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Numerical Simulation of Tumor Growth Based on the Free Boundary Element Discretization

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Abstract. We present an iterative method to numerically simulate the growth and shrinkage of tumor. We transform the free boundary problem describing tumor growth into the boundary integral equations which reduce the dimensionality of the problem by one. By boundary element method, we discretize the boundary integral equations by grid points on the moving boundaries of tumor. We estimate the error of the numerical integration. We design an iterative scheme and implement successfully this scheme to visually and graphically show the evolution of the interface between the tumor and the external tissue at different moments of time. In this paper, the proliferation rate μ is a function of space $\mathbf{x}$ and time t. Our numerical method professor Bei Hu proposed is novel and our numerical results are in agreement with the tumor growth in vivo.

AMS subject classifications: 35R35, 62P10, 65M38

Key words: Free boundary problem, mathematical model of tumor growth, boundary integral equations, Green functions, singular integrals.

1 Introduction

In mathematics, the free boundary problems are partial differential equations (see [1,2]) to be solved for both unknown functions and unknown domain $\Omega(t)$. Tumor growth models are typical free boundary value problems (see [3–5]). The tumor and its boundary change over time. The growth of tumor mass is governed by a balance between cell mitosis and apoptosis. Tumor grows due to reproduction of cells, or shrinks due to the lack of nutrition or cells necrosis. People pay close attention to the evolution of tumor boundary. In previous studies, although mathematical analysis of tumor problems has been done a lot of work (such as papers [6–16] etc.), there is no effective way to numerically compute the changing boundaries of tumor over time. In this article, by boundary

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element method (see [17–22]), we design an iterative algorithm to compute and visually and graphically show the changing boundaries of tumor at different moments in time. Moreover, in previous tumor mathematical models, the proliferation rate μ is always assumed to be a constant (μ describes tumor aggressiveness). Actually, μ should be a function during the growth and shrinkage of tumors. In our tumor model equations (1.1), we consider that μ is a function of space $\mathbf{x}$ and time t. Additionally, we use a simple method to deal with singularities of Green's functions in this paper. Our theoretical and numerical results will have practical value in the clinical tumor research field.

We consider the free boundary value problem modeling the growth of tumor with nonnecrotic core and no inhibitor chemical species (see [13]) as follows:

$$\begin{cases} -\Delta\sigma+\sigma=0 & \text{in } \Omega(t), \\ -\Delta\Big(p+\mu\sigma-\widetilde{\sigma}\dfrac{|\mathbf{x}|^2}{2d}\Big)=0 & \text{in } \Omega(t), \\ \sigma=1 & \text{on } \partial\Omega(t), \\ p=\kappa & \text{on } \partial\Omega(t), \\ \dfrac{\partial p}{\partial n}=-v_n & \text{on } \partial\Omega(t), \end{cases} \tag{1.1}$$

where d is the dimension, $\Omega(t)$ denotes the tumor domain at time t ($0\le t\le T$), σ denotes the concentration of nutrients, p denotes the pressure within the tumor. $\widetilde{\sigma}>0$ is a threshold concentration of nutrients and $\widetilde{\sigma}<1$. The proliferation rate μ measures the aggressiveness of the tumor and μ is a function of space $\mathbf{x}$ and time t. Furthermore, κ denotes the mean curvature, $\overrightarrow{n}$ denotes the outward normal direction, and v_n denotes the velocity of $\partial\Omega(t)$ in the outward normal direction $\overrightarrow{n}$.

The free boundary value problem (1.1) can be rewritten as

$$\begin{cases} -\Delta\sigma+\sigma=0 & \text{in } \Omega(t), \\ -\Delta P=0 & \text{in } \Omega(t), \\ \sigma=1 & \text{on } \partial\Omega(t), \\ P=\kappa+\mu-\widetilde{\sigma}\dfrac{|\mathbf{x}|^2}{2d} & \text{on } \partial\Omega(t), \\ \dfrac{\partial P}{\partial n}=-v_n+\mu\dfrac{\partial\sigma}{\partial n}-\dfrac{\widetilde{\sigma}}{2d}\dfrac{\partial|\mathbf{x}|^2}{\partial n} & \text{on } \partial\Omega(t), \end{cases} \tag{1.2}$$

where $P=p+\mu\sigma-\widetilde{\sigma}\frac{|\mathbf{x}|^2}{2d}$ and $0\le t\le T$.

The rest of the article is structured as follows. The free boundary value problem (1.1) describing tumor growth is transformed into the boundary integral equations in Section 2, which reduce the dimensionality of the problem by one. Namely, a two-dimensional domain problem can be solved via the integration on a one-dimensional boundary curve(at the expense of making the integral singular). By boundary element method, the boundary integral equations are discretized by grid points on the moving