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Free boundary limit of tumor growth model with nutrient

Noemi David* Benoît Perthame†

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Abstract

Both compressible and incompressible porous medium models are used in the literature to describe the mechanical properties of living tissues. These two classes of models can be related using a stiff pressure law. In the incompressible limit, the compressible model generates a free boundary problem of Hele-Shaw type where incompressibility holds in the saturated phase.

Here we consider the case with a nutrient. Then, a badly coupled system of equations describes the cell density number and the nutrient concentration. For that reason, the derivation of the free boundary (incompressible) limit was an open problem, in particular a difficulty is to establish the so-called *complementarity relation* which allows to recover the pressure using an elliptic equation. To establish the limit, we use two new ideas. The first idea, also used recently for related problems, is to extend the usual Aronson-Bénilan estimates in L^∞ to an L^2 setting. The second idea is to derive a sharp uniform L^4 estimate on the pressure gradient, independently of space dimension.

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Introduction

We consider a compressible mechanical model of tumor growth, where the cell motion is driven by the pressure gradient according to Darcy's law. The cell proliferation is governed by a biomechanical form of contact inhibition, that prevents cell division when the total cell density exceeds a critical threshold. The evolution of the cell population density $n \geq 0$ and the concentration of nutrients $c \geq 0$ are described by the following type of system

$$\begin{cases} \partial_t n - \operatorname{div}(n\nabla p) = nG(p,c), & x \in \mathbb{R}^d,\ t \geq 0, \\ \partial_t c - \Delta c + nH(c) = (c_B - c)K(p), \\ c(x,t) \to c_B \quad \text{for } x \to \infty. \end{cases} \tag{1}$$

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The pressure within the tissue is denoted by p, and in the compressible setting, we use for simplicity the following law of state

$$p = n^\gamma, \qquad \gamma > 1. \tag{2}$$

The reaction term $G(p, c)$ is the cell division rate and the lowest value of pressure that prevents cell division is called *homeostatic pressure*, and we denote it by p_H. The concentration $c_B > 0$ is the level of nutrients at the source, namely the network of blood vessels. Here, we consider the vascular phase of tumor growth, after *angiogenesis* has occurred, therefore the vasculature is present both outside and inside the tumor. The term $K \geq 0$ is the rate of nutrient release, which decreases with respect to the pressure. As clinical observation have shown, the mechanical stress generated by the cells shrinks the vessels inside the tumor and effects the blood flow and, by consequence, the nutrients delivery, see [25] for further details. Finally, the term $H \geq 0$ is an increasing function of c and represents the consumption rate of the nutrient by the tumor cells.

The specific form of the reaction term in the equation on c is not fully relevant for our analysis, and we only need the possibility to derive some generic a priori estimates, mostly in L^2. Our study covers, for example, the terms in [27] where the authors take $H = H(p, c)$, $K = 0$ and those in [28] where $K = \mathbb{1}_{\{n=0\}}$, since the authors are considering the avascular phase of tumor growth. For our study, only some general conditions are needed, which are detailed in the next sections.

Motivation and previous works. Models of tumor growth, including (1), possibly with more biological relevance, have been widely used recently. Several surveys are available, as [33]. Numerical schemes for the model at hand, with AP property (asymptotic preserving), have been proposed in [21].

Mechanical models of tumor growth are focused on the effect of the internal pressure which governs the dynamics of the cell population density. This kind of description was initiated in [19] by Greenspan and further developed by Byrne and Chaplain, [6], Friedman, [18], and Lowengrub et al., [23], among the others. The leading assumption is that the birth of a cell generates a mechanical stress on the surrounding cells which start to move under a gradient of pressure. By consequence, the motion of the cells is usually described by Darcy's law

$$\vec{v} = -\nabla p, \tag{3}$$

which relates the velocity to the pressure gradient. This type of models have been extensively used to describe the early stage of tumor growth, the so-called *avascular phase*, see for example [3, 5, 34]. Models of tumor growth that include the effect of viscosity, [29, 14, 31], or more than one species of tissue cells, [11, 22], are also well-developed. For a comprehensive review on this topic we refer the reader to [18, 23, 30, 32].

The equation for the density in the system (1) is based on the continuous mechanical model presented in [7], in which the dynamics of tumor growth are governed by competition for space and contact inhibition. The *homeostatic pressure* is determined by the maximum level of stress that the cells can tolerate, see [7] for further details on the individual-based model that leads to the continuous one.

As explained above, this type of models are usually referred to as *compressible*, since they relate the density and the pressure through a compressible constitutive law, in a fluid mechanical view. A second class of models commonly used to describe tumor growth are free boundary problems, [17]. They are also called geometric or *incompressible* models and describe the tumor as a moving

domain where the density is constant. Free boundary problems arise also from the theory of mixture applied to tumor growth, [8, 9].

Building a link between these two classes of models has attracted the attention of many researchers in recent years. This result has first been achieved in [27] for a purely mechanical model, passing to the so-called *incompressible limit*, as the pressure becomes stiff. Later, it has been studied for a lot of models, which included viscosity [29, 14], different laws of state [15] and more than one species of cells [4]. In each case the limit model turns out to be a free boundary model of Hele-Shaw type.

Our goal is to study the limit $\gamma \to \infty$ in the law of state (2), and prove that the limit solution satisfies a free boundary problem. It has been proved in [27] that (the norms are specified in the next section and we now use the notation n_γ, p_γ, c_γ in place of n, p, c to indicate the dependency upon γ)

$$n_\gamma \to n_\infty, \qquad p_\gamma \to p_\infty, \qquad c_\gamma \to c_\infty,$$

and the limits satisfy the system

$$\begin{cases} \partial_t n_\infty - \operatorname{div}(n_\infty \nabla p_\infty) = n_\infty G(p_\infty, c_\infty), & x \in \mathbb{R}^d,\ t \geq 0, \\ \partial_t c_\infty - \Delta c_\infty + n_\infty H(c_\infty) = (c_B - c_\infty) K(p_\infty), \\ c_\infty(x,t) \to c_B \quad \text{for } x \to \infty, \end{cases} \tag{4}$$

with a *graph* relation between p_∞ and n_∞ given by

$$0 \leq n_\infty \leq 1, \qquad p_\infty(n_\infty - 1) = 0. \tag{5}$$

A remarkable result is the uniqueness of the weak solutions of this system.

However, it was left open in [27] to establish the so-called *complementarity condition*, which reads (in the sense of distributions)

$$p_\infty\big(\Delta p_\infty + G(p_\infty, c_\infty)\big) = 0 \quad \text{in} \quad \mathcal{D}'(\mathbb{R}^d \times (0,\infty)), \tag{6}$$

which follows formally from the equation on n written for the pressure, namely

$$\partial_t p_\gamma = \gamma p_\gamma\big(\Delta p_\gamma + G(p_\gamma, c_\gamma)\big) + |\nabla p_\gamma|^2. \tag{7}$$

The complementarity condition is fundamental because it relates the weak solutions defined by the equations (4) and (5) to the geometric form of the Hele-Shaw problem, where the set $\mathcal{O}(t) := \{x;\, p(x,t) > 0\}$ evolves with the speed determined by the normal component of ∇p_∞. The limit pressure is a solution to the elliptic equation with Dirichlet boundary conditions

$$-\Delta p_\infty = G(p_\infty, c_\infty) \qquad \text{in } \ \mathcal{O}(t) = \{x;\, p_\infty(x,t) > 0\}.$$

The Hele-Shaw problem is a widely studied free boundary model. Although we are only interested in the weak formulation, the regularity of the boundary is also a challenging issue, see [10, 16, 26].

Difficulties and strategies. To handle this problem, we make use of two new estimates which hold because the cell population density satisfies a Porous Medium Equation, which reads

$$\partial_t n_\gamma - \frac{\gamma}{\gamma+1}\Delta n_\gamma^{\gamma+1} = n_\gamma G(p_\gamma, c_\gamma). \tag{8}$$

• The first estimate results from the famous Aronson-Bénilan (AB in short) inequalities for the porous media, [1, 13], which have been extended in various contexts (see [24] for another example). It was used in the purely mechanical case, [27], and it gives the lower bound $\Delta p_\gamma(t) + G(p_\gamma(t)) \geq -C/\gamma t$, with C positive constant. Here, unlike in the case without nutrients, it cannot hold. In fact, as shown in [28], where a semi-explicit travelling wave solution was found, there exists a region where p is constantly equal to zero and G is negative.

Therefore, we show a weaker, but still sufficient, condition

$$\int_0^T \int_{\mathbb{R}^d} |\min(0, \Delta p_\gamma)|^3 \leq C(T).$$

This is proved by working in L^2, rather than with a sub-solution, as it has been recently initiated in [20, 4]. This method has the advantage to be compatible with the L^2 estimates on c_γ and its derivatives. We recall here that Δp_∞ is a bounded measure due to the free boundary of the set $\mathcal{O}(t)$ where the pressure is positive.

• The second new estimate is an L^4 bound on ∇p_γ, independent of the dimension d. In the simple case, where G depends only on p, it results from the kinetic energy relation combined to the AB inequality in L^∞, which is wrong here. We have a new and more general way to derive it, independently of the AB inequality.

Plan of the paper. The paper is organized as follows. The next section is devoted to explain the notations and assumptions and to state the main result of the paper, namely that the complementarity condition holds. The rest of the paper is dedicated to prove this result. We begin in Section 2 presenting standard bounds which are useful for deriving the main new estimates that are stated and proved in Section 3. Finally, in Section 4 we give the proof of the complementarity relation.

1 Notations, assumptions and main result

Notations. We denote $Q = \mathbb{R}^d \times (0, \infty)$, and for $T > 0$ we set $Q_T = \mathbb{R}^d \times (0, T)$. We frequently use the abbreviation form $n(t) := n(x, t)$, $p(t) := p(x, t)$, $c(t) := c(x, t)$. We denote

$$\text{sign}_+ \{w\} = \mathbb{1}_{\{w>0\}} \quad \text{and} \quad \text{sign}_- \{w\} = -\mathbb{1}_{\{w<0\}}.$$

We also define the positive and negative part of w as follows

$$|w|_+ := \begin{cases} w, & \text{for } w > 0, \\ 0, & \text{for } w \leq 0, \end{cases} \quad \text{and} \quad |w|_- := \begin{cases} -w, & \text{for } w < 0, \\ 0, & \text{for } w \geq 0. \end{cases}$$

Assumptions. Considering the growth/reaction terms, the functions G, H and K are assumed to be smooth and we make the following assumption. There exist positive constants β, p_H, p_B (reference pressure of blood vessels) such that

$$\partial_p G < -\beta, \qquad \partial_c G \geq 0, \qquad G(p, c_B) \leq 0, \text{ for } p \geq p_H, \tag{9}$$

$$K'(p) \leq 0, \qquad 0 \leq K(p) \leq 1, \qquad K(p) = 0, \text{ for } p \geq p_B, \tag{10}$$

$$H'(c) \geq 0, \qquad 0 \leq H(c), \qquad H(0) = 0, \tag{11}$$

Furthermore, for a given pressure p, $G(p, c) < 0$ for c small enough. This assumption indicates that the tumor cells die by *necrosis* when the concentration of nutrients is below a survival threshold.

Some standard choices for the reaction terms are

$$G(p, c) = g(p)(c + c_1) - c_2, \qquad H(c) = c, \qquad K(p) = \left| 1 - \frac{p}{p_B} \right|_+,$$

where $c_{1,2}$ are positive constants and g is a decreasing function of p, see [12, 25, 27].

Initial data. The system (1) is completed with initial data. We assume that for some n^0, c^0, the initial data n^0_γ, c^0_γ satisfy

$$0 \leq n^0_\gamma \leq n_H := p_H^{1/\gamma}, \qquad \|n^0_\gamma - n^0\|_{L^1(\mathbb{R}^d)} \xrightarrow[\gamma\to\infty]{} 0, \qquad n^0 \in L^1_+(\mathbb{R}^d), \tag{12}$$

$$0 \leq c^0_\gamma \leq c_B, \qquad \|c^0_\gamma - c^0\|_{L^1(\mathbb{R}^d)} \xrightarrow[\gamma\to\infty]{} 0, \qquad c^0 - c_B \in L^1_+(\mathbb{R}^d). \tag{13}$$

We also assume that there is a positive constant C such that

$$\|\nabla p^0_\gamma\|_{L^2(\mathbb{R}^d)} + \|\Delta p^0_\gamma\|_{L^2(\mathbb{R}^d)} \leq C, \tag{14}$$

$$\|(\partial_t n_\gamma)^0\|_{L^1(\mathbb{R}^d)} + \|(\partial_t c_\gamma)^0\|_{L^1(\mathbb{R}^d)} \leq C, \tag{15}$$

$$\|\nabla c^0_\gamma\|_{L^2(\mathbb{R}^d)} \leq C. \tag{16}$$

Set these conditions on the initial data, we give the definition of weak solution of the system (1) as follows.

Definition 1.1. *Given $T > 0$, a weak solution of the system (1) is a triple $(n_\gamma, p_\gamma, c_\gamma)$ such that,*

$$n_\gamma, p_\gamma, c_\gamma \in L^\infty((0,T), L^p(\mathbb{R}^d)) \quad \forall p \geq 1, \qquad \nabla c_\gamma,\ \nabla p_\gamma \in L^2(\mathbb{R}^d \times (0,T)),$$

and for all $\varphi \in C^1_{comp}(\mathbb{R}^d \times [0,T))$,

$$\int_0^T \int_{\mathbb{R}^d} (-n_\gamma \partial_t \varphi + n_\gamma \nabla p_\gamma \nabla \varphi - n_\gamma G(p_\gamma, c_\gamma)\varphi) = \int_{\mathbb{R}^d} n^0_\gamma \varphi(0),$$

$$\int_0^T \int_{\mathbb{R}^d} (-c_\gamma \partial_t \varphi + \nabla c_\gamma \nabla \varphi + n_\gamma H(c_\gamma)\varphi - (c_B - c)K(p)\varphi) = \int_{\mathbb{R}^d} c^0_\gamma \varphi(0).$$

From [35] we know that a weak solution exists for all $T > 0$.

Compact support. Because our arguments rely on technical calculations, we first simplify the setting assuming that there exists a smooth bounded open domain $\Omega_0 \subset \mathbb{R}^d$, independent of γ, such that for all $\gamma > 1$

$$\mathrm{supp}(n_\gamma^0) \subset \Omega_0.$$

Unlike the solutions of the heat equation, the PME's solutions have a finite speed of propagation, see [35]. This means that, for all $T > 0$, there exists a smooth bounded open domain Ω_T independent of γ such that

$$\mathrm{supp}(n_\gamma(t)) \subset \Omega_T, \qquad \forall t \in [0, T],$$

see Appendix A for the proof. From now on, we consider a solution (n_γ, p_γ) with compact support for all $\gamma > 1$. In the Appendix B, we show how to extend the result to more general solutions.

Main result. We now state the main result of the paper, namely the weak formulation of the complementarity relation.

Theorem 1.2 (Estimates and complementarity relation)**.** *With all the previous assumptions, the limit pressure p_∞ satisfies the relation (6), that means, for all test functions $\zeta \in \mathcal{D}(Q)$, we have*

$$\iint_Q \left(-|\nabla p_\infty|^2 \zeta - p_\infty \nabla p_\infty \nabla \zeta + p_\infty G(p_\infty, c_\infty)\zeta\right) = 0.$$

Furthermore the following estimates hold uniformly in γ

$$\int_0^T \int_{\Omega_T} |\Delta p_\gamma + G(p_\gamma, c_\gamma)|_-^3 \leq C(T), \qquad \int_0^T \int_{\Omega_T} |\nabla p_\gamma|^4 \leq C(T).$$

2 Preliminary Estimates

Let $(n_\gamma, p_\gamma, c_\gamma)$ be a weak solution to the system (1). We recall some standard preliminary bounds on $n_\gamma, p_\gamma, c_\gamma$ and their derivatives, gathered in the following Proposition.

Proposition 2.1 (Direct estimates)**.** *Given $(n_\gamma, p_\gamma, c_\gamma)$ a weak solution of the system (1) for $\gamma > 1$, and $T > 0$, there exists a constant $C(T)$, independent of γ, such that for all $0 \leq t \leq T$*

$$0 \leq n_\gamma \leq n_H, \qquad 0 \leq p_\gamma \leq p_H, \qquad 0 \leq c_\gamma \leq c_B, \tag{17}$$

$$\|n_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq C(T), \qquad \|p_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq C(T), \qquad \|c_\gamma(t) - c_B\|_{L^1(\mathbb{R}^d)} \leq C(T), \tag{18}$$

$$\|\nabla c_\gamma(t)\|_{L^2(\mathbb{R}^d)} \leq C(T), \qquad \|\Delta c_\gamma\|_{L^2(Q_T)} \leq C(T), \qquad \|\partial_t c_\gamma\|_{L^2(Q_T)} \leq C(T), \tag{19}$$

$$\|\partial_t n_\gamma\|_{L^1(Q_T)} \leq C(T), \qquad \|\partial_t p_\gamma\|_{L^1(Q_T)} \leq C(T), \qquad \|\partial_t c_\gamma\|_{L^1(Q_T)} \leq C(T), \tag{20}$$

$$\|\nabla c_\gamma\|_{L^4(Q_T)} \leq C(T), \qquad \|\nabla p_\gamma\|_{L^2(Q_T)} \leq C(T). \tag{21}$$

For the sake of completeness, we now recall the derivation of these bounds.

L^∞ bounds for $n_\gamma, p_\gamma, c_\gamma$. The L^∞ bounds are just consequences of our assumptions on G using the comparison principle.

L^1 bounds on $n_\gamma, p_\gamma, c_\gamma$. These are also standard estimates, noting that

$$\|p(t)\|_{L^1(\mathbb{R}^d)} = \|n(t)p(t)^{\frac{\gamma-1}{\gamma}}\|_{L^1(\mathbb{R}^d)} \leq p_H^{\frac{\gamma-1}{\gamma}} \|n(t)\|_{L^1(\mathbb{R}^d)}.$$

L^2 bounds for the derivatives of c_γ. We now prove the L^2 bounds for $\nabla c_\gamma, \Delta c_\gamma$ and $\partial_t c_\gamma$. We multiply the equation for c_γ by $-\Delta c_\gamma$ and we integrate in space and time

$$-\int_0^t \int_{\mathbb{R}^d} \partial_t c_\gamma \Delta c_\gamma + \int_0^t \int_{\mathbb{R}^d} |\Delta c_\gamma|^2 = \int_0^t \int_{\mathbb{R}^d} (n_\gamma H(c_\gamma) - (c_B - c)K(p_\gamma))\Delta c_\gamma.$$

Integrating by parts and using Young's inequality we obtain

$$\int_0^t \int_{\mathbb{R}^d} \partial_t(\nabla c_\gamma)\nabla c_\gamma + \int_0^t \int_{\mathbb{R}^d} |\Delta c_\gamma|^2 \leq \int_0^t \int_{\mathbb{R}^d} \frac{|n_\gamma H(c_\gamma) - (c_B - c)K(p_\gamma)|^2}{2} + \int_0^t \int_{\mathbb{R}^d} \frac{|\Delta c_\gamma|^2}{2}.$$

Hence, we have

$$\frac{1}{2}\int_{\mathbb{R}^d} |\nabla c_\gamma(t)|^2 + \frac{1}{2}\int_0^t \int_{\mathbb{R}^d} |\Delta c_\gamma|^2 \leq C \int_0^t \left(\|n_\gamma(s)\|^2_{L^1(\mathbb{R}^d)} + \|c_\gamma(s) - c_B\|^2_{L^1(\mathbb{R}^d)} \right) ds + \frac{1}{2}\|\nabla c_\gamma^0\|^2_{L^2(\mathbb{R}^d)},$$

where C is a positive constant depending on n_H, c_B and the L^∞ norms of H and K.

Finally, using the L^1 bounds (18), we obtain

$$\int_{\mathbb{R}^d} |\nabla c_\gamma(t)|^2 + \int_0^t \int_{\mathbb{R}^d} |\Delta c_\gamma|^2 \leq C(T) + \|\nabla c_\gamma^0\|^2_{L^2(\mathbb{R}^d)},$$

for $0 < t \leq T$, and thanks to (16) we conclude the proof of the first and second estimates in (19).

At last, considering the equation for c_γ

$$\partial_t c_\gamma = \Delta c_\gamma - n_\gamma H(c_\gamma) + (c_B - c_\gamma)K(p_\gamma),$$

and using the previous bounds on n_γ, c_γ and Δc_γ we conclude that $\partial_t c_\gamma \in L^2(Q_T)$.

L^1 bounds for the time derivatives of n_γ and p_γ. We differentiate the equation for n_γ and we multiply it by $\operatorname{sign}\{\partial_t n_\gamma\}$

$$\partial_t|\partial_t n_\gamma| - \gamma\Delta(n_\gamma^\gamma|\partial_t n_\gamma|) \leq |\partial_t n_\gamma| G + n_\gamma \partial_p G|\partial_t p_\gamma| + n_\gamma \partial_c G \partial_t c_\gamma \operatorname{sign}\{\partial_t n_\gamma\}. \tag{22}$$

We integrate in space using the monotonicity of G

$$\frac{d}{dt}\|\partial_t n_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq \|G\|_{L^\infty(Q_T)}\|\partial_t n_\gamma(t)\|_{L^1(\mathbb{R}^d)} + \|\partial_c G\|_{L^\infty(Q_T)}\|n_\gamma(t)\|_{L^2(\mathbb{R}^d)}\|\partial_t c_\gamma(t)\|_{L^2(\mathbb{R}^d)}.$$

Thanks to (18) and (19), Gronwall's lemma gives

$$\|\partial_t n_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq C(T)\|(\partial_t n_\gamma)^0\|_{L^1(\mathbb{R}^d)} \leq C(T),$$

where in the last inequality we used (15).

By integrating in $Q_t := \mathbb{R}^d \times (0,t)$ the equation (22), we obtain

$$\|\partial_t n_\gamma(t)\|_{L^1(\mathbb{R}^d)} + \min|\partial_p G| \iint_{Q_t} n_\gamma|\partial_t p_\gamma| \leq C(T),$$

thanks to (15) and the L^1 bounds proved above. Then, for the time derivative of the pressure it holds

$$\|\partial_t p_\gamma\|_{L^1(Q_T)} \leq \iint_{Q_T\cap\{n_\gamma\leq 1/2\}} \gamma n_\gamma^{\gamma-1}|\partial_t n_\gamma| + 2\iint_{Q_T\cap\{n_\gamma\geq 1/2\}} n_\gamma|\partial_t p_\gamma| \leq C(T).$$

We differentiate the equation for c_γ and multiply it by $\operatorname{sign}\{\partial_t c_\gamma\}$

$$\partial_t|\partial_t c_\gamma| - \Delta(|\partial_t c_\gamma|) \leq -\partial_t n_\gamma H \operatorname{sign}\{\partial_t c_\gamma\} - n_\gamma H'|\partial_t c_\gamma| - |\partial_t c_\gamma|K + (c_B - c)K'\partial_t p_\gamma \operatorname{sign}\{\partial_t c_\gamma\}.$$

Integrating in space we obtain

$$\begin{aligned}\frac{d}{dt}\|\partial_t c_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq{}& \|H\|_{L^\infty(Q_T)}\|\partial_t n_\gamma(t)\|_{L^1(\mathbb{R}^d)} + n_H\|H'\|_{L^\infty(Q_T)}\|\partial_t c_\gamma(t)\|_{L^1(\mathbb{R}^d)}\\ &+ c_B\|K'\|_{L^\infty(Q_T)}\|\partial_t p(t)\|_{L^1(\mathbb{R}^d)},\end{aligned}$$

and thanks to the previous bounds and Gronwall's lemma we have

$$\|\partial_t c_\gamma(t)\|_{L^1(\mathbb{R}^d)} \leq C(T)\|(\partial_t c_\gamma)^0\|_{L^1(\mathbb{R}^d)} \leq C(T),$$

and this concludes the proof of (20).

L^4 bound for the gradient of c_γ. Now, we prove that the gradient of c_γ is bounded in L^4. Integration by parts gives

$$\int_{\mathbb{R}^d}|\nabla c_\gamma|^4 = -\int_{\mathbb{R}^d} c_\gamma\Delta c_\gamma|\nabla c_\gamma|^2 - \int_{\mathbb{R}^d} c_\gamma\nabla c_\gamma\cdot\nabla(|\nabla c_\gamma|^2).$$

We use Young's inequality on the first term of the RHS and we get

$$\frac{1}{2}\int_{\mathbb{R}^d}|\nabla c_\gamma|^4 \leq \frac{1}{2}\int_{\mathbb{R}^d} c_\gamma^2|\Delta c_\gamma|^2 - \int_{\mathbb{R}^d} c_\gamma\nabla c_\gamma\cdot\nabla(|\nabla c_\gamma|^2).$$

We write the last term as

$$\begin{aligned}-\int_{\mathbb{R}^d} c_\gamma\nabla c_\gamma\cdot\nabla(|\nabla c_\gamma|^2) &= -2\sum_{i,j}\int_{\mathbb{R}^d} c_\gamma\,\partial_i c_\gamma\,\partial_j c_\gamma\,\partial^2_{i,j}c_\gamma\\ &\leq \frac{1}{4}\int_{\mathbb{R}^d}|\nabla c_\gamma|^4 + 4c_B^2\int_{\mathbb{R}^d}\sum_{i,j}(\partial^2_{i,j}c_\gamma)^2\\ &= \frac{1}{4}\int_{\mathbb{R}^d}|\nabla c_\gamma|^4 + 4c_B^2\int_{\mathbb{R}^d}|\Delta c_\gamma|^2.\end{aligned}$$

Thus, we have

$$\frac{1}{4}\int_{\mathbb{R}^d}|\nabla c_\gamma|^4 \leq \left(\frac{1}{2}+4\right)c_B^2\int_{\mathbb{R}^d}|\Delta c_\gamma|^2.$$

and the L^4 estimate is proved.

L^2 bound for the pressure gradient. Since the pressure satisfies the equation (7), integrating it in space we get

$$\frac{d}{dt}\int_{\mathbb{R}^d} p_\gamma(t) = -\gamma\int_{\mathbb{R}^d}|\nabla p_\gamma(t)|^2 + \gamma\int_{\mathbb{R}^d} p_\gamma(t)G(p_\gamma(t),c_\gamma(t)) + \int_{\mathbb{R}^d}|\nabla p_\gamma(t)|^2.$$

Then, we integrate in time

$$(\gamma-1)\int_0^T\int_{\mathbb{R}^d}|\nabla p_\gamma|^2 = \|p_\gamma(0)\|_{L^1(\mathbb{R}^d)} - \|p_\gamma(T)\|_{L^1(\mathbb{R}^d)} + \gamma\int_0^T\int_{\mathbb{R}^d} p_\gamma G(p_\gamma,c_\gamma),$$
$$(\gamma-1)\int_0^T\int_{\mathbb{R}^d}|\nabla p_\gamma|^2 \le C_0 + \gamma C(T),$$

and this gives, since $\gamma > 1$,

$$\int_0^T\int_{\mathbb{R}^d}|\nabla p_\gamma|^2 \le C(T).$$

3 Stronger a priori estimates on p_γ

To establish the complementarity condition (6) is equivalent to prove the strong compactness of $|\nabla p_\gamma|^2$. One step towards this goal is to prove compactness in space using the classical AB estimate, [1, 13]. Here, major difficulties arise. As explained in the Introduction, since the reaction term can change sign the usual Aronson-Bénilan lower bound cannot hold true, see [27, 28]. Moreover, we cannot apply the comparison principle because of the bad coupling in the system (1). Since the L^∞ bound from below in the AB estimate is missing, we prove an L^3 version, adapting the method presented in [20]. Then, we show that the gradient of the pressure is bounded in $L^4(Q_T)$, which gives the compactness needed to pass to the limit.

Our first goal is to prove the AB estimate on the functional

$$w := \Delta p_\gamma + G(p_\gamma, c_\gamma), \tag{23}$$

which is a variation of the Laplacian in order to take into account the source term, at the same order of Δp_γ, in equation (7).

Theorem 3.1 (Aronson-Bénilan estimate in L^3)**.** *With the assumptions of Section 1 and with $\gamma > \max(1, 2-\frac{4}{d})$, for all $T>0$ there is a constant $C(T)$ depending on T and the previous bounds and independent of γ such that*

$$\int_0^T\int_{\Omega_T}|w|_-^3 \le C(T), \quad \int_0^T\int_{\mathbb{R}^d}|\Delta p_\gamma| \le C(T). \tag{24}$$

Let us point out that because the free boundary is where p_∞ vanishes, it is important that w itself is controlled and not merely pw as in the next estimate.

Theorem 3.2 (L^4 estimate on the pressure gradient)**.** *With the same assumptions as before, given $T>0$, it holds*

$$(\gamma-1)\int_0^T\int_{\Omega_T} p_\gamma|\Delta p_\gamma + G|^2 + \int_0^T\int_{\Omega_T} p_\gamma\sum_{i,j}(\partial^2_{i,j}p_\gamma)^2 \le C(T), \tag{25}$$

$$\int_0^T \int_{\Omega_T} |\nabla p_\gamma|^4 \leq C(T), \tag{26}$$

where C depends on T and previous bounds and is independent of γ.

We recall that in the model independent of c, [27], the AB estimate is much stronger and gives $\Delta p_\gamma(t) + G(p_\gamma(t)) \geq -\frac{1}{\gamma t}$, and the major difficulty is the control of Δp_γ which is provided by Theorem 24. As proved in [26], the L^4 estimate follows from the total energy control when $G = G(p)$, but this uses the strong form of the AB estimate. Therefore, we have invented another proof, which is reminiscent of the energy control, but uses a different treatment of the 'dissipation' terms.

Proof of Theorem 3.1. For the sake of simplicity we forget the index γ in this proof. We compute the time derivative of w and obtain

$$\partial_t w = \Delta(|\nabla p|^2) + \gamma\Delta(pw) + \partial_p G(|\nabla p|^2 + \gamma p w) + \partial_c G\, \partial_t c.$$

The first term is

$$\Delta(|\nabla p|^2) = 2\sum_{i,j}(\partial^2_{i,j} p)^2 + 2\nabla p \cdot \nabla(\Delta p) \geq \frac{2}{d}(\Delta p)^2 + 2\nabla p \cdot \nabla(\Delta p).$$

By definition of w we have

$$2\nabla p \cdot \nabla(\Delta p) = 2\nabla p \cdot \nabla(w - G) = 2\nabla p \cdot \nabla w - 2\partial_p G|\nabla p|^2 - 2\partial_c G \nabla p \cdot \nabla c.$$

Hence, the time derivative satisfies

$$\begin{aligned} \partial_t w \geq & \frac{2}{d}(w - G)^2 + 2\nabla p \cdot \nabla w - \partial_p G|\nabla p|^2 - 2\partial_c G \nabla p \cdot \nabla c \\ & + \gamma\Delta(pw) + \gamma p w\, \partial_p G + \partial_c G\, \partial_t c. \end{aligned} \tag{27}$$

Multiplying (27) by $-|w|_-$, we obtain

$$\begin{aligned} -\partial_t w\, |w|_- \leq & -\frac{2}{d}|w|_-^3 - \frac{4}{d}G|w|_-^2 - \frac{2}{d}G^2|w|_- + \nabla p \cdot \nabla |w|_-^2 + \partial_p G|\nabla p|^2|w|_- \\ & + 2\partial_c G \nabla p \cdot \nabla c|w|_- + \gamma\Delta(p|w|_-)|w|_- + \gamma p\, \partial_p G|w|_-^2 - \partial_c G\, \partial_t c|w|_-. \end{aligned}$$

Hence, using the fact that $\partial_p G < -\beta$ from (9), we integrate in space to obtain

$$\begin{aligned} \frac{d}{dt}\int_{\Omega_T} \frac{|w|_-^2}{2} \leq & -\frac{2}{d}\int_{\Omega_T} |w|_-^3 - \frac{2}{d}\int_{\Omega_T} G^2|w|_- - \beta\int_{\Omega_T} |\nabla p|^2|w|_- \\ & - \frac{4}{d}\int_{\Omega_T} G|w|_-^2 + \underbrace{\int_{\Omega_T} \left[\nabla p \cdot \nabla |w|_-^2 + \gamma\Delta(p|w|_-)|w|_-\right]}_{\mathcal{A}} \\ & \underbrace{-\int_{\Omega_T} \partial_c G\, \partial_t c|w|_-}_{\mathcal{B}} + \underbrace{2\int_{\Omega_T} \partial_c G \nabla p \cdot \nabla c|w|_-}_{\mathcal{C}}, \end{aligned}$$

where C is a positive constant depending on $\|G\|_\infty$ and d. Now we proceed integrating by parts each term.

$$\begin{aligned}\mathcal{A} &= -\int_{\Omega_T} \left[\Delta p|w|_-^2 + \gamma\nabla p\nabla|w|_-|w|_- + \gamma p|\nabla|w|_-|^2\right] \\ &= \int_{\Omega_T} |w|_-^3 + \int_{\Omega_T} G|w|_-^2 + \frac{\gamma}{2}\int_{\Omega_T} \Delta p|w|_-^2 - \gamma\int_{\Omega_T} p|\nabla|w|_-|^2 \\ &= \left(1-\frac{\gamma}{2}\right)\int_{\Omega_T} |w|_-^3 + \left(1-\frac{\gamma}{2}\right)\int_{\Omega_T} G|w|_-^2 - \gamma\int_{\Omega_T} p|\nabla|w|_-|^2.\end{aligned}$$

Next, using (19) and the Cauchy-Schwarz inequality, we obtain

$$\mathcal{B} \leq C\int_{\Omega_T} |w|_-^2 + C.$$

Thanks to Young's inequality and (21), we compute

$$\begin{aligned}\mathcal{C} &\leq \frac{\beta}{2}\int_{\Omega_T} |\nabla p|^2|w|_- + C\int_{\Omega_T} |\nabla c|^4 + C\int_{\Omega_T} |w|_-^2 \\ &\leq \frac{\beta}{2}\int_{\Omega_T} |\nabla p|^2|w|_- + C\int_{\Omega_T} |w|_-^2 + C.\end{aligned}$$

We may now come back to the control of $\frac{d}{dt}\int_{\Omega_T}\frac{|w|_-^2}{2}$. Gathering all the previous bounds, we get the following estimate

$$\frac{d}{dt}\int_{\Omega_T}\frac{|w|_-^2}{2} \leq -\left(\frac{2}{d}-1+\frac{\gamma}{2}\right)\int_{\Omega_T} |w|_-^3 - \frac{\beta}{2}\int_{\Omega_T} |\nabla p|^2|w|_- + C(\gamma+1)\int_{\Omega_T} |w|_-^2 + C.$$

Hence integrating in time we have

$$\begin{aligned}\left(\frac{2}{d}-1+\frac{\gamma}{2}\right)\int_0^T\int_{\Omega_T} |w|_-^3 &\leq C\,(\gamma+1)\int_0^T\int_{\Omega_T} |w|_-^2 + \int_{\Omega_T}\frac{|w^0|_-^2}{2} + C(T) \\ &\leq C\,(\gamma+1)\left(\int_0^T\int_{\Omega_T} |w|_-^3\right)^{\frac{2}{3}} + C(T),\end{aligned}$$

where we used the assumption (14) and C represents different constants depending on T, $|\Omega(T)|$ and previous bounds. This is the place where we strongly use the compact support assumption.

At last, with our assumption that γ is large enough, we obtain

$$\int_0^T\int_{\Omega_T} |w|_-^3 \leq C\left(\int_0^T\int_{\Omega_T} |w|_-^3\right)^{\frac{2}{3}} + C(T),$$

and hence we have proved our main result, that is the first estimate of (24),

$$\int_0^T\int_{\Omega_T} |w|_-^3 \leq C(T).$$

To prove the second estimate, we argue as follows. Since

$$\int_0^T \int_{\Omega_T} (\Delta p + G) \leq C(T),$$

we can also control the positive part of w

$$\int_0^T \int_{\Omega_T} |w|_+ \leq C(T) + \int_0^T \int_{\Omega_T} |w|_- \leq C(T) + C \left(\int_0^T \int_{\Omega_T} |w|_-^3 \right)^{\frac{1}{3}}.$$

Thus it holds

$$\int_0^T \int_{\Omega_T} |\Delta p + G| \leq C(T).$$

Hence, we finally obtain the L^1 estimate for the Laplacian of the pressure

$$\int_0^T \int_{\Omega_T} |\Delta p| \leq C(T),$$

that concludes the proof of Theorem 3.1.

Proof of Theorem 3.2. We consider the equation for the pressure (7), we multiply it by $-(\Delta p_\gamma + G(p_\gamma, c_\gamma))$ and integrate in space. We find successively

$$-\int_{\Omega_T} \partial_t p_\gamma \Delta p_\gamma - \int_{\Omega_T} \partial_t p_\gamma \, G = -\gamma \int_{\Omega_T} p_\gamma |\Delta p_\gamma + G|^2 - \int_{\Omega_T} |\nabla p_\gamma|^2 \Delta p_\gamma - \int_{\Omega_T} |\nabla p_\gamma|^2 G,$$

$$\frac{d}{dt} \int_{\Omega_T} \frac{|\nabla p_\gamma|^2}{2} - \int_{\Omega_T} \partial_t p_\gamma G + \gamma \int_{\Omega_T} p_\gamma |\Delta p_\gamma + G|^2 + \int_{\Omega_T} |\nabla p_\gamma|^2 \Delta p_\gamma \leq \|G\|_{L^\infty} \|\nabla p_\gamma(t)\|_{L^2}^2.$$

We integrate by parts the last term of the LHS and obtain

$$\begin{aligned}
\int_{\Omega_T} |\nabla p_\gamma|^2 \Delta p_\gamma &= \int_{\Omega_T} p_\gamma \Delta(|\nabla p_\gamma|^2) \\
&= 2 \int_{\Omega_T} p_\gamma \nabla p_\gamma \cdot \nabla(\Delta p_\gamma) + 2 \int_{\Omega_T} p_\gamma \sum_{i,j} (\partial_{i,j}^2 p_\gamma)^2 \\
&= -2 \int_{\Omega_T} p_\gamma |\Delta p_\gamma|^2 - 2 \int_{\Omega_T} |\nabla p_\gamma|^2 \Delta p_\gamma + 2 \int_{\Omega_T} p_\gamma \sum_{i,j} (\partial_{i,j}^2 p_\gamma)^2.
\end{aligned}$$

Hence, we conclude that

$$\int_{\Omega_T} |\nabla p_\gamma|^2 \Delta p_\gamma = -\frac{2}{3} \int_{\Omega_T} p_\gamma |\Delta p_\gamma|^2 + \frac{2}{3} \int_{\Omega_T} p_\gamma \sum_{i,j} (\partial_{i,j}^2 p_\gamma)^2.$$

Thus, we have

$$\frac{d}{dt} \int_{\Omega_T} \frac{|\nabla p_\gamma|^2}{2} \underbrace{- \int_{\Omega_T} \partial_t p_\gamma \, G}_{I_1} + \underbrace{\gamma \int_{\Omega_T} p_\gamma |\Delta p_\gamma + G|^2 - \frac{2}{3} \int_{\Omega_T} p_\gamma |\Delta p_\gamma|^2}_{I_2} + \frac{2}{3} \int_{\Omega_T} p_\gamma \sum_{i,j} (\partial_{i,j}^2 p_\gamma)^2 \leq C(T). \tag{28}$$

We can define the function $\overline{G} = \overline{G}(p_\gamma, c_\gamma) = \int_0^{p_\gamma} G(q, c_\gamma) dq$ and then

$$\partial_t p_\gamma \, G(p_\gamma, c_\gamma) = \partial_t \overline{G}(p_\gamma, c_\gamma) - \partial_t c_\gamma \, \partial_c \overline{G}(p_\gamma, c_\gamma).$$

Using this relation the term I_1 can be written as

$$I_1 = -\int_{\Omega_T} \partial_t \overline{G} + \int_{\Omega_T} \partial_c \overline{G} \, \partial_t c_\gamma \geq -\int_{\Omega_T} \partial_t \overline{G} - C$$

thanks to the L^2 bound on $\partial_t c_\gamma$ in (19) and because $|\partial_c \overline{G}| \leq C p_\gamma$. We can estimate the term I_2 from below as follows

$$I_2 \geq (\gamma - 1) \int_{\Omega_T} p_\gamma |\Delta p_\gamma + G|^2 - C \int_{\Omega_T} p_\gamma |G|^2.$$

Therefore

$$I_1 + I_2 \geq (\gamma - 1) \int_{\Omega_T} p_\gamma |\Delta p_\gamma + G|^2 - \int_{\Omega_T} \partial_t \overline{G} - C(T). \tag{29}$$

Combining (28) and (29), we obtain

$$\frac{d}{dt} \int_{\Omega_T} \left[\frac{|\nabla p_\gamma|^2}{2} - \overline{G} \right] + (\gamma - 1) \int_{\Omega_T} p_\gamma |\Delta p_\gamma + G|^2 + \frac{2}{3} \int_{\Omega_T} p_\gamma \sum_{i,j} (\partial^2_{i,j} p_\gamma)^2 \leq C(T).$$

Finally, integrating in time, we obtain the estimate (25) and this proves the first step of Theorem 3.2.

Furthermore, this bound also implies

$$(\gamma - 1) \int_0^T \int_{\Omega_T} p_\gamma |\Delta p_\gamma|^2 \leq C(T). \tag{30}$$

Now, we compute the L^4 norm of the gradient of p_γ, as we did for the gradient of c_γ.

$$\int_{\Omega_T} |\nabla p_\gamma|^4 = -\int_{\Omega_T} p_\gamma \Delta p_\gamma |\nabla p_\gamma|^2 - \int_{\Omega_T} p_\gamma \nabla p_\gamma \cdot \nabla (|\nabla p_\gamma|^2).$$

Applying Young's inequality to the first term, we obtain

$$\frac{1}{2} \int_{\Omega_T} |\nabla p_\gamma|^4 \leq \frac{1}{2} \int_{\Omega_T} p_\gamma^2 |\Delta p_\gamma|^2 - 2 \sum_{i,j} \int_{\Omega_T} p_\gamma \, \partial_i p_\gamma \, \partial_j p_\gamma \, \partial^2_{i,j} p_\gamma.$$

The last term can be upper bounded by

$$\frac{1}{4} \int_{\Omega_T} |\nabla p_\gamma|^4 + 4 \int_{\Omega_T} p_\gamma^2 \sum_{i,j} (\partial^2_{i,j} p_\gamma)^2.$$

Therefore, we obtain

$$\frac{1}{4} \int_{\Omega_T} |\nabla p_\gamma|^4 \leq \frac{1}{2} \int_{\Omega_T} p_\gamma^2 |\Delta p_\gamma|^2 + 4 \int_{\Omega_T} p_\gamma^2 \sum_{i,j} (\partial^2_{i,j} p_\gamma)^2.$$

Since $p \leq p_H$, by (25) and (30) we conclude

$$\int_0^T \int_{\Omega_T} |\nabla p_\gamma|^4 \leq C(T),$$

and this completes the proof of Theorem 3.2.

4 Complementarity relation

Thanks to the bounds provided by Theorem 3.1 and Theorem 3.2, we may obtain the desired compactness on the pressure gradient. This allows us to pass to the incompressible limit and prove the complementarity relation as we state it now.

Theorem 4.1 (Complementarity relation)**.** *With the assumptions of Theorem 3.1, the complementarity condition (6) holds. More precisely, for all test functions $\zeta \in \mathcal{D}(Q)$, the limit pressure p_∞ satisfies*

$$\iint_Q \left(-|\nabla p_\infty|^2 \zeta - p_\infty \nabla p_\infty \cdot \nabla \zeta + p_\infty G(p_\infty, c_\infty)\zeta\right) = 0. \tag{31}$$

This result is related to the geometric form of the Hele-Shaw free boundary problem (while (4) is the weak form). It tells us that the limit solution satisfies

$$\begin{cases} -\Delta p_\infty = G(p_\infty, c_\infty) & \text{in } \mathcal{O}(t) := \{x;\, p_\infty(x,t) > 0\}, \\ p_\infty = 0 & \text{on } \partial\mathcal{O}(t), \end{cases}$$

where, for every $t > 0$, the set $\mathcal{O}(t)$ represents the region occupied by the tumor. Moreover, in the limit, the pressure and the cell population density satisfy the relation

$$p_\infty(1 - n_\infty) = 0. \tag{32}$$

In fact, we may expect that the set $\mathcal{O}(t)$ coincides a.e. with the set where $n_\infty = 1$, hence the classification of *incompressible* model. See [26] for the proof in the case without nutrient. It is not obvious to extend the result in the case at hand.

Proof of Theorem 4.1. Thanks to the bounds in (19), (20) and (21), p_γ and c_γ are locally compact and thus, after the extraction of sub-sequences,

$$p_\gamma \to p_\infty \text{ strongly in } L^1(Q_T), \qquad c_\gamma \to c_\infty \text{ strongly in } L^1(Q_T),$$

when $\gamma \to \infty$, for all $T > 0$. From Theorem 3.2, we also recover the weak convergence of the gradient of the pressure, up to a sub-sequence,

$$\nabla p_\gamma \rightharpoonup \nabla p_\infty \text{ weakly in } L^4(Q_T).$$

From Theorem 3.1, we know that Δp_γ is bounded in L^1. Then, we have local compactness in space for the pressure gradient. To gain compactness in time we use the Aubin-Lions lemma. From the equation for the pressure (7), we have

$$\partial_t(\nabla p_\gamma) = \nabla[\gamma p_\gamma(\Delta p_\gamma + G) + |\nabla p_\gamma|^2],$$

where the RHS is a sum of space derivatives of functions bounded in L^1. In fact, since by (20) and (21), $\partial_t p_\gamma$ and $|\nabla p_\gamma|^2$ are in L^1, from (7) the term $\gamma p_\gamma(\Delta p_\gamma + G)$ is also bounded in L^1. Thus, we can extract a sub-sequence such that

$$\nabla p_\gamma \to \nabla p_\infty \text{ strongly in } L^q(Q_T), \text{ for } 1 \le q < \frac{d}{d-1}.$$

After extraction of a sub-sequence we obtain convergence almost everywhere for ∇p_γ. Then, using the L^4 bound of Theorem 3.2, we have

$$\nabla p_\gamma \to \nabla p_\infty \text{ strongly in } L^q(Q_T), \text{ for } 1 \le q < 4,$$

hence, in particular, also for $q = 2$.

Let $\zeta \in \mathcal{D}(Q)$ be a test function. We consider the equation for p_γ

$$\partial_t p_\gamma = \gamma p_\gamma(\Delta p_\gamma + G(p_\gamma, c_\gamma)) + |\nabla p_\gamma|^2,$$

we multiply it by ζ and we integrate in Q

$$-\frac{1}{\gamma}\iint_Q \left(p_\gamma \partial_t \zeta + |\nabla p_\gamma|^2 \zeta\right) = \iint_Q \left(-|\nabla p_\gamma|^2 \zeta - p_\gamma \nabla p_\gamma \cdot \nabla \zeta + p_\gamma G(p_\gamma, c_\gamma)\zeta\right) \tag{33}$$

Hence, passing to the limit for $\gamma \to \infty$ we obtain the complementarity relation

$$\iint_Q \left(-|\nabla p_\infty|^2 \zeta - p_\infty \nabla p_\infty \cdot \nabla \zeta + p_\infty G(p_\infty, c_\infty)\zeta\right) = 0. \tag{34}$$

This is equivalent to

$$\iint_Q p_\infty \left(\Delta p_\infty + G(p_\infty, c_\infty)\right) \zeta = 0,$$

which means

$$p_\infty \left(\Delta p_\infty + G(p_\infty, c_\infty)\right) = 0, \quad \text{in } \mathcal{D}'(Q),$$

and the proof of Theorem 4.1 is complete.

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Appendix A Compact support property

We now give the proof of the finite speed of propagation property of the solutions of system (1). Our goal is to show that if the initial data satisfy

$$\text{supp}(n_\gamma^0) \subset \Omega_0, \quad \forall \gamma > 1,$$

with Ω_0 independent of γ, then the solutions $n_\gamma(t)$, $p_\gamma(t)$ are compactly supported, uniformly in γ and $t \in [0, T]$, for all $T > 0$. This means that there exists a bounded open domain Ω_T independent of γ such that

$$\text{supp}(n_\gamma(t)) \subset \Omega_T, \quad \forall \gamma > 1, \forall t \in [0, T].$$

For every $\gamma > 1$, the pressure p_γ is a sub-solution to the equation

$$\partial_t p_\gamma \le |\nabla p_\gamma|^2 + \gamma p_\gamma(\Delta p_\gamma + G(0, c_B)), \tag{35}$$

therefore, finding a super-solution with compact support we can control the supports of p_γ and n_γ.

We consider the function

$$\Pi(x,t) = G(0,c_B)\left|S(t) - \frac{|x|^2}{2}\right|_+,$$

where we choose the function S such that it satisfies

$$S'(t) \geq 2G(0,c_B)S(t).$$

We compute the derivatives of Π and we find

$$\begin{aligned}
&\partial_t \Pi(x,t) = G(0,c_B)S'(t)\mathbb{1}_{\{S(t)\geq \frac{|x|^2}{2}\}},\\
&\nabla\Pi(x,t) = -G(0,c_B)x\mathbb{1}_{\{S(t)\geq \frac{|x|^2}{2}\}}, \quad \Delta\Pi(x,t) \leq -d\,G(0,c_B)\mathbb{1}_{\{S(t)\geq \frac{|x|^2}{2}\}}.
\end{aligned}$$

Therefore Π satisfies

$$\begin{aligned}
\partial_t\Pi - |\nabla\Pi|^2 - \gamma\Pi(\Delta\Pi + G(0,c_B)) &\geq (G(0,c_B)S'(t) - G(0,c_B)^2x^2)\mathbb{1}_{\{S(t)\geq \frac{|x|^2}{2}\}} + \gamma\Pi G(0,c_B)(d+1)\\
&\geq (2G(0,c_B)^2S(t) - G(0,c_B)^2x^2)\mathbb{1}_{\{S(t)\geq \frac{|x|^2}{2}\}}\\
&\geq 0.
\end{aligned}$$

Hence, we have proved that for all $T>0$

$$\mathrm{supp}(p_\gamma(t)) \subset \mathrm{supp}(\Pi(t)) \subset B_T,\ \forall\gamma>1, \forall t\in[0,T],$$

where B_T is the open ball with radius $\sqrt{2S(T)}$.

Appendix B Removing the compact support assumption

The proof of the main result of the paper is built on the compact support assumption stated in Section 1. Our goal is to generalize the result removing this condition. Let us note that it is sufficient to extend the Theorem 3.1, since it is the only one for which we used the compact support assumption. Moreover, let us notice that Proposition 2.1 holds true in this framework. We define the functional w as in (23) and we state the following result.

Proposition B.1 (Aronson-Bénilan generalized estimate in L^3)**.** *Let Φ be a test function in $C^2_{comp}(\mathbb{R}^d)$. With the assumptions from (9) to (16), and with $\gamma > \max(1, 2-\frac{4}{d})$, for all $T>0$ there exists a constant $C(T)$ depending on the previous bounds and independent of γ such that*

$$\int_0^T\int_{\mathbb{R}^d} |w|_-^3\Phi \leq C(T), \quad \int_0^T\int_{\mathbb{R}^d} |\Delta p_\gamma|\Phi \leq C(T). \tag{36}$$

Proof. Computing the time derivative of the negative part of w, we have

$$\begin{aligned}
-\partial_t\left(\frac{|w|_-^2}{2}\right) \leq &-\frac{4}{d}|w|_-^3 - \frac{2}{d}G|w|_-^2 - \frac{2}{d}G^2|w|_- + \nabla|w|_-^2\cdot\nabla p + \partial_p G|\nabla p|^2|w|_-\\
&+ 2\partial_c G\nabla p\cdot\nabla c|w|_- + \gamma\Delta(p|w|_-)|w|_- - \partial_c G\,\partial_t c|w|_-.
\end{aligned}$$

as in the proof of Theorem 3.1. We multiply the inequality by Φ and integrate in space

$$\begin{aligned}\frac{d}{dt}\int_{\Omega_T}\frac{|w|_-^2}{2}\Phi \leq &-\frac{2}{d}\int_{\Omega_T}|w|_-^3\Phi-\frac{2}{d}\int_{\Omega_T}G^2|w|_-\Phi-\beta\int_{\Omega_T}|\nabla p|^2|w|_-\Phi \\ &-\frac{4}{d}\int_{\Omega_T}G|w|_-^2\Phi+\underbrace{\int_{\Omega_T}\left[\nabla p\cdot\nabla\left(|w|_-^2\right)\Phi+\gamma\Delta(p|w|_-)|w|_-\Phi\right]}_{\mathcal{A}} \\ &\underbrace{-\int_{\Omega_T}\partial_c G\,\partial_t c|w|_-\Phi}_{\mathcal{B}}+\underbrace{2\int_{\Omega_T}\partial_c G\nabla p\cdot\nabla c|w|_-\Phi}_{\mathcal{C}}.\end{aligned} \tag{37}$$

Now we proceed computing each term.

$$\begin{aligned}\mathcal{A} &= \int_{\mathbb{R}^d}\nabla p\cdot\nabla\left(|w|_-^2\right)\Phi-\gamma\int_{\mathbb{R}^d}\nabla(p|w|_-)\cdot\nabla|w|_-\Phi-\gamma\int_{\mathbb{R}^d}|w|_-\nabla(p|w|_-)\cdot\nabla\Phi \\ &= -\int_{\mathbb{R}^d}\Delta p|w|_-^2\Phi-\int_{\mathbb{R}^d}|w|_-^2\nabla p\nabla\Phi-\gamma\int_{\mathbb{R}^d}|w|_-\nabla p\nabla|w|_-\Phi \\ &\quad -\gamma\int_{\mathbb{R}^d}p|\nabla|w|_-|^2\Phi+\gamma\int_{\mathbb{R}^d}p|w|_-^2\Delta\Phi+\gamma\int_{\mathbb{R}^d}p\nabla\left(\frac{|w|_-^2}{2}\right)\cdot\nabla\Phi \\ &= -\int_{\mathbb{R}^d}\Delta p|w|_-^2\Phi-\int_{\mathbb{R}^d}|w|_-^2\nabla p\cdot\nabla\Phi+\frac{\gamma}{2}\int_{\mathbb{R}^d}\Delta p|w|_-^2\Phi+\frac{\gamma}{2}\int_{\mathbb{R}^d}|w|_-^2\nabla p\cdot\nabla\Phi \\ &\quad -\gamma\int_{\mathbb{R}^d}p|\nabla|w|_-|^2\Phi+\frac{\gamma}{2}\int_{\mathbb{R}^d}p|w|_-^2\Delta\Phi-\frac{\gamma}{2}\int_{\mathbb{R}^d}|w|_-^2\nabla p\cdot\nabla\Phi \\ &= \left(1-\frac{\gamma}{2}\right)\int_{\mathbb{R}^d}|w|_-^3\Phi+\left(1-\frac{\gamma}{2}\right)\int_{\mathbb{R}^d}G|w|_-^2\Phi-\gamma\int_{\mathbb{R}^d}p|\nabla|w|_-|^2\Phi+\mathcal{A}_1,\end{aligned}$$

with

$$\mathcal{A}_1=\frac{\gamma}{2}\int_{\mathbb{R}^d}p|w|_-^2\Delta\Phi-\int_{\mathbb{R}^d}|w|_-^2\nabla p\cdot\nabla\Phi.$$

By the Cauchy-Schwarz inequality we have

$$\mathcal{B}\leq\int_{\mathbb{R}^d}|w|_-^2\Phi+C\int_{\mathbb{R}^d}|\partial_t c|^2\Phi\leq\int_{\mathbb{R}^d}|w|_-^2\Phi+C.$$

Using Young's inequality and (21), we find

$$\begin{aligned}\mathcal{C} &\leq \frac{\beta}{2}\int_{\mathbb{R}^d}|\nabla p|^2|w|_-\Phi+C\int_{\mathbb{R}^d}|\nabla c|^2|w|_-\Phi \\ &\leq \frac{\beta}{2}\int_{\mathbb{R}^d}|\nabla p|^2|w|_-\Phi+C\int_{\mathbb{R}^d}|\nabla c|^4\Phi+C\int_{\mathbb{R}^d}|w|_-^2\Phi \\ &\leq \frac{\beta}{2}\int_{\mathbb{R}^d}|\nabla p|^2|w|_-\Phi+C\int_{\mathbb{R}^d}|w|_-^2\Phi+C.\end{aligned}$$

It remains to treat the term containing the derivatives of Φ

$$\mathcal{A}_1=-\int_{\mathbb{R}^d}|w|_-^2\nabla p\cdot\nabla\Phi+\frac{\gamma}{2}\int_{\mathbb{R}^d}p|w|_-^2\Delta\Phi.$$

We choose a positive function Φ with exponential decay, such that $|\nabla\Phi| \le C\Phi$ and $|\Delta\Phi| \le C\Phi$. Now, we integrate by parts and use Young's inequality

$$\begin{aligned}\mathcal{A}_1 &= 2\int_{\mathbb{R}^d} p|w|_-\nabla|w|_- \cdot \nabla\Phi + \left(1+\frac{\gamma}{2}\right)\int_{\mathbb{R}^d} p|w|_-^2\Delta\Phi \\ &\le \frac{1}{2}\int_{\mathbb{R}^d} p|\nabla|w|_-|^2\Phi + C(\gamma+1)\int_{\mathbb{R}^d}|w|_-^2\Phi.\end{aligned}$$

Finally, the inequality (37) can be written as follows

$$\frac{d}{dt}\int_{\mathbb{R}^d}|w|_-^2\Phi + \left(\frac{2}{d}+\frac{\gamma}{2}-1\right)\int_{\mathbb{R}^d}|w|_-^3\Phi + \frac{\beta}{2}\int_{\mathbb{R}^d}|\nabla p|^2|w|_-\Phi \le C(\gamma+1)\int_{\mathbb{R}^d}|w|_-^2\Phi + C,$$

then, for $\gamma > 2-\frac{4}{d}$, integrating in time we have

$$\int_0^T\int_{\mathbb{R}^d}|w|_-^3\Phi \le \left(\int_0^T\int_{\mathbb{R}^d}|w|_-^3\Phi\right)^{\frac{2}{3}} + C(T),$$

and then we have proved

$$\int_0^T\int_{\mathbb{R}^d}|w|_-^3\Phi \le C(T).$$

By consequence

$$\int_0^T\int_{\mathbb{R}^d}|w|_-^2\Phi \le C(T), \quad \int_0^T\int_{\mathbb{R}^d}|w|_-\Phi \le C(T).$$

Since Φ is a smooth function with compact support

$$\int_0^T\int_{\mathbb{R}^d}(\Delta p + G)\Phi \le C,$$

and then also

$$\int_{\mathbb{R}^d}\Phi|\Delta p + G|_+ = \int_{\mathbb{R}^d}\Phi(\Delta p + G) + \int_{\mathbb{R}^d}\Phi|\Delta p + G|_- \le C(T).$$

Therefore we recover the local L^1 estimate for the Laplacian of the pressure

$$\int_0^T\int_{\mathbb{R}^d}|\Delta p|\Phi \le C.$$

□

Appendix C Optimality of the bound $\nabla p \in L^4$

In Theorem 3.2, we have established the uniform bound $\nabla p \in L^4$, see (26). Here, we aim to show that the exponent 4 cannot be increased. We use the so-called *focusing solution* from [2] that we adapt to the limit $\gamma \to \infty$, i.e., the Hele-Shaw problem. We recall that, for the porous medium equation, the focusing solution consists in a spherical hole filling which generates a stronger singularity than the Barenblatt solution, see [35].

Consider $\alpha > 0$ such that $\nabla p \in L^\alpha(Q_T)$, where p is a solution of the Hele-Shaw problem with Dirichlet boundary conditions in a spherical shell $\{R(t) < |x| < R_1\}$, for a given $R_1 > 0$ and $R(0)$ small enough. Then, to simplify the problem, we fix the external radius R_1 and let p satisfy

$$\begin{cases} -\Delta p = 1, & \text{for} \quad R(t) < |x| < R_1, \\ p(x) = 0, & \text{for} \quad |x| = R(t) \ \text{ or } |x| = R_1, \\ R'(t) = -\nabla p \cdot \vec{n}, & \text{for} \quad |x| = R(t). \end{cases} \tag{38}$$

Here, $\vec{n}$ denotes the inner normal to the ball $B_{R(t)}(0)$. As in [2], $R(t)$ diminishes and vanishes in finite time, generating a singularity $|\nabla p| \to \infty$. The power 4 turns out to be the highest possible integrability in time at this singular time. We treat the case of dimension 2. In higher dimension the radial solutions are more regular and the worse singularity would be obatined for a cylinder with a 2 dimensional basis.

Case $d = 2$. With spherical symmetry, we set $p := p(r)$, $r = |x|$ and equation (38) reads

$$\frac{1}{r}(rp')' = 1.$$

Integrating once, we get, for some $a(t)$

$$p' = -\frac{r}{2} + \frac{a(t)}{r},$$

and the second integration yields

$$p = -\frac{r^2}{4} + a(t)\ln r + b(t).$$

Imposing $p(R_1) = p(R(t)) = 0$, we find

$$b(t) = \frac{R_1^2}{4} - a(t)\ln R_1,$$
$$\frac{R(t)^2}{4} - a(t)\ln R(t) = \frac{R_1^2}{4} - a(t)\ln R_1.$$

Hence for $R(t) \approx 0$, we have

$$a(t) \approx -\frac{R_1^2}{4\ln R(t)}, \qquad R'(t) \approx \frac{1}{R(t)\ \ln R(t)}. \tag{39}$$

Therefore there is $T > 0$ when $R(T^-) = 0$ and as $t \approx T$, we compute

$$\int_0^T \int_{B_{R_1}(0)} |\nabla p(x)|^\alpha dx dt = \int_0^T \int_{R(t)}^{R_1} |p'(r)|^\alpha r dr dt \approx \int_0^T \int_{R(t)}^{R_1} \frac{|a(t)|^\alpha}{r^{\alpha-1}} dr dt.$$

The singularity at T is thus driven by

$$\int_0^T \frac{|a(t)|^\alpha}{R(t)^{\alpha-2}} dt \approx \int_0^T \frac{1}{|\ln R(t)|^\alpha\, R(t)^{\alpha-2}} dt \approx \int_0^{R(0)} \frac{1}{|\ln R|^{\alpha-1} R^{\alpha-3}} dR$$

by the change of variable $R = R(t)$ and using equation (39). We recall that we have chosen $R(0)$ small enough.

This integral is finite for $1 \le \alpha \le 4$ and infinite for $\alpha > 4$.

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