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MATHEMATICAL AND NUMERICAL ANALYSIS OF AN ACID-MEDIATED CANCER INVASION MODEL WITH NONLINEAR DIFFUSION*

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Abstract. In this paper, we study the existence of weak solutions of the nonlinear cancer invasion parabolic system with density-dependent diffusion operators. To establish the existence result, we use regularization, the Faedo-Galerkin approximation method, some a priori estimates, and compactness arguments. Furthermore in this paper, we present results of numerical simulations for the considered invasion system with various nonlinear density-dependent diffusion operators. A standard Galerkin finite element method with the backward Euler algorithm in time is used as a numerical tool to discretize the given cancer invasion parabolic system. The theoretical results are validated by numerical examples.

Key words. cancer invasion, density-dependent diffusion, Faedo-Galerkin approximation, finite element method

AMS subject classifications. 35D30, 65M60, 35K57

1. Introduction. Mathematical models of tumor invasion towards healthy cells can be modelled either using a discrete cell-based approach that focuses on individual cell behavior [1] or by using a continuum approach [2] that deals with the evolution of cancer cell densities. Continuum-based cancer models are helpful to clinically identify a significant size of a tumor with the current imaging techniques. Therefore, for a better understanding of the continuum tumor growth, mathematical models may eventually open the door for successful cancer treatments, as well as the development of new drugs and therapies of cancer research. In the field of mathematical modelling in cancer biology, a lot of research has focused on cancer invasion models, which have been used to describe the development of the tumor, the interaction of the tumor with the normal cells, the taxis effect of cancer cells, and the production of H^+ ions by the tumor; see, for example, [1, 2, 15, 20, 21, 23, 33, 34, 49, 50].

Tumor cells expressing the glycolytic phenotype, which results in increased acid production and the diffusion of that acid into the surrounding healthy tissue, create the environment in which tumor cells can survive and proliferate, whereas the healthy cells are unable to survive. This idea is known as acid-mediated tumor invasion and was first modelled by Gatenby and Gawlinski in [23] using reaction-diffusion systems. Furthermore, the acid-mediated cancer invasion is accepted by many researchers, and many mathematical models have been developed in the literature to explore the relationships between tumor invasion, tissue acidity, and energy requirements; see [27, 31, 32, 33, 34, 49] and also the references therein. An overview of the development of one such model and related topics can be found in the survey articles [3, 38].

The description of the interaction of cancer cells and healthy tissue is incorporated in the form of coupled parabolic partial differential equations, and the model is called cancer invasion parabolic system. The unknown quantities of the cancer invasion reaction-diffusion system are the density of cancer cells $u(x,t)$, the density of healthy cells $v(x,t)$, and the concentration of the extracellular lactic acid $w(x,t)$ in the excess of normal tissue acid concentrations. Thus, the mathematical model of the cancer cells' interaction with healthy cells is given by the

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nonlinear parabolic system [34]:

$$
\begin{aligned}
&u_t - \mathrm{div}(D_1(u)\nabla u) = \rho_1 u\left(1 - \frac{u}{k_1} - \frac{v}{k_2}\right) - \delta_1 uw, && (x,t) \in Q_T,\\
&v_t = \rho_2 v\left(1 - \frac{u}{k_1} - \frac{v}{k_2}\right) - \delta_2 vw, && (x,t) \in Q_T,\\
&w_t - \mathrm{div}(D_2(w)\nabla w) = \rho_3 u\left(1 - \frac{w}{k_3}\right) - \delta_3 w, && (x,t) \in Q_T,\\
&u(x,t) = w(x,t) = 0, && (x,t) \in \Sigma_T,\\
&u(x,0) = u_0(x), v(x,0) = v_0(x), w(x,0) = w_0(x), && x \in \Omega,
\end{aligned}
\tag{1.1}
$$

where $Q_T = \Omega \times (0,T)$, $\Sigma_T = \partial\Omega \times (0,T)$, and $T > 0$ is the final time. Here, Ω is a bounded domain in $\mathbb{R}^N$ with smooth boundary $\partial\Omega$. On the other hand, $D_1(u)$ and $D_2(w)$ represent the density-dependent diffusion coefficients of the cancer density (u) and the acid concentration (w), respectively. Further, ρ_1 and ρ_2, respectively, represent the cancer cells' and healthy cells' proliferation rates, and ρ_3 denotes the rate of production of excess acid by tumor cells. Moreover, k_1, k_2, and k_3 denote the carrying capacities of the cancer cells, the healthy tissues, and the acid concentrations, respectively. The constants δ_1 represents the rate of acid-mediated tumor cells death, δ_2 represents the rate of acid-mediated healthy cells death, and δ_3 represents the rate of clearance of excess acid by combined buffering and vascular evacuation. The homogeneous Dirichlet boundary condition means that the model (1.1) is self-contained and has no population on the boundary $\partial\Omega$. The functions $u_0(x)$, $v_0(x)$, and $w_0(x)$ are the initial densities of u, v, and the concentration w, respectively.

Recently, much research has focused on the existence of solutions of biological models; see, for example, [4, 5, 7, 9, 39, 40, 41, 42, 43, 44]. The key areas of the study presented in this paper are the existence of weak solutions and the numerical analysis of nonlinear density-dependent diffusion cancer invasion models. Before discussing our main results, it is noteworthy to discuss the literature related to this work. Walker and Webb proved the existence of unique global classical solutions for a system of nonlinear partial differential equations in a cancer invasion model using maximal regularity results and some a priori estimates in [57]. Rodrigo considered a nonlinear system of differential equations arising in tumor invasion and proved local existence and uniqueness of solutions using the Schauder fixed point theorem in [36]. Szymanska et al. considered a system of reaction-diffusion-taxis partial differential equations to represent the invasion of cancer cells and subsequently proved global existence of solutions in [50]. Furthermore, they also provided numerical simulation results for their model to show the effect of the nonlocal terms in [50]. Tao and Wang considered a mathematical model of cancer invasion of tissue in [54], which incorporates the interaction of cancer cells with an extra cellular matrix, and they studied global existence of solutions in two- and three-dimensional domains. Global existence of a unique classical solution to the chemotaxis-haptotaxis model of cancer invasion of tissue is proved in [52]. A free boundary problem modeling the cell cycle and cell movement in multi-cellular tumor spheroids is considered, and the existence of solutions is studied in [51]. Kano and Ito [29] considered a mathematical cancer invasion model with some constraints and established global existence of solutions using the Schauder fixed point theorem.

Recently, Graham and Ayati considered a mathematical model for the collective cell motility using a nonlinear diffusion term that is able to capture in a unified way directed and undirected collective cell motility in [25]. Further, by using numerical simulations of a nonlinear diffusion model, they demonstrated a mechanism that accounts for the difference in the motility properties of the cells. In the previous mentioned papers, the diffusion coefficients of the unknown functions are considered constant or a function of the space variables. However, diffusion functions of cancer invasion models need not always be constant. It is well understood from the literature that a density-dependent nonlinear diffusion of the unknown is more realistic than a constant diffusion coefficient for tumor invasion models; see, for example, [25, 46]. Studies of the existence of solutions of tumor invasion models with nonlinear diffusion models are considered in only few papers in the literature. In particular, Ito et al. established local existence and uniqueness of solutions of approximate systems of 1D tumor invasion models with nonlinear diffusion in [28]. Tao and Winkler studied the global existence of solutions for a chemotaxis-haptotaxis nonlinear diffusion model using the Schauder fixed point theorem in [55]. Tao and Cui considered a nonlinear diffusion model consisting of three reaction-diffusion-taxis partial differential equations describing interactions between cancer cells, matrix degrading enzymes, and the host tissue, and they established existence of solutions using a fixed point argument in [53]. In [35], a mathematical model focusing on the effect of HSPs on the tumor cell migration was proposed, and the local existence of a unique positive weak solution was obtained using an iterative procedure.

Subsequently, a number of numerical methods were proposed in the literature for the computations of cancer invasion and the related continuum mathematical models. The finite difference method [12, 13], the finite volume method [30], and the method of lines [24] are the most commonly used methods in the literature for cancer migration models. Zheng et al. [58] and Peterson et al. [37] proposed adaptive finite element methods in two-dimensional (2D) domains for vascularized tumor models to simulate the angiogenesis process. Further, discontinuous Galerkin finite element methods were successfully applied in [19] for haptotaxis-chemotaxis problems in 2D domains. To study tumor growth based on the continuum theory of mixtures, a 2D mixed finite element method was proposed in [16]. Recently, Vilanova et al. [56] performed numerical simulations for discrete/continuum tumor angiogenesis models using the finite element method with a growth of capillaries in 2D spatial domains. An implicit level-set finite element numerical scheme for reaction-diffusion-advection equations related to tumor invasion models on an evolving in-time-hypersurface for two-dimensional domains was proposed and studied in [45]. A positivity-preserving finite element method was proposed and studied for a related chemotaxis-type problem (not for cancer invasion models) in [47, 48] for both two- and three-dimensional spatial domains.

As we have seen, several studies of theoretical and numerical techniques for cancer invasion and metastasis models incorporate linear diffusion. Many of these papers examine the spread of cancer cells using a system of partial differential equations, where the cancer cell migration is modelled by linear random motility. In contrast to the above mentioned papers, literature concerning the existence of solutions and their numerical studies for tumor invasion models with nonlinear diffusion operators is rather limited. As far as the authors are aware, there is no paper available in the literature related to the study of existence and uniqueness of weak solutions of the cancer invasion model (1.1) with nonlinear density-dependent diffusion. Therefore, in this work, we have made an attempt to study the existence of weak solutions and a priori error estimates for the proposed finite element method of the tumor invasion model with nonlinear diffusion operators.

To reduce the number of parameters in the given system (1.1), we use the following dimensionless form. Let $L = 0.1\,\text{cm}$ and $\tau = \frac{L^2}{D}$ (where $D \simeq 10^{-6}\text{cm}^2\ \text{s}^{-1}$) be the characteristic length and time scales, respectively. Using these characteristic and reference values, we define the dimensionless variables as

$$\tilde{u} = \frac{u}{k_1}, \qquad \tilde{v} = \frac{v}{k_2}, \qquad \tilde{w} = \frac{w}{k_3}, \qquad \tilde{x} = \frac{x}{L}, \qquad \tilde{t} = \frac{t}{\tau}.$$

Employing these dimensionless variables in the system (1.1) and omitting the tilde afterwards, the dimensionless form of equations (1.1) in $\Omega \times (0, I)$ becomes

$$
\begin{aligned}
&u_t - \operatorname{div}(d_1(u)\nabla u) = \lambda u(1-u-v) - \chi uw, && (x,t) \in Q_T,\\
&v_t = \rho v(1-u-v) - \eta vw, && (x,t) \in Q_T,\\
&w_t - \operatorname{div}(d_2(w)\nabla w) = \alpha u(1-w) - \beta w, && (x,t) \in Q_T,
\end{aligned} \tag{1.2}
$$

where

$$
\begin{aligned}
d_1(u) &= \frac{\tau D_1(u)}{L^2}, \qquad d_2(w) = \frac{\tau D_2(w)}{L^2}, \qquad \lambda = \tau\rho_1, \qquad \chi = \tau k_3 \delta_1,\\
\eta &= \tau k_3 \delta_2, \qquad \alpha = \tau \rho_3 \frac{k_1}{k_2}, \qquad \beta = \tau\delta_3, \qquad \rho = \rho_2 \tau
\end{aligned}
$$

are the dimensionless quantities. Without loss of generality, in this work we assume that the dimensionless quantities $\lambda, \chi, \eta, \alpha, \beta$, and ρ all are positive constants. This assumption helps us to prove the existence of weak solutions (u, v, w) of the system. Moreover, we define the nonlinear terms of the cancer invasion system as

$$
\begin{aligned}
f(u,v,w) &:= \lambda u(u+v) + \chi uw,\\
g(u,v,w) &:= \rho v(u+v) + \eta vw,\\
h(u,w) &:= \alpha uw + \beta w,
\end{aligned}
$$

and for some technical reasons, we extend the functions as follows so that they are measurable on Q_T and continuous with respect to the solutions u, v, and w:

$$
f(u,v,w) = \begin{cases} f(0,v,w) & \text{if } v \geq 0 \text{ and } w \geq 0,\\ f(u,0,w) & \text{if } u \geq 0 \text{ and } w \geq 0,\\ f(u,v,0) & \text{if } u \geq 0 \text{ and } v \geq 0, \end{cases} \tag{1.3}
$$

$$
g(u,v,w) = \begin{cases} g(0,v,w) & \text{if } v \geq 0 \text{ and } w \geq 0,\\ g(u,0,w) & \text{if } u \geq 0 \text{ and } w \geq 0,\\ g(u,v,0) & \text{if } u \geq 0 \text{ and } v \geq 0, \end{cases} \tag{1.4}
$$

$$
h(u,w) = \begin{cases} h(0,w) & \text{if } w \geq 0,\\ h(u,0) & \text{if } u \geq 0. \end{cases} \tag{1.5}
$$

Furthermore, we assume the following hypotheses to prove the mentioned results for the weak solutions of the given reaction-diffusion system (1.1). The Caratheodory functions $d_i(s)\zeta$, $i = 1, 2$, are continuous functions with respect to s and ζ such that

- (H_1) $d_i(s)\zeta \cdot \zeta \geq \psi_i |\zeta|^2, \psi_i > 0, i = 1, 2$, for all $s \in \mathbb{R}, \zeta \in \mathbb{R}^N$.
- (H_2) For any $k \geq 0$ there exists a constant $c_k > 0$ and a function $A_{i,k}(x,t) \in L^2(Q_T)$, $i = 1, 2$, such that $|d_i(s)\zeta| \leq A_{i,k}(x,t) + c_k|\zeta|$ for almost every x in Ω and for all $s \in \mathbb{R}$ such that $|s| \leq k$.
- (H_3) $[d_i(s)\zeta - d_i(s)\zeta'] \, [\zeta - \zeta'] \geq 0, i = 1, 2$.
- (H_4) $|d_i'(s)| \leq B, B > 0, i = 1, 2$, for all $s \in \mathbb{R}$.

These assumptions are assumed to hold for almost every (x,t) in Q_T, for every s in $\mathbb{R}$, and for every ζ, ζ' in $\mathbb{R}^N$, $\zeta \neq \zeta'$. For more details regarding these hypotheses, one can consult [10, 11] and also the references therein. Throughout the manuscript, C denotes a generic positive constant that may change from line to line.

We establish the existence and uniqueness of weak solutions for the system (1.1) under the hypotheses (H_1)–(H_3). The existence of weak solutions of the given parabolic system is established by means of regularization, the Faedo-Galerkin approximation method, some a priori estimates, and compactness arguments. Then, we implement the Galerkin finite element method for the tumor model and prove second-order convergence of the above-mentioned numerical method using error estimates and computational results. We would like to mention that the numerical treatment of the system (1.2) is challenging due to the highly nonlinear terms and the heterogeneous spatio-temporal dynamics of the model.

The paper is organized as follows. In Section 2, we prove the existence of weak solutions of the given dimensionless parabolic system (1.2) using the Faedo-Galerkin approximation method. Furthermore, the variational formulation of the model, the finite element discretization, the solution procedure for the nonlinear system, and the a priori error estimates for nonlinear diffusion are presented in Section 3.

2. Solvability of the cancer invasion system. This section is devoted to the study of the existence of weak solutions of the given parabolic system (1.2). Here, first we provide the definition of weak solutions, and then we use the Faedo-Galerkin approximation method to prove the existence of weak solutions of the approximate problem. Then, a priori estimates and compactness arguments help us to establish global existence of weak solutions of the given system (1.2).

DEFINITION 2.1. *A weak solution of the cancer invasion system* (1.2) *is a triple* (u, v, w) *of non-negative functions in the function spaces*

$$
\begin{aligned}
&u, w \in L^\infty(Q_T) \cap L^2(0, T; H_0^1(\Omega)) \cap C([0, T]; L^2(\Omega)),\\
&v \in C([0, T]; L^2(\Omega)),\\
&d_1(u), d_2(w) \in L^2(0, T; H_0^1(\Omega)),\\
&u_t, w_t \in L^2(0, T; H^{-1}(\Omega)),
\end{aligned}
$$

which satisfy the weak formulation

$$
\begin{aligned}
&-\int_0^T \langle u, \phi_{1t}\rangle\, dt + \int_{Q_T} d_1(u)\nabla u \nabla \phi_1 \, dxdt + \int_{Q_T} f(u, v, w)\phi_1 \, dxdt\\
&\qquad\qquad = \int_{Q_T} \lambda u \phi_1 dxdt + \int_\Omega u_0(x)\phi_1(x, 0)dx,\\
&-\int_0^T \langle v, \phi_{2t}\rangle\, dt + \int_{Q_T} g(u, v, w)\phi_2 \, dxdt\\
&\qquad\qquad = \int_{Q_T} \rho v \phi_2 dxdt + \int_\Omega v_0(x)\phi_2(x, 0)dx,\\
&-\int_0^T \langle w, \phi_{3t}\rangle\, dt + \int_{Q_T} d_2(w)\nabla w \nabla \phi_3 \, dxdt + \int_{Q_T} h(u, w)\phi_3 \, dxdt\\
&\qquad\qquad = \int_{Q_T} \alpha u \phi_3 dxdt + \int_\Omega w_0(x)\phi_3(x, 0)dx,
\end{aligned}
\tag{2.1}
$$

for all $\phi_1, \phi_3 \in L^2(0, T; H_0^1(\Omega))$ *and* $\phi_2 \in C([0, T]; L^2(\Omega))$, *with* $\phi_i(\cdot, T) = 0$, $i = 1, 2, 3$. *Here,* $\langle \cdot, \cdot \rangle$ *denotes the duality pair between* $H_0^1(\Omega)$ *and* $H^{-1}(\Omega)$.

THEOREM 2.1. *Under the hypotheses* (H_1)–(H_3) *and assuming that the initial conditions satisfy* $u_0(x), v_0(x), w_0(x) \in L^\infty(\Omega)$, *the reaction-diffusion system* (1.2) *possesses at least one weak solution* (u, v, w) .

A major difficulty in the analysis of the reaction-diffusion system (1.2) are the nonlinear diffusion terms. In order to overcome this difficulty, it is fair to work with the following regularized problem instead of the original system (1.1):

$$
\begin{aligned}
&u_t^\varepsilon - \operatorname{div}(d_1(u^\varepsilon)\nabla u^\varepsilon) + f^\varepsilon(u^\varepsilon, v^\varepsilon, w^\varepsilon) = \lambda u^\epsilon, && (x,t) \in Q_T,\\
&v_t^\varepsilon + g^\varepsilon(u^\varepsilon, v^\varepsilon, w^\varepsilon) = \rho v^\epsilon, && (x,t) \in Q_T,\\
&w_t^\varepsilon - \operatorname{div}(d_2(w^\varepsilon)\nabla w^\varepsilon) + h^\varepsilon(u^\varepsilon, w^\varepsilon) = \alpha u^\epsilon, && (x,t) \in Q_T,
\end{aligned} \tag{2.2}
$$

with the initial and boundary conditions

$$
\begin{aligned}
&u^\varepsilon(x,0) = u_0(x), \quad v^\varepsilon(x,0) = v_0(x), \quad w^\varepsilon(x,0) = w_0(x), && \text{in } \Omega,\\
&u^\varepsilon(x,t) = w^\varepsilon(x,t) = 0, && \text{in } \Sigma_T,
\end{aligned}
$$

where

$$
f^\varepsilon = \frac{f}{1+\varepsilon|f|}, \qquad g^\varepsilon = \frac{g}{1+\varepsilon|g|}, \qquad h^\varepsilon = \frac{h}{1+\varepsilon|h|}.
$$

THEOREM 2.2. *Assume that the hypotheses* (H_1) *and* (H_3) *hold and that the initial conditions satisfy* $u_0(x), v_0(x), w_0(x) \in L^\infty(\Omega)$. *Then the approximate problem* (2.2) *possesses a weak solution* $(u^\varepsilon, v^\varepsilon, w^\varepsilon)$ *in the function spaces*

$$
\begin{aligned}
&u^\varepsilon, w^\varepsilon \in L^\infty(Q_T) \cap L^2(0,T; H_0^1(\Omega)) \cap C([0,T]; L^2(\Omega)),\\
&v^\varepsilon \in C([0,T]; L^2(\Omega)),\\
&d_1(u^\varepsilon), d_2(w^\varepsilon) \in L^2(0,T; H_0^1(\Omega)),\\
&u_t^\varepsilon, w_t^\varepsilon \in L^2(0,T; H^{-1}(\Omega)),
\end{aligned}
$$

satisfying the following weak formulation:

$$
\begin{aligned}
-\int_0^T \langle u^\varepsilon, \phi_{1t}\rangle\, dt + \int_{Q_T} d_1(u^\varepsilon)\nabla u^\varepsilon \nabla\phi_1\, dxdt + \int_{Q_T} f^\varepsilon(u^\varepsilon, v^\varepsilon, w^\varepsilon)\phi_1\, dxdt&\\
= \int_{Q_T} \lambda u^\varepsilon \phi_1 dxdt + \int_\Omega u_0(x)\phi_1(x,0)dx&,\\
-\int_0^T \langle v^\varepsilon, \phi_{2t}\rangle\, dt + \int_{Q_T} g^\varepsilon(u^\varepsilon, v^\varepsilon, w^\varepsilon)\phi_2\, dxdt&\\
= \int_{Q_T} \rho v^\varepsilon \phi_2 dxdt + \int_\Omega v_0(x)\phi_2(x,0)dx&,\\
-\int_0^T \langle w^\varepsilon, \phi_{3t}\rangle\, dt + \int_{Q_T} d_2(w^\varepsilon)\nabla w^\varepsilon \nabla\phi_3\, dxdt + \int_{Q_T} h^\varepsilon(u^\varepsilon, w^\varepsilon)\phi_3\, dxdt&\\
= \int_{Q_T} \alpha u^\varepsilon \phi_3 dxdt + \int_\Omega w_0(x)\phi_3(x,0)dx&,
\end{aligned} \tag{2.3}
$$

for all $\phi_1, \phi_3 \in L^2(0,T; H_0^1(\Omega))$ *and* $\phi_2 \in C([0,T]; L^2(\Omega))$, *with* $\phi_i(\cdot, T) = 0$, $i = 1, 2, 3$.

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2.1. Galerkin approximation method. To prove Theorem 2.2, which asserts the existence of weak solutions of the approximate problem (2.2), we use the Faedo-Galerkin approximation method. First, consider the following spectral problem [6]: Find $z \in H_0^1(\Omega)$ and a number κ such that

$$\begin{aligned} (\nabla z, \nabla \phi)_{L^2(\Omega)} &= \kappa\,(z,\phi)_{L^2(\Omega)}\,, && \text{for all } \phi \in H_0^1(\Omega),\\ z &= 0, && \text{on } \partial\Omega. \end{aligned}$$

This spectral problem possesses a sequence of real eigenvalues $\{\kappa_l\}_{l=1}^{\infty}$, and the corresponding eigenfunctions form a basis $\{e_l\}_{l=1}^{\infty}$ that is orthogonal in $H_0^1(\Omega)$ and orthonormal in $L^2(\Omega)$. Furthermore, we assume without loss of generality that $\kappa_1 = 0$.

Now, we look for a finite-dimensional approximate solution of the system (2.2) in the form of sequences $(u_n^\varepsilon)_{n>1}$, $(v_n^\varepsilon)_{n>1}$, and $(w_n^\varepsilon)_{n>1}$ defined for $t \geq 0$ and $x \in \overline{\Omega}$ by

$$\begin{aligned} &u_n^\varepsilon(x,t) = \sum_{l=1}^{n} c_{1,n,l}(t)e_l(x), \qquad v_n^\varepsilon(x,t) = \sum_{l=1}^{n} c_{2,n,l}(t)e_l(x), \quad \text{and}\\ &w_n^\varepsilon(x,t) = \sum_{l=1}^{n} c_{3,n,l}(t)e_l(x), \end{aligned}$$

where $e_l(x)$ is the sequence of eigenfunctions as defined above.

Our aim is to determine a set of coefficients $\{c_{i,n,l}\}_{l=1}^{n}$, $i = 1,2,3$, such that, for $k = 1,2,\ldots,n$,

$$\begin{aligned} &\langle \partial_t u_n^\varepsilon, e_k\rangle + \int_\Omega d_1(u_n^\varepsilon)\nabla u_n^\varepsilon \nabla e_k\,dx + \int_\Omega f^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)e_k\,dx = \int_\Omega \lambda u_n^\varepsilon e_k dx,\\ &\langle \partial_t v_n^\varepsilon, e_k\rangle + \int_\Omega g^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)e_k\,dx = \int_\Omega \rho v_n^\varepsilon e_k dx,\\ &\langle \partial_t w_n^\varepsilon, e_k\rangle + \int_\Omega d_2(w_n^\varepsilon)\nabla w_n^\varepsilon \nabla e_k\,dx + \int_\Omega h^\varepsilon(u_n^\varepsilon, w_n^\varepsilon)e_k\,dx = \int_\Omega \alpha u_n^\varepsilon e_k dx, \end{aligned} \tag{2.4}$$

where ∂_t denotes the partial derivative with respect to time. Moreover, the initial conditions are given by

$$\begin{aligned} &u_n^\varepsilon(x,0) := u_{0,n}(x) = \sum_{l=1}^{n} c_{1,n,l}(0)e_l(x), \quad v_n^\varepsilon(x,0) := v_{0,n}(x) = \sum_{l=1}^{n} c_{2,n,l}(0)e_l(x), \quad \text{and}\\ &w_n^\varepsilon(x,0) := w_{0,n}(x) = \sum_{l=1}^{n} c_{3,n,l}(0)e_l(x). \end{aligned}$$

Further, it is obvious that the above solutions with our choice of basis functions for u_n^ε, v_n^ε, and w_n^ε also satisfy the assumed boundary conditions of the system.

Now, the system (2.4) can be rewritten in the following form with the help of the normality of the basis,

$$
\begin{aligned}
c'_{1,n,k}(t) &= -\int_\Omega d_1(u_n^\varepsilon)\nabla u_n^\varepsilon \nabla e_k\, dx - \int_\Omega f^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon) e_k\, dx + \int_\Omega \lambda u_n^\varepsilon e_k,\\
&=: F_1^k\left(t, \{c_{1,n,l}\}_{l=1}^n, \{c_{2,n,l}\}_{l=1}^n, \{c_{3,n,l}\}_{l=1}^n\right),\\
c'_{2,n,k}(t) &= -\int_\Omega g^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon) e_k\, dx + \int_\Omega \rho v_n^\varepsilon e_k dx,\\
&=: F_2^k\left(t, \{c_{1,n,l}\}_{l=1}^n, \{c_{2,n,l}\}_{l=1}^n, \{c_{3,n,l}\}_{l=1}^n\right),\\
c'_{3,n,k}(t) &= -\int_\Omega d_2(w_n^\varepsilon)\nabla w_n^\varepsilon \nabla e_k\, dx - \int_\Omega h^\varepsilon(u_n^\varepsilon, w_n^\varepsilon) e_k\, dx + \int_\Omega \alpha u_n^\varepsilon e_k dx,\\
&=: F_3^k\left(t, \{c_{1,n,l}\}_{l=1}^n, \{c_{3,n,l}\}_{l=1}^n\right).
\end{aligned}
\tag{2.5}
$$

In the next step, we prove the existence of a local solution of the obtained ODE system (2.5). Let $t^* \in (0,T)$, and set $U = [0,t^*]$. Choose $r > 0$ large enough such that the ball $B_r \in \mathbb{R}^N$ contains the three vectors $\{c_{i,n,l}(0)_{l=1}^n\}$, $i = 1,2,3$, and then set $V = \overline{B_r}$. Let us take $F_i = \{F_i^k\}_{k=1}^m$, $i = 1,2,3$, and suppose that each function $F_i : U \times V \to \mathbb{R}^N$ is a Caratheodory function.

Using the hypothesis (H_2) and (1.3)–(1.5), the components of F_i, $i = 1,2,3$, can be bounded on $U \times V$ as follows:

$$
\begin{aligned}
&\left|F_1^k\left(t, \{c_{1,n,l}\}_{l=1}^n, \{c_{2,n,l}\}_{l=1}^n, \{c_{3,n,l}\}_{l=1}^n\right)\right|\\
&\quad\le d_1\left(\sum_{l=1}^n c_{1,n,l} e_l\right)\left(\int_\Omega |\sum_{l=1}^n c_{1,n,l}\nabla e_l|^2 dx\right)^{\frac12}\left(\int_\Omega |\nabla e_k|^2 dx\right)^{\frac12}\\
&\qquad + \frac{\text{meas}(\Omega)}{\varepsilon}\left(\int_\Omega |e_k|^2\right)^{\frac12} + \lambda\left(\int_\Omega |\sum_{l=1}^n c_{1,n,l} e_l|^2 dx\right)^{\frac12}\left(\int_\Omega |\nabla e_k|^2 dx\right)^{\frac12}\\
&\quad\le C(r,n),
\end{aligned}
$$

where the positive constant $C(r,n)$ depends only on r, n, and the given data. Similar calculations for F_i, $i = 2,3$, show that

$$
\begin{aligned}
\left|F_2^k\left(t, \{c_{1,n,l}\}_{l=1}^n, \{c_{2,n,l}\}_{l=1}^n, \{c_{3,n,l}\}_{l=1}^n\right)\right| &\le C(r,n),\\
\left|F_3^k\left(t, \{c_{1,n,l}\}_{l=1}^n, \{c_{3,n,l}\}_{l=1}^n\right)\right| &\le C(r,n),
\end{aligned}
$$

where the positive constant $C(r,n)$ depends only on r, n. Thus, according to the standard ODE theory, there exists absolutely continuous functions $\{c_{1,n,l}\}_{l=1}^n$, $\{c_{2,n,l}\}_{l=1}^n$, and $\{c_{3,n,l}\}_{l=1}^n$ satisfying the initial conditions of the system such that for almost all $t \in [0,t^*)$ for some $t^* > 0$, the following equations hold on $[0,t^*)$:

$$
\begin{aligned}
c_{1,n,l}(t) &= c_{1,n,l}(0) + \int_0^t F_1^l(\tau, \{c_{1,n,m}(\tau)\}_{m=1}^n, \{c_{2,n,m}(\tau)\}_{m=1}^n, \{c_{3,n,m}(\tau)\}_{m=1}^n) d\tau,\\
c_{2,n,l}(t) &= c_{2,n,l}(0) + \int_0^t F_2^l(\tau, \{c_{1,n,m}(\tau)\}_{m=1}^n, \{c_{2,n,m}(\tau)\}_{m=1}^n, \{c_{3,n,m}(\tau)\}_{m=1}^n) d\tau,\\
c_{3,n,l}(t) &= c_{3,n,l}(0) + \int_0^t F_3^l(\tau, \{c_{1,n,m}(\tau)\}_{m=1}^n, \{c_{3,n,m}(\tau)\}_{m=1}^n) d\tau.
\end{aligned}
$$

Therefore, on $[0, t^*)$, the set of functions $\{c_{1,n,l}\}_{l=1}^n$, $\{c_{2,n,l}\}_{l=1}^n$, and $\{c_{3,n,l}\}_{l=1}^n$ are well defined and also are approximate solutions of the system (2.2) with given initial data. Next, to show global existence of the Faedo-Galerkin approximate solution, we want to derive a priori estimates for the solutions $(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)$ in various Banach spaces. Here we let $\tilde{T}$ be an arbitrary time in the interval $[0, t^*)$, and, to derive a priori estimates for the approximate solutions, we prove the following lemma.

LEMMA 2.1. *Suppose that the hypotheses (H_1)–(H_3) hold true and that $u_0(x), v_0(x)$, and $w_0(x)$ are in $L^\infty(\Omega)$. Then there exists a constant $C > 0$ independent of n such that*

$$\begin{aligned} \|(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)\|_{L^\infty(0,\tilde{T},L^2(\Omega))} &\le C, \\ \|(\nabla u_n^\varepsilon, \nabla w_n^\varepsilon)\|_{L^2(Q_{\tilde{T}})} &\le C, \\ \|(\partial_t u_n^\varepsilon, \partial_t v_n^\varepsilon, \partial_t w_n^\varepsilon)\|_{L^2(0,\tilde{T},H^{-1}(\Omega))} &\le C. \end{aligned}$$

Proof. For given absolutely continuous coefficients $b_{i,n,l}(t)$, $i = 1, 2, 3$, we set $\phi_{i,n}(x,t) = \sum_{l=1}^{n} b_{i,n,l}(t) e_l(x)$ with $\phi_i(\cdot, T) = 0$, $i = 1, 2, 3$. It follows from (2.4) that the Faedo-Galerkin solutions satisfy the following weak formulation for each fixed t,

(2.6)
$$\begin{aligned} \int_\Omega \partial_t u_n^\varepsilon \phi_{1,n} dx + \int_\Omega d_1(u_n^\varepsilon) \nabla u_n^\varepsilon \nabla \phi_{1,n} dx + \int_\Omega f^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon) \phi_{1,n} dx &= \int_\Omega \lambda u_n^\varepsilon \phi_{1,n} dx, \\ \int_\Omega \partial_t v_n^\varepsilon \phi_{2,n} dx + \int_\Omega g^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon) \phi_{2,n} dx &= \int_\Omega \rho v_n^\varepsilon \phi_{1,n} dx, \\ \int_\Omega \partial_t w_n^\varepsilon \phi_{3,n} dx + \int_\Omega d_2(w_n^\varepsilon) \nabla w_n^\varepsilon \nabla \phi_{3,n} dx + \int_\Omega h^\varepsilon(u_n^\varepsilon, w_n^\varepsilon) \phi_{3,n} dx &= \int_\Omega \alpha u_n^\epsilon \phi_{1,n} dx. \end{aligned}$$

After substituting $\phi_{1,n} = u_n^\varepsilon$, $\phi_{2,n} = v_n^\varepsilon$, and $\phi_{3,n} = w_n^\varepsilon$, respectively, in (2.6), we use the hypotheses (H_1)–(H_2) and the definition of the nonlinear functions $f^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)$, $g^\varepsilon(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)$, and $h^\varepsilon(u_n^\varepsilon, w_n^\varepsilon)$. Then, by Young's inequality, we get

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \int_\Omega \left(|u_n^\varepsilon|^2 + |v_n^\varepsilon|^2 + |w_n^\varepsilon|^2 \right) dx + \int_\Omega \left(\psi_1 |\nabla u_n^\varepsilon|^2 + \psi_2 |\nabla w_n^\varepsilon|^2 \right) dx \\ \le C \int_\Omega \left(|u_n^\varepsilon|^2 + |v_n^\varepsilon|^2 + |w_n^\varepsilon|^2 \right) dx, \end{aligned} \tag{2.7}$$

where the constant $C > 0$ depends only on the given data. Furthermore, using Gronwall's inequality in (2.7), we get

$$\int_\Omega \left(|u_n^\varepsilon(x, \tilde{T})|^2 + |v_n^\varepsilon(x, \tilde{T})|^2 + |w_n^\varepsilon(x, \tilde{T})|^2 \right) dx \le C \tag{2.8}$$

for some constant $C > 0$, which depends only on the given data and is independent of n. This allows us to conclude that

$$\|(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)\|_{L^\infty(0,\tilde{T},L^2(\Omega))} \le C.$$

Use (2.8) in (2.7) to get the bound

$$\int_0^{\tilde{T}} \int_\Omega \left(\psi_1 |\nabla u_n^\varepsilon|^2 + \psi_2 |\nabla w_n^\varepsilon|^2 \right) dx \le C$$

for some constant $C > 0$ independent of n. Thus, we conclude that

$$\|(\nabla u_n^\varepsilon, \nabla w_n^\varepsilon)\|_{L^2(Q_{\tilde{T}})} \leq C. \tag{2.9}$$

Choose $\phi_{i,n} = \phi_i \in L^2(0, T, H_0^1(\Omega))$, $i = 1, 2, 3$, respectively, in the first, second, and third equation of (2.6). Using the inequalities (2.8), (2.9) and from the boundedness of the solutions, we can show that there exists a constant $C > 0$ independent of n with

$$\left| \int_0^{\tilde{T}} \langle \partial_t u_n^\varepsilon, \phi_1 \rangle dt \right| \leq C \|\phi_1\|_{L^2(0,T,H_0^1(\Omega))},$$
$$\left| \int_0^{\tilde{T}} \langle \partial_t v_n^\varepsilon, \phi_2 \rangle dt \right| \leq C \|\phi_2\|_{L^2(0,T,H_0^1(\Omega))},$$
$$\left| \int_0^{\tilde{T}} \langle \partial_t w_n^\varepsilon, \phi_3 \rangle dt \right| \leq C \|\phi_3\|_{L^2(0,T,H_0^1(\Omega))}.$$

This verifies that

$$\|(\partial_t u_n^\varepsilon, \partial_t v_n^\varepsilon, \partial_t w_n^\varepsilon)\|_{L^2(0,\tilde{T},H^{-1}(\Omega))} \leq C$$

and concludes the proof of the lemma. $\square$

Now, we have to show that the local solutions constructed earlier can be extended to the whole time interval $[0, T]$ (independently of n). We are using similar ideas as in [8, 39] to show the global existence of solutions of the system (2.4). By (2.8), we get

$$\sum_{i=1}^{3} |c_{i,n,l}(t)_{l=1,2,\ldots,n}|^2 = \|u_n^\varepsilon(x,t)\|_{L^2(\Omega)}^2 + \|v_n^\varepsilon(x,t)\|_{L^2(\Omega)}^2 + \|w_n^\varepsilon(x,t)\|_{L^2(\Omega)}^2 \leq C$$

for some constant $C > 0$ independent of t and n and for any arbitrary t in the interval $[0, t^*)$. Define the set

$$\mathcal{A} = \{t \in [0, T); \text{there exists a solution of (2.4) in } [0, t)\}.$$

The above local existence result shows that $\mathcal{A}$ is non-empty. Let $\bar{t} \in A$ and $0 < t_1 < t_2 < \bar{t}$. Then we get

$$|c_{i,n,l}(t_1) - c_{i,n,l}(t_2)| \leq c \int_{t_1}^{t_2} |F_i(\tau)| d\tau, \qquad i = 1, 2, 3. \tag{2.10}$$

Since $F_i(t)$, $i = 1, 2, 3$, are in L^1, it is easy to understand that $t \to c_{i,n,l}(t)$, $i = 1, 2, 3$, is uniformly continuous on $[0, \tilde{t}]$. Therefore, we can solve the ODE system (2.5) at time $\tilde{t}$ with the solution defined on the interval $[0, \tilde{t} + \delta]$ for some $\delta = \delta(\tilde{t}) > 0$. This proves that $\mathcal{A}$ is open.

Now consider the sequence $\{t_j\}_{j>1} \subset A$ such that $t_j \to \tilde{t}$ as $j \to \infty$. Let $\{c_{i,n,l}^j(t)\}$, $i = 1, 2, 3$, denote the solutions of (2.4) such that

$$c_{i,n,l}^j(t) = \begin{cases} c_{i,n,l}^j(t) & \text{if } t \in [0, t_l), \\ c_{i,n,l}^j(t_l) & \text{if } t \in [t_l, \tilde{t}). \end{cases}$$

Since from (2.10) and the previous arguments, $\{c_{i,n,l}^j\}_{l=1}^n$, $i = 1, 2, 3$, are bounded and equicontinuous on $[0, \tilde{t})$, there exists a convergent subsequence which converges to a limit

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point $\{c_{i,n,l}\}_{l=1}^{n}$, $i = 1, 2, 3$, as $j \to \infty$. Hence, by the Lebesgue dominated convergence theorem, this limit solves the ODE system (2.5), where the solutions exist on the interval $[0, \tilde{t})$. This proves that $\mathcal{A}$ is closed. Consequently, this result shows that the Faedo-Galerkin approximate solutions can be extended to the whole interval on $[0, T]$.

LEMMA 2.2. *The solution triple* $(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)$ *of the approximate system is non-negative.*

Proof. Choose $\phi_{1,n} = -u_n^{-\varepsilon}$, $\phi_{2,n} = -v_n^{-\varepsilon}$, and $\phi_{3,n} = -w_n^{-\varepsilon}$ in (2.6), respectively, where $u_n^{-\varepsilon} = \max(0, -u_n^\varepsilon)$, $v_n^{-\varepsilon} = \max(0, -v_n^\varepsilon)$, and $w_n^{-\varepsilon} = \max(0, -w_n^\varepsilon)$. Then integrating over $(0, t)$ with $0 < t < T$ and using the hypotheses (H_1)–(H_2), we get

$$\begin{aligned} \frac{1}{2}\frac{d}{dt}\int_\Omega \left(|u_n^{-\varepsilon}|^2 + |v_n^{-\varepsilon}|^2 + |w_n^{-\varepsilon}|^2\right) dx + \int_\Omega \left(\psi_1 |\nabla u_n^{-\varepsilon}|^2 + \psi_2 |\nabla w_n^{-\varepsilon}|^2\right) dx \\ \leq C \int_\Omega \left(|u_n^{-\varepsilon}|^2 + |v_n^{-\varepsilon}|^2 + |w_n^{-\varepsilon}|^2\right) dx \end{aligned} \tag{2.11}$$

for some positive $C > 0$, which depends only on the given data. In the above inequality, we have used the assumptions on the nonlinear functions f, g, and h. According to the non-negativity of the right-hand side of (2.11) and the initial conditions, we get

$$\frac{1}{2}\frac{d}{dt}\int_\Omega \left(|u_n^{-\varepsilon}|^2 + |v_n^{-\varepsilon}|^2 + |w_n^{-\varepsilon}|^2\right) dx \leq 0.$$

This proves non-negativity of the solutions u_n^ε, v_n^ε, and w_n^ε. ∎

Proof of Theorem 2.2. Combining the above results, from Lemma 2.1, and using standard compactness arguments, the sequences $(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon)_n$ have convergent subsequences (which are also denoted by $u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon$). Thus, there exist limit functions $u^\varepsilon, v^\varepsilon, w^\varepsilon$ such that, as $n \to \infty$, we get

$$\begin{aligned}
(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon) &\rightharpoonup (u^\varepsilon, v^\varepsilon, w^\varepsilon) && \text{weakly-* in } L^\infty(Q_T) \text{ and a.e in } Q_T,\\
(u_n^\varepsilon, w_n^\varepsilon) &\rightharpoonup (u^\varepsilon, w^\varepsilon) && \text{weakly in } L^2(0,T;H_0^1(\Omega)),\\
d_1(u_n^\varepsilon)\nabla u_n^\varepsilon &\rightharpoonup \varrho_1 && \text{weakly in } L^2(Q_T),\\
d_2(w_n^\varepsilon)\nabla w_n^\varepsilon &\rightharpoonup \varrho_2 && \text{weakly in } L^2(Q_T),\\
(\partial_t u_n^\varepsilon, \partial_t v_n^\varepsilon, \partial_t w_n^\varepsilon) &\rightharpoonup (\partial_t u^\varepsilon, \partial_t v^\varepsilon, \partial_t w^\varepsilon) && \text{weakly in } L^2(0,T;H^{-1}(\Omega)),\\
f(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon) &\to f(u^\varepsilon, v^\varepsilon, w^\varepsilon) && \text{a.e in } Q_T,\\
g(u_n^\varepsilon, v_n^\varepsilon, w_n^\varepsilon) &\to g(u^\varepsilon, v^\varepsilon, w^\varepsilon) && \text{a.e in } Q_T,\\
h(u_n^\varepsilon, w_n^\varepsilon) &\to h(u^\varepsilon, w^\varepsilon) && \text{a.e in } Q_T.
\end{aligned}$$

First, by a similar type of arguments as in [39] and the monotonicity property (H_3) of the nonlinear diffusion operator, we can easily show that $d_1(u^\varepsilon)\nabla u^\varepsilon = \varrho_1$ and $d_2(w^\varepsilon)\nabla w^\varepsilon = \varrho_2$. Moreover, by integrating equation (2.6) from 0 to T, using integration by parts, the construction of the Faedo-Galerkin solutions, and the previous convergence results, it follows that the weak formulation (2.3) hold true when $n \to \infty$.

From these results, we conclude that there exists a weak solution $(u^\varepsilon, v^\varepsilon, w^\varepsilon)$ of the approximate system (2.2), which satisfies the weak formulation (2.3). This concludes the proof of Theorem 2.2. ∎

2.2. Weak solutions of the cancer invasion system. In this section we establish the existence of non-negative weak solutions of the original problem (1.1) using the hypotheses (H_1)–(H_3), the weak solutions of the approximate problem (2.1), some a priori estimates, and compactness arguments by finally letting the parameter ε tends to zero.

LEMMA 2.3. *Assume that the hypotheses (H_1)–(H_3) and (1.3)–(1.4) hold true. If $u_0(x)$, $v_0(x)$, and $w_0(x)$ in $L^\infty(\Omega)$ are non-negative, then the solution triple $(u^\varepsilon, v^\varepsilon, w^\varepsilon)$ is non-negative. Moreover there exists some constant C such that*

$$\begin{aligned}
\|(u^\varepsilon, v^\varepsilon, w^\varepsilon)\|_{L^\infty(0,T,L^2(\Omega))} &\leq C,\\
\|(u^\varepsilon, v^\varepsilon, w^\varepsilon)\|_{L^\infty(Q_T)} &\leq C,\\
\|(\nabla u^\varepsilon, \nabla w^\varepsilon)\|_{L^2(Q_T)} &\leq C,\\
\|(\partial_t u^\varepsilon, \partial_t v^\varepsilon, \partial_t w^\varepsilon)\|_{L^2(0,T,H^{-1}(\Omega))} &\leq C.
\end{aligned}$$

Proof. We use the previous convergence results for (2.6) and take $\phi_1 = (u^\varepsilon)^{p-1}$, $\phi_2 = (v^\varepsilon)^{p-1}$, and $\phi_3 = (w^\varepsilon)^{p-1}$, respectively, in the first, second, and third equations of (2.6), where $p > 1$. Then, from (H_1)–(H_2) and the assumptions for the nonlinear functions, we get

$$\frac{1}{2}\frac{d}{dt}\int_\Omega (|u^\varepsilon|^p + |v^\varepsilon|^p + |w^\varepsilon|^p)\,dx \leq C\int_\Omega (|u^\varepsilon|^p + |v^\varepsilon|^p + |w^\varepsilon|^p)\,dx,$$

where the constant $C > 0$ depends only on the given data. By an application of Gronwall's inequality and repeating the same procedure as in the proof of Lemma 2.1, we get

$$\int_\Omega (|u^\varepsilon(x,t)|^p + |v^\varepsilon(x,t)|^p + |w^\varepsilon(x,t)|^p)\,dx \leq C$$

for some constant $C > 0$ that depends only on the given data. This allows us to conclude that

$$\|(u^\varepsilon, v^\varepsilon, w^\varepsilon)\|_{L^\infty(Q_T)} \leq C. \tag{2.12}$$

By similar arguments as in the proof the Lemma 2.1 and using (2.12), we obtain the following result:

$$\begin{aligned}
\|(u^\varepsilon, v^\varepsilon, w^\varepsilon)\|_{L^2(0,T,H_0^1(\Omega))} &\leq C,\\
\|(\partial_t u^\varepsilon, \partial_t v^\varepsilon, \partial_t w^\varepsilon)\|_{L^2(0,T,H^{-1}(\Omega))} &\leq C,
\end{aligned}$$

where $C > 0$ is a positive constant depending only on the given data. □

Proof of Theorem 2.1. According to Lemma 2.3 and standard compactness arguments, we can extract convergent subsequences (which are also denoted by $(u^\varepsilon, v^\varepsilon, w^\varepsilon)$). Thus, there exist limit functions (u, v, w) such that, as ε tends to zero, we obtain

$$\begin{aligned}
(u^\varepsilon, v^\varepsilon, w^\varepsilon) &\rightharpoonup (u, v, w) && \text{weakly-* in } L^\infty(Q_T) \text{ and a.e in } Q_T,\\
(u^\varepsilon, w^\varepsilon) &\rightharpoonup (u, w) && \text{weakly in } L^2(0,T;H^1(\Omega)),\\
d_1(u^\varepsilon)\nabla u^\varepsilon &\rightharpoonup \varrho_1 && \text{weakly in } L^2(Q_T),\\
d_2(w^\varepsilon)\nabla w^\varepsilon &\rightharpoonup \varrho_2 && \text{weakly in } L^2(Q_T),\\
(\partial_t u^\varepsilon, \partial_t v^\varepsilon, \partial_t w^\varepsilon) &\rightharpoonup (\partial_t u, \partial_t v, \partial_t w) && \text{weakly in } L^2(0,T;H^{-1}(\Omega)),\\
f(u^\varepsilon, v^\varepsilon, w^\varepsilon) &\to f(u, v, w) && \text{a.e in } Q_T,\\
g(u^\varepsilon, v^\varepsilon, w^\varepsilon) &\to g(u, v, w) && \text{a.e in } Q_T,\\
h(u^\varepsilon, w^\varepsilon) &\to h(u, w) && \text{a.e in } Q_T.
\end{aligned}$$

By a similar type of arguments as in [39] and the monotonicity property of the nonlinear diffusion operator, we can easily show that $d_1(u)\nabla u = \varrho_1$ and $d_2(w)\nabla w = \varrho_2$. Now, recalling the fact that u and w in $L^\infty(Q_T) \cap L^2(0,T;H_0^1(\Omega))$ and $u_t, v_t, w_t \in L^2(0,T;H^{-1}(\Omega))$, we conclude that the solution (u, v, w) belongs to the space $C([0,T], L^2(\Omega))$. This proves the existence of weak solutions of the cancer invasion system (1.1). □

3. Finite element method for the cancer invasion system. In this section, we present a finite element scheme for the considered model equations. We consider the dimensionless form (1.2) of the given mathematical model and the variational forms (2.1) of the cancer cells density equation, the healthy cells density equation, and the equation for the concentration of the extracellular acid to develop the scheme. We first present the temporal discretization of the coupled variational system (2.1). In particular, the application of a backward Euler time discretization is investigated for the system. Further, an iteration of fixed point-type is applied to handle the nonlinear terms in the cancer parabolic system. Moreover, the choice of finite elements for the spatial discretization of the system (2.1) is also discussed in this section.

3.1. Temporal discretization. Let $0 = t^0 < t^1 < \cdots < t^{\mathcal{N}} = T$ be a decomposition of the considered time interval $[0, T]$, and let $\delta_t = t^{n+1} - t^n$, $n = 0, 1, \ldots, \mathcal{N} - 1$, denote the uniform time step. Define the backward difference quotient by $\bar{\partial} f^n = \frac{f(\cdot,t_n) - f(\cdot,t_{n-1})}{\delta_t}$. Also, we use $u^n(x) := u(x, t^n)$, $v^n(x) := v(x, t^n)$, $w^n(x) := w(x, t^n)$ to denote the function values at time t^n. After applying the implicit backward Euler discretization scheme, which is A-stable, the semi-discrete (continuous in space) form of the system (2.1) reads as follows: For given u^{n-1}, v^{n-1}, and w^{n-1} with $u^0 = u_0$, $v^0 = v_0$, and $w^0 = w_0$, find $u^n, v^n, w^n \in H_0^1(\Omega)$ such that

$$\begin{aligned}
&\left(\frac{u^n - u^{n-1}}{\delta_t}, \phi\right) + a_u(u^n; \tilde{u}^n; \tilde{v}^n; \tilde{w}^n, \phi) = 0,\\
&\left(\frac{v^n - v^{n-1}}{\delta_t}, \phi\right) + a_v(v^n; \tilde{v}^n; \tilde{u}^n; \tilde{w}^n, \phi) = 0,\\
&\left(\frac{w^n - w^{n-1}}{\delta_t}, \phi\right) + a_w(w^n; \tilde{u}^n; \tilde{w}^n, \phi) = b\left(u^n, \phi\right),
\end{aligned} \tag{3.1}$$

for all $\phi \in H_0^1(\Omega)$, where

$$\begin{aligned}
a_u(u; \tilde{u}; \tilde{v}; \tilde{w}, \phi) &= \int_\Omega d_1(\tilde{u}) \nabla u \cdot \nabla \phi \, dx - \lambda \int_\Omega u(1 - \tilde{u} - \tilde{v}) \phi \, dx - \chi \int_\Omega u \tilde{w} \phi \, dx\\
a_v(v; \tilde{v}; \tilde{u}; \tilde{w}, \phi) &= \eta \int_\Omega v \tilde{w} \phi \, dx - \rho \int_\Omega v(1 - \tilde{u} - \tilde{v}) \phi \, dx,\\
a_w(w; \tilde{u}, \tilde{w}, \phi) &= \int_\Omega d_2(\tilde{w}) \nabla w \cdot \nabla \phi \, dx + \int_\Omega w(\alpha \tilde{u} + \beta) \phi \, dx,\\
b(u, \phi) &= \int_\Omega \alpha u \phi \, dx.
\end{aligned}$$

3.2. Fixed point iteration. An iteration of fixed point-type [22] is proposed to treat the nonlinear and coupled terms semi-implicitly. We briefly explain the steps of the fixed point iteration for the nonlinear term in the cancer density equation in the time interval (t^{n-1}, t^n). Let $u_0^n = u^{n-1}$. Then the nonlinear integral terms in the cancer density equation are replaced by

$$\int_\Omega \left(\lambda u_k^n (1 - u_k^n - v_k^n) - \chi u_k^n w_k^n\right) \phi \, dx \simeq \int_\Omega \left(\lambda u_k^n (1 - u_{k-1}^n - v_{k-1}^n) - \chi u_k^n w_{k-1}^n\right) \phi \, dx,$$

for $k = 0, 1, 2, \ldots$ Furthermore, we iterate until the residual of the system is less than the prescribed threshold value (10^{-8}) or until a given maximal number of iterations is reached. Finally, we set $u^n = u_{k-1}^n$ and advance to the next time step.

Using the prescribed fixed point iteration, the linearized (semi-implicit) form of the semi-discrete system (3.1) reads: For given $u_0^n = u^{n-1}$, $v_0^n = v^{n-1}$, and $w_0^n = w^{n-1}$, find u_k^n, v_k^n, and w_k^n such that for all $\phi \in H_0^1(\Omega)$

$$
\begin{aligned}
&(u_k^n, \phi) + \delta_t a_u \left(u_k^n; u_{k-1}^n; v_{k-1}^n; w_{k-1}^n, \phi\right) = \left(u^{n-1}, \phi\right), \\
&(w_k^n, \phi) + \delta_t a_w \left(w_k^n; u_k^n, \phi\right) = \delta_t b\left(u_k^n, \phi\right) + \left(w^{n-1}, \phi\right), \\
&(v_k^n, \phi) + \delta_t a_v \left(v_k^n; v_{k-1}^n; u_k^n; w_k^n, \phi\right) = \left(v^{n-1}, \phi\right),
\end{aligned} \tag{3.2}
$$

for $k = 0, 1, 2, \dots$ In the computations, the iteration converges within two or three iterations with a residual error of 10^{-8}, and the number of iterations increase when δ_t is increased.

3.3. Finite element discretization. Let Ω_h be a triangulation of Ω into tetrahedral cells. Suppose that $V_h \subset H_0^1(\Omega)$ and $Q_h \subset H^1(\Omega)$ are conforming finite element (finite-dimensional) subspaces consisting of piecewise polynomials of degree r associated with Ω_h. We have the following approximation properties from [14],

$$
\begin{aligned}
&\inf_{s_h \in Q_h} \|s - s_h\|_0 \leqslant C h^{r+1} \|s\|_{r+1}, \qquad \forall s \in H^1(\Omega) \cap H^{r+1}(\Omega), \\
&\inf_{s_h \in Q_h} \|s - s_h\|_1 \leqslant C h^{r} \|s\|_{r+1}, \qquad \forall s \in H^1(\Omega) \cap H^{r+1}(\Omega),
\end{aligned}
$$

and the inverse inequality,

$$
\|s_h\|_\infty \leqslant C h^{-\frac{N}{2}} \|s_h\|_0, \qquad \forall s_h \in Q_h,
$$

where C is a constant independent of h, and for the space dimension $N = 2$ or 3. Moreover, define the finite element ansatz functions as

$$
u_h^n(x) = \sum_{i=1}^{\mathcal{N}} u_i^n \phi_i(x), \quad v_h^n(x) = \sum_{i=1}^{\mathcal{N}} v_i^n \phi_i(x), \quad w_h^n(x) = \sum_{i=1}^{\mathcal{N}} w_i^n \phi_i(x).
$$

The discrete form of the functions in (3.2) leads to a system of linearized (semi-implicit) system of algebraic equations

$$
\begin{aligned}
(M + \delta_t A^u)\, \mathcal{U}^n &= M\, \mathcal{U}^{n-1}, \\
(M + \delta_t A^v)\, \mathcal{V}^n &= M\, \mathcal{V}^{n-1}, \\
(M + \delta_t A^w)\, \mathcal{W}^n &= M\, \mathcal{W}^{n-1} + \delta_t F,
\end{aligned}
$$

where $\mathcal{U}^n = \mathrm{vec}(\mathcal{U}^n)$, $\mathcal{V}^n = \mathrm{vec}(\mathcal{V}^n)$, and $\mathcal{W}^n = \mathrm{vec}(\mathcal{W}^n)$ are the vectorization of the solution matrices $\mathcal{U}^n = [u_j^n]$, $\mathcal{V}^n = [v_j^n]$, and $\mathcal{W}^n = [w_j^n]$, respectively. Denote the fully discrete solutions by $u_{h,k}^n$, $v_{h,k}^n$, and $w_{h,k}^n$ at a fixed point iteration step $k = 0, 1, 2, \dots$ Here, the entries of the mass, stiffness matrices, and source vector at the iteration step k are given by

$$\begin{aligned}
M_{ij} &= \int_{\Omega_h} \phi_i(x)\,\phi_j(x)\,dx,\\
A^u_{ij} &= \int_{\Omega_h} d_1(u^n_{h,k-1})\nabla\phi_i(x)\cdot\nabla\phi_j(x)\,dx - \lambda\int_{\Omega_h}\phi_i(x)\,(1-u^n_{h,k-1}-v^n_{h,k-1})\,\phi_j(x)\,dx\\
&\qquad -\chi\int_{\Omega_h}\phi_i(x)\,w^n_{h,k-1}\,\phi_j(x)\,dx,\\
A^v_{ij} &= \eta\int_{\Omega_h}\phi_i(x)\,w^n_{h,k}\,\phi_j(x)\,dx - \rho\int_{\Omega_h}\phi_i(x)\,(1-u^n_{h,k-1}-v^n_{h,k-1})\,\phi_j(x)\,dx,\\
A^w_{ij} &= \int_{\Omega_h} d_2(w^n_{h,k-1})\nabla\phi_i(x)\cdot\nabla\phi_j(x)\,dx + \int_{\Omega_h}\phi_i(x)\,(\alpha u^n_{h,k-1}+\beta)\,\phi_j(x)\,dx,\\
F_i &= \alpha\int_{\Omega_h} u^n_{h,k}\,\phi_i(x)\,dx.
\end{aligned}$$

3.4. Analysis of the error estimates. We first study error estimates for the proposed finite element numerical scheme. For simplicity, we no longer indicate the subscript k of the fixed point iteration and use (u^n_h, v^n_h, w^n_h) to denote the numerical solution instead of $(u^n_{h,k}, v^n_{h,k}, w^n_{h,k})$. Hence, the fully discretized system is given in the following form:

$$\begin{aligned}
(u^n_h,\phi) + \delta_t a_u\left(u^n_h;u^n_h;v^n_h;w^n_h,\phi\right) &= \left(u^{n-1}_h,\phi\right),\\
(w^n_h,\phi) + \delta_t a_w\left(w^n_h;u^n_h,\phi\right) &= \delta_t b\left(u^n_h,\phi\right) + \left(w^{n-1}_h,\phi\right),\\
(v^n_h,\phi) + \delta_t a_v\left(v^n_h;v^n_h;u^n_h;w^n_h,\phi\right) &= \left(v^{n-1}_h,\phi\right).
\end{aligned} \tag{3.3}$$

From Theorem 2.1, we know that the exact solution of (1.1) satisfies

$$\|(u,v,w)\|_\infty \le K. \tag{3.4}$$

Here, K is positive constant and $t\in[0,I]$. Furthermore, we assume the following hypothesis, which will be proved at the end of the section:

$$\|(U^n,V^n,W^n)\|_\infty \le K, \tag{3.5}$$

where (U^n,V^n,W^n) is the numerical solution of (3.1) and K is the same constant as in (3.4).

THEOREM 3.1. *Assume that* (3.4) *and* (3.5) *hold. Let* (u,v,w) *and* (U^n,V^n,W^n) *be the exact and numerical solutions, respectively. Then we have the error estimate*

$$\|S^n - s(x,t_n)\|_0 \le Ch^2 + C\delta t,$$

where $S^n = (U^n,V^n,W^n)$ *and* $s=(u,v,w)$. *Here we use piecewise linear polynomial finite elements associated with* Ω_h.

Proof. Let $s^n := s(\cdot,t_n)$ be the exact solution of (1.1) and S^n be the numerical solution of (3.3). Let S^n_h denote the Ritz projection of s^n, and define the approximation error

$$S^n - s^n = S^n - S^n_h + S^n_h - s^n = \xi^n + \Lambda^n.$$

The projection error estimate follows from the error estimates of the Ritz projection. Therefore we get

$$\|\Lambda^n\|_0 \le Ch^2.$$

Then, we estimate ξ^n. Using the properties of the Ritz projection, we get

$$\begin{aligned}
&\int_\Omega \bar{\partial}\xi_1^n \phi_1 dx + \int_\Omega d_1(U^n)\nabla\xi^n\nabla\phi_1 dx \\
&= \int_\Omega \bar{\partial}U^n\phi_1 dx + \int_\Omega (d_1(U^n)\nabla U^n\phi_1 dx - \int_\Omega \bar{\partial}u_h^n\phi_1 dx - \int_\Omega d_1(U^n)\nabla u_h^n\phi_1 dx \\
&= \int_\Omega \lambda(1-U^n-V^n)U^n\phi_1 dx + \int_\Omega \chi U^n W^n\phi_1 dx - \int_\Omega \lambda(1-u^n-v^n)u^n\phi_1 dx \\
&\quad - \int_\Omega \chi u^n w^n\phi_1 dx - \int_\Omega \bar{\partial}\Lambda_1^n\phi_1 dx \\
&\quad - \int_\Omega (\bar{\partial}u^n - u_t^n)\phi dx - \int_\Omega (d_1(U^n)-d_1(u^n))\nabla u_h^n\nabla\phi_1 dx.
\end{aligned}$$

In the above equation, by taking $\phi_1 = \xi_1^n$ and using (H_1), (H_4), we obtain

$$\begin{aligned}
&\frac{1}{2}\bar{\partial}\|\xi_1^n\|^2 + \psi_1\|\nabla\xi_1^n\|^2 \\
&\quad \le C_K\|U^n-u^n\|\|\xi_1^n\| + B\|U^n-u^n\|\|\nabla\xi_1^n\| + (\|\bar{\partial}\Lambda_1^n\| + \|\bar{\partial}u^n - u_t^n\|)\|\xi_1^n\|.
\end{aligned}$$

Using Young's inequality, the boundedness of u^n and U^n, and the positivity of the second term on the left-hand side leads to

$$\bar{\partial}\|\xi_1^n\|^2 \le C(\|\xi_1^n\|^2 + R_n),$$

where R_n is defined as $R_n = \|\Lambda_1^n\| + \|\bar{\partial}\Lambda_1^n\|^2 + \|\bar{\partial}u^n - u_t^n\|^2$. From the definition of $\bar{\partial}$ and by simple algebraic calculations, we get

$$(1-C\delta_t)\|\xi_1^n\|^2 \le \|\xi_1^{n-1}\|^2 + C\delta_t R_n.$$

For sufficiently small δ_t, we now obtain the inequality

$$\|\xi_1^n\|^2 \le (1+C\delta_t)\|\xi_1^{n-1}\|^2 + C\delta_t R_n.$$

It is easy to see that $\|\bar{\partial}u^n - u_t^n\| \le C(u)\delta_t$ and $\|\bar{\partial}\Lambda_1^n\| \le C(u)h^2$. This shows that R_n defined above satisfies $R_n \le C(u)(h^2+\delta_t)$, and therefore we get

$$\|\xi_1^n\|^2 \le (1+C\delta_t)\|\xi_1^{n-1}\|^2 + C(u)(h^2+\delta_t).$$

Similarly, we find

$$\|\Lambda_1^n\|^2 \le (1+C\delta_t)\|\Lambda_1^{n-1}\|^2 + C(u)(h^2+\delta_t).$$

Hence,

$$\|\xi_1^n\|^2 + \|\Lambda_1^n\|^2 \le (1+C\delta_t)(\|\xi_1^{n-1}\|^2 + \|\Lambda_1^{n-1}\|^2) + C(u)(h^2+\delta_t).$$

Applying successive iteration, we obtain

$$\|\xi_1^n\|^2 + \|\Lambda_1^n\|^2 \le (1+C\delta_t)(\|\xi_1^0\|^2 + \|\Lambda_1^0\|^2) + C(u)(h^2+\delta_t).$$

Hence, we conclude that

$$\|\xi_1^n\|^2 + \|\Lambda_1^n\|^2 \le C(u)(h^2+\delta_t).$$

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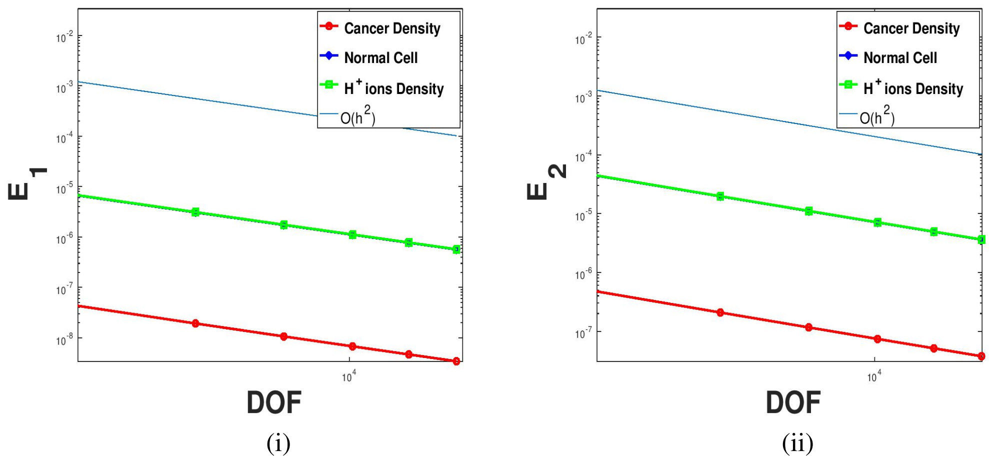

FIG. 3.1. *Error plots of the cancer cell density, the normal cell density, and the H^+ions density obtained with different mesh levels. Panel (i) and (ii), respectively, represent the logarithmic values of the error norms E_1 and E_2 of the solution of the system* (3.7) *against the logarithmic value of the DOF for Example* 3.2.

Similarly, we find

$$\|\xi^n\|^2 + \|\Lambda^n\|^2 \le C(s)(h^2 + \delta_t). \qquad \square$$

Next, we prove the validity of (3.5).

Proof of (3.5). For $t = 0$, the result is obvious from (3.4). Assume that the numerical solution U^{n-1} at t_{n-1} is bounded. Therefore,

$$\begin{aligned} \|U^n\|_\infty &\le \|U^n - u^n\|_\infty + \|u^n\|_\infty \le \|\xi_1^n\|_\infty + \|\Lambda_1^n\|_\infty + \|u^n\|_\infty \\ &\le Ch^{-\frac{N}{2}}(\|\xi_1^n\|_0 + \|\Lambda_1^n\|_0) + K \\ &\le C\left(\frac{\delta_t}{h^{N/2}} + h^{2-\frac{N}{2}}\right) + K. \end{aligned} \tag{3.6}$$

Thus,

$$\|U^n\|_\infty \le K + 1.$$

Similarly, we show that

$$\|V^n\|_\infty \le K + 1 \quad \text{and} \quad \|W^n\|_\infty \le K + 1.$$

Hence, the inequality is true for every n. $\square$

3.5. Numerical results. The numerical scheme for the system (1.2) is implemented using Freefem++ library functions [26], and the system of algebraic equations are solved using UMFPACK [17, 18]. The computations are performed on the square domain $\Omega = [0, 1]^2$. All computations are carried out using an Intel Core i7-7700 CPU with 3.60Hz and 8 GB RAM.

3.6. Convergence study. In the following cancer invasion models, the system (3.7) represents a model with linear diffusion operators, whereas (3.8) represents a model with

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TABLE 3.1
Errors and order of convergence with the error norms E_1 and E_2 for Example 3.2.

	DOF	E_1	Order	E_2	Order
	1681	4.5042e-08	—	4.7567e-07	—
	3721	1.9297e-08	2.0905	2.0800e-07	2.0401
	6561	1.0690e-08	2.0532	1.1609e-07	2.0272
u	10201	6.7873e-09	2.0356	7.3975e-08	2.0193
	14641	4.6915e-09	2.0256	5.1239e-08	2.0142
	19881	3.4366e-09	2.0192	3.7582e-08	2.0107
	1681	6.9363e-06	—	4.4149e-05	—
	3721	3.0843e-06	1.9988	1.9633e-05	1.9986
	6561	1.7352e-06	1.9994	1.1046e-05	1.9993
v	10201	1.1106e-06	1.9996	7.0699e-06	1.9996
	14641	7.7132e-07	1.9997	4.9099e-06	1.9997
	19881	5.6670e-07	1.9998	3.6074e-06	1.9998
	1681	7.0027e-06	—	4.4393e-05	—
	3721	3.1125e-06	1.9998	1.9732e-05	1.9998
	6561	1.7508e-06	1.9999	1.1100e-05	1.9999
w	10201	1.1205e-06	1.9999	7.1039e-06	1.9999
	14641	7.7816e-07	2.0000	4.9333e-06	2.0000
	19881	5.7171e-07	2.0000	3.6245e-06	1.9999

nonlinear diffusion operators:

$$\begin{aligned} &u_t - d_1\Delta u - \lambda u(1-u-v) + \chi uw = f_u, && (x,t)\in Q_T,\\ &v_t - \rho v(1-u-v) + \eta vw = f_v, && (x,t)\in Q_T,\\ &w_t - d_2\Delta w - \alpha u(1-w) + \beta w = f_w, && (x,t)\in Q_T, \end{aligned} \tag{3.7}$$

and

$$\begin{aligned} &u_t - d_1\nabla((1+u)\nabla u) - \lambda u(1-u-v) + \chi uw = f_u, && (x,t)\in Q_T,\\ &v_t - \rho v(1-u-v) + \eta vw = f_v, && (x,t)\in Q_T,\\ &w_t - d_2\nabla((1+w)^2\nabla w - \alpha u(1-w) + \beta w = f_w, && (x,t)\in Q_T, \end{aligned} \tag{3.8}$$

where f_u, f_v, and f_w are chosen in such a way that the functions u, v, w in Examples 3.2–3.3 satisfy (3.7) and (3.8).

EXAMPLE 3.2.

$$u = t(x-x^2)(y-y^2), \quad v = (1-t)(x-x^2)(y-y^2), \quad \text{and} \quad w = (1+t)(x-x^2)(y-y^2).$$

EXAMPLE 3.3.

$$u = e^t \cos x \sin y, \quad v = e^{-t}\cos x \cos y, \quad \text{and} \quad w = e^t \sin x \sin y.$$

Furthermore, we choose the parameter values of the models (3.7) and (3.8) as

$$d_1 = 0.001,\ \lambda = 0.25,\ \chi = 0.1,\ \rho = 0.25,\ \eta = 10,\ d_3 = 0.005,\ \alpha = 0.1,\ \text{and}\ \beta = 0.05.$$

A set of finite element computations on uniformly refined meshes with time step $\delta_t = h^2$ are performed. In addition, we use the following errors norms to compare the discretization

TABLE 3.2
Errors and order of convergence with the error norms E_1 and E_2 for Example 3.3.

	DOF	E_1	Order	E_2	Order
	1681	1.0537e-05	—	6.9414e-05	—
	3721	4.6866e-06	1.9983	3.0924e-05	1.9941
	6561	2.6368e-06	1.9993	1.7409e-05	1.9971
u	10201	1.6876e-06	1.9996	1.1146e-05	1.9982
	14641	1.1720e-06	1.9998	7.7422e-06	1.9988
	19881	8.6109e-07	1.9999	5.6888e-06	1.9991
	1681	1.0545e-05	—	7.0327e-05	—
	3721	4.6929e-06	1.9967	4.6929e-06	1.9919
	6561	2.6410e-06	1.9985	2.6410e-06	1.9960
v	10201	1.6905e-06	1.9991	1.6905e-06	1.9976
	14641	1.1741e-06	1.9995	1.1741e-06	1.9984
	19881	8.6264e-07	1.9996	8.6264e-07	1.9988
	1681	6.2387e-06	—	3.9607e-05	—
	3721	2.7720e-06	2.0007	1.7597e-05	2.0009
	6561	1.5591e-06	2.0004	9.8968e-06	2.0005
w	10201	9.9776e-07	2.0002	6.3335e-06	2.0003
	14641	6.9287e-07	2.0002	4.3981e-06	2.0002
	19881	5.0904e-07	2.0001	3.2312e-06	2.0001

errors and the order of convergence of the proposed numerical scheme,

$$E_1 := L^2(0,T;L^2(\Omega)) = \left(\int_0^T \left(\|u(t)-u_h(t)\|^2_{L^2(\Omega)}\right)dt\right)^{\frac{1}{2}},$$
$$E_2 := L^\infty(0,T;L^2(\Omega)) = \sup_{i=1,2,3,\ldots,n} \|u(t^i)-u_h(t^i)\|_{L^2(\Omega)}.$$

Finally, the computational results are presented in Tables 3.1–3.4 and Figures 3.1–3.4. It is clearly confirmed that the optimal order of convergence (approximately two) is attained for both cases (linear and nonlinear diffusion operators) with piecewise linear triangular P_1 finite elements .

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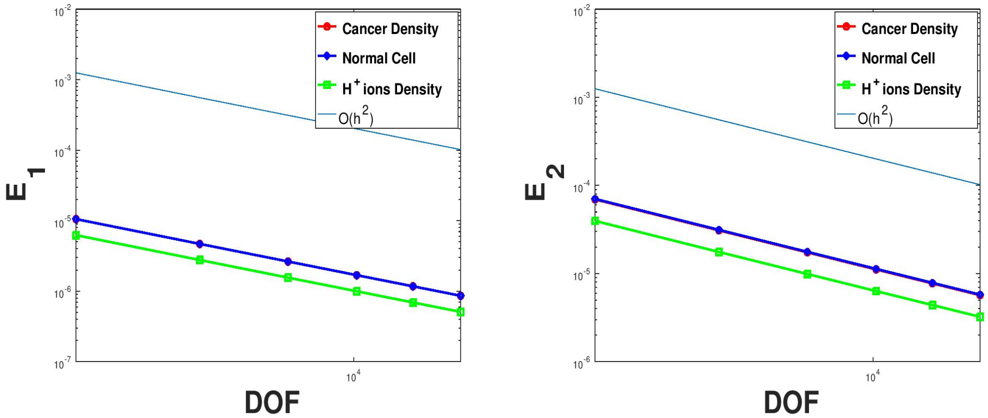
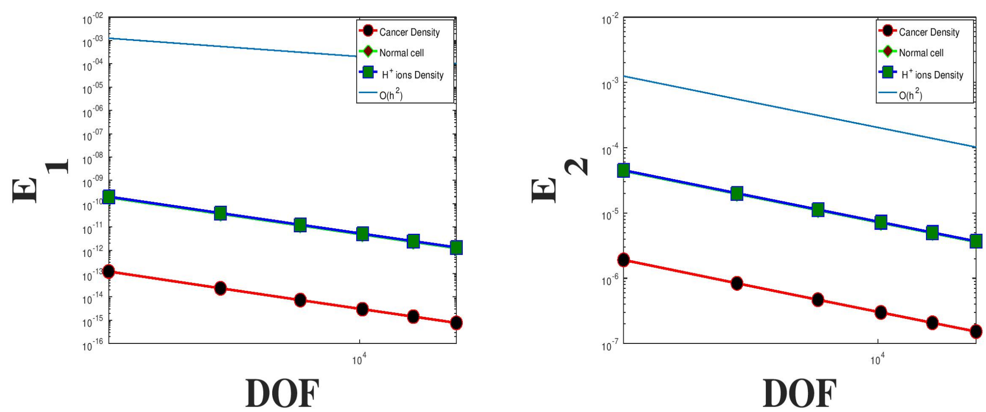


(i) (ii)

FIG. 3.2. *Error plots of the cancer cell density, the normal cell density, and the H^+ions density obtained with different mesh levels. Panel (i) and (ii), respectively, represent the logarithmic values the error norms of E_1 and E_2 of the solution of the system* (3.7) *against the logarithmic value of the DOF for Example* 3.3.



(i) (ii)

FIG. 3.3. *Error plots of the cancer cell density, the normal cell censity, and the H^+ions density obtained with different mesh levels. Panel (i) and (ii), respectively, represent the logarithmic values of the error norms E_1 and E_2 of the solution of the system* (3.8) *against the logarithmic value of the DOF for Example* 3.2 *with nonlinear diffusion.*

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TABLE 3.3
Errors and order of convergence with the error norms E_1 and E_2 for Example 3.2 with nonlinear diffusion.

	DOF	E_1	Order	E_2	Order
	1681	1.2346e-13	—	1.9090e-06	—
	3721	2.3467e-14	2.0236	8.3750e-07	2.0320
	6561	7.3113e-15	2.0134	4.6869e-07	2.0178
u	10201	2.9726e-15	2.0083	2.9928e-07	2.0101
	14641	1.4281e-15	2.0052	2.0765e-07	2.0048
	19881	7.6942e-16	2.0030	1.5257e-07	1.9996
	1681	1.8494e-10	—	4.4149e-05	—
	3721	3.6587e-11	1.9991	1.9633e-05	1.9986
	6561	1.1584e-11	1.9994	1.1046e-05	1.9993
v	10201	4.7464e-12	1.9996	7.0699e-06	1.9996
	14641	2.2895e-12	1.9997	4.9099e-06	1.9997
	19881	1.2360e-12	1.9997	3.6074e-06	1.9998
	1681	1.9933e-10	—	4.5149e-05	—
	3721	3.9373e-11	2.0000	2.0066e-05	2.0001
	6561	1.2458e-11	2.0000	1.1287e-05	2.0001
w	10201	5.1026e-12	2.0000	7.2236e-06	2.0000
	14641	2.4607e-12	2.0000	5.0164e-06	2.0000
	19881	1.3282e-12	2.0000	3.6855e-06	2.0000

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TABLE 3.4
Errors and order of convergence with the error norms E_1 and E_2 for Example 3.3 with nonlinear diffusion.

	DOF	E_1	Order	E_2	Order
	1681	3.4667e-10	—	6.9414e-05	—
	3721	6.8420e-11	1.9983	3.0924e-05	1.9941
	6561	2.1637e-11	1.9993	1.7409e-05	1.9971
u	10201	8.8602e-12	1.9996	1.1146e-05	1.9982
	14641	4.2722e-12	1.9998	7.7422e-06	1.9988
	19881	2.3058e-12	1.9999	5.6888e-06	1.9991
	1681	3.3635e-10	—	7.0327e-05	—
	3721	6.6524e-11	1.9992	3.1359e-05	1.9919
	6561	2.1052e-11	1.9999	1.7660e-05	1.9960
v	10201	8.6229e-12	2.0000	1.6905e-06	1.9976
	14641	4.1582e-12	2.0001	7.8552e-06	1.9984
	19881	2.2444e-12	2.0001	5.7722e-06	1.9988
	1681	1.6587e-10	—	4.3215e-05	—
	3721	3.2721e-11	2.0008	1.9198e-05	2.0012
	6561	1.0348e-11	2.0004	1.0797e-05	2.0006
w	10201	4.2376e-12	2.0002	6.9094e-06	2.0003
	14641	2.0433e-12	2.0002	4.7980e-06	2.0003
	19881	1.1029e-12	2.0001	3.5250e-06	2.0001

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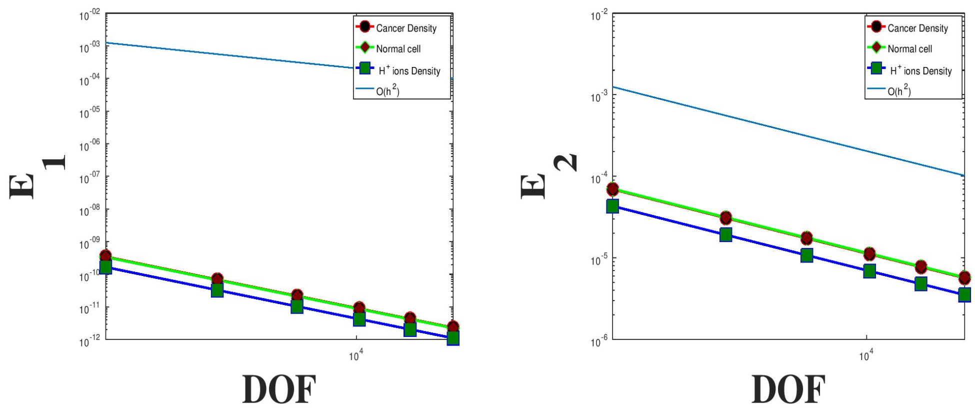

(i) (ii)

FIG. 3.4. *Error plots of the cancer cell density, the normal cell density, the H^+ions density obtained with different mesh levels. Panel (i) and (ii), respectively, represent the logarithmic values of the error norms E_1 and E_2 of the solution of the system* (3.8) *against the logarithmic value of the DOFs for Example 3.3 with nonlinear diffusion.*

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