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On a moving boundary problem associated with a mathematical model of breast cancer

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Abstract

This paper is associated with a nonlinear parabolic moving boundary problem raised from the mathematical modeling of the behavior of the breast avascular cancer tumors at their first stage. This model is a modification of the previous works. Using the weak form of the proposed problem, the uniqueness of the solution is proved. Based on the finite difference method, a variable time step approach is proposed to solve the problem, numerically. It is shown that the numerical approach preserves the positivity of the solution and is unconditionally stable. To show the robustness and ability of the numerical method, the numerical and exact solutions are discussed and compared for two examples with the exact solutions.

Keywords. Moving boundary, Breast cancer, Uniqueness, Variable time step.
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1. Introduction

Oncologic mathematics is a pivotal discipline that has been of interest to many scientists. Today solution to oncologic problems has crucial importance and a considerable amount of scientific literature has been devoted to the employment of mathematical models and approaches to predict and describe the behavior of cancer tumors and the physiologic and morphologic aspects of developments of tumors [2, 3, 16, 17]. Investigation of avascular tumors has been the main goal of much research for instance [2, 3, 6, 16]. The avascular stage which is the early stage of tumor formation happens in the absence of a vascular network. The passing from the avascular phase to vascular phase is influenced by the capability of the tumor to produce new blood vessels which ultimately enter into the tumor to obtain blood and oxygen supply and micro-circulation. According to the importance of detecting and investigating the avascular tumors to treat them, this study is devoted to a mathematical model of the initial growth stage of breast cancer known as ductal carcinoma in situ (DCIS).

Breast cancer, as the second leading cause of cancer death in women, is the subject of extensive studies in recent years [1, 4, 5, 7, 12, 13, 18–20]. Detecting the cancer at the initial growth phase and analyzing its behavior in this stage may be very helpful to treat this disease. To analyze and simulate the behavior and development of DSIS, mathematical models are very useful tools. Many studies have been conducted in the literature concerned with the mathematical modeling and investigation of the models. For instance, Franks et.al. established a mathematical model for DSIS based on the compliant basement membrane tensions, the cell movement, and the interactions between the forces caused by the proliferation of tumor cells [5]. Nicolien T. Van Ravesteyn et al. provided a comprehensive study of the existing modeling of DCIS in [17]. Xu et al. have studied a number of moving boundary models of DCIS as direct and inverse problems [18–20]. M. Garshasbi developed an iterative computational approach based on space marching and mollification methods to solve an inverse moving boundary problem concerned with the DSIS models [5].

In this paper in the wake of previous studies associated with DCIS models, we consider a modified model proposed by Xu et al. ([18, 19]) as a nonlinear moving boundary problem. In this problem, determination of the unknown

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moving boundary is one of our goals which deals with a nonlocal boundary condition. In the moving boundary problems, besides the fixed boundaries of the domain, there are boundaries across them where phase change takes place which is time-dependent and maybe not known a priori. Usually, many conditions such as thermodynamic equilibrium conditions are to be held on the moving boundaries. The moving boundary problems with unknown moving boundaries are highly nonlinear and except for some simple cases, analytical solutions do not exist for them. Because of the applications and importance of these kinds of problems, many numerical approaches have been proposed to solve them in the literature [8–11, 15, 18–20]. In this work, we consider a modified form of a one-dimensional DCIS model, as a moving boundary problem. After investigating the uniqueness of the solution of this problem, a numerical approach is developed to solve this problem. The organization of this work is as follows:

In section 2, the mathematical formulation of the growth of an avascular tumor within the breast is briefly introduced. The uniqueness of the solution of the problem is proved in section 3. In section 4, we develop a numerical method based on the finite difference approach to solve the main problem numerically and the positivity of the numerical solution is demonstrated. To show the ability of the numerical method, some test problems are considered in section 5.

2. Problem statement

In this section, we consider a moving boundary problem concerned with the avascular tumor growth within the breast duct, i.e. DCIS. At the first stage of cancer development, the tumor is noninvasive and has not extended to other parts of the breast. However, without any treatments, it spreads to the tissues surrounding the duct and becomes threatening to life. To characterize DCIS, many phenomena and assumptions may be considered and usually, the models are so complex. In this study, we focus on the mathematical model of nutrient concentration. Considering the diffusion and consumption as two pivotal processes that can control the distribution of nutrients for DCIS, we may drive the following equation for nutrient concentration (for more details regard to the DCIS models we refer the readers to [5, 18, 19] and the reference therein)

$$\frac{\partial u}{\partial t} + \nabla.(uv) = D\nabla^2 u - k_\rho(u)\rho - \alpha k_p(u)p, \tag{2.1}$$

where p, ρ, and u denote the densities of the proliferating cells, the surrounding fluid, and the nutrient, D shows the diffusion coefficient, $k_p(u)$ and $k_\rho(u)$ are proliferating and fluid rates and v is the local velocity of cells. According to the literature, one may consider the rates as the following positive functions [4, 12]

$$k_p(u) = \frac{A_p u^{m_p}}{u_1 + \alpha_p u^{m_p}},\ k_\rho(u) = \frac{A_\rho u^{m_\rho}}{u_2 + \alpha_\rho u^{m_\rho}}, \tag{2.2}$$

where $A_p,\ A_\rho,\ m_p \geq 1,\ m_\rho \geq 1,\ u_1,\ u_2,\ \alpha_p$ and α_ρ are known constants.

We consider that the local velocity of cells is zero, the tumor is spherically symmetric and its boundary changes with time as $r = s(t)$. Implying these assumptions and considering the appropriate initial and boundary conditions, we consider the problem of determination of $(u(x,t), s(t))$ from the DCIS diffusion model as follows

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} - \lambda(u,x,t)u + F(x,t),\ (x,t) \in \Omega_t = (0, s(t)] \times (0,T), \tag{2.3}$$

$$u(x,0) = f(x),\ 0 \leq x \leq s(t), \tag{2.4}$$

$$u_x(0,t) = 0,\ 0 < t < T, \tag{2.5}$$

$$u(s(t),t) = g(t),\ 0 < t < T, \tag{2.6}$$

$$\frac{ds}{dt} = \mu \int_0^{s(t)} (u(x,\tau) - u_0)d\tau,\ s(0) = s_0 > 0, \tag{2.7}$$

where $F(x,t),\ T,\ f(x), g(t), u_0, \mu$, and s_0 are known. The problem (2.3)-(2.7) has been studied in the literature for $\lambda = \lambda(t),\ \lambda = \lambda(x)$, and $\lambda = \lambda(x,t)$ as direct and inverse problems [5, 18–20]. In this study, based on the problem assumptions, we study a modify form of the one-dimensional DCIS moving boundary problem for $\lambda = \lambda(u, x, t)$. In the next section the uniqueness of solution of problem (2.3)-(2.7) is discussed.

3. Properties of solution

In this section we address some important properties of solutions of problem (2.3)-(2.7). First we rewrite the problem using $x = \xi s(t)$ as an equivalent nonlinear fixed domain initial-boundary value problem of parabolic type. Implying this new variable changes $x \in [0, s(t)]$ to $\xi \in [0, 1]$. Let

$$\begin{aligned} v(\xi, t) &= u(\xi s(t), t),\ \hat{\lambda}(v(\xi, t), \xi, t) = \lambda(u(\xi s(t), t), \xi s(t), t), \\ \hat{F}(\xi, t) &= F(\xi s(t), t),\ \hat{f}(\xi) = f(\xi s(t)). \end{aligned} \tag{3.1}$$

From now on, for simplicity let us replace ξ by x and omit the hat sing. Then problem (2.3)-(2.7) can be derived as

$$\frac{\partial v}{\partial t} = \frac{1}{s^2(t)}\frac{\partial^2 v}{\partial x^2} + \frac{x s'(t)}{s(t)}\frac{\partial v}{\partial x} - \lambda(v, x, t)v(x, t) + F(x, t),\ (x, t) \in \Omega, \tag{3.2}$$

$$v(x, 0) = f(x),\ 0 \le x \le 1, \tag{3.3}$$

$$v_x(0, t) = 0,\ 0 < t < T, \tag{3.4}$$

$$v(1, t) = g(t),\ 0 < t < T, \tag{3.5}$$

$$s(t) = s_0 e^{\mu \int_0^t \int_0^1 (v(x,\tau) - u_0) dx d\tau},\ 0 < t < T,\ s(0) = s_0, \tag{3.6}$$

where $\Omega = (0, 1) \times (0, T]$. Let make the following assumptions:

(A1) $v(x, t) \in C^{1,2}(\Omega)$, and $v(x, t) > u_0$. Then one may find a positive constant C such that $\mid u(x, t) \mid < C$.

(A2) $\lambda : C^{1,2} \times (0, 1] \times (0, T) \to \mathbb{R}$ is continuous in all arguments and is Lipschitz continuous with respect to u, with the Lipschitz constant L, i.e.

$$\parallel \lambda(u, x, t) - \lambda(v, x, t) \parallel \le L \parallel u - v \parallel . \tag{3.7}$$

To show the uniqueness of solution of problem (3.2)-(3.6), using the weak form of this problem and the following lemma may be very helpful.

Lemma 3.1. *In problem (3.2)-(3.6), we have*

(I) $0 < s_0 \le s(t) \le s_0 e^{\mu(C - u_0)t}$,

(II) $0 \le s'(t) \le \mu(C - u_0)s(t)$.

Proof. Using equations (3.6) and (2.7) and considering assumption (A1), we obtain (I) and (II). □

Suppose

$$H_0^1(\Omega) = \{\phi \in H^1(\Omega) \mid \phi(1, t) = 0\}.$$

Concern to the the inner product in the space $H^1[0, 1]$, one may conclude that for all $\phi \in H_0^1(\Omega)$, the weak form of problem (3.2)-(3.6) is

$$\langle v_t, \phi \rangle = \frac{-1}{s^2}\langle v_x, \phi_x \rangle - \frac{s'}{s}\langle v_x, x\phi \rangle + \langle \lambda v, \phi \rangle + \langle F, \phi \rangle, \tag{3.8}$$

$$v(x, 0) = f(x), \tag{3.9}$$

$$s(t) = s_0 e^{\mu \int_0^t \int_0^1 (v(x,\tau) - u_0) dx d\tau}, s(0) = s_0, \tag{3.10}$$

where $\langle ., . \rangle$ denotes the inner product.

Theorem 3.2. *The weak solution of problem (3.2)-(3.6) is unique.*

Proof. Suppose that (v^1, s_1) and (v^2, s_2) are solutions of problem (3.8)-(3.10), and $\lambda_i \equiv \lambda(v^i, x, t);\ i = 1, 2$. Then we have: for $i = 1$

$$\begin{aligned} \left\langle v_t^1, \phi \right\rangle &= \frac{-1}{s_1^2} \left\langle v_x^1, \phi_x \right\rangle - \frac{s_1'}{s_1} \left\langle v_x^1, x\phi \right\rangle + \left\langle \lambda_1 v^1, \phi \right\rangle + \left\langle F, \phi \right\rangle, && (3.11)\\ v^1(x,0) &= f(x), && (3.12)\\ s_1(t) &= s_0 e^{\mu \int_0^t \int_0^1 (v^1(x,\tau) - u_0) dx d\tau}, s_1(0) = s_0, && (3.13) \end{aligned}$$

and for $i = 2$

$$\begin{aligned} \left\langle v_t^2, \phi \right\rangle &= \frac{-1}{s_2^2} \left\langle v_x^2, \phi_x \right\rangle - \frac{s_2'}{s_2} \left\langle v_x^2, x\phi \right\rangle + \left\langle \lambda_2 v^2, \phi \right\rangle + \left\langle F, \phi \right\rangle, && (3.14)\\ v^2(x,0) &= f(x), && (3.15)\\ s_2(t) &= s_0 e^{\mu \int_0^t \int_0^1 (v^2(x,\tau) - u_0) dx d\tau}, && (3.16)\\ s_2(0) &= s_0. && (3.17) \end{aligned}$$

Let $w = v^1 - v^2, s_w = s_1 - s_2$, and $\lambda_w = \lambda_1 - \lambda_2$. Subtracting (3.14), (3.15) and (3.16) from (3.11), (3.12) and (3.13), respectively obtains

$$\begin{aligned} \left\langle w_t, \phi \right\rangle &= \frac{-1}{s_1^2} \left\langle w_x, \phi_x \right\rangle - \left(\frac{1}{s_1^2} - \frac{1}{s_2^2} \right) \left\langle v_x^2, \phi_x \right\rangle - \frac{s_1'}{s_1} \left\langle w, x\phi_x \right\rangle \\ &\quad - \left(\frac{s_1'}{s_1^2} - \frac{s_2'}{s_2^2} \right) \left\langle v^2, x\phi \right\rangle + \left\langle \lambda_1 v^1 - \lambda_2 v^2, \phi \right\rangle, && (3.18)\\ w(x,0) &= 0, && (3.19)\\ s_w(t) &= s_0 \left(e^{\mu \int_0^t \int_0^1 (v^1(x,\tau) - u_0) dx d\tau} - e^{\mu \int_0^t \int_0^1 (v^2(x,\tau) - u_0) dx d\tau} \right), && (3.20)\\ s_w(0) &= 0. && (3.21) \end{aligned}$$

In equation (3.18), if we consider $\phi = w$, then we derive

$$\begin{aligned} \frac{1}{2}\frac{d}{dt}\|w\|^2 &= \frac{-1}{s_1^2}\|w_x\|^2 - \left(\frac{1}{s_1^2} - \frac{1}{s_2^2} \right) \left\langle v_x^2, w_x \right\rangle - \frac{s_1'}{s_1} \left\langle w, xw_x \right\rangle - \left(\frac{s_1'}{s_1^2} - \frac{s_2'}{s_2^2} \right) \left\langle v^2, xw \right\rangle \\ &\quad + \left\langle \lambda_1 w, w \right\rangle + \left\langle (\lambda_1 - \lambda_2) v^2, w \right\rangle. && (3.22) \end{aligned}$$

Let us recall that according to the Young inequality, for every $\mu, \nu \in H^0(0,1)$ and $\epsilon > 0$, we have

$$\langle \mu, \nu \rangle \leq \frac{1}{2\epsilon}\|\mu\|^2 + \frac{\epsilon}{2}\|\nu\|^2. \qquad (3.23)$$

Then using the Young inequality and considering the assumption (A2) yield

$$\begin{aligned} \frac{1}{2}\frac{d}{dt}\|w\|^2 \leq\ & \frac{-1}{s_1^2}\|w_x\|^2 + \frac{\epsilon_1}{2}\|w_x\|^2 \\ & + \frac{1}{2\epsilon_1}\|v^2\|^2 \left(\frac{(s_1+s_2)^2 s_w^2}{s_1^4 s_2^4} \right) + \frac{\epsilon_2}{2}\|w_x||^2 \\ & + \frac{1}{2\epsilon_2} \left(\frac{s_1'}{s} \right)^2 \|w\|^2 + \frac{\epsilon_3}{2}\|v_x^2||^2 \\ & + \frac{1}{2\epsilon_3} \left(\frac{s_1'}{s_1} - \frac{s_2'}{s_2} \right)^2 \|w\|^2 + C_M^2\|w\|^2 \\ & + \frac{\epsilon_4}{2} L^2 \|w||^2 \|v^1||^2 + \frac{1}{2\epsilon_4}\|w\|^2, \qquad (3.24) \end{aligned}$$

where $\epsilon_i, i = 1, 2, 3, 4$ are arbitrary constants and C_M is chosen such that $|\lambda(v, x, t)| \leq C_M$. On the other hand using Lemma 3.1 we have

$$0 \leq s_1'(t) \leq \mu(C - u_0)s_1(t), \tag{3.25}$$

$$0 \leq s_2'(t) \leq \mu(C - u_0)s_2(t). \tag{3.26}$$

Subtracting (3.26) and (3.25) yields

$$0 \leq s_w' \leq \mu(C - u_0)s_w. \tag{3.27}$$

Now if we multiple both sides of inequality (3.27) by s_w, we see that

$$\frac{1}{2}\frac{d}{dt}(s_w^2) \leq \mu(C - u_0)s_w^2. \tag{3.28}$$

One can combine the estimates (3.24) and (3.28) to give

$$\begin{aligned} \frac{1}{2}\frac{d}{dt}\left(\|w\|^2 + s_w^2\right) \quad \leq \quad & \left(\frac{-1}{s_1^2} + \frac{\epsilon_1}{2} + \frac{\epsilon_2}{2}\right)\|w_x\|^2 \\ & + \left(\frac{1}{2\epsilon_2}\frac{s_1'}{s} + \frac{1}{2\epsilon_3}\left(\frac{s_1'}{s_1} - \frac{s_2'}{s_2}\right) + C_M^2 + \frac{\epsilon_4}{2}L^2\|v^1\|^2 + \frac{1}{2\epsilon_4}\right)\|w\|^2 \\ & + \left(\frac{1}{2\epsilon_1}\|v^2\|^2\left(\frac{(s_1 + s_2)^2}{s_1^4 s_2^4}\right) + \mu(C - u_0)\right)s_w^2. \end{aligned} \tag{3.29}$$

We can choose the constants $\epsilon_i;\ i = 1, 2$ such that the coefficient of $\|w_x\|^2$ in (3.29) be negative. Consequently we may conclude that there is a function $\alpha = \alpha(t) \in L^2(0, T)$ such that

$$\frac{1}{2}\frac{d}{dt}\left(\|w\|^2 + s_w^2\right) \leq \alpha(s_w^2 + \|w\|^2). \tag{3.30}$$

On the other hand, it is clear that the initial conditions for $\|w\|$ and s_w are zero. Hence implying the Gronwall inequality we see that $\|w\|^2 = 0,\ s_w^2 = 0$. □

4. A variable time step method

To solve the proposed nonlinear problem, in this section a numerical method based on the finite differences approach is established. To this end, the "$x - t$" domain is partitioned using a fixed space step Δx and variable time step Δt. According to the variable time step method, the time step Δt_n at each time level t_n is obtained such that the interface or moving boundary moves exactly Δx during the time interval $[t_n, t_{n+1}]$ [8, 9]. Hence in this approach we deal with the determination of the time step $\Delta t_n = t_{n+1} - t_n$ such that the moving boundary moves from the position $n\Delta x$ to the position $(n+1)\Delta x$. To establish the numerical approach, we focus on problem (2.3)-(2.7) and use a backward implicit finite difference approach to discretize the problem. Consider the space domain is divided into N subintervals using the step size Δx. Without losing the generality, because of considering the problem in the scaled and non-dimensional form, we suppose that $0 \leq x \leq 1$ and Ns_0 is one on the node points. Therefore using (2.3)-(2.6), we may write the problem in finite difference form as

$$\frac{u_i^{n+1} - u_i^n}{\Delta t_n} = \frac{u_{i+1}^{n+1} - 2u_i^{n+1} + u_{i-1}^{n+1}}{\Delta x^2} - \lambda_i^n u_i^{n+1} + F_i^{n+1}, \tag{4.1}$$

$$u_i^0 = f_i \equiv f(x_i),\ i = 0, 1, \cdots, Ns_0, \tag{4.2}$$

$$u_{-1}^{n+1} = u_1^{n+1}, \tag{4.3}$$

$$u_{Ns_0+n+1}^{n+1} = g_n \equiv g(t_n), \tag{4.4}$$

where $x_i = i\Delta x,\ F_i^n = F(x_i, t_n)$ and $u_i^n,\ \lambda_i^n$ denote the approximate values of $u(x_i, t_n)$ and $\lambda(u(x_i, t_n), x_i, t_{n+1})$, respectively.

We use equations (2.7) and (2.7) to determine the variable time steps. First at $t = 0$, we have

$$\mu \frac{\Delta x}{\Delta t_0} \simeq \int_0^{s_0} (u(\xi, 0) - u_0) d\xi. \tag{4.5}$$

Using (4.5) one can easily find the first time step Δt_0. At any time level, let $r_n = \frac{\Delta t_n}{\Delta x}$, then finite difference approach (4.1)-(4.4) yields the following system of equations

$$G_n U^{n+1} = d_n, \tag{4.6}$$

where

$$G_n = \begin{pmatrix} b_0 & c_0 & 0 & 0 & \dots & 0 \\ a_1 & b_1 & c_1 & 0 & \dots & 0 \\ 0 & a_2 & b_2 & c_2 & \dots & 0 \\ & & \ddots & \ddots & \ddots & \\ & & & & & \\ 0 & 0 & \dots & & a_{Ns_0+n-1} & b_{Ns_0+n-1} \end{pmatrix},$$

$$\begin{aligned} a_i &= -r_n, \ i = 0, 1, \cdots, \ Ns_0 + n - 1, \\ b_i &= 1 + 2r_n + \Delta t_n \lambda_i^n, \ i = 0, 1, \cdots, \ Ns_0 + n - 1, \\ c_0 &= -2r_n, \ c_i = -r_n, \ i = 0, 1, \cdots, \ Ns_0 + n - 1, \\ U^n &= \begin{pmatrix} u_0^{n+1} & u_1^{n+1} & \dots & u_{Ns_0+n-1}^{n+1} \end{pmatrix}^T, \end{aligned}$$

$$d_n = \begin{pmatrix} d_n^1 & d_n^2 & \dots & d_n^{Ns_0+n-2} & d_n^{Ns_0+n-1} \end{pmatrix}^T.$$

$$\begin{aligned} d_n^1 &= u_0^n + \Delta t_n F_0^{n+1}, \\ d_n^k &= u_k^n + \Delta t_n F_k^{n+1}; k = 1, 2, \dots, Ns_0 + n - 2, \\ d_{Ns_0+n-1}^n &= u_{Ns_0+n-1}^n + \Delta t_n F_{Ns_0+n-1}^{n+1} + r_n g_{n+1}. \end{aligned}$$

Solving linear system (4.6) and using (2.7) we have

$$\begin{aligned} \frac{\Delta x}{\Delta t_n} &\simeq \frac{1}{\mu} \int_0^{s_0+n\Delta x} (u(\xi, t_n) - u_0) d\xi \\ &\simeq \frac{\Delta x}{2\mu} \left((u_0^n - u_0) + (u_{Ns_0+n}^n - u_0) + 2 \sum_{j=1}^{Ns0+n-1} (u_j^n - u_0) \right). \end{aligned}$$

Therefore, we may find Δt_n as

$$\Delta t_n = \frac{2\mu}{(u_0^n - u_0) + (u_{Ns_0+n}^n - u_0) + 2 \sum_{j=1}^{Ns0+n-1} (u_j^n - u_0)}. \tag{4.7}$$

Theorem 4.1. *If $1 + \lambda_i^n \Delta t_n > 0$; $i = 0, 1, \cdots, Ns_0 + n$, and $F_i^n > 0$; $i = 0, 1, \cdots, Ns_0 + n$, then finite difference method (4.2)-(4.7), preserves the positivity of solution of problem (2.3)- (2.7).*

Proof. At each time level, the approximate solution U^n is obtained by solving linear system (4.6). It is clear that considering the positivity of $1 + \lambda_i^n \Delta t_n$; $i = 0, 1, Ns_0 + n$ yields that G_n is a is strictly diagonally dominant tridiagonal matrix. In addition in $G_n = (\gamma_{m,p})_{(Ns_0+n)\times(Ns_0+n)}$, we find that $\gamma_{m,m} > 0$; $m = 1, 2, \cdots, Ns_0 + n$, and $\gamma_{m,p} \leq 0$; $m \neq p$. Hence one can easily see that G_n is a M-matrix too. Therefor G_n is nonsingular and the elements of G_n^{-1} are positive [14]. Considering the assumptions of this statement, we find that the elements of $U^n = G_n^{-1} d_n$ are positive. ∎

Theorem 4.2. *Under assumptions of Theorem 4.1, the solution of finite difference method (4.2)-(4.7), is unconditionally stable.*

Proof. To investigate the stability of the proposed finite difference approach, considering a separated solution $u_i^n = \theta_n e^{j\beta i\Delta x}$ and substituting it in (4.1), yield

$$\gamma_{i,i-1}\theta_{n+1}e^{j\beta(i-1)\Delta x} + \gamma_{i,i}\theta_{n+1}e^{j\beta i\Delta x} + \gamma_{i,i+1}\theta_{n+1}e^{j\beta(i+1)\Delta x} = d_{ni}, \tag{4.8}$$

where d_{ni} is the elements of right hand side vector d_n in (4.6), $j = \sqrt{-1}$ and $\beta \in [0, \pi]$ shows the real spatial wave number. Note that to analyze the stability of the method, we only need consider $u_i^n = \theta_n e^{j\beta i\Delta x}$ instead of d_n^i in (4.8). Thus we obtain

$$\theta_{n+1} = \frac{\theta_n}{\gamma_{i,i-1}e^{-j\beta\Delta x} + \gamma_{i,i} + \gamma_{i,i+1}e^{j\beta\Delta x}}. \tag{4.9}$$

Now if we consider (4.8) as $\theta_{n+1} = \eta\theta_n$, then the method is stable if $\mid \eta \mid < 1$, that is

$$\mid \frac{1}{\gamma_{i,i-1}e^{-j\beta\Delta x} + \gamma_{i,i} + \gamma_{i,i+1}e^{j\beta\Delta x}} \mid < 1. \tag{4.10}$$

We claim that this inequality is satisfied for each $n = 1, 2, \cdots, N - Ns_0$ and $i = 1, 2, \cdots, Ns_0 + n$. To prove this claim first let $i = 1$, then we have

$$\begin{aligned} \mid \frac{1}{\eta} \mid^2 &= \mid b_0 + c_0 e^{j\beta\Delta x} \mid^2 \\ &= b_0^2 + c_0^2 + 2b_0c_0\cos(\beta\Delta x) \geq (b_0 - c_0)^2 \\ &\geq (b_0 - c_0)^2 = (1 + 4r_n + \Delta t_n\lambda_i^n)^2 > 1. \end{aligned} \tag{4.11}$$

This show for $i = 1$, our claim is satisfied. For $i = 2, \cdots, Ns_0 + n - 2$, we have $c_i = a_i$ and can obtain

$$\begin{aligned} \mid \frac{1}{\eta} \mid^2 &= \mid a_i e^{-j\beta\Delta x} + b_i + c_i e^{j\beta\Delta x} \mid^2 = \mid a_i(e^{-j\beta\Delta x} + e^{j\beta\Delta x}) + b_i \mid^2 \\ &= (b_0 + 2c_0\cos(\beta\Delta x))^2 \geq (1 + \Delta t_n\lambda_i^n)^2 > 1. \end{aligned}$$

Similar to $i = 1$, one may conclude that for $i = Ns_0 + n - 1$, the clam is true and this complete the proof of this statement. □

5. Numerical experiments

In this section to show the reliability and robustness of our proposed numerical approach, we implement the proposed numerical method for a test problem. The exact solution of the test problem is used as a criteria to evaluate the approximate solution. We use MATLAB R2014a software to implement the numerical procedure. Following l_2-error norm is used to evaluate the accuracy of the numerical results

$$E = \frac{\left[(1/(N - Ns_0 + 1)(Ns_0 + 1))\Sigma_{j=0}^{N-Ns_0}\Sigma_{i=0}^{Ns_0+j} \mid u(i\Delta x, t_j + \Delta t_j) - u_i^j \mid^2\right]^{1/2}}{\left[(1/(N - Ns_0 + 1)(Ns_0 + 1))\Sigma_{j=0}^{N-Ns_0}\ \Sigma_{i=0}^{Ns_0+j} \mid v(ih, jl) \mid^2\right]^{1/2}}. \tag{5.1}$$

In addition, we use the following formula to compute the rate of convergency (P)

$$P = \frac{ln(E_k/E_l)}{ln(\Delta x_k/\Delta x_l)}. \tag{5.2}$$

TABLE 1. The relative l_2 error norms at iteration $n = 10$ for Example 5.1.

Δx	$\frac{1}{20}$	$\frac{1}{40}$	$\frac{1}{80}$	$\frac{1}{160}$	$\frac{1}{320}$	$\frac{1}{640}$	$\frac{1}{1280}$	$\frac{1}{2560}$
l_2-error	0.36832	0.08423	0.05147	0.04231	0.01903	0.00901	0.00498	0.00312
P	–	2.12899	1.91514	1.84231	1.76231	1.71324	1.68376	1.62567

Example 5.1. In the problem (2.3)-(2.7) suppose

$$\begin{aligned} F(x,t) &= e^{2t}\cos x + e^{2t}\cos x \sin(e^{2t}\cos x) \\ f(x) &= \cos x,\ \lambda(u,x,t) = \sin(u),\ g(t) = e^{2t}\cos(2arccot(e^{3.4949-\frac{e^{2t}}{2}})) \\ s_0 &= 0.1,\ u_0 = 0,\ \mu = 1. \end{aligned}$$

One may find that the exact solution of this problem is

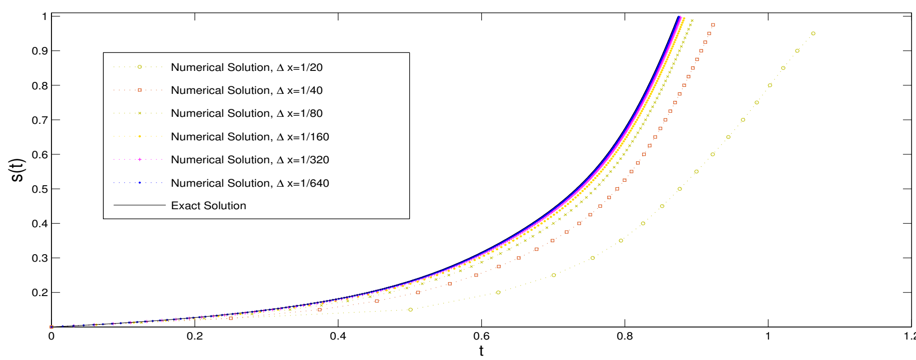

FIGURE 1. The exact and approximate moving boundary function $s(t)$ with respect to different values of Δx for Example 5.1.

$$u(x,t) = e^{2t}\cos x,\ \ s(t) = 2arccot(e^{3.4949-\frac{e^{2t}}{2}}). \tag{5.3}$$

Table 1 shows the relative l_2 error norms between the numerical and exact solutions when the space mesh steps varies from $\Delta x = \frac{1}{20}$ to $\Delta x = \frac{1}{2560}$. This table shows that decreasing Δx, increases the accuracy of the numerical results.

In Figure 1, the exact and approximate moving boundary functions $s(t)$ are shown for $\Delta x = \frac{1}{40}, \frac{1}{80}, \frac{1}{160}, \frac{1}{320}, \frac{1}{640}$. The numerical results are in good agreement with the exact solution when r Δx considered appropriable small. Some computed time mesh-nodes for $\Delta x = \frac{1}{600}$ and the values of u at $x = \frac{1}{30}$ are reported in Table 2.

TABLE 2. Computed time nodes when $\Delta x = \frac{1}{600}$, and the exact and numerical solutions for u at $x = \frac{1}{30}$ for Example 5.1.

t	0.12648	0.22507	0.29852	0.35586	0.40204	0.44017	0.47236	0.50011
u_exact	1.28355	1.56331	1.81068	2.03072	2.22722	2.40368	2.56352	2.70981
u_appr.	1.27200	1.55141	1.78917	1.99915	2.22383	2.41721	2.65609	2.81184

At $x = s_0$, we plot the numerical and exact solutions for $u(x,t)$ in Figure 4.

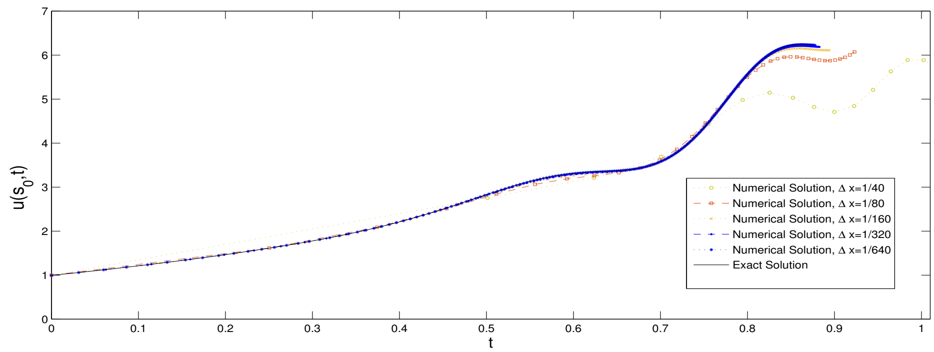

FIGURE 2. The exact and approximate solutions for $u(s_0, t)$, with respect to different values of Δx for Example 5.2.

TABLE 3. The relative l_2 error norms at iteration $n = 10$ for Example 5.2.

Δx	$\frac{1}{20}$	$\frac{1}{40}$	$\frac{1}{80}$	$\frac{1}{160}$	$\frac{1}{320}$	$\frac{1}{640}$	$\frac{1}{1280}$	$\frac{1}{2560}$
l_2-error	0.13052	0.01683	0.00367	0.00112	0.00043	0.00018	0.00008	0.00004
P	–	2.9566	2.5899	2.28814	2.06137	1.90037	1.77863	1.66739

Example 5.2. As the second test problem, let suppose

$$\begin{aligned} F(x,t) &= -\frac{1}{2}e^{\frac{t}{2}}\cosh x + \frac{e^t\cosh^3 x}{1+e^{\frac{3t}{2}}\cosh^2 x}, \\ f(x) &= \cosh x,\ \lambda(u,x,t) = \frac{u^2}{1+u^2},\ g(t) = e^{\frac{t}{2}}\cosh(2arccoth(e^{4.99657-2e^{\frac{t}{2}}})), \\ s_0 &= 0.1,\ u_0 = 0,\ \mu = 1. \end{aligned}$$

The exact solution of problem (2.3)-(2.7) with the above assumptions is

$$u(x,t) = e^{\frac{t}{2}}\cosh x,\ s(t) = 2arccoth(e^{4.99657-2e^{\frac{t}{2}}}). \tag{5.4}$$

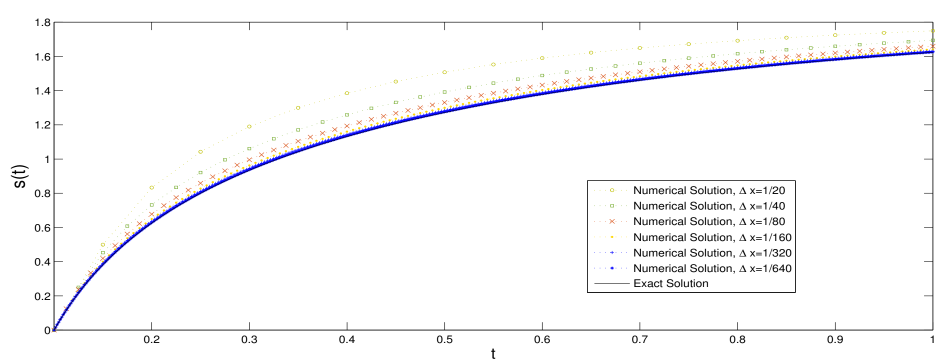

FIGURE 3. The exact and approximate moving boundary function $s(t)$ with respect to different values of Δx for Example 5.2.

The relative l_2 error norms between the numerical and exact solutions for $\Delta x = \frac{1}{20}, ..., \Delta x = \frac{1}{2560}$ are shown in Table 3. It is clear that the accuracy of the numerical results is increased when we decrease Δx.

In Figure 3, we demonstrate the plot of exact and approximate moving boundary functions $s(t)$, for $\Delta x = \frac{1}{40}, \frac{1}{80}, \frac{1}{160}, \frac{1}{320}, \frac{1}{640}$. We see that the numerical results are in good agreement with the exact solution for small Δx. For $\Delta x = \frac{1}{600}$, and $x = \frac{1}{30}$, some computed time mesh-nodes and the values of u at these points are considered in Table 4.

TABLE 4. Computed time nodes when $\Delta x = \frac{1}{600}$, and the exact and numerical solutions for u at $x = \frac{1}{30}$ for Example 5.2.

t	0.03435	0.07053	0.10480	0.13733	0.16827	0.19775	0.225898	0.25280
u_exact	1.01751	1.03608	1.05399	1.07127	1.08797	1.10413	1.11978	1.13494
u_appr.	1.01755	1.03614	1.05404	1.07133	1.08803	1.10420	1.11985	1.13502

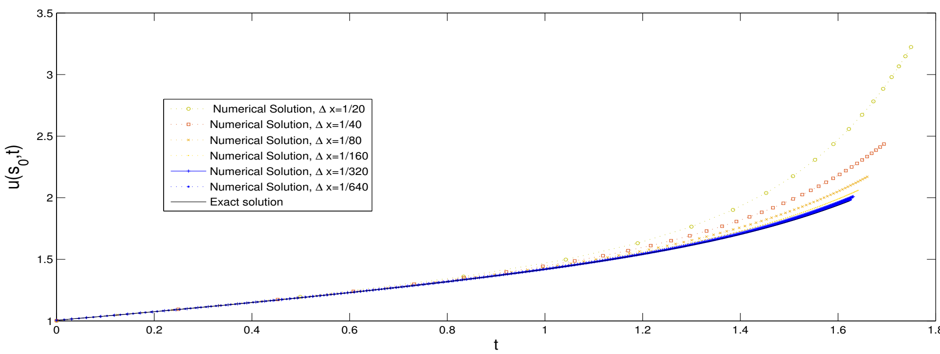

FIGURE 4. The exact and approximate solutions for $u(s_0, t)$, with respect to different values of Δx for Example 5.2.

The plot of numerical and exact solutions for $u(x, t)$ at $x = s_0$, is shown in Figure 4.

6. Conclusion

This paper concerns a mathematical model of diffusion of breast cancer at the first stage named DCIS, as a nonlinear moving boundary problem. For the proposed moving boundary problem, the uniqueness of the solution is proved. A numerical method based on a variable time step finite difference approach is developed to solve the problem. It is shown that the numerical method preserves the positivity of the solution and is unconditionally stable. For two test problems, the numerical results are shown which show the numerical results are in good agreement with the exact solutions.

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