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Research Article

Quantitative Analysis for the Spread Range of Malignant Tumor Based on Lie Symmetry

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It provided a powerful new way for predicting the growth trend of malignant tumor and assisting the treatment of cancer patients. Firstly, a one-dimensional mathematical model for the dynamic proliferation of malignant tumors is established on the premise of related simplification and hypothesis. Secondly, according to the Lie symmetry theory, we deduce the multigroup allowed infinitely small generating elements of partial differential equations and obtain the analytic form of the exact invariant solution. Finally, the influence of the model condition parameters (oxygen concentration and inhibitor concentration) on the tumor multiplication time index T is analyzed and discussed. The results showed that when the concentration of the nutrient substance is higher than the critical concentration, the multiplication time of the tumor region approximately decreased firstly and then increased in the linear form about tumor radius under different oxygen concentrations, and at the same radius, the oxygen concentration is lower, and the multiplication time is longer; the multiplication time of the tumor region approximately decreased in the exponential form about tumor radius under different inhibitor concentrations, and at the same radius, the inhibitor concentration is higher, and the multiplication time is bigger, which are consistent with the experimental and clinical observation.

1. Introduction

Malignant tumors can cause canceration, proliferation, and metastasis of cancer cells after surgical resection; it has the characteristics of unlimited and endless proliferation, which is a great threat to human life. Therefore, the growth law of malignant tumors and their evolution theory has been an important subject to study and conquer cancer in modern medicine [1]. In recent years, more and more studies have introduced mathematical modeling methods into the study of tumor cell growth trends, which are mainly divided into two types: 1. an ordinary differential equation model based on fitting clinical trial data (such as the exponential model [2], logistic model [3], Gompertz model [4], and cellular automata model [5]); 2. based on the idea that the volume of tumor does not increase indefinitely in the process of tumor growth is due to the balance between the proliferation and death of cells in tumor, people began to use partial differential equations to establish mathematical models of malignant tumor growth. This research in this area can be found in literature studies [6–13]. No matter which type, there will be a common problem in the aforementioned research, that is, the solution of the mathematical model. Most of the current researchers focus on the approximate simulation of the computer numerical algorithm; however, there are some limitations such as time consuming and energy consuming and continuous quantitative display analysis cannot be carried out. If we can establish the mathematical model of tumor diffusion and calculate its growth law, it will be of great practical value for the rapid prediction and precise treatment of tumor indication. In the 19th century, the mathematician Lie firstly expounded the concept of symmetry of differential equations and gave a general integration method of equations, that is, Lie symmetry analysis [14], which is equivalent to linear and nonlinear equations, constant coefficient and variable coefficient equations, and is applicable to both ordinary and partial differential equations. In fact, Lie symmetry analysis theory has become the only universal and effective method to solve differential equations.

There is no report on using Lie symmetry analysis to study the tumor diffusion equation at home and abroad. It is a very difficult task because there are many biological control factors involved in the process of tumor growth. In this paper, a simple one-dimensional free-boundary partial differential equation system is used to describe the dynamic diffusion range of the tumor. After transformation and deduction, several sets of Lie symmetry generators of the system are given, and the exact analytical solution expressions of the system are given successfully by combining the invariant solution technique. The effects of nutrient concentration and inhibitor concentration of the boundary condition on the tumor dynamic index with multiplication time were simulated, which is meaningful for therapeutic strategies.

2. Mathematical Model of Malignant Tumor Proliferation

Considering the interaction between malignant tumor cell and the surrounding microenvironment, the tumor cell is taken as the coordinate origin, a malignant tumor is located on the surface (that is oxy plane) of a cancer cell, the spheroids of tumor cells are symmetrical and incompressible, and the drug inhibits cell growth by proportional concentration. The density of tumor cells in reproduction is p, the density of tumor cells in the dormant state is q, the density of tumor cells that have died but not yet disappeared is d, the speed of cell movement is v, the pressure between the tumor cells is π, the radius of the tumor is $R(t)$ at the time t, the space occupied by the tumor is $r < R(t)$, and the interface of the tumor is $\Gamma(t)$. According to the research ideas of Geresnpan, Adam, Chaplian, and Byren [15] and using the reaction-diffusion principle of chemical substances, the degradation of the substrate causes tumor cells to migrate through tissues and then spread to other parts, thus forming tumor metastasis. Consider the interaction among tumor cells, collagenase IV, nutritional inhibitors, proteolytic enzymes, and host tissues, as shown in Figure 1.

Combining with the law of mass conservation, ignoring the tumor cells invade normal surrounding tissues, and the vertical direction of diffusion is nonindependence, so the one-dimensional mathematical model of spatial dynamics of malignant tumors is [15]

$$\begin{aligned} u_t &= f(u) - (uc_x)_x, \\ c_t &= -g(c,p), \\ p_t &= h(u,c) - Kp, \\ f(u) &> 0, g_c(c,u) < 0, g_u(c,u) > 0. \end{aligned} \tag{1}$$

u, c, and p represent the concentration of invasive cells, extracellular matrix, and protease, f, g, and h represent the nutrient consumption function, inhibitor consumption function, and protease dependent function, and K is the protease attenuation coefficient; they can be typical selected as

$$f = \alpha u (\alpha < 0), \quad g = ue^{-c}. \tag{2}$$

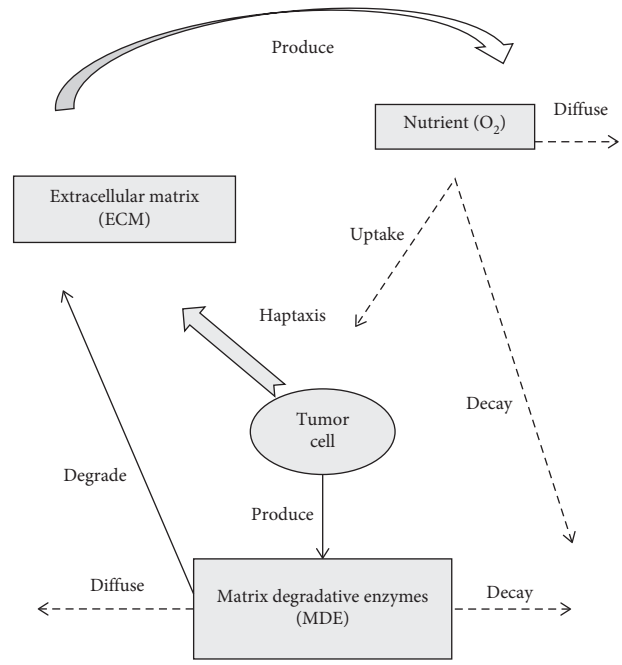

Figure 1: Interactions between the main components in the microenvironment.

Considering that the synthesis and decay time of protease are much shorter than the time of cell invasion, equation (1) can be simplified as follows:

$$\begin{aligned} u_t &= ac - (uc_x)_x, \\ c_t &= -ue^{-c}. \end{aligned} \tag{3}$$

Model (3) assumes that malignant tumors have homogeneous globular structures, that is, only living cells without dead cells in tumor and that all living cells are in a state of reproduction, which is an ideal situation.

3. Lie Symmetry of Diffusion Equations

Set independent variable as $\mathbf{x} = (t, x)$ and dependent variable $\mathbf{u} = (u, c)$, and total differential operators and one- or two-order partial derivatives are considered:

$$\begin{aligned} D_i &= \frac{\partial}{\partial x_i} + u_i^a \frac{\partial}{\partial u^\alpha} + u_{ij}^a \frac{\partial}{\partial u_j^\alpha}, \\ u_i^\alpha &= D_i(u^\alpha), u_{ij}^\alpha = D_i\left(u_j^\alpha\right) = D_i D_j(u^\alpha). \end{aligned} \tag{4}$$

Considering a finitesimal transformation group with a single parameter,

$$\begin{aligned} t^* &= t + \varepsilon\xi_1(t,x,u,c), x^* = x + \varepsilon\xi_2(t,x,u,c), \\ u^* &= u + \varepsilon\eta_1(t,x,u,c), c^* = c + \varepsilon\eta_2(t,x,u,c). \end{aligned} \tag{5}$$

According to the extension theory of Lie group, the generators of (5) and the one- or two-order extension vector fields are

$$X = \xi_i(\mathbf{x},\mathbf{u})\frac{\partial}{\partial x_i} + \eta_i(\mathbf{x},\mathbf{u})\frac{\partial}{\partial u^i}, X^{(1)}$$

$$= X + \zeta_i^{(1)w}(\mathbf{x},\mathbf{u},\partial\mathbf{u})\frac{\partial}{\partial u_i^w},$$

$$X^{(2)} = X^{(1)} + \zeta_{i_1 i_2}^{(2)v}\left(\mathbf{x},\mathbf{u},\partial\mathbf{u},\partial^2\mathbf{u}\right)\frac{\partial}{\partial u_{i_1 i_2}^v}, \tag{6}$$

$$\zeta_i^{(1)w} = D_i\zeta^w - \left(D_i\xi_j\right)u_j^w, \zeta_{i_1 i_2}^{(2)v}$$

$$= D_{i_2}\zeta_{i_1}^{(1)w} - \left(D_{i_2}\xi_j\right)u_{i_1 j}^w (i,j,w,i_1,i_2 = 1,2).$$

The invariance of equation (3) under transformation (5) can be expressed as

$$X^{(2)}\left[u_t - ac + (uc_x)_x\right] = 0,$$
$$X^{(1)}\left[c_t + ue^{-c}\right] = 0. \tag{7}$$

For solving the partial differential equation (7), it is easy to get expressions with the following coefficient functions:

$$X_1 = \frac{\partial}{\partial t},$$
$$X_2 = \frac{\partial}{\partial x}, \tag{8}$$
$$X_3 = \frac{\partial}{\partial c} + u\frac{\partial}{\partial u}.$$

By defining the commutator operation, that is, Lie bracket $[,]$ in the space of partial differential operators, which is made up of all generators of the invariant group of equation (3), the corresponding 4-dimensional Lie algebraic structure $\{X\}$ can be obtained; it is easy to know that there is a set of bases (8), which are independent and are closed to each other.

4. Invariant Solution of Diffusion Equations

If $\mathbf{u} = J(\mathbf{x})$ is an invariant solution of the partial differential equations $F^m(\mathbf{x},\mathbf{u},\partial\mathbf{u},\partial^2\mathbf{u}) = 0$, the solution is derived from point symmetry of infinitesimal generating element $X = \xi_i(\mathbf{x},\mathbf{u})(\partial/\partial x^i) + \eta_i(\mathbf{x},\mathbf{u})(\partial/\partial u^i)$ of partial differential equations if and only if satisfied $X(J) = 0$. The group invariant solution of the equation combined with the separation of variables can reduce the number of independent variables, and then converting to ordinary differential equations provides a way to obtain exact solutions of partial differential equations [16].

We mainly discuss invariant solutions of the combinatorial form of symmetric operators $X_1 + X_3$ about the Lie point transformation group (8) corresponding to diffusion equation (3) of the malignant tumor. $(X_1 + X_3)J = 0$ gives three new independent variables.

$x, \phi_1 = c - t, \phi_2 = ue^{-t}$, so we can get

$$u_t = e^t\phi_2(x),$$
$$u_x = e^t\phi_2'(x),$$
$$c_t = 1, \tag{9}$$
$$c_x = \phi_1'(x),$$
$$c_{xx} = \phi_1''(x).$$

By substituting (9) into (3), the ordinary differential with the new independent variable can be obtained:

$$\phi_1''(x) + \phi_1'^2 + (1-\alpha) = 0,$$
$$\phi_2(x) = -e^{-\phi_1(x)}. \tag{10}$$

So, we get the general solution of equation (3):

$$u(t,x) = -e^{-t}\left|A_2\cos\left(\sqrt{1-\alpha}\,(A_1 - x)\right)\right|,$$
$$c(t,x) = t + \ln\left|A_2\cos\left(\sqrt{1-\alpha}\,(A_1 - x)\right)\right| (\alpha < 0). \tag{11}$$

A_1 and A_2 are arbitrary constants.

5. Example Simulation

Set the initial and boundary conditions for diffusion equation (3) as follows:

$$u(x,0) = u_0(x),$$
$$c(x,0) = c_0(x),$$
$$(0 \le x \le R_0),$$
$$R(0) = R_0,$$
$$\frac{\partial u}{\partial x}(0,t) = 0, \tag{12}$$
$$\frac{\partial c}{\partial x}(0,t) = 0,$$
$$u(R(t),t) = \overline{u},$$
$$c(R(t),t) = \overline{c}.$$

$\overline{u}$ and $\overline{c}$ represent the tumor obtains the concentration of nutrients and inhibitory substances from the boundary.

The growth function of tumor cells is

$$S(u,c) = \lambda(u - \widetilde{u}) - \gamma c. \tag{13}$$

$\widetilde{u}$ is the critical value of nutrient concentration.

The change of tumor volume is entirely determined by the proliferation and death of tumor cells, so the tumor radius satisfies

$$\frac{\mathrm{d}R(t)}{\mathrm{d}t} = \frac{1}{R^2(t)}\int_0^{R(t)} S(u,c)x^2\mathrm{d}x. \tag{14}$$

Setting the tumor growth rate is k per unit time, in clinical application, the time required for the tumor volume radius increase for double is an important parameter in characteristics of tumor growth. T is the multiplication time, so

$$T = \frac{\ln 2}{R'(t)} R(t). \tag{15}$$

By substituting (11), (13), and (14) into (15), we can get

$$T\left(R(t), t, R_0, \overline{u}, \overline{c}, \widetilde{u}, \alpha, \lambda, \gamma\right) = \frac{\ln 2}{R'(t)} R(t)$$

$$= \frac{\ln 2}{\int_0^{R(t)} \left[\lambda\left(-e^{-t}\cos\left(\sqrt{1-\alpha}\, x\right) - \widetilde{u}\right) - \gamma\left(t + \ln\cos\left(\sqrt{1-\alpha}\, x\right)\right]x^2 dx} R^3(t) \tag{16}$$

$$u(R(t), t) = -e^{-t}\cos\left(\sqrt{1-\alpha}\, R(t)\right) = \overline{u}, c(R(t), t) = t + \ln\cos\left(\sqrt{1-\alpha}\, R(t)\right) = \overline{c}.$$

When $\alpha = -0.01$, $\overline{c} = 0$, $\widetilde{u} = 0.15$, $\lambda = \gamma = 1$, and $R_0 = 0.5$, we make nutrient concentration $\overline{u}$ take different values, we simulate the multiplication curve of (16), and we can obtain Figure 2.

As can be seen from Figure 1, the multiplication time decreases before the inflection point and increases at an increasing rate after the inflection point when the oxygen concentration is fixed. It can be explained entirely from the point of view of biological nutrition that when the tumor is full of nutrients, it is in a rapid growth stage; when the oxygen concentration decreases, the diffusion of nutrients becomes more difficult, and the tumor growth rate began to slow down; and when the tumor increases into a stable stage, oxygen is more difficult to enter, so the multiplication time tends to be infinite, the oxygen concentration is higher, the trend weakens, and at last, it degenerates into the approximate exponential form. Therefore, we can effectively treat the spread of malignant tumors by cutting off the access to nutrition and making the nutrients obtain lower than the critical concentration.

When $\alpha = -0.01$, $\overline{u} = 0.3$, $\widetilde{u} = 0.15$, $\lambda = \gamma = 1$, and $R_0 = 0.01$, we make inhibitor concentration $\overline{c}$ take different values, we simulate the multiplication curve of (16), and we can obtain Figure 3.

As can be seen from Figure 2, the tumor cells grow up gradually and eventually become dormant when there is no inhibitor concentration. Fixing the inhibitor concentration, multiplication time showed an exponential increase with the radius of the tumor, and the radius of the tumor area tends to decrease until it becomes zero eventually as the tumor cell growth is inhibited; thus, the multiplication time becomes longer until it reaches infinity. At the same radius, with the inhibitor concentration increase, the difference of growth is more obvious, and the multiplication time is greater, which is also consistent with the actual situation. Therefore, it is a therapeutic strategy that to increase the amount of inhibitory substances to inhibit the growth of malignant tumors.

In order to illustrate the correctness of the Lie symmetry method, comparing the literature [17], its results show that the growth rate of tumor cells is directly proportional to the oxygen concentration, that is, when the oxygen concentration is higher, the growth of tumor cells is faster, and when the oxygen concentration is lower, the growth of tumor cells is slower. This is consistent with the conclusion of Figure 2 by the Lie symmetry method. Similarly, comparing the literature [18], its results show that increasing of inhibitor concentration not only reduces the vessel density of tumor peripheral but also blocks the mature vessels in the tumor center, which causes the vascular network in tumor tissue to be unsmoothed, so the channels for nutrition and transport of the metabolite are destroyed. The total cell number and tumor size were significantly inhibited. This is consistent with the conclusion of Figure 3 by the Lie symmetry method.

6. Conclusion

At present, Lie symmetry analysis method is widely used in the field of mathematical and physical equations, which has achieved rich research results. The diffusion model of malignant tumor can be simplified as a free-boundary problem of one-dimensional nonlinear partial differential equations; there are many numerical approximation methods for its solution, but with the help of Lie symmetry, the four-dimensional Lie algebra of allowable Lie symmetry can be obtained, and the exact analytical solution of dynamic diffusion can be constructed by using the generalized invariant solution. From this study, we can see that there is a critical nutrient concentration in the process of malignant tumor growth. Nutrient concentration and inhibitor concentration can change the multiplication time of tumor cell volume (number). With

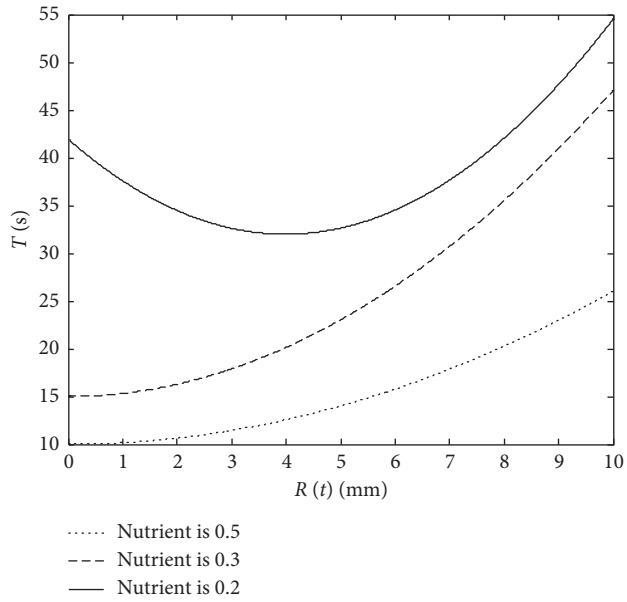

Figure 2: The trend of multiplication time T with $R(t)$ under different nutrient concentrations.

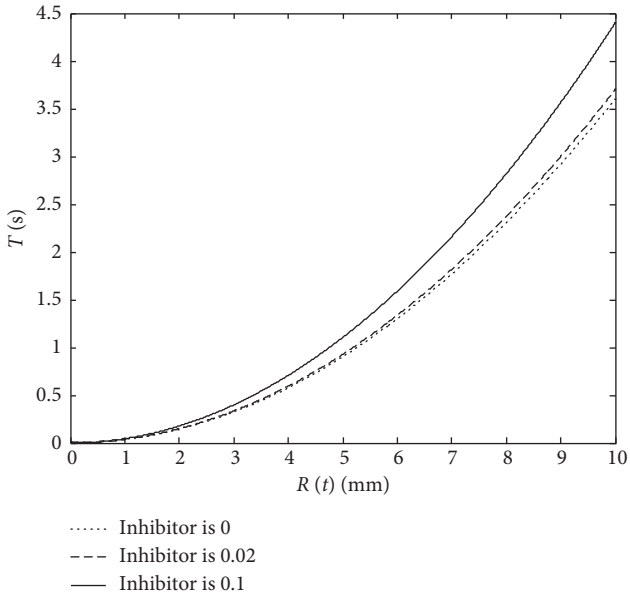

Figure 3: The trend of multiplication time T with $R(t)$ under different inhibitor concentrations.

the increase of oxygen concentration, the curve of multiplication time can be changed from U-type to approximately linear type, and with the increase of inhibitor concentration, the more obvious the difference between exponential growth curve, the lower oxygen concentration, and higher inhibitor concentration makes the multiplication time longer, so the clinical rational matching of nutrients and inhibitory substances can effectively block the spread of malignant tumors. The Lie symmetry analysis method can be further extended to more complex tumor growth and prediction therapy.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The author declares that there are no conflicts of interest regarding the publication of this paper.

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