Journal of Computational Physics 364 (2018) 73–94

Contents lists available at ScienceDirect

Journal of Computational Physics

www.elsevier.com/locate/jcp

An accurate front capturing scheme for tumor growth models with a free boundary limit

Jian-Guo Liu [a], Min Tang [b], Li Wang [c], Zhennan Zhou [d,*]

[a] Department of Mathematics and Department of Physics, Duke University, United States
[b] Department of Mathematics, Institute of Natural Sciences and MOE-LSC, Shanghai Jiao Tong University, China
[c] Department of Mathematics, Computational and Data-Enabled Science and Engineering Program, State University of New York at Buffalo, United States
[d] Beijing International Center for Mathematical Research, Peking University, China

ARTICLE INFO

Article history:
Received 29 August 2017
Received in revised form 6 March 2018
Accepted 7 March 2018
Available online 9 March 2018

Keywords:
Hele–Shaw equation
Free boundary problem
Front capturing scheme
Tumor growth model
Prediction-correction method

ABSTRACT

We consider a class of tumor growth models under the combined effects of density-dependent pressure and cell multiplication, with a free boundary model as its singular limit when the pressure-density relationship becomes highly nonlinear. In particular, the constitutive law connecting pressure p and density ρ is $p(\rho) = \frac{m}{m-1}\rho^{m-1}$, and when $m \gg 1$, the cell density ρ may evolve its support according to a pressure-driven geometric motion with sharp interface along its boundary. The nonlinearity and degeneracy in the diffusion bring great challenges in numerical simulations. Prior to the present paper, there is lack of standard mechanism to numerically capture the front propagation speed as $m \gg 1$. In this paper, we develop a numerical scheme based on a novel prediction-correction reformulation that can accurately approximate the front propagation even when the nonlinearity is extremely strong. We show that the semi-discrete scheme naturally connects to the free boundary limit equation as $m \to \infty$. With proper spatial discretization, the fully discrete scheme has improved stability, preserves positivity, and can be implemented without nonlinear solvers. Finally, extensive numerical examples in both one and two dimensions are provided to verify the claimed properties in various applications.

1. Introduction

In this paper, we are concerned with a tumor growth model for the cell density function $\rho(\mathbf{x}, t)$, whose governing equation is given by:

$$\frac{\partial}{\partial t}\rho - \nabla \cdot (\rho \nabla p(\rho)) = \rho G(c, p), \quad \mathbf{x} \in \mathbb{R}^d,\ t \geq 0, \tag{1}$$

where $c(\mathbf{x}, t)$ represents the nutrient concentration and is a uniformly bounded function; $p(\rho)$ is the pressure that depends on the cell density through a state equation. In the present paper, we consider

$$p(\rho) = \frac{m}{m-1}\rho^{m-1}, \tag{2}$$

* Corresponding author.
E-mail address: zhennan@bicmr.pku.edu.cn (Z. Zhou).

https://doi.org/10.1016/j.jcp.2018.03.013
0021-9991/

as in [25] and other possible forms can be found in [28]. The tumor cells are transported according to the Darcy's law, whose velocity is determined by the negative gradient of the pressure, and they proliferate with a growth rate that depends on both the nutrient concentration and the pressure. The growth rate $G(c, p)$ is assumed to be monotonically increasing in the c variable, monotonically decreasing in the p variable and may take negative values, i.e., $\frac{\partial}{\partial c}G(c, p) \geq 0$, $\frac{\partial}{\partial p}G(c, p) \leq 0$. We complement this system with an initial condition that satisfies

$$\rho(0, x) = \rho^{ini}(x) \geq 0, \qquad \rho^{ini} \in L^1 \cap L^\infty. \tag{3}$$

It has been proved in [25] that, under some assumptions for the initial density, when $m \to \infty$, the solution of (1) converges to the solution of a free boundary problem supported on $\Omega(t)$. The geometric motion of $\Omega(t)$ is governed by the limiting pressure p_∞. To understand this, we first derive the equation for p. Multiplying equation (1) by $p'(\rho)$, it becomes

$$\frac{\partial}{\partial t}p = \rho p'(\rho)\Delta p + |\nabla p|^2 + p'(\rho)\rho G(c, p)\,,$$

and since $p(\rho) = \frac{m}{m-1}\rho^{m-1}$, we find the equation for p that writes

$$\frac{\partial}{\partial t}p = (m-1)p\Delta p + |\nabla p|^2 + (m-1)pG(c, p)\,. \tag{4}$$

Sending $m \to \infty$ in the above equation, we formally have the following 'complementary relation':

$$p_\infty\big(\Delta p_\infty + G(c, p_\infty)\big) = 0\,. \tag{5}$$

$\Omega(t)$ is the support of p_∞ and the normal velocity of its boundary $\partial\Omega$ is given by $v = -\nabla p_\infty \cdot \hat{n}$, where $\hat{n}(x, t)$ is the unit outer normal direction on the boundary. In the limit of $m \to \infty$, the constitutive relation (2) is no longer satisfied by ρ_∞ and p_∞. Instead, if starts with a characteristic function, ρ_∞ remains a characteristic function of $\Omega(t)$ along dynamics, and p_∞ satisfies

$$p_\infty \in P_\infty(\rho) = \begin{cases} 0, & 0 \leq \rho_\infty < 1, \\ [0, \infty), & \rho_\infty = 1. \end{cases} \tag{6}$$

The limit of $m \to \infty$ connects two different kinds of descriptions of solid tumor: one describes the dynamics of the cell population density, and the other considers the 'geometric' motion of the solid tumor by free boundary problems. Similar limits have also been considered in the congested crowd transport models, or the congested aggregation models [1,4,12]. Besides, there are other types of tumor-growth models that consist of Cahn–Hilliard equations that can yield a free boundary problem in the sharp interface limit, e.g. [17,29].

In terms of numerics, there are several challenges in simulating the tumor growth models with $m > 1$. The first one is due to the degeneracy of the diffusion in (1), whose solution profile has sharp interfaces near its support and the boundaries of the support propagate with a finite speed [30]. Owing to the lack of smoothness of degenerate problems, parabolic solvers may lose the convergence order, which results in incorrect propagation speed of the sharp interfaces. Many numerical methods have been proposed for the simulations of degenerate parabolic equations, including the finite element method [2,6], finite volume scheme [5,13], finite difference method [19,22], relaxation scheme which exhibits the merit of the Jin–Xin relaxation model [18,23], discontinuous Galerkin method [32], or some approach based on perturbation and regularization [27]. However, to the best of our knowledge, no existing numerical methods have ever investigate the possibility of preserving the free boundary limit of the degenerate reaction-diffusion equation.

The second challenge lies in the nonlinear term, which becomes more severe when $m \gg 1$. The reason is that, when $m \gg 1$, numerical errors in the density ρ will be greatly magnified in the pressure p when ρ is close to 1, see Fig. 1 for a schematic plot. Note here, the pressure p still takes the form of (2). Moreover, incorrect numerical approximation of the pressure p implies incorrect support of the density ρ, which conversely results in noticeable error in the density ρ. On the other hand, if one simulates the equation of p in (4) instead, small errors in p will induce large errors in ρ when p is close to 0, as in Fig. 1. This results in noticeable errors in the support of ρ. Therefore, strong nonlinearity due to large m indeed raises great computational challenge.

In general, there are two traditional approaches to handle nonlinear terms. One is to use a fully implicit scheme and solve the resulting discrete nonlinear system by iterative methods. However, as m increases, the growing multiplicity and stiffness of the Jacobi matrix of the resulting algebraic system make the implementation of iterative methods infeasible. The other choice is to treat the nonlinear term semi-implicitly, for example, as in the authors' previous work [20]. Like most numerical schemes for porous media type equations, the method in [20] leads to satisfactory results for moderate m, but when m increases, there is a fast decrease in the size of spatial grids and time steps in order to get a consistent numerical approximation. This is because, if not doing so, either the scheme is unstable or the numerical front position deviates from its true location. Therefore, traditional ways of treating moderate nonlinearity is not enough for the strong nonlinearity here, and new methods need to be developed, which is the goal our paper.