Existence result and free boundary limit of a tumor growth model with necrotic core

Samiha Belmor

October 14, 2022

Abstract

We analyze a system of cross-diffusion equations that models the growth of an avascular-tumor spheroid. The model incorporates two nonlinear diffusion effects, degeneracy type and superdiffusion. We prove the global existence of weak solutions and justify the convergence towards the free boundary problem of the Hele-Shaw type when the pressure gets stiff. We also investigate the convergence rate of the solutions in $L^1$–Lebesgue spaces.

1 Introduction

We consider a compressible model of tumor growth with initial data. It takes the following form

\begin{align}
\partial_t n_l - \text{div}(n_l \nabla p) &= G(c)n_l - K_D(c)n_l, \quad \text{in } Q_T \equiv Q \times (0, T), \\
\partial_t n_d - \text{div}(n_d \nabla p) &= K_D(c)n_l - \mu n_d, \quad \text{in } Q_T \equiv Q \times (0, T), \\
\partial_t c &= d\Delta c - f(c)n_l, \quad \text{in } Q_T, \\
n_l \nabla p \cdot n &= n_d \nabla p \cdot n = 0, \quad \text{on } \Sigma_T \equiv \partial Q \times (0, T), \\
c &= c_\infty \text{ on } \Sigma_T, \\
(n_l|_{t=0}, n_d|_{t=0}, c|_{t=0}) &= (n_0^l, n_0^d, c^0),
\end{align}

where $Q$ is a bounded domain in $\mathbb{R}^d$ with Lipschitz boundary $\partial Q$, $T$ is a positive number, $n$ is the unit outward normal to $\partial Q$ and

\begin{equation}
n = n_l + n_d, \quad P = p_\kappa = \kappa \frac{n}{1-n}, \quad \kappa \geq 0,
\end{equation}

We assume there is a continuous motion of cells within the tumor, we indicate this movement by the velocity fields $\vec{v}$ so that by Darcy’s law [17], we have

\begin{equation}
\vec{v} = -\nabla P \quad \text{in } Q, \quad \kappa > 0.
\end{equation}

This problem was proposed by Ward and King in [1,2], and modified later by Shangbin [3] which assumes that the tumor is ball-shaped and all the functions are radially symmetric in space. In the model the cells are classified in two phases: $n_l$ refer to live tumor cells and $n_d$ refer to dead tumor cells, $c$ represents the concentration of nutrients that the live cells receive from its boundary, $d$ is the diffusion coefficient of nutrient which is supposed to be a positive constant. $G(c)$ is the growth rate of tumor cells when nutrient supplement is at level $c$, $K_D(c)$ is the death rate of tumor cells when nutrient supplement at level $c$, the dead cells are removed at rate $\mu$ which is a positive constant independent of $c$. When the oxygen and nutrients are insufficient in the central regions due to the lack of the vessel formation, the cell proliferation rate decrease under the activity of cell killing agents, the inner core of the tumor will therefore enter into a necrotic state. Note that necrotic is not a reversible process, which means dead cells are never be live cells again, and only live cells consume nutrients with the consumption rate $f(c)$. Mathematically we have the following biological assumptions on the growth rate and the reaction terms, which are quite similar to the one stated in [3].

2020 Mathematics subject classification. Primary: 35B45, 35B65, 35D30, 35Q92

Key words and phrases. Existence; incompressible limit; free boundary problem; two cell population; rate of convergence; necrotic.
• (A1) \( f \in C^1[0, \infty), f' > 0 \), and \( f(0) = 0 \).
• (A2) \( \gamma \in C^1[0, \infty), \gamma' > 0 \), and \( \gamma(0) = 0 \).
• (A3) \( D_s \in C^1[0, \infty), K_s < 0, K_s(c) \geq 0 \) for \( c \geq 0 \).
• (A 4) \( \mu > K_s(0) > 0 \).

The condition (A4) means that when there is no nutrient the dead core may not necessarily increase. We shall not call the expressions of the functions \( f(c), \gamma(c) \), and \( K_s(c) \) here, for the reader references, we refer to [1, 2].

Continuum mechanical models are used in the literature to describe the mechanical properties of tissue growth, different models describing tumors consisting of different kinds of cells, we mention, Bertsch et al. [22] considered model for healthy and tumor cells. Jonathan et al. [23] constructed a model for proliferating cells and quiescent cells. Model of non-necrotic tumors was given by Byrne et al. in [24]. One can also model tissue growth by considering free boundary models [25, 26] where the tumor treated as an expanding domain in (t) and describe its movement and shape by the motion of the boundary. A specific type of convergence established via the so-called incompressible limit has been used to draw a connection between these two types of models.

The rigorous justification of the incompressible limit has been studied vastly in different contexts relying on the generality of the system, the type of the system (Navier-Stokes model [12], Cahn-Hilliard type model [13], Cahn-Hilliard-Brinkman type model [13], Keller-Segel model [15], Patlak-Keller-Segel model [16] or Parabolic type model [17]), the modeling context (Darcy’s law, or Brinkman’s law [18]), the pressure law (power-law [19], or singular law [20]) as well as the type of the initial data considered (well-prepared or ill-prepared). The mathematical justification of the incompressible limit was first initiated by Bénilan and Crandall [21] for the filtration equations \( \partial_t n = \Delta \rho \) where \( \rho(s) = s^\gamma \) with ill-prepared initial data. This work are then extended by several authors in different settings, for recent work we mention [9, 19, 27, 28, 29]. The limit model in each case is a Hele-Shaw type free boundary model.

The core of the analysis in this paper is to study the existence assertion for (1)-(6), and establish the convergence rate of the solution \( (n_0, c_0) \).

We note that by combining (1) and (2), we obtain the total density \( n \) equation, which solves the problem

\[
\partial_t n - \Delta (H_n) = G(c) n_t - \mu n_d \equiv R_n \quad \text{in } Q_T.
\]  

where

\[
H_n := \int_0^{a_n} s \rho_k(s) ds = p_k + \kappa \ln (1 - n_k). \tag{9}
\]

As a result, if we formally set \( \kappa \to 0 \), we will encounter the following problem

\[
\partial_t n_0 - \Delta p_0 = G(c_0) n_{t,0} - \mu n_{d,0} \equiv R_0 \quad \text{in } D'(Q_T),
\]

\[
\partial_t n_{t,0} - \text{div}(n_{t,0} \nabla p_0) = G(c) n_{t,0} - K_s(c_0) n_{t,0} \quad \text{in } D'(Q_T)
\]

\[
\partial_t n_{d,0} - \text{div}(n_{d,0} \nabla p_0) = K_s(c_0) n_{t,0} - \mu n_{d,0} \quad \text{in } D'(Q_T)
\]

\[
\frac{\partial c_0}{\partial t} = d \Delta c_0 - f(c_0) n_{t,0} \quad \text{in } Q_T
\]

\[
n_{t,0} \nabla p_0 \cdot n = n_{d,0} \nabla p_0 \cdot n = 0 \quad \text{on } \Sigma_T \equiv \partial Q \times (0, T),
\]

\[
\nabla p_0 \cdot n = 0 \quad \text{on } \Sigma_T,
\]

\[
c = c_\infty \text{ on } \Sigma_T,
\]

\[
n_0(x, 0) = n_{t,0} + n_{d,0} \text{ on } Q.
\]

Multiplying the total density equation (8) by \( p'(n_k) \) we find an equation of the pressure

\[
\frac{\partial p_k}{\partial t} - \left( \frac{p_k}{\kappa} + p_k \right) \Delta p_k - |\nabla p_k|^2 = \frac{1}{\kappa} (p_k + \kappa)^2 (n_{t,k} G(c_k) - \mu n_{d,k}). \tag{10}
\]

Passing formally to the limit \( \kappa \to 0 \) into (10), we can reach the so-called complementarity relation.

\[
- p_0^2 \Delta p_0 = p_0^2 (n_{t,0} G(c_0) - \mu n_{d,0}). \tag{11}
\]
It is not difficult to derive from (7) that when \( \kappa \) goes to 0, we expect having the relation \((1 - \eta_0)\eta_0 = 0\) in the sens of distribution. This relation leads to decomposition of the domain in two parts. \( P(t) = \{ x, \ p(t, x) > 0 \} \) and its complementary \( P'(t) = \{ x, \ p(t, x) = 0 \} \). Unlike the complementarity relation that was established in [8], the authors were unable to recover the usual relation due to the lack of compactness in time, nevertheless, using the Aubin-Lions theorem, we may prove the relation (11) directly. The proof of the convergence follows from the following estimate

\[
\int_{Q_T} (\partial_t H_\kappa(n_\kappa))^2 + \sup_{t \in \left[0, T\right]} \int_Q |\nabla H_\kappa(n_\kappa)|^2 \leq C, \tag{12}
\]

that is \( H_\kappa \) is bounded function in \( L^2(0, T; W^{1,2}(Q)) \). Before we introduce our complete results, the following assumptions about the model’s components are made throughout this paper: We assume that the model is equipped with non-negative and ill-prepared initial data in the sens that

\[
P_\kappa^0 = p(n_\kappa^0) \in L^\infty(Q), \quad n_\kappa \in L^1(Q), \quad |n_\kappa - n_\kappa^0|_{L^1(Q)} \rightarrow 0 \quad \text{as } \kappa \rightarrow 0. \tag{13}
\]

\[
c_\kappa \in L^1(Q), \quad |c_\kappa - c_\kappa^0|_{L^1(Q)} \rightarrow 0 \quad \text{as } \kappa \rightarrow 0. \tag{14}
\]

**Main results.** Before stating our main result, we first introduce the definition of the weak solution for the initial-boundary value problem of parabolic system.

**Definition 1.1.** (Weak solution) We call that \((n_1, n_d, c)\) a solution of system (1)-(6) on \((0, T)\), if the components \((n_1, n_d, c)\) are all non-negative, and satisfy

- \((H 1)\) \( n_1, n_d, c \in L^\infty(Q_T) \),
- \((H 2)\) \( p, c \in L^2((0, T); W^{1,2}(Q)) \),

and satisfy (1)-(6) in distributional sense. More precisely,

\[
\int_Q (n_1 \varphi)|_{\xi = t} - \int_Q n_1^0 \varphi|_{\xi = 0} + \int_{Q_t} (n_1 \nabla p \nabla \varphi) dx dt = \int_{Q_t} R_1 \varphi dx dt, \tag{15}
\]

for all \( t \in [0, T] \) and \( \varphi \in C^2(\overline{Q_T}) \) such that \( \varphi \geq 0 \) in \( Q_T \) and \( \varphi|_{\partial Q} = 0 \). Similarly, for \( n_d \) and \( c \) we have

\[
\int_Q (n_d \varphi)|_{\xi = t} - \int_Q n_d^0 \varphi|_{\xi = 0} + \int_{Q_t} (n_d \nabla p \nabla \varphi) dx dt = \int_{Q_t} R_2 \varphi dx dt, \tag{16}
\]

\[
\int_Q (c \varphi)|_{\xi = t} - \int_Q c^0 \varphi|_{\xi = 0} - d \int_{Q_t} (c \partial_\nu \varphi + c \Delta \varphi) dx dt + \int_0^t \int_{\partial Q} c_\infty \partial_\nu \varphi = \int_{Q_t} F \varphi dx dt, \tag{17}
\]

where, \( R_1 \equiv G(c)n_1 - K_D(c)n_1, R_2 \equiv K_D(c)n_1 - \mu n_d, F = f(c)n_1, \) and \( \partial_\nu \) is the outward unit normal derivative at the boundary. Note that since we are looking for solutions \((n_1, n_d, c)\) with

\[
(n_1, n_d, c) \in (W^{1,1}((0, T), W^{-1,1}(Q)))^3,
\]

we have

\[
(n_1, n_d, c) \in (C((0, T), W^{-1,1}(Q)))^3.
\]

**Theorem 1.1.** (Existence Theorem) Assume the initial data are non-negative and smooth, namely, that

\((H1)\) \( c^0 \in L^\infty(Q) \cap H^1(Q) \)

\((H2)\) \( n_1^0 \in L^\infty(Q), \quad n_d^0, n_0^0 \in L^\infty(Q) \cap W_0^{1,2}(Q), \)

\((H3)\) \( n_1^0, n_d^0, c^0 \geq 0, \quad \|n_1^0\|_{L^\infty(Q)} = 1 - \theta < 1, \) for some \( \theta \in (0, 1) \).

Then there is a weak solution to (1)-(6). We set

\[
c_{\text{max}} := \max\{|c_0|_{L^\infty(\Omega)}, |c_\infty|_{L^\infty(\partial \Omega)}\}, \quad G_m = \sup_{\xi \in [0, c_{\text{max}}]} G(\xi), \quad F_m = \sup_{\xi \in [0, c_{\text{max}}]} f(\xi). \tag{18}
\]
We recall that the global existence result was considered in [30] for systems similar to (1)-(6), but with different reaction terms and boundary conditions. Here we take another approach to drive the existence results.

**Theorem 1.2.** (Incompressible Limit) Let the assumptions of Theorem 1.1 hold. Assume:

- \( G'(\xi) < -\alpha, \quad \alpha > 0, \quad \text{and} \quad \xi \in [0, c_{\text{max}}] \).
- \( n_0 \) is measurable and, \( \int_{\Omega} \int_{0}^{n_0} H_k(\xi) d\xi < \infty \).

Let’s denote by \( (n_k, n_{1,k}, n_{d,k}, c_k) \) the solution obtained in Theorem 1.1. Then as \( k \to 0 \), we have the following convergences:

\[
(n_k, n_{1,k}, n_{d,k}, c_k) \to (n_0, n_{1,0}, n_{d,0}, c_0) \quad \text{weakly in} \quad (C(0, T; L^2(Q)))^4,
\]

\[
H_k \to p_0 \quad \text{strongly in} \quad C(0, T; L^1(Q)),
\]

\[
\nabla p_k \to \nabla p_0 \quad \text{weakly in} \quad L^2(0, T; W^{1,2}(Q)),
\]

\[
\nabla p_k \to \nabla p_0 \quad \text{strongly in} \quad L^2(0, T; (L^2(Q))^d),
\]

Let’s denote by \( (n_0, n_{1,0}, n_{d,0}, c_0) \) the limit solution, which satisfies

\[
- \int_{Q_T} n_0 \partial_t \phi dx dt + \int_{Q_T} \nabla p_0 \nabla \phi dx dt = \int_{Q_T} R_0 \phi dx dt
\]

\[
- \int_{Q_T} n_{1,0} \partial_t \phi dx dt + \int_{Q_T} n_{1,0} \nabla p_0 \nabla \phi dx dt = \int_{Q_T} R_{1,0} \phi dx dt
\]

\[
- \int_{Q_T} n_{d,0} \partial_t \phi dx dt + \int_{Q_T} n_{d,0} \nabla p_0 \nabla \phi dx dt = \int_{Q_T} R_{2,0} \phi dx dt
\]

\[
- \int_{Q_T} c_0 \partial_t \phi dx dt + d \int_{Q_T} \nabla c_0 \nabla \phi dx dt = -\int_{Q_T} f(c_0) n_{1,0} \phi dx dt
\]

**Theorem 1.3.** (Convergence rate) Under the assumptions of Theorem 1.2 and the assumptions 13-14. Then for all \( T > 0 \) there exists a unique pair function \( (n_k, c_k) \in C^1(0, T; L^1(Q)) \) such that \( (n_k, c_k) \) converges strongly to \( (n_0, c_0) \) in \( L^\infty(0, T; L^1(Q)) \) with the following convergence rate

\[
\sup_{t \in (0, T)} \|n_k(t) - n_0(t)\|_{L^1(Q)} \leq \|n_k(0) - n_0(0)\|_{L^1(Q)} + G_{mf} \|n_k\|_{L^1(Q)},
\]

\[
\sup_{t \in (0, T)} \|c_k(t) - c_0(t)\|_{L^1(Q)} \leq \|c_k(0) - c_0(0)\|_{L^1(Q)} + F_{mf} \|n_k\|_{L^1(Q)}.
\]

### 1.1 A family of approximate problems and proof of the Theorem 1.1

We approximate the degenerate problem (1)-(6) by a sequence of non-degenerate parabolic problem, and show that their solutions converge to the solution of the degenerate problem when the regularization parameter tends to zero. The regularization is adapted from [4]. For small \( \epsilon > 0 \) we define:

\[
\chi_{\epsilon}(n) := \begin{cases} \kappa \epsilon & \text{if } n < 0 \\ \kappa \frac{n+\epsilon}{1-n^2} & \text{if } 0 \leq n \leq 1 - \epsilon \\ \kappa \frac{1}{\epsilon^2} & \text{if } n \geq 1 - \epsilon \\
\end{cases}
\]

\[
\chi_{\epsilon,\gamma}(n) := \begin{cases} \kappa \epsilon & \text{if } n < 0 \\ \kappa \frac{(2+\epsilon)}{(1-n^2)} & \text{if } 0 \leq n \leq 1 - \epsilon \\ \kappa \frac{1}{\epsilon^2} & \text{if } n \geq 1 - \epsilon \\
\end{cases}
\]
thus the approximation of the system (33)-(39) is given by
\[ \begin{align*}
\partial_t n &= \text{div}(\chi(n)\nabla n) + G(c)\mu n|c| - \mu|n_{d,e}| \equiv R_e, \quad \text{in } \Sigma_T \equiv \partial Q \times (0,T) \\
\partial_t n_{d,e} &= \text{div}(\chi(n_{d,e})\nabla n_{d,e}) + G(c)\mu n_{d,e} - K_D(c)\mu n_{d,e}, \quad \text{in } \Sigma_T \equiv \partial Q \times (0,T) \\
\partial_t c_e &= d\Delta c_e - f(c_e)n_{d,e}, \quad \text{in } Q_T \\
\chi(n)\partial_t n &= \chi(n)\partial_t n_{d,e} = \chi(n)\partial_t n_{d,e} = 0 \quad \text{on } \Sigma_T \equiv \partial Q \times (0,T),
\end{align*} \]

which is non-degenerate parabolic. Therefore, the problem (33)-(39) possesses a solution, which we denote by \((n_e, n_{d,e}, c_e)\).

**Proof.** We first show the non-negativity and boundedness of all components of the solution to the non-degenerate approximation using the comparison principle (see, [4]). Per hypothesis, the boundary/initial data for our system are non-negative. Moreover, we see that
\[ R_1(0, n_{d,e}, c_e) = f(0) = 0, \]
thus, zero is subsolution to \(n_{d,e}\) and \(c_e\). According to (A3), and since \(n_{1,e}\) and \(c_e\) are non-negative, we have
\[ R_2(n_{1,e}, 0, c_e) = K_D(c_e)n_{1,e} \geq 0, \]
we conclude the non-negativity of \(n_{d,e}\). The non-negativity of \(n_e\) is an immediate consequence. Now we will establish the \(L^\infty\) a priori estimates for \(n_e\) using the so-called true upper-barriers technique; we set
\[ n_e = n_{1,e} + n_{d,e}, \]
we introduce the barrier function \(n_\omega = \omega + 1\), where \(\omega\) is a solution of the following elliptic problem
\[ \begin{align*}
\Delta \omega &= -1 \quad \text{in } Q, \\
\omega|_{\partial Q} &= 0.
\end{align*} \]
The maximum principle for elliptic equations [5] implies that \(\omega \geq 0\) in \(Q\) and
\[ 1 \leq n_\omega(x) \leq 1 + K, \quad x \in Q, \]
for some constant \(K \geq 0\). Furthermore, we observe that \(n_\omega^0 = n_e|_{t=0} \leq n_\omega|_{t=0}, \quad 0 = n_\omega|_{\partial Q} \leq n_\omega|_{\partial Q}\).

Since \(n_\omega\) is a time-independent function, it follows that
\[ \begin{align*}
\partial_t n_\omega - \text{div}(\chi(n_\omega)\nabla n_\omega) - G(c_e)n_{1,e} + \mu n_{d,e} &= 0 + \frac{k}{\epsilon^2} - G(c_e)n_\omega \geq \frac{k}{\epsilon^2} - G_m(1 + K) \geq 0 \\
&= \partial_t n_e - \text{div}(\chi(n_e)\nabla n_e) - G(c_e)n_{1,e} + \mu n_{d,e}
\end{align*} \]
for all sufficiently small \(\epsilon > 0\). Hence \(n_\omega\) is an upper-solution for the total density \(n\) i.e. \(n_\omega \geq n_e\). It follows that, by the parabolic comparison principle there exists an \(\epsilon_0^*\) such that
\[ 0 \leq n_e \leq C_\epsilon^* \]
for all \(0 < \epsilon < \epsilon_0^*\), and \(C_\epsilon^*\) is a positive constant, which also implies
\[ 0 \leq n_{1,e}, n_{d,e} \leq C_\epsilon^*. \]
To show the uniform boundedness of \(c_e\), we define the constant \(c_{\max} := \max\{||d||_{L^\infty(Q)}, |c_\infty|_{L^\infty(\partial Q)}\}\)
\[ \partial_t c_{\max} - d\Delta c_{\max} + f(c_{\max})n_{1,e} = f(c_{\max})n_{1,e} \geq 0, \]
where we used the nonnegativity of \(n_{1,e}\), this shows that if \(c_{\max}\) is sufficiently large, it is an upper solutions for \(c_e\), and, thus, the uniform boundedness using the comparison principle. \(\square\)
The following lemma shows that the total population \( n \) is uniformly bounded away from the singularity, i.e., the case \( n = 1 \) is never attained for all sufficiently small \( \varepsilon > 0 \).

**Lemma 1.1.** Under the hypothesis of Theorem (11), there exist \( \rho > 0 \) and \( \varepsilon_0 > 0 \) such that \( n_\varepsilon \leq 1 - \rho \) in \( Q_T \) for all \( 0 < \varepsilon < \varepsilon_0 \).

**Proof.** Let \( \varepsilon_0 > 0 \), we construct a suitable barrier function and consider the elliptic problem

\[
\begin{align*}
\Delta \varphi(x) &= -\lambda_1, \quad x \in Q, \\
\varphi(x)|_{\partial Q} &= \lambda_2.
\end{align*}
\]

(40)

The constants \( \lambda_1 \) and \( \lambda_2 \) are defined by

\[
\lambda_1 := \sup_{0 < \varepsilon < \varepsilon_0} \left\{ \| R_\varepsilon \|_{L^\infty(Q_T)} \right\},
\]

\[
\lambda_2 := \sup_{0 < \varepsilon < \varepsilon_0} \left\{ \| H_\varepsilon(n^0) \|_{L^\infty(Q)} \right\},
\]

where \( H_\varepsilon \) is given by

\[
H_\varepsilon(n^0) = \int_0^{n^0} \chi_\varepsilon(\xi)d\xi = \int_0^{n^0} \frac{\xi + \varepsilon}{(1 - \xi)^2}d\xi.
\]

(41)

We point out that for sufficiently small \( \varepsilon_1 < \varepsilon_0 \) the constants \( \lambda_1 \) and \( \lambda_2 \) can be chosen uniform for all \( 0 < \varepsilon_1 < \varepsilon_0 \). Moreover, the solution \( \varphi \) of (40) is bounded on \( Q \), and by the maximum principle for elliptic problems \([6]\) it follows that \( \varphi > \lambda_2 \) in \( Q \). For \( \varepsilon < \varepsilon_1 \) we define \( Y_\varepsilon := H_\varepsilon^{-1}(\varphi) \) and observe that

\[
\partial_t Y_\varepsilon - \Delta (H_\varepsilon(Y_\varepsilon)) = \lambda_1 = \| R_\varepsilon \|_{L^\infty(Q_T)} \geq \partial_t n_\varepsilon - \Delta (H_\varepsilon(n_\varepsilon)),
\]

in \( Q_T \). Furthermore, the boundary conditions indicate that

\[
Y_\varepsilon|_{\partial Q} = H_\varepsilon^{-1}(\varphi)|_{\partial Q} = H_\varepsilon^{-1}(\lambda_2) \geq n_\varepsilon|_{\partial Q} = 0.
\]

Since the function \( H_\varepsilon^{-1} \) is a monotone function, the initial data then satisfies

\[
Y_\varepsilon|_{t=0} = H_\varepsilon^{-1}(\varphi)|_{t=0} \geq H_\varepsilon^{-1}(\lambda_2) \geq H_\varepsilon^{-1}(H_\varepsilon(n^0)) = n^0.
\]

As a result, the function \( Y_\varepsilon \) is an upper solution for \( n_\varepsilon \). Using the fact that \( \varphi \) is bounded in \( Q \) and that \( H_\varepsilon \) converges point-wise to infinity in the interval \((0,1)\), we conclude that there exist \( 0 < \varepsilon_0 \leq \varepsilon_1 \) and \( \rho \in (0,1) \) such that \( \varepsilon_0 \leq P_\varepsilon = H_\varepsilon^{-1}(\varphi) < 1 - \rho \) for all \( 0 < \varepsilon < \varepsilon_0 \). We particularly emphasize that the nondegenerate approximations for the total population are uniformly bounded away from the singularity i.e

\[
\| n_\varepsilon(\cdot,t) \|_{L^\infty(Q)} \leq 1 - \rho, \quad \forall \varepsilon < \varepsilon_0, \quad t \geq 0.
\]

Next we show that the solutions of the regularized system (33)-(39) converge as \( \varepsilon \to 0 \) to a solution of the degenerate problem \((n,n_1,n_\mu,c)\). On the other hand we have \( \lim_{\varepsilon \to \infty} H_\varepsilon(1) = \infty \), since \( n_\varepsilon \) is uniformly bounded we can find \( \beta_\rho \) such that \( H_\varepsilon(n_\varepsilon(t,x)) \) is uniformly bounded from above and below for all sufficiently small \( \varepsilon \) i.e:

\[
0 \leq H_\varepsilon(n_\varepsilon(t,x)) < \beta_\rho < \infty.
\]

We write the equation (33) in terms of the Laplacian

\[
\partial_t n_\varepsilon = \Delta H_\varepsilon(n_\varepsilon) + R_\varepsilon
\]

where \( R_\varepsilon \in L^\infty(Q_T) \). For \( T > 0 \), we define the local parabolic cylinder \( Q_T : Q \times (T,T+1] \). From the classical theory of parabolic equations \([3]\), it is known that the solution \( n_\varepsilon \in C^\alpha(Q_T) \) for some \( \alpha > 0 \) and

\[
\| n_\varepsilon \|_{C^\alpha(Q_T)} \leq K(\| R_\varepsilon \|_{L^\infty(Q_T)}),
\]

(42)
\[ \|c_e\|_{C^0(Q_T)} \leq W(\|f_e\|_{L^\infty(Q_T)}), \]  

where \( K \) and \( W \) are non-decreasing functions that depend on the upper and lower bounds of \( H_e \) and \( c_e \) respectively. Since \( R_e \) is uniformly bounded (relatively to \( \epsilon \)), \( n_e \) is bounded in \( C^0(Q_T) \), which is compactly embedded in \( \mathcal{C}^0(Q_T) \), thus we have a strong convergence in \( \mathcal{C}(Q_T) \) in norm as \( \epsilon \to 0 \), i.e.

\[ n_e \to n_* \quad \text{in} \quad \mathcal{C}(\overline{Q}_T). \]

Since \( n_{l,e} \) and \( n_{d,e} \) are uniformly bounded under the \( L^\infty(Q_T) \) norm, it follows when \( \epsilon \to 0 \)

\[ n_{l,e} \to n_{l,*} \quad n_{d,e} \to n_{d,*} \quad \text{w} - * \quad \text{in} \quad L^\infty(Q_T). \]

We have \( n_e = n_{l,e} + n_{d,e} \) and due to the uniqueness of the limit we get \( n_* = n_{l,*} + n_{d,*} \). It remains to prove now that the functions \( n_{l,*} \) and \( n_{d,*} \) are indeed solutions of the original system. As a weak solution, \( n_{l,*} \) has to satisfy for any \( \varphi \in C^2(Q_T) \)

\[ \int_Q (n_{l,*}\varphi)|_{\xi=T} - \int_Q (n_{l,*}\varphi)|_{\xi=T} + \int_Q (\chi_{n_{l,*}}(n_*)\nabla n_\varphi \nabla \varphi) = \int_Q (G(c_\epsilon)n_{l,*} - K_d(c_\epsilon)n_{l,*}\varphi) \quad (44) \]

where \( 0 \leq \tau \leq t \leq T \). We know that for any \( \epsilon > 0 \) the following equation is verified for \( n_{l,e} \)

\[ \int_Q (n_{l,e}\varphi)|_{\xi=T} - \int_Q (n_{l,e}\varphi)|_{\xi=T} + \int_Q (\chi_{n_{l,e}}(n_e)\nabla n_e \nabla \varphi) = \int_Q (G(c_\epsilon)n_{l,e} - K_d(c_\epsilon)n_{l,e}\varphi) \quad (45) \]

As \( \epsilon \to 0 \) in (45) the convergence of the third term is not clear, thus we give estimates for the residual term

\[ Y_\epsilon = \int_{Q_T} (\chi_{n_{l,e}}(n_*)\nabla n_\varphi \nabla \varphi) - \int_{Q_T} (\chi_{n_{l,e}}(n_e)\nabla n_e \nabla \varphi) \quad (46) \]

and show that \( Y_\epsilon \) vanishes as \( \epsilon \to 0 \). The idea is we treat the region, where the total density is small enough. For \( \delta \in (0,1) \) and sufficiently small \( \epsilon_0 > 0 \) we define the open set

\[ Q_{T,\delta} = \{(x,t) \in Q : (n_{l,e} + n_{d,e}) < \delta, \quad \text{and} \quad (n_{l,*} + n_{d,*}) < \delta, \quad \forall \epsilon < \epsilon_0\}, \]

and decompose \( Y_\epsilon \) over \( Q_{T,\delta} \) and its complement \( Q_{T,\delta}^c \). To this end, we define the integrals

\[ Y_\epsilon = I_\epsilon(\delta) + J_\epsilon(\delta), \]

\[ := \int_{Q_{T,\delta}} (\chi_{n_{l,e}}(n_*)\nabla n_\varphi \nabla \varphi) - \int_{Q_{T,\delta}} (\chi_{n_{l,e}}(n_e)\nabla n_e \nabla \varphi), \]

\[ + \int_{Q_{T,\delta}} (\chi_{n_{l,e}}(n_*)\nabla n_\varphi \nabla \varphi) - \int_{Q_{T,\delta}} (\chi_{n_{l,e}}(n_e)\nabla n_e \nabla \varphi), \]

- **Estimates for \( I_\epsilon(\delta) \):** Multiplying the equation (33) by \( n_e \) and integrating over \( \Omega \), we obtain

\[ \frac{1}{2} \frac{d}{dt} \|n_e\|^2 \|L^2(\Omega) + \int_{Q_T} \chi_{n_e}(n_e) |\nabla n_e|^2 dx = \int_{Q_T} (G(c_\epsilon)n_{l,e} - \mu n_{d,e})n_e, \]

integrating over time we get

\[ \frac{1}{2} \|n_e(T)\|^2 \|L^2(\Omega) + \int_{Q_T} \chi_{n_e}(n_e) |\nabla n_e|^2 dt dx = \int_{Q_T} (G(c_\epsilon)n_{l,e} - \mu n_{d,e})n_e dt dx + \frac{1}{2} \|n_e^0\|^2 \|L^2(\Omega). \]

From the uniform boundness of the cell density, we deduce

\[ \int_{Q_T} \chi_{n_{l,e}}(n_e) |\nabla n_e|^2 dt dx \leq \int_{Q_T} \chi_{n_e}(n_e) |\nabla n_e|^2 dt dx \leq \int_{Q_T} (G(c_\epsilon)n_{l,e} - \mu n_{d,e})n_e dt dx + \frac{1}{2} \|n_e^0\|^2 \|L^2(\Omega) < C, \]

for some constant \( C > 0 \). From Lemma[11], the constant \( C \) is independent of \( \epsilon > 0 \). Moreover, we can write

\[ \chi_{n_{l,e}}(n_e) \|\nabla n_e\|^2 = \sqrt{\chi_{n_{l,e}}(n_e)} \|\chi_{n_{l,e}}(n_e) \|\nabla n_e\|^2, \]
thus we have shown
\[ \left\| \sqrt{\chi_{n,e}(n_e)} \nabla n_e \right\|_{L^2(Q_T)} \leq C, \]  
(47)
this allows us to use Hölder’s inequality to estimate the second integral of \( I_e \)
\[ \left| \int_{Q_T} \chi_{n,e}(n_e) \nabla n_e \nabla \varphi dxdt \right| \leq \left\| \chi_{n,e}(n_e) \right\|_{L^2(Q_T)} \left\| \nabla \varphi \right\|_{L^2(Q_{T,T})} \]
\[ \leq C \left( \int_{Q_{T,T}} \kappa_\delta n_e(x,t) + e \left( \frac{1}{1 - n_e(x,t)} \right)^2 \right)^{\frac{1}{2}} \leq C \frac{\delta \kappa}{(1 - 2\delta)} \| \varphi \|_{L^2((0,T),H^1(Q))}. \]
We follow the same steps to estimate the second term of the integral \( I_e(\delta) \), therefore the existence of \( \epsilon_0 > 0 \) such that for all sufficiently small \( \epsilon < \epsilon_0 \)
\[ I_e(\delta) \leq C \| \varphi \|_{L^2((0,T),H^1(Q))}. \]  
(48)
Next we estimate \( I_e(\delta) \) for \( \delta > 0 \). Restricted to the domain \( Q^c_{T,\delta} = Q_T \setminus \overline{Q_{T,\delta}} \). The solution \( n_e \) satisfy the estimate of Lemma 1.1 and (42) uniformly, and the Hölder exponent \( \alpha \) is independent of \( \epsilon > 0 \). Indeed, if \( \epsilon > 0 \) is sufficiently small, then \( n_e \) is bounded in \( Q^c_{T,\delta} \). Consequently, the term
\[ \left( \int_{Q_{T,T}} \kappa_\delta n_e(x,t) + e \left( \frac{1}{1 - n_e(x,t)} \right)^2 \right)^{\frac{1}{2}} \leq C \frac{\delta \kappa}{(1 - 2\delta)} \| \varphi \|_{L^2((0,T),H^1(Q))}. \]
is uniformly bounded from above and below by a positive constant which is independent of \( \epsilon > 0 \).
Now we need to show that
\[ \nabla n_{1,e} \rightharpoonup \nabla n_{1,s} \quad L^2(Q_{T,\delta}). \]  
(50)
From (49) and (47) we have
\[ \int_{Q^c_{T,\delta}} |\nabla n_{1,e}|^2 \leq \frac{C}{\delta}. \]
where \( C \) is a constant independent of \( \epsilon \). This implies weak-convergence for a subsequence in \( L^2(Q_{T,\delta}) \).
Moreover, we have \( \nabla n_{1,e} \) converges in \( D'(Q_{T,\delta}) \) to \( \nabla n_{1,s} \), because of the uniform convergence in \( C(Q_{T,\delta}) \), the limit in \( D'(Q_{T,\delta}) \) is unique and, thus, we obtain the weak convergence of \( \nabla n_{1,e} \) to \( \nabla n_{1,s} \) over \( Q_{T,\delta} \). To resume, from Lemma 1.1 we have as \( \epsilon \to 0 \)
\[ \chi_{n,e}(n_e) \rightharpoonup \chi_{n,s}(n_s) \quad \text{in} \quad C(Q_T), \]
and from the weak convergence of \( \nabla n_{1,e} \) to \( \nabla n_{1,s} \), we obtain finally for every \( \delta > 0 \),
\[ \lim_{\epsilon \to 0} I_e(\delta) = 0. \]
To conclude the proof, we pick any \( \eta > 0 \). From (48) we obtain that there exists \( \delta(\eta) \), and \( \epsilon \leq \epsilon_0(\delta(\eta)) \leq \frac{\eta}{4} \). Since \( I_e(\delta(\eta)) \) is independent of \( \delta \).
\[ \forall \eta > 0, \exists \epsilon(\eta) = \min \{ \epsilon_0(\eta), \epsilon_1(\eta) \}, \]  
such that for \( \epsilon \leq \epsilon(\eta) \), we have \( R_e \leq \eta \). Thus \( R_e \to 0 \) as \( \epsilon \to 0 \). The same procedure can be carried out for the remaining components.

2 Incompressible limit as \( \kappa \to 0 \) (Proof of Theorem 1.2)
This section is devoted to the proof of the incompressible limit, i.e. when \( \kappa \to 0 \). Thanks to the result proven in the previous section, cf. Theorem 1.1, we know that for each \( \kappa > 0 \) there exists
\((n_k, n_{1,k}, n_{d,k}, c_k)\) that verify (1)-(5) in a weak sense:
\[
\partial_t n_k - \Delta (H_k(n_k)) = G(c_k)n_{1,k} - \mu d_{1,k} \equiv R_k \quad \text{in } D'(Q_T),
\]
\[
\partial_t n_{1,k} - \text{div}(n_{1,k} \nabla p_k) = G(c_k)n_{1,k} - K_D(c_k)n_{1,k} \quad \text{in } D'(Q_T),
\]
\[
\partial_t n_{d,k} - \text{div}(n_{d,k} \nabla p_k) = K_D(c_k)n_{1,k} - \mu n_{d,k}, \quad \text{in } D'(Q_T),
\]
\[
\partial_t c_k = \partial c_{\epsilon_0} \equiv 0 \text{ on } \Sigma_T,
\]
\[
(n_k, n_{1,k}, n_{d,k}, c_k) \Big|_{t=0} = (n_k(0), n_{1,k}(0), n_{d,k}(0), c_k(0)) \quad \text{on } Q.
\]

From the previous section, we have
\[
n_{1,k} \geq 0, \quad n_{d,k} \geq 0, \quad c_k \geq 0, \quad n_k \leq n_{M,k}, \quad c_k \leq c_{\text{max}},
\]
where \(n_M\) is independent of \(k\). Thus as \(k \to 0\), we have
\[
(n_k, n_{1,k}, n_{d,k}, c_k) \to (n_0, n_{d,0}, n_{d,0}, c_0), \quad w^* \in L^\infty(Q_T).
\]

Lemma 2.1. Let the assumptions of Theorem 2.1 and (A1)-(A4) hold, the following estimates hold true for all \(T > 0\), with constants \(C = C(T) > 0\):
\[
\int_Q \left( \partial_t c_k \right)^2 + \sup_{t \in [0,T]} \int_Q |\nabla c_k|^2 \leq C.
\]
\[
\int_Q \left( \partial_t n_{1,k} \right)^2 + \sup_{t \in [0,T]} \int_Q |\nabla n_{1,k}|^2 \leq C.
\]
\[
\int_Q \left( \partial_t n_{d,k} \right)^2 + \sup_{t \in [0,T]} \int_Q |\nabla n_{d,k}|^2 \leq C.
\]

Proof. We multiply the equation (54) by \(\partial_t c_k\) and integrate in space and time,
\[
\int_I \int_Q \left( \partial_t c_k \right)^2 = -\frac{d}{2} \int_I \int_Q \partial_t |\nabla c_k|^2 + \int_I \int_Q \partial_t c_k f(c_k) n_{k,l},
\]
where \(0 \leq \tau \leq t \leq T\). We apply Young’s inequality on the second r.h.s
\[
= \frac{d}{2} \int_Q |\nabla c_k|^2 \big|_{\xi = \tau} + \int_I \int_Q \partial_t c_k f(c_k) n_{k,l}
\]
\[
\leq \frac{d}{2} \int_Q |\nabla c_k|^2 \big|_{\xi = \tau} + \frac{1}{2} \int_I \int_Q |\partial_t c_k|^2 + \frac{1}{2} \int_I \int_Q |f(c_k) n_{k,l}|^2.
\]

Letting \(\tau\) be zero, we get
\[
\frac{1}{2} \int_Q |\partial_t c_k|^2 + \frac{1}{2} \int_Q |\nabla c_k|^2 \big|_{\xi = t}
\]
\[
\leq \frac{1}{2} \int_Q |\nabla c_0|^2 + \frac{1}{2} \int_Q |f(c_k) n_{k,l}|^2,
\]
(18) and (58) implies that
\[
\int_Q |\partial_t c_k|^2 \leq C, \quad \sup_{t \in [0,T]} \int_Q |\nabla c_k|^2 \leq C'.
\]

To derive the estimates for \(n_{1,k}\), we multiply equation (52) by \(\partial_t n_{1,k}\) and integrate in space and time we get
\[
\int_I \int_Q |\partial_t n_{1,k}|^2 = -\int_I \int_Q n_{1,k} \nabla p_k \partial_t (\nabla n_{1,k}) + \int_I \int_Q \partial_t n_{1,k} (G(c_k)n_{1,k} - K_D(c_k)n_{1,k}).
\]
Young’s inequality implies
\[ \int_t^\tau \int_Q |\partial_\xi n_{i,k}|^2 + \frac{1}{2} \int_Q |\nabla n_{i,k}|^2 |\xi=\tau| \leq -\frac{1}{2} \int_t^\tau \int_Q |n_{i,k} \nabla p_k|^2 + \frac{1}{2} \int \int_Q |\nabla n_{i,k}|^2 |\xi=\tau| \\
+ \frac{1}{2} \int_t^\tau \int_Q |\partial_\xi n_{i,k}|^2 + \frac{1}{2} \int_t^\tau \int_Q |(G(c_k)n_{i,k} - K_D(c_k)n_{i,k})|^2, \]

letting \( \tau = 0 \), we obtain
\[ \frac{1}{2} \int_Q |\partial_\xi n_{i,k}|^2 + \frac{1}{2} \int_Q |\nabla n_{i,k}|^2 \leq \frac{1}{2} \int_Q |\nabla n_{i,k}^0|^2 + \frac{1}{2} \int_Q |(G(c_k)n_{i,k} - K_D(c_k)n_{i,k})|^2, \]

the assumptions A2-A3 lead to
\[ \int_Q |\partial_\xi n_{i,k}|^2 \leq C', \quad \sup_{t \in [0,T]} \int_Q |\nabla n_{i,k}|^2 \leq C'. \] (65)

To drive estimates for \( n_{d,k} \), we follow the same procedures as above
\[ \int_Q |\partial_t n_{d,k}|^2 \leq C', \quad \sup_{t \in [0,T]} \int_Q |\nabla n_{d,k}|^2 \leq C'. \] (66)

Our main a priori estimate is the following:

**Lemma 2.2.** Thanks to the estimates provided in Lemma 2.7, we have
\[ \int_Q |D_t H_k(n_k)|^2 + \sup_{t \in [0,T]} \int_Q |\nabla H_k(n_k)|^2 \leq C \] (67)

**Proof.** To derive the estimates for \( H_k(n_k) \), let
\[ \Psi(n_k, n_{k,\ell}, n_{k,d}, c_k) := \int_0^{n_k} \chi_k(\xi) \psi(\xi, n_{k,\ell}, n_{k,d}, c_k) d\xi, \] (68)

where \( \chi_k(\xi) = \kappa_\xi(1 - \xi)^{-2} \), and \( \psi(\xi, n_{k,\ell}, n_{k,d}, c_k) = G(c_k)n_{i,k} - \mu n_{d,k} - \xi + \xi \).

We have
\[ \int_t^\tau \int_Q |\partial_\xi \Psi(n_k, n_{i,k}, n_{d,k}, c_k)| = \int_Q |\Psi(n_k, n_{i,k}, n_{d,k}, c_k)| |_{\xi=t} - \int_Q |\Psi(n_k, n_{i,k}, n_{d,k}, c_k)| |_{\xi=\tau}. \] (69)

Multiplying the equation of the total density (51) by \( \partial_\xi (H(n_k)) \) and integrating over space and time, we obtain
\[ \int_t^\tau \int_Q \chi_k(n_k)(\partial_\xi n_k)^2 = \int_t^\tau \int_Q |\partial_\xi (H(n_k))| ^2 n_k \\
= \int_t^\tau \int_Q \text{div}(\chi_k(n_k) \nabla n_k) \partial_\xi (H(n_k)) + \int_t^\tau \int_Q |\partial_\xi (H(n_k))| \psi(n_k, n_{k,\ell}, n_{k,d}, c_k) \\
= -\int_t^\tau \int_Q \chi_k(n_k) \nabla n_k \partial_\xi (\nabla H(n_k)) + \int_t^\tau \int_Q |\partial_\xi (H(n_k))| \psi(n_k, n_{k,\ell}, n_{k,d}, c_k) \\
= -\frac{1}{2} \int_t^\tau \int_Q |\partial_\xi \chi_k(n_k) \nabla n_k|^2 + \int_t^\tau \int_Q |\partial_\xi (H(n_k))| \psi(n_k, n_{k,\ell}, n_{k,d}, c_k). \]

Where we used integration by parts in the second step. Thus, using the identity (69) we obtain
\[ \int_t^\tau \int_Q |\partial_\xi \Psi(n_k, n_{i,k}, n_{d,k}, c_k)| = \int_t^\tau \int_Q \int_0^{n_k} \chi_k(\xi) \partial_\xi \psi(\xi, n_{i,k}, n_{d,k}, c_k) + \int_t^\tau \int_Q |\partial_\xi n_k \chi_k(n_k) \psi(n_k, n_{i,k}, n_{d,k}, c_k) \\
= \int_t^\tau \int_Q \int_0^{n_k} \chi_k(\xi) (\partial_\xi n_{i,k} \partial n_{i,k} \psi(\xi, n_{i,k}, n_{d,k}, c_k) + \partial_\xi n_{d} \partial n_{i,k} \psi(\xi, n_{i,k}, n_{d,k}, c_k) \\
+ \partial_\xi \partial_\xi \psi(\xi, n_{i,k}, n_{d,k}, c_k) + \int_t^\tau \int_Q |\partial_\xi (H(n_k))| \psi(n_k, n_{i,k}, n_{d,k}, c_k), \]
it follows that
\[
\int_0^t \int_Q \chi_k(n_k)(\partial_t n_k)^2 + \frac{1}{2} \int_Q |\chi_k(n_k)\nabla n_k|^2 |_{t=\tau} \\
= \frac{1}{2} \int_Q |\chi_k(n_k)\nabla n_k|^2 |_{t=\tau} + \int_0^t \Psi(n_k,n_{1,k},n_{d,k},c_k) |_{t=\tau} - \int_0^t \Psi(n_k,n_{1,k},n_{d,k},c_k) |_{t=\tau} \\
+ \int_0^t \int_Q \chi_k(\zeta)(\partial_{\zeta} n_1 \partial_{\zeta} \psi(\zeta,n_{1,k},n_{d,k},c_k) + \partial_{\zeta} n_1 \partial_{\zeta} \psi(\zeta,n_{1,k},n_{d,k},c_k) \\
+ \partial_\zeta c \partial_\zeta \psi(\zeta,n_{1,k},n_{d,k},c_k).
\]

Lemma 1.1 and (58) imply that there exists \( \kappa_0 > 0 \) such that \( n_k \) satisfy \( n_k \leq n_M < 1 \) in \( Q_T \) for all \( 0 < \kappa < \kappa_0 \). Consequently, \( \chi_k(n_k) \) is positive and uniformly bounded from above by a constant which is independent from \( \kappa \), i.e.
\[
0 < \chi_k(n_k(t,x)) = \kappa n_k(t,x)(1 - n_k(t,x))^{-2} \leq \kappa n_M(1 - n_M)^{-2} = \frac{p(n_M)}{(1 - n_M)} \leq C, \quad (t,x) \in Q_T.
\]

Applying Young’s inequality on the last integral we can estimate
\[
\int_0^t \int_Q \chi_k(n_k)(\partial_t n_k)^2 + |\partial_\zeta c |^2 \leq C \int_0^t \int_Q (|\partial_\zeta \psi(\zeta,n_{1,k},n_{d,k},c_k) |^2 + |\partial_\zeta n_1 |^2 + |\partial_\zeta c |^2)^2 + \int_0^t \sum_i (|\partial_i \psi(\zeta,n_{1,k},n_{d,k},c_k) |^2),
\]

estimates (64), (65), (66), and (70) and setting \( \tau = 0 \), lead to
\[
\int_Q \chi_k(n_k)(\partial_t n_k)^2 \leq C', \quad \sup_{t \in [0,T]} \int_Q |\chi_k(n_k)\nabla n_k|^2 \leq C'.
\]

since \( n_k \) is uniformly bounded, we have
\[
\int_Q (\partial_t H_k(n_k))^2 = \int_Q \chi_k(n_k)(\partial_t n_k)^2 \leq ||\chi_k(n_k)||_{L^\infty(Q_T)} \int_Q \chi_k(n_k)(\partial_t n_k)^2 \leq C'
\]

which implies
\[
\int_Q (\partial_t H_k(n_k))^2 \leq C', \quad \sup_{t \in [0,T]} \int_Q |\nabla H_k(n_k)|^2 \leq C'. \tag{73}
\]

This shows that the family \( \Gamma_k = H_k(n_k) \), for \( 0 < \kappa < \kappa_0 \), is uniformly bounded in \( W = \{ u \in L^\infty(0,T;H^1(Q)) \mid \partial_\zeta u \in L^2(0,T;L^2(Q)) \} \), which is compactly embedded into \( C(0,T;L^2(Q)) \) by Aubin-Lions’ Lemma. Consequently, there exists \( \Gamma_0 \in C(0,T;L^2(Q)) \) such that
\[
\Gamma_k \to \Gamma_0 \quad \text{in} \quad C(0,T;L^2(Q)) \quad \text{as} \quad \kappa \to 0.
\]

We have from the definition of \( H(n_k) = p_k - \kappa \ln(1 - n_k) \), which implies that \( p_0 = \Gamma_0 \), therefore (21) holds.

The next proposition shows the energy estimate, we introduce the quantity
\[
\Phi_k(n) = \int_0^n H_k(s)ds.
\]

**Proposition 2.1.** (Energy estimate) Let the above assumptions hold. Then, the following estimate is valid
\[
||\Phi_k(n_k)||_{L^\infty(0,T;L^1(Q))} + ||\nabla H_k(n_k)||_{L^2(Q_T)}^2 \leq C \tag{74}
\]
where \( C \) is a constant independent of \( \kappa \).
Proof. We multiply the equation (51) by $H_\kappa(n_\kappa)$ and integrate over space, we have
\[
\frac{d}{dt} \int_Q \Phi_\kappa(n_\kappa)dx + \int_Q |\nabla H_\kappa(n_\kappa)|^2dx = \int_Q (G(c_\kappa)n_{1,x} - \mu n_{d,x}))H_\kappa(n_\kappa)dx
\] (75)
inserting the expression of $H_\kappa(n_\kappa)$, we get
\[
\frac{d}{dt} \int_Q \Phi_\kappa(n_\kappa)dx + \int_Q |\nabla H_\kappa(n_\kappa)|^2dx \leq (G_m + \mu) \int_Q n_\kappa(p_\kappa + \kappa \ln(1 - n_\kappa))
\]
(65)
\[
\leq (G_m + \mu) \left( \int_Q p_\kappa - \kappa n_\kappa + \kappa \int_Q n_\kappa \ln(1 - n_\kappa) \right)
\] (77)
after time integrating, we get
\[
\int_Q \Phi_\kappa(n_\kappa)dx + \int_{Q_T} |\nabla H_\kappa(n_\kappa)|^2dxdt \leq (G_m + \mu) \int_{Q_T} n_\kappa(p_\kappa + \kappa \ln(1 - n_\kappa))
\] (78)
\[
\leq (G_m + \mu) \left( \int_{Q_T} p_\kappa - \kappa n_\kappa dx + \kappa \int_{Q_T} n_\kappa \ln(1 - n_\kappa) dx dt \right) + \int_Q \Phi(n_0)dx.
\] (79)
Taking into account (H6), $n_\kappa$ is bounded in $L^1$, and $x \to x \ln(1 - x)$ is uniformly bounded on $[0, n_M]$, thus the right hand side integrals are uniformly bounded.

$L^2$ Estimate for pressure gradient: We may write
\[
\int_{Q_T} |\nabla H_\kappa(n_\kappa)|^2dxdt \leq \int_{Q_T} n_\kappa^2|\nabla p_\kappa|^2dxdt \leq C,
\] given that $n_\kappa$ is uniformly bounded in $L^\infty$, we get
\[
\int_{Q_T} |\nabla p_\kappa|^2dxdt \leq C,
\] (80)
taking Friedrich’s inequality into account we deduce that $p_\kappa \in L^2(Q_T)$. Consequently, the sequence $(\nabla p_\kappa)_\kappa$ converges in the strong topology of $L^2(0, T; L^2(Q))$ to $\nabla p_0$ and thus (23) holds.

3 Complementarity relation

The usual strategy to prove the complementarity relation is to prove the strong convergence of the gradient pressure $\nabla p_\kappa$, and pass to the limit in the equation for the pressure (10). Since we have no control on $\partial_1 p_\kappa$, we will be able to detect the limit only after the proof of the strong compactness of $\nabla H_\kappa$, thanks to the uniform estimates established in the previous section. More precisely we prove the following complementarity relation
\[
- p_0^2 \Delta p_0 = p_0^2 (G(c_0)n_{1,0} - \mu n_{d,0}).
\] (81)
We know that
\[
\Delta H_\kappa(n_\kappa) = \partial_t n_\kappa - (G(c_\kappa)n_{1,x} - \mu n_{d,x}),
\] (82)
and
\[
\Delta p_\kappa = \Delta H_\kappa - \kappa \Delta \ln(1 - n_\kappa).
\]
From (13), (62), and (63), and the inequality $\ln(1 - n_\kappa) \leq \ln(1 - n_M) \leq 0$ we deduce that $\Delta H_\kappa$ and $\Delta p_\kappa$ are bounded in $L^\infty(0, T; L^1(Q))$, therefore we have local compactness in space for $\nabla H_\kappa$. To ensure time compactness we apply the Aubin-Lions lemma. We may write
\[
\partial_t (\nabla H_\kappa) = \nabla (\partial_t H_\kappa)
\] = $\nabla [\partial_t (p_\kappa + \kappa \ln(1 - n_\kappa))]
\] = $\nabla [\frac{p_\kappa}{p_\kappa + \kappa} \partial_t p_\kappa]
\] = $\nabla \left[ \frac{p_\kappa}{p_\kappa + \kappa} (p_\kappa + \kappa R_\kappa + p_\kappa \Delta p_\kappa) + \frac{p_\kappa}{p_\kappa + \kappa} |\nabla p_\kappa|^2 \right]$,.
from (67), (80) and (82) \( \partial_t H_k \L 2 p_k \), and \( \Delta p_k \) are bounded functions in \( L^1 \), on the other hand, given that \( n_{k_x} \) and \( p_k \) are uniformly bounded in \( L^\infty \), we deduce that the r.h.s term is a sum of space derivatives of functions bounded in \( L^1 \). Consequently, we can extract a sub-sequence such that

\[
\nabla H_k \to \nabla p_0 \quad \text{strongly in} \quad L^1(Q_T).
\]

After extraction of a sub-sequence we obtain convergence almost everywhere for \( \nabla H_k \).

Let \( \varphi \in \mathcal{D}(Q_T) \) be a test function. We consider the equation (82), and multiply it by \( \kappa \partial_t \varphi \), we obtain

\[
(p_k + \kappa)^2 \Delta H_k = \frac{\kappa^2}{(1 - \kappa)^2} \partial_t n_k - (p_k + \kappa)^2 (G(c_k)n_{1,k} - \mu n_{d,k}),
\]

we multiply it by \( \varphi \) and we integrate over \( Q_T \)

\[
\kappa^2 \int_{Q_T} (\Delta H_k - \frac{1}{(1 - \kappa)^2} \partial_t n_k + R_k) \varphi + 2\kappa \int_{Q_T} (\Delta H_k - R_k) p_k \varphi = \int_{Q_T} 2p_k \varphi \nabla p_k \nabla H_k + p_k^2 \nabla H_k \nabla \varphi - p_k^2 R_k \varphi.
\]

Thanks to the bounds provided the previous section. From (61), (62), (63), and (67), \( c_k, n_{1,k}, n_{d,k} \), and \( H_k \) are compactly embedded in \( C(0, T; L^2(Q)) \) which is continuously embedded in \( C(0, T; L^1(Q)) \), \( p_k \) is uniformly bounded in \( L^2(Q_T) \) and thus, after the extraction of sub-sequences, we can pass to the limit for \( \kappa \to 0 \) in the product and obtain the complementarity relation

\[
\int_{Q_T} (2p_0 |\nabla p_0|^2 + \frac{p_0^2 \nabla p_0 \nabla \varphi}{2} - p_0^2 R_k \varphi) \, dx \, dt,
\]

which is equivalent to

\[-\Delta p_0 = G(c_0)n_{1,0} - \mu n_{d,0}, \quad \mathcal{D}'(Q_T).
\]

4 Convergence rate: proof of Theorem 1.3

Recently, the authors of the paper [10] proved the \( L^{4/3} \)-convergence rate using interpolation with BV bound. Here we prove the result in \( L^1 \) directly without using interpolation with BV bound. We define the function \( \varphi \) to be the solution of the following parabolic equation in \( (0, T) \times Q \)

\[
\begin{cases}
\partial_t \varphi = (\lambda(t) + \varepsilon) \Delta \varphi \\
\varphi(t, 0) = 0 \\
\varphi(0, x) = \varphi_0,
\end{cases}
\]

(83)

where \( \varepsilon \) is a small regularization parameter, and the function \( \lambda \) is defined by

\[
\lambda(t, x) := \int_0^1 H'(\zeta n_{k} + (1 - \zeta)n_{k'}) d\zeta.
\]

(84)

for \( 0 < k' < k \), and \( H \) is defined by (2). Our approach is based on the following Lemma which appeared in the investigation of Lipschitz semigroup continuous for bacterial biofilm model [31]

Lemma 4.1. The problem (83) has a unique solution \( \varphi \) which satisfies

\[
\varphi \in L^\infty((0, T) \times Q) \cap L^\infty(0, T; W^1(2)(Q)), \quad \Delta \varphi \in L^2((0, T) \times Q).
\]

Moreover, the solution \( \varphi \) is subject to the inequalities

\[
\|\varphi(t)\|_{L^\infty(Q)} \leq \|\varphi_0\|_{L^\infty(Q)},
\]

(85)

\[
\|\varphi(t)\|^2_{W^1(2)(Q)} + C\varepsilon \int_0^1 \|\Delta \varphi(\xi)\|^2_{L^2(Q)} \, d\xi \leq \|\varphi_0\|^2_{W^1(2)(Q)},
\]

(86)
Proof. We have from the previous section \((n_\varepsilon, c_\varepsilon, n_\varepsilon', c_\varepsilon') \in (C(0, T; L^2(Q)) \cap L^\infty((0, T) \times Q))^4\), then the function \(\lambda\) satisfies
\[
\lambda \in L^\infty((0, T) \times Q), \quad \text{and} \quad \lambda(t, x) \geq 0. \tag{87}
\]
Therefore the problem \((83)\) with \(\varepsilon > 0\) is a non-degenerate parabolic equation. To drive the estimates for \(\varphi\) we use the maximum principle. We multiply equation \((83)\) by \(|\varphi - \|\varphi_0\|_\infty|\), and integrate in space we get
\[
\frac{1}{2} \frac{d}{dt} \int_Q (|\varphi - \|\varphi_0\|_\infty|)^2 \leq 0, \tag{88}
\]
after time integration we get
\[
\frac{1}{2} \int_Q (|\varphi(t) - \|\varphi_0\|_\infty|)^2 \leq 0. \tag{89}
\]
So \(|\varphi - \|\varphi_0\|_\infty|^2 = 0\), thus we get \(\|\varphi\|_\infty \leq \|\varphi_0\|_\infty\). To drive the estimate \((86)\), we multiply equation \((83)\) by \(\Delta \varphi\) and integrate in space
\[
\int_Q \partial_t |\nabla \varphi|^2 + \int_Q (\lambda(t) + \varepsilon)|\Delta \varphi|^2 = 0, \tag{90}
\]
we integrate in time, and considering \((87)\) we get
\[
\int_Q |\nabla \varphi(t)|^2 + C \varepsilon \int_0^t \int_Q |\Delta \varphi|^2 \leq \int_Q |\nabla \varphi(0)|^2, \tag{91}
\]
thus \((86)\). We omit here the investigation of the existence and uniqueness, for the reader reference’s see [5]. This finishes the proof of Lemma [4.1]. \(\square\)

Now we proceed to Proof Theorem 1.3

Proof of Theorem 1.3

We consider \(W(t) = n_\varepsilon(t) - n_\varepsilon'(t)\), and \(Z(t) = c_\varepsilon(t) - c_\varepsilon'(t)\), for \(0 < \varepsilon < \varepsilon\). Then these functions satisfy the following equations
\[
\partial_t (W(t)) - \Delta (\lambda(t) W(t)) = R(t) = G(c_\varepsilon - c_\varepsilon')(n_{l,\varepsilon} - n_{l,\varepsilon'}) - \mu(n_{d,\varepsilon} - n_{d,\varepsilon'}), \tag{92}
\]
and
\[
\partial_t (Z(t)) - d\Delta (Z(t)) = R_3(t) = -f(c_\varepsilon - c_\varepsilon')(n_{l,\varepsilon} - n_{l,\varepsilon'}). \tag{93}
\]
Let \(\varphi_0 \in C_0^\infty(Q)\) be an arbitrary function, and \(\varphi\) be a solution of the problem \((83)\). We test equation \((92)\) against \(\varphi(t)\) and integrate in space and time we obtain
\[
\int_Q W(t) \varphi(t) dx - \int_Q W(0) \varphi(0) dx + \int_0^t \int_Q (\partial_t \varphi - \lambda(\varphi) \Delta \varphi) W(\varphi) d\xi dx
= \int_0^t \int_Q \varepsilon \Delta \varphi W(\varphi) d\xi dx + \int_0^t \int_Q R(\varphi) \varphi d\xi dx,
\]
where we used the fact that \(\varphi(t)\) solves \((83)\). Using Young’s inequality and estimate \((85)\)
\[
\int_Q W(t) \varphi(t) \leq \sqrt{\varepsilon} \left( \int_0^t \left( \|W(t)\|_L^2(Q) + \varepsilon \|\Delta \varphi\|_L^2(Q) \right) d\xi \right)
+ \|\varphi_0\|_L^\infty(Q) \left( \|W(0)\|_L^1(Q) + \int_0^t \|R(\xi)\|_L^1(Q) d\xi \right).
\]
Now taking the limit \(\varepsilon \to 0^+\) and using estimate \((85)\), we derive
\[
\int_Q W(t) \varphi(t) \leq \|\varphi_0\|_L^\infty(Q) \left( \|W(0)\|_L^1(Q) + \int_0^t \|R(\xi)\|_L^1(Q) d\xi \right), \tag{94}
\]
for every ϕ₀ ∈ C₀∞(Q). Taking now any function ϕ₀ ∈ L∞(Q) and approximate it by a sequence ϕₙ₀ ∈ C₀∞(Q) such that ∥ϕₙ₀∥∞ ≤ ∥ϕ₀∥L∞(Q) and ∥ϕₙ₀ − ϕ₀∥₁ → 0 as n → ∞ thus (94) is valid for every ϕ₀ ∈ L∞(Q). Therefore we get

\[ \|W(t)\|_{L¹(Q)} \leq \|W(0)\|_{L¹(Q)} + \int_0^t \|R(ξ)\|_{L¹(Q)}dξ, \]

which implies

\[ \|n_κ(t) - n_κ'(t)\|_{L¹(Q)} \leq \|n_κ(0) - n_κ'(0)\|_{L¹(Q)} + C, \]

from (20), n_κ converge in the strong topology of C(0, T; L¹(Q)) to n₀ (due to the continuous embedding C(0, T; L²(Q)) → C(0, T; L¹(Q))). Consequently, taking κ' → 0 we deduce the following rate of the convergence in L¹(Q)

\[ \|n_κ(t) - n₀(t)\|_{L¹(Q)} \leq \|n_κ(0) - n₀(0)\|_{L¹(Q)} + C, \]

where C is a positive constant defined as

\[ C = Gmf\|n_κ\|_{L¹(Q)}. \]

The second estimate of the convergence rate (31) can be proved analogously.

References

[1] J. Ward, J. King. Mathematical modeling of avascular-tumor growth, IMA J. Math. Appl. Med. Biol. 14: 53–75, 1997.

[2] J. Ward, J. King. Mathematical modeling of avascular-tumor growth II: Modelling growth saturation, IMA J. Math. Appl. Med. Biol. 15:1–42, 1997.

[3] S. Cui. Existence of a stationary solution for the modified Ward–King tumor growth model. Advances in Applied Mathematics, 36(4):421-445, 2006.

[4] H. Amman. Nonhomogeneous linear and quasilinear elliptic and parabolic boundary value problems, Function Spaces, Differential Operators and Nonlinear Analysis, Teubner-Texte Math., 133, 9–126, 1993.

[5] O. Ladyzhenskaya, O. Solonnikov and N. Ural'tseva, Linear and Quasilinear Equations of Parabolic Type (transl. from Russian), AMS, Providence, RI, 1967.

[6] M. Renardy and R. C. Rogers, An Introduction to Partial Differential Equations, 2nd edition, Springer Verlag, New York, 2004.

[7] F. Bubba, B. Perthame, C. Pouchol, and M. Schmidtchen. Hele-Shaw limit for a system of two reaction-(cross-)diffusion equations for living tissues. Arch. Rational. Mech. Anal. 236:735–766, 2020.

[8] P. Degond, S. Hecht, N. Vauchelet, Incompressible limit of a continuum model of tissue growth for two cell populations. arXiv preprint arXiv:1809.05442, 2018.

[9] N. David and B. Perthame. Free boundary limit of a tumor growth model with nutrient. Journal de Mathématiques Pures et Appliquées, 2021.

[10] N. David, T. Debiec, B. Perthame . Convergence rate for the incompressible limit of nonlinear diffusion-advection equations. arXiv preprint arXiv:2108.00787, 2021.

[11] H. Triebel, Interpolation Theory, Functional Spaces, Differential Operators, North-Holland, Amsterdam, 1978.

[12] N. Vauchelet, E. Zatorska . Incompressible limit of the Navier—Stokes model with a growth term. Nonlinear Analysis, 163:34-59, 2017.
[13] M. Ebenbeck, H. Garcke. On a Cahn–Hilliard–Brinkman Model for Tumor Growth and Its Singular Limits. SIAM Journal on Mathematical Analysis, 51(3):1868-1912, 2019.

[14] H. Garcke, A. Novick-Cohen. A singular limit for a system of degenerate Cahn-Hilliard equations. Advances in Differential Equations, 5(4-6):401-434, 2000.

[15] C. Elbar, B. Perthame, A. Poulain. Degenerate Cahn-Hilliard and incompressible limit of a Keller-Segel model. arXiv preprint [arXiv:2112.10394] 2021.

[16] Q. He, H. L. Li, B. Perthame. Incompressible limits of Patlak-Keller-Segel model and its stationary state. arXiv preprint [arXiv:2203.13099] 2022.

[17] B. Perthame, F. Quirós, and J. L. Vázquez. The Hele-Shaw asymptotics for mechanical models of tumor growth. Arch. Ration. Mech. Anal., 212(1):93–127, 2014.

[18] B. Perthame and N. Vauchelet. Incompressible limit of a mechanical model of tumour growth with viscosity. Philos. Trans. Roy. Soc. A, 373(2050):20140283, 16, 2015.

[19] J.-G. Liu and X. Xu. Existence and incompressible limit of a tissue growth model with autophagy. arXiv:2102.03844v3, 2021.

[20] S. Hecht and N. Vauchelet. Incompressible limit of a mechanical model for tissue growth with non-overlapping constraint. Communications in Mathematical Sciences, 15(7):1913–1932, 2017.

[21] P. Bénilan, P. M. G. Crandall. The continuous dependence on $\phi$ of solutions of $u_t - \Delta \phi(u) = 0$. Indiana University Mathematics Journal, 30(2):161–177, 1981.

[22] M. Bertsch, D. Hilhorst, H. Izuhara, & M. Mimura. A nonlinear parabolic-hyperbolic system for contact inhibition of cell-growth. Differ. Equ. Appl, 4(1):137-157, 2012.

[23] J. A. Sherratt, M. A. Chaplain. A new mathematical model for avascular tumour growth. Journal of mathematical biology, 43(4):291-312, 2001.

[24] H. M. Byrne and M. A. J. Chaplain. Growth of nonnecrotic tumors in the presence and absence of inhibitors, Math. Biosciences, 130:151-181, 1995.

[25] A. Friedman. A hierarchy of cancer models and their mathematical challenges. Discrete and Continuous Dynamical Systems Series B, 4(1):147–160, 2004.

[26] A. Friedman. Mathematical analysis and challenges arising from models of tumor growth. Mathematical Models and Methods in Applied Sciences, 17(supp01):1751–1772, 2007.

[27] C. M. Elliott, M. A. Herrero, J. R. King, and J. R. Ockendon. Themesa problem: Diffusion patterns for $u_t = \nabla (u^m \nabla u)$ as $m \to 0$. IMA journal of applied mathematics, 37(2):147–154, 1986.

[28] T. Debiec, B. Perthame, M. Schmidtchen, and N. Vauchelet. Incompressible limit for a two-species model with coupling through Brinkman’s law in any dimension. Journal de Mathématiques Pures et Appliquées, 145:204–239, 2021.

[29] T. Debiec and M. Schmidtchen. Incompressible limit for a two-species tumour model with coupling through Brinkman’s law in one dimension. Acta Applicandae Mathematicae, 169(1):593–611, 2020.

[30] M. Bertsch, R. Dal Passo, and M. Mimura. A free boundary problem arising in a simplified tumour growth model of contact inhibition. Interfaces Free Bound, 12:235-250, 2010.

[31] M. A. Efendiev, S. Zelik, H. J. Eberl. Existence and longtime behavior of a biofilm model. Communications on Pure and Applied Analysis, 8(2):509–531 2009.

E-mail address, Samiha BELMOR: belmor.samiha@gmail.com