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Incompressible limit of a continuum model of tissue growth for two cell populations

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Abstract

This paper investigates the incompressible limit of a system modelling the growth of two cells population. The model describes the dynamics of cell densities, driven by pressure exclusion and cell proliferation. It has been shown that solutions to this system of partial differential equations have the segregation property, meaning that two population initially segregated remain segregated. This work is devoted to the incompressible limit of such system towards a free boundary Hele Shaw type model for two cell populations.

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1 Introduction

Diversity is key in biology. It appears at all kind of level from the human scale to the microscopic scale, with million of cells types; each scales impacting on the others. During development, the coexistence of different cells types following different rules impact on the growth of tissue and then on the global structures. In a more specific case, this can be observed in cancerous tissue

with the invasion of tumour cells in an healthy tissue creating a abnormal growth. Furthermore, cancerous cells are not playing all the same roles. They can be proliferative or quiescent depending of their positions, ages, ... To study the influence of these diverse cells on each others from a theoretical view, we introduce mathematical model for multiple populations. In this paper we are interesting in the global dynamics and interactions of the two populations, meaning that we focus specifically on continuous models.

In the already existing literature on macroscopic model, we distinguish two categories. The most common ones involved partial differential equations (PDE) in which cells are represented by densities. These models have been widely used to model growth of tissue [10, 29], in particular for tumor growth [1, 7, 9, 15]. Another way to model tissue growth is by considering free boundary models [16, 17, 20]. In these models the tissue is described by a domain and its growth and movement are driven by the motion of the boundary. The link between these two types of model has been made via an incompressible limit in [21, 22, 24, 26, 27, 28]. This link is interesting as both models have their advantages. On the one hand PDE relying models, also called mechanical models, are widely studied with many numerical and analytical tools. On the other hand free boundary models are closer to the biologic vision of the tissue and allow to study motion and dynamics of the tissue. This paper aims to extend the link between the mechanical and the free boundary models, in the case of multiple populations system.

In the specific case of multiple populations, several mathematical models have been already introduced. In particular in population dynamics, the famous Lotka-Volterra system [23] models the dynamics of a predator-prey system. This model has been extended to nonlinear diffusion Lotka-Volterra systems [3, 4, 5, 8]. For the tumor growth modelling (see e.g. [13]), some models focus on mechanical property of tissues such as contact inhibition [6, 2, 19] and mutation [18]. They have been extended to multiple populations [18, 30]. Solutions to these models may have some interesting spatial pattern known as segregation [5, 11, 25, 30].

The two cell populations system under investigation in this paper is an extension on a simplest cell population model proposed in [10, 27]. Let $n(x, t)$ be the density of a single category of cell depending on the position $x \in \mathbb{R}^d$ and the time $t > 0$, and let $p(x, t)$ be the mechanical pressure of the system. The pressure is generated by the cell density and is defined via a pressure law $p = P(n)$. This pressure exerted on cells induces a motion with a velocity field $v = v(x, t)$ related to the pressure through the Darcy's law. The proliferation is modelled by a growth term $G(p)$ which is pressure dependent. With this assumption, the mathematical model reads

$$\begin{aligned} \partial_t n + \nabla \cdot (nv) &= nG(p), & \text{on } \mathbb{R}^d \times \mathbb{R}^+, \\ v &= -\nabla p, & p = P(n). \end{aligned}$$

In [22, 24, 26, 27, 28], the pressure law is given by $P(n) = \frac{\gamma}{\gamma-1} n^{\gamma-1}$ which allows to recover the porous medium equation. However, in many tissues, cells may not overlap, implying that the maximal packing density should be bounded by 1. To take into account this non-overlapping constraint, the pressure law $P(n) = \epsilon \frac{n}{1-n}$ has been taken in [21]. This latter choice of pressure law has also been taken in the present paper. For this one population model, it has been showed in [21], that at the incompressible limit, $\epsilon \rightarrow 0$ (or $\gamma \rightarrow +\infty$ depending on the pressure expression), the model converges towards a Hele-Shaw type free boundary problem.

The previous model has the particularity to derive from the free energy

$$\mathcal{E}(n) = \int_{\mathbb{R}} P(n(x)) dx.$$

as a gradient flow for the Wasserstein metric. Using this property we derive a model for two species of cells. Let us denote $n_1(x, t)$ and $n_2(x, t)$ the two cell densities depending on the

position $x \in \mathbb{R}^d$ and the time $t > 0$. We assume that the pressure depends on the total density $n = n_1 + n_2$. As the pressure depends on a parameter ϵ , we introduce this dependency in the notation. We define the free energy for the two cell populations by,

$$\mathcal{E}(n_\epsilon) = \int_{\mathbb{R}} P(n_{1\epsilon}(x) + n_{2\epsilon}(x)) dx.$$

Restricting to the one dimensional case, the system of equation deriving from this free energy is then defined by,

$$\partial_t n_{1\epsilon} - \partial_x(n_{1\epsilon} \partial_x p_\epsilon) = n_{1\epsilon} G_1(p_\epsilon), \quad (1)$$

$$\partial_t n_{2\epsilon} - \partial_x(n_{2\epsilon} \partial_x p_\epsilon) = n_{2\epsilon} G_2(p_\epsilon), \quad (2)$$

$$p_\epsilon = P(n_\epsilon) = \epsilon \frac{n_\epsilon}{1 - n_\epsilon}, \quad (3)$$

$$n_\epsilon = n_{1\epsilon} + n_{2\epsilon}, \quad (4)$$

with G_1, G_2 the growth functions, and p_ϵ the pressure.

The existence of solution for system (1)-(4) has been proven in [6, 2] for a compact domain $(-L, L)$ with $L > 0$, with Neumann homogeneous boundary condition. In particular, it is shown that at a fix $\epsilon > 0$, given initial conditions $n_{1\epsilon}^{\text{ini}}$ and $n_{2\epsilon}^{\text{ini}}$ satisfying,

$$\exists \zeta^0 \in \mathbb{R} \text{ such that } n_{1\epsilon}^{\text{ini}} = n_\epsilon^{\text{ini}} \mathbf{1}_{x \leq \zeta^0} \text{ and } n_{2\epsilon}^{\text{ini}} = n_\epsilon^{\text{ini}} \mathbf{1}_{x \geq \zeta^0}, \quad (5)$$

and

$$n_{1\epsilon}^{\text{ini}}, n_{2\epsilon}^{\text{ini}} \geq 0 \text{ and } 0 < A_0 \leq n_{1\epsilon}^{\text{ini}} + n_{2\epsilon}^{\text{ini}} \leq B_0 \quad (6)$$

then there exists $\zeta_\epsilon \in C([0, \infty)) \cap C^1((0, \infty))$ such that

$$n_{1\epsilon}(t, x) = n_\epsilon(t, x) \mathbf{1}_{x \leq \zeta_\epsilon(t)} \quad \text{and} \quad n_{2\epsilon}(t, x) = n_\epsilon(t, x) \mathbf{1}_{x \geq \zeta_\epsilon(t)}, \quad (7)$$

and $n_{1\epsilon}$ and $n_{2\epsilon}$ respectively satisfy (1) on $\{(t, x), x \leq \zeta_\epsilon(t)\}$ and (2) on $\{(t, x), x \geq \zeta_\epsilon(t)\}$. In addition $n_\epsilon = n_{1\epsilon} + n_{2\epsilon}$ is solution to:

$$\begin{cases} \partial_t n_\epsilon - \partial_x(n_\epsilon \partial_x p_\epsilon) = n_\epsilon G_1(p_\epsilon) & \text{on } \{(t, x), x \leq \zeta_\epsilon(t)\}, \\ \partial_t n_\epsilon - \partial_x(n_\epsilon \partial_x p_\epsilon) = n_\epsilon G_2(p_\epsilon) & \text{on } \{(t, x), x \geq \zeta_\epsilon(t)\}, \\ n_\epsilon(t, \zeta_\epsilon(t)^-) = n_\epsilon(t, \zeta_\epsilon(t)^+), \\ \zeta_\epsilon'(t) = -\partial_x p(t, \zeta_\epsilon(t)^-) = -\partial_x p(t, \zeta_\epsilon(t)^+), \\ \partial_x n_\epsilon(\pm L, 0) = 0 \text{ for } t > 0. \end{cases} \quad (8)$$

In [2], the reaction term is not the same than in this paper, however it is easy to see that there proof can be extended to our system under a set of assumptions for the growth functions which will be defined latter in this paper.

The aim of this paper is is to study the incompressible limit $\epsilon \rightarrow 0$ for the two populations systems. When the two species are not in contact, the system is equivalent to the one population model [21], this is why we limit ourself in this paper to the case where the two populations are initially in contact. To use the solutions defined in [2], we restrict the space to a compact domain $(-L, L)$ with $L > 0$ and assume (5) and (6) are verified. Outside the domain $(-L, L)$, the system will be equivalent to the one population model.

We firstly remark that by adding (1) and (2), we get,

$$\partial_t n_\epsilon - \partial_x(n_\epsilon \partial_x p_\epsilon) = n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon) \text{ in } (-L, L). \quad (9)$$

Multiplying by $P'(n_\epsilon)$ we find an equation for the pressure,

$$\partial_t p_\epsilon - \left(\frac{p_\epsilon^2}{\epsilon} + p_\epsilon\right) \partial_{xx} p_\epsilon - |\partial_x p_\epsilon|^2 = \frac{1}{\epsilon} (p_\epsilon + \epsilon)^2 (n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon)) \text{ in } (-L, L). \quad (10)$$

Formally, passing at the limit $\epsilon \rightarrow 0$, we expect the relation,

$$-p_0^2 \partial_{xx} p_0 = p_0^2 (n_{10} G_1(p_0) + n_{20} G_2(p_0)) \text{ in } (-L, L).$$

In addition, passing formally to the limit $\epsilon \rightarrow 0$ into (3), it appears clearly that $(1 - n_0)p_0 = 0$. We consider the domain $\Omega_0(t) = \{x \in (-L, L), p_0(x, t) > 0\}$, then, from the latter identity, $n_0 = 1$ on Ω_0 . Moreover, from the segregation property, we have $n_{1\epsilon} n_{2\epsilon} = 0$ when the two densities are initially segregated. Passing to the limit $\epsilon \rightarrow 0$ into this relation implies $n_{10} n_{20} = 0$. Then we may split $\Omega_0(t)$ into two disjoint sets $\Omega_1(t) = \{x \in (-L, L), n_{10}(x, t) = 1\}$ and $\Omega_2(t) = \{x \in (-L, L), n_{20}(x, t) = 1\}$. Formally, it is not difficult to deduce from (10) that when $\epsilon \rightarrow 0$, we expect to have the relation

$$-p_0^2 \partial_{xx} p_0 = \begin{cases} p_0^2 G_1(p_0) & \text{on } \Omega_1(t), \\ p_0^2 G_2(p_0) & \text{on } \Omega_2(t). \end{cases}$$

Then we obtain a free boundary problem of Hele-Shaw type: On $\Omega_1(t)$, we have $n_{10} = 1$ and $-\partial_{xx} p_0 = G_1(p_0)$, on $\Omega_2(t)$, we have $n_{20} = 1$ and $-\partial_{xx} p_0 = G_2(p_0)$.

The outline of the paper is the following. In Section 2 we expose the main results of this paper, which are the convergence of the continuous model (1)-(4) when $\epsilon \rightarrow 0$ to a Hele-Shaw free boundary model, and uniqueness for this limiting model. Section 3 is devoted to the proof of these main results. The proof on the convergence relies on some a priori estimate and compactness techniques. We use Hilbert duality method to establish uniqueness of solution to the limiting system. Finally in Section 4, we present some numerical simulations of the system (1)-(4) when ϵ is going to 0 and simulations of a specific application on tumor spheroid growth.

2 Main results

In this paper we aim to prove the incompressible limit $\epsilon \rightarrow 0$ of the two populations model with non overlapping constraint (1)-(4) in one dimension. We first introduce a list of assumptions on the growth terms and the initial conditions. For the growth, we consider the following set of assumptions:

$$\left\{ \begin{array}{l} \exists G_m > 0, \quad \|G_1\|_\infty \leq G_m, \quad \|G_2\|_\infty \leq G_m, \\ G'_1, G'_2 < 0, \quad \text{and } \exists P_M^1, P_M^2 > 0, \quad G_1(P_M^1) = 0 \text{ and } G_2(P_M^2) = 0, \\ \exists \gamma > 0, \quad \min\left(\inf_{[0, P_M^1]} |G'_1|, \inf_{[0, P_M^2]} |G'_2|\right) = \gamma, \\ P_M := \max(P_M^1, P_M^2), \quad \exists g_m \geq 0, \quad \min\left(\inf_{[0, P_M]} G_1, \inf_{[0, P_M]} G_2\right) \geq -g_m. \end{array} \right. \quad (11)$$

The set of assumptions on the growth rate is standard and similar to the one in [21]. The parameters P_M^1 and P_M^2 are called homeostatic pressures which represent the maximal pressure that the tissue can handle before starting dying. For the initial datas, we assume that there

exists $\epsilon_0 > 0$ such that, for all $\epsilon \in (0, \epsilon_0)$, for all $x \in (-L, L)$,

$$\left\{ \begin{array}{l} 0 \leq n_{1\epsilon}^{\text{ini}}, \quad 0 \leq n_{2\epsilon}^{\text{ini}}, \quad n_{\epsilon}^{\text{ini}} = n_{1\epsilon}^{\text{ini}} + n_{2\epsilon}^{\text{ini}}, \quad 0 < A_0 \leq n_{\epsilon}^{\text{ini}} \leq B_0, \quad \partial_x n_{\epsilon}^{\text{ini}}(\pm L) = 0, \\ \exists \zeta^0 \in (-L, L) \text{ such that } n_{1\epsilon}^{\text{ini}} = n_{\epsilon}^{\text{ini}} \mathbf{1}_{x \leq \zeta^0} \text{ and } n_{2\epsilon}^{\text{ini}} = n_{\epsilon}^{\text{ini}} \mathbf{1}_{x \geq \zeta^0}, \\ p_{\epsilon}^{\text{ini}} := \epsilon \frac{n_{\epsilon}^{\text{ini}}}{1 - n_{\epsilon}^{\text{ini}}} \leq P_M := \max(P_M^1, P_M^2), \\ \max(\|\partial_x n_{1\epsilon}^{\text{ini}}\|_{L^1(-L, L)}, \|\partial_x n_{2\epsilon}^{\text{ini}}\|_{L^1(-L, L)}) \leq C, \\ \exists n_1^{\text{ini}}, n_2^{\text{ini}} \in L_+^1(-L, L), \text{ such that } \|n_{1\epsilon}^{\text{ini}} - n_1^{\text{ini}}\|_{L^1(-L, L)} \rightarrow 0 \\ \text{and } \|n_{2\epsilon}^{\text{ini}} - n_2^{\text{ini}}\|_{L^1(-L, L)} \rightarrow 0, \text{ as } \epsilon \rightarrow 0. \end{array} \right. \quad (12)$$

These initial conditions imply that $n_{1\epsilon}^{\text{ini}}$ and $n_{2\epsilon}^{\text{ini}}$ are uniformly bounded in $W^{1,1}(-L, L)$. Notice also that the existence of ζ^0 being the interface between the two species implies that the two populations are initially segregated.

From [2], we recover that at a fix $\epsilon > 0$ under assumption (11), given initial conditions $n_{1\epsilon}^{\text{ini}}$ and $n_{2\epsilon}^{\text{ini}}$ satisfying (12), then there exists $\zeta_{\epsilon} \in C([0, \infty)) \cap C^1((0, \infty))$ such that $n_{1\epsilon}$ and $n_{2\epsilon}$ verify (7) and $n_{1\epsilon}$ and $n_{2\epsilon}$ respectively satisfy (1) on $\{(t, x), x \leq \zeta_{\epsilon}(t)\}$ and (2) on $\{(t, x), x \geq \zeta_{\epsilon}(t)\}$. In addition $n_{\epsilon} = n_{1\epsilon} + n_{2\epsilon}$ is solution to (8).

Remark 1. Considering $n_{1\epsilon}$ and $n_{2\epsilon}$ defined previously, we have for $i = 1, 2$

$$\partial_t n_{i\epsilon} = \partial_t n_{\epsilon}(t, x) \mathbf{1}_{x \leq \zeta_{\epsilon}(t)} + n_{\epsilon} \zeta'_{\epsilon}(t) \delta_{x=\zeta_{\epsilon}(t)}.$$

Given (8), for all $\varphi \in C_c^{\infty}(-L, L)$ we compute, for $i = 1, 2$

$$\begin{aligned} \int_{\mathbb{R}} \partial_t n_{i\epsilon} \varphi \, dx &= \int_{-\infty}^{\zeta_{\epsilon}(t)} \partial_t n_{\epsilon} \varphi \, dx + n_{\epsilon}(t, \zeta_{\epsilon}(t)) \zeta'_{\epsilon}(t) \varphi(\zeta_{\epsilon}(t)) \\ &= \int_{-L}^{\zeta_{\epsilon}(t)} \partial_x (n_{\epsilon} \partial_x p_{\epsilon}) \varphi \, dx + \int_{-L}^L n_{i\epsilon} G_i(p_{\epsilon}) \varphi \, dx + n_{\epsilon}(t, \zeta_{\epsilon}(t)) \zeta'_{\epsilon}(t) \varphi(\zeta_{\epsilon}(t)) \\ &= - \int_{-L}^{\zeta_{\epsilon}(t)} n_{\epsilon} \partial_x p_{\epsilon} \partial_x \varphi \, dx + n_{\epsilon}(t, \zeta_{\epsilon}(t)) \partial_x p_{\epsilon}(t, \zeta_{\epsilon}(t)) \varphi(\zeta_{\epsilon}(t)) \\ &\quad + \int_{-L}^L n_{i\epsilon} G_i(p_{\epsilon}) \varphi \, dx - n_{\epsilon}(t, \zeta_{\epsilon}(t)) \partial_x p_{\epsilon}(t, \zeta_{\epsilon}(t)) \varphi(\zeta_{\epsilon}(t)) \\ &= \int_{-L}^L n_{i\epsilon} \partial_x p_{\epsilon} \partial_x \varphi \, dx + \int_{-L}^L n_{i\epsilon} G_i(p_{\epsilon}) \varphi \, dx \\ &= \int_{-L}^L (\partial_x (n_{i\epsilon} \partial_x p_{\epsilon}) + n_{i\epsilon} G_i(p_{\epsilon})) \varphi \, dx. \end{aligned}$$

Hence $n_{1\epsilon}$ and $n_{2\epsilon}$ are weak solutions to (1) and (2) on $(-L, L)$ respectively. This result will be used in the following.

Considering this particular solution, we are going to show the incompressible limit $\epsilon \rightarrow 0$ for system (1)-(4). The main result is the following

Theorem 1. *Let $T > 0$, $Q_T = (0, T) \times (-L, L)$. Let G_1, G_2 and $(n_{1\epsilon}^{\text{ini}}), (n_{2\epsilon}^{\text{ini}})$ satisfy assumptions (11)–(12). After extraction of subsequences, the densities $n_{1\epsilon}, n_{2\epsilon}$ and the pressure p_{ϵ} , solutions defined in (7)–(8), converge strongly in $L^1(Q_T)$ as $\epsilon \rightarrow 0$ towards the respective limit $n_{10}, n_{20} \in L^{\infty}([0, T]; L^1(-L, L)) \cap BV(Q_T)$, and $p_0 \in BV(Q_T) \cap L^2([0, T]; H^1(-L, L))$.*

Moreover, these functions satisfy, for all $(t, x) \in Q_T$,

$$0 \leq n_{10}(t, x) \leq 1, \quad 0 \leq n_{20}(t, x) \leq 1, \quad (13)$$

$$0 < A_0 e^{-g_m t} \leq n_0(t, x) \leq 1, \quad 0 \leq p_0 \leq P_M, \quad (14)$$

$$\partial_t n_0 - \partial_{xx} p_0 = n_{10} G_1(p_0) + n_{20} G_1(p_0), \quad \text{in } \mathcal{D}'(Q_T), \quad (15)$$

where $n_0 = n_{10} + n_{20}$, and

$$\partial_t n_{10} - \partial_x(n_{10} \partial_x p_0) = n_{10} G_1(p_0), \quad \text{in } \mathcal{D}'(Q_T), \quad (16)$$

$$\partial_t n_{20} - \partial_x(n_{20} \partial_x p_0) = n_{20} G_2(p_0), \quad \text{in } \mathcal{D}'(Q_T), \quad (17)$$

complemented with Neumann boundary conditions $\partial_x p_0(\pm L) = 0$. Moreover, we have the relations

$$(1 - n_0)p_0 = 0, \quad (18)$$

and

$$n_{10} n_{20} = 0, \quad (19)$$

and the complementary relation

$$p_0 \left(\partial_{xx} P_0 + \int_0^t (n_{10} G_1(p_0) + n_{20} G_2(p_0)) ds + n_0^{\text{ini}} - 1 \right) = 0. \quad (20)$$

where P_0 is defined by $P_0(t, x) = \int_0^t p_0(s, x) ds$.

Remark 2. Introducing the set $\Omega_0 = \{p_0 > 0\}$, we deduce that on Ω_0 we have

$$-\partial_{xx} P_0 = \int_0^t (n_{10} G_1(p_0) + n_{20} G_2(p_0)) ds + n_0^{\text{ini}} - 1.$$

Deriving with respect to t , we find formally

$$-\partial_{xx} p_0 = n_{10} G_1(p_0) + n_{20} G_2(p_0).$$

We recognise the Hele-Shaw model. Noticing also that taking $t = 0$ into the relation (20), we recover the expected relation $p_0^{\text{ini}} n_0^{\text{ini}} = p_0^{\text{ini}}$.

The proof of this convergence result is given in Section 3. It is straightforward to observe that adding (1) and (2) provides an equation on the total density similar to the one found in the one species case [21, 27]. Then we use a similar strategy for the proof relying on a compactness method. However the presence of the two populations generate some technical difficulties. To overcome them, we use the segregation property. Notice that this paper is written in the specific case where the two species are separated by one interface, but could be generalised to many interfaces. Using the segregation of the species we are able to obtain a priori estimates on the densities, the pressure and their spatial derivatives. Compactness in time is deduced thanks to the Aubin-Lions theorem. The proof of convergence follows from these new estimates. However, the lack of estimates on the time derivative makes obtaining the complementary relation difficult, then we are not able to recover the usual relation but the one stated in (20) which may be seen as an integral in time of the usual one as explained in the above remark.

To complete the result on the asymptotic limit of the model, an uniqueness result for the Hele-Shaw free boundary model for two populations is provided in Proposition 1 in §3.4. The proof of this uniqueness result for the limiting problem is based on Hilbert's duality method.

3 Proof of the main results

This section is devoted to the proof of Theorem 1, whereas in Section 3.4 the uniqueness of the solution to the Hele Shaw system is established. We first establish some a priori estimates.

3.1 A priori estimates

3.1.1 Nonnegativity principle

The following Lemma establishes the nonnegativity of the densities.

Lemma 1. *Let $(n_{1\epsilon}, n_{2\epsilon}, p_\epsilon)$ be a solution to (1) and (2) such that $n_{1\epsilon}^{\text{ini}} \geq 0$, $n_{2\epsilon}^{\text{ini}} \geq 0$ and $G_m < \infty$. Then, for all $t \geq 0$, $n_{1\epsilon}(t) \geq 0$ and $n_{2\epsilon}(t) \geq 0$.*

Proof. To show the nonnegativity we use the Stampacchia method. We multiply (1) by $\mathbf{1}_{n_{1\epsilon} < 0}$ and denote $|n|_- = \max(0, -n)$ for the negative part, we get

$$\mathbf{1}_{n_{1\epsilon} < 0} \partial_t n_{1\epsilon} - \mathbf{1}_{n_{1\epsilon} < 0} \partial_x (n_{1\epsilon} \partial_x p_\epsilon) = \mathbf{1}_{n_{1\epsilon} < 0} n_{1\epsilon} G_1(p_\epsilon).$$

With the above notation, it reads

$$\partial_t |n_{1\epsilon}|_- - \partial_x (|n_{1\epsilon}|_- \partial_x p_\epsilon) = |n_{1\epsilon}|_- G_1(p_\epsilon).$$

We integrate in space, using assumption (11) and $\partial_x p_\epsilon(\pm L, t) = p'_\epsilon(n_\epsilon) \partial_x n_\epsilon(\pm L, t) = 0$, we deduce

$$\frac{d}{dt} \int_{-L}^L |n_{1\epsilon}|_- dx \leq \int_{-L}^L |n_{1\epsilon}|_- G_1(p_\epsilon) dx \leq G_m \int_{-L}^L |n_{1\epsilon}|_- dx.$$

Then we integrate in time,

$$\int_{-L}^L |n_{1\epsilon}|_- dx \leq e^{G_m t} \int_{-L}^L |n_{1\epsilon}^{\text{ini}}|_- dx.$$

With the initial condition $n_{1\epsilon}^{\text{ini}} > 0$ we deduce $n_{1\epsilon} > 0$. With the same method we can show that if $n_{2\epsilon}^{\text{ini}} > 0$ we have $n_{2\epsilon} > 0$. \square

Remark 3. We notice that the positivity gives a formal proof of the segregation of any solution of (1)-(4). Indeed, defining $r_\epsilon = n_{1\epsilon} n_{2\epsilon}$ and multiplying (1) by $n_{2\epsilon}$, (2) by $n_{1\epsilon}$ and adding, we obtain the following equation for r_ϵ ,

$$\partial_t r_\epsilon - \partial_x r_\epsilon \partial_x p_\epsilon - 2r_\epsilon \partial_{xx} p_\epsilon = r_\epsilon (G_1(p_\epsilon) + G_2(p_\epsilon)).$$

Given that $r_\epsilon^{\text{ini}} = 0$, we get that $r_\epsilon = 0$ at all time.

3.1.2 A priori estimates

To show the compactness result we establish a priori estimate on the densities, pressure and their derivatives. We first compute the equation on the total density. As shown earlier $n_{1\epsilon}$ and $n_{2\epsilon}$ are respectively weak solutions of (1) and (2). By summing the two equations we deduce that n_ϵ is a weak solution of (9). Notice that this equation can be rewritten as,

$$\partial_t n_\epsilon - \partial_{xx} H(n_\epsilon) = n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon), \quad (21)$$

with $H(n) = \int_0^n u P'(u) du = P(n) - \epsilon \ln(P(n) + \epsilon) + \epsilon \ln \epsilon$.

We establish the following a priori estimates

Lemma 2. *Let us assume that (11) and (12) hold. Let $(n_{1\epsilon}, n_{2\epsilon}, p_\epsilon)$ be a solution to (1)–(4). Then, for all $T > 0$, and $t \in (0, T)$, we have the uniform bounds in $\epsilon \in (0, \epsilon_0)$,*

$$\begin{aligned} n_{1\epsilon}, n_{2\epsilon} &\text{ in } L^\infty([0, T]; L^1 \cap L^\infty(-L, L)); \\ 0 \leq p_\epsilon \leq P_M, \quad 0 < A_0 e^{-g_m t} \leq n_\epsilon(t) \leq \frac{P_M}{P_M + \epsilon} \leq 1. \end{aligned}$$

Moreover, we have that $(n_{1\epsilon})_\epsilon$ and $(n_{2\epsilon})_\epsilon$ are uniformly bounded in $L^\infty([0, T], W^{1,1}(-L, L))$ and $(p_\epsilon)_\epsilon$ is uniformly bounded in $L^1([0, T], W^{1,1}(-L, L))$.

Proof. **Comparison principle.**

The usual comparison principle is not true for this system of equations. However we are able to show some comparison between the total density and n_M defined by $n_M = \frac{P_M}{\epsilon + P_M}$ where P_M is defined in (12). We deduce from (21) that

$$\begin{aligned} \partial_t(n_\epsilon - n_M) - \partial_{xx}(H(n_\epsilon) - H(n_M)) &\leq n_{1\epsilon} G_1(P(n_\epsilon)) - n_M \mathbf{1}_{x \leq \zeta_\epsilon(t)} G_1(P_M) \\ &\quad + n_{2\epsilon} G_2(P(n_\epsilon)) - n_M \mathbf{1}_{x \geq \zeta_\epsilon(t)} G_2(P_M), \end{aligned}$$

where we use the monotonicity of G_1 and G_2 from assumption (11).

Notice that, since the function H is nondecreasing, the sign of $n_\epsilon - n_M$ is the same as the sign of $H(n_\epsilon) - H(n_M)$. Moreover,

$$\partial_{xx} f(y) = f''(y) |\partial_x y|^2 + f'(y) \partial_{xx} y,$$

so for $y = H(n_\epsilon) - H(n_M)$ and $f(y) = y_+$ the positive part, the so-called Kato inequality reads $\partial_{xx} f(y) \geq f'(y) \partial_{xx} y$. Thus multiplying the latter equation by $\mathbf{1}_{n_\epsilon - n_M > 0}$ and given (7) we obtain

$$\begin{aligned} \partial_t |n_\epsilon - n_M|_+ - \partial_{xx} |H(n_\epsilon) - H(n_M)|_+ &\leq (n_\epsilon - n_M) \mathbf{1}_{x \leq \zeta_\epsilon(t)} G_1(P(n_\epsilon)) \mathbf{1}_{n_\epsilon - n_M > 0} \\ &\quad + (n_\epsilon - n_M) \mathbf{1}_{x \geq \zeta_\epsilon(t)} G_2(P(n_\epsilon)) \mathbf{1}_{n_\epsilon - n_M > 0} \\ &\quad + n_M (G_1(P(n_\epsilon)) - G_1(P(n_M)) + G_2(P(n_\epsilon)) - G_2(P(n_M))) \mathbf{1}_{n_\epsilon - n_M > 0}. \end{aligned}$$

Since the function P is increasing and G_1 and G_2 are decreasing (see (11)), we deduce that the last term is nonpositive. Then, integrating on $(-L, L)$ and using $\partial_x n_\epsilon(\pm L, t) = 0$, we deduce

$$\begin{aligned} \frac{d}{dt} \int_{-L}^L |n_\epsilon - n_M|_+ dx &\leq \partial_x |H(n_\epsilon) - H(n_M)|_+(L, t) - \partial_x |H(n_\epsilon) - H(n_M)|_+(-L, t) \\ &\quad + \int_{-L}^{\zeta_\epsilon(t)} (n_\epsilon - n_M) \mathbf{1}_{n_\epsilon - n_M > 0} G_1(P(n_\epsilon)) dx \\ &\quad + \int_{\zeta_\epsilon(t)}^L (n_\epsilon - n_M) \mathbf{1}_{n_\epsilon - n_M > 0} G_2(P(n_\epsilon)) dx \\ &\leq G_m \int_{-L}^L |n_\epsilon - n_M|_+ dx. \end{aligned}$$

Then, integrating in time, we deduce

$$\int_{-L}^L |n_\epsilon - n_M|_+ dx \leq e^{G_m t} \int_{-L}^L |n_\epsilon^{\text{ini}} - n_M|_+ dx = 0.$$

L^∞ bounds.

From (12), we have $p_\epsilon^{\text{ini}} \leq P_M$. Since the function P is inscreasing, we have $n_\epsilon^{\text{ini}} \leq n_M$. With the above comparison principle, we conclude that $n_\epsilon \leq n_M$. We deduce easily with the non-negativity principle (1) that $0 \leq p_\epsilon \leq P_M$, $0 \leq n_{1\epsilon} \leq n_M$ and $0 \leq n_{2\epsilon} \leq n_M$.

Estimates from below.

From above, we deduce that the pressure is bounded by P_M . Hence, using assumption (11) we deduce

$$\partial_t n_\epsilon - \partial_{xx} H(n_\epsilon) = n_{1\epsilon} G_1(P(n_\epsilon)) + n_{2\epsilon} G_2(P(n_\epsilon)) \geq -n_\epsilon g_m.$$

Let us introduce $n_m := A_0 e^{-g_m t}$. We deduce

$$\partial_t(n_m - n_\epsilon) - \partial_{xx}(H(n_m) - H(n_\epsilon)) \leq -(n_m - n_\epsilon)g_m.$$

As above, for the comparison principle, we may use the positive part and the Kato inequality to deduce

$$\partial_t |n_m - n_\epsilon|_+ - \partial_{xx} |H(n_m) - H(n_\epsilon)|_+ \leq -|n_m - n_\epsilon|_+ g_m.$$

Integrating in space and in time as above, we deduce that $|n_m - n_\epsilon|_+ = 0$.

L^1 bounds of n_ϵ , $n_{1\epsilon}$, $n_{2\epsilon}$ and p_ϵ .

Integrating (21) on $(-L, L)$ and using the nonnegativity of the densities from Lemma 1 as well as the Neumann boundary conditions, we deduce

$$\frac{d}{dt} \|n_\epsilon\|_{L^1(-L, L)} \leq G_m \|n_\epsilon\|_{L^1(-L, L)}.$$

Integrating in time, we deduce

$$\|n_\epsilon\|_{L^1(-L, L)} \leq e^{G_m t} \|n_\epsilon^{\text{ini}}\|_{L^1(-L, L)}.$$

Since $n_{1\epsilon} \geq 0$ and $n_{2\epsilon} \geq 0$, we deduce the uniform bounds on $\|n_{1\epsilon}\|_{L^1(-L, L)}$ and on $\|n_{2\epsilon}\|_{L^1(-L, L)}$.

From the relation (3), we deduce $p_\epsilon = n_\epsilon(\epsilon + p_\epsilon)$. Moreover, the bound $p_\epsilon \leq P_M := \max(P_M^1, P_M^2)$ implies

$$\|p_\epsilon\|_{L^1(-L, L)} \leq (\epsilon + P_M) \int_{-L}^L |n_\epsilon| dx \leq C e^{G_m t} \|n_\epsilon^{\text{ini}}\|_{L^1(-L, L)}.$$

L^1 estimates on the x derivatives.

Recalling (7), we can reformulate (9) by

$$\partial_t n_\epsilon - \partial_{xx} H(n_\epsilon) = n_\epsilon G(p_\epsilon, t, x) \tag{22}$$

with $G(p, t, x) = G_1(p) \mathbf{1}_{x \leq \zeta_\epsilon(t)} + G_2(p) \mathbf{1}_{x \geq \zeta_\epsilon(t)}$. The space derivative of this growth function is given by,

$$\partial_x G(p, t, x) = (G_1(p) - G_2(p)) \delta_{x=\zeta_\epsilon(t)} + G_1'(p) \partial_x p \mathbf{1}_{x \leq \zeta_\epsilon(t)} + G_2'(p) \partial_x p \mathbf{1}_{x \geq \zeta_\epsilon(t)}.$$

We derive (22) with respect to x ,

$$\begin{aligned} \partial_t \partial_x n_\epsilon - \partial_{xx} (\partial_x H(n_\epsilon)) &= \partial_x n_\epsilon G(p_\epsilon, t, x) + n_\epsilon (G_1(p_\epsilon) - G_2(p_\epsilon)) \delta_{x=\zeta_\epsilon(t)} \\ &\quad + n_\epsilon (G_1'(p_\epsilon) \mathbf{1}_{x \leq \zeta_\epsilon(t)} + G_2'(p_\epsilon) \mathbf{1}_{x \geq \zeta_\epsilon(t)}) \partial_x p_\epsilon. \end{aligned}$$

We multiply by $\text{sign}(\partial_x n_\epsilon) = \text{sign}(\partial_x p_\epsilon)$ and use the Kato inequality,

$$\begin{aligned} \partial_t |\partial_x n_\epsilon| - \partial_{xx} (|\partial_x H(n_\epsilon)|) &\leq |\partial_x n_\epsilon| G(p_\epsilon, t, x) \\ &\quad + n_\epsilon (G_1(p_\epsilon) - G_2(p_\epsilon)) \delta_{x=\zeta_\epsilon(t)} \text{sign}(\partial_x n_\epsilon) \\ &\quad + n_\epsilon (G_1'(p_\epsilon) \mathbf{1}_{x \leq \zeta_\epsilon(t)} + G_2'(p_\epsilon) \mathbf{1}_{x \geq \zeta_\epsilon(t)}) |\partial_x p_\epsilon|. \end{aligned}$$

We integrate in space on $(-L, L)$. Using the fact that $\max_{[0, P_M^1]} G_1' \leq -\gamma < 0$ and $\max_{[0, P_M^2]} G_2' \leq -\gamma < 0$ (see (11)) and that $\partial_x H(n_\epsilon)(\pm L, t) = H'(n_\epsilon) \partial_x n_\epsilon(\pm L, t) = 0$,

$$\begin{aligned} \partial_t \int_{-L}^L |\partial_x n_\epsilon| dx &\leq G_m \int_{-L}^L |\partial_x n_\epsilon| dx - \gamma \int_{-L}^L n_\epsilon |\partial_x p_\epsilon| dx \\ &\quad + n_\epsilon(t, \zeta_\epsilon(t)) |G_1(p_\epsilon(t, \zeta_\epsilon(t)) - G_2(p_\epsilon(t, \zeta_\epsilon(t)))|. \end{aligned}$$

Using Gronwall's lemma and the uniform bound on n_ϵ and G_1 and G_2 (see (11)), we deduce that, for all $t > 0$,

$$\|\partial_x n_\epsilon(t)\|_{L^1(-L, L)} + \gamma \int_0^t \int_{-L}^L n_\epsilon |\partial_x p_\epsilon| dx ds \leq C e^{G_m t} (\|\partial_x n_\epsilon^{\text{ini}}\|_{L^1(-L, L)} + 1). \quad (23)$$

This concludes the proof for the estimate on $\partial_x n_\epsilon$. Then,

$$\|\partial_x p_\epsilon\|_{L^1(-L, L)} = \int_{-L}^L |\partial_x p_\epsilon| dx = \int_{-L}^L \frac{\epsilon}{(1-n_\epsilon)^2} |\partial_x n_\epsilon| dx.$$

We split the latter integral in two: either $n_\epsilon \leq 1/2$ and then $\frac{\epsilon}{(1-n_\epsilon)^2} \leq C$; either $n_\epsilon \geq 1/2$,

$$\begin{aligned} \|\partial_x p_\epsilon\|_{L^1(-L, L)} &\leq C \int_{n_\epsilon \leq 1/2} |\partial_x n_\epsilon| dx + \int_{n_\epsilon \geq 1/2} |\partial_x p_\epsilon| dx \\ &\leq C \int_{n_\epsilon \leq 1/2} |\partial_x n_\epsilon| dx + 2 \int_{n_\epsilon \geq 1/2} \frac{1}{2} |\partial_x p_\epsilon| dx \\ &\leq C \|\partial_x n_\epsilon(t)\|_{L^1(-L, L)} + 2 \int_{n_\epsilon \geq 1/2} n_\epsilon |\partial_x p_\epsilon| dx. \end{aligned}$$

Then, we integrate in time and we deduce using (23)

$$\|\partial_x p_\epsilon\|_{L^1(Q_T)} \leq C' e^{G_m T} (\|\partial_x n_\epsilon\|_{L^1(-L, L)} + 1).$$

Hence we have a uniform bound on $\partial_x p_\epsilon$ in $L^1(Q_T)$. To recover the estimate on $\partial_x n_{1\epsilon}$ and $\partial_x n_{2\epsilon}$ we deduce from (7),

$$\begin{aligned} \partial_x n_{1\epsilon} &= \partial_x n_\epsilon \mathbf{1}_{x \leq \zeta_\epsilon(t)} + n_\epsilon \delta_{x=\zeta_\epsilon(t)}, \\ \partial_x n_{2\epsilon} &= \partial_x n_\epsilon \mathbf{1}_{x \leq \zeta_\epsilon(t)} - n_\epsilon \delta_{x=\zeta_\epsilon(t)}. \end{aligned}$$

So

$$\|\partial_x n_{1\epsilon}\|_{L^1(-L, L)} = \int_{x \leq \zeta_\epsilon(t)} \partial_x n_{1\epsilon} dx + n_\epsilon(t, \zeta_\epsilon(t)) \leq \|\partial_x n_\epsilon\|_{L^1(-L, L)} + \|n_{1\epsilon}\|_\infty,$$

and

$$\|\partial_x n_{2\epsilon}\|_{L^1(-L, L)} = \int_{x \geq \zeta_\epsilon(t)} \partial_x n_{2\epsilon} dx - n_\epsilon(t, \zeta_\epsilon(t)) \leq \|\partial_x n_\epsilon\|_{L^1(-L, L)} + \|n_{2\epsilon}\|_\infty$$

This concludes the proof. \square

3.1.3 L^2 estimate for $\partial_x p$

Lemma 3 (L^2 estimate for $\partial_x p$). *Let us assume that (11) and (12) hold. Let $(n_{1\epsilon}, n_{2\epsilon}, p_\epsilon)$ be a solution to (1)–(4). Then, for all $T > 0$ we have a uniform bound on $\partial_x p_\epsilon$ in $L^2(Q_T)$.*

Proof. For a given function ψ we have, multiplying (4) by $\psi(n_\epsilon)$,

$$\partial_t n_\epsilon \psi(n_\epsilon) - \partial_x (n_\epsilon \partial_x p_\epsilon) \psi(n_\epsilon) = (n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon)) \psi(n_\epsilon).$$

Integrating on $(-L, L)$, we have

$$\frac{d}{dt} \int_{-L}^L \Psi(n_\epsilon) dx + \int_{-L}^L n_\epsilon \partial_x n_\epsilon \cdot \partial_x p_\epsilon \psi'(n_\epsilon) dx = \int_{-L}^L (n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon)) \psi(n_\epsilon) dx,$$

where Ψ is an antiderivative of ψ . We choose $\psi(n) = \epsilon(\ln(n) - \ln(1-n) + \frac{1}{1-n})$ so that $n_\epsilon \psi'(n_\epsilon) = P'(n_\epsilon)$. Inserting the expression of ψ , we get

$$\frac{d}{dt} \int_{-L}^L \epsilon n_\epsilon \ln\left(\frac{n_\epsilon}{1-n_\epsilon}\right) dx + \int_{-L}^L |\partial_x p_\epsilon|^2 dx \leq G_m \int_{-L}^L \epsilon n_\epsilon \left| \ln(n_\epsilon) - \ln(1-n_\epsilon) + \frac{1}{1-n_\epsilon} \right| dx.$$

After integrating in time and using the expression of the pressure (3), we have

$$\begin{aligned} & \int_{-L}^L \epsilon n_\epsilon \ln\left(\frac{p_\epsilon}{\epsilon}\right) dx - \int_{-L}^L \epsilon n_\epsilon^{\text{ini}} \ln\left(\frac{n_\epsilon^{\text{ini}}}{1-n_\epsilon^{\text{ini}}}\right) dx + \int_0^T \int_{-L}^L |\partial_x p_\epsilon|^2 dx dt \\ & \leq G_m \int_0^T \int_{-L}^L \left(\epsilon n_\epsilon \left| \ln\left(\frac{p_\epsilon}{\epsilon}\right) \right| + p_\epsilon \right) dx. \end{aligned}$$

Then, to prove that $\partial_x p_\epsilon \in L^2(Q_T)$, we are left to find a uniform bound on $\int_{-L}^L \epsilon n_\epsilon \left| \ln\left(\frac{p_\epsilon}{\epsilon}\right) \right| dx$. Using the expression of p_ϵ in (3), we have

$$\begin{aligned} \int_{-L}^L \epsilon n_\epsilon \left| \ln\left(\frac{p_\epsilon}{\epsilon}\right) \right| dx & \leq \int_{-L}^L \epsilon n_\epsilon |\ln p_\epsilon| dx + \epsilon \ln(\epsilon) \int_{-L}^L n_\epsilon dx \\ & \leq \int_{-L}^L (1-n_\epsilon) p_\epsilon |\ln p_\epsilon| dx + \epsilon \ln(\epsilon) \int_{-L}^L n_\epsilon dx \end{aligned}$$

Since n_ϵ is bounded in L^1 , the second term of the right hand side is uniformly bounded with respect to ϵ . Moreover given that $0 \leq p_\epsilon \leq P_M$ and $x \mapsto x |\ln x|$ is uniformly bounded on $[0, P_M]$, we get

$$\int_{-L}^L (1-n_\epsilon) p_\epsilon |\ln(p_\epsilon)| dx \leq C \int_{-L}^L \mathbf{1}_{p_\epsilon > 0} dx \leq 2LC.$$

This concludes the proof. □

3.2 Proof of theorem 1

3.2.1 Convergence

In the last paragraph we have found a priori estimates for the densities and their space derivatives. To use a compactness argument, we need to obtain estimates on the time derivative. To do so, we are going to use the Aubin Lions theorem [31].

According to Lemma 3, $n_{1\epsilon} \partial_x p_\epsilon$ and $n_{2\epsilon} \partial_x p_\epsilon$ are in $L^2(Q_T)$. Moreover thanks to Lemma 2, we have that $n_{1\epsilon} G_1(p_\epsilon)$ and $n_{2\epsilon} G_2(p_\epsilon)$ are uniformly bounded in $L^\infty([0, T]; L^1 \cap L^\infty(-L, L))$, so $\partial_t n_{1\epsilon}$ and $\partial_t n_{2\epsilon}$ are uniformly bounded in $L^2([0, T], W^{-1,2}(-L, L))$. We also have $n_{1\epsilon}$ and $n_{2\epsilon}$ bounded in $L^1([0, T], W^{1,1}(-L, L))$. Since we are working in one dimension, we have the following embeddings

$$W^{1,1}(-L, L) \subset L^1(-L, L) \subset W^{-1,2}(-L, L).$$

The Aubin Lions theorem implies that $\{u \in L^1([0, T], W_{loc}^{1,1}(-L, L)); \dot{u} \in L^2([0, T], W^{-1,2}(-L, L))\}$ is compactly embedded in $L^1([0, T], L^1(-L, L))$. So we can extract strongly converging subsequences $n_{1\epsilon}$ and $n_{2\epsilon}$ in $L^1(Q_T)$. The convergence of the pressure follows from the same kind of computation.

3.2.2 Limit model

From the above results, up to extraction of subsequences, $(n_{1\epsilon})_\epsilon$, $(n_{2\epsilon})_\epsilon$, and $(p_\epsilon)_\epsilon$ converge strongly in $L^1(Q_T)$ and a.e. towards some limits denoted n_{10} , n_{20} , and p_0 , respectively. Moreover, due to the uniform estimate on $(\partial_x p_\epsilon)_\epsilon$ in $L^2(Q_T)$ from Lemma 3, we may extract a subsequence, still denoted $(\partial_x p_\epsilon)_\epsilon$, which converges weakly in $L^2(Q_T)$ towards $\partial_x p_0$. Passing to the limit in the uniform estimates of Lemma 2 gives (13) and n_{10}, n_{20}, n_0, p_0 belongs to $BV(Q_T)$.

Then, we recall that

$$\partial_t n_\epsilon - \partial_{xx}(p_\epsilon - \epsilon \ln(p_\epsilon + \epsilon)) = n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon).$$

From the uniform bounds on p_ϵ , we get,

$$\epsilon \ln \epsilon \leq \epsilon \ln(p_\epsilon + \epsilon) \leq \epsilon \ln(P_M + \epsilon).$$

Thus, the term in the Laplacian converges strongly to p_0 . Then, thanks to the strong convergence of n_ϵ and p_ϵ , we deduce that in the sense of distributions

$$\partial_t n_0 - \partial_{xx} p_0 = n_{10} G_1(p_0) + n_{20} G_2(p_0).$$

Moreover, let $\phi \in W^{1,\alpha}(Q_T)$ with $\phi(T, x) = 0$ ($\alpha > 2$) be a test function. We multiply equation (1) by ϕ and integrate using the Neumann boundary conditions, we get

$$\begin{aligned} - \int_0^T \int_{-L}^L n_{1\epsilon} \partial_t \phi \, dt dx - \int_{-L}^L n_{1\epsilon}^{ini}(x) \phi(0, x) \, dx + \int_0^T \int_{-L}^L n_{1\epsilon} \partial_x p_\epsilon \partial_x \phi \, dx dt \\ = \int_0^T \int_{-L}^L n_{1\epsilon} G_1(p_\epsilon) \phi \, dx dt. \end{aligned}$$

Due to the strong convergence of $n_{1\epsilon}$ and p_ϵ , we can pass easily to the limit $\epsilon \rightarrow 0$ into the first term of the left hand side and into the term in the right hand side. For the second term, we use the assumptions on the initial data to pass into the limit. For the third term, we can pass to the limit in a product of a weak-strong convergence from standard arguments, then we arrive at

$$\begin{aligned} - \int_0^T \int_{-L}^L n_{10} \partial_t \phi \, dt dx - \int_{-L}^L n_1^{ini}(x) \phi(0, x) \, dx + \int_0^T \int_{-L}^L n_{10} \partial_x p_0 \partial_x \phi \, dx dt \\ = \int_0^T \int_{-L}^L n_{10} G_1(p_0) \phi \, dx dt, \end{aligned}$$

for any test function $\phi \in W^{1,\alpha}(Q_T)$. Then we obtain the weak formulation of (16) with Neumann boundary conditions on p_0 . We proceed by the same token to recover (17).

Passing into the limit in the relation $(1 - n_\epsilon)p_\epsilon = \epsilon n_\epsilon$ implies

$$(1 - n_0)p_0 = 0.$$

We can also pass to the limit for the segregation and deduce $n_{10}n_{20} = 0$. To conclude the proof of Theorem 1, we are left to establish the relation (20).

3.3 Complementary relation

In this section we want to pass to the limit in the equation for the pressure (10). However, this task can not be performed easily since we only have uniform estimates on the gradient of n and p , whereas we need strong convergence of the gradient to pass to the limit in (10). Then we propose to work on the time antiderivative. Let us denote $q_\epsilon = p_\epsilon - \epsilon \ln(p_\epsilon + \epsilon)$. Then, we have proved above that $q_\epsilon \rightarrow p_0$ strongly as $\epsilon \rightarrow 0$, and

$$\partial_t n_\epsilon - \partial_{xx} q_\epsilon = n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon). \quad (24)$$

Let us introduce Q_ϵ a time antiderivative of q_ϵ , $Q_\epsilon(t, x) := \int_0^t q_\epsilon(s, x) ds$. From the strong convergence of q_ϵ , we deduce that $Q_\epsilon \rightarrow P_0 := \int_0^t p_0(s, x) ds$ as $\epsilon \rightarrow 0$. By a simple time integration of (24), we have

$$\partial_{xx} Q_\epsilon = n_\epsilon - n_\epsilon^{\text{ini}} - \int_0^t (n_{1\epsilon} G_1(p_\epsilon) + n_{2\epsilon} G_2(p_\epsilon)) ds. \quad (25)$$

From Lemma 2, we deduce that $\partial_{xx} Q_\epsilon$ is uniformly bounded in $L^1 \cap L^\infty([0, T] \times (-L, L))$. Moreover, using the relation $q_\epsilon = p_\epsilon - \epsilon \ln(p_\epsilon + \epsilon)$, we get

$$\partial_t \partial_x Q_\epsilon = \partial_x q_\epsilon = \frac{p_\epsilon}{p_\epsilon + \epsilon} \partial_x p_\epsilon.$$

From the uniform bound on $\partial_x p_\epsilon$ in $L^2(Q_T)$ in Lemma 3, we deduce that the sequence $(\partial_t \partial_x Q_\epsilon)_\epsilon$ is uniformly bounded in $L^2([0, T] \times (-L, L))$. Thus we have obtained that the sequence $(\partial_x Q_\epsilon)_\epsilon$ is uniformly bounded in $H^1([0, T] \times (-L, L))$. We deduce from the compact embedding of $H^1(Q_T)$ into $L^2(Q_T)$ that we can extract a subsequence, still denoted $(\partial_x Q_\epsilon)_\epsilon$, converging strongly in $L^2(Q_T)$ and weakly in $H^1(Q_T)$ towards a limit denoted $\overline{\partial Q}$. Since $Q_\epsilon \rightarrow P_0$ as $\epsilon \rightarrow 0$, we deduce $\overline{\partial Q} = \partial_x P_0$.

Thus, we can pass to the limit $\epsilon \rightarrow 0$ into the equation (25). We obtain

$$n_0 - n_0^{\text{ini}} - \partial_{xx} P_0 = \int_0^t (n_{10} G_1(p_0) + n_{20} G_2(p_0)) ds.$$

Multiplying by p_0 and using the relation $p_0 n_0 = p_0$, we deduce the complementary relation (20). This concludes the proof of Theorem 1.

3.4 Uniqueness of solutions

In this section, we focus on the uniqueness of solutions to the limiting problem (15)–(19). We first observe that from (15) and (19), we have

$$\partial_t n_0 - \partial_{xx}(n_0 p_0) = n_{10} G_1(p_0) + n_{20} G_2(p_0), \quad \text{in } \mathcal{D}'(Q_T). \quad (26)$$

Since we have the segregation property given by (19), we deduce that the support of n_{10} and of n_{20} are disjoint. Then, by taking test functions with support included in the support of n_{10} or of n_{20} in the weak formulation of (26), we deduce that

$$\partial_t n_{10} - \partial_{xx}(n_{10} p_0) = n_{10} G_1(p_0), \quad \text{in } \mathcal{D}'(Q_T), \quad (27)$$

$$\partial_t n_{20} - \partial_{xx}(n_{20} p_0) = n_{20} G_2(p_0), \quad \text{in } \mathcal{D}'(Q_T). \quad (28)$$

We are going to prove that system (27)–(28) complemented with the segregation property (19) and the relation (18) admits a unique solution. More precisely our result reads:

Proposition 1. *Let us assume that assumptions (11) on G_i , $i = 1, 2$ holds. There exists a unique solution (n_{10}, n_{20}, p_0) to the problem (27)-(28)-(18)-(19) with $0 \leq n_{i0} \leq 1$ for $i = 1, 2$.*

Proof. We follow the idea developped in [27] and adapt the Hilbert's duality method. Consider two solutions (n_{10}, n_{20}, p_0) and $(\widetilde{n}_{10}, \widetilde{n}_{20}, \widetilde{p}_0)$ of the system (27)-(28)-(18)-(19). Making the difference and denoting $q_i = n_{i0}p_0$ and $\widetilde{q}_i = \widetilde{n}_{i0}\widetilde{p}_0$, for $i = 1, 2$, we have

$$\begin{aligned} \partial_t(n_{10} - \widetilde{n}_{10}) - \partial_{xx}(q_1 - \widetilde{q}_1) &= n_{10}G_1(p_0) - \widetilde{n}_{10}G_1(\widetilde{p}_0), & \text{in } \mathcal{D}'(Q_T), \\ \partial_t(n_{20} - \widetilde{n}_{20}) - \partial_{xx}(q_2 - \widetilde{q}_2) &= n_{20}G_2(p_0) - \widetilde{n}_{20}G_2(\widetilde{p}_0), & \text{in } \mathcal{D}'(Q_T). \end{aligned}$$

We first observe that on the set $\{n_{10} > 0\} \cap \{p_0 > 0\}$, we have $q_1 = p_0$ from (18). Hence we have $n_{10}G_1(p_0) = n_{10}G_1(q_1)$. The same observation holds for the other terms in the right hand side of these latter equations. For any suitable test functions ψ_1 and ψ_2 , we have, for $i = 1, 2$,

$$\iint_{Q_T} \left[(n_{i0} - \widetilde{n}_{i0})\partial_t\psi_i + (q_i - \widetilde{q}_i)\partial_{xx}\psi_i + (n_{i0}G_i(q_i) - \widetilde{n}_{i0}G_i(\widetilde{q}_i))\psi_i \right] dxdt = 0. \quad (29)$$

This can be rewritten as, for $i = 1, 2$,

$$\iint_{Q_T} (n_{i0} - \widetilde{n}_{i0} + q_i - \widetilde{q}_i) \left(A_i\partial_t\psi_i + B_i\partial_{xx}\psi_i + A_iG_i(q_i)\psi_i - C_iB_i\psi_i \right) dxdt = 0, \quad (30)$$

where

$$A_i = \frac{n_{i0} - \widetilde{n}_{i0}}{n_{i0} - \widetilde{n}_{i0} + q_i - \widetilde{q}_i}, \quad B_i = \frac{q_i - \widetilde{q}_i}{n_{i0} - \widetilde{n}_{i0} + q_i - \widetilde{q}_i}, \quad C_i = -\widetilde{n}_{i0} \frac{G_i(q_i) - G_i(\widetilde{q}_i)}{q_i - \widetilde{q}_i},$$

and we define $A_i = 0$ as soon as $n_{i0} = \widetilde{n}_{i0}$ and $B_i = 0$ as soon as $q_i = \widetilde{q}_i$, whatever is the value of their denominators. It is shown in Lemma 4 below that, for $i = 1, 2$, we have $0 \leq A_i \leq 1$, $0 \leq B_i \leq 1$, $0 \leq C_i \leq \gamma$.

The idea of the Hilbert's duality method consists in solving the *dual problem*, which is defined here by, for any smooth function Φ_i , $i = 1, 2$,

$$\begin{cases} A_i\partial_t\psi_i + B_i\partial_{xx}\psi_i + A_iG_i(q_i)\psi_i - C_iB_i\psi_i = A_i\Phi_i, & \text{in } Q_T, \\ \partial\psi_i(\pm L) = 0 & \text{in } (0, T), \quad \psi_i(\cdot, T) = 0 & \text{in } (-L, L). \end{cases} \quad (31)$$

If such a system admits a smooth solution, then, by choosing ψ_i as a test function in (30), we get

$$\iint_{Q_T} (n_{i0} - \widetilde{n}_{i0} + q_i - \widetilde{q}_i) A_i \Phi_i dxdt = 0.$$

From the expression of A_i , we deduce

$$\iint_{Q_T} (n_{i0} - \widetilde{n}_{i0}) \Phi_i dxdt = 0,$$

for any smooth function Φ_i , $i = 1, 2$. It is obvious to deduce the uniqueness for the density. Uniqueness for the pressure will follow from (29).

However, the dual problem (31) is not uniformly parabolic and its coefficients are not smooth. Then, in order to make this step rigorous, a regularization procedure is required. It can be done exactly as in [27, p 109-110]. For the sake of completeness of this paper, this regularizing procedure is recalled in Appendix A. \square

Lemma 4. *Under assumptions (11), we have $0 \leq A_i \leq 1$, $0 \leq B_i \leq 1$, $0 \leq C_i \leq \gamma$, for $i = 1, 2$.*

Proof. We observe that, for $i = 1, 2$, $n_{i0} > \widetilde{n}_{i0}$ implies $q_i \geq \widetilde{q}_i$. Indeed, either $\widetilde{n}_{i0} = 0$ and then $\widetilde{q}_i = 0 \leq q_i$, or $0 < \widetilde{n}_{i0} < 1$ and then from the segregation property (19) we have $\widetilde{n}_0 = \widetilde{n}_{i0}$ and from the relation $(1 - \widetilde{n}_0)\widetilde{p}_0 = 0$ we deduce that $\widetilde{p}_0 = 0$, thus $\widetilde{q}_i = 0 \leq q_i$. Similarly, for $i = 1, 2$, $\widetilde{n}_{i0} > n_{i0}$ implies $\widetilde{q}_i \geq q_i$. By setting $A_i = 0$ whenever $\widetilde{n}_{i0} = n_{i0}$, we conclude that $0 \leq A_i \leq 1$.

By the same token, we show that, for $i = 1, 2$, $q_i \geq \widetilde{q}_i$ implies $n_{i0} \geq \widetilde{n}_{i0}$. Indeed, from $q_i = n_{i0}p_0 > 0$, we deduce that $n_{i0} > 0$ which implies $n_0 = n_{i0}$, and then $p_0 > 0$ implies from (18) that $n_{i0} = 1 \geq \widetilde{n}_{i0}$. Hence, $0 \leq B_i \leq 1$.

Finally, the bound on C_i is a direct consequence of the fact that G_i is nonincreasing and Lipschitz (see (11)) and that $0 \leq \widetilde{n}_{i0} \leq 1$. \square

4 Numerical simulations

4.1 Numerical scheme

The numerical simulations are performed using a finite volume method similar as the one proposed in [12, 14]. The scheme used for the conservative part is a classical explicit upwind scheme. To facilitate the reading of this paper, we recall here the scheme used. We divide the computational domain into finite-volume cells $C_j = [x_{j-1/2}, x_{j+1/2}]$ of uniform size Δx with $x_j = j\Delta x$, $j \in \{1, \dots, M_x\}$, and $x_j = \frac{x_{j-1/2} + x_{j+1/2}}{2}$ so that

$$-L = x_{1/2} < x_{3/2} < \dots < x_{j-1/2} < x_{j+1/2} < \dots < x_{M_x-1/2} < x_{M_x+1/2} = L,$$

and define the cell average of functions $n_1(t, x)$ and $n_2(t, x)$ on the cell C_j by

$$\bar{n}_{\beta_j}(t) = \frac{1}{\Delta x} \int_{C_j} n_{\beta}(t, x) dx, \quad \beta \in \{1, 2\}.$$

The scheme is obtained by integrating system (1)-(2) over C_j and is given by

$$\bar{n}_{\beta_j}^{k+1} = -\frac{F_{\beta,j+1/2}^k - F_{\beta,j-1/2}^k}{\Delta x} + \bar{n}_{\beta_j}^{k+1} G_{\beta}(p_j^k) \quad \text{for } \beta = 1, 2, \quad (32)$$

where $F_{\beta,j+1/2}^k$ are numerical fluxes approximating $-n_{\beta}^k u_{\beta}^k := -n_{\beta}^k \partial_x(p_{\beta}^k)$ and defined by:

$$F_{\beta,j+1/2}^k = (u_{\beta,j+1/2}^k)^+ \bar{n}_{\beta_j}^k + (u_{\beta,j+1/2}^k)^- \bar{n}_{\beta_{j+1}}^k, \quad \beta \in \{1, 2\},$$

where

$$u_{\beta,j+1/2}^k = \begin{cases} -\frac{p_{j+1}^k - p_j^k}{\Delta x}, & \forall j \in \{2, \dots, M_x - 1\}, \\ 0, & \text{otherwise,} \end{cases}$$

with the discretized pressure

$$p_j^k = \frac{\epsilon n_j^k}{1 - n_j^k}, \quad n_j^k = \bar{n}_{1_j}^k + \bar{n}_{2_j}^k.$$

We use the usual notation $(u)^+ = \max(u, 0)$ and $(u)^- = \min(u, 0)$ for the positive part and, respectively, the negative part of u . Neumann boundary conditions are also implemented at the boundaries of the computational model.

In order to illustrate the time dynamics for the model, we plot in Fig 1 the densities computed thanks to the above scheme for $\epsilon = 1$ at different times : (a) $t = 0$, (b) $t = 0.1$, (c) $t = 0.3$, (d) $t = 0.6$, (e) $t = 1$ and (f) $t = 2$. For this numerical simulation, the densities are initialized by

$$n_1^{\text{ini}}(x) = 0.98 \mathbf{1}_{[-L; 0.25]}(x) \quad \text{and} \quad n_2^{\text{ini}}(x) = 0.98 \mathbf{1}_{[0.25; L]}(x), \quad (33)$$

with $L = 5$, and the growth rates are defined by

$$G_1(p) = 10(1 - p/2) \quad \text{and} \quad G_2(p) = 10(1 - p). \quad (34)$$

We recall that we have defined the parameters P_M^1 and P_M^2 as the values of the pressure for which the growth functions vanish (see (11)). In this case their numerical values are given by $P_M^1 = 2$ and $P_M^2 = 1$. Then, we define

$$N_{M\epsilon}^1 = p^{-1}(P_M^1) = \frac{P_M^1}{\epsilon + P_M^1} \quad \text{and} \quad N_{M\epsilon}^2 = p^{-1}(P_M^2) = \frac{P_M^2}{\epsilon + P_M^2}. \quad (35)$$

Since the growth functions are different, clearly $N_{M\epsilon}^2 < N_{M\epsilon}^1$.

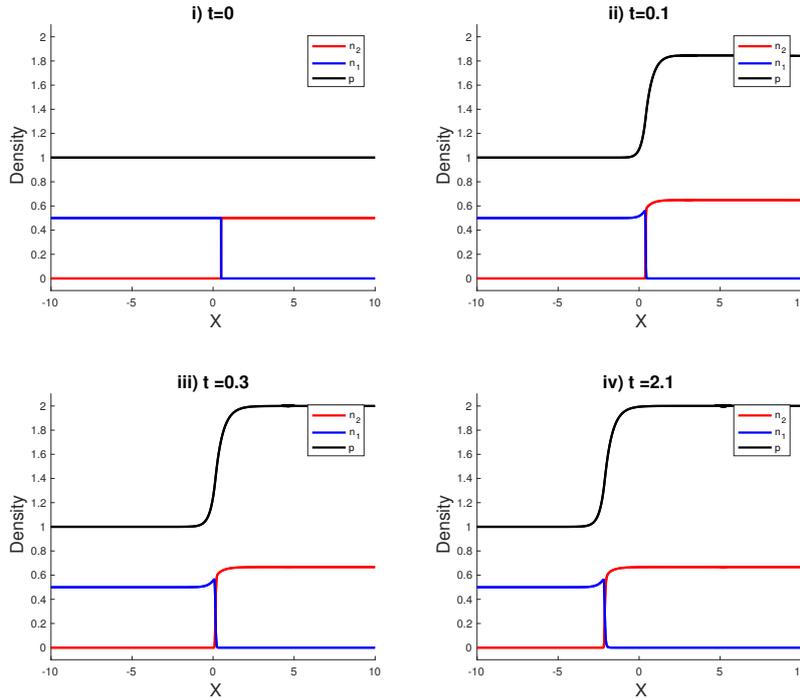


Figure 1: Densities n_1 (red), n_2 (blue) and pressure p as functions of position x at different times: a) $t = 0$, b) $t = 0.1$, c) $t = 0.3$, d) $t = 0.6$, e) $t = 1$ and f) $t = 2$; in the case $\epsilon = 1$ with the initial densities and growth rate defined by (33)-(34).

In Fig 1 the red and blue species are initially segregated and equal to 0.5. At first the dynamics is driven by the growth term, so the two species grow and reach their respective maximal packing values $N_{M\epsilon}^1$ and $N_{M\epsilon}^2$. Once this value is reached ($t = 1, 2$ on both panel (ii), (iii) and (iv)), we observe two phenomena. First a bump is created on the left side of the interface, in the domain of n_2 . This bump help the total densities to stay continuous, as it joins the two maximal densities. It also means that, at the interface, the pressure is going to be higher than the limit pressure P_M^2 . Then the derivative of the pressure at the interface is positive, which induces a motion of the interface representing the fact that the red species n_1 pushes the blue species n_2 . This motion of the interface is the second phenomenon which is observed.

4.2 Influence of the parameter ϵ

In order to illustrate our main result on the limit $\epsilon \rightarrow 0$, we show, in this section, some numerical simulations of the model (1)-(2) when ϵ goes to 0. We also compare with the analytical solution of the limiting Hele-Shaw free boundary model. To perform these simulations we use the numerical scheme (32) complemented with the initial condition (33) and the growth function (34). For the limiting model, we use the initial conditions

$$n_1^{\text{ini}}(x) = \mathbf{1}_{[-L;0.25]}(x) \quad \text{and} \quad n_2^{\text{ini}}(x) = \mathbf{1}_{[0.25;L]}(x),$$

and the growth function (34). The analytical expressions of the solution to the limiting Hele-Shaw system is computed in [14].

Fig 2 displays the time dynamics of the densities for different values of ϵ : (a) $\epsilon = 1$, (b) $\epsilon = 0.1$, (c) $\epsilon = 0.01$, and (d) $\epsilon = 0.001$, along with solution to the Hele-Shaw system (e). For all simulations, the densities are plotted at times $t = 0.5$, $t = 1$ and $t = 1.5$.

We observe in Fig. 2 that the time dynamics of the numerical solutions is similar for each case and follows the dynamics presented above for the case $\epsilon = 1$. The main difference observed is the maximal packing value $N_{M\epsilon}^1$ and $N_{M\epsilon}^2$. Indeed since the maximal packing values are given by (35), when $\epsilon \rightarrow 0$, the maximal packing value converges to 1. This is consistent with the numerical results shown in Fig. 2. In addition we observe that as ϵ decreases the stiffness of the densities increases. In overall we observe that as $\epsilon \rightarrow 0$ densities converge to Heaviside functions.

4.3 Particular solutions: tumor spheroid

One interested application of this study is tissue development. Since we consider a system with two populations of cells, we can for example consider the case of tumour with proliferative cells, whose density is denoted n_2 , and quiescent cells, whose density is denoted n_1 .

Solution of the limiting Hele-Shaw problem. We assume that initially the tumor is a spheroid centered in 0 and is composed by a spherical core representing the quiescent cells surrounded by a ring representing the proliferative cells. Then, we are looking for particular solution of the limiting Hele-Shaw problem (1)-(2) under the form:

$$n_1(t, x) = \mathbf{1}_{\Omega_1(t)}(x) \quad \text{with} \quad \Omega_1(t) = \{n_1(x, t) = 1\} = B_{[-R_1(t), R_1(t)]},$$

$$n_2(t, x) = \mathbf{1}_{\Omega_2(t)}(x) \quad \text{with} \quad \Omega_2(t) = \{n_2(x, t) = 1\} = B_{(-L, L)} \setminus B_{[-R_1(t), R_1(t)]}.$$

The radius $R_1(t)$, with $R_1(t) < L$, is computed according to the geometric motion rules

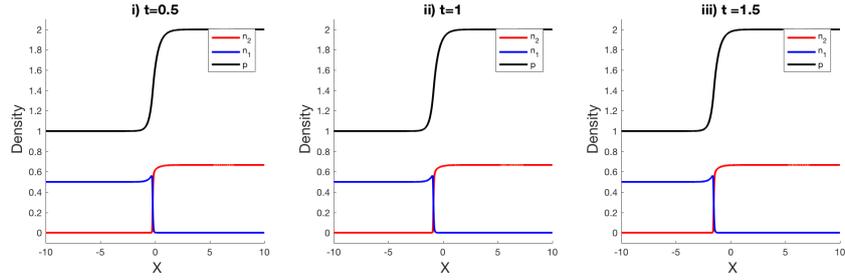
$$\begin{cases} R_1'(t) = -\partial_x p(R_1(t)), \\ R_1(0) = R_1^0, \end{cases}$$

where p is the solution of

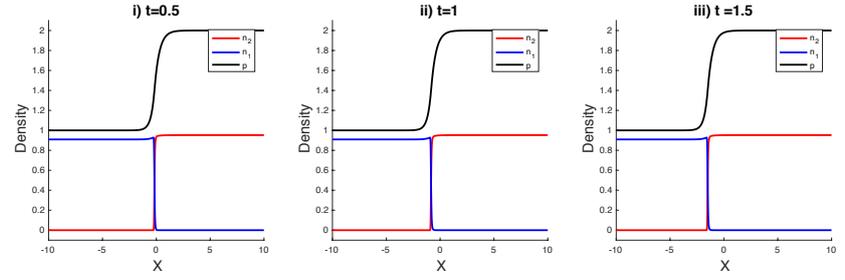
$$-\partial_{xx} p = n_1 G_1(p) + n_2 G_2(p) \quad \text{in} \quad \Omega_1(t) \cup \Omega_2(t).$$

Such functions n_1 and n_2 are solutions to the limiting Hele-Shaw problem (1)-(2). Indeed by differentiating the densities, in the distributional sense, we get,

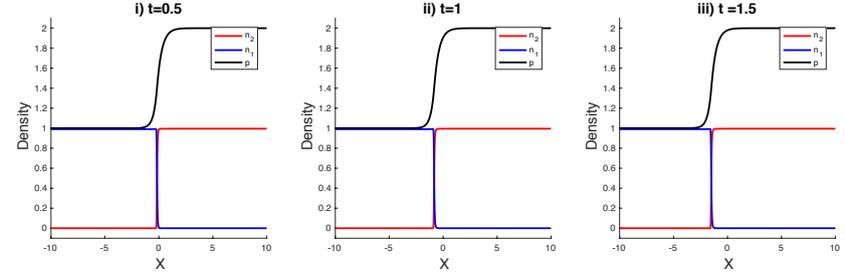
$$\begin{aligned} \partial_t n_1 &= R_1'(t) (\delta_{x=R_1(t)} - \delta_{x=-R_1(t)}), \\ \partial_x (n_1 \partial_x p) &= (\delta_{x=R_1(t)} - \delta_{x=-R_1(t)}) \partial_x p + \mathbf{1}_{[-R_1(t), R_1(t)]} \partial_{xx} p. \end{aligned}$$



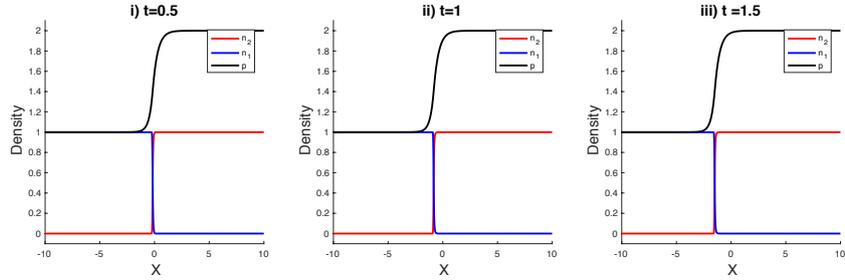
(a) $\epsilon = 1$



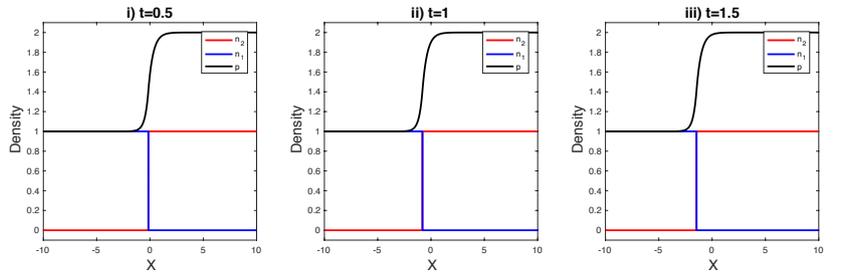
(b) $\epsilon = 0.1$



(c) $\epsilon = 0.01$



(d) $\epsilon = 0.001$



(e) Hele-Shaw system

Figure 2: Densities n_1 (red), n_2 (blue) as functions of position x at different times: (i) $t = 0.5$, (ii) $t = 1$, (iii) $t = 1.5$; and for different values of ϵ : (a) $\epsilon = 1$, (b) $\epsilon = 0.1$, (c) $\epsilon = 0.01$, (d) $\epsilon = 0.001$, (e) Hele-Shaw system.

Since $R_1'(t) = -\partial_x p(R_1(t))$, it follows that

$$\partial_t n_1 - \partial_x(n_1 \partial_x p) = \mathbf{1}_{[-R_1(t), R_1(t)]} G_1(p) = n_1 G_1(p).$$

By applying the same computation on n_2 we get,

$$\partial_t n_2 - \partial_x(n_2 \partial_x p) = n_2 G_2(p).$$

Analytical solution. As this paper is reduced to the case of dimension 1, we can compute the exact solution of the limiting Hele-Shaw problem (1)-(2) with this initial configuration for some simple expression of the growth terms G_1 and G_2 . For instance, let us suppose that the growth terms are linear,

$$G_1(p) = g_1(P_M^1 - p) \quad \text{and} \quad G_2(p) = g_2(P_M^2 - p).$$

This choice means that as the pressure increases, the tumor will grow more slowly, until the pressure reach a critical value (P_M^1 or P_M^2 depending of the species) where the growth rate takes negative values, modelling the apoptosis of cells. The solution of the pressure equation is given by,

$$p(x, t) = \begin{cases} (P_M^1 - P_M^2) \frac{\sqrt{g_2} \sinh(\sqrt{g_2}(R_1(t) - L)) \cosh(\sqrt{g_1}x)}{\lambda} & \text{on } \Omega_1(t), \\ (P_M^1 - P_M^2) \frac{\sqrt{g_1} \cosh(\sqrt{g_2}(x - L)) \sinh(\sqrt{g_1}R_1(t))}{\lambda} & \text{on } \Omega_2(t). \end{cases}$$

with

$$\lambda = \sqrt{g_1} \cosh(\sqrt{g_2}(R_1 - L)) \sinh(\sqrt{g_1}R_1) - \sqrt{g_2} \sinh(\sqrt{g_2}(R_1 - L)) \cosh(\sqrt{g_1}R_1),$$

Computing the derivatives at the interface $R_1(t)$ we deduce that,

$$R_1'(t) = -\sqrt{g_1 g_2} (P_M^1 - P_M^2) \frac{\sinh(\sqrt{g_2}(R_1(t) - L)) \cosh(\sqrt{g_1}R_1(t))}{\lambda}. \quad (36)$$

We are interested in the study of the evolution of R_1 in time, in function of the parameters g_1, g_2, P_M^1, P_M^2 . Given that $0 \leq R_1(t) \leq L$, it is straightfoward that $\lambda \leq 0$. From (36), we deduce that the sign of $R_1'(t) \geq 0$ is the same as the sign of $P_M^1 - P_M^2$.

Numerical simulations Finally we show some simulations of the mechanical problem for the case of spheroid tumor growth. We run the simulations with $\epsilon = 0.01$ as we have shown in Section 4.2 that the simulations are close enough from the free boundary model. We consider two populations with the same space configuration as at the beginning of this section,

$$n_1 = 0.5 \mathbf{1}_{B_{[-R_1(t), R_1(t)]}} \quad \text{and} \quad n_2 = 0.5 \mathbf{1}_{B_{[-L, L] \setminus [-R_1(t), R_1(t)]}},$$

with

$$R_1(0) = 0.5 \quad \text{and} \quad R_2(0) = 1.5.$$

We fix the parameter ϵ to the value 1. The growth rates are going to defined the dynamics of the two populations. In the first example, we choose growth functions such that we observe death of the inner species n_1 , which corresponds to the apoptosis of one population of cells. The growth functions are defined by

$$G_1(p) = 10(1 - p) \quad \text{and} \quad G_2(p) = 10(1 - p/2), \quad (37)$$

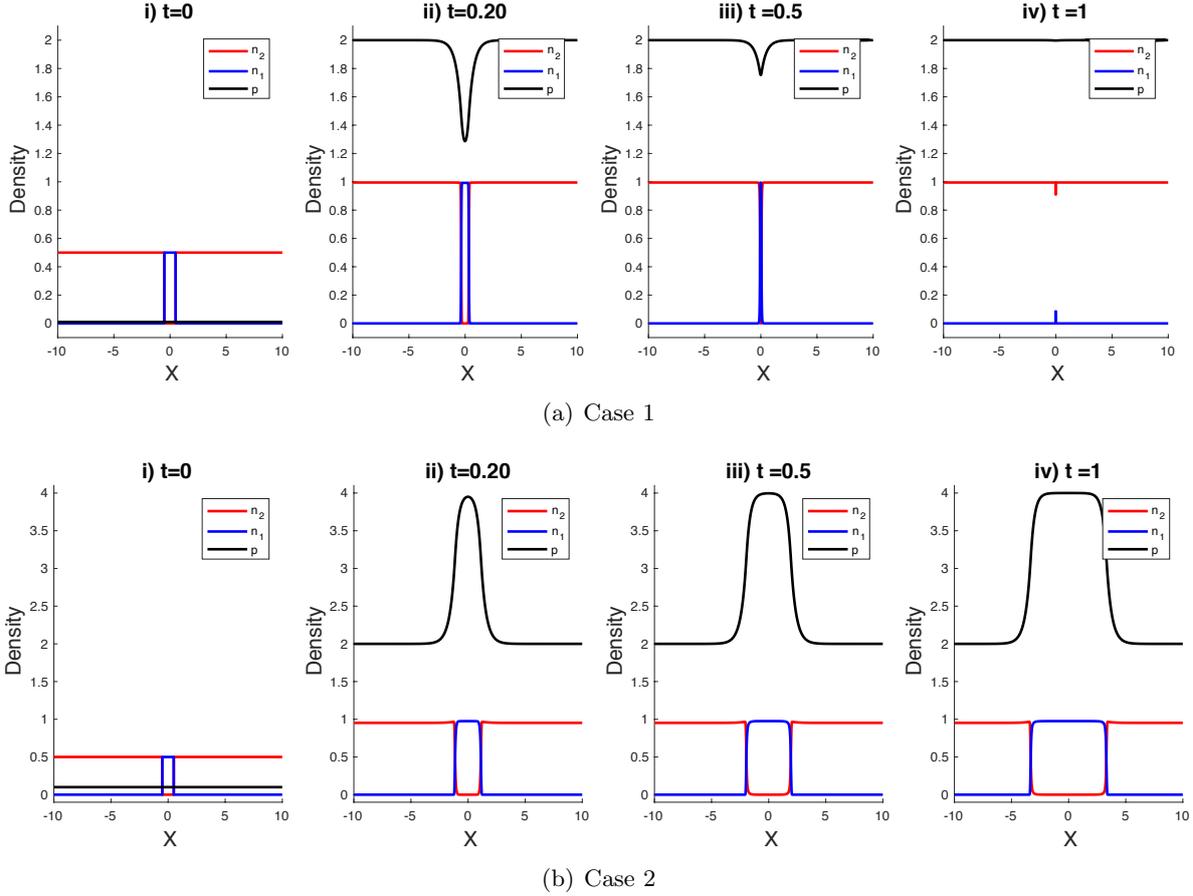


Figure 3: Densities n_1 (red), n_2 (blue) and p (black) as functions of position x for different growth function at different times: (i) $t = 0.3$, (ii) $t = 0.6$, (iii) $t = 1$, (iv) $t = 1.5$.

In a second example we display an example where the species n_1 grows and pushes the surrounding species n_2 .

$$G_1(p) = 10(4 - p) \quad \text{and} \quad G_2(p) = 10(1 - p/2). \quad (38)$$

In Fig 3, we display the time dynamics of the densities of these two examples at different time step: (i) $t = 0$, (ii) $t = 0.1$, (iii) $t = 0.3$, (iv) $t = 0.6$, (v) $t = 1$. It illustrates the two different behaviours mentioned above by (37) and (38). In Fig 3 (a) the red species grows and the blue species disappears since the pressure in the domain is bigger that P_M^1 . In Fig 3 (b), the blue species pushes the red species and propagates.

A Uniqueness of solutions: Regularized dual problem

In this appendix we prove rigorously Proposition 1 using a regularization procedure for the dual problem 31. We follow closely the ideas in [27, p 109-110] which are recall here for the sake of completeness of this paper. Since the coefficients A_i, B_i are not strictly positive and not smooth, then we need to regularize the problem 31. For $i = 1, 2$, let A_i^k, B_i^k, C_i^k and G_i^k be sequences of smooth functions such that,

$$\begin{cases} \|A_i - A_i^k\|_{L^2(Q_T)} < \frac{\alpha_i}{k}, & \frac{1}{k} < A_i^k \leq 1, \\ \|B_i - B_i^k\|_{L^2(Q_T)} < \frac{\beta_i}{k}, & \frac{1}{k} < B_i^k \leq 1, \\ \|C_i - C_i^k\|_{L^2(Q_T)} < \frac{\delta_{1,i}}{k}, & 0 \leq C_i^k \leq M_{1,i}, \quad \|\partial_t C_i^k\|_{L^1(Q_T)} \leq K_{1,i}, \\ \|G_i(q_i) - G_i^k\|_{L^2(Q_T)} < \frac{\delta_{2,i}}{k}, & |G_i^k| < M_{2,i}, \quad \|\partial_x G_i^k\|_{L^2(Q_T)} \leq K_{2,i}, \end{cases}$$

for some constant $\alpha_i, \beta_i, \delta_{1,i}, \delta_{2,i}, M_{1,i}, M_{2,i}, K_{1,i}, K_{2,i}$. For any smooth function $\Phi_i, i = 1, 2$, we consider the following regularised dual system,

$$\begin{cases} \partial_t \psi_i^k + \frac{B_i^k}{A_i^k} \partial_{xx} \psi_i^k + G_i^k \psi_i^k - C_i^k \frac{B_i^k}{A_i^k} \psi_i^k = \Phi_i, & \text{in } Q_T, \\ \partial_x \psi_i^k(\pm L) = 0 & \text{in } (0, T), \quad \psi_i^k(\cdot, T) = 0 & \text{in } (-L, L). \end{cases} \quad (39)$$

As the coefficients $\frac{B_i^k}{A_i^k}$ for $i = 1, 2$, are positive, continuous and bounded below away from zero, the dual equation is uniformly parabolic in Q_T . Then we can solve it and we denote ψ_i^k the solution of (39). This solution ψ_i^k is smooth and can be used as a test function in (30).

Using (30) and (39), for $i = 1, 2$,

$$\iint_{Q_T} (n_{i0} - \widetilde{n}_{i0}) \Phi_i \, dxdt = I_{1,i} - I_{2,i} - I_{3,i} + I_{4,i},$$

where

$$\begin{aligned} I_{1,i} &= \iint_{Q_T} (n_{i0} - \widetilde{n}_{i0} + q_i - \widetilde{q}_i) \frac{B_i^k}{A_i^k} (A_i - A_i^k) (\Delta \psi_i^k - C_i^k \psi_i^k) \, dxdt, \\ I_{2,i} &= \iint_{Q_T} (n_{i0} - \widetilde{n}_{i0} + q_i - \widetilde{q}_i) (B_i - B_i^k) (\Delta \psi_i^k - C_i^k \psi_i^k) \, dxdt, \\ I_{3,i} &= \iint_{Q_T} (n_{i0} - \widetilde{n}_{i0}) (G_i(q_i) - G_i^k) \psi_i^k \, dxdt, \\ I_{4,i} &= \iint_{Q_T} (n_{i0} - \widetilde{n}_{i0} + q_i - \widetilde{q}_i) B_i (C_i - C_i^k) \psi_i^k \, dxdt. \end{aligned}$$

We intend to show that at the limit $k \rightarrow +\infty$, $I_{j,i}$ converges to 0 for $j = 1, 2, 3, 4$ and $i = 1, 2$. To show the convergence, we are going to find estimates on ψ_i^k and its derivative:

- As ψ_i^k is solution of (39) with C_i^k nonnegative and G_i^k uniformly bounded, from the maximum principle we get,

$$\|\psi_i^k\|_{L^\infty(Q_T)} \leq \kappa_1,$$

where κ_1 is independent of k .

- Multiplying (39) by $\partial_{xx}\psi_i^k - C_i^k\psi_i^k$ and integrating on $\Omega \times (t, T)$, we get

$$\begin{aligned}
& \frac{1}{2} \|\partial_x \psi_i^k(t)\|_{L^2(-L, L)}^2 + \iint_{\Omega \times (t, T)} \frac{B_i^k}{A_i^k} |\partial_{xx} \psi_i^k - C_i^k \psi_i^k|^2 dx dt = - \int_{-L}^L (C_i^k \frac{(\psi_i^k)^2}{2})(t) dx \\
& + \iint_{(-L, L) \times (t, T)} \left(-\partial_t C_i^k \frac{(\psi_i^k)^2}{2} - G_i^k |\partial_x \psi_i^k|^2 - \psi_i^k \partial_x G_i^k \partial_x \psi_i^k + C_i^k G_i^k (\psi_i^k)^2 \right. \\
& \quad \left. + \psi_i^k \partial_{xx} \Phi_i - \Phi_i C_i^k \psi_i^k \right) dx dt \\
& \leq K \left(1 - t + \int_t^T \|\partial_x \psi_i^k(s)\|_{L^2(-L, L)}^2 ds \right), \tag{40}
\end{aligned}$$

with K a constant independent of k . By using Gronwall lemma we get the following bound,

$$\sup_{0 \leq t \leq T} \|\partial_x \psi_i^k\|_{L^2(Q_T)} \leq \kappa_2,$$

with κ_2 independent of k .

- Using (40), we get

$$\left\| \left(\frac{B_i^k}{A_i^k} \right)^{1/2} (\partial_{xx} \psi_i^k - C_i^k \psi_i^k) \right\|_{L^2(Q_T)} \leq \kappa_3,$$

with κ_3 independent of k .

We use these bounds to prove the convergence of the integrals $I_{j,i}$ for $j = 1, 2, 3, 4$ and $i = 1, 2$. We get,

$$\begin{aligned}
I_{1,i} &= \tilde{K} \iint_{Q_T} \frac{B_i^k}{A_i^k} |A_i - A_i^k| |\partial_{xx} \psi_i^k - C_i^k \psi_i^k| dx dt \leq \tilde{K} \left(\frac{B_i^k}{A_i^k} \right)^{1/2} (A_i - A_i^k) \|_{L^2(Q_T)} \\
&\leq \tilde{K} k^{1/2} \| (A_i - A_i^k) \|_{L^2(Q_T)} \leq \tilde{K} \alpha k^{-1/2} \\
I_{2,i} &= \tilde{K} \iint_{Q_T} |B_i - B_i^k| |\partial_{xx} \psi_i^k - C_i^k \psi_i^k| dx dt \leq \tilde{K} \left(\frac{A_i^k k^{1/2}}{B_i^k} \right)^{1/2} (B_i - B_i^k) \|_{L^2(Q_T)} \\
&\leq \tilde{K} k^{1/2} \| (B_i - B_i^k) \|_{L^2(Q_T)} \leq \tilde{K} \beta k^{-1/2}, \\
I_{3,i} &= \iint_{Q_T} |n_{i0} - \tilde{n}_{i0}| |G_1(q_1) - G_i^k| |\psi_i^k| dx dt \leq \tilde{K} \| (G_i(q_i) - G_i^k) \|_{L^2(Q_T)} \leq \tilde{K} \frac{\delta_{2,i}}{n}, \\
I_{4,i} &= \tilde{K} \iint_{Q_T} B_i |C_i - C_i^k| |\psi_i^k| dx dt \leq \tilde{K} \| (C_i - C_i^k) \|_{L^2(Q_T)} \leq \frac{\tilde{K}}{n}.
\end{aligned}$$

where \tilde{K} is a constant independent of k . It justifies that $\lim_{k \rightarrow +\infty} I_{j,i} = 0$ for $j = 1, 2, 3, 4$ and $i = 1, 2$. Then

$$\lim_{k \rightarrow +\infty} \iint_{Q_T} (n_{i0} - \tilde{n}_{i0}) \Phi_i dx dt = 0,$$

for any smooth function Φ_i for $i = 1, 2$. This implies that $n_{10} = \tilde{n}_{10}$ and $n_{20} = \tilde{n}_{20}$. Then, we deduce from (29),

$$\iint_{Q_T} \left[(q_i - \tilde{q}_i) \partial_{xx} \psi_i + n_{i0} (G_i(q_i) - G_i(\tilde{q}_i)) \psi_i \right] dx dt = 0.$$

By using $\psi_i = q_i - \tilde{q}_i$, we recover $q_i = \tilde{q}_i$ for $i = 1, 2$. It concludes the proof.

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