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Phase-field model and its splitting numerical scheme for tissue growth

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ABSTRACT

We consider phase-field models and associated numerical methods for tissue growth. The model consists of the Cahn–Hilliard equation with a source term. In order to solve the equations accurately and efficiently, we propose a hybrid method based on an operator splitting method. First, we solve the contribution from the source term analytically and redistribute the increased mass around the tissue boundary position. Subsequently, we solve the Cahn–Hilliard equation using the nonlinearly gradient stable numerical scheme to make the interface transition profile smooth. We then perform various numerical experiments and find that there is a good agreement when these computational results are compared with analytic solutions.

1. Introduction

The mathematical modeling and computational simulation of tumor growth dynamics can yield important insights into tumor progression, help to explain experimental and clinical observations, and help with assessing optimal treatment strategies [28]. Much research has focused on modeling tumor growth using a diffuse interface model, in which sharp interfaces are replaced by narrow transition layers (see [7,28], and references therein). The building block in the diffuse interface model is the Cahn–Hilliard (CH) equation [5]. The CH equation exhibits useful properties, such as separating two different materials in modeling interface problems. However, it has some drawbacks in the case of modeling tissue growth. When we model tissue growth with the CH equation we add an extra source term to the equation. If the proliferation rate is large, then the volume fraction becomes greater than one, which is far from the physical quantity. We note that the tumor growth model has been studied in order to explain the complex dynamics of the behavior of tumor cells. General reviews relating to tumor growth can be found in [1,21,24]. For mass balances in cellular biological media, see [13,14], and for a summary relating to the shape of tumors, see [23]. Applications of diffuse-interface tumor growth models have recently been proposed in relation to both tumor growth [11,12] and surfaces of tumor mass [10]. The evolution of tumors has also been described using a reaction–diffusion equation in [2].

The main purpose of this paper is to present a phase-field model for application to fundamental tissue growth along with accurate and efficient numerical solutions. In comparison with conventional tumor growth models using phase-field methods [6,22,26,28,29], the proposed model admits useful features, such as keeping the minimum and maximum of the volume fraction close to zero and one, an ability to handle large values for the proliferation parameter, and yielding a

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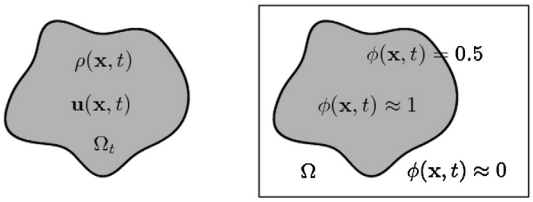

Fig. 1. Schematic of the tumor in the phase-field model. In (a) $\rho(\mathbf{x},t)$ represents the density, $\mathbf{u}(\mathbf{x},t)$ the velocity field, and Ω_t the domain of the tumor. (b) displays that $\phi(\mathbf{x},t)$ is approximately 1 on the inside and 0 on the outside of the tumor. The interface of the tumor is represented as $\phi(\mathbf{x},t) = 0.5$.

robust and accurate numerical scheme. In particular, the first feature is important from a physical point of view, because the volume fraction should not be greater than one.

The rest of the paper is organized as follows. In Section 2, we describe a mathematical model for tissue growth. In Section 3, we provide a new numerical method for the tissue growth model. We perform several numerical experiments on the effect of the proposed method in Section 4. In Section 5, we provide a summary and present our conclusions.

2. Mathematical model

We develop a simple mathematical model for describing the dynamics of early stage of tumor growth in the absence of a necrotic core. Let $\rho(\mathbf{x},t)$ be the density of the tumor and $\mathbf{u}(\mathbf{x},t)$ the velocity field in the tumor at position $\mathbf{x}$ and time t. The conservation of mass gives

$$\rho_t(\mathbf{x},t) + \nabla\cdot[\rho(\mathbf{x},t)\mathbf{u}(\mathbf{x},t)] = \lambda_p\rho(\mathbf{x},t) \text{ in } \Omega_t, \tag{1}$$

where λ_p is the proliferation rate and Ω_t is the tumor domain [3] (see Fig. 1).

Let us assume that the density in the tumor is constant, i.e., $\rho(\mathbf{x},t) \equiv \rho_0$. Then, Eq. (1) becomes

$$\nabla\cdot\mathbf{u}(\mathbf{x},t) = \lambda_p \text{ in } \Omega_t. \tag{2}$$

In order to develop a phase-field model for Eq. (1), let us introduce the phase-field function ϕ, which is the volume fraction of the tumor cell. Therefore, $\phi \approx 1$ in the tumorous phase Ω_t and $\phi \approx 0$ in the healthy tissue phase $\Omega\setminus\Omega_t$. The function also has a smooth transition between 0 and 1. We interpret the level set, $\phi = 0.5$, as the tissue interface. First, we extend the tissue domain to Ω which is time-independent and embeds Ω_t. Then, we can approximate with $\rho = \rho_0\phi$ in Ω. Plugging this into Eq. (1), we have

$$\phi_t(\mathbf{x},t) + \nabla\cdot[\phi(\mathbf{x},t)\mathbf{u}(\mathbf{x},t)] = \lambda_p\phi(\mathbf{x},t) \text{ in } \Omega.$$

Under the assumption that the density is constant, the effect of the velocity field $\mathbf{u}$ is to distribute the increased mass to the boundary of the tissue. We model this advection term with a relaxation term in the CH equation, i.e., $-M\Delta[F'(\phi(\mathbf{x},t)) - \epsilon^2\Delta\phi(\mathbf{x},t)]$, where M represents mobility, $F(\phi) = 0.25\phi^2(\phi-1)^2$, and ϵ is a small positive parameter. Therefore, the proposed model for Eq. (1) is given as

$$\phi_t(\mathbf{x},t) = M\Delta\mu(\mathbf{x},t) + \lambda_p\phi(\mathbf{x},t),\ \mathbf{x}\in\Omega,\ t>0, \tag{3}$$

$$\mu(\mathbf{x},t) = F'(\phi(\mathbf{x},t)) - \epsilon^2\Delta\phi(\mathbf{x},t), \tag{4}$$

where μ is the chemical potential and ϵ is the gradient energy coefficient related to the following total energy of the system (3)–(4) with $\lambda_p = 0$.

$$\mathcal{E} = \int_\Omega \left(F(\phi) + 0.5\epsilon^2|\nabla\phi|^2\right)\mathrm{d}\mathbf{x} \tag{5}$$

The boundary conditions are $\dfrac{\partial\phi}{\partial\mathbf{n}} = \dfrac{\partial\mu}{\partial\mathbf{n}} = 0$ on $\partial\Omega$, where $\mathbf{n}$ is the outward normal vector to the domain boundary $\partial\Omega$.

We note that if $\lambda_p = 0$, then Eqs. (3) and (4) reduce to the classical CH equation. The CH equation, a fourth-order parabolic equation was originally derived to describe the phase separation and coarsening phenomena in a melted binary alloy [4,5]. For further details on the physical, mathematical, and numerical derivations of the binary CH equation, see the review paper [19,25].

3. Numerical method

In this section, we propose an efficient and accurate numerical method, based on an operator splitting technique for solving the governing Eqs. (3) and (4).