Table 2, that number of iterations required for defined tolerance for OR method is sufficiently less as compare to finite difference method for converged solution. It means computational space required for OR method is less, which enables scheme to execute faster and give results in short time interval without using extra memory of computing machines. In OR method, relaxation parameter plays an important role. In fact, convergence and hence the number of iterations depends on the values of parameter. In order to obtain the best parameter value, we have compared different values of  $\omega$  to comment on its effect on number of iterations. In the figure 1, graphical representation of number of iterations required for the converged solution for different values of relaxation parameter is presented. We can observe that for  $h = 1.1$ , proposed numerical scheme gives converged solution after 26973 iterations against the tolerance  $10^{-11}$ .

To provide a fair comparison of these methods for converged solutions, we have also analyzed the time history and shown in figure 2. We can observe the nonlinearity in the solution from figure 2. It is to be noted that Finite Difference scheme achieves the value of converged solution a bit earlier than RK4, around  $t = 185$ , but OR convergence is most improved form which gets its same converged results much earlier approximately at  $t = 162$ . Moreover, for large values of  $t$ , converged solution takes place far earlier through OR method in comparison with RK4 and FD. It gives one of efficient feature of proposed scheme.

Figure 2. Time history of  $x(t)$  through three schemes.



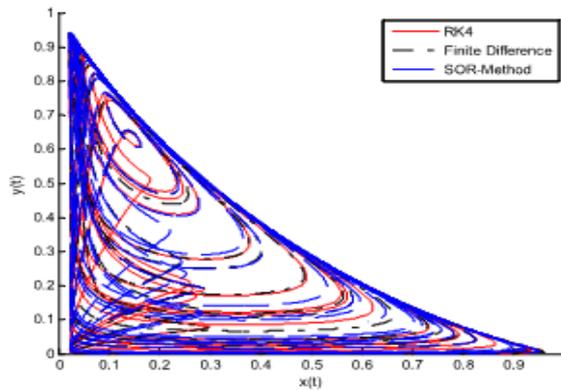


Figure 3. Strange attractor of Cancer model in xy-space

To observe the chaotic behavior for defined parameter values of the cancer model, we created the phase portraits in figure 3 and 4. Figure 3 gives the strange attractor of cancer model sketched through RK4, Finite Difference and OR method.

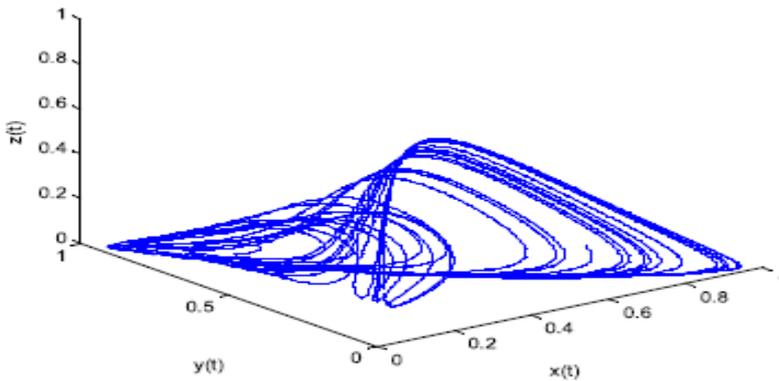


Figure 4. Strange attractor of Cancer model in xyz-space

We can notice that the phase portrait between tumor cells and healthy host cells is periodic and chaotic for defined growth, inhibiting and killing rates. Differences in results can be viewed clearly in xy-plane. Figure 4 is three dimensional sketch of chaotic system through OR method.

### CONCLUSION

Mathematical models of cancer are often complex and are unlikely to be amenable to standard mathematical analysis and therefore are nearly always solved by means of computational solution. Such computational solutions, either numerical or simulation-based, require a great deal of computing power, which has only recently become widely available. It seems clear that we have now seen the emergence of computational models as the dominant tool in mathematical models of cancer.

The aim of this work was to analyze the mathematical model describing the growth of a tumor in the presence of a nutrient, the concentration of which is not only subject to natural production and consumption processes. The considered model has the form of a system of ordinary equations and is solved by Over-Relaxation

method. Results are compared for Runge-Kutta 4 (RK4), Finite Difference methods, using different computational aspects.

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