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Incompressible limit and well-posedness of PDE models of tissue growth

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Incompressible limit and well-posedness of PDE models of tissue growth

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Ai miei genitori,
Marco e Francesca

Incompressible limit and well-posedness of PDE models of tissue growth

Abstract

Both compressible and incompressible porous medium models have been used in the literature to describe the mechanical aspects of living tissues, and in particular of tumor growth. Using a stiff pressure law, it is possible to build a link between these two different representations. In the incompressible limit, compressible models generate free boundary problems of Hele-Shaw type where saturation holds in the moving domain. Our work aims at investigating the stiff pressure limit of reaction-advection-porous medium equations motivated by tumor development. Our first study concerns the analysis and numerical simulation of a model including the effect of nutrients. Then, a coupled system of equations describes the cell density and the nutrient concentration. For this reason, the derivation of the pressure equation in the stiff limit was an open problem for which the strong compactness of the pressure gradient is needed. To establish it, we use two new ideas: an L^3-version of the celebrated Aronson-Bénilan estimate, also recently applied to related problems, and a sharp uniform L^4-bound on the pressure gradient. We further investigate the sharpness of this bound through a finite difference upwind scheme, which we prove to be stable and asymptotic preserving. Our second study is centered around porous medium equations including convective effects. We are able to extend the techniques developed for the nutrient case, hence finding the complementarity relation on the limit pressure. Moreover, we provide an estimate of the convergence rate at the incompressible limit. Finally, we study a multi-species system. In particular, we account for phenotypic heterogeneity, including a structured variable into the problem. In this case, a cross-(degenerate)-diffusion system describes the evolution of the phenotypic distributions. Adapting methods recently developed in the context of two-species systems, we prove existence of weak solutions and we pass to the incompressible limit. Furthermore, we prove new regularity results on the total pressure, which is related to the total density by a power law of state.

Keywords: porous medium equation, tumor growth, Aronson-Bénilan estimate, free boundary, Hele-Shaw problem

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Résumé

Les modèles de milieux poreux, en régime compressible ou incompressible, sont utilisés dans la littérature pour décrire les propriétés mécaniques des tissus vivants et en particulier de la croissance tumorale. Il est possible de construire un lien entre ces deux différentes représentations en utilisant une loi de pression raide. Dans la limite incompressible, les modèles compressibles conduisent à des problèmes de frontières libres de type Hele-Shaw. Nos travaux visent à étudier la limite de pression raide des équations de type milieu poreux motivées par le développement tumoral. Notre première étude concerne l'analyse et la simulation numérique d'un modèle incluant l'effet des nutriments. Ensuite, un système d'équations, dont le couplage est délicat, décrit la densité cellulaire et la concentration en nutriments. Pour cette raison, la dérivation de l'équation de pression dans la limite incompressible était un problème ouvert qui nécessite la compacité forte du gradient de pression. Pour l'établir, nous utilisons deux nouvelles idées : une version L^3 de la célèbre estimation d'Aronson-Bénilan, également utilisée récemment pour des problèmes connexes, et une estimation L^4 sur le gradient de pression (où l'exposant 4 est optimal). Nous étudions en outre l'optimalité de cette estimation par un schéma numérique upwind aux différences finies, que nous montrons être stable et *asymptotic preserving*. Notre deuxième étude est centrée sur l'équation de milieux poreux avec effets convectifs. Nous étendons les techniques développées pour le cas avec nutriments, trouvant ainsi la relation de complémentarité sur la pression limite. De plus, nous fournissons une estimation du taux de convergence à la limite incompressible. Enfin, nous étudions un système multi-espèces. En particulier, en tenant compte de l'hétérogénéité phénotypique, nous incluons une variable structurée dans le problème. Par conséquent, un système de diffusion croisée et dégénérée décrit l'évolution des distributions phénotypiques. En adaptant des méthodes récemment développées pour des systèmes à deux équations, nous prouvons l'existence de solutions faibles et nous passons à la limite incompressible. En outre, nous prouvons de nouveaux résultats de régularité sur la pression totale, qui est liée à la densité totale par une loi de puissance.

Mots clés : équation des milieux poreux, croissance tumorale, estimation d'Aronson-Bénilan, frontière libre, problème de Hele-Shaw

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Abstract

Tra i modelli matematici per la crescita dei tessuti, ed in particolare per la crescita tumorale, sia modelli cosiddetti comprimibili sia modelli incomprimibili sono largamente utilizzati in letteratura. Passando al limite incomprimibile, i modelli comprimibili generano modelli a frontiera libera del tipo Hele-Shaw, in cui si ha saturazione nel dominio. L'obiettivo di questa tesi è quello di analizzare il limite *stiff pressure* (pressione rigida) di equazioni del tipo reazione-convezione-diffusione degenere (dei mezzi porosi). Il primo lavoro riguarda l'analisi e la simulazione numerica di un modello che include la presenza di nutrienti. Un sistema di equazioni descrive l'evoluzione della densità cellulare e della concentrazione di nutrienti. In questo caso, la derivazione dell'equazione della pressione nel limite incomprimibile rappresentava un problema irrisolto, per il quale era necessario trovare la compattezza forte del gradiente della pressione. Al fine di dimostrarla, sono state utilizzate due tecniche: una versione L^3 della celebre stima di Aronson e Bénilan, e una stima L^4 ottimale sul gradiente della pressione. Inoltre, si è investigato numericamente l'ottimalità di questa stima utilizzando uno schema upwind alle differenze finite, che si dimostra essere stabile e *asymptotic preserving*. Il secondo lavoro si concentra sulle equazioni dei mezzi porosi che includono un termine di convezione. Sono state quindi estese le tecniche sviluppate nel modello con nutrienti e ricavata la relazione di complementarietà della pressione limite. Inoltre, viene fornita una stima della velocità di convergenza del limite incomprimibile. Infine, si analizza un modello multi-specie. In particolare, è stata presa in considerazione l'eterogeneità fenotipica, includendo una variabile strutturata nel modello. In questo caso, un sistema del tipo diffusione (degenere) incrociata descrive l'evoluzione delle distribuzioni fenotipiche. Adattando metodi recentemente sviluppati nel contesto di sistemi di due specie, si prova l'esistenza di soluzioni deboli e si passa al limite *stiff*. Inoltre, vengono forniti nuovi risultati di regolarità sulla pressione totale, la quale è legata alla densità totale tramite una legge di potenza.

Parole chiave: equazione dei mezzi porosi, crescita tumorale, stima di Aronson-Bénilan, frontiera libera, problema di Hele-Shaw

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[60] Noemi David and Tomasz Dębiec and Benoit Perthame, Convergence rate for the incompressible limit of nonlinear diffusion-advection equations, *ArXiv Preprint, arXiv:2108.00787*, 2021, https://arxiv.org/abs/2108.00787v1, Accepted for publication in Annales de l'Institut Henri Poincaré C,

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Chapter 1

Introduction

Mathematical modelling of living tissue is one of the most fascinating and challenging problems in mathematical biology. The description and understanding of the mechanisms driving cell migration and proliferation can benefit remarkably from mathematical analysis and simulations. While the former may lead to a more comprehensive view of the qualitative properties and asymptotic behavior of the biological problem, the latter may provide useful parameters suitable for comparison with biological observations. Moreover, mathematical models can provide new insights on those aspects that are more difficult to access experimentally. On the other hand, the modelling of biological phenomena is nowadays one of the most prolific sources of involved and challenging mathematical questions, in particular regarding the analysis of partial differential equations (PDEs). In the last decades, nonlinear and degenerate PDEs and systems motivated by the description of living tissues have been widely investigated. In particular, in this thesis we are interested in problems arising in the modelling of tumor growth.
One of the most crucial aspects to be taken into account in this context is the multiscale nature of cancer development. Indeed, the phenomenon involves several processes occurring at different spatial and temporal scales. This complexity is well represented in the extremely vast literature available today. From individual-based models describing the process from a microscopic viewpoint, to PDE systems representing the tissue as a continuum, the modelling of tumor growth has been largely addressed during the last six decades. One of the most interesting mathematical problems arising in this context concerns the question of bridging the gap between different scales or representations. In particular, among models describing tumor growth from a macroscopic viewpoint, it is possible to identify two main types of descriptions. On the one hand, the space-time evolution of the cell population density can be naturally described by reaction-diffusion equations. On the other hand, a more geometrical perspective is also frequently used, since the tumor can be seen as a domain whose boundary evolves in time. This thesis is centered around the question of how to link these two different representations, namely continuity equations and free boundary problems, through asymptotic analysis.

1.1 Mechanical models of tissue growth

During the last decades, mathematical models of cancer growth have been increasingly applying a mechanical perspective to the problem, adopting a fluid dynamic viewpoint. In fact, at the macroscopic level living tissues can be seen as fluids moving through a porous medium, namely, the extra-cellular matrix (ECM). Continuous models describing the development of tumors usually consist of nonlinear partial differential equations. The temporal and spatial evolution of the cell population density can indeed be described through reaction-diffusion equations and systems. In mechanical models of tumor growth the pressure generated by the birth of new cells plays an essential role both in the dynamics that drive the cell movement, as well as in cell proliferation and death. Besides systems of PDEs based on conservation laws, a second main type of macroscopic models has been largely applied to the description of living tissues and, in particular, tumors: free boundary problems. Indeed, a more "geometrical" perspective can be assumed as the tumor is seen as a domain whose moving boundary evolves in time.

We now give a brief overview of these two types of macroscopic models. Let us stress the fact that, as aforementioned, this thesis is centered around the analytical challenges arising from the problem of bridging the gap between these two different representations. Although our focus does not concern the biomedical applications of such problems, for the sake of completeness we here provide a brief and simplified biological introduction on cancer growth.

1.1.1 Biological background on tumor development

The main feature characterizing cancer growth is certainly the acquired capacity of malignant cells to replicate uncontrollably. Despite the complexity of the phenomenon, that leads to an amount of about one hundred different types of cancer, it has been suggested that malignant growth is a manifestation of the combination of six essential functional capabilities: self-sufficiency in growth signals, insensitivity to growth-inhibitory signals, evasion of apoptosis, limitless replicative potential, sustained angiogenesis, and tissue invasion and metastasis [95].

Among the principal dynamics that drive the tumor cells movement there is space competition. In fact, cells tend to avoid overcrowding, moving towards less congested regions and searching for the space necessary in order to divide. Thus, before the occurrence of different movement processes such as, for instance, chemotaxis, cell motion is mainly triggered by the gradient of the pressure. Moreover, space availability plays a central role in cell proliferation as well. Indeed, a bio-mechanical form of contact inhibition prevents cell multiplication in regions with a high pressure/congestion. Sensing the level of mechanical stress around them, cells control their proliferation in order not to overcome a critical threshold of packaging, which is determined by the compression that cells experience, [37].

It is possible to identify two main phases during the development of solid tumors: the avascular and vascular phases. Initially, neoplastic cells aggregate to form a quasi-spherical cluster. The size of the mass is so small that these very early stages of cancer growth can be studied only in laboratory experiments. Studying 3D cancer spheroids *in vitro* it is possible to recognize their internal structure. They are usually formed by an outer rim of cells that reproduce fast and without control, an intermediate layer of quiescent cells, and a core of dead cells. This internal region contains cells that have died by *necrosis*. Unlike *apoptosis*, which is the natural end of the cell cycle, necrosis is induced by the lack of nutrients in the surrounding environment. Since avascular tumors do not have direct access to blood vessels, they receive the nutrient supply by diffusion. For this reason, they tend to adopt a well-defined symmetrical shape with an outer nutrient-rich rim and a dead core spaced out by a non-proliferating annulus, [40].

In order to provide themselves with blood vessels, tumor cells induce a mechanisms called *angiogenesis*. Tumor cells lacking oxygen produce angiogenic factors that diffuse into the host tissue and activate the endothelial cells lining into the blood vessels. After breaking the basement membrane, endothelial cells migrate towards the tumor and generate a new network of blood supply. During the vascular phase the cancer grows much faster and its structure and shape change significantly compared to avascular tumors. The new vessels are usually formed very quickly, thus they lack muscular tone and may easily collapse under the pressure generated by the surrounding cells. This decreases the level of oxygen in certain regions which induces hypoxia. Consequently, angiogenic factors are secreted, neovascularization occurs and cells start proliferating again. For this reason, the composition and spatial organization of the tumor changes dynamically during the vascular phase. Later, tumor cells may enter the blood vessels and be transported to other regions, creating *metastasis* which represent the most dangerous side of the disease.

1.1.2 Density-based models

Reaction-diffusion equations and systems are one of the most common mathematical models used to describe tissue growth at the macroscopic level. The evolution in space and time of the cell population density is classically described by the continuity equation of fluid mechanics

$$\frac{\partial \varrho}{\partial t}(x,t) - \nabla \cdot \vec{J} = f(x,t), \tag{1.1}$$

where $\vec{J} = \vec{J}(\varrho, \nabla\varrho, \vec{v})$ is the flux which is usually related to the mass density $\varrho = \varrho(x,t)$, its gradient and/or to a vector field $\vec{v}$ given by a constitutive law. On the right-hand side, f denotes the growth/degradation of the tissue. The reaction term may depend on the space and time variables, on the density itself, or on other quantities involved in tumor growth such as, for instance, the pressure of the tissue or the concentration of nutrients. This class of macroscopic models based on conservation equations are usually referred to as *density-based models*.
Early models were centered around the interaction between cancer cells and other chemical species such as, for instance, nutrients (oxygen or glucose), lactate or carbon dioxide, which play an important role in the evolution of tumors. In particular, the modelling of nutrient availability and diffusion has attracted a lot of attention in the context of avascular tumors. As mentioned above, until the tumor is able to provide itself with its own blood supply its evolution and size is inherently related to nutrient diffusion, see [33, 139] and references therein. Later, mathematical models started including also tumor cell movement rather than only nutrient diffusion and consumption. The cells can move via convection [151], active motion (diffusion) [145], or chemotaxis [122, 133], *i.e.* the directed movement of cells towards a chemical concentration. For a complete review of mathematical models of avascular tumors we refer the reader to [139].
More recently, mathematical models have been directed more and more on the mechanical aspects of tumor development rather than only environmental ones. One of the first examples in this direction is the model introduced by Greenspan in 1975, which builds on the early models based on nutrients availability by including a notion of pressure. In [92], the author relates the tumor internal pressure $p = p(x,t)$ to the cell velocity field, proposing a model that was later further elaborated by Byrne and Chaplain [34]. The common feature of these models is that tumors can be seen as fluids flowing through a porous medium represented by the ECM. As mentioned above, cells have the tendency to avoid over-crowding. Therefore, they move down pressure gradients, away from congested regions. For this reason, mechanical models of tumor growth usually link the velocity field $\vec{v}$ to the pressure by the *Darcy law*, *i.e.*

$$\vec{v} = -\kappa \nabla p, \tag{1.2}$$

where κ represents the ratio between permeability and viscosity.
Another step towards a more mechanical description of living tissue is the influence that over-crowding and congestion exert not only on cell motion but also on cell proliferation and death. One of the earliest examples in this direction has been proposed by Byrne and Drasdo in [37]. The authors develop a mechanical model where the pressure plays a fundamental role not only as the driving force of cells movement, but also as the main growth-limiting factor. As aforementioned, the competition for space is indeed crucial in the development of tumors since cells tend

to multiply less in highly congested regions due to contact inhibition. Therefore, the authors describe the evolution of the cell population density through a conservation law as (1.1), where the flux is $\vec{J} = \varrho\vec{v}$ with velocity field $\vec{v}$ given by (1.2), and the stress-regulated proliferation is represented by a pressure-penalised reaction term f

$$\frac{\partial \varrho}{\partial t} - \nabla \cdot (\varrho \vec{v}) = f(p_H - p), \tag{1.3}$$

where p_H denotes the *homeostatic pressure*, *i.e.* the lowest level of pressure that prevents cell division. Above this value cell division is inhibited due to the mechanical stress generated by the pressure. For this reason, the authors assume $f(p_H - p) = s_0 H(p_H - p)$, where s_0 denotes the local growth rate and H is the Heaviside step function. The model has to be closed by a law of state of the pressure, *i.e.* $p = P(\varrho)$.
The model in [37] has later attracted vast interest, in particular for its asymptotic behavior as the stiffness of the pressure increases. In fact, a properly chosen pressure law allows to build a link between Eq. (1.3) and the incompressible (or "geometrical") models that will be introduced in the following section. Two of the most common pressure laws in this context are the power law and the singular pressure law. Power laws as the following

$$p = P_m(\varrho) = \frac{m}{m-1}\left(\frac{\varrho}{\varrho_c}\right)^{m-1}, \qquad m > 1,$$

where ϱ_c represents the maximum packing density of cells, are also well known in applications to fluid mechanics. Combining the power law with Darcy's law (1.2), one can see that the continuity equation (1.3) actually reduces to a porous medium equation (PME) that well represents the behaviour of the tumor cells moving through the extra-cellular matrix.
The singular pressure law

$$p = P_\varepsilon(\varrho) = \varepsilon\frac{\varrho}{1-\varrho}, \qquad \varepsilon > 0,$$

is often specifically used to model tissue growth since the singularity at $\varrho = 1$ directly imposes a constraint on the maximum cell-population density, *i.e.* $\varrho \leqslant 1$. At the microscopic level, this singularity is equivalent to forcing non-overlapping constraints on the cells (particles) that compose the tissue.
Despite having very different forms, these two pressure laws actually exhibit a very similar asymptotic behavior as $\gamma \to \infty$ and $\varepsilon \to 0$. Assuming, without loss of generality, that $\varrho_c = 1$, in both cases the tumor pressure tends to become more and more stiff around the value $\varrho = 1$ and the model can be naturally represented through a more geometrical viewpoint. Both limits generate free boundary problems where a saturation constraint holds. Before going into further details regarding the asymptotic behavior of porous medium models, we briefly introduce the most common features of tumor growth models based on a free boundary formulation.

1.1.3 Free boundary problems

Besides density-based models consisting of reaction-diffusion equations, among macroscopic models of tumor growth one can identify a second main category of models. Rather than describing the evolution of the cell population density in space and time, *free boundary problems* represent the tumor as a domain $\Omega(t)$ with a moving boundary. Therefore, the unknowns of the problem are both the free boundary $\partial\Omega(t)$ and the solution of the partial differential equation set in $\Omega(t)$. This kind of problems is widely used in the modelling of tumor growth, in particular when dealing with avascular tumors or in vitro spheroids, which usually exhibit well-defined boundaries.

Moreover, multi-species models are also largely adopted, since early stages tumors are often formed by different layers of distinguished types of cells: an outer rim of proliferating cells, an inner region of quiescent cells and a core of necrotic cells. Therefore, several tumor growth models describe segregated populations through free boundary problems involving multiple interfaces, see for instance [34, 35].
Let us give an example of a classical free boundary model of cancer growth which takes into account only one species of cells (proliferating cells) and in which cell proliferation is only nutrient-limited. Let $\alpha, \beta > 0$ be positive given constants and let us denote by $\partial_\nu p$ the outward normal derivative of the pressure. The evolution of the pressure $p = p(x,t)$ and the nutrient concentration $c = c(x,t)$ are described as follows

$$\begin{cases} \partial_t c &= \Delta c - \alpha c, & \text{in } \Omega(t), \\ \Delta p &= f(c), & \text{in } \Omega(t), \\ V &= -\partial_\nu p, & \text{on } \partial\Omega(t), \end{cases} \qquad \begin{cases} p &= \beta k, & \text{on } \partial\Omega(t), \\ c &= c_B, & \text{on } \partial\Omega(t), \\ c(x,0) &= c_0(x), & \text{in } \Omega(0), \end{cases}$$

where $\Omega(0)$ and c_0 are given, and c_B is the level of nutrients outside of the spheroid, see [80]. The density of the population is assumed to be constant inside $\Omega(t)$. For this reason, these problems are usually referred to as *incompressible models*. Unlike the classical condition of fluid incompressibility (*i.e.* a divergence-free velocity field), due to the presence of a reaction term f (*i.e.* cell multiplication) the divergence of the flow does not vanish.
The above system takes into account surface tension, *i.e.* the pressure on the boundary is proportional to the mean curvature k. If one assumes $p = 0$ on the moving boundary, the problem reduces to a Hele-Shaw type problem (HS in short), which is a well known free boundary problem that will be presented more in detail in the following sections.
Let us notice that the velocity law of the free boundary coincides with Darcy's law, which means that cells are escaping regions with higher pressure. In fact, there is a close relation between the HS problem and the conservation law (1.1). As already mentioned, through the so-called *incompressible limit* it is possible to bridge the gap between these two different representations of the same phenomenon, namely density-based models and free boundary problems. The analytical (and numerical) study of this limit for different PDEs and systems is the main subject of this manuscript.

1.2 Notation and preliminaries

For the sake of clarity, let us introduce some notation and preliminary results that will be used throughout the thesis.

Notation. Given a function $w : \mathbb{R}^d \to \mathbb{R}$, we define its positive sign and negative sign

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

We also define its positive part and negative part as follows

$$(w)_+ := \begin{cases} w, & \text{for } w > 0, \\ 0, & \text{for } w \leqslant 0, \end{cases} \qquad (w)_- := \begin{cases} -w, & \text{for } w < 0, \\ 0, & \text{for } w \geqslant 0, \end{cases}$$

as well as its absolute value $|w| := (w)_+ + (w)_-$.

Given a general set A, we denote by $\mathbb{1}_A$ its characteristic function, namely

$$\mathbb{1}_A(x) = \begin{cases} 1, & \text{for } x \in A, \\ 0, & \text{otherwise.} \end{cases}$$

Let $\Omega \subset \mathbb{R}^d$ be an open subset. We denote by $L^p(\Omega)$ and $W^{m,p}(\Omega)$ the usual Lebesgue and Sobolev spaces, respectively, where $1 \leqslant p \leqslant \infty$ and $m \in \mathbb{N}$. As usual, we indicate $H^m(\Omega) := W^{m,2}(\Omega)$. Given a function $f \in L^p(\Omega)$, we often use the abbreviated form $\|f\|_p := \|f\|_{L^p(\Omega)}$.
We denote by $< \cdot, \cdot >$ the standard duality pairing between $(H^1(\Omega))'$ and $H^1(\Omega)$.
We denote by $C^\infty_{comp}(\mathbb{R}^d \times (0,\infty))$ the space of smooth functions with compact support in $\mathbb{R}^d \times (0,\infty)$. We also use the notation $\mathcal{D}(\mathbb{R}^d \times (0,\infty))$ to indicate the same space, and we denote by $\mathcal{D}'(\mathbb{R}^d \times (0,\infty))$ the space of distributions.

Useful inequalities. Let us recall some important inequalities and embedding theorems that we will frequently use in this thesis.

Proposition 1.2.1 (Kato inequality). *Let $\Omega \subset \mathbb{R}^d$ be a bounded open subset, and let $w \in L^1_{loc}(\mathbb{R}^d)$ be a function such that $\Delta w \in L^1_{loc}(\mathbb{R}^d)$. Then $\Delta(w)_-$ is a Radon measure and the following holds*

$$\Delta(w)_- \geqslant \text{sign}_-(w)\Delta w, \qquad \text{in } \mathcal{D}'(\mathbb{R}^d). \tag{1.4}$$

Proposition 1.2.2 (Poincaré inequality). *Let $1 \leqslant p < \infty$ and let $\Omega \subset \mathbb{R}^d$ be an open and bounded subset. There exists C depending on Ω and p such that for every $u \in W^{1,p}_0(\Omega)$, we have*

$$\|u\|_{L^p(\Omega)} \leqslant C\|\nabla u\|_{L^p(\Omega)}. \tag{1.5}$$

Proposition 1.2.3 (Poincaré-Wirtinger inequality). *Let $1 \leqslant p < \infty$ and let $\Omega \subset \mathbb{R}^d$ be an open and bounded subset. There exists C depending on Ω and p such that for every $u \in W^{1,p}(\Omega)$, we have*

$$\|u - u_\Omega\|_{L^p(\Omega)} \leqslant C\|\nabla u\|_{L^p(\Omega)}, \tag{1.6}$$

where u_Ω is the mean of u on Ω i.e.

$$u_\Omega = \frac{1}{|\Omega|}\int_\Omega u \,\mathrm{d}x.$$

Proposition 1.2.4 (Compact embeddings of Sobolev spaces). *Let $\Omega \subset \mathbb{R}^d$ be an open and bounded subset with Lipschitz boundary. Let $j \geqslant 0$ and $m \geqslant 1$ be integers and let $1 \leqslant p < \infty$. Then, the following embeddings are compact*

- *if $mp > d$, we have*

$$\begin{aligned} &W^{j+m,p}(\Omega) \to C^j(\bar{\Omega}), \\ &W^{j+m,p}(\Omega) \to W^{j,q}(\Omega), \qquad 1 \leqslant q < \infty, \end{aligned}$$

  so, in particular,

$$W^{m,p}(\Omega) \to L^q(\Omega), \qquad 1 \leqslant q < \infty,$$

- *if $mp = d$, we have*

$$W^{j+m,p}(\Omega) \to W^{j,q}(\Omega), \qquad 1 \leqslant q < \infty,$$

- *if $mp < d$, we have*

$$W^{j+m,p}(\Omega) \to W^{j,q}(\Omega), \qquad 1 \leqslant q < p^* = \frac{dp}{d-mp}.$$

Compactness theorems. We recall two classical results on compactness that will be used in the following parts of the thesis.

Proposition 1.2.5 (Aubin-Lions lemma). *Let X_0, X and X_1 be three Banach spaces with $X_0 \subset X \subset X_1$. Suppose X_0 is compactly embedded in X and that X is continuously embedded in X_1. For $1 \leqslant p, q \leqslant \infty$, let*

$$W := \{u \in L^p(0,T;X_0) |\ \partial_t u \in L^q(0,T;X_1)\}.$$

Then

- *if $p < \infty$, then the embedding of W into $L^p(0,T;X)$ is compact,*
- *if $p = \infty$ and $q > 1$, then the embedding of W in $C(0,T;X)$ is compact.*

Proposition 1.2.6 (Fréchet–Kolmogorov theorem). *Let $S \subset L^p(\mathbb{R}^d)$ be a bounded subset. Assume that*

$$\lim_{|h|\to 0} \int_{\mathbb{R}^d} |f(x+h) - f(x)|^p \,\mathrm{d}x = 0,$$

uniformly in $f \in S$. Then, for any $\Omega \subset \mathbb{R}^d$, the set $\{f_{|\Omega}|\ f \in S\}$ is relatively compact. If $\forall \varepsilon > 0$ there exists a bounded set Ω_ε such that $\|f\|_{L^p(\mathbb{R}^d \setminus \Omega_\varepsilon)} < \varepsilon$ for any $f \in S$, then S is relatively compact.

1.3 Incompressible limit of porous medium models

Mathematical models based on porous medium type equations (or, more generally, filtration equations) have been vastly applied to problems arising in biology and medicine, as well as to the modelling of crowd motion and fluid dynamics.
One of the most interesting problems related to these equations is to understand their asymptotic behavior as the pressure law becomes stiff. As aforementioned, this limit has recently attracted particular interest in the context of tumor growth modelling. However, its study has a very long history which originates in the seminal works on the classical porous medium equation (PME). Before introducing the incompressible limit, its derivation and its recent applications, let us give a brief overview of the PME and its main properties. For a complete picture on the theory of the porous medium equation we refer the reader to the monograph of Vázquez, *cf.* [150].

1.3.1 The porous medium equation

The porous medium equation (PME) is a well known nonlinear, degenerate parabolic equation. It represents the simplest example of a nonlinear parabolic equation and it reads as follows

$$\frac{\partial u}{\partial t} = \Delta u^m, \quad x \in \mathbb{R}^d,\ t > 0, \tag{1.7}$$

with exponent $m > 1$. At first sight it might appear as a simple variation of the heat equation (HE), to which it is indeed equivalent when $m = 1$. However, the degeneracy of the PME induces several properties that drastically separate it from its linear and uniformly parabolic counterpart. The most recognizable characteristic that sets apart the PME from the HE is the property of finite speed of propagation. In fact, it is well known that solutions which are initially compactly supported remain so at any finite time, see [127]. This property is in stark contrast to the infinite speed of propagation of solutions of the HE, which is a direct consequence of the strong maximum principle. As a consequence, a moving boundary appears, separating the two sets $\{x;\ u(x,t) > 0\}$ and $\{x;\ u(x,t) = 0\}$. The speed of this boundary is determined by the gradient of the density-related pressure, defined as follows

$$p = \frac{m}{m-1} u^{m-1}. \tag{1.8}$$

Indeed, let us notice that the PME can be written as a continuity equation with velocity field given by Darcy's law, namely

$$\vec{v} = -\nabla p, \tag{1.9}$$

$$\frac{\partial u}{\partial t} + \nabla \cdot (u\vec{v}) = 0. \tag{1.10}$$

The so-called *pressure transformation* (1.8) is frequently used in the analysis of porous medium type equations. This change of variables is very useful in that it induces a self-contained equation satisfied by the pressure, namely

$$\frac{\partial p}{\partial t} = (m-1)p\Delta p + |\nabla p|^2. \tag{1.11}$$

The above equation clearly shows that the PME behaves in very different ways around the value $p \approx 0$. Indeed, when p is larger than zero, the parabolic part is dominant and thus the equation is a nonlinear perturbation of the HE plus a lower order term. On the other hand, when p approaches zero the equation is a perturbation of the eikonal equation

$$\frac{\partial p}{\partial t} = |\nabla p|^2,$$

which is highly hyperbolic. Therefore, around the value of degeneracy, the PME is of *mixed type*, and by consequence it exhibits mixed properties. From the last equation it is possible to notice that the finite velocity of the free boundary, $\partial\{x;\ u(x,t) = 0\} = \partial\{x;\ p(x,t) = 0\}$, coincides with the velocity field of the density, (1.9). For this reason, in the framework of diffusion equations, the porous medium equation is also referred to as *slow diffusion*, while the same equation for $m < 1$ is called *fast diffusion*.

Physical interpretation

Let us mention here the first notable application of the porous medium equation and its derivation in the context of fluid mechanics, which is due to Leibenzon (1930) and Muskat (1933). They describe the flow of a gas in a porous medium through the following system

$$\begin{cases} \dfrac{\partial \varrho}{\partial t} + \nabla \cdot (\varrho \vec{v}) = 0, \\ \vec{v} = -\dfrac{\mu}{\nu} \nabla p, \quad p = P(\varrho), \end{cases}$$

where $\varrho(x,t)$ indicates the gas density, which evolves under the usual continuity equation, and $p(x,t)$ denotes the density-related pressure. The positive constants ν and μ represent the viscosity of the fluid and the permeability of the medium, respectively. The velocity field is linked to the pressure through the second equation of the system. The closure relation between pressure and density is given by the barotropic power law

$$p = P(\varrho) = p_o \varrho^\gamma,$$

where $\gamma = 1$ for isothermal gases and $\gamma > 1$ for adiabatic gas flows. Therefore, one can rewrite the continuity equation of the density as follows

$$\frac{\partial \varrho}{\partial t} = \nabla \cdot \left(\frac{\mu}{\nu} \varrho \nabla p\right) = p_0 \frac{\mu}{\nu} \nabla \cdot (\varrho \nabla \varrho^\gamma) = p_0 \frac{\mu}{\nu} \frac{\gamma}{\gamma+1} \Delta \varrho^{\gamma+1}.$$

To recover the classical porous medium equation, we choose $\mu = \nu$ and $p_0 = (\gamma+1)/\gamma$. Therefore, taking $\gamma + 1 = m$ we get (1.7) and (1.8).

Regularity

The definition of a class of weak solutions for Eq. (1.7) was first given in the one dimensional case in [127], where the authors prove existence and uniqueness of solutions in that class. We here give the definition of weak solution to Eq. (1.7) which is the one we will always consider throughout the subsequent chapters of the thesis.

Definition 1.3.1 (Weak solution of the PME)**.** A locally integrable function u defined in $\mathbb{R}^d \times (0,T)$ is said to be a weak solution of (1.7) with initial condition given by $u_0 \in L^1(\mathbb{R}^d)$ if

(i) $u^m \in L^2(0,T; H^1(\mathbb{R}^d))$,

(ii) u satisfies

$$\int_0^T \int_{\mathbb{R}^d} \left(\nabla u^m \cdot \nabla \varphi - u \frac{\partial \varphi}{\partial t}\right) \mathrm{d}x \, \mathrm{d}t = \int_{\mathbb{R}^d} u_0(x) \varphi(x,0) \, \mathrm{d}x,$$

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

It is well known that for compactly supported initial data u_0, even if continuous, the porous medium equation does not admit a global classical solution due to its degeneracy (*i.e.* due to the appearance of a free boundary). In fact, for compactly supported initial data, it is not possible to have a solution of the Cauchy problem whose gradient is continuous in space. The discontinuity of u_x was proven in [100], where for the one-dimensional problem, the author proves that there always exists a point of discontinuity of $u_x(t)$ for each $t > 0$, even for smooth initial data, $u_0 \in C^\infty(\mathbb{R})$. Nonetheless, in spatial neighborhoods of points in which $u(x,t)$ takes positive values, weak solutions satisfy the problem in the classical sense. In particular, if we lift the initial data so that $u_\varepsilon(\cdot,0) \geqslant \varepsilon$, then there exists a unique classical solution, $u_\varepsilon \geqslant \varepsilon$.
An explicit formula is available for *source solutions* of Eq. (1.7), *i.e.* $u(x,t)$ such that $u(x,t) \to M\delta(x)$ as $t \to 0$, where $M := \int u_0(x) \, \mathrm{d}x$. The so-called Barenblatt solution is a self-similar profile given by the following expression

$$B(x,t;M) := t^{-\alpha} F(x/t^\beta), \qquad F(\xi) := (C - \kappa|\xi|^2)_+^{\frac{1}{m-1}},$$

where

$$\alpha = \frac{d}{2+d(m-1)}, \quad \beta = \frac{1}{2+d(m-1)}, \quad \kappa = \frac{\alpha(m-1)}{2md},$$

and $C > 0$ is a constant determined by the mass M. This profile gives the simplest example of solution that does not satisfy the equation in the classical sense.

The regularity of solutions of the porous medium equation was extensively studied for decades, originating from the works of Aronson, Caffarelli, Crandall, Friedman, and Pierre in the '70s. In [7], Aronson investigates the problem in dimension one, analysing the free boundary of compactly supported solutions. In order to give a more precise characterisation of the free boundary, *i.e.* the curves that separate $\{(x,t); u(x,t) > 0\}$ from $\{(x,t); u(x,t) = 0\}$, the author proves a lower bound on the second derivative of the pressure. Assuming that $\operatorname{essinf}_{\operatorname{supp} u_0}(p_0)_{xx} \geqslant -\alpha$ for some $\alpha > 0$, then $\partial^2_{xx} p(x,t) \geqslant -\alpha$ for all (x,t) such that $u(x,t) > 0$. This estimate was later established in any spatial dimension by Aronson and Bénilan, [9], and is now named after the two authors

$$\Delta p = \Delta\left(\frac{m}{m-1} u^{m-1}\right) \geqslant -\frac{1}{kt}, \qquad \text{with } k = m - 1 + \frac{2}{d}. \tag{1.12}$$

Let us mention that this lower bound on the Laplacian of the pressure is used by the authors to prove that there exists a unique strong and continuous solution to the Cauchy problem with L^1-bounded initial data. The Aronson-Bénilan estimate (AB in short) is usually referred to as the fundamental estimate in the theory of the porous medium equation and it will be further discussed in Section 1.4.

Let us come back to the regularity of solutions in dimension one. The free boundary of the set $\Omega(t) := \{x;\ u(x,t) > 0\}$ consists of two monotone curves: there exist $\zeta_i(t)$, $i = 1, 2$, such that

$$\Omega(t) = \{x;\ \zeta_1(t) < u(x,t) < \zeta_2(t)\},$$

where both $-\zeta_1(t)$ and $\zeta_2(t)$ are monotone increasing, see [100], and Lipschitz continuous for positive times, see [7]. In 1979, Caffarelli and Friedman proved that ζ_i are actually continuously differentiable after a certain time $t = t_i^*$, [41]. At this point, there can be a jump discontinuity of the velocities $\zeta_i'(t)$, therefore the Lipschitz regularity of the interfaces is optimal in dimension one.

A fundamental step forward in the quest for the regularity properties of the PME was made in [42] where the authors prove Hölder continuity of both the free boundary and $u(x,t)$ in any dimension. Later in 1987, Caffarelli, Vázquez and Wolanski show that the free boundary of the solution is Lipschitz continuous after a certain waiting time, see [44]. For dimension $d > 1$ such condition is needed since the free boundary velocity $|\nabla p|$, may blow up in finite time. This occurs if the initial support contains empty patches that close after a certain finite time t^* usually referred to as *focusing time*. This behavior has indeed attracted a lot of attention in relation to the global regularity issue. The first study is due to Graveleau [90] after which the solution is named. The Graveleau solution, also called *focusing solution*, is a radially symmetric self-similar solution whose initial support is contained outside of a ball. Thanks to the finite speed of propagation, the "hole" shrinks in finite time, t^*. This solution represents the simplest example that shows that global Lipschitz continuity cannot always be expected. Indeed, for $d \geqslant 2$, the solution is smooth on its support only after the focusing time t^*, after which the initial "hole" has closed up (or *focused*), [8, 11]. For more insights on the regularity of PME's solutions in Sobolev spaces we refer the reader to [84].

Filtration equation

In 1982, Crandall and Pierre extend the Aronson-Bénilan inequality for a broader class of degenerate and nonlinear equations. Investigating the regularity of the filtration equation, namely $u_t = \Delta\varphi(u)$, where φ is a continuous, non-decreasing function with $\varphi(0) = 0$. In [58] the authors

prove an L^∞-lower bound on $u_t = \Delta\varphi(u)$.
In [18], Bénilan and Crandall establish the continuous dependence of the filtration equation on φ using nonlinear semi-group theory which enables them to allow for cases of φ being a monotone graph. As a matter of fact, their paper also covers the first result on the incompressible limit, which consists of letting $m \to \infty$, upon choosing $\varphi(z) = z^m$. The authors prove a convergence result in the particular case of non-negative initial data such that $\|u_0\|_\infty \leqslant 1$.

1.3.2 From the PME to the Hele-Shaw problem

A question that has fascinated many researchers in the last few decades is to understand the behavior of the porous medium equation as the exponent m becomes larger and larger. As it is now well known, a compactly supported solution u_m develops sharp interfaces as $m \to \infty$. In particular, the appearance of a saturated region occurs, *i.e.* a zone where $u_\infty = 1$, which is closely related to the domain of a free boundary problem known as the *Hele-Shaw problem*. Despite being quite different from a mathematical viewpoint, the PME and the Hele-Shaw problem share a crucial common feature. In fact, in both cases the flow is induced by Darcy's law.
Before introducing the underlying principles behind the *incompressible limit* $m \to \infty$ and summarizing the early results in the literature, let us give a short overview of the Hele-Shaw problem.

The Hele-Shaw problem

The Hele-Shaw problem is a free boundary problem which was first introduced to model the injection of a fluid into a laminar cell, see [138]. The fluid surface expands in the small gap between two parallel flat plates that form the cell, also called *Hele-Shaw cell*, named after Henry Selby Hele-Shaw who studied the phenomenon in 1898. In 1972, Richardson analyses the Hele-Shaw problem for a point source injected into an infinite cell. Originally the model was motivated by applications to plastic industry, in particular to injection moulding, see [138].
The same problem was then approached from a variational point of view by Elliot and Janovský. In [74], they consider a finite cell and a finite source. Moreover, the injected fluid is assumed to be incompressible and the pressure variations which are perpendicular to the cell surface are neglected, since the space between the plates is infinitesimally small. This property is the main characteristic of the Hele-Shaw flow. The fluid "blows" from the injection point with constant rate Q. Hence, after a certain time t the increment of the fluid blob is Qt volume units.
As already mentioned the main feature of the Hele-Shaw flow is the fact that the movement of the fluid is governed by Darcy's law (1.2), where κ is a positive constant that depends on the fluid viscosity and the depth of the cell. From now on, without loss of generality we assume $\kappa = 1$.

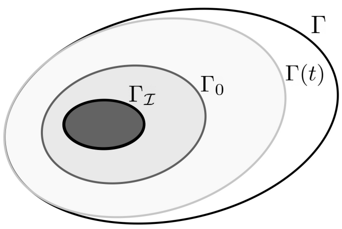

Figure 1.1: Domain of the Hele-Shaw problem

The problem is set as displayed in Fig.1.1. The curve $\Gamma_{\mathcal{I}}$ is the curve through which the fluid is blown into the cell at velocity Q. At time $t = 0$, the fluid occupies the region between $\Gamma_{\mathcal{I}}$

and Γ_0 denoted Ω_0, while $\Omega(t)$ is the area occupied at time $t > 0$ included between $\Gamma_{\mathcal{I}}$ and $\Gamma(t)$. We denote by Ω the entire domain, *i.e.* the region included between $\Gamma_{\mathcal{I}}$ and the exterior fixed boundary Γ.
Since the fluid is assumed to be incompressible the velocity field is divergence free in the region it occupies, namely

$$\Delta p = 0, \text{ in } \Omega(t).$$

The pressure on $\Gamma(t)$ is assumed to be constantly equal to zero and the normal velocity of the free boundary $\Gamma(t)$ is equal to the opposite of the normal derivative of the pressure $V = -\partial_\nu p$. The flow is assumed to be tangential to the outer boundary of the cell, therefore $\partial_\nu p = 0$ on Γ. Let us assume that for some function $l = l(x)$, the moving boundary and the fluid surface can be defined as

$$\begin{aligned}\Gamma(t) &= \{x;\ t - l(x) =: S(x,t) = 0\},\\ \Omega(t) &= \{x;\ l(x) < t\}.\end{aligned}$$

The Hele-Shaw problem in the sense of Elliot-Janovský [74] can be stated as follows.

Problem 1.3.2 (Original Hele-Shaw problem). *Find $l(x)$ and $p(x,t)$, $x \in \Omega$ and $t \in (0,T]$ such that*

$$\begin{cases} l(x) = 0, & \textit{for } x \in \Omega_0,\\ \Delta p(x,t) = 0, & \textit{for } x \in \Omega(t), \end{cases} \qquad \begin{cases} p = 0, & \textit{on } \Gamma(t),\\ \partial_\nu p = -V, & \textit{on } \Gamma(t),\\ \partial_\nu p = Q, & \textit{on } \Gamma_{\mathcal{I}},\\ \partial_\nu p = 0, & \textit{on } \Gamma. \end{cases} \tag{1.13}$$

As observed in [74], the Hele-Shaw problem is actually a Stefan problem with zero specific heat. Indeed, if we replace $\Delta p = 0$ by $c\partial_t p - \Delta p = 0$ where p represents the temperature of water and $c > 0$ is the specific heat, Problem 1.13 describes the evolution of the surface of contact between water and melting ice.
As shown in [107], cusp-like singularities may appear on the free boundary, therefore the Hele-Shaw problem does not necessarily have a global classical solution. A weaker notion of solution is then introduced. Using the Baiocchi's transform it is possible to find an equivalent problem which consists of an elliptic variational inequality. Let w be the transform of p, namely

$$w(x,t) = \begin{cases} 0, & \text{for } x \in \Omega \setminus \Omega_0,\ t \in [0, l(x)],\\ \displaystyle\int_{l(x)}^t p(x,\tau)\,\mathrm{d}\tau, & \text{for } x \in \Omega \setminus \Omega_0,\ t \in [l(x), T],\\ \displaystyle\int_0^t p(x,\tau)\,\mathrm{d}\tau, & \text{for } x \in \Omega_0,\ t \in [0,T]. \end{cases}$$

Let $\mathbb{1}_{\Omega_0}$ be the characteristic function of Ω_0. Then, w satisfies the following complementarity problem

$$\begin{cases} -\Delta w - (\mathbb{1}_{\Omega_0} - 1) \geqslant 0, \quad w \geqslant 0,\\ (-\Delta w - (\mathbb{1}_{\Omega_0} - 1))w = 0, \end{cases} \qquad \begin{cases} \partial_\nu w = Qt & \text{on } \Gamma_{\mathcal{I}},\\ \partial_\nu w = 0 & \text{on } \Gamma,\\ w = 0,\ \partial_\nu w = 0 & \text{on } \Gamma(t). \end{cases} \tag{1.14}$$

This problem is equivalent to the following variational formulation for which existence and uniqueness results are proven in [74].

Problem 1.3.3 (Variational inequality formulation of the HS problem)**.** *Let* $\mathcal{H} = \{v \in H^1(\Omega);\ v \geqslant 0$ *almost everywhere in* $\Omega\}$. *Find* $w(t) \in \mathcal{H}$ *for each* $t \in (0,T)$ *such that for all* $v \in \mathcal{H}$

$$\int_\Omega \nabla w \cdot \nabla (v-w)\,\mathrm{d}x \geqslant \int_\Omega (\mathbb{1}_{\Omega_0}(x) - 1)(v-w)\,\mathrm{d}x + \int_\Gamma Qt(v-w)\,\mathrm{d}\sigma. \tag{1.15}$$

The Hele-Shaw problem in a bounded domain Ω with a point source is analogously studied in [55], where the authors prove the well-posedness of the variational inequality formulation.

Incompressible limit of the Cauchy problem

Following the work of Bénilan and Crandall on the continuous dependence of the filtration equation [18], the asymptotic behaviour of the following Cauchy problem attracted increasing attention

$$\begin{cases} \dfrac{\partial u}{\partial t} = \Delta u^m, & x \in \mathbb{R}^d,\ t > 0, \\ u(x,t) = u_0(x) \geqslant 0, & u_0 \in L^1(\mathbb{R}^d) \cap L^\infty(\mathbb{R}^d). \end{cases} \tag{1.16}$$

Before briefly reviewing the seminal works on the incompressible limit achieved from the late '80s, let us give a formal and intuitive explanation of the leading mechanisms behind this asymptotics. The PME can be rewritten as a continuity equation as follows

$$\frac{\partial u_m}{\partial t} = \nabla \cdot (D(u_m)\nabla u_m), \qquad\qquad D(u_m) = m u_m^{m-1},$$

where we highlight the dependency upon the parameter m using subscripts. It is immediate to see that when $m \to \infty$ the non-linear density-dependent diffusivity coefficient $D(u_m)$ behaves as follows

$$D(u_m) \xrightarrow{m\to\infty} \begin{cases} 0, & \text{when } u < 1, \\ \infty, & \text{when } u > 1. \end{cases} \tag{1.17}$$

As a consequence, there exists a region in which the limit solution u_∞ is constantly equal to 1 and outside of which it coincides with the initial data. Indeed, since the diffusivity coefficient blows up where the initial data is larger than 1, the solution instantaneously collapses to the level 1 as $m \to \infty$. On the other hand, where $u_0 < 1$ the diffusivity coefficient vanishes and thus the solution "stays still" as $m \to \infty$. This heuristic argument suggests that in the limit the solution of the Cauchy problem (1.16) converges to a stationary limit $u_\infty = u_\infty(x)$.
In [73], Elliott *et al.* show the formation of a plateau-like region, which they refer to as *mesa*, of nearly constant density u_m, for $m \approx \infty$, using formal asymptotic expansions and working with radial solutions. The authors conjecture that there exists a region where the limit profile of the solution is nearly constant and outside of which it approximates the initial data u_0, although they do not provide a rigorous derivation. Moreover, they show that the *mesa* region is associated with the variational inequality formulation of the Hele-Shaw problem. This will be proven rigorously in [45] for star-shaped initial data, in [142] for radially symmetric initial data and in [17] in a more general setting.
In [45], Caffarelli and Friedman consider the limit of the Cauchy problem (1.16) assuming weaker conditions on the initial data with respect to the work on the filtration equation by Bénilan and Crandall [18]. In fact, they are the first to include the case in which the L^∞-norm of the initial data is greater than 1. The "stationarity" of the limit density, *i.e.* $u_\infty = u_\infty(x)$, is deduced upon combining three tools: uniform bounds, the AB estimate, and the conservation of mass. First of

all, as explained above, Prob. (1.16) admits a unique non-negative weak solution u_m. Using the comparison principle, it is immediate to see that the solution satisfies

$$0 \leqslant u_m \leqslant \|u_0\|_\infty. \tag{1.18}$$

As a consequence, u_m converges weakly* in L^∞ to some limit u_∞, up to a subsequence. Here, the classical Aronson-Bénilan estimate (1.12) proven in [9] plays an essential role in that it gives

$$\frac{\partial u_m}{\partial t} \geqslant -\frac{u_m}{(m-1+\frac{2}{d})t}\ .$$

Therefore, for any $\psi \in C_0^\infty(\mathbb{R}^d \times (0,\infty)), \psi \geqslant 0$, the above inequality implies

$$-\iint u_m \frac{\partial \psi}{\partial t}\,\mathrm{d}x\,\mathrm{d}t \geqslant -\iint \frac{u_m}{(m-1+\frac{2}{d})t}\psi\,\mathrm{d}x\,\mathrm{d}t \longrightarrow 0,$$

and consequently

$$-\iint u_\infty \frac{\partial \psi}{\partial t}\,\mathrm{d}x\,\mathrm{d}t \geqslant 0.$$

It is then possible to conclude that for any $t > s > 0$

$$u_\infty(\cdot,t) \geqslant u_\infty(\cdot,s), \qquad \text{almost everywhere in } \mathbb{R}^d. \tag{1.19}$$

Finally, the mass conservation property of the PME and the convergence of u_m in $C((0,\infty), L^1(\mathbb{R}^d))$ proven in [18] imply

$$\begin{array}{ccc} \displaystyle\int_{\mathbb{R}^d} u_m(x,t)\,\mathrm{d}x & = & \displaystyle\int_{\mathbb{R}^d} u_m(x,s)\,\mathrm{d}x, \\ \downarrow & & \downarrow \\ \displaystyle\int_{\mathbb{R}^d} u_\infty(x,t)\,\mathrm{d}x & = & \displaystyle\int_{\mathbb{R}^d} u_\infty(x,s)\,\mathrm{d}x, \end{array}$$

which combined with Eq. (1.19) leads to $u_\infty(x,t) = u_\infty(x)$, namely the limit u_∞ is time-independent.

In [45] the authors also show that $0 \leqslant u_\infty \leqslant 1$. In fact, if $\|u_0\|_\infty < 1$, they infer that $u_\infty = u_0$ in a different way and independently from the result in [18]. When $\|u_0\|_\infty \geqslant 1$ they show that

$$u_\infty(x) = \begin{cases} 1, & \text{for } x \in A, \\ u_0(x), & \text{for } x \notin A, \end{cases} \tag{1.20}$$

where A is defined as the non-coincidence set of the solution to the following variational inequality problem

$$w \in L^1(\mathbb{R}^d),\ \Delta w \in L^1(\mathbb{R}^d),\ -\Delta w - (u_0 - 1) \geqslant 0,\ w \geqslant 0,\ (-\Delta w - (u_0-1))w = 0,\ \text{a.e. in } \mathbb{R}^d, \tag{1.21}$$

which means

$$u_\infty = \Delta w + u_0. \tag{1.22}$$

In fact, the authors prove that

$$w(x_0) := \int_{\mathbb{R}^d} (u_0(x) - u_\infty(x))\Gamma_{x_0}(x)\,\mathrm{d}x,$$

is the unique solution of Prob. (1.21), where Γ_{x_0} is the fundamental solution of $-\Delta$. Secondly, they show that u_∞ satisfies (1.20) with $A = \{w > 0\}$, [45, Theorem 5.3] and therefore they infer the uniqueness of the limit.

Let us mention that in [45] the authors impose strong geometric assumptions on the initial data, such as u_0 continuously differentiable in its support and star shaped with respect to the origin. These assumptions are weakened by Sacks in [142], where only radial symmetry is assumed, and later by Bénilan *et al.* in [17], where taking $u_0 \in L^1(\mathbb{R}^d)$ is sufficient.

It is worth noting that the variational inequality problem (1.21) is the equivalent, in the whole space $\mathbb{R}^d$, of the Hele-Shaw problem (1.14) studied by Elliot and Janovský, in the case of initial data given by a *patch*, *i.e.* $u_0 = \mathbb{1}_{\Omega_0}$. However, there is a main difference between the Hele-Shaw problem (1.13)-(1.15) and the limit problem generated by the PME in the asymptotic $m \to \infty$: the "stationarity" of the solution. Indeed, while the solution of Eq. (1.15) depends on time and the free boundary is a moving interface, the limit density $u_\infty = u_\infty(x)$ is independent of time, as is the solution $w = w(x)$ of (1.21). It is interesting to notice that this is not in contrast with the dynamics that drive the Hele-Shaw flow. As explained above, the Hele-Shaw flow is induced by Darcy's law, *i.e.* the velocity field has the same direction as the gradient of the pressure. In Section 1.3.1 we analyzed the physical meaning of the PME, which is also induced by Darcy's law, *cf.* (1.10), with velocity field given by $-\nabla p$ where the pressure is $p = mu^{m-1}/(m-1)$. As one can deduce from Eq. (1.11) set in the whole space $\mathbb{R}^d$, as $m \to \infty$ the pressure vanishes instantaneously, thus the limit pressure is equal to zero almost everywhere, as is its gradient. Therefore, there is no evolution in the limit problem, which can be seen as a "stationary" Hele-Shaw problem.

The picture drastically changes if we set the porous medium equation in a bounded domain with non-trivial boundary conditions, as explained in the following paragraph.

The boundary valued problem

The limit $m \to \infty$ of the PME set in a bounded domain with homogeneous Dirichlet or Neumann boundary conditions was first studied in [17], where the authors prove $u_m \to u_0 + \Delta w$, with w a solution of corresponding variational inequalities. For both conditions, the limit solution is stationary and the variational inequality system coincides with a "motionless" Hele-Shaw problem.

The asymptotic behavior changes significantly for the Cauchy-Dirichlet problem with non-homogeneous boundary conditions

$$\begin{cases} \dfrac{\partial u_m}{\partial t} = \Delta u_m^m, & x \in \Omega,\ t > 0, \\ u_m(x, 0) = u_0(x) \geqslant 0, & x \in \Omega, \\ u_m(x,t)^m = g(x,t) \geqslant 0, & x \in \partial\Omega,\ t > 0, \end{cases} \tag{1.23}$$

where $\Omega \subset \mathbb{R}^d$ is an open subset with non-empty boundary $\partial\Omega$. In 2001, Gil and Quirós analysed the incompressible limit for the above problem for time-independent boundary data $g = g(x)$, [87].

Let us point out that as $m \approx \infty$, $u_m^m \approx p_m$. Hence, imposing the boundary condition in (1.23) is equivalent to fixing the value of the pressure on the boundary. Usually the quantity $v_m = u^m$

is referred to as the *generalized pressure*.

Let us notice that given a set Ω large enough, the case $g \equiv 0$ coincides with the problem studied by Caffarelli and Friedman in [45] in the whole space $\mathbb{R}^d$. Indeed, in [87] Gil and Quirós are able to recover the same result from a different perspective by focusing on the role of the pressure rather than the density itself. This is indeed the main novelty introduced by the authors who center the analysis around p_m rather than u_m. For vanishing Dirichlet boundary data, *i.e.* $g \equiv 0$, the "stationarity" of the limit Hele-Shaw problem can be seen by analyzing the asymptotic behavior of p_m. Indeed, in the limit, the pressure vanishes almost everywhere. This can be easily seen by letting $m \to \infty$ in the pressure equation (1.11). In conjunction with the uniform essential bounds, this immediately yields $\|\nabla p_\infty\|_{L^2(\Omega\times(0,T))} = 0$, by the following argument

$$\int_0^T \int_\Omega |\nabla p_m|^2 \,\mathrm{d}x\,\mathrm{d}t = \frac{1}{m-2}\int_\Omega (p_m^0 - p_m(T))\,\mathrm{d}x \xrightarrow{m\to\infty} 0. \tag{1.24}$$

Therefore, the boundary of the limit HS problem is actually motionless.

The central role of the pressure in [87] is motivated by the fact that for non-vanishing boundary data the pressure p_m that solves (1.23) does not vanish as $m \to \infty$. Indeed, if $g \geqslant 0$ is non-trivial, the pressure is "forced" to be positive somewhere near the outer boundary $\partial\Omega$. Since the pressure gradient is no longer zero, the motion of the free boundary $\partial\{p_\infty > 0\}$ is governed by Darcy's law $V = -\partial_\nu p_\infty$. Let us also stress that the mass conservation property no longer holds since there is a source term on the boundary of Ω. Consequently, the proof of the "stationarity" of u_∞, which relies on the AB estimate reported above, fails. Similarly, the proof of $\|\nabla p_\infty\|_{L^2} = 0$ by Eq. (1.24) no longer holds true due to the fact that the boundary term arising from the integration by parts no longer vanishes.

As a consequence, the main effect induced by imposing non-vanishing boundary data is the "nonstationarity" of the limit problem, which here turns out to be the standard Hele-Shaw problem

$$\begin{cases} \Delta p(x,t) &= 0, \qquad \text{in } \{x;\ p(x,t) > 0\},\\ \quad V &= -\partial_\nu p, \quad \text{on } \partial\{x;\ p(x,t) > 0\}. \end{cases}$$

As already mentioned, using the Baiocchi transform $w(x,t) = \int_0^t p(x,\tau)\,\mathrm{d}\tau$ the HS problem can be rewritten as a variational inequality problem. Let Ω_0 be the initial pressure support, *i.e.* $\operatorname{supp}(p_0) = \Omega_0$, then w satisfies the variational inequality

$$-\Delta w - (\mathbb{1}_{\Omega_0} - 1) \geq 0, \quad w \geq 0, \quad (-\Delta w - (\mathbb{1}_{\Omega_0} - 1))w = 0, \tag{1.25}$$

with boundary data $w = \int_0^t g(x,\tau)\,\mathrm{d}\tau$ on $\partial\Omega$.

In [87] the authors prove that for time-independent boundary data, *i.e.* $g = g(x)$, the pressure p_m related to the solution of the PME (1.23) converges to the weak solution of the Hele-Shaw problem in the sense of Elliot-Janovský, namely

$$p_m \to p_\infty, \qquad \text{strongly in } L^1(\Omega\times(0,T)),$$

and p_∞ is the solution of (1.25) with $\Omega_0 = \{x;\ p(x,0) > 0\}$.

In order to obtain this result, the authors introduce a new definition of weak solution of the HS problem, and prove that the limit p_∞ satisfies this weak formulation. It is our interest to introduce this definition since, from now on, we will only deal with this notion of weak solution rather than the original one by Elliot-Janovský. In [87] it is proven that the two solutions coincide in the case of initial data given by a patch.

Definition 1.3.4 (Weak solution of the Hele-Shaw problem)**.** Let $u_0 \in L^2(\Omega)$, $u_0 \geqslant 0$ and $g \in L^2_{loc}([0,T); H^1(\Omega))$, $g \geq 0$. The pair of non-negative and measurable functions (u,p) is a weak solution of the Hele-Shaw problem in Ω with initial data u_0 and boundary data g, if

(i) $u \in L^2_{loc}([0,\infty); L^2(\Omega)), p \in L^2_{loc}([0,\infty); H^1(\Omega))$,

(ii) $\forall \varphi \in C^{2,1}_{comp}(\Omega \times [0,\infty))$ vanishing on $\partial\Omega \times (0,\infty)$, u satisfies

$$\int_0^\infty \int_\Omega \left(u \frac{\partial \varphi}{\partial t} - \nabla p \cdot \nabla \varphi \right) \mathrm{d}x \, \mathrm{d}t + \int_\Omega u_0 \varphi(x,0) \, \mathrm{d}x = 0, \tag{1.26}$$

(iii)

$$p \in \Phi(u) := \begin{cases} 0, & 0 \leqslant u < 1, \\ [0,\infty), & u = 1, \end{cases} \tag{1.27}$$

(iv) $p - g \in L^2_{loc}([0,\infty); W^{1,2}_0(\Omega))$.

The authors prove that the solution (u,p) defined above is unique. Moreover, let $\bar{p}$ be the solution of the Hele-Shaw problem (1.25) in the sense of Elliot-Janovský with initial support $\Omega_0 = \{\bar{p}_0 > 0\}$. By [87, Corollary 4.5], $\bar{p} = p$, where p is the solution in the sense of Definition 1.3.4 with initial data given by $u_0 = \mathbb{1}_{\Omega_0}$.
Let us give a formal derivation of Eq. (1.26) as the limit of the porous medium equation, *i.e.* we formally deduce that the limit (u_∞, p_∞) is a solution in the sense of Definition 1.3.4. First of all, we can write the PME as follows

$$\frac{\partial u_m}{\partial t} = \Delta \left(\frac{m-1}{m} p_m \right)^{\frac{m}{m-1}}. \tag{1.28}$$

Hence, by passing formally to the limit $m \to \infty$ we find

$$\frac{\partial u_\infty}{\partial t} = \Delta p_\infty, \tag{1.29}$$

whose weak formulation is given by Eq. (1.26).
Moreover, the relation between p_m and u_m implies

$$\left(\frac{m}{m-1} p_m \right)^{\frac{m}{m-1}} = u_m^m = \frac{m-1}{m} p_m u_m,$$

from which we can formally recover $p_\infty = p_\infty u_\infty$, namely

$$p_\infty (1 - u_\infty) = 0, \tag{1.30}$$

which is equivalent to the graph relation $p_\infty \in \Phi(u_\infty)$ in Eq. (1.27). This relation is fundamental in the theory of the incompressible limit of the PME, and, as we will show in the following chapters, different methods to derive it have been provided in the literature. We will be referring to this relation as *saturation relation*, since it implies that in regions of positive pressure the density is totally saturated, *i.e.* $u_\infty \equiv 1$. This is consistent with the fact that (u_∞, p_∞) is a solution of the Hele-Shaw problem, where an incompressible fluid moves under Darcy's law.

Moreover, combining formally Eq. (1.30) and Eq. (1.29) we have $\Delta p_\infty(t) = 0$ in $\{x;\ p_\infty(x,t) > 0\}$, *i.e.* we recover once again the standard equation of the Hele-Shaw problem. This can also be inferred from

$$p_\infty \Delta p_\infty = 0, \tag{1.31}$$

which can be obtained by passing to the limit in the pressure equation (1.11).
The above equation on the limit pressure is usually referred to as *complementarity relation*. To prove Eq. (1.31) rigorously for porous medium-reaction-advection equations is an involved analytical challenge that has recently attracted great interest in the context of living tissue models.

1.3.3 Recent developments: tumor growth models

Emanating from the early works on the mesa problem for the porous medium equation, research began branching out in different directions. In this section, we aim at giving a brief overview of different extensions of the porous medium equation, applications of the models obtained this way to tumor growth description, as well as techniques used to study their respective incompressible limits analytically.
The first generalisation concerns the inclusion of a pressure-dependent growth term, and was proposed in [130]. As we presented in Section 1.3.2, the limit of the PME Cauchy problem is stationary, unless we set the equation in a bounded domain and impose non-trivial boundary conditions that act like a sort of "injection" of fluid, hence inducing a moving boundary with speed related to the pressure gradient. If the Cauchy problem is set in the whole space, "nonstationarity" can be induced by a different mechanism, which is the source/sink effect obtained by including a reaction term into the equation. As in the boundary valued problem, the "injection" of new mass implies that the set $\{p_\infty > 0\}$ is non-empty and its dynamics is governed by a Hele-Shaw-type flow.
Most recently, the inclusion of migratory processes, *i.e.* local and non-local drift terms, as a model extension received a lot of attention. We also aim at shortly presenting the results on the incompressible limit for models using different pressure laws, or different relations between velocity field and pressure. We conclude the section by mentioning cross-reaction-diffusion models, where a system of two or more interacting species is considered.

Models including cell proliferation

The first generalisation concerns the inclusion of a pressure-dependent growth term proposed in [130] by Perthame, Quirós and Vázquez. The authors present a tumor growth model that originates from the one by Byrne and Drasdo, [37]. The cells move according to Darcy's law, and the tissue pressure $p = p(x,t)$ is generated by the cell population density $n = n(x,t)$ through the compressible law of state $p(n) = mn^{m-1}/m - 1$, $m > 2$. As shown in Sec. 1.3.1, in conjunction with Darcy's law this leads to a porous medium-type diffusion. In addition, they include a proliferation term, $nG(p)$, which models cells divisions with a pressure-penalised rate

$$\frac{\partial n_m}{\partial t} - \nabla \cdot\ (n_m \nabla p_m) = n_m G(p_m). \tag{1.32}$$

As mentioned in Section 1.1, cells are less "willing" to divide in packed regimes. Therefore, the proliferation rate, G, is assumed to be a decreasing function of the pressure

$$G'(p) < 0, \qquad G(p_H) = 0, \tag{1.33}$$

where, as in [37], the homeostatic pressure p_H represents the lowest level of pressure that prevents cell multiplication due to contact inhibition.

Their paper is seminal in that the authors were the first to perform the rigorous stiff pressure limit in the presence of growth terms. In this case, the pressure equation (1.11) reads

$$\frac{\partial p_m}{\partial t} = (m-1)p_m(\Delta p_m + G(p_m)) + |\nabla p_m|^2. \tag{1.34}$$

Therefore, as for the boundary valued problem with non-trivial boundary conditions (1.23), the proof of $\|\nabla p_\infty\|_{L^2} = 0$ fails, due to the non-trivial reaction term, namely

$$\int_0^T \int_{\mathbb{R}^d} |\nabla p_m|^2 \,\mathrm{d}x\,\mathrm{d}t = \frac{m-1}{m-2}\int_0^T \int_{\mathbb{R}^d} p_m G(p_m)\,\mathrm{d}x\,\mathrm{d}t + \frac{1}{m-2}\int_{\mathbb{R}^d} (p_m^0 - p_m(T))\,\mathrm{d}x \nrightarrow 0. \tag{1.35}$$

Therefore, the region $\Omega(t) := \{x;\ p_\infty(x,t) > 0\}$ is non-empty and evolves under a Hele-Shaw flow. In fact, passing formally to the limit in the pressure equation, one can obtain the following problem

$$p_\infty(\Delta p_\infty + G(p_\infty)) = 0, \tag{1.36}$$

$$p_\infty \geqslant 0, \quad 0 \leqslant n_\infty \leqslant 1, \quad p_\infty(1-n_\infty) = 0. \tag{1.37}$$

Let us recall that Eq. (1.36) is known in the literature as *complementarity relation*, and it is the equivalent of Eq. (1.31) for non-trivial reaction terms. Once again we find the saturation relation (1.37), which implies that the positivity set of the pressure is contained in the saturation region of the density, namely $\Omega(t) \subset \{x;\ n_\infty(x,t) = 1\}$. In the presence of non-negative growth rate G (which is the case here since it is possible to prove that $0 \leqslant p_\gamma \leqslant p_H$ uniformly) the two sets actually coincide. Indeed, let us assume there exists (x,t) such that $n_\infty(x,t) = 1$ and $p_\infty(x,t) = 0$. Taking $m \to \infty$ in Eq. (1.32) it is easy to see that $n_\infty(x,t)$ should growth exponentially with rate $G(0)$, which is a contradiction since $0 \leqslant n_\infty \leqslant 1$.

Let us point out that, in order to have a complete representation of the solution behavior in the limit, Eq. (1.36) is not sufficient. In fact, the complementarity relation does not tell us what is the behavior of the limit solution in the *mushy regions*, namely those regions in which $p_\infty = 0$ and $n_\infty < 1$ and in which the density grows exponentially. Thus, in order to have a full description of the limit problem, the equation on the limit density (which is the analogue of (1.29)) is necessary

$$\frac{\partial n_\infty}{\partial t} - \Delta p_\infty = n_\infty G(p_\infty). \tag{1.38}$$

Indeed, in [130] the authors show that n_∞ is a weak solution of a reaction-Hele-Shaw problem in the sense of Definition 1.3.4.

Let us notice that passing to the limit in the pressure equation (1.34) is much more involved than obtaining Eq. (1.38) from Eq. (1.32). Indeed, the *weak* compactness of ∇p_m in $L^2(\mathbb{R}^d \times (0,T))$ can be easily inferred from Eq. (1.35). Therefore, the strong compactness of p_m and n_m is absolutely sufficient for the Hele-Shaw limit of (1.32). On the other hand, this is not true when attempting to infer the complementarity relation (1.36). In order to prove it rigorously, the *strong* compactness of the *pressure gradient* is indispensable. To this purpose, obtaining a certain control on Δp_m is one of most common strategies. Let us point out that since the pressure has "corners" on the moving boundary, we cannot expect Δp_m to be more regular than a measure. In [130] using the comparison principle, the authors show that the Laplacian of the pressure satisfies an Aronson-Bénilan type estimate, namely

$$\Delta p_m + G(p_m) \gtrsim -\frac{C}{mt}, \qquad \text{for } t > 0. \tag{1.39}$$

Combining this estimate with a time-regularising argument, the authors are able to prove the complementarity relation (1.36).

To complete the description of (1.38) as a Hele-Shaw flow, one should include the velocity of the moving boundary $\partial\Omega(t) = \partial\{x;\ p_\infty(x,t) > 0\}$. From Eq. (1.34), one can infer $\partial_t p_\infty = |\nabla p_\infty|^2$. Hence, at least at a formal level, the speed should be $V = |\nabla p_\infty|$. This is indeed true if the initial data is the characteristic function of a bounded set, as was proven in [130] and later in [123]. However, allowing for the presence of mushy regions introduces a novelty in the characterisation of the limit problem. As conjectured in [130], the presence of regions where $0 < n_\infty < 1$ influences the velocity of the free boundary. Let us show with a formal argument how the velocity of the moving boundary should be related to the pressure in the case of non-empty mushy regions, see [102]. We denote by n_∞^I and n_∞^E the value of n_∞ inside and outside of $\Omega(t)$, respectively. Integrating Eq. (1.38) and formally applying Reynold's transport theorem, we obtain

$$\begin{aligned}
\int_{\mathbb{R}^d} n_\infty G(p_\infty)\,\mathrm{d}x &= \frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} n_\infty\,\mathrm{d}x\\
&= \frac{\mathrm{d}}{\mathrm{d}t}\left(\int_{\Omega(t)} n_\infty\,\mathrm{d}x + \int_{\mathbb{R}^d\setminus\Omega(t)} n_\infty\,\mathrm{d}x\right)\\
&= \int_{\Omega(t)} \frac{\partial n_\infty^I}{\partial t}\,\mathrm{d}x + \int_{\partial\Omega(t)} V\left(n_\infty^I - n_\infty^E\right)\mathrm{d}\sigma + \int_{\mathbb{R}^d\setminus\Omega(t)} \frac{\partial n_\infty^E}{\partial t}\,\mathrm{d}x\\
&= \int_{\Omega(t)} \Delta p_\infty\,\mathrm{d}x + \int_{\partial\Omega(t)} V\left(n_\infty^I - n_\infty^E\right)\mathrm{d}\sigma + \int_{\mathbb{R}^d} n_\infty G(p_\infty)\,\mathrm{d}x\\
&= \int_{\partial\Omega(t)} \left(\partial_\nu p_\infty + V\left(1 - n_\infty^E\right)\right)\mathrm{d}\sigma + \int_{\mathbb{R}^d} n_\infty G(p_\infty)\,\mathrm{d}x,
\end{aligned}$$

where V indicates the normal velocity of $\partial\Omega(t)$. This suggests that, in the presence of mushy regions, the normal boundary velocity under which $\partial\Omega(t)$ evolves satisfies $V(1 - n_\infty^E) = -\partial_\nu p_\infty$, see (1.40). This result was rigorously proven in [102] through a *viscosity solutions* approach. The authors pass to the limit in Eq. (1.32) and show locally uniform convergence of the density away from the free boundary $\partial\{p_\infty > 0\}$. Moreover, they prove locally uniform convergence of the pressure (as long as the limit is continuous) and that p_∞ is the viscosity solution of the following Hele-Shaw problem

$$\begin{cases} -\Delta p_\infty &= G(p_\infty), \qquad\qquad \text{in } \{p_\infty > 0\},\\[1ex] V &= \dfrac{|\nabla p_\infty|}{1 - \min(1, n_\infty^E)}, \quad \text{on } \partial\{p_\infty > 0\}, \end{cases} \tag{1.40}$$

where the normal velocity law was only formally presumed in [130], but not rigorously proven. As already mentioned, outside of $\Omega(t)$ the density grows exponentially, thus the external density is given by $n_\infty^E(x,t) = n_0(x)e^{G(0)t}$. When the trace of n_∞ from the set $\{n_\infty < 1\}$ vanishes, *i.e.* $n_\infty^E = 0$ on $\partial\Omega(t)$, we obtain once again the classical Hele-Shaw flow, namely, the boundary moves under Darcy's law.

Let us stress the fact that, as the velocity law suggests, the density shows jump discontinuities

at the free boundary. Moreover, the velocity blows up when the density reaches value 1. As a consequence, if at a certain time $s > t$ a new *mesa* of non-zero measure appears outside of $\{p_\infty(t) > 0\}$, the pressure becomes instantaneously positive in the new *nucleated* region, hence exhibiting time discontinuities.
The equivalence between Eq. (1.37)-(1.38) and the free boundary problem (1.40) was further studied in [123], where Mellet *et al.* prove that the velocity law of the free boundary holds both in a weak (distributional) and in a measure theoretical sense. In the same paper, they also provide an L^4-bound of the pressure gradient that relies on the Aronson-Bénilan estimate (1.39).

Non-monotone case

Let us point out that if $0 \leqslant p_m^0 \leqslant p_H$, then by the comparison principle the solution of (1.32) is bounded by p_H for all times. Therefore, the reaction term $n_m G(p_m)$ induces always a non-negative source/growth and the total mass is non-decreasing. In fact, the monotonicity properties

$$\frac{\partial \varrho_\infty}{\partial t} \geqslant 0, \qquad \frac{\partial p_\infty}{\partial t} \geqslant 0,$$

can be deduced from the AB estimate (1.39), see [130] for the detailed proof. This no longer holds true if the reaction term can be either a source or a sink. A major difference in this case is given by the fact that when the reaction is not necessarily non-negative the inclusion $\{p_\infty > 0\} \subset \{n_\infty = 1\}$ is strict. Let us mention that, if G can take negative values, the proof that the two sets coincide given above does not apply.
Therefore, n_∞ might be continuous on some regions of the free boundary $\partial\{p_\infty > 0\}$. In particular, this happens when the pressure gradient is continuous as well, as shown in [131] for travelling waves solutions in dimension 1. On the one hand, if $|\nabla p_\infty| > 0$ on $\partial\{n_\infty = 1\}$ then the boundary is expanding with a Hele-Shaw-type flow, with velocity given by (1.40). On the other hand, if $|\nabla p_\infty| = 0$, the boundary might recede. In fact, since $(1 - n_\infty^E)V = |\nabla p_\infty|$, if the pressure gradient vanishes, either the velocity of the boundary is zero or $n_\infty^E = 1$, *i.e.* the limit density is continuous across the free boundary. In the latter case, as proven in [93] through a viscosity solution approach, a retraction of the saturated region might occur.
It is interesting to notice that in the case of non-monotone reaction terms, the movement of the free boundary is not only determined by the Hele-Shaw flow, but it also depends on a completely different dynamics generated by the loss of mass.

Models including local and non-local drifts

A different mechanism that may generate an alternation of forward and backward movements of the free boundary, even in the absence of growth terms, is the presence of a force field.
In 2010, Kim and Lei introduced the notion of viscosity solution for the porous medium equation with drift

$$\frac{\partial n_m}{\partial t} = \Delta n_m^m + \nabla \cdot (n_m \nabla \Phi), \quad \text{with } \Phi : \mathbb{R}^d \to \mathbb{R},$$

and they prove that it coincides with the weak solution in the distributional sense [106]. Using the same viscosity approach, in [1] Alexander *et al.* study the link between the Hele-Shaw model with drift

$$\begin{cases} -\Delta p &= \Delta \Phi, & \text{in } \{p > 0\}, \\ \quad V &= -(\nabla p + \nabla \Phi) \cdot \nu, & \text{on } \partial\{p > 0\}, \end{cases}$$

and the congested crowd motion model

$$\begin{cases} \dfrac{\partial n}{\partial t} - \nabla \cdot (n \nabla \Phi) = 0, & \text{where } n < 1, \\ 0 \leqslant n \leqslant 1, \end{cases}$$

where the latter constraint comes from the singular limit in the nonlinear diffusion term. To prove the equivalence of the two models, they study the asymptotics of the porous medium equation with drift as $m \to \infty$. They show that the viscosity solution converges locally uniformly to a solution of the Hele-Shaw model. At the same time, using the metric setting of the 2-Wasserstein space, they infer the convergence to the aforementioned congested crowd motion model. To this purpose, they assume the potential Φ to be sub-harmonic, *i.e.* $\Delta\Phi > 0$. While the convergence in the 2-Wasserstein distance holds for general initial data $0 \leqslant n_0 \leqslant 1$, the locally uniform limit holds only for patches, *i.e.* $n^0 = \mathbb{1}_{\Omega_0}$, with Ω_0 a compact set in $\mathbb{R}^d$. Let us also mention that the authors are able to estimate the convergence rate of the solutions as $m \to \infty$ in the 2-Wasserstein distance. In fact, they find

$$\sup_{t\in[0,T]} W_2(n_m(t), n_\infty(t)) \leqslant \frac{C}{m^{1/24}}. \tag{1.41}$$

The result in [1] was later extended in [57] by Craig *et al.* to a model with non-local interaction potential $\mathcal{N} : \mathbb{R}^d \to \mathbb{R}$, *i.e.*

$$\frac{\partial n_m}{\partial t} = \Delta n_m^m + \nabla \cdot (n_m \nabla \mathcal{N} \star n_m).$$

The main novelty they introduce is that they are able to study the incompressible limit despite lack of convexity. In fact, unlike the congested drift equation studied in [1], the energy related to the aggregation equation through the 2-Wasserstein gradient flow structure is not semi-convex, see [57]. A different approach for the incompressible limit for Eq. (1.32) was taken in [53], where a transport-growth distance is introduced so that Eq. (1.32) can be understood as a gradient flow with respect to said metric.
The question of how to pass to the limit $m \to \infty$ in the porous medium equation with a drift and a non-trivial source term has been addressed in [103]. The authors propose a model with a generic vector field $\vec{b} : \mathbb{R}^d \times \mathbb{R}^+ \to \mathbb{R}^d$ as drift term, namely

$$\frac{\partial n_m}{\partial t} - \Delta n_m^m + \nabla \cdot (n_m \vec{b}) = n_m G, \tag{1.42}$$

with growth rate $G = G(x, t)$. Through viscosity solutions methods, they prove that as $m \to \infty$ the model converges to a free boundary problem of Hele-Shaw type. Their work improves the results previously achieved in [1], extending the class of initial data from patches to any continuous and compactly supported function bounded between zero and one.

Different pressure laws and relations

As indicated above, in certain contexts Darcy's law may not be the appropriate relation that links the velocity field to the mechanical pressure. Depending on the modelling context and the model complexity, the pressure is incorporated in the fluid velocity through Stokes flow, Brinkman's law or Navier–Stokes' law. We briefly present recent works on the incompressible limit for different pressure laws and relations.

Singular Pressure. As already mentioned, parallel to the advances in the context of incompressible limits with power-law pressures, it has been observed that the singular pressure law of the form

$$p_\varepsilon(n) = \varepsilon \frac{n}{1-n}, \tag{1.43}$$

can be used to model living tissue, see for instance [96]. Let us recall that (1.43) already introduces an incompressibility condition in the sense that the pressure blows up when the cell density reaches the saturated regime, $n = 1$. Thus, singular pressure laws of this kind are encountered in scenarios when non-overlap conditions are enforced already at a population-level, see for instance [69, 128] in the context of congestive collective crowd motion, and [21, 22] in the context of traffic flow modelling. In [96] the authors are able to show that the pressure in (1.43) is suitable to pass to the incompressible limit using a generalisation of the Aronson-Bénilan argument by Crandall and Pierre, *cf.* [58].

Brinkman Law. Unlike Darcy's law, using the Brinkman law

$$-\nu\Delta W + W = p(n),$$

accounts for visco-elastic effects, [37]. Based on this observation, in [132] the authors propose a modification of the above model, Eq. (1.32), incorporating the Brinkman law

$$\frac{\partial n}{\partial t} - \nabla\cdot\ (n\nabla W) = nG(p).$$

Different from the Darcy law setting, the authors are forced to use a different set of techniques since the problem is no longer degenerate parabolic but, instead, of transport nature. While, at first glance, the Brinkman law has a regularising effect on the velocity field, it makes obtaining compactness of the pressure a hard endeavour. Using a kinetic reformulation and controlling oscillations in the pressure finally yields the required compactness to pass to the incompressible limit and obtain a visco-elastic version of the complementarity relation, *cf.* [132, Theorem 1.1]. For pressure laws of the form $p_\varepsilon(n) = \varepsilon \mathbb{1}_{n\geqslant 1}\log(n)$, quite recently, explicit travelling wave profiles were obtained by [114].

Navier-Stokes flow. It is important to stress that both Darcy's law and Brinkman's law are, at least, formally related to the Navier-Stokes law which can therefore be seen as the most general relation between the fluid velocity and the mechanical pressure. In [148] the authors prove the incompressible limit for a proliferating species whose velocity is linked to the pressure through the Navier-Stokes law thus generalising the case without birth and death processes of [110]. The authors use the fact that the growth rate is linear in the pressure so that weak compactness of the pressure suffices in order to pass to the limit, so long as the density itself is strongly compact. While the weak compactness of the pressure follows from a renormalisation argument the strong compactness of the density is based on a compactness propagation argument introduced (and later refined) in [14, 30, 29].

Active Motion. In [129] the authors extend the model of [130] by an additional active motion term in form of a linear diffusion term. They are able to rigorously perform the incompressible limit. In fact, they obtain the same complementarity relation as in the absence of active motion without relying on the Aronson-Bénilan by imposing certain conditions on the initial data. Nonetheless, the restriction on the initial data can be dropped by employing the argument of Crandall and Pierre, in [58]. In [147] the authors propose a very similar model based on Brinkman's law, including a linear diffusion term. They observe that travelling waves exist and analyse their profile.

Fractional Diffusion. In 2015, Vázquez opened another both fascinating and challenging research direction by addressing the mesa problem in the fractional pressure case, *cf.* [150]. More precisely, he studies the incompressible limit, $m \to \infty$, in the fractional porous medium equation,

$$\frac{\partial n_m}{\partial t} + (-\Delta)^{-s}(n_m)^m = 0,$$

for $s \in (0,1)$. Unlike the case of classical porous medium type diffusion, the limiting profile exhibits tails and does not remain compactly supported. The analysis is of orders of magnitude harder since the classical theory discussed in Section 1.3.2 relies on comparison principles and the fact that it is known what happens to the Barenblatt profiles in the incompressible limit. In the fractional setting the source solutions are not known explicitly. Nonetheless, they are the starting point of the analysis of [150]. Many questions remain open, in particular the inclusion of other processes such as reactions and drifts.

Multi-Species Systems

Recently, there has been a growing interest in multi-phase extensions of the models presented above. Instead of merely modelling the evolution of a single species, say, cancer tissue, other phases such as quiescent cells, healthy tissue, dead tissue, are incorporated into the model. The extension to multiple interacting species not only leads to interesting behaviors, such as phase separation, but also raises novel mathematical challenges such as the loss of regularity at internal layers, *i.e.* regions where two or more phases get in contact.
In 2018, Carrillo *et al.* consider the following cross(-reaction)-diffusion system

$$\begin{cases} \dfrac{\partial n_1}{\partial t} - \dfrac{\partial}{\partial x}\left(n_1 \dfrac{\partial \chi'(n)}{\partial x}\right) = n_1 F_1(p) + n_2 G_1(p), & x \in \mathbb{R},\ t > 0, \\ \dfrac{\partial n_2}{\partial t} - \dfrac{\partial}{\partial x}\left(n_2 \dfrac{\partial \chi'(n)}{\partial x}\right) = n_1 F_2(p) + n_2 G_2(p), \end{cases}$$

where the single species n_1, n_2 evolve under nonlinear diffusion represented by $\chi'(n)$, which indicates the opposition to the congestion generated by the total population density $n = n_1 + n_2$. Using methods from optimal transport, the authors prove the existence of solutions in the one dimensional case, [47].
This result was later extended by Gwiazda *et al.* to higher dimensions in the case where χ' is related to the total density by a power law, [94]. Therefore, since both species evolve under Darcy's law, the joint population n satisfies a porous medium-type equation with pressure given by $p(n) = \chi'(n) = n^\gamma$, $\gamma > 1$.
Let us mention that in the following parts of the thesis we will use both this simple power law without coefficients and (1.8). Indeed, the two respective equations are equivalent apart from a re-scaling coefficient.
The existence result in [94] relies on applying a uniformly parabolic regularisation to the system and then obtaining the compactness needed to pass to the limit. Certainly, to this end, the nonlinearity of the cross-diffusion terms $n_i \nabla p, i = 1, 2$, represents the most involved challenge. Unlike in [47], only weak compactness is known on the single species n_i (since BV-estimates are

not available for $d > 1$). Hence, the authors proceed by deducing the strong compactness of the pressure gradient. To this end, they prove an L^2-version of the Aronson-Bénilan estimate which provides a bound on the Laplacian of the pressure

$$(\Delta p)_- \in L^\infty(0,T;L^2(\mathbb{R}^d)), \qquad \Delta p \in L^1(\mathbb{R}^d \times (0,T)).$$

However, in order to obtain the above regularity results on the pressure, the authors enforce a technical condition on the reaction rates, namely $F_1(0) + F_2(0) = G_1(0) + G_2(0)$. Later, an existence result for a cross-diffusion model of the same form was obtained by Price and Xu avoiding this strong assumption, [135]. In fact, their argument does not rely on any control on the second derivatives of $p = n^\gamma$, but it rather focuses on directly studying the compactness of $\nabla n^{\gamma+1}$.

The incompressible limit for this kind of two-species porous medium models has attracted a lot of attention as well. Due to the hyperbolic flavour of the single species equations (in contrast with the parabolic nature of the joint density equation) to infer the required compactness represents a remarkably challenging problem. In [31], Bubba *et al.* have established the rigorous incompressible limit for the same model as the one in [94] as $\gamma \to \infty$ in the pressure law. However, the lack of regularity is such that only a one-dimensional result could be obtained. Indeed, the authors are not able to deduce the strong time-compactness of the pressure in dimension greater than one. This is due to the fact that the proof relies on an L^1-version of the Aronson-Bénilan estimate which only holds in the one-dimensional case. As detailed in the following section, this particular control requires the Sobolev embedding $W^{1,1}(\mathbb{R}) \subset L^\infty(\mathbb{R})$.

Let us mention that, in a similar fashion, a one-dimensional result could be obtained, see [67], when the pressure is given by the singular law (1.43) using the generalisation of the Aronson-Bénilan estimate introduced in [58].

In 2020, [71] proposed a two-cell-type model coupled with nutrients to study the effect of autophagy on tumour growth. In their work they, too, consider an incompressible limit, however the results remains formal due to difficulties similar to that of the system without nutrients treated by [31, 67]. The multi-dimensional case for a pressure generated in form of a power law was later successfully addressed in [115] through a different argument that does not rely on high order estimates on the pressure $p = n^\gamma$. On the contrary, the authors' effort is focused on the quantity $v = n^{\gamma+1}$ which is the power of the density that appears in the porous medium form of the equation. In this way, they are able to directly show the strong compactness of the gradient, ∇v, avoiding the issue of the strong time-compactness on the pressure itself.

Thanks to the higher regularity of the pressure induced by Brinkman's law, a more complete picture on the two-species system was available earlier in this case, see [65, 66]. For early works on (reaction)-cross-diffusion system we refer the reader to [23, 24, 97] and references therein.

1.4 Regularity *à la* Aronson-Bénilan: a short review

As briefly presented in the previous section, the Aronson-Bénilan estimate is a well known and powerful tool which has been widely applied and adapted in the context of porous medium equations. This estimate and its variations constitute very useful results in that they provide a control on the second order derivatives of the pressure. Therefore, the AB estimate is often used in order to show regularity as well as to obtain the compactness needed to pass to the incompressible limit. Here we aim at giving a short overview of this bound, its origin and some variations. For a complete review we refer the reader to [26].

1.4.1 The original estimate: lower bound on Δp

The original AB estimate provides a lower bound on the Laplacian of the pressure and it has been proven in 1979 by Aronson and Bénilan in [9]. The core of the proof is the application of the comparison principle for quasi-linear parabolic operators. Here we present a formal proof.

Let $m > 1$ and $w := \Delta p$. Let us recall Eq. (1.11), *i.e.* the pressure equation

$$\frac{\partial p}{\partial t} = (m-1)p\Delta p + |\nabla p|^2.$$

We compute

$$\begin{aligned}\frac{\partial w}{\partial t} &= \Delta\left(\frac{\partial p}{\partial t}\right)\\ &= \Delta\big((m-1)pw + |\nabla p|^2\big)\\ &= (m-1)w^2 + 2(m-1)\nabla p\cdot\nabla w + (m-1)p\Delta w + 2\nabla p\cdot\nabla\Delta p + 2\sum_{i,j}\left(\frac{\partial^2 p}{\partial x_i\partial x_j}\right)^2\\ &\geqslant (m-1)w^2 + 2m\nabla p\cdot\nabla w + (m-1)p\Delta w + \frac{2}{d}(\Delta p)^2,\end{aligned}$$

and thus

$$\frac{\partial w}{\partial t} \geqslant \left(m-1+\frac{2}{d}\right)w^2 + 2m\nabla p\cdot\nabla w + (m-1)p\Delta w.$$

Assuming p is smooth and bounded away from zero, the above inequality implies that w is a supersolution of a quasi-linear parabolic operator. Let $\tau > 0$. The function

$$W(t) := -\frac{1}{\alpha(t+\tau)}, \quad \text{with } \alpha := m-1+\frac{2}{d},$$

is a subsolution of the same operator, since

$$W'(t) = \frac{1}{\alpha(t+\tau)^2} = \alpha W(t)^2.$$

Let us assume that, for τ small enough, $w(x,0) = \Delta p(x,0) \geqslant -\frac{1}{\alpha\tau} = W(0)$. Therefore, by the comparison principle for uniformly parabolic operators we find $w(x,t) \geqslant -\frac{1}{\alpha(t+\tau)}$ for $t > 0$ and for any $\tau > 0$. Letting $\tau \to 0$ we finally find

$$w(x,t) \geqslant -\frac{1}{(m-1+\frac{2}{d})t}, \tag{1.44}$$

namely, the classical AB estimate (1.12).

Let us notice that the above estimate is independent of any regularisation argument. Therefore, it can be understood in the sense of distributions for any solution obtained as the limit of regular solutions, see [9]. Let us report the gist of the argument for the sake of completeness. In order to apply the comparison principle for quasi-linear parabolic operator we need to approximate the solution of the PME taking $u_{0,\varepsilon}(x) = u_0(x) + \varepsilon$. For such initial data, the PME is no longer degenerate and there exists a unique solution that satisfies $u_\varepsilon \in C^\infty(\mathbb{R}^d \times (0,\infty))$ and

$u_\varepsilon(x,t) \geqslant \varepsilon$. Consequently, the pressure $p_\varepsilon = \frac{m}{m-1}u_\varepsilon^{m-1} \in C^\infty(\mathbb{R}^d \times (0,\infty))$ is bounded away from zero as well. Then, we can apply the above argument and the AB estimate (1.44) holds for p_ε uniformly in ε. One can show that $p_\varepsilon \to p$ in $L^1_{loc}(\mathbb{R}^d \times (0,\infty))$, *cf.* [149, Lemma 9.5]. Hence, for any $\varphi \in C_c^\infty(\mathbb{R}^d \times (0,\infty))$, $\varphi \geqslant 0$, we have

$$\int_0^\infty \int_{\mathbb{R}^d} \left(\Delta p_\varepsilon + \frac{1}{\alpha t} \right) \varphi \,\mathrm{d}x\,\mathrm{d}t \geqslant 0,$$

and, thus

$$\int_0^\infty \int_{\mathbb{R}^d} \left(p_\varepsilon \Delta\varphi + \frac{1}{\alpha t}\varphi \right) \mathrm{d}x\,\mathrm{d}t \geqslant 0,$$

$$\downarrow$$

$$\int_0^\infty \int_{\mathbb{R}^d} \left(p \Delta\varphi + \frac{1}{\alpha t}\varphi \right) \mathrm{d}x\,\mathrm{d}t \geqslant 0,$$

and this completes the proof, *i.e.* Eq. (1.12) holds in the sense of distributions.

1.4.2 Including reactions and drifts: L^∞-estimates

Starting from the seminal paper by Perthame *et al.*, several variations of the Aronson-Bénilan estimate have been proposed in the literature for reaction-advection equations with porous medium diffusion, as well as for cross-diffusion systems.

AB estimate with reaction terms

The first generalisation of the AB estimate for an equation including a pressure-dependent reaction term, Eq. (1.32), is due to [130]. Under conditions (1.33), and assuming $0 \leqslant p^0 \leqslant p_H$, one can prove $0 \leqslant p \leqslant p_H$ in $\mathbb{R}^d \times (0,\infty)$. Let us define the non-negative quantity

$$r_G := \min_{0 \leqslant p \leqslant p_H} (G(p) - pG'(p)) \geqslant 0. \tag{1.45}$$

Since the equation includes a reaction term, the functional on which it is possible to infer a lower bound is different from the one considered in the classical AB estimate. Indeed, the authors define $w := \Delta p + G(p)$. Therefore, the pressure equation (1.34) now reads

$$\frac{\partial p}{\partial t} = (m-1)pw + |\nabla p|^2. \tag{1.46}$$

Computing $\partial_t w$, we find

$$\begin{aligned}
\frac{\partial w}{\partial t} &= (m-1)\Delta(pw) + 2\nabla p \cdot \nabla \Delta p + 2\sum_{i,j}\left(\frac{\partial^2 p}{\partial x_i \partial x_j}\right)^2 + G'(p)\frac{\partial p}{\partial t} \\
&\geqslant (m-1)p\Delta w + (m-1)w\Delta p + 2(m-1)\nabla p \cdot \nabla w + 2\nabla p \cdot \nabla(w - G) \\
&\quad + G'(p)(m-1)pw + G'(p)|\nabla p|^2 \\
&= (m-1)p\Delta w + (m-1)w^2 - (m-1)wG + 2m\nabla p \cdot \nabla w + G'(p)(m-1)pw - G'(p)|\nabla p|^2
\end{aligned}$$

$$\geqslant (m-1)p\Delta w + (m-1)w^2 + 2m\nabla p \cdot \nabla w - (m-1)(G(p) - pG'(p))w,$$

where in the last inequality we used the fact that $-G'(p) \geqslant 0$. Since $(m-1) > 0$ and $-(m-1)(G(p) - pG'(p)) \leqslant 0$ we can again apply the comparison principle. In fact, treating p as a known function with enough regularity, w is a supersolution of a quasi-linear parabolic operator. Let us define

$$W_G(t) := -r_G \frac{e^{-(m-1)r_G t}}{1 - e^{-(m-1)r_G t}}.$$

Then, $W(t)$ is a solution to $W_G' = (m-1)W_G(t)^2 - (m-1)r_G W_G(t)$. In particular, it is a subsolution of the same parabolic operator. Therefore, we recover

$$\Delta p + G(p) \geqslant -r_G \frac{e^{-(m-1)r_G t}}{1 - e^{-(m-1)r_G t}}. \tag{1.47}$$

As for the case $G = 0$, the above estimate holds independently of any regularity. Consequently, it is possible to prove that this lower bound holds in the sense of distributions for a larger class of functions obtained as the limit of solutions with enough regularity. Let us notice that for $t \sim 0$, the above estimate turns out to be $\Delta p + G(p) \gtrsim -\frac{1}{(m-1)t}$.

AB estimate with drift terms

A similar lower bound on the Laplacian of the pressure was also provided in [105], for a model including a general drift $\vec{b} : \mathbb{R}^d \times (0, \infty) \to \mathbb{R}^d$. The equation of the model is given by taking $G = 0$ in Eq. (1.42). In this case, the pressure satisfies

$$\frac{\partial p}{\partial t} = (m-1)p(\Delta p + \nabla \cdot \vec{b}) + |\nabla p|^2 + \nabla p \cdot \vec{b}. \tag{1.48}$$

The authors assume the drift to have continuous space derivatives up to the third order, and to be continuously differentiable in time, *i.e.* $\vec{b} \in C^{3,1}_{x,t}$. Under this assumption, following the idea developed by Aronson and Bénilan, they are able to find a subsolution of a suitable parabolic operator in order to estimate Δp on one side. Once again, since for any weak solution n of the drift-PME equation there exists a sequence of strictly positive classical solutions $n_\varepsilon > 0$ that converges to n in $L^1(\mathbb{R}^d \times (0, \infty))$, it is sufficient to prove that the AB estimate holds for such regular solutions.

Let $w := \Delta p$. Upon computing the time derivative, we obtain

$$\begin{aligned}
\frac{\partial w}{\partial t} &= (m-1)\Delta(pw) + (m-1)\Delta(p\nabla \cdot \vec{b}) + 2\nabla p \cdot \nabla w + 2\sum_{i,j}\left(\frac{\partial^2 p}{\partial x_i \partial x_j}\right)^2 + \Delta(\nabla p \cdot \vec{b}) \\
&= (m-1)p\Delta w + 2m\nabla p \cdot \nabla w + (m-1)w^2 + (m-1)w\nabla \cdot \vec{b} + 2(m-1)\nabla p \cdot \nabla(\nabla \cdot \vec{b}) \\
&\quad + (m-1)p\Delta(\nabla \cdot \vec{b}) + 2\sum_{i,j}\left(\frac{\partial^2 p}{\partial x_i \partial x_j}\right)^2 + \nabla p \cdot \Delta \vec{b} + 2\sum_{i,j}\frac{\partial^2 p}{\partial x_i \partial x_j}\frac{\partial v^i}{\partial x_j} + \nabla w \cdot \vec{b}.
\end{aligned} \tag{1.49}$$

Using Young's inequality, we have

$$\left|(m-1)w\nabla\cdot\vec{b}+2\sum_{i,j}\frac{\partial^2 p}{\partial x_i\partial x_j}\frac{\partial v^i}{\partial x_j}\right|\leqslant\frac{m-1}{2}w^2+\frac{m-1}{2}\left(\nabla\cdot\vec{b}\right)^2+\sum_{i,j}\left(\frac{\partial^2 p}{\partial x_i\partial x_j}\right)^2+\sum_{i,j}\left(\frac{\partial v^i}{\partial x_j}\right)^2$$
$$\leqslant\left(\frac{m-1}{2}-\frac{1}{d}\right)w^2+2\sum_{i,j}\left(\frac{\partial^2 p}{\partial x_i\partial x_j}\right)^2+mC,$$

where in the last inequality we used $\sum p_{i,j}^2=2\sum p_{i,j}^2-\sum p_{i,j}^2\leqslant 2\sum p_{i,j}^2-(\Delta p)^2/d$. Moreover,

$$\left|\nabla p\cdot\Delta\vec{b}+2(m-1)\nabla p\cdot\nabla(\nabla\cdot\vec{b})\right|\leqslant m|\nabla p|^2+mC,$$

$$(m-1)p\Delta(\nabla\cdot\vec{b})\leqslant Cm.$$

Thus, Eq. (1.49) becomes

$$\frac{\partial w}{\partial t}\geqslant(m-1)p\Delta w+2m\nabla p\cdot\nabla w+(m-1)w^2-m|\nabla p|^2-\left(\frac{m-1}{2}-\frac{1}{d}\right)w^2+\nabla w\cdot\vec{b}+Cm.$$

Here C indicates a positive universal constant, and depends on the L^∞-norms of the space derivatives of $\vec{b}$. Assuming p to be a known smooth function, the above inequality can be written as

$$\mathcal{L}(w)\geqslant 0,$$

where $\mathcal{L}$ is a quasi-linear parabolic operator. As before, we look for a subsolution. In [105] the authors suppose that $\Delta p(x,0)\geqslant-\frac{1}{\tau}$ for some $\tau\geqslant 0$. Therefore, p is uniformly bounded, *i.e.* there exists a positive constant C_0 such that $|p(x,t)|\leqslant C_0$. Let

$$W_{\vec{b}}:=-\frac{C_1}{t+\tau}+p-C_2,$$

where $C_i, i=1,2$ are positive constants, to be chosen later, such that $C_1\geqslant 1$ and $C_2\geqslant C_0$. Then

$$w(x,0)=\Delta p(x,0)\geqslant-\frac{1}{\tau}\geqslant-\frac{C_1}{\tau}+p(x,0)-C_2=W_{\vec{b}}(x,0).$$

It is straightforward to see that $W_{\vec{b}}$ satisfies

$$\mathcal{L}(W_{\vec{b}})=\frac{C_1}{(t+\tau)^2}+\frac{\partial p}{\partial t}-(m-1)p\Delta p-m|\nabla p|^2-\left(\frac{m-1}{2}+\frac{1}{d}\right)\left(-\frac{C_1}{t+\tau}+p-C_2\right)^2-\nabla p\cdot\vec{b}+Cm.$$

Substituting Eq. (1.48) into the above equation, and estimating $|\nabla p\cdot\vec{b}|\leqslant Cm$, we obtain

$$\mathcal{L}(W_{\vec{b}})\leqslant\frac{C_1}{(t+\tau)^2}+(1-m)|\nabla p|^2-\left(\frac{m-1}{2}+\frac{1}{d}\right)\frac{C_1^2}{(t+\tau)^2}-\left(\frac{m-1}{2}+\frac{1}{d}\right)(C_2-p)^2+Cm$$
$$\leqslant\frac{C_1}{(t+\tau)^2}-\left(\frac{m-1}{2}+\frac{1}{d}\right)\frac{C_1^2}{(t+\tau)^2}-\left(\frac{m-1}{2}+\frac{1}{d}\right)(C_2-p)^2+Cm,$$

where in the last inequality we used $m>1$. Choosing $C_1:=d$ and $C_2:=C_0+\sqrt{4dC}$ we obtain

$\mathcal{L}(W_{\vec{b}}) \leqslant 0$. Therefore, by applying the comparison principle and taking $\tau \to 0$, we have

$$\Delta p \geqslant -\frac{C_1}{t} - C_2. \tag{1.50}$$

Let us stress a main difference between the previous AB estimates Eq. (1.44), Eq. (1.47) and the above estimate with drift proven in [105]: the lower bound (1.50) does not vanish as $m \to \infty$. Although the bound provides a control from below of the Laplacian of the pressure, it is not sufficient to pass to the incompressible limit in the pressure equation (1.48) by applying the same argument used in the reaction case in [130]. Indeed, the fact that the lower side of the inequality converges to zero in the limit plays an essential role in the proof by [130]. As explained in the following sections, in this case another strategy is required in order to obtain the strong compactness of the pressure gradient.

1.4.3 Variations in different norms: L^p-estimates

For certain porous medium equations and systems it is not possible to find a lower bound on Δp, *i.e.* a subsolution as in Eqs. (1.44, 1.47 1.50). Therefore, since it is not clear how to bound the L^∞-norm of the negative part of Δp, researchers have been searching for weaker estimates on the same quantity. This idea was first developed in [94] where Gwiazda, Perthame, and Świerczewska-Gwiazda prove the existence of solutions to the following cross-diffusion system

$$\begin{cases} \dfrac{\partial n_1}{\partial t} - \nabla \cdot (n_1 \nabla p) = n_1 F_1(p) + n_2 G_1(p), \\ \dfrac{\partial n_2}{\partial t} - \nabla \cdot (n_2 \nabla p) = n_1 F_2(p) + n_2 G_2(p), \\ p = (n_1 + n_2)^\gamma, \quad \gamma > 1, \end{cases} \tag{1.51}$$

where n_1, n_2 represent the densities of two different populations, F_1, G_2 the growth rates of each population and F_2, G_1 the cross-growth rates. The pressure to which each species is subject is given by a power law of the total population density, $n = n_1 + n_2$. Therefore, the equation on n looks like a porous medium equation (up to a factor $\gamma/\gamma + 1$)

$$\frac{\partial n}{\partial t} = \frac{\gamma}{\gamma + 1} \Delta n^{\gamma+1} + n_1 F(p) + n_2 G(p),$$

where $F := F_1 + F_2$ and $G := G_1 + G_2$. The fact that the reaction term in the equation is not directly proportional to the density n is a crucial difference with respect to the one-species case. Denoting $\sigma_i := n_i/n$ and $R(\sigma_i, p) = \sigma_1 F(p) + \sigma_2 G(p)$, one can rewrite the density equation as follows

$$\frac{\partial n_\gamma}{\partial t} = \frac{\gamma}{\gamma + 1} \Delta n_\gamma^{\gamma+1} + n_\gamma R_\gamma,$$

and thus

$$\frac{\partial p_\gamma}{\partial t} = \gamma p_\gamma (\Delta p_\gamma + R_\gamma) + |\nabla p_\gamma|^2,$$

where we pointed out the dependence on γ. Although the equation looks similar to (1.34), the term R_γ also depends on the density fractions. Hence, it is not possible to look for subsolutions, *i.e.* finding an L^∞-bound on the negative part of $\Delta p_\gamma + R_\gamma$. Consequently, the Aronson-Bénilan estimate was extended in weaker norms:

- in [94] the authors prove $((\Delta p_\gamma + R_\gamma)(t))_- \in L^2(\mathbb{R}^d)$. Although this estimate is not sufficient in order to pass to the incompressible limit, (since time-compactness of the pressure is missing for Sys. (1.51)) let us point out that this estimate can be obtained uniformly with respect to γ. In [94], the authors use it to apply the Aubin-Lions lemma and prove the existence of weak solutions of Sys. (1.51) for any fixed $\gamma > 1$.

• the same approach was later used in [31] for dimension $d = 1$. The authors prove $((\Delta p_\gamma + R_\gamma)(t))_- \in L^1(\mathbb{R})$ uniformly in γ and successively they recover the complementarity relation in the incompressible limit. Indeed, in the one dimensional case time-compactness of the pressure is available.

Now we briefly presents the gist of the proofs, starting from the one-dimensional case.

L^1-Aronson-Bénilan estimate

The proof relies on the following *a priori* estimates

$$\frac{\partial p}{\partial x} \in L^2_{x,t}, \qquad \frac{\partial \sigma_i}{\partial x} \in L^1_{x,t}, \quad \text{for } i = 1, 2. \tag{1.52}$$

Moreover, let us assume that the initial pressure is compactly supported. Then, thanks to the finite speed of propagation property of porous medium equations, the pressure remains compactly supported for all finite times, *i.e.* for all $T > 0$ there exists $\Omega \subset \mathbb{R}$ independent of $\gamma > 1$ such that

$$\operatorname{supp}(p(t)) \subset \Omega, \quad \forall t \in [0, T],\ \forall \gamma > 1.$$

As usual we define $w := \Delta p + R$ and compute the time derivative

$$\begin{aligned}\frac{\partial w}{\partial t} &= \gamma \frac{\partial^2 (pw)}{\partial x^2} + \frac{\partial^2}{\partial x^2}\left(\left|\frac{\partial p}{\partial x}\right|^2\right) + \frac{\partial R}{\partial t}\\ &= \gamma \frac{\partial^2 (pw)}{\partial x^2} + 2\frac{\partial p}{\partial x}\frac{\partial (w-R)}{\partial x} + 2\left|\frac{\partial^2 p}{\partial x^2}\right|^2 + \frac{\partial R}{\partial t}.\end{aligned} \tag{1.53}$$

Since we aim at estimating the negative part of w, we multiply by $\operatorname{sign}_-(w)$ to obtain

$$\begin{aligned}\frac{\partial (w)_-}{\partial t} \leqslant{}& \gamma \frac{\partial^2 (p(w)_-)}{\partial x^2} + 2\frac{\partial p}{\partial x}\frac{\partial (w)_-}{\partial x} - 2\frac{\partial p}{\partial x}\frac{\partial R}{\partial x}\operatorname{sign}_-(w) + 2|w-R|^2 \operatorname{sign}_-(w)\\ &+ \operatorname{sign}_-(w)\frac{\partial R}{\partial t},\end{aligned} \tag{1.54}$$

where we used Kato's inequality. Let us notice that

$$\operatorname{sign}_-(w)\frac{\partial R}{\partial t} \leqslant \gamma p (w)_- R_p + \operatorname{sign}_-(w)|\nabla p|^2 + \left|(F-G)\frac{\partial \sigma_1}{\partial t}\right| \leqslant \left|(F-G)\frac{\partial \sigma_1}{\partial t}\right|, \tag{1.55}$$

since $R_p \leqslant 0$. As explained above, the main novelty of this approach is to integrate the inequality and using *a priori* estimates in order to achieve a control on $(w)_-$ in a weaker norm. Let us notice that, by integrating (1.54) in space, the first term on the right-hand side vanishes. As will be explained below, this term will instead play a crucial role in the L^2-AB estimate. We obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega (w)_-\,\mathrm{d}x \leqslant 2\int_\Omega \frac{\partial p}{\partial x}\frac{\partial (w)_-}{\partial x}\,\mathrm{d}x + 2\int_\Omega \left|\frac{\partial p}{\partial x}\right|\left|\frac{\partial R}{\partial x}\right|\mathrm{d}x - 2\int_\Omega (w)_-^2\,\mathrm{d}x + 4\int_\Omega (w)_- R\,\mathrm{d}x$$
$$+ 2\int_\Omega |R|^2\,\mathrm{d}x + \int_\Omega \left|(F-G)\frac{\partial \sigma_1}{\partial t}\right|\mathrm{d}x.$$

Using the boundedness of R_p, F, and G, one can see

$$2\int_\Omega \left|\frac{\partial p}{\partial x}\right|\left|\frac{\partial R}{\partial x}\right|\mathrm{d}x \leqslant C\int_\Omega \left|\frac{\partial p}{\partial x}\right|^2\mathrm{d}x + C\sum_{i=1}^2\int_\Omega \left|\frac{\partial p}{\partial x}\right|\left|\frac{\partial \sigma_i}{\partial x}\right|\mathrm{d}x \leqslant C + C\left\|\frac{\partial p}{\partial x}\right\|_\infty,$$

where we used the *a priori* estimates (1.52). Moreover, computing $\partial_t\sigma_1$, it is possible to prove

$$\int_\Omega \left|(F-G)\frac{\partial \sigma_1}{\partial t}\right|\mathrm{d}x \leqslant C + \left\|\frac{\partial \sigma_1}{\partial x}\right\|_{L^1}\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty} \leqslant C + C\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty}.$$

Therefore, we have

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega (w)_-\,\mathrm{d}x &\leqslant 2\int_\Omega \frac{\partial p}{\partial x}\frac{\partial (w)_-}{\partial x}\,\mathrm{d}x - 2\int_\Omega (w)_-^2\,\mathrm{d}x + C\int_\Omega (w)_-\,\mathrm{d}x + C + C\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty}\\
&= -2\int_\Omega \frac{\partial^2 p}{\partial x^2}(w)_-\,\mathrm{d}x - 2\int_\Omega (w)_-^2\,\mathrm{d}x + C\int_\Omega (w)_-\,\mathrm{d}x + C + C\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty}\\
&= -2\int_\Omega (w-R)(w)_-\,\mathrm{d}x - 2\int_\Omega (w)_-^2\,\mathrm{d}x + C\int_\Omega (w)_-\,\mathrm{d}x + C + C\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty}\\
&\leqslant 2\int_\Omega (w)_-^2\,\mathrm{d}x - 2\int_\Omega (w)_-^2\,\mathrm{d}x + C\int_\Omega (w)_-\,\mathrm{d}x + C + C\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty}\\
&= C\int_\Omega (w)_-\,\mathrm{d}x + C + C\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty}.
\end{aligned}$$

Let us mention that this only works since we are in dimension one. In fact, for any dimension d greater than one, the factor multiplying $\int (w)_-^2$ would be $2(1-1/d) > 0$. Therefore, due to the positivity of the coefficient, we would not be able to apply Gronwall's lemma or to absorb this higher order term.

Before applying Gronwall's lemma, we have to estimate the L^∞-norm of the pressure gradient. Let us recall that for the classical porous medium equation the pressure is always Lipschitz in dimension one. We now show that this holds (uniformly in γ) also for Sys. (1.51); however, due to a different argument. Thanks to Sobolev's embedding theorem in dimension one, we have

$$\begin{aligned}
\left\|\frac{\partial p}{\partial x}\right\|_{L^\infty(\Omega)} \leqslant \left\|\frac{\partial^2 p}{\partial x^2}\right\|_{L^1(\Omega)} = \int_\Omega \left|\frac{\partial^2 p}{\partial x^2}\right|\mathrm{d}x &\leqslant \int_\Omega (w - 2(w)_- + |R|)\,\mathrm{d}x\\
&\leqslant \int_\Omega (\Delta p + 2(w)_- + 2|R|)\,\mathrm{d}x\\
&\leqslant C + C\int_\Omega (w)_-\,\mathrm{d}x.
\end{aligned}$$

Hence, we finally have

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega (w)_-\,\mathrm{d}x \leqslant C + C\int_\Omega (w)_-\,\mathrm{d}x,$$

and, provided $(w(x,0))_- \in L^1(\mathbb{R})$, by Gronwall's lemma we have (uniformly in γ)

$$\left(\frac{\partial^2 p}{\partial x^2} + R\right)_- \in L^\infty(0,T;L^1(\mathbb{R})). \tag{1.56}$$

L^2-Aronson-Bénilan estimate

As aforementioned, the above L^1-estimate can only work for $d=1$. In fact, the first L^p-extension of the Aronson-Bénilan estimate was developed for any dimension and $p=2$, see [94]. The argument is similar to the one-dimensional case, but the inequality on w is multiplied by $-(w)_-$ instead by simply $\text{sign}_-(w)$. Hence, from

$$\begin{aligned}\frac{\partial w}{\partial t} &= \gamma\Delta(pw) + \Delta\left(\left|\frac{\partial p}{\partial x}\right|^2\right) + \frac{\partial R}{\partial t}\\
&= \gamma\Delta(pw) + 2\nabla p\cdot\nabla(w-R) + 2\sum_{i,j}\left|\frac{\partial^2 p}{\partial x_i\partial x_j}\right|^2 + \frac{\partial R}{\partial t}\\
&\geqslant \gamma\Delta(pw) + 2\nabla p\cdot\nabla(w-R) + \frac{2}{d}\left|\Delta p\right|^2 + \frac{\partial R}{\partial t},\end{aligned}$$

we obtain

$$\frac{1}{2}\frac{\partial(w)_-^2}{\partial t} \leqslant \gamma\Delta(p(w)_-)(w)_- + 2(w)_-\nabla p\cdot\nabla(w)_- + 2(w)_-\nabla p\cdot\nabla R - \frac{2}{d}(w)_-\left|w-R\right|^2 - \frac{\partial R}{\partial t}(w)_-.$$

Developing the last term in a similar fashion as in Eq. (1.55), gives

$$\begin{aligned}-\frac{\partial R}{\partial t}(w)_- &= -\frac{\partial p}{\partial t}R_p(w)_- - (F(p)-G(p))\frac{\partial\sigma_1}{\partial t}(w)_-\\
&= \gamma p(w)_-^2R_p - |\nabla p|^2R_p(w)_- - (F(p)-G(p))\frac{\partial\sigma_1}{\partial t}(w)_-\\
&\leqslant -|\nabla p|^2R_p(w)_- - (F(p)-G(p))\frac{\partial\sigma_1}{\partial t}(w)_-,\end{aligned}$$

and hence

$$\begin{aligned}\frac{1}{2}\frac{\partial(w)_-^2}{\partial t} \leqslant{}& \gamma\underbrace{\Delta(p(w)_-)(w)_- + \nabla p\cdot\nabla(w)_-^2}_{\mathcal{D}} + \underbrace{(w)_-|\nabla p|^2R_p}_{\mathcal{N}\leqslant 0} + \underbrace{2(w)_-\nabla p\cdot\nabla\sigma_1(F(p)-G(p))}_{\mathcal{B}_1}\\
&-\frac{2}{d}(w)_-^3 + C(w)_-^2 + C(w)_- - \underbrace{(F(p)-G(p))\frac{\partial\sigma_1}{\partial t}(w)_-}_{\mathcal{B}_2},\end{aligned} \tag{1.57}$$

where $C>0$ is independent of γ. The core of the proof is still the same. After integrating in space over Ω, we aim at using Gronwall's lemma. However, the treatment of some terms is different with respect to the L^1-estimate. For instance, the terms including the gradient of σ_1

cannot be bounded in the same way, since for $d \geqslant 2$ the BV-bounds of the density fractions and the L^∞-bound on the pressure gradient no longer hold. Let us mention that for a certain bounded and continuous function $\mathcal{F} = \mathcal{F}(\sigma_1, \sigma_2, p)$, the equation on σ_1 reads

$$\frac{\partial \sigma_1}{\partial t} = \nabla \sigma_1 \cdot \nabla p + \mathcal{F}.$$

As shown in [94], the "bad" terms, $\mathcal{B}_1$ and $\mathcal{B}_2$, can be treated using integration by parts as follows

$$\begin{aligned}\int_\Omega \mathcal{B}_1 + \mathcal{B}_2 \,\mathrm{d}x &= \int_\Omega (F(p) - G(p)) \nabla \sigma_1 \cdot \nabla p (w)_- \,\mathrm{d}x - \int_\Omega (F(p) - G(p)) \mathcal{F}(w)_- \,\mathrm{d}x \\ &\leqslant C \int_\Omega (w)_- \,\mathrm{d}x - \int_\Omega \sigma_1 (F(p) - G(p)) \Delta p (w)_- \,\mathrm{d}x - \int_\Omega (F'(p) - G'(p)) \sigma_1 |\nabla p|^2 (w)_- \,\mathrm{d}x \\ &\quad - \int_\Omega \sigma_1 (F(p) - G(p)) \nabla p \cdot \nabla (w)_- \,\mathrm{d}x.\end{aligned}$$

Let us focus the attention on the last term on the right-hand side. Indeed, the other terms can be bounded using $\Delta p = w - R$, integration by parts, and $\nabla p \in L^\infty_t L^2_x$. Using Young's inequality, we have

$$- \int_\Omega \sigma_1 (F(p) - G(p)) \nabla p \cdot \nabla (w)_- \leqslant \frac{1}{2} \int_\Omega \frac{|F(p) - G(p)|^2}{p} |\nabla p|^2 + \frac{1}{2} \int_\Omega p |\nabla (w)_-|^2. \tag{1.58}$$

Here is where the technical condition assumed in [94] is used. In fact, the authors impose

$$F(0) = G(0). \tag{1.59}$$

Therefore, the first integral on the right-hand side is uniformly bounded. It remains to treat one "bad term" which is the integral including $|\nabla (w)_-|^2$ in Eq. (1.58). In order to absorb it, we use the dissipation term $\mathcal{D}$ in Eq. (1.57). Indeed, as we mentioned before, unlike for the L^1-estimate this term does not disappear. Using again integration by parts and $\Delta p = w - R$, we have

$$\begin{aligned}\int_\Omega \mathcal{D} &\leqslant \left(1 - \frac{\gamma}{2}\right) \int_\Omega (w)_-^3 + \left(1 - \frac{\gamma}{2}\right) \int_\Omega R (w)_-^2 - \gamma \int_\Omega p |\nabla (w)_-|^2 \\ &\leqslant \left(1 - \frac{\gamma}{2}\right) \int_\Omega (w)_-^3 + \frac{1}{2} \int_\Omega R (w)_-^2 - \gamma \int_\Omega p |\nabla (w)_-|^2,\end{aligned} \tag{1.60}$$

where in the last inequality we used the fact that R is always non-negative. Therefore, the last integral on the right-hand side helps absorbing the last one in Eq. (1.58).

Finally, combining these estimates with Eq. (1.57), we find

$$\frac{\mathrm{d}}{\mathrm{d}t} \int_\Omega \frac{(w)_-^2}{2} \leqslant \left(1 - \frac{\gamma}{2} - \frac{2}{d}\right) \int_\Omega (w)_-^3 + C \int_\Omega (w)_-^2 + C \int_\Omega (w)_- + C. \tag{1.61}$$

Assuming $\gamma > \max(1, 2 - 4/d)$, we can apply Gronwall's lemma to obtain

$$(\Delta p + R)_- \in L^\infty(0, T; L^2(\mathbb{R}^d)), \tag{1.62}$$

which is uniform in γ, since the constant C is independent of γ.

1.5 Contents of the thesis

In this thesis we develop further the theory on the incompressible limit of porous medium models motivated by tumor growth. This section is devoted to presenting the novelties introduced in this work, which is structured in three parts:

- **Part I** concerns the analysis of the stiff limit of a mechanical tumor growth model and its numerical simulation. In Chapter 2 we analyse the incompressible limit of a model including the presence of nutrients (for instance, oxygen or glucose). As explained above, during the development of cancers the lack of nutrients in the center of the tumoral mass induces cell death by necrosis, generating a *necrotic core*. As a consequence, models that account for nutrient availability allow for non-positive reaction terms. From an analytical viewpoint, this turns out to be a crucial difference with respect to models without nutrients, such as the purely mechanical model studied in [130]. In this chapter, we consider a system of reaction-diffusion equations whose bad coupling makes the comparison principle, used in [130] to recover the AB estimate in L^∞, fail. Therefore, in order to recover the complementarity relation in the stiff limit, we rely on two new techniques: an L^3-version of the AB estimate, and a *sharp* uniform L^4-bound on the pressure gradient which allows us to recover the required regularity in order to pass to the limit. Chapter 3 concerns the numerical simulation of this kind of porous medium models of tumor growth. We present an upwind finite difference scheme of the purely mechanical model for which we prove stability results and the asymptotic preserving property as $\gamma \to \infty$. We also test our scheme for models including a nutrient, both in the *in vitro* and *in vivo* cases, and including necrotic cells in the system. Finally, we numerically verify the sharpness of the L^4-bound of the pressure gradient, computing the norms of the focusing solution in dimension 2.

- **Part II** is focused on the incompressible limit of a reaction-porous medium equation including convective effects. As mentioned in Introduction, the asymptotic behavior of this kind of equations has already been addressed in the literature. However, the complementarity relation that allows to recover the limit pressure as the solution of an elliptic equation was still an open problem. In Chapter 4, we present a proof which is based on extending and blending the two techniques presented in Chapter 2: the L^4-bound of the pressure gradient and the L^3-version of the Aronson-Bénilan estimate. We are able to extend these results to the case including convective effects, as well as to substantially reduce the conditions on the drift term imposed in the previous literature. To this end, we apply the L^4-control in order to recover the AB estimate. We also prove uniqueness of the weak solution of the limit Hele-Shaw problem. Chapter 5 deals with estimating the convergence rate of the incompressible limit analysed in Chapter 4. This question has been rarely addressed in the literature. In this chapter we present a simple and flexible proof of how to obtain an estimate for the convergence rate in the $L^\infty_t H^{-1}_x$-norm for nonlinear and degenerate diffusion equations including convection, in both the power law and the singular pressure law cases.

- **Part III** concerns the analysis of a tumor growth model structured by phenotypic trait. We consider a cross-diffusion model where each phenotypic density evolves under Darcy's law, and the pressure is related to the total population density. We prove the existence of weak solutions as well as the incompressible limit as the pressure becomes stiff. Moreover, we recover regularity results that, to the best of our knowledge, are novel in the multi-species case.

Now we summarize the main contributions of this thesis in some greater detail.

1.5.1 Incompressible limit of tumor growth models including nutrients: analysis and simulations

Free boundary limit of a model with nutrient

As mentioned in the previous section, the behavior of the free boundary of PME's solutions changes drastically if we allow for non-monotonicity, namely if the growth rate can assume negative values. In the context of cancer growth modelling this happens, for instance, if the presence of nutrients is taken into account. The nutrients (for instance glucose or oxygen) are brought by the blood vessels and diffuse into the tumor where they are consumed by cancer cells. However, if the level of nutrients is not high enough, cells may die by necrosis, as it happens in the center of avascular tumors after they have reached a certain size. Therefore, modelling nutrient presence means allowing for cell death, *i.e.* assuming that the growth rate G depends both on the pressure p and on the nutrient concentration c, and that $G(p,c) < 0$ for c small enough. This type of models implicitly distinguishes proliferating cells from necrotic cells. Although several multi-species models describing proliferating, necrotic or quiescent cells are available in the literature, we focus on a model that only considers the first type of cells. Consequently, the cell population density may vanish in regions contained in its initial support.
The incompressible limit for a model including nutrients was already addressed in the seminal work [130], where the authors consider a system of PDEs including a nutrient concentration which satisfies a reaction-diffusion equation. As for the purely mechanical model (1.32), they pass to the stiff limit in the density equation obtaining (1.38). However, they leave open the question of how to recover the complementarity relation, namely

$$p_\infty(\Delta p_\infty + G(p_\infty, c_\infty)) = 0. \tag{1.63}$$

In fact, the method the authors developed for the purely mechanical model does not apply in this case. The reason lies in the fact that the fundamental Aronson-Bénilan estimate (1.39) fails. In fact, since G may now take negative values, we can no longer apply the comparison principle in order to bound the quantity $w := \Delta p + G(p,c)$ by a subsolution that vanishes as $m \to \infty$. Indeed, after a certain time, a region may appear where the pressure is constantly equal to zero and the reaction rate is negative. Therefore $\Delta p + G(p,c) \gtrsim -1/mt$ cannot hold.
Our work aims at solving this open problem. We consider the following model including nutrients

$$\begin{cases} \dfrac{\partial n}{\partial t} - \nabla \cdot (n \nabla p) = nG(p,c), & x \in \mathbb{R}^d,\ t \geqslant 0, \\ p = n^\gamma, & \gamma > 1, \\ \partial_t c - \Delta c + nH(c) = (c_B - c)K(p), & \\ c(x,t) \to c_B & \text{for } x \to \infty. \end{cases}$$

Unlike [130], we consider nutrient consumption (with given rate H) as well as nutrient release from the vasculature (with given rate K).
In order to prove the complementarity relation (1.63) we derive a weaker version of the Aronson-Bénilan estimate, in the spirit of the L^2-estimate proven in [94], whose derivation was explained in Section 1.4.3. In this case, we are able to obtain an equation which is analogous to (1.61). However, there is an essential difference in the case including nutrients. Since the reaction rate $G(p,c)$ does not have a sign, we are not able to bound the corresponding integral as in (1.60). Therefore, the positive constant C in front of $\int (w)_-^2$ in (1.61) is no longer independent of γ. As a consequence, we are not able to use Gronwall's lemma to infer $(\Delta p + G(p,c))_- \in L^\infty(0,T; L^2(\mathbb{R}^d))$

uniformly in γ. However, we are still able to prove the following result.

Proposition 1.5.1 (L^3-version of the AB estimate)**.** *The following control holds uniformly with respect to* γ

$$(\Delta p + G(p,c))_- \in L^3(\mathbb{R}^d \times (0,T)).$$

This bound allows us to deduce $\Delta p \in L^1(\mathbb{R}^d \times (0,T))$ which, together with the L^1-control of $\partial_t p$, is enough to infer the strong compactness of ∇p in $L^q_{x,t}$ for $1 \leqslant q \leqslant d/(d-2)$. Since we aim at proving the complementarity relation, we know that the strong compactness of the pressure gradient in $L^2_{x,t}$ is needed. Therefore, we need to prove a higher uniform control.

Proposition 1.5.2 (Sharp L^4-bound of the gradient)**.** *The following estimate holds uniformly with respect to* γ

$$|\nabla p| \in L^4(\mathbb{R}^d \times (0,T)).$$

Moreover, this estimate is sharp, namely, there exists a solution such that $\|\nabla p\|_{L^q}$ *blows up as* $\gamma \to \infty$ *for every* $q > 4$.

This control on the gradient was already achieved in [123], where the authors consider the purely mechanical model. However, their argument deeply relies on the L^∞-AB control, which fails in our case. We develop a new proof which does not rely on any control on Δp. Moreover, we are the first to show that this uniform estimate is *sharp*. Indeed, a counterexample is given by the *focusing solution* discussed in Sec. 1.3.1. We analyze this property using an asymptotic argument and we later investigated it numerically, as presented below.

Numerical simulation of a mechanical model of tumor growth

We propose a simple finite difference scheme to analyze the purely mechanical model introduced in [130]

$$\frac{\partial n}{\partial t} - \nabla \cdot (n \nabla p) = nG(p), \qquad p = n^\gamma, \quad \gamma > 1.$$

The numerical simulation of tissue growth models of porous medium type has attracted a lot of interest in recent years, see, for instance, [114, 112, 113, 25] and references therein. The main challenges are represented by the lack of regularity near the free boundary and the stiffness of solutions that occurs when $\gamma \to \infty$.

We propose the following upwind scheme in dimension one

$$\frac{d}{dt} n_i = \frac{n_{i+1/2} q_{i+1/2} - n_{i-1/2} q_{i-1/2}}{\Delta x} + n_i G(p_i), \qquad \text{with} \quad q_{i+1/2} = \frac{p_{i+1} - p_i}{\Delta x}, \tag{1.64}$$

where we define

$$n_{i+1/2} = \begin{cases} n_i, & \text{if } \; q_{i+1/2} \leqslant 0, \\ n_{i+1}, & \text{if } \; q_{i+1/2} > 0. \end{cases}$$

The simplicity of the scheme allows us to prove several stability estimates. In particular, we prove BV-controls on both the semi-discrete scheme and the fully discrete scheme, obtained using Euler implicit discretization in time. Moreover, we prove the asymptotic preserving (AP) property of the scheme as $\gamma \to \infty$.

Proposition 1.5.3 (Asymptotic preserving property)**.** *Given* n_i, p_i *a solution of scheme* (1.64) *with* $\gamma > 1$. *Then, for all* i, *we have*

$$n_i \xrightarrow{\gamma \to \infty} n_{\infty,i}, \qquad \text{in } L^p(0,T), \text{ for all } 1 \leqslant p < \infty,$$

$$p_i \xrightarrow{\gamma\to\infty} p_{\infty,i}, \qquad \textit{in } L^p(0,T), \textit{ for all } 1 \le p < \infty,$$
$$q_{i+\frac{1}{2}} \xrightarrow{\gamma\to\infty} q_{\infty,i+\frac{1}{2}}, \quad \textit{weakly in } L^2(0,T).$$

and the limit satisfies

$$0 = p_{\infty,i}\left(\frac{p_{i+1} - 2p_i + p_{i-1}}{|\Delta x|^2} p_{\infty,i} + G(p_{\infty,i})\right),$$
$$\frac{d}{dt} n_{\infty,i} = \frac{n_{\infty,i+1/2}q_{\infty,i+1/2} - n_{\infty,i-1/2}q_{\infty,i-1/2}}{\Delta x} + n_{\infty,i}G(p_{\infty,i}).$$

We then derive a discrete version of the Aronson-Bénilan estimate. As frequently illustrated before, this estimate is fundamental in the analysis of both the classical PME and the related tissue growth models. Therefore, it is our interest to analyze whether such estimate is also discretely satisfied by our upwind scheme. This purpose was addressed by Monsaingeon in [124] for a tracking front scheme of the classical PME, *i.e.* Eq. (1.7). We manage to infer the same estimate in the case of a fixed grid, for $\gamma = 1$ and $\gamma \approx \infty$. Our main contribution in this direction is the proof of the AB estimate in the case of non-trivial pressure-dependent reaction terms.

Proposition 1.5.4 (Discrete Aronson-Bénilan estimate)**.** *Let* $\alpha > 0$, $G(p) = \alpha(p_H - p)$ *and*

$$w_i := \delta_x^2 p_i + G(p_i) = \frac{p_{i+1} - 2p_i + p_{i-1}}{(\Delta x)^2} + G(p_i), \quad \forall i.$$

Then, for $\gamma = 1$ *and* $\gamma \approx \infty$*, scheme* (1.64) *satisfies the Aronson-Bénilan estimate, namely*

$$w_i \geqslant -\frac{1}{\gamma t}, \qquad \forall i.$$

We perform several numerical simulations to test the accuracy of our scheme. We test it both for the classical PME and for tumor growth models including nutrients and/or necrotic cells. At last, we perform numerical simulations to investigate the sharpness of the L^4-estimate on the pressure gradient mentioned before, *cf.* Lemma 1.5.2. We consider a radial focusing solution, *i.e.* a solution of the Hele-Shaw problem whose initial data is a spherical shell. By computing the L^q-norm of ∇p we verify the worsening of the blow up at the focusing time as $q > 4$.

1.5.2 Incompressible limit of a tumor growth model including convective effects: regularity and convergence rate

Stiff limit of a model with drift: regularity and complementarity relation

Besides the passive movement generated by the pressure gradient, tumor cells can undergo active forces as, for instance, the attraction due to the concentration of a certain chemical, or as a result of self-propulsion as in the Keller-Segel model. In the latter case the velocity field is given by the convolution of the density with the Newtonian potential, $\mathcal{N} \star n$. In this part of the thesis, we analyse the regularity properties and the incompressible limit of the following nonlinear diffusion-advection equation

$$\frac{\partial n}{\partial t} - \nabla \cdot (n(\nabla p + \nabla V)) = nG, \tag{1.65}$$

where $V : \mathbb{R}^d \times (0, \infty) \to \mathbb{R}$ is given.

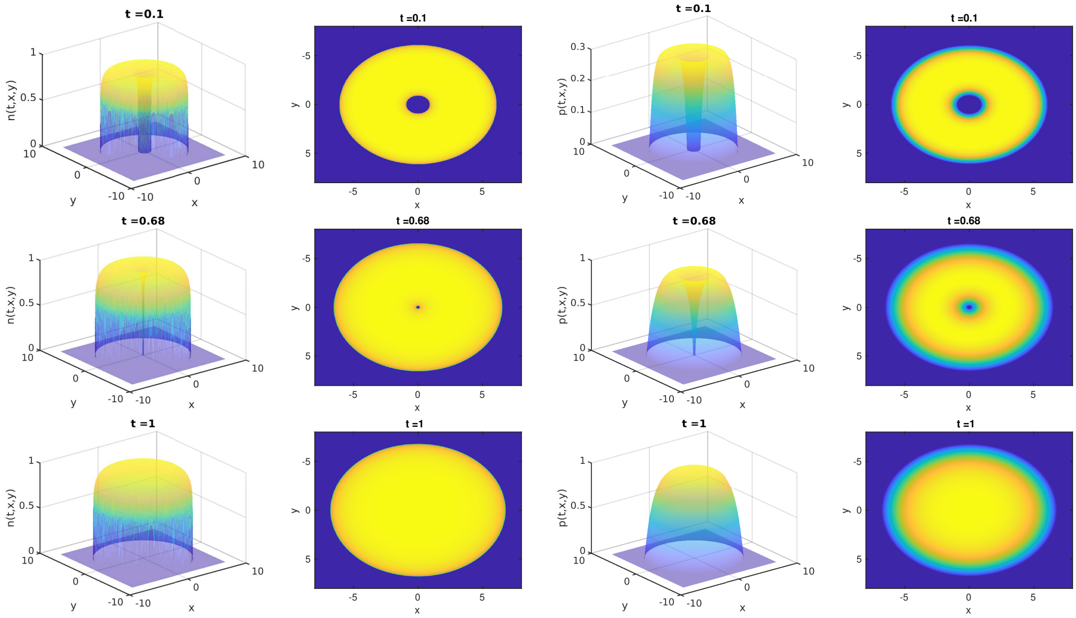

Figure 1.2: *Focusing solution: density (left) and pressure (right).* Numerical solution of the focusing problem with $\gamma = 10$, $\Delta x = 0.02$, initial internal radius 1.

Several works on the free boundary limit of porous medium equations incorporating advection terms can be found in the literature, see for instance [1, 57, 103]. However, to find the *complementarity relation*, *i.e.* the elliptic equation satisfied by p_∞ in its positivity set, was still an open question. As in the case including nutrients, the main difficulty consists in proving the L^2-strong compactness of the pressure gradient. We address this problem for Eq. (1.65) with $p = n^\gamma$ and a pressure-dependent growth rate $G = G(p)$.
Under suitable assumptions on V, we prove that as $\gamma \to \infty$ the solution to Eq. (1.65) converges to a limit (n_∞, p_∞) that satisfies the following statement.

Proposition 1.5.5 (Complementarity relation with drift). *The limit (n_∞, p_∞) solves*

$$p_\infty(\Delta p_\infty + \Delta V + G(p_\infty)) = 0, \qquad p_\infty(1 - n_\infty) = 0.$$

To this end, we extend the techniques that we developed in the case with nutrients: the L^3-version of the Aronson-Bénilan estimate and the L^4-bound on the pressure gradient. In particular, the latter is a novelty in the context of porous medium-advection equations.
We also aim at weakening the assumptions on the drift V with respect to the existing literature. To this end, we use $\nabla p \in L^4$ to deduce the AB estimate, although the two arguments could be made one independent of the other. Moreover, let us stress that an L^∞-version of the Aronson-Bénilan estimate was already obtained by [103] in the drift case, Eq. (1.50), as illustrated in Section 1.4. However, to obtain this lower bound, the authors require a $C^{3,1}_{x,t}$-control on ∇V. In order to achieve the much weaker L^3-bound we considerably reduce this assumption, asking only for $D^2 V \in L^\infty_{x,t}$ and $\Delta \nabla V \in L^{12/5}_{x,t}$.
Finally, we give a proof of the uniqueness of the limit solution adapting Hilbert's duality method.

Proposition 1.5.6 (Uniqueness of the limit solution). *There exists at most one distributional solution such that for all $T > 0$ the couple $(n_\infty, p_\infty) \in L^\infty(\mathbb{R}^d \times (0,T)) \times L^2(0,T; H^1(\mathbb{R}^d))$ is a* *solution to the following system*

$$\begin{cases} \dfrac{\partial n_\infty}{\partial t} - \Delta p_\infty - \nabla \cdot (n_\infty \nabla V) = n_\infty G(p_\infty), & \mathcal{D}'(\mathbb{R}^d \times (0,T)), \\ p_\infty(1-n_\infty) = 0, & a.e. \ in \ \mathbb{R}^d \times (0,T). \end{cases} \tag{1.66}$$

Stiff limit of a model with drift: convergence rate

Despite the vast literature on the incompressible limit of porous medium models including advection, the question of how to estimate the convergence rate of the solutions has been rarely addressed. A first result is provided by Alexander, Kim and Yao in [1], where the authors find a polynomial rate of 1/24 in the 2-Wasserstein distance, Eq. (1.41). Our aim is to estimate the convergence rate in the $L^\infty_t \dot{H}^{-1}_x$-norm. In particular, for both the power and the singular laws

$$p_\gamma = \frac{\gamma}{\gamma-1} n_\gamma^{\gamma-1} \quad \text{or} \quad p_\varepsilon = \varepsilon \frac{n_\varepsilon}{1-n_\varepsilon},$$

we study the convergence of solutions n_γ (respectively n_ε) of Eq. (1.65) as $\gamma \to \infty$ (respectively $\varepsilon \to 0$) and we find the following polynomial rate.

Proposition 1.5.7 (Convergence rate in $\dot{H}^{-1}$)**.** *Under suitable assumptions on $V = V(x,t)$ and $G = G(x,t)$, for all $T > 0$, there exists a unique function $n_\infty \in C([0,T); L^1(\mathbb{R}^d))$ such that the sequence n_γ (resp. n_ε) converges as $\gamma \to \infty$ (resp. $\varepsilon \to 0$) to n_∞ strongly in $L^\infty(0,T; \dot{H}^{-1}(\mathbb{R}^d))$ with the following rate*

$$\sup_{t\in[0,T]} \|n_\gamma(t) - n_\infty(t)\|_{\dot{H}^{-1}(\mathbb{R}^d)} \leqslant \frac{C(T)}{\gamma^{1/2}} + \|n_\gamma^0 - n_\infty^0\|_{\dot{H}^{-1}(\mathbb{R}^d)}.$$

Moreover, thanks to this result we are able to provide a new proof of the saturation relation in Eq. (1.66) which does not require the strong convergence of the density or the pressure.

We here present the gist of the methods that we apply in Chapter 5 to estimate the convergence rate. Our strategy relies on considering $\varphi_\gamma := \mathcal{K} \star n_\gamma$, where $\mathcal{K}$ is the fundamental solution of the Laplace equation. Then, we have

$$-\Delta \varphi_\gamma = n_\gamma.$$

For $\gamma' > \gamma > 1$, we consider the following equation

$$\frac{\partial(n_\gamma - n_{\gamma'})}{\partial t} = \Delta(A_\gamma - A_{\gamma'}) + \nabla \cdot ((n_\gamma - n_{\gamma'})\nabla V) + (n_\gamma - n_{\gamma'})G,$$

where A_γ is chosen appropriately depending on the law of state of the pressure. Multiplying the above equation by $\varphi_\gamma - \varphi_{\gamma'}$, we obtain

$$\begin{aligned} \frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2 \,\mathrm{d}x &= \int_{\mathbb{R}^d} (n_{\gamma'} - n_\gamma)(A_\gamma(n_\gamma) - A_{\gamma'}(n_{\gamma'}))\,\mathrm{d}x \\ &- \int_{\mathbb{R}^d} (n_\gamma - n_{\gamma'})\nabla(\varphi_\gamma - \varphi_{\gamma'}) \cdot \nabla V \,\mathrm{d}x + \int_{\mathbb{R}^d} G(t,x)(n_\gamma - n_{\gamma'})(\varphi_\gamma - \varphi_{\gamma'})\,\mathrm{d}x. \end{aligned}$$

Under suitable assumptions on G and V, we are able to find

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}|\nabla(\varphi_\gamma-\varphi_{\gamma'})|^2\,\mathrm{d}x+\int_{\mathbb{R}^d}(n_\gamma-n_{\gamma'})(A_\gamma(n_\gamma)-A_{\gamma'}(n_{\gamma'}))\,\mathrm{d}x\leqslant C\int_{\mathbb{R}^d}|\nabla(\varphi_\gamma-\varphi_{\gamma'})|^2\,\mathrm{d}x.$$

Manipulating the second term on the left-hand side in a proper way (depending on the pressure law under consideration) and applying the Gronwall inequality, we can deduce

$$\sup_{t\in[0,T]}\|\nabla(\varphi_\gamma-\varphi_{\gamma'})(t)\|_{L^2(\mathbb{R}^d)}\leqslant C\left(\frac{1}{\sqrt{\gamma}}+\frac{1}{\sqrt{\gamma'}}\right)+\|\nabla(\varphi_\gamma-\varphi_{\gamma'})(0)\|_{L^2(\mathbb{R}^d)}. \tag{1.67}$$

Passing to the limit $\gamma'\to\infty$ we infer the result in Proposition 1.5.7.

1.5.3 A multi-species model structured by phenotype

As discussed in Section 1.3.3, multi-species models of cross-reaction-diffusion equations have been widely studied during the last decade. The different natures of the single species equations and the total population equation introduce involved challenges to the analysis. Existence and regularity results for these models have been provided recently by [47, 94, 101] and the incompressible limit has been addressed in one spatial dimension in [31] and then extended in multiple dimensions by [115].

We aim at extending these recent results for a model structured by a phenotypic trait. Phenotypic heterogeneity plays a central role in the development of tumors. Cells with different gene expressions can develop higher aggressivity that lead to faster invasion. An interesting phenomenon called "growth or go" has been observed in certain tumors. It consists in the fact that cells with higher mobility are less aggressive and have a diminished growth rate with respect to cells with a lower mobility. This dichotomy has been analysed through a structured model by Lorenzi *et al.* in [118], where the authors perform a formal asymptotic analysis to show the appearance of accelerating fronts.

In this part of the thesis we consider a similar structured system

$$\begin{cases}\dfrac{\partial n}{\partial t}(y,x,t)-\nabla\cdot(n(y,x,t)\nabla p(x,t))=nR(y,p), & (y,x,t)\in[0,1]\times\mathbb{R}^d\times(0,\infty),\\[2mm] \varrho(x,t)=\displaystyle\int_0^1 n(y,x,t)\,\mathrm{d}y,\quad p(x,t)=\varrho(x,t)^\gamma, & \end{cases} \tag{1.68}$$

which in some way extends the two-species system (1.51) to an infinitely-many-species problem. We only analyse the case of constant mobility rates which, unlike in [118], do not depend on the structured variable y.

The main contribution of our work consists in three results: the existence of weak solutions n_γ, p_γ of (1.68), the incompressible limit of such solutions as $\gamma\to\infty$, and additional regularity results on p_γ. The first two results are obtained as an extension of the methods developed in [135] and [115], respectively. The main difference with respect to the works by [94] and [31] is the fact that the focus is no longer centered around the pressure itself, but rather on the quantity $v:=\varrho^{\gamma+1}$. Working with ∇v rather than ∇p, it is possible to infer strong compactness in $L^2_{x,t}$ without any control on the Laplacian Δp which was the case in [31, 94]. Following this approach and adapting it to the structured case, we are able to prove both existence of weak solutions and pass to the stiff limit $\gamma\to\infty$. Unlike [115], where the authors assume the reaction terms to depend only on a certain nutrient concentration, we consider pressure-penalised reaction terms. Therefore, we also need to prove strong compactness of the pressure itself in order to pass to the limit in this nonlinear term. This issue was left open in [115] since to control $\partial_t p$ uniformly in γ is still an open question. However, assuming to have compactly supported solutions, *i.e.* $\operatorname{supp}(\varrho(t)) \subset \Omega \subset \mathbb{R}^d$ for $0 \leqslant t \leqslant T$, we are able to prove strong compactness of p simply using Poincaré inequality and the strong compactness of ∇p.

Proposition 1.5.8 (Existence of solutions and incompressible limit)**.** *Given $n_0 \in L^\infty([0,1] \times \mathbb{R}^d) \cap L^1([0,1] \times \mathbb{R}^d)$, $n_0 \geqslant 0$, there exists $n \in L^\infty([0,1] \times \mathbb{R}^d \times (0,\infty)) \cap L^1([0,1] \times \mathbb{R}^d \times (0,\infty))$, $n \geqslant 0$, such that $\nabla p \in L^2(\mathbb{R}^d \times (0,\infty))$, that satisfies Sys. (1.68) in the sense of distributions. Moreover, assuming ϱ_0 is compactly supported in $\mathbb{R}^d$, after extraction of a subsequence, the triple $(n_\gamma, \varrho_\gamma, p_\gamma)$ converges weakly* in $L^\infty(\mathbb{R}^d \times (0,\infty))$ to $(n_\infty, \varrho_\infty, p_\infty)$ which satisfies the following Hele-Shaw problem*

$$\begin{aligned}
\frac{\partial \varrho_\infty}{\partial t} &= \Delta p_\infty + \int_0^1 n_\infty R(y, p_\infty)\, \mathrm{d}y, && \text{in } \mathcal{D}'(\mathbb{R}^d \times (0,\infty)),\\
p_\infty\left(\Delta p_\infty + \int_0^1 n_\infty R(y, p_\infty)\, \mathrm{d}y\right) &= 0, && \text{in } \mathcal{D}'(\mathbb{R}^d \times (0,\infty)),\\
p_\infty(\varrho_\infty - 1) &= 0, && \text{a.e. in } \mathbb{R}^d \times (0,\infty).
\end{aligned}$$

Although no control on Δp is needed neither to prove existence nor to pass to the incompressible limit, it still represents a challenging and interesting question by itself. Therefore, we also aim at understanding if an L^2-version of the AB estimate holds for this structured model as well. As illustrated in Section 1.4.3, this control was proven in [94] for the two-species counterpart, (1.62). However, the authors had to impose a restrictive condition on the reaction terms, *i.e.* (1.59). We manage to remove this assumption by performing a different treatment of the "bad term", *i.e.* the first integral in Eq. (1.58). In fact, we first prove the following control on the pressure gradient.

Proposition 1.5.9 (L^4-estimate)**.** *There exists a constant $C(T)$ such that for any $0 \leqslant \alpha < \frac{1}{\gamma}$ the following estimate holds true*

$$\kappa(\alpha) \int_0^T \int_\Omega \frac{|\nabla p|^4}{p^{1-\alpha}}\, \mathrm{d}t \leqslant C(T),$$

with $\kappa(\alpha) := \frac{\alpha}{6}(1 - \alpha\gamma)$.

By using this result, we are able to find an L^2-AB estimate which is the analogue of (1.62). Indeed, applying Young's inequality, the integral in (1.58), for which the technical assumption $F(0) = G(0)$ was needed, now can be treated as follows

$$\int_0^1 \int_\Omega \sigma R(y,p) \nabla p \cdot \nabla(w)_- \,\mathrm{d}x\,\mathrm{d}y \leqslant \frac{\|\mathcal{R}\|_\infty}{4} \int_\Omega \frac{|\nabla p|^4}{p^{1-\alpha}}\,\mathrm{d}x + \frac{3}{4}\int_\Omega p^{1-\alpha} |\nabla(w)_-|^{4/3}\,\mathrm{d}x, \tag{1.69}$$

where

$$\mathcal{R} := \int_0^1 \sigma(y) R(y,p)\,\mathrm{d}y, \quad \text{and} \quad \sigma(y,x,t) := \frac{n(y,x,t)}{\varrho(x,t)}.$$

Thanks to the previous proposition the first term on the right-hand side of (1.69) is bounded, while the second one can be absorbed in the term $-\gamma \int_\Omega p|\nabla(w)_-|^2$ which will appear analogously as in (1.60). Therefore, we recover the following Aronson-Bénilan estimate for the structured system (1.68) without imposing any special conditions on the reaction term (which we always consider monotonically decreasing with respect to the pressure).

Proposition 1.5.10 (L^2-Aronson-Bénilan estimate)**.** *For all $T > 0$, there exists a constant $C(T)$ independent of γ, such that for all $t \in [0,T]$ we have*

$$\int_\Omega (\Delta p(t) + \mathcal{R})_-^2 \leqslant C(T), \qquad \int_0^T \int_\Omega (\Delta p + \mathcal{R})_-^3 \,\mathrm{d}t \leqslant C(T).$$

1.6 Discussions and perspectives

Mathematical models motivated by tissue growth and movement represent one of the most stimulating sources of challenging mathematical questions, in particular, in the context of analysis of PDEs. In this thesis we contribute to the study of the asymptotic behavior and well-posedness theory of porous medium equations and systems motivated by tumor development. This topic has been largely addressed by many researchers and, in recent years, remarkable results have been achieved in the understanding of these problems. Nevertheless, this field presents several challenging questions that remain open, in particular regarding the well-posedness of cross-diffusion systems and the Hele-Shaw limit with surface tension.

1.6.1 Existence results on cross-diffusion systems

As we already mentioned, degenerate cross-diffusion systems are particularly involved to treat due to the difficulty of proving strong compactness on at least one of the quantities involved. Many variations of System (1.51) have been investigated in the literature, and some of these problems represent long-standing open questions.

Different drifts

In Chapter 4, we study the incompressible limit of a porous medium model including convective effects, *i.e.* Eq. (1.65). Neglecting reaction processes and coupling Eq. (1.65) with an analogous equation for a second species that moves accordingly to Darcy's law and a different drift, we obtain the following system

$$\begin{cases} \dfrac{\partial n_1}{\partial t} - \nabla \cdot (n_1(\nabla p + \nabla V_1)) = 0, \\[2ex] \dfrac{\partial n_2}{\partial t} - \nabla \cdot (n_2(\nabla p + \nabla V_2)) = 0, \\[2ex] p = (n_1+n_2)^\gamma, \quad \gamma > 1, \end{cases}$$

where the pressure depends on the joint population density. Despite major efforts applied by different research groups, this problem remains the simplest example of a nonlinear cross-diffusion system for which the existence of solutions has not been established yet. Although both the densities and the pressure gradient are weakly compact, passing to the limit would require strong convergence of one of the two terms involved. The strategies based on the Aronson-Bénilan estimate used for systems like (1.51) do not seem to hold in this case. Only one result has been obtained in the one-dimensional case, see [101]. However, the authors need to impose a restrictive condition, namely that the two species stay segregated for all times, *i.e.* $-\partial_x V_1 \geqslant -\partial_x V_2$ and $x_1 > x_2$ for $x_i \in \{n_i^0 > 0\}, i = 1,2$.

Different mobilities

Including different mobility coefficients, $\mu_1 \neq \mu_2$, into System (1.51) increments even more the complexity of proving the existence of weak solutions

$$\begin{cases} \dfrac{\partial n_1}{\partial t} - \mu_1 \nabla \cdot (n_1 \nabla p) = n_1 F_1(p) + n_2 G_1(p), \\[2ex] \dfrac{\partial n_2}{\partial t} - \mu_2 \nabla \cdot (n_2 \nabla p) = n_1 F_2(p) + n_2 G_2(p), \\[2ex] p = (n_1 + n_2)^\gamma, \quad \gamma > 1. \end{cases}$$

Nowadays, no well-posedness results on the above system are available in the literature. Indeed, the whole set of methods developed for the previously presented models built upon the fact that the sum of the two equations generates a porous medium type equation. Due to the asymmetry of the degenerate diffusion terms, those techniques cannot be applied in this case. In fact, it is not clear how to find uniform *a priori* estimates on the pressure gradient, which are essential to the analysis of the system. Moreover, instabilities may occur under certain conditions, as noticed in [104, 117].

In [104], Kim and Tong considered a similar model in dimension $d = 2$, and showed local-in-time well-posedness of the related free boundary problem imposing specific assumptions to avoid instabilities. They assume that $G_1 \equiv F_2 \equiv G_2 \equiv 0$, and $n_1 + n_2 \leqslant 1$, and analyse the free boundary problem

$$\begin{cases} -\nabla \cdot ((\mu n_1 + \nu n_2) \nabla p) = n_1 F_1(p), & \text{if } n_1 + n_2 = 1, \\ p = 0, & \text{if } n_1 + n_2 < 1. \end{cases}$$

They assume that at the initial time, both the tumor, $n_1 = \mathbb{1}_\Omega$, and the surrounding healthy tissue, $n_2 = \mathbb{1}_{\tilde{\Omega} \setminus \Omega}$, are given by patches, with $\Omega \subset\subset \tilde{\Omega}$. Numerical results in [117] show that if $\mu_1 < \mu_2$ a certain radially symmetric solution is stable, while for $\mu_1 > \mu_2$ instabilities may occur. Therefore, Kim and Tong assume $\mu_1 < \mu_2$. However, they notice that instabilities may still occur at the contact interface between the two species, and thus they impose specific geometrical assumptions on Ω and $\tilde{\Omega}$.

1.6.2 Relation to Mean-Field Games

As mentioned above, in order to pass to the incompressible limit in Eq. (1.65) we manage to weaken the assumptions imposed on the drift term, see Chapter 4. However, further improvements in this direction are expected. In particular, it is of interest to find optimal conditions on V under which to obtain the sharp estimate $\nabla p \in L^4_{x,t}$ and the strong compactness of the pressure. This would be important in view of applications to the following mean field game, where a Hamilton-Jacobi equation and a continuity equation are coupled, and the system with unknowns $\varphi(x,t)$ (value function), $n(x,t)$ (density), and $p(x,t)$ (pressure), is closed with incompressibility conditions on n and p

$$\begin{cases} \dfrac{\partial \varphi}{\partial t} + \dfrac{|\nabla \varphi|^2}{2} - \nabla \varphi \cdot \nabla p = 0, \\[2ex] \dfrac{\partial n}{\partial t} + \nabla \cdot (n(\nabla \varphi - \nabla p)) = 0, \end{cases} \quad \text{and} \quad \begin{cases} p \geq 0, \ p(1-n) = 0, \\[2ex] \varphi(x,T) = \Phi(x), \ n(x,0) = n^0(x). \end{cases} \tag{1.70}$$

The model was first proposed in [143]. Due to the nonvariational formulation of the problem, proving the existence of solutions remains open and remarkably obstinate to solve. A possible approach could be to apply Schauder's fixed point theorem on the pressure p, but it requires strong stability and uniqueness results. For this reason, extending the new regularity results that we obtained in Chapter 4 represents a possible strategy in order to address the problem.

1.6.3 Cahn-Hilliard model and surface tension

In mathematical modelling of living tissues dynamics a crucial aspect to consider is the surface tension between different phases. Indeed, experimental measurements have shown that surface tension plays an important role in cell-segregation and cluster formation, [78]. For this reason, mechanical models of tumor growth that include this effect are more relevant from a biological viewpoint with respect to the models we presented, in which the pressure is always vanishing on the moving boundary. On the other hand, accounting for jump discontinuities of the pressure on the interface also induces several challenging mathematical questions.
One of the most used models that accounts for surface tension is the well known Cahn-Hilliard equation (CH in short). Models of CH type have been widely used in tumor growth modelling; we refer the reader to [51, 79, 152] and references therein.
The model describes the interaction between two phases (tissues, or more broadly fluids) whose densities are denoted by n_1, n_2. In the context of living tissues, we assume that cells constituting the phase $i = 1$ are tumor cells, while the second phase represents the surrounding environment. Therefore, we denote $n = n_1/(n_1 + n_2)$ the relative cell density of interest. The degenerate CH model reads as follows

$$\begin{cases} \dfrac{\partial n}{\partial t} - \nabla \cdot (n \nabla \mu) = nG(\mu), \\ \qquad\qquad\qquad \mu = n^\gamma - \delta \Delta n. \end{cases} \tag{1.71}$$

By definition, the so-called *effective pressure*, μ, is formed by two potentials that represent, respectively, the repulsion between cells, n^γ, and the surface tension, $\delta \Delta n$, where $\sqrt{\delta}$ is the width of the interface in which partial mixing of the two components n_1, n_2 occurs.
The relation between the Cahn-Hilliard equation and the Hele-Shaw model with surface tension has attracted vast interest. In [2], the authors prove that, in the sharp interface limit, level surfaces of solutions to the Cahn-Hilliard equation with constant mobility tend to solutions of the Hele-Shaw problem with surface tension, provided that classical solutions of the latter exist, which was proven in [75]. A similar result was recently obtained by Kroemer and Laux in [108] where the authors prove convergence of weak solutions of the CH equation to the HS model. Let us mention that in these two works no reaction term is taken into account in the equation. A step forward in this direction has been achieved in [72], where the authors consider a relaxed version of the CH model (1.71), and prove convergence of solutions as $\gamma \to \infty$. However, it is still an open question how to directly pass to the stiff limit in the degenerate CH equation (1.71) and to obtain the following HS model

$$\begin{cases} -\Delta \mu &= G(\mu), \quad \text{in } \Omega(t) := \{x;\ p(x,t) > 0\}, \\ \quad \mu &= -\delta \Delta n, \quad \text{on } \partial\Omega(t), \end{cases} \qquad \begin{cases} p(1-n) &= 0, \\ p - \delta \Delta n &= \mu. \end{cases}$$

In particular, it is of interest to find a rigorous way to link the jump of the pressure on the moving boundary to its mean curvature for the model including reaction terms.

Part I

Incompressible limit of tumor growth models including nutrients: analysis and simulations

Chapter 2

Free boundary limit of a tumor growth model with nutrients

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 estimate 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 the space dimension.

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2.1 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 bio-mechanical form of contact inhibition that prevents cell division when the total cell density exceeds a critical threshold. The evolution of the cell population density $n(x,t) \geqslant 0$ and the concentration of nutrients $c(x,t) \geqslant 0$ are described by the following type of system

$$\begin{cases} \dfrac{\partial n}{\partial t} - \nabla \cdot (n \nabla p) = nG(p,c), & x \in \mathbb{R}^d,\ t \geqslant 0, \\ \dfrac{\partial c}{\partial t} - \Delta c + nH(c) = (c_B - c)K(p), \\ c(x,t) \to c_B \quad \text{for } x \to \infty. \end{cases} \tag{2.1}$$

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

$$p = n^\gamma, \qquad \gamma > 1. \tag{2.2}$$

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 in 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 $K \geqslant 0$ is the rate of nutrient release, which decreases with respect to the pressure. As clinical observations have shown, the mechanical stress generated by the cells shrinks the vessels inside the tumor and affects the blood flow; by consequence, the nutrient delivery decreases, see [121] for further details. Finally, the term $H \geqslant 0$ is an increasing function of c and represents the nutrient consumption rate.
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 [130] where the authors take $H = H(p,c)$, $K = 0$ and those in [131] 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.

Motivations and previous works. Models of tumor growth, including (2.1), possibly with more biological relevance, have been widely used recently. Several surveys are available, as [139]. Numerical schemes for the model at hand, with AP property (asymptotic preserving), have been proposed in [112].
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 [92] by Greenspan and further developed by Byrne and Chaplain, [36], Friedman, [81], and Lowengrub et al., [119], 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 $\vec{v} = -\nabla p$. This type of models have been extensively used to describe the early stage of tumor growth, the so-called *avascular phase*, see for example [28, 34, 146]. Models of tumor growth that include the effect of viscosity, [132, 65, 136], or more than one species of tissue cells, [47, 117], are also well-developed. For a comprehensive overview of this topic we refer the reader to [81, 119, 134, 137].
The equation for the density in system (2.1) is based on the continuous mechanical model presented in [37], 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; we refer the reader to [37] 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 cancer growth are free boundary problems, [80]. 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, [38, 39].

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 [130] 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, [132, 65], different laws of state, [67] and more than one species of cells, [31]. 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 (2.2), and prove that the limit solution satisfies a free boundary problem. It has been proved in [130] 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

$$\begin{cases} \dfrac{\partial n_\infty}{\partial t} - \nabla \cdot (n_\infty \nabla p_\infty) = n_\infty G(p_\infty, c_\infty), & x \in \mathbb{R}^d,\ t \geqslant 0, \\ \dfrac{\partial c_\infty}{\partial t} - \Delta c_\infty + n_\infty H(c_\infty) = (c_B - c_\infty) K(p_\infty), & \\ c_\infty(x,t) \to c_B \quad \text{for } x \to \infty, & \end{cases} \tag{2.3}$$

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

$$0 \leqslant n_\infty \leqslant 1, \qquad p_\infty(n_\infty - 1) = 0. \tag{2.4}$$

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

However, it was left open in [130] to establish the so-called *complementarity condition*, which reads (in the sense of distributions)

$$p_\infty\big(\Delta p_\infty + G(p_\infty, c_\infty)\big) = 0 \quad \text{in} \quad \mathcal{D}'(\mathbb{R}^d \times (0,\infty)), \tag{2.5}$$

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

$$\partial_t p_\gamma = \gamma p_\gamma \big(\Delta p_\gamma + G(p_\gamma, c_\gamma)\big) + |\nabla p_\gamma|^2. \tag{2.6}$$

The complementarity condition is fundamental because it relates the weak solutions defined by equations (2.3) and (2.4) to the geometric form of the Hele-Shaw problem, where the set $\Omega(t) := \{x;\, p(x,t) > 0\}$ 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

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

The Hele-Shaw model is a widely studied free boundary problem. Although we are only interested in the weak formulation, the regularity of the boundary is also a challenging issue, see [43, 77, 123].

Difficulties and strategies. To handle this problem, we make use of two new estimates which hold because the cell population density satisfies the following equation of porous medium type

$$\frac{\partial n_\gamma}{\partial t} - \frac{\gamma}{\gamma+1}\Delta n_\gamma^{\gamma+1} = n_\gamma G(p_\gamma, c_\gamma). \tag{2.7}$$

• The first estimate results from the famous Aronson-Bénilan (AB in short) inequalities for the porous media, [9, 58], which have been extended in various contexts (see [120] for another example). It was adapted to a purely mechanical tumor growth model, [130], and it gives the lower bound $\Delta p_\gamma(t) + G(p_\gamma(t)) \geqslant -C/\gamma t$, with C positive constant. Here, unlike in the case without nutrients, it cannot hold. In fact, as shown in [131], where a semi-explicit travelling wave solution was found, there exists a region where p_γ is constantly equal to zero and G is negative. Therefore, we show a weaker, but still sufficient, condition

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

This is proved by working in L^2 rather than with a sub-solution, as it has been recently initiated in [31, 94]. This method has the advantage to be compatible with the L^2-estimates on c_γ and its derivatives. We recall that Δp_∞ is a bounded measure due to the free boundary of the set $\Omega(t)$ 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 estimate.

Plan of the paper. The paper is organized as follows. The next section is devoted to explain the notation 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 2.3 presenting standard bounds which are useful for deriving the main new estimates that are stated and proved in Section 2.4. Finally, in Section 2.5 we give the proof of the complementarity relation.

2.2 Notation, assumptions and main result

Notation. We denote $Q = \mathbb{R}^d \times (0,\infty)$, and for $T > 0$ we set $Q_T = \mathbb{R}^d \times (0,T)$. Given a bounded subset $\Omega \subset \mathbb{R}^d$, we denote $\Omega_T := \mathbb{R}^d \times (0,T)$. We frequently use the abbreviated form $n(t) := n(x,t)$, $p(t) := p(x,t)$, $c(t) := c(x,t)$.

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

$$\partial_p G < -\beta, \qquad \partial_c G \geqslant 0, \qquad G(p, c_B) \leqslant 0, \text{ for } p \geqslant p_H, \tag{2.8}$$

$$K'(p) \leqslant 0, \qquad 0 \leqslant K(p) \leqslant 1, \qquad K(p) = 0, \text{ for } p \geqslant p_B, \tag{2.9}$$

$$H'(c) \geqslant 0, \qquad 0 \leqslant H(c), \qquad H(0) = 0. \tag{2.10}$$

Furthermore, for a given pressure p, $G(p,c) < 0$ for c small enough. This assumption indicates that 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, c_2 are positive constants and g is a decreasing function of p, see [52, 121, 130].

Initial data. System (2.1) is endowed with initial data n_γ^0, c_γ^0. We assume that for some n^0, c^0, the initial data n_γ^0, c_γ^0 satisfy

$$0 \leqslant n_\gamma^0 \leqslant n_H := p_H^{1/\gamma}, \qquad \|n_\gamma^0 - n^0\|_{L^1(\mathbb{R}^d)} \xrightarrow[\gamma\to\infty]{} 0, \qquad n^0 \in L^1_+(\mathbb{R}^d), \tag{2.11}$$

$$0 \leqslant c_\gamma^0 \leqslant c_B, \qquad \|c_\gamma^0 - c^0\|_{L^1(\mathbb{R}^d)} \xrightarrow[\gamma\to\infty]{} 0, \qquad c^0 - c_B \in L^1_+(\mathbb{R}^d). \tag{2.12}$$

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

$$\|\nabla p_\gamma^0\|_{L^2(\mathbb{R}^d)} + \|\Delta p_\gamma^0\|_{L^2(\mathbb{R}^d)} \leqslant C, \tag{2.13}$$

$$\|(\partial_t n_\gamma)^0\|_{L^1(\mathbb{R}^d)} + \|(\partial_t c_\gamma)^0\|_{L^1(\mathbb{R}^d)} \leqslant C, \tag{2.14}$$

$$\|\nabla c_\gamma^0\|_{L^2(\mathbb{R}^d)} \leqslant C. \tag{2.15}$$

Set these conditions on the initial data, we give the definition of weak solution of system (2.1) as follows.

Definition 2.2.1. Given $T > 0$, a weak solution of system (2.1) is a triple $(n_\gamma, p_\gamma, c_\gamma)$ such that,

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

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

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

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

From standard methods, see [94, 135, 149], 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 $\gamma > 1$

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

Unlike the solutions of the heat equation, the PME's solutions have a finite speed of propagation, see [149]. This means that, for all $T > 0$, there exists a smooth bounded open domain Ω independent of γ such that

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

see Appendix 2.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 2.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 2.2.2 (Estimates and complementarity relation)**.** *With all the previous assumptions, the limit pressure p_∞ satisfies the relation (2.5), that means, for all test functions $\zeta \in \mathcal{D}(Q)$, we have*

$$\iint_Q \left(-|\nabla p_\infty|^2 \zeta - p_\infty \nabla p_\infty \nabla \zeta + p_\infty G(p_\infty, c_\infty)\zeta\right) \mathrm{d}x\, \mathrm{d}t = 0.$$

Furthermore the following estimates hold uniformly in γ

$$\iint_{\Omega_T} (\Delta p_\gamma + G(p_\gamma, c_\gamma))_-^3 \, \mathrm{d}x\, \mathrm{d}t \leqslant C(T), \qquad \iint_{\Omega_T} |\nabla p_\gamma|^4 \, \mathrm{d}x\, \mathrm{d}t \leqslant C(T).$$

2.3 Preliminary Estimates

Let $(n_\gamma, p_\gamma, c_\gamma)$ be a weak solution to system (2.1). We recall some standard preliminary bounds on $n_\gamma, p_\gamma, c_\gamma$ and their derivatives, gathered in the following Proposition.

Proposition 2.3.1 (Direct estimates)**.** *Let $(n_\gamma, p_\gamma, c_\gamma)$ be a weak solution of system (2.1). For all $T > 0$, the following holds independently of γ*

$$0 \leqslant n_\gamma \leqslant n_H, \; 0 \leqslant p_\gamma \leqslant p_H, \; 0 \leqslant c_\gamma \leqslant c_B, \tag{2.16}$$

$$n_\gamma, \; p_\gamma, \; c_\gamma(t) - c_B \in L^\infty(0, T, L^1(\mathbb{R}^d)), \tag{2.17}$$

$$c_\gamma \in L^\infty(0, T, H^1(\mathbb{R}^d)) \cap L^2(0, T, H^2(\mathbb{R}^d)), \tag{2.18}$$

$$\partial_t n_\gamma, \; \partial_t p_\gamma \in L^1(Q_T), \quad \partial_t c_\gamma \in L^2(Q_T) \tag{2.19}$$

$$c_\gamma \in L^4(Q_T), \quad p_\gamma \in L^2(0, T, H^1(\mathbb{R}^d)). \tag{2.20}$$

Proof. **L^∞-bounds for $n_\gamma, p_\gamma, c_\gamma$.** The L^∞-bounds follow from the comparison principle and our assumptions on G. For the sake of completeness, we recall the argument. From equation (2.7) we have

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

Multiplying by $\text{sign}_+\{n_\gamma - n_H\}$ we obtain

$$\begin{aligned}\partial_t(n_\gamma - n_H)_+ - \frac{\gamma}{\gamma+1}\Delta((n_\gamma^{\gamma+1} - n_H^{\gamma+1})_+) \leqslant & G(p_\gamma, c_\gamma)(n_\gamma - n_H)_+ \\ & + n_H(G(p_\gamma, c_\gamma) - G(p_H, c_\gamma))\text{sign}_+(n_\gamma - n_H).\end{aligned}$$

since, thanks to the assumptions on G, we have $G(p_H, c_\gamma) \leqslant 0$.
Integrating in space yields

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} (n_\gamma(t) - n_H)_+ \, \mathrm{d}x \leqslant \|G\|_\infty \int_{\mathbb{R}^d} (n_\gamma(t) - n_H)_+ \, \mathrm{d}x,$$

because $(G(p_\gamma, c_\gamma) - G(p_H, c_\gamma))\text{sign}_+(n_\gamma - n_H) \leqslant 0$, since G is decreasing with respect to p_γ. By the assumption (2.11) and thanks to Gronwall's lemma, we find $n_\gamma \leqslant n_H$ and therefore $p_\gamma \leqslant p_H$.

Using the same argument with the $\mathrm{sign}_-(n_\gamma)$ we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}(n_\gamma(t))_-\,\mathrm{d}x \leqslant C\int_{\mathbb{R}^d}(n_\gamma(t))_-\,\mathrm{d}x.$$

By Gronwall's lemma we deduce

$$\int_{\mathbb{R}^d}(n_\gamma(t))_-\,\mathrm{d}x \leqslant e^{Ct}\int_{\mathbb{R}^d}(n_\gamma^0)_-\,\mathrm{d}x,$$

and, since the initial data is non-negative by assumption (2.11), this yields $n_\gamma \geqslant 0$ and $p_\gamma \geqslant 0$. The same argument applies to c_γ and then we have $c_\gamma \geqslant 0$. From the equation for c_γ it holds

$$\partial_t(c_\gamma - c_B)_+ - \Delta(c-c_B)_+ \leqslant -\,n_\gamma H(c_\gamma)\mathrm{sign}_+(c_\gamma - c_B) - K(p)(c_\gamma - c_B)_+.$$

Since H, K and n_γ are always non-negative, we get

$$\partial_t(c_\gamma - c_B)_+ - \Delta(c-c_B)_+ \leqslant 0,$$

which gives

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}(c-c_B)_+\,\mathrm{d}x \leqslant 0.$$

Since $c_\gamma^0 \leqslant c_B$, by assumption (2.12), we conclude that $c_\gamma \leqslant c_B$. **L^1-bounds on $n_\gamma, p_\gamma, c_\gamma$.**

These are also standard estimates, noting that

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

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

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

Integrating by parts and using Young's inequality we obtain

$$\begin{aligned}&\int_0^t\int_{\mathbb{R}^d}\partial_t\left(\frac{|\nabla c_\gamma|^2}{2}\right)\mathrm{d}x\,\mathrm{d}s + \int_0^t\int_{\mathbb{R}^d}|\Delta c_\gamma|^2\,\mathrm{d}x\,\mathrm{d}s\\ &\qquad\leqslant \int_0^t\int_{\mathbb{R}^d}\frac{|n_\gamma H(c_\gamma) - (c_B - c_\gamma)K(p_\gamma)|^2}{2}\,\mathrm{d}x\,\mathrm{d}s + \int_0^t\int_{\mathbb{R}^d}\frac{|\Delta c_\gamma|^2}{2}\,\mathrm{d}x\,\mathrm{d}s.\end{aligned}$$

Hence, we have

$$\begin{aligned}&\frac{1}{2}\int_{\mathbb{R}^d}|\nabla c_\gamma(t)|^2\,\mathrm{d}x + \frac{1}{2}\int_0^t\int_{\mathbb{R}^d}|\Delta c_\gamma|^2\,\mathrm{d}x\,\mathrm{d}s\\ &\qquad\leqslant C\int_0^t\left(\|n_\gamma(s)\|^2_{L^1(\mathbb{R}^d)} + \|c_\gamma(s) - c_B\|^2_{L^1(\mathbb{R}^d)}\right)\mathrm{d}s + \frac{1}{2}\|\nabla c_\gamma^0\|^2_{L^2(\mathbb{R}^d)},\end{aligned}$$

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 (2.17), we obtain

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

for $0 < t \leqslant T$, and thanks to (2.15) we conclude the proof of the first and second estimates in (2.18).

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 $\mathrm{sign}(\partial_t n_\gamma)$

$$\partial_t |\partial_t n_\gamma| - \gamma \Delta(n_\gamma^\gamma |\partial_t n_\gamma|) \leqslant |\partial_t n_\gamma| G + n_\gamma \partial_p G |\partial_t p_\gamma| + n_\gamma \partial_c G \partial_t c_\gamma \mathrm{sign}(\partial_t n_\gamma). \tag{2.21}$$

We integrate in space using the monotonicity of G

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

Thanks to (2.17) and (2.18), Gronwall's lemma gives

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

where in the last inequality we used (2.14).

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

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

thanks to (2.14) and the L^1 bounds proved above. Then, for the time derivative of the pressure, it holds

$$\|\partial_t p_\gamma\|_{L^1(Q_T)} \leqslant \iint_{Q_T \cap \{n_\gamma \leqslant 1/2\}} \gamma n_\gamma^{\gamma-1} |\partial_t n_\gamma| \,\mathrm{d}x \,\mathrm{d}t + 2 \iint_{Q_T \cap \{n_\gamma \geqslant 1/2\}} n_\gamma |\partial_t p_\gamma| \,\mathrm{d}x \,\mathrm{d}t \leqslant C(T).$$

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

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

Integrating in space we obtain

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

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

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

and this concludes the proof of (2.19).

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

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

We use Young's inequality on the first term of the right-hand side and we get

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

We write the last term as

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

Thus, we have

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

and the L^4-estimate is proven.

L^2-bound for the pressure gradient. Since the pressure satisfies equation (2.6), integrating it in space we get

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

Then, we integrate in time

$$\begin{aligned}
&(\gamma - 1)\int_0^T \int_{\mathbb{R}^d} |\nabla p_\gamma|^2 \, \mathrm{d}x \, \mathrm{d}t = \|p_\gamma(0)\|_{L^1(\mathbb{R}^d)} - \|p_\gamma(T)\|_{L^1(\mathbb{R}^d)} + \gamma \int_0^T \int_{\mathbb{R}^d} p_\gamma G(p_\gamma, c_\gamma) \, \mathrm{d}x \, \mathrm{d}t, \\
&(\gamma - 1)\int_0^T \int_{\mathbb{R}^d} |\nabla p_\gamma|^2 \, \mathrm{d}x \, \mathrm{d}t \leqslant C_0 + \gamma C(T),
\end{aligned}$$

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

$$\int_0^T \int_{\mathbb{R}^d} |\nabla p_\gamma|^2 \, \mathrm{d}x \, \mathrm{d}t \leqslant C(T).$$

□

2.4 Stronger a priori estimates on p_γ

To establish the complementarity condition (2.5) 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, [9, 58]. 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 [130, 131]. Moreover, we cannot apply the comparison principle because of the bad coupling in system (2.1). Since the L^∞ bound from below in the AB estimate is missing, we prove an L^3 version, adapting the method presented in [94]. 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

$$w := \Delta p_\gamma + G(p_\gamma, c_\gamma), \tag{2.22}$$

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 (2.6).

Theorem 2.4.1 (Aronson-Bénilan estimate in L^3). *With the assumptions of Section 2.2 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*

$$\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T), \qquad \iint_{\Omega_T} |\Delta p_\gamma| \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T). \tag{2.23}$$

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

$$(\gamma - 1) \iint_{\Omega_T} p_\gamma |\Delta p_\gamma + G|^2 \,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} p_\gamma \sum_{i,j} (\partial^2_{i,j} p_\gamma)^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T), \tag{2.24}$$

$$\iint_{\Omega_T} |\nabla p_\gamma|^4 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T), \tag{2.25}$$

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

We recall that in the model independent of c_γ, [130], the AB estimate is much stronger and gives $\Delta p_\gamma(t) + G(p_\gamma(t)) \geqslant -\frac{1}{\gamma t}$, and the major difficulty is the control of Δp_γ which is provided by Theorem 2.4.1. As proved in [123], 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 use another argument, which is reminiscent of the energy control, but treats differently of the "dissipation" terms.

Proof of Theorem 2.4.1. For the sake of simplicity we forget the index γ and $\mathrm{d}x\,\mathrm{d}t$ in the integration. 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

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

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

$$\begin{aligned}\partial_t w \geqslant &\frac{2}{d}(w-G)^2 + 2\nabla p\cdot\nabla w - \partial_p G|\nabla p|^2 - 2\partial_c G\nabla p\cdot\nabla c \\ &+\gamma\Delta(pw) + \gamma pw\,\partial_p G + \partial_c G\,\partial_t c.\end{aligned} \tag{2.26}$$

Multiplying (2.26) by $-(w)_-$, we obtain

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

Hence, using the fact that $\partial_p G < -\beta$ from (2.8), we integrate in space to obtain

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

Now, we proceed integrating by parts the first term,

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

Next, using (2.18) and the Cauchy-Schwarz inequality, we obtain

$$\mathcal{B} \leqslant C\int_\Omega (w)_-^2 + C.$$

Thanks to Young's inequality and (2.20), we compute

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

We may now come back to the control of $\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \frac{(w)_-^2}{2}$. Gathering all the previous bounds, we get the following estimate

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \frac{(w)_-^2}{2} \leqslant -\left(\frac{2}{d}-1+\frac{\gamma}{2}\right)\int_\Omega (w)_-^3 - \frac{\beta}{2}\int_\Omega |\nabla p|^2 (w)_- + C(\gamma+1)\int_\Omega (w)_-^2 + C.$$

Hence integrating in time we have

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

where we used assumption (2.13) 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

$$\iint_{\Omega_T}(w)_-^3 \leqslant C\left(\iint_{\Omega_T}(w)_-^3\right)^{\frac{2}{3}} + C(T),$$

and hence we have proved our main result, that is the first estimate of (2.23),

$$\iint_{\Omega_T}(w)_-^3 \leqslant C(T).$$

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

$$\iint_{\Omega_T}(\Delta p + G) \leqslant C(T),$$

we can also control the positive part of w

$$\iint_{\Omega_T}(w)_+ \leqslant C(T) + \iint_{\Omega_T}(w)_- \leqslant C(T) + C\left(\iint_{\Omega_T}(w)_-^3\right)^{\frac{1}{3}}.$$

Thus it holds

$$\iint_{\Omega_T}|\Delta p + G| \leqslant C(T).$$

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

$$\iint_{\Omega_T}|\Delta p| \leqslant C(T),$$

that concludes the proof of Theorem 2.4.1.

Proof of Theorem 2.4.2. We consider the equation for the pressure (2.6), we multiply it by $-(\Delta p_\gamma + G(p_\gamma, c_\gamma))$ and integrate in space. We find successively

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

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

We integrate by parts the last term of the left-hand side and obtain

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

Hence, we conclude that

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

Thus, we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \frac{|\nabla p_\gamma|^2}{2} \underbrace{- \int_\Omega \partial_t p_\gamma\, G}_{I_1} + \underbrace{\gamma\int_\Omega p_\gamma|\Delta p_\gamma + G|^2 - \frac{2}{3}\int_\Omega p_\gamma|\Delta p_\gamma|^2}_{I_2} + \frac{2}{3}\int_\Omega p_\gamma\sum_{i,j}(\partial^2_{i,j}p_\gamma)^2 \leqslant C(T). \tag{2.27}$$

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

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

thanks to the L^2-bound on $\partial_t c_\gamma$ in (2.18) and because $|\partial_c\overline{G}| \leqslant Cp_\gamma$. We can estimate the term I_2 from below as follows

$$I_2 \geqslant (\gamma-1)\int_\Omega p_\gamma|\Delta p_\gamma + G|^2 - C\int_\Omega p_\gamma|G|^2.$$

Thus, we find

$$I_1 + I_2 \geqslant (\gamma-1)\int_\Omega p_\gamma|\Delta p_\gamma + G|^2 - \int_\Omega \partial_t\overline{G} - C(T). \tag{2.28}$$

Combining (2.27) and (2.28), we have

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

Finally, integrating in time, we obtain estimate (2.24), and this proves the first step of Theorem 2.4.2.

Furthermore, this bound also implies

$$\iint_{\Omega_T} p_\gamma |\Delta p_\gamma|^2 \leqslant C(T). \tag{2.29}$$

We compute the L^4-norm of the gradient of p_γ, as we did for the gradient of c_γ,

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

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

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

The last term can be bounded from above as follows

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

Therefore, we obtain

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

Since $p_\gamma \leqslant p_H$, by (2.24) and (2.29) we conclude

$$\iint_{\Omega_T} |\nabla p_\gamma|^4 \leqslant C(T),$$

and this completes the proof of Theorem 2.4.2.

2.5 Complementarity relation

Thanks to the bounds provided by Theorem 2.4.1 and Theorem 2.4.2, 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 2.5.1 (Complementarity relation)**.** *With the assumptions of Theorem 2.4.1, the complementarity condition (2.5) holds. More precisely, for all test functions $\zeta \in \mathcal{D}(Q)$, the limit pressure p_∞ satisfies*

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

This result is related to the geometric form of the Hele-Shaw free boundary problem (while (2.3) is the weak form). It tells us that the limit solution satisfies

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

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

$$p_\infty(1 - n_\infty) = 0.$$

Therefore, $\Omega(t) \subset \{x; n_\infty(x,t) = 1\}$, hence the classification of *incompressible* model. In the purely mechanical case the two sets actually coincide almost everywhere, see [123].

Proof of Theorem 2.5.1. Thanks to the bounds in (2.18), (2.19) and (2.20), p_γ and c_γ are locally compact. Thus, after the extraction of subsequences, we have

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

when $\gamma \to \infty$, for all $T > 0$. From Theorem 2.4.2, we also recover the weak convergence of the gradient of the pressure, up to a subsequence, *i.e.*

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

From Theorem 2.4.1, 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 equation (2.6), we have

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

where the right-hand side is a sum of space derivatives of functions bounded in L^1. In fact, since by (2.19) and (2.20), $\partial_t p_\gamma$ and $|\nabla p_\gamma|^2$ are in L^1, from (2.6) the term $\gamma p_\gamma(\Delta p_\gamma + G)$ is also bounded in L^1. Thus, we can extract a subsequence such that

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

After the extraction of a subsequence, we obtain convergence almost everywhere for ∇p_γ. Then, using the L^4-bound of Theorem 2.4.2, we have

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

hence, in particular, also for $q = 2$.
Let $\zeta \in \mathcal{D}(Q)$ be a test function. We consider the equation for p_γ

$$\frac{\partial p_\gamma}{\partial t} = \gamma p_\gamma(\Delta p_\gamma + G(p_\gamma, c_\gamma)) + |\nabla p_\gamma|^2,$$

we multiply it by ζ and we integrate in Q

$$-\frac{1}{\gamma}\iint_Q \left(p_\gamma \partial_t \zeta + |\nabla p_\gamma|^2 \zeta\right) \mathrm{d}x \, \mathrm{d}t = \iint_Q \left(-|\nabla p_\gamma|^2 \zeta - p_\gamma \nabla p_\gamma \cdot \nabla \zeta + p_\gamma G(p_\gamma, c_\gamma)\zeta\right) \mathrm{d}x \, \mathrm{d}t.$$

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

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

This is equivalent to
$$\iint_Q p_\infty \left(\Delta p_\infty + G(p_\infty, c_\infty)\right) \zeta \,\mathrm{d}x\,\mathrm{d}t = 0,$$
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 2.5.1 is complete.

2.A Compact support property

We give the proof of the finite speed of propagation property of solutions of system (2.1). Our goal is to show that, if the initial data satisfy
$$\operatorname{supp}(n_\gamma^0) \subset \Omega_0, \quad \forall \gamma > 1,$$
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 independent of γ such that
$$\operatorname{supp}(n_\gamma(t)) \subset \Omega, \quad \forall \gamma > 1, \, \forall t \in [0, T].$$
For every $\gamma > 1$, the pressure p_γ is a sub-solution to equation
$$\partial_t p_\gamma \leqslant |\nabla p_\gamma|^2 + \gamma p_\gamma (\Delta p_\gamma + G(0, c_B)).$$
Thus, by finding a supersolution 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
$$S'(t) \geqslant 2G(0, c_B) S(t).$$
We compute the derivatives of Π and we find
$$\begin{aligned}
\partial_t \Pi(x,t) &= G(0, c_B) S'(t) \mathbb{1}_{\{S(t) \geqslant \frac{|x|^2}{2}\}}, \\
\nabla \Pi(x,t) &= -G(0, c_B) x \mathbb{1}_{\{S(t) \geqslant \frac{|x|^2}{2}\}}, \\
\Pi \Delta \Pi(x,t) &= \Pi \left(-d \; G(0, c_B) \mathbb{1}_{\{S(t) \geqslant \frac{|x|^2}{2}\}} + G(0, c_B)|x| \delta_{\{S(t) = \frac{|x|^2}{2}\}} \right) = -dG(0, c_B)\Pi.
\end{aligned}$$
Therefore Π satisfies
$$\begin{aligned}
\partial_t \Pi - |\nabla \Pi|^2 - \gamma \Pi (\Delta \Pi + G(0, c_B)) &\geqslant (G(0, c_B) S'(t) - G(0, c_B)^2 x^2) \mathbb{1}_{\{S(t) \geqslant \frac{|x|^2}{2}\}} + \gamma \Pi G(0, c_B)(d+1) \\
&\geqslant (2G(0, c_B)^2 S(t) - G(0, c_B)^2 x^2) \mathbb{1}_{\{S(t) \geqslant \frac{|x|^2}{2}\}} \\
&\geqslant 0.
\end{aligned}$$

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 $\sqrt{2S(T)}$.

2.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 2.2. Our goal is to generalize the result removing this condition. Let us note that it is sufficient to extend Theorem 2.4.1, since it is the only one for which we used the compact support assumption. Moreover, let us notice that Proposition 2.3.1 holds true in this framework. We define the functional w as in (2.22) and we state the following result.

Proposition 2.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 (2.8) to (2.15), and with $\gamma > \max(1, 2-\frac{4}{d})$, for all $T > 0$ there exists a constant $C(T)$ depending on previous bounds and independent of γ such that*

$$\int_0^T \int_{\mathbb{R}^d} (w)_-^3\, \Phi \leqslant C(T), \qquad \int_0^T \int_{\mathbb{R}^d} |\Delta p| \Phi \leqslant C(T).$$

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

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

as in the proof of Theorem 2.4.1. We multiply the inequality by Φ and integrate in space

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t} \int_\Omega \frac{(w)_-^2}{2} \Phi \leqslant & -\frac{2}{d} \int_\Omega (w)_-^3\, \Phi - \frac{2}{d} \int_\Omega G^2 (w)_- \Phi - \beta \int_\Omega |\nabla p|^2 (w)_- \Phi \\ & - \frac{4}{d} \int_\Omega G (w)_-^2\, \Phi + \underbrace{\int_\Omega \left[\nabla p \cdot \nabla \left((w)_-^2\right) \Phi + \gamma \Delta (p(w)_-)(w)_- \Phi\right]}_{\mathcal{A}} \\ & \underbrace{- \int_\Omega \partial_c G\, \partial_t c(w)_- \Phi}_{\mathcal{B}} + \underbrace{2 \int_\Omega \partial_c G \nabla p \cdot \nabla c (w)_- \Phi}_{\mathcal{C}}.\end{aligned} \tag{2.30}$$

Now we proceed computing each term,

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

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

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

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

Using Young's inequality and (2.20), we find

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

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 $|\nabla\Phi| \leqslant C\Phi$ and $|\Delta\Phi| \leqslant C\Phi$. Now, we integrate by parts and use Young's inequality

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

Finally, inequality (2.30) can be written as follows

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

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

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

and then we have proved

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

By consequence

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

Since Φ is a smooth function with compact support

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

and then also

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

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

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

□

2.C Sharpness of the bound $\nabla p \in L^4$

In Theorem 2.4.2, we have established the uniform bound $\nabla p_\gamma \in L^4_{x,t}$, see (2.25). Here, we aim at showing that the exponent 4 cannot be increased. We use the so-called *focusing solution* of the porous medium equation, see for instance [11], which consists in a spherical hole filling which generates a stronger singularity than the Barenblatt solution, see [149]. We consider the limit $\gamma \to \infty$, *i.e.* the Hele-Shaw problem, that was already studied in detail in [10] for a larger class of operators.

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

$$\begin{cases} -\Delta p = 1, & \text{for} \quad R(t) < |x| < R_1, \\ p(x) = 0, & \text{for} \quad |x| = R(t) \ \text{ or } |x| = R_1, \\ R'(t) = -\nabla p \cdot \nu, & \text{for} \quad |x| = R(t). \end{cases} \tag{2.31}$$

Here, ν denotes the inner normal to the ball $B_{R(t)}(0)$. As in [11], $R(t)$ 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 worst singularity would be obtained for a cylinder with a 2 dimensional basis.

Case $d = 2$. With spherical symmetry, we set $p = p(r)$, $r := |x|$, and the first equation in (2.31) 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

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

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

$$a(t) \approx -\frac{R_1^2}{4\ln R(t)}, \qquad\qquad R'(t) \approx \frac{1}{R(t)\ \ln R(t)}. \tag{2.32}$$

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 (2.32). We recall that we have chosen $R(0)$ small enough.
This integral is finite for $1 \leqslant \alpha \leqslant 4$ and infinite for $\alpha > 4$.

Chapter 3

An asymptotic preserving scheme for a tumor growth model of porous medium type

Abstract

Mechanical models of tumor growth based on a porous medium approach have been attracting a lot of interest both analytically and numerically. In this paper, we study the stability properties of a finite difference scheme for a model where the density evolves down pressure gradients and the growth rate depends on the pressure and possibly nutrients. Based on the stability results, we prove the scheme to be asymptotic preserving (AP) in the incompressible limit. Numerical simulations are performed in order to investigate the regularity of the pressure. We study the sharpness of the L^4-uniform bound of the gradient, the limiting case being a solution whose support contains a bubble which closes-up in finite time generating a singularity, the so-called focusing solution.

This chapter is taken from N. D. and X. Ruan. *An asymptotic preserving scheme for a tumor growth model of porous medium type*, ESAIM: M2AN, (2021).

3.1 Introduction

We consider a model of tumor growth describing the evolution of the cell population density $n(x,t)$ through a porous medium equation with a source,

$$\frac{\partial n}{\partial t} - \nabla(n\nabla p) = nG(p), \qquad x \in \mathbb{R}^d, t > 0, \tag{3.1}$$

where p is the internal pressure of the tumor, defined by the law of state

$$p = n^\gamma, \qquad \gamma > 1. \tag{3.2}$$

The non-linearity and degeneracy of the diffusion term bring several difficulties to the numerical analysis of the model, and many numerical schemes have been proposed in the literature, *cf.* [112, 25, 113, 124]. In this paper, we investigate the properties of solutions of Eq. (3.1), which for simplicity we consider in one dimension, using the following upwind scheme

$$\frac{d}{dt}n_i = \frac{n_{i+1/2}q_{i+1/2} - n_{i-1/2}q_{i-1/2}}{\Delta x} + n_i G(p_i), \qquad \text{with} \qquad q_{i+1/2} = \frac{p_{i+1} - p_i}{\Delta x},$$

and where we define $n_{i+\frac{1}{2}}$ in the upwind manner

$$n_{i+1/2} = \begin{cases} n_i, & \text{if } q_{i+1/2} \leqslant 0, \\ n_{i+1}, & \text{if } q_{i+1/2} > 0. \end{cases}$$

Extension to higher dimensions is straightforward for tensor product grids and thus omitted here. On the one hand, the simplicity of the scheme allows us to prove analytical properties which do not apply to more complex ones. We prove stability results and the asymptotics preserving (AP) property of the scheme as $\gamma \to \infty$. On the other hand, despite its simplicity, we perform numerical tests that show the good efficiency of the scheme for different reaction terms G as well as for $\gamma \gg 1$.

We are also interested in analysing numerically the regularity of the so-called *focusing solution* of Eq. (3.1), whose support is initially contained outside of a compact set, see for instance [11]. Due to the degeneracy of the diffusion, the inner hole closes up in finite time and singularities occur due to this topological change. In particular, we perform numerical tests to study the blow-up of the L^p-norms of the pressure gradient, which are uniformly (with respect to γ) bounded for $p \leq 4$, as recently proved in [61]. This regularity is actually sharp, and the focusing solution represents the limiting case since the L^p-norms of its gradient blow up for $p > 4$ as $\gamma \to \infty$. Our aim is to obtain a numerical verification of the study of the optimal exponent from [61].

Motivations. Models as Eq. (3.1), possibly including advection terms or coupled with a second equation, have been largely applied to the description of tissue and tumor growth. They are based on the mechanical aspects that drive cell motion and proliferation. Describing the fact that cells move down pressure gradients, the flow velocity in Eq. (3.1) is given by Darcy's law, namely $\vec{v} = -\nabla p$.

Besides driving the cells movement, the pressure also controls the cell proliferation through an inhibitory effect, since the division rate is lower at higher pressure values. Therefore, we make the following assumption on the growth rate G: there exist positive constants α and p_H such that

$$G'(p) \leqslant -\alpha, \qquad G(p_H) = 0, \tag{3.3}$$

where p_H represents the so-called *homeostatic pressure*, namely the lowest level of pressure that prevents cell multiplication due to contact inhibition.

Later in the paper, we also consider an extension of the model where G depends both on the pressure and the concentration of a nutrient (for instance, oxygen or glucose), denoted by $c(x,t)$. In this case, Eq. (3.1) would be coupled with an equation on c that depends both on the environmental conditions (*in vitro* or *in vivo*) and on the stage of the tumor development (*avascular* or *vascular*). We refer the reader to [131] for the formulation of the Hele-Shaw problem with nutrient and its traveling wave solutions.

As mentioned above, the density actually satisfies a porous medium type equation, which can be directly recovered combining the pressure law, Eq. (3.2), and Eq. (3.1), namely

$$\frac{\partial n}{\partial t} = \frac{\gamma}{\gamma+1}\Delta n^{\gamma+1} + nG(p).$$

As the solution of the classical porous medium equation (PME), n evolves with finite speed of propagation, since the diffusion term degenerates when $n = 0$. Thus, if the initial data has compact support, the solution remains compactly supported at any time and exhibits a moving front, which is the interface that separates $\{n > 0\}$ and $\{n = 0\}$.
As shown in [130], as $\gamma \to \infty$, the pressure p_γ of Eq. (3.1) converges strongly in L^1 to a function p_∞ which is a solution of a Hele-Shaw free boundary problem defined on the set $\Omega(t) := \{x,\ p_\infty(x,t) > 0\}$, in which p_∞ satisfies an elliptic equation. The so-called *incompressible limit* of Eq. (3.1) has attracted a lot of interest in the last decades and a vast literature on the topic is now available, *cf.* [130, 67, 102]. The Hele-Shaw limit has also been studied for several extensions of the model at hand, we refer the reader to [61, 60, 63, 129, 132, 31, 66] for models including nutrients, viscosity, active motion, convective effects or a second species of cells.
The complete proof can be found in [130, 102], while here we present a formal argument to explain the link between the compressible model and the free boundary formulation. Upon multiplying Eq. (3.1) by $\gamma n^{\gamma-1}$, we recover the equation satisfied by the pressure, which reads

$$\frac{\partial p}{\partial t} = \gamma p(\Delta p + G(p)) + |\nabla p|^2. \tag{3.4}$$

Then passing formally to the limit $\gamma \to \infty$ we find the *complementarity relation*

$$p_\infty(\Delta p_\infty + G(p_\infty)) = 0.$$

This implies that the limit pressure has to satisfy the elliptic equation $-\Delta p_\infty = G(p_\infty)$ in the tumor region $\Omega(t)$.

Our contribution.

∘ *Asymptotic preserving property.* In this paper, we show that, as $\gamma \to \infty$, the aforementioned scheme is asymptotic preserving and the solution converges to a solution of the following finite difference equation

$$p_i(\delta_x^2 p_i + G(p_i)) = 0,$$

where we denote $\delta_x^2 p_i := (p_{i+1} - 2p_i + p_{i-1})/|\Delta x|^2$.

∘ *Aronson-Bénilan estimate.* The derivation of the complementarity relation in the continuous case is deeply related to a lower bound on the quantity $w := \Delta p + G(p)$, namely $w \gtrsim -\frac{C}{\gamma t}$, *cf.* [130]. This bound is an adaptation of the Aronson-Bénilan (AB in short) estimate, which is a well-known and powerful tool in the theory of porous medium equations.
It is our aim to recover a discrete version of this lower bound for our scheme. This purpose has been already addressed in the literature, in particular we refer the reader to [124] for a tracking front scheme for which the author proves the Aronson-Bénilan estimate for the classical porous medium equation (namely, with no reaction terms), and for any $\gamma > 1$. Unlike [124], we keep a fixed grid and show that the AB estimate holds also for a restricted class of pressure-penalized growth rates $G = G(p)$, only in the cases $\gamma = 1$ and $\gamma \approx \infty$ which is our interest for the Hele-Shaw limit. To the best of our knowledge, we are the first to prove the discrete version of the AB estimate for a nontrivial pressure-dependent reaction term in the porous medium equation. It is not the main goal of this paper to prove the convergence of the scheme as $\Delta x \to 0$, nevertheless,

we want to point out that this estimate could be useful in this direction.

∘ *Focusing solution.* The solutions of Eq. (3.1) exhibit different kind of singularities in the incompressible limit $\gamma \to \infty$. For instance, the limit density n_∞ shows jump discontinuities across the boundary of the tumor region $\partial\Omega(t)$, while the pressure p_∞ can develop singularities in time. In fact, when a new saturated region is generated outside $\Omega(t)$, *i.e.* when $n_\infty(\cdot, s)$ becomes 1 in a set of positive measure contained outside the original tumor region, for some $s > t$, the pressure instantaneously becomes positive in the same set, according to the relation $p_\infty(1 - n_\infty) = 0$. Moreover, time discontinuities can also appear when the set $\Omega(t)$ undergoes certain topological changes, for instance when the support contains a hole which closes up at time $t = T^*$, which is called *focusing time*. This particular solution is referred to as *focusing solution*. The hole filling problem has attracted a lot of attention since it represents the limiting case for several regularity results. For instance, in [11], Aronson and Graveleau use the focusing solution to show that the Hölder continuity of the pressure gradient is optimal, for dimension $d \geqslant 2$. In fact, the pressure gradient blows up at the focusing time T^*.
In [61], the authors prove that the L^4-norm of ∇p_γ is uniformly bounded with respect to γ. Then, they show that this uniform estimate is optimal using the focusing solution as a counter-example. Through an asymptotic argument on a radial solution, they compute that 4 is the highest possible order of integrability for the gradient of the pressure of the Hele-Shaw problem. One of the main interests of this paper is to numerically investigate and confirm this property of the focusing solution. To this end, we perform 2-dimensional simulations with initial data given by the characteristic function of a spherical shell. The results obtained by computing the L^p-norms of the pressure gradient clearly show its singularity at the focusing time and confirm the worsening of the blow-up as the exponents become greater than 4. At the best of our knowledge, there are no numerical inspections of this sharpness result in the literature, although the focusing solution has been deeply studied both analytically and numerically [11, 10, 8].

Previous works. The numerical simulation of the tumor growth model (3.1) is challenging in two aspects, the lack of regularity of solutions near the free boundary, which is a common difficulty of porous medium equations, and the stiffness appearing in the Hele-Shaw limit $\gamma \to \infty$. The numerical study of porous medium equations lasts for decades and a variety of algorithms have been proposed. An early study of the finite difference method can be found in [91]. Further studies on the finite difference method include the interface tracking algorithm, [15, 124], which works perfectly in 1D by separating the computation of the free boundaries and the solutions inside the support, a WENO scheme, [116], which eliminates the oscillations around the free boundaries, and so on. There is also an extensive study on the finite volume method, [25, 76] and various finite element methods, including an early study of the convergence analysis, [140], the locally discontinuous Galerkin method, [153], and the adaptive mesh, [13, 12, 126]. The relaxation scheme, which is originally designed for conservation laws, [99], can be extended to porous medium equations successfully as well, [50, 125]. Besides the methods on Euler coordinates, there is an increasing interest in designing Lagrangian methods, see for example [32, 49, 46, 48, 111]. Despite the extensive study of the numerical methods for porous medium equations, the algorithm preserving the free boundary limit is rarely studied. A fully implicit solver is generally needed. A recent work shows that one way to avoid a fully implicit scheme is to construct a semi-implicit scheme by combining the relaxation scheme with the prediction-correction formulation, [112].

Contents of the paper. The semi-discrete scheme and the analysis of its properties are presented in Section 3.2. We prove stability providing a priori estimates on the main quantities and their derivatives, Subsec. 3.2.1. Let us point out that these estimates are uniform with respect to γ, and therefore stability holds for any $\gamma > 1$. Then, we prove the asymptotic preserving property of the scheme, Subsec. 3.2.2 and recover a discrete version of the Aronson-Bénilan estimate for a nontrivial reaction term, Subsec. 3.2.3. We introduce the implicit scheme in Section 3.3, and we extend the uniform a priori estimates previously derived on the semi-discrete scheme. The solvability of the scheme is proven in detail in Appendix 3.A. We report the results of several numerical simulations in Section 3.4. We test the accuracy of the scheme using the explicit Barenblatt profile, and we compare the numerical solutions with γ large to the exact solutions of the *in vitro* and *in vivo* model with nutrients. Moreover, we apply our scheme to a two-species model of tumor growth, where both populations evolve under a porous medium mechanics. Finally, we report the results of the 2-dimensional simulations on the focusing solution which confirm the sharpness of the L^4-uniform bound of ∇p.

3.2 The semi-discrete scheme

To better focus on the analysis of the upwind discretization in space, we start from the semi-discrete scheme. For simplicity, only the one dimensional problem is considered. The scheme for the multi-dimensional problem with tensor product grids can be analyzed similarly.

We suppose the domain is a closed interval $\Omega = [-X, X]$. We choose a uniform mesh with mesh size $\Delta x = \frac{X}{M_x}$, where $2M_x$ is the number of sub-intervals. Denote $n_i(t)$ and $p_i(t)$ to be the numerical approximations of $n(t, x_i)$ and $p(t, x_i)$, where $x_i = i\Delta x$ for $i \in I = \{-M_x, -M_x + 1, \ldots, M_x\}$. Then the semi-discrete finite difference scheme for Eq. (3.1) is

$$\frac{d}{dt}n_i = \frac{n_{i+1/2}q_{i+1/2} - n_{i-1/2}q_{i-1/2}}{\Delta x} + n_i G_i, \quad i \in I, \tag{3.5}$$

with

$$q_{i+1/2} = \frac{p_{i+1} - p_i}{\Delta x}, \quad G_i = G(p_i). \tag{3.6}$$

The Neumann boundary condition is applied so that $n_{-M_x-1} = n_{-M_x+1}$ and $n_{M_x+1} = n_{M_x-1}$. We define $n_{i+\frac{1}{2}}$ in the upwind manner

$$n_{i+1/2} = \begin{cases} n_i, & \text{if } \ q_{i+1/2} \leqslant 0, \\ n_{i+1}, & \text{if } \ q_{i+1/2} > 0. \end{cases} \tag{3.7}$$

Multiplying Eq. (3.5) by $\gamma n_i^{\gamma-1}$ we recover the finite difference equation on the pressure

$$\frac{d}{dt}p_i = \gamma n_i^{\gamma-1}\left(\frac{n_{i+1/2} - n_i}{\Delta x}q_{i+1/2} + \frac{n_i - n_{i-1/2}}{\Delta x}q_{i-1/2}\right) + \gamma p_i\left(\delta_x^2 p_i + G_i\right), \tag{3.8}$$

where

$$\delta_x^2 p_i := \frac{q_{i+1/2} - q_{i-1/2}}{\Delta x}.$$

Assumptions. In order to prove stability results such as L^∞ control and discrete BV-estimates, we need to make the following assumptions: we assume that there exists positive constants C

and p_H (homeostatic pressure) such that

$$
\begin{aligned}
0 \leqslant p_i^0 \leqslant p_H, \qquad \Delta x \sum_i |n_i^0| \leqslant C \qquad \Delta x \sum_i |p_i^0| \leqslant C,\\
\sum_i |n_{i+1}^0 - n_i^0| \leqslant C, \qquad \Delta x \sum_i \left| \left(\frac{d}{dt} n_i\right)^0 \right| \leqslant C.
\end{aligned}
\tag{3.9}
$$

In the following section we will prove that thanks to Gronwall's lemma the above regularity of the initial data propagates along time.

3.2.1 Stability results

Now we prove the positivity preserving property of the semi-discrete scheme (3.5), and the *a priori* estimates that imply stability for any $\gamma > 1$.

Theorem 3.2.1 (A priori estimates). *Let $T > 0$ and $n_H := p_H^{1/\gamma}$ and assume* (3.3) *and* (3.9) *hold true. Then, for all $0 \leqslant t \leqslant T$, we have*

(i) $0 \leqslant n_i(t) \leqslant n_H$, $0 \leqslant p_i(t) \leqslant p_H$, $\forall i$,

(ii) $\Delta x \sum_i |n_i(t)| \leqslant C(T)$, $\Delta x \sum_i |p_i(t)| \leqslant C(T)$,

(iii) $\sum_i |n_{i+1}(t) - n_i(t)| \leqslant C(T)$,

(iv) $\Delta x \sum_i \left|\frac{d}{dt} n_i(t)\right| \leqslant C(T)$, $\int_0^T \Delta x \sum_i \left|\frac{d}{dt} p_i\right| \mathrm{d}t \leqslant C(T)$,

(v) $\int_0^T \Delta x \sum_i \left|\frac{p_{i+1}-p_i}{\Delta x}\right|^2 \mathrm{d}t \leqslant C(T)$.

for some positive constants $C(T)$ depending on T and independent of γ.

Proof. **L^∞ estimates.** Combining Eq. (3.6) and Eq. (3.7) we recover

$$
\gamma n_i^{\gamma-1} \frac{n_{i+1/2} - n_i}{\Delta x} q_{i+1/2} = \begin{cases} 0 & \text{if } q_{i+1/2} < 0,\\ \gamma n_i^{\gamma-1} \dfrac{n_{i+1} - n_i}{\Delta x} \dfrac{p_{i+1} - p_i}{\Delta x} & \text{if } q_{i+1/2} > 0, \end{cases}
$$

and

$$
\gamma n_i^{\gamma-1} \frac{n_i - n_{i-1/2}}{\Delta x} q_{i-1/2} = \begin{cases} \gamma n_i^{\gamma-1} \dfrac{n_i - n_{i-1}}{\Delta x} \dfrac{p_i - p_{i-1}}{\Delta x} & \text{if } q_{i-1/2} < 0,\\ 0 & \text{if } q_{i-1/2} > 0. \end{cases}
$$

Therefore, the equation on the pressure, Eq. (3.8), reads

$$
\frac{d}{dt} p_i = \gamma p_i^{(\gamma-1)/\gamma} \left(\frac{n_{i+1} - n_i}{\Delta x} (q_{i+1/2})_+ + \frac{n_i - n_{i-1}}{\Delta x} (q_{i-1/2})_- \right) + \gamma p_i \left(\delta_x^2 p_i + G_i\right),
$$

where $(\cdot)_+$ and $(\cdot)_-$ denote the positive and negative parts, respectively.
To begin with, we prove the non-negativity of $n_i(t)$ and $p_i(t)$. In fact, if $n_i = 0$ at $t = t_0$, by scheme (3.5), we have

$$
\frac{d}{dt} n_i = \frac{n_{i+1/2} - n_i}{\Delta x} q_{i+1/2} + \frac{n_i - n_{i-1/2}}{\Delta x} q_{i-1/2}
$$

$$
\begin{aligned}
&= \frac{(n_{i+1}-n_i)_+}{\Delta x}(q_{i+1/2})_+ + \frac{(n_i - n_{i-1/2})_-}{\Delta x}(q_{i-1/2})_- \\
&\geq 0,
\end{aligned}
$$

which implies that n_i and p_i can never be negative.

As for the upper bound, let us notice that the following inequality holds

$$
\frac{d}{dt}p_i \leqslant \left(q_{i+1/2}\right)_+^2 + \left(q_{i-1/2}\right)_-^2 + \gamma p_i(\delta_x^2 p_i + G_i). \tag{3.10}
$$

Let us assume that at time $t = t_0$, $\max_i p_i = p_H$. For simplicity of notations, we denote $p_{\bar{i}} = \max_i p_i$. It is easy to check that $\left(q_{\bar{i}+1/2}\right)_+ = \left(q_{\bar{i}-1/2}\right)_- = 0$, $\delta_x^2 p_{\bar{i}} \leq 0$ and $G_{\bar{i}} = 0$. Then, inequality (3.10) shows that

$$
\frac{d}{dt}p_{\bar{i}} \leq 0,
$$

which implies that p_i can never be greater than p_H, and thus n_i can never be greater than n_H. ***L^1*-estimate.** To prove estimates *(ii)*, we compute the sum of Eq. (3.5) for all i, and we find successively

$$
\frac{d}{dt}\left(\Delta x \sum_i n_i\right) = \sum_i (n_{i+1/2}q_{i+1/2} - n_{i-1/2}q_{i-1/2}) + \Delta x \sum_i n_i G(p_i) = \Delta x \sum_i n_i G(p_i),
$$

$$
\frac{d}{dt}\left(\Delta x \sum_i n_i\right) \leqslant G(0)\Delta x \sum_i n_i,
$$

where in the last inequality we use the assumptions on the growth term, *cf.* Eq. (3.3). By Gronwall's lemma and Eq. (3.9), we have

$$
\Delta x \sum_i |n_i(t)| \leqslant e^{G(0)t}\Delta x \sum_i |n_i^0| \leqslant C(T), \text{ for } 0 \leqslant t \leqslant T.
$$

Upon using the L^∞-bound of the pressure, we finally obtain

$$
\Delta x \sum_i |p_i(t)| \leqslant p_H^{(\gamma-1)/\gamma}\Delta x \sum_i |n_i(t)| \leqslant C(T).
$$

***BV*-estimate.** We now subtract the equation for n_i from the equation for n_{i+1} and multiply by $\mathrm{sign}(n_{i+1}-n_i)$

$$
\begin{aligned}
\frac{d}{dt}|n_{i+1}-n_i| \leq & \frac{1}{\Delta x}(n_{i+3/2}|q_{i+3/2}| - 2n_{i+1/2}|q_{i+1/2}| + n_{i-1/2}|q_{i-1/2}|) \\
& + (n_{i+1}G(p_{i+1}) - n_i G(p_i))\mathrm{sign}(n_{i+1}-n_i)).
\end{aligned}
$$

We sum over i to obtain

$$
\begin{aligned}
\frac{d}{dt}\left(\sum_i |n_{i+1}-n_i|\right) \leqslant & \frac{1}{\Delta x}\sum_i (n_{i+3/2}|q_{i+3/2}| - 2n_{i+1/2}|q_{i+1/2}| + n_{i-1/2}|q_{i-1/2}|) \\
& + \sum_i \left[|n_{i+1}-n_i|G(p_i) + n_{i+1}(G(p_{i+1}) - G(p_i))\mathrm{sign}(n_{i+1}-n_i)\right]
\end{aligned}
$$

$$\leqslant \sum_i |n_{i+1} - n_i| G(p_i),$$

where in the last inequality we use the monotonicity of G, Eq. (3.3). In fact, since G' is negative, $\text{sign}(n_{i+1} - n_i) = \text{sign}(p_{i+1} - p_i) = -\text{sign}(G(p_{i+1}) - G(p_i))$. Finally, we get

$$\frac{d}{dt} \sum_i |n_{i+1} - n_i| \leqslant G(0) \sum_i |n_{i+1} - n_i|,$$

and thus we recover *(iii)* thanks to Gronwall's lemma and the assumptions on the initial data, Eq. (3.9),

$$\sum_i |n_{i+1}(t) - n_i(t)| \leqslant e^{G(0)t} \sum_i |n_{i+1}^0 - n_i^0| \leqslant C(T), \text{ for } 0 \leqslant t \leqslant T.$$

Estimates on the time derivatives. Now we give the proof of the boundedness of the time derivatives, *(iv)*. Deriving Eq. (3.5) with respect to time, we obtain

$$\frac{d}{dt}\left(\frac{d}{dt} n_i\right) \Delta x = \frac{d}{dt}\left(n_{i+1/2} q_{i+1/2} - n_{i-1/2} q_{i-1/2} + n_i G(p_i) \Delta x\right).$$

We multiply by $\text{sign}\left(\frac{d}{dt} n_i\right)$

$$\begin{aligned}\frac{d}{dt}\left(\left|\frac{d}{dt} n_i\right|\right) \Delta x = & \underbrace{\frac{d}{dt}\left(n_{i+1/2} q_{i+1/2}\right) \text{sign}\left(\frac{d}{dt} n_i\right)}_{A_i} \underbrace{- \frac{d}{dt}\left(n_{i-1/2} q_{i-1/2}\right) \text{sign}\left(\frac{d}{dt} n_i\right)}_{B_i} \\ & + \left(G(p_i)\left|\frac{d}{dt} n_i\right| + n_i G'(p_i)\left|\frac{d}{dt} p_i\right|\right) \Delta x.\end{aligned} \tag{3.11}$$

We now compute A_i and B_i

$$\begin{aligned}A_i &= \left[\frac{d}{dt} n_{i+1/2} \left(q_{i+1/2}\right)_+ - \frac{d}{dt} n_{i+1/2} \left(q_{i+1/2}\right)_- + n_{i+1/2} \frac{d}{dt} q_{i+1/2}\right] \text{sign}\left(\frac{d}{dt} n_i\right) \\ &\leqslant \left|\frac{d}{dt} n_{i+1}\right| \left(q_{i+1/2}\right)_+ - \left|\frac{d}{dt} n_i\right| \left(q_{i+1/2}\right)_- + \frac{n_{i+1/2}}{\Delta x}\left|\frac{d}{dt} p_{i+1}\right| - \frac{n_{i+1/2}}{\Delta x}\left|\frac{d}{dt} p_i\right|, \\ B_i &= \left[-\frac{d}{dt} n_{i-1/2} \left(q_{i-1/2}\right)_+ + \frac{d}{dt} n_{i-1/2} \left(q_{i-1/2}\right)_- - n_{i-1/2} \frac{d}{dt} q_{i-1/2}\right] \text{sign}\left(\frac{d}{dt} n_i\right) \\ &\leqslant -\left|\frac{d}{dt} n_i\right| \left(q_{i-1/2}\right)_+ + \left|\frac{d}{dt} n_{i-1}\right| \left(q_{i-1/2}\right)_- - \frac{n_{i-1/2}}{\Delta x}\left|\frac{d}{dt} p_i\right| + \frac{n_{i-1/2}}{\Delta x}\left|\frac{d}{dt} p_{i-1}\right|.\end{aligned}$$

Upon summing over i, we find

$$\sum_i (A_i + B_i) \leqslant 0,$$

and then, from Eq. (3.11), we have

$$\frac{d}{dt}\left(\Delta x \sum_i \left|\frac{d}{dt} n_i\right|\right) \leqslant \Delta x \sum_i G(p_i) \left|\frac{d}{dt} n_i\right|,$$

since G' is negative. Hence, we obtain

$$\Delta x \sum_i \left| \frac{d}{dt} n_i \right| \leqslant e^{G(0)t} \Delta x \sum_i \left| \left(\frac{d}{dt} n_i \right)^0 \right| \leqslant C(T), \text{ for } 0 \leqslant t \leqslant T. \tag{3.12}$$

It remains to prove the estimate on the time derivative of the pressure. We compute

$$\int_0^T \Delta x \sum_i \left| \frac{d}{dt} p_i \right| \mathrm{dt} \leqslant \int_0^T \Delta x \sum_i \gamma n_i^{\gamma-1} \left| \frac{d}{dt} n_i \right| \mathbb{1}_{\{n_i \leqslant 1/2\}} \, \mathrm{dt} + 2 \int_0^T \Delta x \sum_i n_i \left| \frac{d}{dt} p_i \right| \mathbb{1}_{\{n_i \geqslant 1/2\}} \, \mathrm{dt}. \tag{3.13}$$

Thanks to Eq. (3.12) the first term in the right-hand side is bounded.
Let us denote $\beta := \min_i |G'(p_i)|$. We sum Eq. (3.11) over i and we integrate in time to obtain

$$\Delta x \sum_i \left| \frac{d}{dt} n_i \right| + \beta \int_0^T \Delta x \sum_i n_i \left| \frac{d}{dt} p_i \right| \mathrm{dt} \leqslant G(0) \int_0^T \Delta x \sum_i \left| \frac{d}{dt} n_i \right| \mathrm{dt} + \Delta x \sum_i \left| \left(\frac{d}{dt} n_i \right)^0 \right| \leqslant C(T),$$

where the last inequality comes from Eq. (3.12). Thanks to this bound, we know that

$$\int_0^T \Delta x \sum_i n_i \left| \frac{d}{dt} p_i \right| \mathrm{dt} \leqslant C(T),$$

and from Eq. (3.13) we finally find

$$\int_0^T \Delta x \sum_i \left| \frac{d}{dt} p_i \right| \mathrm{dt} \leqslant C(T).$$

L^2-estimate on the pressure gradient. We sum for all i the inequality satisfied by the pressure, Eq. (3.10), namely

$$\begin{aligned}
\sum_i \frac{d}{dt} p_i &\leqslant \sum_i \left(\frac{p_{i+1} - p_i}{\Delta x} \right)_+^2 + \sum_i \left(\frac{p_i - p_{i-1}}{\Delta x} \right)_-^2 + \gamma \sum_i p_i (\delta_x^2 p_i + G_i) \\
&\leqslant \sum_i \left| \frac{p_{i+1} - p_i}{\Delta x} \right|^2 + \gamma \sum_i \frac{p_i p_{i+1} - 2p_i^2 + p_{i-1} p_i}{|\Delta x|^2} + \gamma \sum_i p_i G_i \\
&= \sum_i \left| \frac{p_{i+1} - p_i}{\Delta x} \right|^2 - \gamma \sum_i \left| \frac{p_{i+1} - p_i}{\Delta x} \right|^2 + \gamma \sum_i p_i G_i.
\end{aligned}$$

Hence, we have

$$(\gamma - 1) \sum_i \left| \frac{p_{i+1} - p_i}{\Delta x} \right|^2 \leqslant - \sum_i \frac{d}{dt} p_i + \gamma \sum_i p_i G_i,$$

and, upon integrating in time, we recover

$$\int_0^T \Delta x \sum_i \left| \frac{p_{i+1} - p_i}{\Delta x} \right|^2 \mathrm{dt} \leqslant \frac{1}{\gamma - 1} \Delta x \sum_i p_i^0 - \Delta x \sum_i p_i(T) + \frac{\gamma}{\gamma - 1} \int_0^T \Delta x \sum_i p_i G_i \, \mathrm{dt}.$$

Thus *(v)* follows from the assumptions on G and p_i^0, *cf.* Eqs. (3.3, 3.9), and the estimates *(ii)* proven above.

$\square$

3.2.2 The asymptotic-preserving property

As mentioned in the introduction, it is well-known that when $\gamma \to \infty$ the porous medium-type equation (3.1) turns out to be a free boundary problem of Hele-Shaw type. In particular, passing to the limit in the equation of the pressure

$$\frac{\partial p}{\partial t} = \gamma p(\Delta p + G(p)) + |\nabla p|^2,$$

allows to recover the *complementarity relation*, namely

$$p_\infty(\Delta p_\infty + G(p_\infty)) = 0,$$

in the sense of distributions.
We show that the semi-discrete scheme (3.5) satisfies the same property and thus is asymptotic preserving (AP) as $\gamma \to \infty$. First of all, let us prove the following convergence result (where we point out the dependence of the solution on γ in the notation).

Theorem 3.2.2 (Convergence result)**.** *Given $n_{\gamma,i}, p_{\gamma,i}$ a solution of scheme* (3.5) *with $\gamma > 1$. Then, for all i, we have*

$$n_{\gamma,i} \xrightarrow{\gamma\to\infty} n_{\infty,i}, \qquad \textit{in } L^p(0,T), \textit{ for all } 1 \leqslant p < \infty,$$

$$p_{\gamma,i} \xrightarrow{\gamma\to\infty} p_{\infty,i}, \qquad \textit{in } L^p(0,T), \textit{ for all } 1 \leq p < \infty,$$

$$q_{\gamma,i+\frac{1}{2}} \xrightarrow{\gamma\to\infty} q_{\infty,i+\frac{1}{2}}, \qquad \textit{weakly in } L^2(0,T).$$

Proof. Thanks to the uniform bounds *(ii), (iv)* stated in Theorem 3.2.1, by standard compactness arguments we infer the convergence of $n_{\gamma,i}$ and $p_{\gamma,i}$ in $L^1(0,T)$. Since both the density and the pressure are bounded uniformly in $L^\infty(0,T)$, they converge strongly, up to a subsequence, in any $L^p(0,T)$, with $1 \leqslant p < \infty$.
Finally, the a priori bound *(v)* of Theorem 3.2.1 yields the weak convergence of $q_{\gamma,i+\frac{1}{2}}$ in $L^2(0,T)$. $\square$

Now we prove the asymptotic preserving property of the scheme. First of all, let us recall the equation satisfied by the pressure

$$\frac{d}{dt}p_i - \gamma n_i^{\gamma-1}\left(\frac{n_{i+1/2}-n_i}{\Delta x}q_{i+1/2} + \frac{n_i - n_{i-1/2}}{\Delta x}q_{i-1/2}\right) = \gamma p_i\left(\delta_x^2 p_i + G_i\right). \tag{3.14}$$

Since

$$\left|\gamma n_i^{\gamma-1}\left(\frac{n_{i+1/2}-n_i}{\Delta x}q_{i+1/2} + \frac{n_i - n_{i-1/2}}{\Delta x}q_{i-1/2}\right)\right| \leqslant \left(q_{i+1/2}\right)_+^2 + \left(q_{i-1/2}\right)_-^2,$$

thanks to Theorem 3.2.1 we know that the left-hand side of Eq. (3.14) is uniformly bounded in $L^1(0,T)$. Testing Eq. (3.14) against a function $\varphi \in C^1_{comp}(0,T)$, we obtain

$$\int_0^T p_i\left(\delta_x^2 p_i + G(p_i)\right)\varphi\,\mathrm{d}t = -\frac{1}{\gamma}\left(\int_0^T p_i\varphi'\,\mathrm{d}t - \int_0^T \gamma n_i^{\gamma-1}\left(\frac{n_{i+1/2}-n_i}{\Delta x}q_{i+1/2} + \frac{n_i - n_{i-1/2}}{\Delta x}q_{i-1/2}\right)\varphi\,\mathrm{d}t\right).$$

Hence, passing to the limit $\gamma \to \infty$ using Theorem 3.2.2, we recover

$$p_{\infty,i}(\delta_x^2 p_{\infty,i} + G(p_{\infty,i})) = 0,$$

which is the discrete formulation of the complementarity relation.
We now pass to the limit also in the equation for the density, which reads

$$\frac{d}{dt} n_i = \frac{n_{i+1/2} q_{i+1/2} - n_{i-1/2} q_{i-1/2}}{\Delta x} + n_i G_i.$$

Multiplying by a test function, we obtain

$$-\int_0^T n_i \varphi' \,\mathrm{d}t = \int_0^T \frac{n_{i+1/2} q_{i+1/2} - n_{i-1/2} q_{i-1/2}}{\Delta x} \varphi \,\mathrm{d}t + \int_0^T n_i G(p_i) \varphi \,\mathrm{d}t,$$

hence, thanks to Theorem 3.2.2, we find (in the weak sense)

$$\frac{d}{dt} n_{\infty,i} = \frac{n_{\infty,i+1/2} q_{\infty,i+1/2} - n_{\infty,i-1/2} q_{\infty,i-1/2}}{\Delta x} + n_{\infty,i} G(p_{\infty,i}).$$

3.2.3 Stronger estimate on the pressure - The Aronson-Bénilan estimate

In [130], Perthame, Quirós and Vázquez recover the compactness needed to pass to the limit in Eq. (3.4) relying on a lower bound on the Laplacian of the pressure. In fact, they extend the celebrated Aronson-Bénilan estimate of the PME to the case of non-trivial reaction term, *i.e.* $G \neq 0$, proving the following bound

$$\Delta p + G(p) \gtrsim -\frac{C}{\gamma t}. \tag{3.15}$$

It is our interest to investigate whether this lower bound on the second derivatives still holds for Eq. (3.5), in order to obtain a discrete counterpart of a fundamental property of porous medium-type equations.
We are able to prove the discrete version of the Aronson-Bénilan estimate, Eq. (3.15), for $\gamma = 1$ and $\gamma \approx \infty$ and for a pressure-dependent growth term of the form $G(p) = \alpha(p_H - p)$. It remains an open question how to recover the discrete AB estimate for $\gamma > 1$ and for a general reaction term G. The discrete version of the AB property for non-trivial reaction terms could be extremely useful in order to pass to the limit as Δx vanishes and therefore to prove the convergence of the scheme.

Theorem 3.2.3 (Aronson-Bénilan estimate)**.** *Let $G(p) = \alpha(p_H - p)$, with $\alpha \geqslant 0$. We set*

$$w_i := \delta_x^2 p_i + G(p_i) = \frac{p_{i+1} - 2p_i + p_{i-1}}{(\Delta x)^2} + G(p_i), \qquad \forall i.$$

Then, for $\gamma = 1$ and $\gamma \approx \infty$, scheme (3.5) satisfies the Aronson-Bénilan estimate, i.e.

$$w_i \geqslant -\frac{1}{\gamma t}, \qquad \forall i.$$

Proof. As in [130], it is sufficient to prove

$$\frac{d\underline{w}}{dt} \geq \gamma(\underline{w})^2, \qquad \text{with } \underline{w} := \min_i\{w_i\}.$$

• **Case $\gamma = 1$.**

We have $p_i = n_i$ and thus scheme (3.5) can be reformulated as

$$\frac{dp_i}{dt} = p_i w_i + (q^+_{i+\frac{1}{2}})^2 + (q^-_{i-\frac{1}{2}})^2,$$

where $q^+_{i+\frac{1}{2}} = \max\{q_{i+\frac{1}{2}}, 0\}$ and $q^-_{i-\frac{1}{2}} = \max\{-q_{i-\frac{1}{2}}, 0\}$, and it further implies that

$$\frac{dw_i}{dt} = \delta_x^2(p_i w_i) + \delta_x^2[(q^+_{i+\frac{1}{2}})^2] + \delta_x^2[(q^-_{i-\frac{1}{2}})^2] - \alpha p_i w_i - \alpha(q^+_{i+\frac{1}{2}})^2 - \alpha(q^-_{i-\frac{1}{2}})^2. \tag{3.16}$$

In order to consider the evolution of the minimal w_i we denote

$$w_j := \min_i w_i.$$

On the one hand, it is easy to see that

$$\delta_x^2(p_j w_j) \geq w_j \delta_x^2 p_j. \tag{3.17}$$

On the other hand, by definition

$$w_j = \frac{q_{j+\frac{1}{2}} - q_{j-\frac{1}{2}}}{\Delta x} + \alpha(p_H - p_j),$$

and the inequality $w_j \leq w_{j+1}$ indicates that

$$q_{j+\frac{3}{2}} + q_{j-\frac{1}{2}} \geq q_{j+\frac{1}{2}}(2 + \alpha|\Delta x|^2).$$

As a result,

$$\begin{aligned} q^+_{j+\frac{3}{2}} + q^+_{j-\frac{1}{2}} &\geq \max\{q_{j+\frac{3}{2}} + q_{j-\frac{1}{2}},\, 0\} \\ &\geq \max\{q_{j+\frac{1}{2}}(2 + \alpha|\Delta x|^2),\, 0\} \\ &= q^+_{j+\frac{1}{2}}(2 + \alpha|\Delta x|^2). \end{aligned}$$

And then, by Jensen's inequality, we get

$$(q^+_{j+\frac{3}{2}})^2 + (q^+_{j-\frac{1}{2}})^2 \geq (q^+_{j+\frac{1}{2}})^2(2 + \alpha|\Delta x|^2),$$

or equivalently,

$$\delta_x^2[(q^+_{j+\frac{1}{2}})^2] \geq \alpha(q^+_{j+\frac{1}{2}})^2. \tag{3.18}$$

Similarly, we recover $\delta_x^2[(q^-_{j-\frac{1}{2}})^2] \geq \alpha(q^-_{j-\frac{1}{2}})^2$. Upon combining Eq. (3.17) with Eq. (3.16) and adding and subtracting $G(p_j)w_j$, we get

$$\frac{dw_i}{dt} \geqslant w_i^2 - G(p_j)w_j + \delta_x^2[(q^+_{i+\frac{1}{2}})^2] + \delta_x^2[(q^-_{i-\frac{1}{2}})^2] - \alpha p_i w_i - \alpha(q^+_{i+\frac{1}{2}})^2 - \alpha(q^-_{i-\frac{1}{2}})^2,$$

which yields

$$\frac{dw_i}{dt} \geqslant w_i^2 - G(p_j)w_j - \alpha p_i w_i,$$

thanks to Eq. (3.18). Finally, using the definition of G and assuming without loss of generality that $w_j \leqslant 0$, we obtain

$$\frac{dw_i}{dt} \geq w_i^2,$$

which implies

$$w_j \geq -\frac{1}{t}.$$

• **Case $\gamma \approx \infty$.**

Now, we prove the AB estimate for γ very large. We recall that

$$\frac{d}{dt}p_i = \gamma n_i^{\gamma-1}\left(\frac{n_{i+1/2}-n_i}{\Delta x}q_{i+1/2} + \frac{n_i - n_{i-1/2}}{\Delta x}q_{i-1/2}\right) + \gamma p_i\left(\delta_x^2 p_i + G_i\right),$$

and we use the following definitions

$$w_i = \delta_x^2 p_i + G(p_i) = \frac{q_{i+1/2}-q_{i-1/2}}{\Delta x} + G(p_i), \qquad\qquad q_{i+\frac{1}{2}} = \frac{n_{i+1}^{\gamma} - n_i^{\gamma}}{\Delta x}.$$

Computing the time derivative of $q_{i+1/2}$ we find

$$\frac{1}{\gamma}\frac{d}{dt}q_{i+1/2} = \frac{1}{|\Delta x|^2}\left[n_{i+1}^{\gamma-1}\left(n_{i+3/2}q_{i+3/2} - n_{i+1/2}q_{i+1/2}\right) - n_i^{\gamma-1}\left(n_{i+1/2}q_{i+1/2} - n_{i-1/2}q_{i-1/2}\right)\right].$$

Hence,

$$\begin{aligned}\frac{1}{\gamma}\frac{d}{dt}w_i =& \frac{1}{|\Delta x|^3}\left[n_{i+1}^{\gamma-1}\left(n_{i+3/2}q_{i+3/2} - n_{i+1/2}q_{i+1/2}\right) - n_i^{\gamma-1}\left(n_{i+1/2}q_{i+1/2} - n_{i-1/2}q_{i-1/2}\right)\right]\\ &+ \frac{1}{|\Delta x|^3}\left[-n_i^{\gamma-1}\left(n_{i+1/2}q_{i+1/2} - n_{i-1/2}q_{i-1/2}\right) + n_{i-1}^{\gamma-1}\left(n_{i-1/2}q_{i-1/2} - n_{i-3/2}q_{i-3/2}\right)\right]\\ &- \frac{\alpha}{\gamma}\left(\gamma n_i^{\gamma-1}\left(\frac{n_{i+1/2}-n_i}{\Delta x}q_{i+1/2} + \frac{n_i-n_{i-1/2}}{\Delta x}q_{i-1/2}\right) + \gamma p_i\left(\delta_x^2 p_i + G_i\right)\right).\end{aligned} \tag{3.19}$$

Once again we define $\min_i w_i =: w_j$. Let us notice that, for $\gamma \approx \infty$, we have

$$n_{j+1}^{\gamma-1}n_{j+2} \approx p_{j+1},$$

since

$$n_{j+1}^{\gamma-1}n_{j+2} = (p_{j+1})^{\frac{\gamma-1}{\gamma}}(p_{j+2})^{\frac{1}{\gamma}}.$$

Analogously, we also have

$$n_j^{\gamma-1}n_{j+1/2} \approx p_j \qquad n_j^{\gamma-1}n_{j-1/2} \approx p_j.$$

Thus, when $\gamma \approx \infty$, from Eq. (3.19) we recover

$$\frac{1}{\gamma}\frac{d}{dt}w_j = \frac{1}{(\Delta x)^3}\left[n_{j+1}^{\gamma-1}\left(n_{j+3/2}q_{j+3/2} - n_{j+1/2}q_{j+1/2}\right) - n_j^{\gamma-1}\left(n_{j+1/2}q_{j+1/2} - n_{j-1/2}q_{j-1/2}\right)\right]$$

$$
\begin{aligned}
&+\frac{1}{(\Delta x)^3}\left[-n_j^{\gamma-1}\left(n_{j+1/2}q_{j+1/2}-n_{j-1/2}q_{j-1/2}\right)+n_{j-1}^{\gamma-1}\left(n_{j-1/2}q_{j-1/2}-n_{j-3/2}q_{j-3/2}\right)\right]\\
&-\alpha p_j w_j-\frac{\alpha}{\Delta x}n_i^{\gamma-1}\big((n_{i+1/2}-n_i)q_{i+1/2}+(n_i-n_{i-1/2})q_{i-1/2}\big)\\
\approx\ &\frac{1}{(\Delta x)^3}\left[p_{j+1}\left(q_{j+3/2}-q_{j+1/2}\right)-p_j\left(q_{j+1/2}-q_{j-1/2}\right)\right]\\
&+\frac{1}{(\Delta x)^3}\left[-p_j\left(q_{j+1/2}-q_{j-1/2}\right)+p_{j-1}\left(q_{j-1/2}-q_{j-3/2}\right)\right]-\alpha p_j w_j\\
\geqslant\ &\frac{p_{j+1}w_{j+1}-2p_jw_j+p_{j-1}w_{j-1}}{(\Delta x)^2}\\
\geq\ &w_j^2,
\end{aligned}
$$

where we assumed again $w_j \leqslant 0$. Hence

$$\frac{d}{dt}w_j \gtrapprox \gamma w_j^2,$$

thus the result is proven.

□

3.3 The fully discrete implicit scheme

Now we consider the fully discrete implicit scheme and show that all the properties for the semi-discrete scheme hold for the fully discrete scheme if the time step Δt is small enough. Similar to Section 3.2, we only consider the one dimensional problem and the scheme for the multidimensional problem is straightforward. In space, we use the same notations as in Section 3.2. We denote N_i^k to be the numerical approximation of $n(t_k, x_i)$, where $t_k = k\Delta t$ and $x_i = i\Delta x$, $k \geq 0$, $i \in I$. Then $P_i^k := \left(N_i^k\right)^\gamma$ is the numerical approximation of $p(t_k, x_i)$ and the fully implicit scheme can be written as

$$\delta_t N_i^k = \frac{N_{i+\frac12}^{k+1}Q_{i+\frac12}^{k+1} - N_{i-\frac12}^{k+1}Q_{i-\frac12}^{k+1}}{\Delta x} + N_i^{k+1}G_i^{k+1}, \tag{3.20}$$

where

$$\delta_t N_i^k = \frac{N_i^{k+1}-N_i^k}{\Delta t}, \quad Q_{i+\frac12}^k = \frac{P_{i+1}^k - P_i^k}{\Delta x}, \quad G_i^k = G(P_i^k) \leq G(0),$$

and

$$N_{i+1/2}^k = \begin{cases} N_i^k, & \text{if } Q_{i+1/2}^k < 0,\\ N_{i+1}^k, & \text{if } Q_{i+1/2}^k > 0.\end{cases}$$

For simplicity, we introduce

$$A(U,V) = VQ_+(U,V) - UQ_-(U,V), \qquad \text{for } U, V \geq 0, \tag{3.21}$$

where $Q(U,V) = (V^\gamma - U^\gamma)/\Delta x$ and

$$Q_+(U,V) = \max\{Q(U,V), 0\}, \quad Q_-(U,V) = \max\{-Q(U,V), 0\}.$$

A direct computation shows that

$$\partial_1 A(U,V) = -\gamma H(U,V)U^{\gamma-1} - Q_-(U,V) \le 0,$$
$$\partial_2 A(U,V) = \gamma H(U,V)V^{\gamma-1} + Q_+(U,V) \ge 0,$$

where

$$H(U,V) = \begin{cases} U, & \text{if } Q(U,V) < 0, \\ V, & \text{if } Q(U,V) > 0. \end{cases}$$

With the notations defined above, scheme (3.20) can be reformulated as

$$(1-\Delta t G_i^{k+1})N_i^{k+1} - \nu\left(A_{i+\frac{1}{2}}^{k+1} - A_{i-\frac{1}{2}}^{k+1}\right) = N_i^k, \tag{3.22}$$

where $\nu = \Delta t/\Delta x$ and

$$A_{i+\frac{1}{2}}^{k+1} = A(N_i^{k+1}, N_{i+1}^{k+1}) = N_{i+\frac{1}{2}}^{k+1} Q_{i+\frac{1}{2}}^{k+1}.$$

Theorem 3.3.1 (A priori estimates)**.** *Let $T > 0$ and $n_H := p_H^{1/\gamma}$, $\Delta t < 1/G(0)$ and $k(T) = \lfloor T/\Delta t \rfloor$. Then, there exists a unique solution N_i^k of Eq. (3.22) satisfying*

(i) $0 \leqslant N_i^k \leqslant n_H$, $0 \leqslant P_i^k \leqslant p_H$, $\forall t > 0, \forall i$, *and* $\forall n$,

(ii) $\Delta x \sum_i N_i^k \leqslant C(T), \Delta x \sum_i P_i^k \leqslant C(T)$,

(iii) let M_i^k be a non-negative solution satisfying Eq. (3.22), then $\Delta x \sum_i |M_i^k - N_i^k| \leqslant C(T)$,

(iv) if $\sum_i |N_{i+1}^0 - N_i^0| \leqslant C$, *then* $\sum_i |N_{i+1}^k - N_i^k| \leqslant C(T)$,

(v) $\Delta x \sum_i |\delta_t N_i^k| \leqslant C(T)$, $\Delta x \sum_i |\delta_t P_i^k| \leqslant C(T)$,

(vi) $\Delta t \Delta x \sum_{j=0}^k \sum_i |Q_{i+\frac{1}{2}}^j|^2 \leqslant C(T)$,

for some positive constant $C(T)$ depending on T and independent of γ.

Proof. **Solvability and L^∞ estimate.** When $\Delta t < 1/G(0)$ and $0 \le N_i^k \le p_H^{\frac{1}{\gamma}}$ for all i, we claim that there exists a unique solution N_i^{k+1} satisfying $0 \le N_i^{k+1} \le p_H^{\frac{1}{\gamma}}$.
The proof relies on the the existence of sub- and supersolutions. When $\bar N_i = p_H^{\frac{1}{\gamma}}$ for all i, we have $G(\bar N_i^\gamma) < 0$ and $A(\bar N_i, \bar N_{i+1}) = 0$, which implies that

$$(1-\Delta t G(\bar N_i^\gamma))\bar N_i - \nu\left(A(\bar N_i, \bar N_{i+1}) - A(\bar N_{i-1}, \bar N_i)\right) \ge N_i^k$$

and thus $\bar N_i = p_H^{\frac{1}{\gamma}}$ is a supersolution. Similarly, we can prove that $\bar N_i = 0$ is a subsolution. Then following the proof in [3], we can prove the existence and uniqueness of the solution. The detailed proof can be found in Appendix 3.A.
***L^1* estimate.** Summing up Eq. (3.20) over i, we have

$$\Delta x \sum_i N_i^{k+1} - \Delta x \sum_i N_i^k = \Delta t \Delta x \sum_i N_i^{k+1} G_i^{k+1} \le G(0)\Delta t \Delta x \sum_i N_i^{k+1}.$$

As a result, when $\Delta t \le \alpha/G(0)$ with $\alpha < 1$, we have

$$\Delta x \sum_i N_i^k \le \frac{1}{(1-\Delta t G(0))^k} \Delta x \sum_i N_i^0 \le \frac{1}{(1-\alpha)^{\frac{G(0)T}{\alpha}}} \Delta x \sum_i N_i^0,$$

where $T = k\Delta t$. Further, we have $\sum_i P_i^k \le p_H^{\gamma-1} \sum_i N_i^k \le C(T)$.

L^1-contraction. Denote M_i^k to be another non-negative solution satisfying Eq. (3.22), or more specifically

$$(1 - \Delta t G_{M,i}^{k+1}) M_i^{k+1} - \nu \left(A_{M,i+\frac{1}{2}}^{k+1} - A_{M,i-\frac{1}{2}}^{k+1} \right) = M_i^k,$$

where

$$G_{M,i}^k = G(P_{M,i}^k) \text{ with } P_{M,i}^k = (M_i^k)^\gamma,\ A_{M,i+\frac{1}{2}}^{k+1} = A_{i+\frac{1}{2}}(M_i^{k+1}, M_{i+1}^{k+1}).$$

Subtracting the equation for N_i^k from the equation for M_i^k, we get

$$I_1 - \nu \left(A_{M,i+\frac{1}{2}}^{k+1} - A_{N,i+\frac{1}{2}}^{k+1} \right) + \nu \left(A_{M,i-\frac{1}{2}}^{k+1} - A_{N,i-\frac{1}{2}}^{k+1} \right) = M_i^k - N_i^k,$$

where the term I_1 is defined as

$$\begin{aligned} I_1 &= \left[(1 - \Delta t G_{M,i}^{k+1}) M_i^{k+1} - (1 - \Delta t G_{N,i}^{k+1}) N_i^{k+1} \right] \\ &= (1 - \Delta t G_{M,i}^{k+1})(M_i^{k+1} - N_i^{k+1}) - \Delta t (G_{M,i}^{k+1} - G_{N,i}^{k+1}) N_i^{k+1} \\ &= (1 - \Delta t G_{M,i}^{k+1})(M_i^{k+1} - N_i^{k+1}) - \Delta t G'(P_{\eta,i}^{k+1}) N_i^{k+1} (P_{M,i}^{k+1} - P_{N,i}^{k+1}) \end{aligned}$$

where $P_{\eta,i}^{k+1} = (\eta_i^{k+1})^\gamma$ with η_i^{k+1} being some non-negative number between M_i^{k+1} and N_i^{k+1}. Noticing that $G'(\cdot) \le 0$ and the fact that $P_{M,i}^{k+1} - P_{N,i}^{k+1}$ shares the same sign with $M_i^{k+1} - N_i^{k+1}$, we have that

$$I_1 \mathrm{sign}(M_i^{k+1} - N_i^{k+1}) \ge (1 - \Delta t G(0)) |M_i^{k+1} - N_i^{k+1}| + \Delta t \min_p |G'(p)| N_i^{k+1} \left| P_{M,i}^{k+1} - P_{N,i}^{k+1} \right|.$$

In fact, we can further prove that

$$\begin{aligned} I_1 \mathrm{sign}(M_i^{k+1} - N_i^{k+1}) &\ge (1 - \Delta t G(0)) |M_i^{k+1} - N_i^{k+1}| \\ &\quad + \Delta t \min_p |G'(p)| \max\{M_i^{k+1}, N_i^{k+1}\} \left| P_{M,i}^{k+1} - P_{N,i}^{k+1} \right| \\ &\ge (1 - \Delta t G(0)) |M_i^{k+1} - N_i^{k+1}|. \end{aligned} \tag{3.23}$$

By the mean value theorem, we have

$$A_{M,i+\frac{1}{2}}^{k+1} - A_{N,i+\frac{1}{2}}^{k+1} = \alpha_i^{k+1} \left(M_i^{k+1} - N_i^{k+1} \right) + \beta_{i+1}^{k+1} \left(M_{i+1}^{k+1} - N_{i+1}^{k+1} \right)$$

where $\alpha_i^{k+1} \le 0$ and $\beta_i^{k+1} \ge 0$ are defined as

$$\begin{aligned} \alpha_i^{k+1} &:= \partial_1 A(\xi_i^{k+1}, M_{i+1}^{k+1}) = \frac{A(M_i^{k+1}, M_{i+1}^{k+1}) - A(N_i^{k+1}, M_{i+1}^{k+1})}{M_i^{k+1} - N_i^{k+1}}, \\ \beta_i^{k+1} &:= \partial_2 A(N_i^{k+1}, \eta_{i+1}^{k+1}) = \frac{A(N_i^{k+1}, M_{i+1}^{k+1}) - A(N_i^{k+1}, N_{i+1}^{k+1})}{M_{i+1}^{k+1} - N_{i+1}^{k+1}}, \end{aligned}$$

for some ξ_i^{k+1}, η_i^{k+1} between M_i^{k+1} and N_i^{k+1}. As a result,

$$\left(A_{M,i+\frac{1}{2}}^{k+1} - A_{N,i+\frac{1}{2}}^{k+1} \right) \mathrm{sign}(M_i^{k+1} - N_i^{k+1}) \le \alpha_i^{k+1} \left| M_i^{k+1} - N_i^{k+1} \right| + \beta_{i+1}^{k+1} \left| M_{i+1}^{k+1} - N_{i+1}^{k+1} \right|. \tag{3.24}$$

Similarly, we can prove that

$$\left(A^{k+1}_{M,i-\frac{1}{2}} - A^{k+1}_{N,i-\frac{1}{2}}\right) \mathrm{sign}(M_i^{k+1} - N_i^{k+1}) \geq \alpha_{i-1}^{k+1} \left|M_{i-1}^{k+1} - N_{i-1}^{k+1}\right| + \beta_i^{k+1} \left|M_i^{k+1} - N_i^{k+1}\right|. \tag{3.25}$$

Combining Eqs. (3.23, 3.24, 3.25), we finally get

$$\begin{aligned}&\left(1 - \Delta t G(0) - \nu\alpha_i^{k+1} + \nu\beta_i^{k+1}\right)\left|M_i^{k+1} - N_i^{k+1}\right| - \nu\beta_{i+1}^{k+1}\left|M_{i+1}^{k+1} - N_{i+1}^{k+1}\right| \\ &+ \nu\alpha_{i-1}^{k+1}\left|M_{i-1}^{k+1} - N_{i-1}^{k+1}\right| \leq \left|M_i^k - N_i^k\right|.\end{aligned}$$

Summing over i, we have

$$(1 - \Delta t G(0)) \sum_i |M_i^{k+1} - N_i^{k+1}| \leq \sum_i |M_i^k - N_i^k|.$$

which indicates that, when $\Delta t < 1/G(0)$,

$$\Delta x \sum_i \left|M_i^k - N_i^k\right| \leq \frac{1}{(1 - \Delta t G(0))^k} \Delta x \sum_i \left|M_i^0 - N_i^0\right| \leq C(T), \tag{3.26}$$

since we assumed that $\Delta x \sum_i \left|M_i^0 - N_i^0\right| \leq C$.
***BV*-estimate.** When $\Delta t < 1/G(0)$, by taking $M_i^k = N_{i+1}^k$ in Eq. (3.26), we get that,

$$\sum_i |N_{i+1}^k - N_i^k| \leq \frac{1}{(1 - \Delta t G(0))^k} \sum_i |N_{i+1}^0 - N_i^0| \leq C(T),$$

where in the last inequality we used the assumption $\sum_i |N_{i+1}^0 - N_i^0| \leqslant C$.
Estimate on time derivative. The boundedness of the discrete time derivative of the density comes directly from the L^1-contraction (3.26). Assuming $\Delta t < 1/G(0)$ and taking $M_i^k = N_i^{k+1}$ in Eq. (3.26), we have that

$$\Delta x \sum_i |\delta_t N_i^k| \leq \frac{1}{(1 - \Delta t G(0))^k} \Delta x \sum_i |\delta_t N_i^0| \leq C(T). \tag{3.27}$$

Analogous to the semi-discrete case, we can prove an estimate of the discrete time derivative of the pressure. Denoting $k(T) = \lfloor T/\Delta t \rfloor$, where $\lfloor x \rfloor$ is the largest integer that is less or equal than x, then we are able to prove that

$$\Delta t \Delta x \sum_{n=1}^{k(T)} \sum_i \left|\delta_t P_{N,i}^k\right| \leqslant C(T). \tag{3.28}$$

The proof is similar to the semi-discrete case. To begin with, we have that

$$|\delta_t P_{N,i}^k| = |\delta_t P_{N,i}^k| \mathbb{1}_{\{\max\{N_i^k, N_i^{k+1}\} \leq \frac{1}{2}\}} + |\delta_t P_{N,i}^{k+1}| \mathbb{1}_{\{\max\{N_i^k, N_i^{k+1}\} > \frac{1}{2}\}}.$$

The first term is uniformly bounded in γ thanks to Eq. (3.27) and

$$\begin{aligned}|\delta_t P_{N,i}^k| \mathbb{1}_{\{\max\{N_i^k, N_i^{k+1}\} \leqslant \frac{1}{2}\}} &\leq \gamma \max\{(N_i^k)^{\gamma-1}, (N_i^{k+1})^{\gamma-1}\} |\delta_t N_i^k| \mathbb{1}_{\{\max\{N_i^k, N_i^{k+1}\} \leqslant \frac{1}{2}\}} \\ &\leq \frac{\gamma}{2^{\gamma-1}} |\delta_t N_i^k|.\end{aligned} \tag{3.29}$$

To give an estimate of the second term, we recall the first inequality in Eq. (3.23), *i.e.*

$$
\begin{aligned}
I_1 \mathrm{sign}(M_i^{k+1} - N_i^{k+1}) \geq & (1 - \Delta t G(0))|M_i^{k+1} - N_i^{k+1}| \\
& + \Delta t \min_p |G'(p)| \max\{M_i^{k+1}, N_i^{k+1}\} \left| P_{M,i}^{k+1} - P_{N,i}^{k+1} \right| .
\end{aligned}
$$

And then following a similar procedure as before, we have that

$$
\begin{aligned}
&\left(1 - \Delta t G(0) - \nu \alpha_i^{k+1} + \nu \beta_i^{k+1}\right) \left|M_i^{k+1} - N_i^{k+1}\right| \\
&\qquad + \Delta t \min_p |G'(p)| \max\{M_i^{k+1}, N_i^{k+1}\} \left| P_{M,i}^{k+1} - P_{N,i}^{k+1} \right| \\
&\qquad - \nu \beta_{i+1}^{k+1} \left|M_{i+1}^{k+1} - N_{i+1}^{k+1}\right| + \nu \alpha_{i-1}^{k+1} \left|M_{i-1}^{k+1} - N_{i-1}^{k+1}\right| \\
&\qquad \leq \left|M_i^k - N_i^k\right| .
\end{aligned}
$$

Now taking $M_i^k = N_i^{k+1}$, dividing both sides by Δt and summing over i and $k = 0, 1, \ldots,$ we proved that

$$
\begin{aligned}
&\min_p |G'(p)| \Delta t \Delta x \sum_{k=1}^{k(T)} \sum_i \max\{N_i^k, N_i^{k+1}\} \left|\delta_t P_{N,i}^k\right| \\
\leq & \Delta x \sum_i \left|\delta_t N_i^0\right| - \Delta x \sum_i \left|\delta_t N_i^{k(T)}\right| + G(0) \Delta t \Delta x \sum_{k=1}^{k(T)} \sum_i |\delta_t N_i^k| \leq C(T),
\end{aligned}
$$

which further implies that

$$
\begin{aligned}
\Delta t \Delta x & \sum_{k=1}^{k(T)} \sum_i |\delta_t P_{N,i}^k| \mathbb{1}_{\{\max\{N_i^k, N_i^{k+1}\} > \frac{1}{2}\}} \\
& \leq 2 \Delta t \Delta x \sum_{k=1}^{k(T)} \sum_i \max\{N_i^k, N_i^{k+1}\} |\delta_t P_{N,i}^k| \\
& \leq C(T).
\end{aligned}
\tag{3.30}
$$

The conclusion (3.28) is then obvious by combining Eq. (3.29) and Eq. (3.30).
***L^2*-estimate on the pressure gradient.** Rewriting Eq. (3.20) to be

$$
\delta_t N_i^k = \frac{N_{i+\frac{1}{2}}^{k+1} - N_i^{k+1}}{\Delta x} Q_{i+\frac{1}{2}}^{k+1} + \frac{N_i^{k+1} - N_{i-\frac{1}{2}}^{k+1}}{\Delta x} Q_{i-\frac{1}{2}}^{k+1} + N_i^{k+1} (\delta_x^2 P_i^{k+1} + G_i^{k+1})
$$

and multiplying both sides by $\gamma (N_i^{k+1})^{\gamma - 1}$, we get

$$
\gamma (N_i^{k+1})^{\gamma-1} \delta_t N_i^k \leq \left(Q_{i+\frac{1}{2}}^{k+1}\right)_+^2 + \left(Q_{i-\frac{1}{2}}^{k+1}\right)_-^2 + \gamma P_i^{k+1} (\delta_x^2 P_i^{k+1} + G_i^{k+1}),
$$

by the following argument. By definition of $Q^{k+1}_{i+\frac{1}{2}}$ we have

$$\gamma(N_i^{k+1})^{\gamma-1}\frac{N^{k+1}_{i+\frac{1}{2}}-N_i^{k+1}}{\Delta x}Q^{k+1}_{i+\frac{1}{2}}=\begin{cases}0, & \text{if } Q^{k+1}_{i+\frac{1}{2}}<0,\\ \gamma(N_i^{k+1})^{\gamma-1}\frac{N^{k+1}_{i+1}-N_i^{k+1}}{\Delta x}Q^{k+1}_{i+\frac{1}{2}} & \text{if } Q^{k+1}_{i+\frac{1}{2}}>0,\end{cases}$$

and moreover, when $N^{k+1}_{i+1}\geqslant N_i^{k+1}$ convexity implies

$$\gamma(N_i^{k+1})^{\gamma-1}\frac{N^{k+1}_{i+1}-N_i^{k+1}}{\Delta x}\leqslant Q^{k+1}_{i+\frac{1}{2}}.$$

Noticing that $\delta_t P_i^k\leq\gamma(N_i^{k+1})^{\gamma-1}\delta_t N_i^k$ due to the convexity, we prove

$$\delta_t P_i^k\leq\left(Q^{k+1}_{i+\frac{1}{2}}\right)^2_+ +\left(Q^{k+1}_{i-\frac{1}{2}}\right)^2_- +\gamma P_i^{k+1}(\delta_x^2 P_i^{k+1}+G_i^{k+1}).\tag{3.31}$$

Summing Eq. (3.31) over all i, we have

$$\begin{aligned}\delta_t\sum_i P_i^k &\leq \sum_i\left(Q^{k+1}_{i+\frac{1}{2}}\right)^2_+ +\sum_i\left(Q^{k+1}_{i-\frac{1}{2}}\right)^2_- +\sum_i\gamma P_i^{k+1}(\delta_x^2P_i^{k+1}+G_i^{k+1})\\ &=(1-\gamma)\sum_i|Q^{k+1}_{i+\frac{1}{2}}|^2+\gamma\sum_i P_i^{k+1}G_i^{k+1}\\ &\leq(1-\gamma)\sum_i|Q^{k+1}_{i+\frac{1}{2}}|^2+\gamma G(0)\sum_i P_i^{k+1}.\end{aligned}$$

Then summing over $n=0,1,2,\dots$ and dividing both sides by $\gamma-1$, we get

$$\Delta t\Delta x\sum_{j=0}^k\sum_i|Q^j_{i+\frac{1}{2}}|^2\leq\frac{\Delta x\sum_i P_i^0-\Delta x\sum_i P_i^k}{\gamma-1}+\frac{\gamma}{\gamma-1}G(0)\Delta t\Delta x\sum_{j=0}^k\sum_i P_i^j\leq C(T).$$

□

3.4 Numerical simulations

Now we present some numerical results on Eq. (3.1) and for some extensions of the model including the effect of a nutrient. In particular, we are interested in the performance of the implicit scheme (3.20) for large values of γ, hence confirming the AP property of the scheme.

3.4.1 Accuracy test: the Barenblatt solution

At first, we consider the simplest example in order to test the accuracy of the scheme as γ increases. Let us take the standard porous medium equation in dimension 1, *i.e.* Eq. (3.1) with trivial reaction terms

$$\frac{\partial n}{\partial t}=\frac{\partial^2 n^{\gamma+1}}{\partial x^2},$$

where for sake of simplicity we take $p = \frac{\gamma+1}{\gamma} n^\gamma$. We take as initial data the delayed Barenblatt solution

$$n(x,0) = \frac{1}{t_0^\beta}\left(C - \beta\frac{\gamma}{2(\gamma+1)}\frac{x^2}{t_0^{2\beta}}\right)_+^{\frac{1}{\gamma}}, \tag{3.32}$$

with $t_0 = 0.01$, $\beta = 1/(\gamma+2)$ and C a positive constant to be chosen later.

We compare the numerical solution of the scheme to the Barenblatt profile for $\gamma = 3$, $\gamma = 12$, $\gamma = 40$. We compute the L^1-error for $\Delta x = 1/2^k$, with $k = 4, 5, 6, 7, 8$ and $\Delta t = 10^{-5}$.

We choose $[-15, 15]$ to be the spatial computational domain and $T = 0.1$ as final time. Upon defining $N_x = 30/\Delta x$, the error at time $t_j := j\Delta t$ is given by

$$err_1(t_j) = \sum_{i=1}^{N_x} |N_i^j - n(i\Delta x, t_j)|\Delta x. \tag{3.33}$$

In the formula of the exact solution, Eq. (3.32), we choose $C = 1$ for $\gamma = 3$ and $C = 0.1$ for $\gamma = 12, 40$. In Figure 3.1, the plots of both the analytical solution and the numerical solution are displayed. We notice that as γ increases, the moving boundary becomes sharper and sharper and this affects the accuracy of the scheme as can be seen in Figure 3.2, where on the left we display the error (3.33) along time till $T = 0.1$, and on the right we show the spatial convergence of our scheme by plotting the following error

$$\|err_1(t > 0.05)\|_\infty = \max_{j\Delta t > 0.05}\left\{\sum_{i=1}^{N_x} |N_i^j - n(i\Delta x, j\Delta t)|\Delta x\right\}, \tag{3.34}$$

with respect to Δx and for different values of γ. When checking the spatial convergence rate, we consider the maximal error over a period as in (3.34) to get rid of the affect due to oscillation as shown on the left of Figure 3.2. As shown in the figure, our scheme is roughly first order accurate in space, which is consistent with our intuition since the first order upwind finite difference discretization is applied in space.

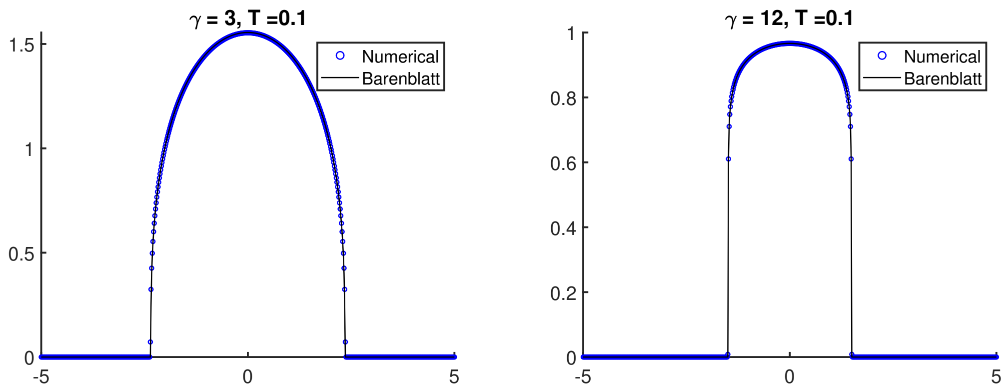

Figure 3.1: Porous Medium Equation in 1D: we compare the analytical solution and the numerical solution for $\gamma = 3$ (left) and $\gamma = 12$ (right), with $\Delta x = 1/64$ and $\Delta t = 0.01\Delta x$.

The oscillations of the error along time confirm the effect of the free boundary on the accuracy.

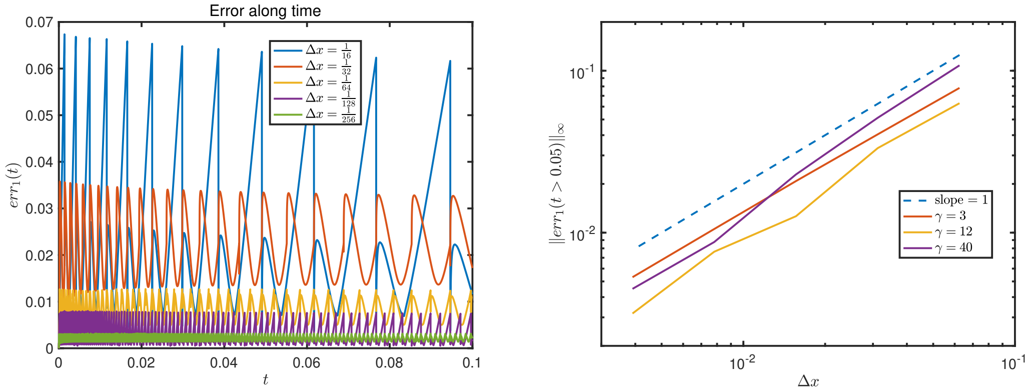

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Figure 3.2: Porous Medium Equation in 1D: Left: plot of the error along time for $\gamma = 12$. Right: plot of the error (3.34) with respect to Δx for different values of γ.

3.4.2 1D model with nutrient: *in vitro* and *in vivo*

Including the effect of a nutrient (*e.g.* oxygen) into the model, the density equation (3.1) is coupled with an equation for the nutrient concentration $c(x,t)$, to obtain the system

$$\begin{cases} \dfrac{\partial n}{\partial t} - \nabla \cdot (n \nabla p) = nG(p,c), \\ \tau \dfrac{\partial c}{\partial t} - \Delta c + H(n,c) = 0, \end{cases}$$

where H denotes the nutrient consumption and τ is a time scaling parameter. Since the nutrient diffuses much faster than the tumor invasion, it is usual to take $\tau = 0$. The consumption term H can take different forms, depending on which stage of tumor growth we put under investigation.

For instance, if one considers an *in vitro* setting, which means that the tumor is developing surrounded by an homogeneous liquid, then the level of nutrient is assumed to be constant outside the region occupied by the tumor, while inside it is consumed linearly, with a rate $\psi(n)$ depending on the tumor cell population density. The model reads

$$\begin{cases} -\Delta c + \psi(n)c = 0, & \text{in } \{n > 0\}, \\ c = c_B, & \text{in } \mathbb{R}^d \setminus \{n > 0\}. \end{cases} \tag{in vitro}$$

The consumption rate $\psi(n)$ is always non-negative and vanishes for $n = 0$.

A second kind of models are the *in vivo* models, which include the effect of the blood vessels that deliver the nutrient supply. During the early stages of tumor growth, the vasculature is present only outside the tumor region (*avascular phase*), and the equation reads

$$-\Delta c + \psi(n)c = (c_B - c)\mathbb{1}_{\{n=0\}}. \tag{in vivo}$$

On the other hand, if the tumor is already in its *vascular phase*, we have

$$-\Delta c + \psi(n)c = (c_B - c)K(p), \tag{in vivo: vascular}$$

where K is the nutrient release rate which depends on the pressure. In particular, we assume it to decrease with respect to the pressure to describe the shrinking effect of the mechanical stress generated by the cells on the vessels, which may cause the reduction of nutrients delivery, *cf.* [121]. We refer the reader to [131] for an extensive study of the Hele-Shaw model in both the *in vitro* and *in vivo* cases.
From now on, we assume that the growth term G depends only on the nutrient concentration, forgetting the effect of the pressure. Then, passing to the *incompressible limit* $\gamma \to \infty$, we obtain the limit problem

$$\begin{cases} \dfrac{\partial n_\infty}{\partial t} - \nabla \cdot (n_\infty \nabla p_\infty) &= n_\infty G(c_\infty), \\ -\Delta c_\infty + H(n_\infty, c_\infty) &= 0, \end{cases}$$

and since it holds $p_\infty(1 - n_\infty) = 0$, the density is constantly equal to 1 in the set $\{p_\infty > 0\}$.
As shown in [61], one can also pass to the limit in the equation for the pressure, which leads to the Hele-Shaw problem

$$\begin{cases} -\Delta p_\infty &= G(c_\infty), & \text{in } \Omega(t), \\ \quad p_\infty &= 0, & \text{on } \partial\Omega(t), \end{cases}$$

where $\Omega(t) := \{x \mid p_\infty(x,t) > 0\}$.

In vitro model: comparison with the exact solution of the Hele-Shaw problem

We consider the model (in vitro) in 1D with linear growth, *i.e.* $G(c) = c$, and $\psi(n) = n$, namely

$$\begin{cases} \partial_t n - \partial_x(n \partial_x p) &= nc, \\ -\partial_{xx} c + nc &= 0, & \text{in } \{n > 0\}, \\ c &= c_B, & \text{in } \mathbb{R}^d \setminus \{n > 0\}. \end{cases} \tag{3.35}$$

We take as initial density $n(x,0)$ the characteristic function of the interval $[-R_0, R_0]$, with $R_0 > 0$. Then, passing to the incompressible limit, the density remains always a patch, with support $[-R(t), R(t)]$. Therefore, we have

$$n_\infty = \mathbb{1}_{[-R(t),R(t)]}. \tag{3.36}$$

Thus, as computed in [113], the explicit solution is

$$c_\infty = \begin{cases} \dfrac{c_B \cosh(x)}{\cosh(R(t))}, & \text{for } x \in [-R(t), R(t)], \\ c_B, & \text{for } x \notin [-R(t), R(t)], \end{cases}$$

and

$$p_\infty = \begin{cases} -\dfrac{c_B \cosh(x)}{\cosh(R(t))} + c_B, & \text{for } x \in [-R(t), R(t)], \\ 0, & \text{for } x \notin [-R(t), R(t)]. \end{cases} \tag{3.37}$$

The velocity of the front is

$$R'(t) = c_B \tanh(R(t)).$$

We perform numerical simulations using our scheme for system (3.35) for $\gamma = 80$ and compare the results to the exact solution (3.36)-(3.37). We use the computational domain $[-5, 5]$ and

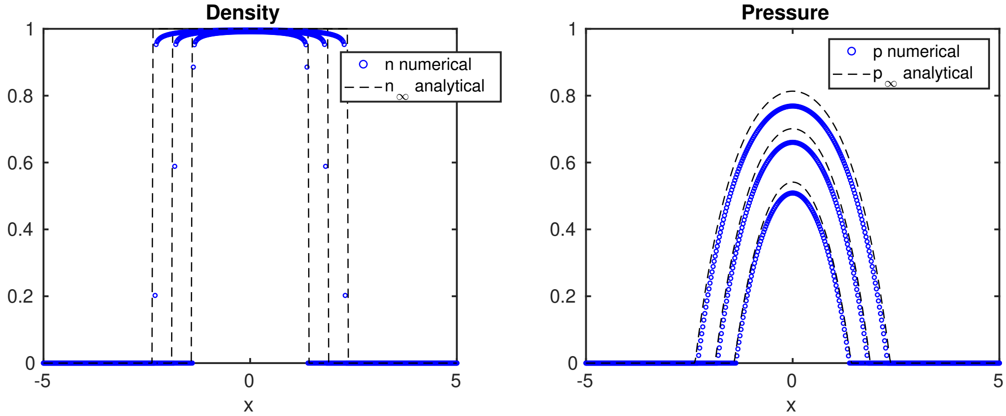

Figure 3.3: *In vitro* model in 1D: comparison between the numerical solution and the analytical solution at different times, t=0.5, t=1, t=1.5, with $\gamma = 80$, $\Delta x = 0.025$ and $\Delta t = 10^{-6}$.

choose as initial data

$$n(x,0) = (p_\infty(x,0))^{\frac{1}{\gamma}}\,, \tag{3.38}$$

with p_∞ defined by (3.37). We also set $c_B = 1$, $R(0) = 1$, $\Delta x = 0.025$ and $\Delta t = 10^{-6}$, *cf.* Fig. 3.3.

In vivo model: comparison with the exact solution

Using again a characteristic function as initial data, in the limit $\gamma \to \infty$ the model (in vivo) reads

$$-\partial_{xx} c_\infty + c_\infty = (c_B - c_\infty)\mathbb{1}_{\{n=0\}},$$

with $\{n = 0\} = \mathbb{R} \setminus [-R(t), R(t)]$. Thus, the explicit solution is given by

$$c_\infty = \begin{cases} \dfrac{c_B}{e^{R(t)}}\cosh(R(t)), & \text{for } x \in [-R(t), R(t)], \\ c_B - c_B \sinh(R(t))e^{-|x|}, & \text{for } x \notin [-R(t), R(t)], \end{cases}$$

cf. [113]. The limit pressure is

$$p_\infty = \begin{cases} -\dfrac{c_B G_0}{e^{R(t)}}\cosh(x) + \dfrac{c_B G_0}{e^{R(t)}}\cosh(R(t)), & \text{for } x \in [-R(t), R(t)], \\ 0, & \text{for } x \notin [-R(t), R(t)], \end{cases} \tag{3.39}$$

with a front invasion speed given by

$$R'(t) = c_B G_0 \frac{\sinh R(t)}{e^{R(t)}}.$$

As for the previous case, we perform numerical simulations using our scheme for the system (in vivo) with $\gamma = 80$ and compare the results to the exact solution. As before we choose (3.38) as initial data where the pressure is defined by (3.39) and we set $c_B = 1$, $R(0) = 1$, $\Delta x = 0.025$ and $\Delta t = 10^{-6}$, *cf.* Fig. 3.4. As in [112], we notice that the scheme is more accurate for the *in vivo* model than for the *in vitro*.

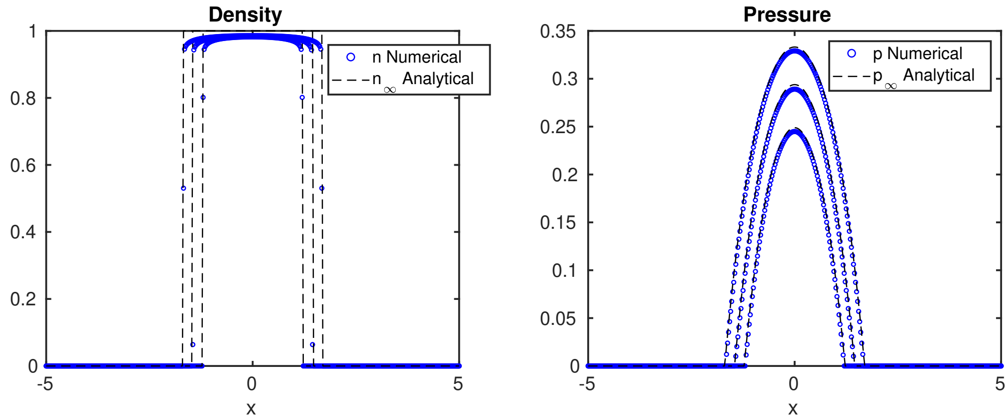

Figure 3.4: *In vivo* model in 1D: comparison between the numerical solution and the analytical solution at different times, t=0.5, t=1, t=1.5, with $\gamma = 80$, $\Delta x = 0.025$ and $\Delta t = 10^{-6}$.

3.4.3 Two-species model: proliferating and necrotic cells

We consider a model including a second species of cells. Indeed, at the early stages of its growth, the tumor mass develop a necrotic core of dead cells, which is surrounded by a rim of quiescent or proliferating cells. The model reads

$$\begin{cases} \dfrac{\partial n_P}{\partial t} - \dfrac{\partial}{\partial x}\left(n_P \dfrac{\partial p}{\partial x}\right) = n_P G(c), \\ \dfrac{\partial n_D}{\partial t} - \dfrac{\partial}{\partial x}\left(n_D \dfrac{\partial p}{\partial x}\right) = n_P (G(c))_-, \end{cases} \tag{3.40}$$

where n_P and n_D represent the cell densities of proliferating and necrotic (dead) cells. The total population density and the pressure are, respectively, $n = n_P + n_D$, $p = n^\gamma$.
Since in this case the growth rate $G = G(c)$ can be negative, the proliferating cells die and turn into necrotic with the same rate. In particular, we assume there exists a positive constant $\bar{c}$ such that $G(c) < 0$ if $c < \bar{c}$, to indicate that the cells die because of the lack of nutrients.
We use the scheme (3.20) for both the equations on n_P and n_D and we test it for both (in vitro) and (in vivo). We take as computational domain $[-6, 6]$, and we set $c_B = 1$,

$$G(c) = \begin{cases} 12 & \text{if } c < 0.4, \\ -15 & \text{if } c \geqslant 0.4, \end{cases}$$

and as initial data

$$n_P^0 = \mathbb{1}_{[-1,1]}, \qquad n_D^0 = 0.$$

The numerical simulations for the *in vitro* and *in vivo* environments are displayed along time in Fig. 3.5 and Fig. 3.6, respectively.

3.4.4 2D model: the focusing problem

The focusing solution of the porous medium equation is the solution of Eq. (3.1) with an initial data whose support is contained outside of a compact set. At finite time the empty bubble closes

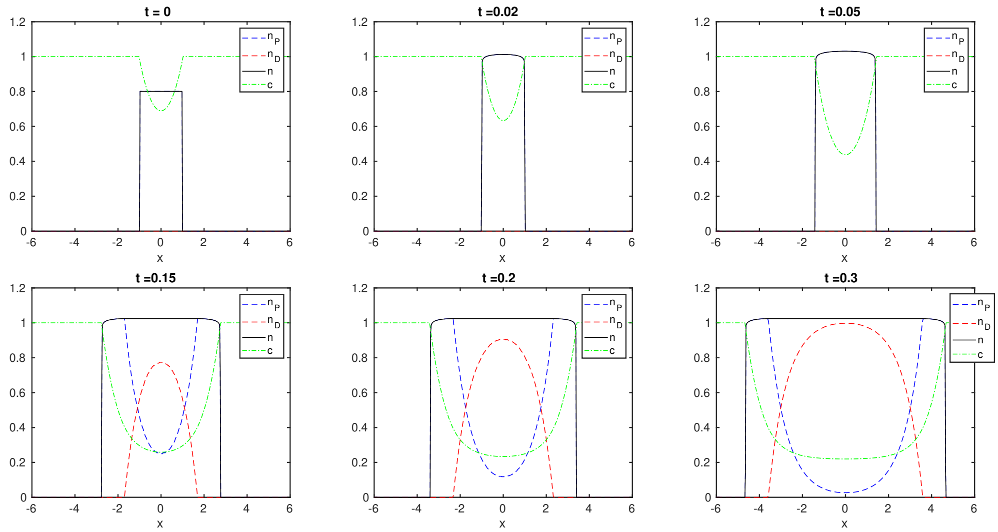

Figure 3.5: *In vitro* two-species model in 1D: plot of n_P, n_D, n, c with $\gamma = 80$, $\Delta x = 0.025$ and $\Delta t = 10^{-4}$.

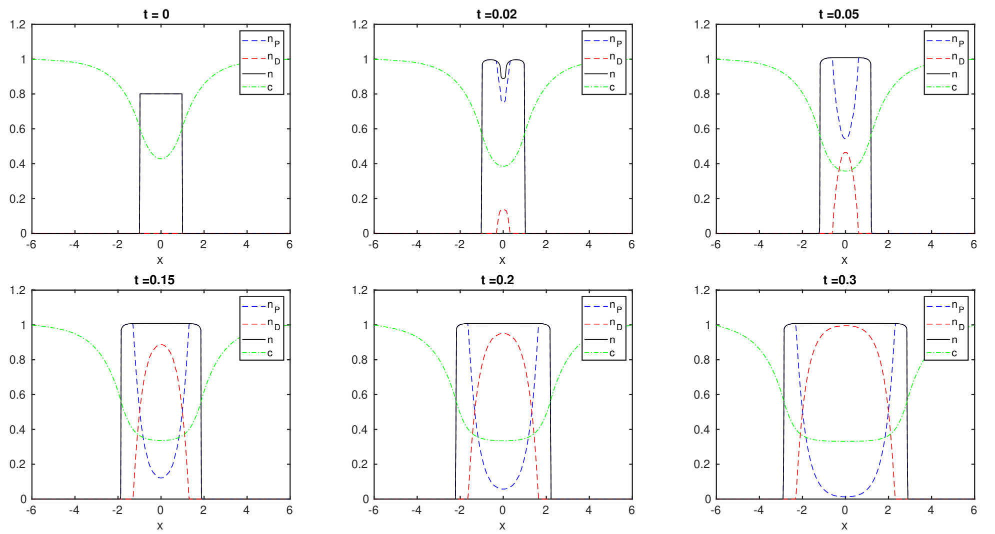

Figure 3.6: *In vivo* two-species model in 1D: plot of n_P, n_D, n, c with $\gamma = 80$, $\Delta x = 0.025$ and $\Delta t = 10^{-4}$.

up and the topological change of the support generates a singularity of the pressure gradient. In [61], the authors show that the pressure gradient is uniformly bounded with respect to γ in $L^4(\mathbb{R}^d \times (0,T))$. Then, they prove the sharpness of this uniform bound using the focusing solution as counterexample.

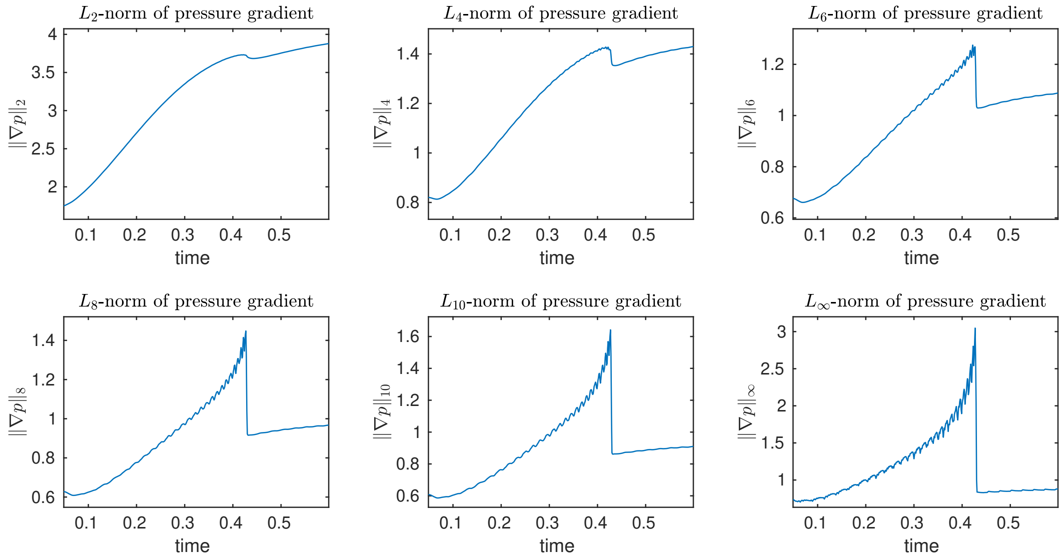

Figure 3.7: *Focusing solution: pressure gradient norms.* Plot of the pressure gradient norms along time, from the left ot the right, from the top down, $L^2, L^4, L^6, L^8, L^{10}, L^\infty$-norm, with $\gamma = 10$, $\Delta x = 0.02$, $\Delta t = 0.001$, $p_H = 1$ and initial internal radius 0.6.

The Hele-Shaw problem in a spherical shell is defined by the following system

$$\begin{cases} -\Delta p_\infty = G(p_\infty) & \text{in } \Omega(t), \\ V \quad = -\partial_\nu p_\infty & \text{on } \partial\Omega(t), \end{cases} \tag{3.41}$$

where ν and V denote the outward normal and the normal velocity of the free boundary, with

$$\Omega(t) = \{x;\ R_1(t) \leqslant |x| \leqslant R_2(t)\}.$$

In [61] the authors compute the asymptotic behaviour of the L^p-norms in space and time of the gradient of a radial solution, choosing for the sake of simplicity a constant reaction term and external radius $R_2(t) = R_2$ fixed. They show that the L^p-norms are *uniformly* bounded (with respect to γ) if and only if $p \leqslant 4$, which confirms that the uniform L^4-bound of the PME solution gradient is optimal.

We use our fully discrete scheme (3.20) in 2D to verify this interesting behaviour. We approximate the solution of system (3.41), taking $\gamma = 10$, which is a value that well approximate the behaviour of the solution as $\gamma \to \infty$.

We take as computational domain $[-8, 8] \times [-8, 8]$ and $G(p) = 1 - p$. The initial data is given by

$$n(x, y) = \begin{cases} 0.8 & \text{if} \quad 0.6 < \sqrt{x^2 + y^2} < 6, \\ 0 & \text{otherwise.} \end{cases} \tag{3.42}$$

The plots of the L^q_x-norms of $\nabla p(t)$, with $q = 2, 4, 6, 8$, are displayed along time in Fig. 3.7. We notice that at the focusing time, which is around $t = 0.428$, the norms with exponent larger than 4 develop a singularity. We also present 3D plots of the solution and its pressure as time evolves, *cf.* Fig. 3.8 and Fig. 3.9. In order to better show the behaviour and the shape of the focusing

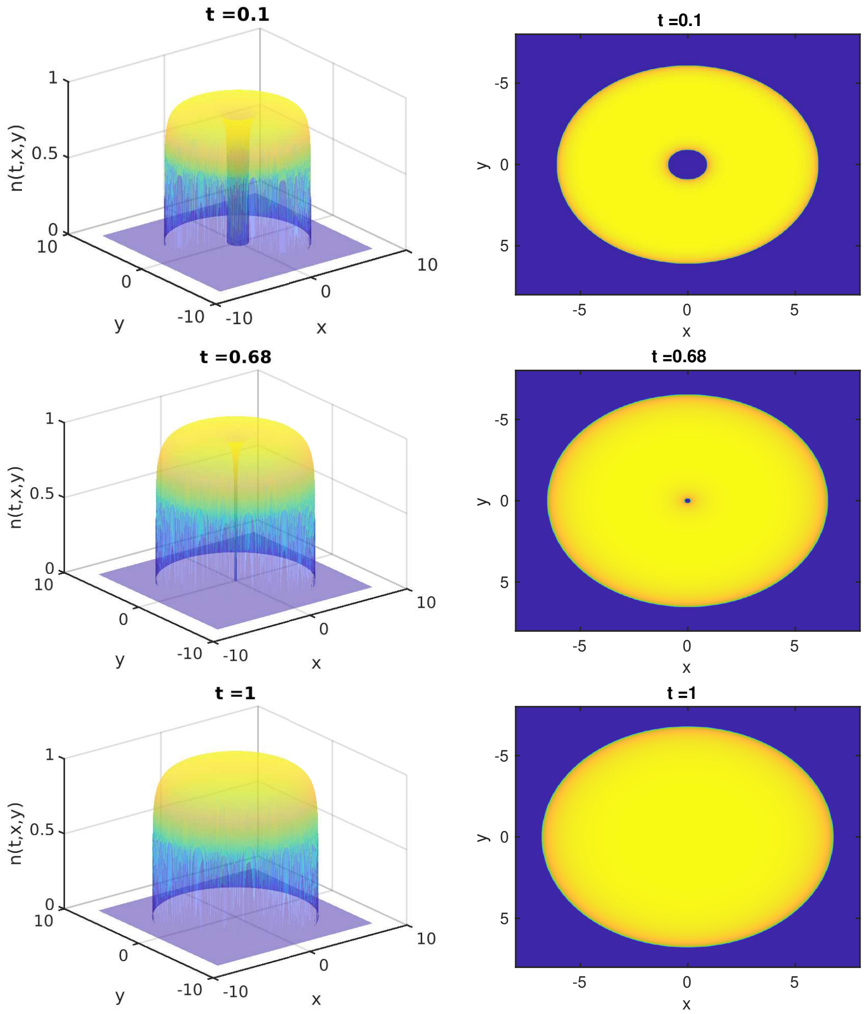

Figure 3.8: *Focusing solution (density).* Numerical solution of the focusing problem with $\gamma = 10$, $\Delta x = 0.02$, initial internal radius 1.

solution, we choose to take a larger initial internal radius. Hence, we take it to be equal to 1 rather than 0.6 in Eq. (3.42).

3.5 Conclusions

We studied the properties of an upwind finite difference scheme for a mechanical model of tumor growth proving stability results which allowed us to infer the asymptotic preserving property of the scheme in the so-called incompressible limit. We performed numerical simulations in order to investigate the sharpness of the L^4-uniform bound of the pressure gradient, using the focusing solution as limiting example.

The question of how to derive the Aronson-Bénilan estimate for a fixed grid and $\gamma > 1$ remains completely open and faces several technical difficulties, due to the stronger non-linearity of the

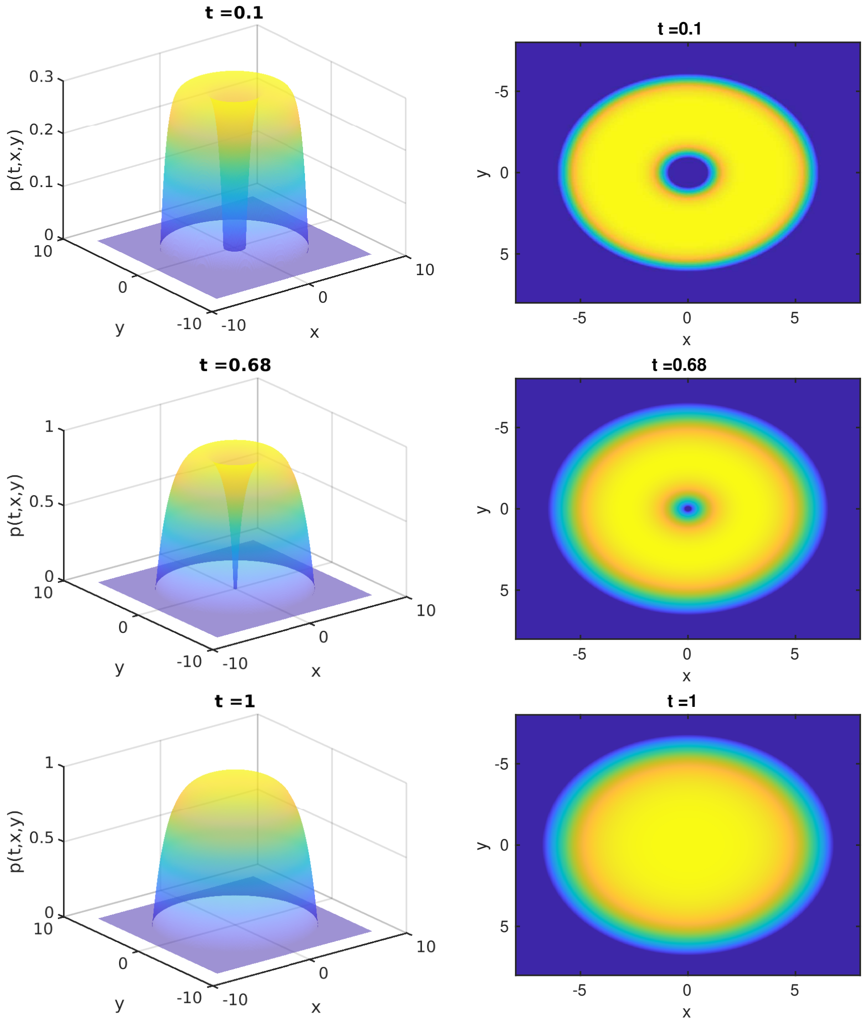

Figure 3.9: *Focusing solution (pressure).* Numerical solution of the focusing problem with $\gamma = 10$, $\Delta x = 0.02$, initial internal radius 1.

equation. Moreover, as aforementioned, it could be of use in order to pass to the limit as $\Delta x \to 0$ in the semi-discrete scheme. Extending our approach on the Aronson-Bénilan estimate to finite difference schemes for cross-reaction-diffusion systems of porous medium type could also represent a challenging problem.

3.A Proof of the solvability of (3.22)

The following theorem, which is a generalization of [3, Theorem A.1] holds.

Theorem 3.A.1. *Denote $\bar{n}_i(t)$ and $\underline{n}_i(t)$ to be two solutions of the system of equations*

$$\frac{dn_i(t)}{dt} + (1-\alpha_i(t))n_i(t) - \nu\left[A(n_i(t), n_{i+1}(t)) - A(n_{i-1}(t), n_i(t))\right] = N_i^k, \quad i \in I, \tag{3.43}$$

where $A(n_i(t), n_{i+1}(t))$ is defined from (3.21), $\nu = \Delta t/\Delta x$, $\alpha_i(t) = \Delta t G(n_i^\gamma(t))$ and $\Delta t < 1/G(0)$, with a super- and a sub-solution initial data, respectively, i.e.

$$\bar{n}_i(0) = p_H^{\frac{1}{\gamma}}, \quad \underline{n}_i(0) = 0.$$

Then we have
(i) $\bar{n}_i(t)$ and $\underline{n}_i(t)$ are nonnegative for all $t > 0$ and $i \in I$.
(ii) $\bar{n}_i(t)$ and $\underline{n}_i(t)$ are super- and sub-solutions for all $t > 0$ and $i \in I$.
(iii) $\bar{n}_i(t) \geq \underline{n}_i(t)$ for all $t > 0$ and $i \in I$.
(iv) for any $i \in I$, both $\bar{n}_i(t)$ and $\underline{n}_i(t)$ converges to the same limit, which is the unique solution of (3.22).

Proof. (i) We prove the case of supersolution. The proof for the case of subsolution is similar. Consider the moment t^* when $\bar{n}_i(t)$ first reach 0 for some i_0, i.e. $\bar{n}_{i_0}(t^*) = 0$ while $\bar{n}_i(t^*) \geq 0$ for all $i \neq i_0$, then $A(\bar{n}_{i_0}(t), \bar{n}_{i_0+1}(t)) \geq 0$, $A(\bar{n}_{i_0-1}(t), \bar{n}_{i_0}(t)) \leq 0$ and thus

$$\frac{d\bar{n}_{i_0}(t^*)}{dt} = \nu \left[A(\bar{n}_{i_0}(t), \bar{n}_{i_0+1}(t)) - A(\bar{n}_{i_0-1}(t), \bar{n}_{i_0}(t))\right] + N_{i_0}^k \geq 0,$$

via the evolution equation (3.43). As a result, $\bar{n}_i(t)$ can't change signs and thus remain nonnegative for all $t \geq 0$.

(ii) Here we prove the case of subsolution. The proof for the case of supersolution is similar. Denote

$$\underline{z}_i(t) = \frac{d\underline{n}_i(t)}{dt}, \quad \underline{\alpha}_i(t) = \Delta t G(\underline{n}_i^\gamma(t)), \quad \underline{A}_{i+\frac{1}{2}}(t) = A(\underline{n}_i(t), \underline{n}_{i+1}(t)),$$

then $\underline{z}_i(0) \geq 0$ for all i since $\underline{n}_i(0)$ is a subsolution. Differentiating (3.43), we get

$$\begin{aligned}&\frac{d\underline{z}_i(t)}{dt} + (1 - \underline{\alpha}_i(t))\underline{z}_i(t) - \underline{\alpha}_i'(t)\underline{n}_i(t) - \nu\left[\partial_1 \underline{A}_{i+\frac{1}{2}} - \partial_2 \underline{A}_{i-\frac{1}{2}}\right]\underline{z}_i(t) \\ =&\nu \partial_2 \underline{A}_{i+\frac{1}{2}} \underline{z}_{i+1}(t) - \nu \partial_1 \underline{A}_{i-\frac{1}{2}} \underline{z}_{i-1}(t).\end{aligned}$$

Noticing that $\underline{\alpha}_i'(t) = 0$ when $\underline{z}_i(t) = 0$, the function $\underline{z}_i(t)$ can't change signs following a similar argument as in (i), which implies that $\underline{z}_i(t) \geq 0$ for all $t \geq 0$. Then combining with (3.43), we have that

$$(1 - \underline{\alpha}_i(t))\underline{n}_i(t) - \nu\left[\underline{A}_{i+\frac{1}{2}}(t) - \underline{A}_{i-\frac{1}{2}}(t)\right] \leq N_i^k, \text{ for all } t \geq 0,$$

which shows that $\underline{n}_i(t)$ is always a subsolution.

(iii) Denote $w_i(t) = \bar{n}_i(t) - \underline{n}_i(t)$, then initially we have $w_i(0) \geq 0$ for all i. We wish to show that $w_i(t) \geq 0$ for all $t \geq 0$ and $i \in I$. For simplicity of notation, we denote

$$\bar{\alpha}_i(t) = \Delta t G(\bar{n}_i^\gamma(t)), \quad \underline{\alpha}_i(t) = \Delta t G(\underline{n}_i^\gamma(t)).$$

Noticing (3.3) and the fact that both $\bar{n}_i(t)$ and $\underline{n}_i(t)$ are nonnegative, when $\Delta t < 1/G(0)$, we have $\bar{\alpha}_i(t) \leq 1$ and $\underline{\alpha}_i(t) \leq 1$. A direct computation shows that

$$\begin{aligned}(1 - \bar{\alpha}_i(t))\bar{n}_i(t) - (1 - \underline{\alpha}_i(t))\underline{n}_i(t) &= (1 - \bar{\alpha}_i(t))w_i(t) + (\underline{\alpha}_i(t) - \bar{\alpha}_i(t))\underline{n}_i(t) \\ &= (1 - \bar{\alpha}_i(t) + \beta_i(t))w_i(t),\end{aligned}$$

where $\beta_i(t) = -\Delta t G'(\eta_i^\gamma(t))\gamma\eta_i^{\gamma-1}(t)\underline{n}_i(t) \geq 0$ for some nonnegative $\eta_i(t)$ between $\bar{n}_i(t)$ and

$\underline{n}_i(t)$. By (3.43) and the fact that $\bar{n}_i(t)$ and $\underline{n}_i(t)$ are super- and subsolutions, we have

$$(1 - \bar{\alpha}_i(t) + \beta_i(t))w_i(t) - \nu \left[A_{i+\frac{1}{2}}(\bar{n}_i, \bar{n}_{i+1}) - A_{i-\frac{1}{2}}(\bar{n}_{i-1}, \bar{n}_i)\right] \\ + \nu \left[A_{i+\frac{1}{2}}(\underline{n}_i, \underline{n}_{i+1}) - A_{i-\frac{1}{2}}(\underline{n}_{i-1}, \underline{n}_i)\right] \geq 0.$$

Combining the above inequality with the following expression

$$A_{i+\frac{1}{2}}(\bar{n}_i, \bar{n}_{i+1}) - A_{i+\frac{1}{2}}(\underline{n}_i, \underline{n}_{i+1}) = \partial_1 A_{i+\frac{1}{2}}(\xi_i, \bar{n}_{i+1})w_i + \partial_2 A_{i+\frac{1}{2}}(\underline{n}_i, \eta_{i+1})w_{i+1},$$

where $\partial_1 A_{i+\frac{1}{2}}(\xi_i, \bar{n}_{i+1}) \leq 0$ with some ξ_i between $\bar{n}_i$ and $\underline{n}_i$ and $\partial_2 A_{i+\frac{1}{2}}(\underline{n}_i, \eta_{i+1}) \geq 0$ with some η_{i+1} between $\bar{n}_{i+1}$ and $\underline{n}_{i+1}$, we have

$$\left[1 - \bar{\alpha}_i(t) + \beta_i(t) - \nu \left(\partial_1 A_{i+\frac{1}{2}}(\xi_i, \bar{n}_{i+1}) - \partial_2 A_{i-\frac{1}{2}}(\underline{n}_{i-1}, \eta_i)\right)\right] w_i(t) \\ - \nu \partial_2 A_{i+\frac{1}{2}}(\underline{n}_i, \eta_{i+1})w_{i+1}(t) + \nu \partial_1 A_{i-\frac{1}{2}}(\xi_{i-1}, \underline{n}_i)w_{i-1}(t) \geq 0.$$

Multiplying both sides by $\mathbb{1}_{\{w_i<0\}}$ and summing over i, we get

$$-\sum_i (1 - \bar{\alpha}_i(t) + \beta_i(t))w_i^- + I_1 + I_2 \geq 0,$$

where $w_i^- = \max\{-w_i, 0\}$ and

$$I_1 = \nu \sum_i \partial_2 A_{i-\frac{1}{2}}(\underline{n}_{i-1}, \eta_i)w_i(\mathbb{1}_{\{w_i<0\}} - \mathbb{1}_{\{w_{i-1}<0\}}),$$
$$I_2 = -\nu \sum_i \partial_1 A_{i+\frac{1}{2}}(\xi_i, \underline{n}_{i+1})w_i(\mathbb{1}_{\{w_i<0\}} - \mathbb{1}_{\{w_{i+1}<0\}}).$$

It is worth noticing that

$$w_i(\mathbb{1}_{\{w_i<0\}} - \mathbb{1}_{\{w_{i\pm1}<0\}}) \leq 0,$$

which implies that $I_1 \leq 0$, $I_2 \leq 0$ and further

$$\sum_i (1 - \bar{\alpha}_i(t) + \beta_i(t))w_i^- \leq 0. \tag{3.44}$$

It is easy to see from (3.44) that we must have $w_i^-(t) \equiv 0$, i.e. $w_i(t) \geq 0$ for all $t > 0$.
(iv) The monotonicity of $\bar{n}_i(t)$ and $\underline{n}_i(t)$ indicates that there exist the limits

$$\bar{N}_i = \lim_{t\to\infty} \bar{n}_i(t), \quad \underline{N}_i = \lim_{t\to\infty} \underline{n}_i(t).$$

Denote $W_i = \bar{N}_i - \underline{N}_i$, we can show that

$$\left[1 - \Delta t G(\bar{N}_i^\gamma) + \beta_i(t) - \nu \left(\partial_1 A_{i+\frac{1}{2}}(\xi_i, \bar{N}_{i+1}) - \partial_2 A_{i-\frac{1}{2}}(\underline{N}_{i-1}, \eta_i)\right)\right] W_i \\ - \nu \partial_2 A_{i+\frac{1}{2}}(\underline{N}_i, \eta_{i+1})W_{i+1} + \nu \partial_1 A_{i-\frac{1}{2}}(\xi_{i-1}, \underline{N}_i)W_{i-1} = 0,$$

for some ξ_i's and η_i's. Summing over all i, we have

$$\sum_i \left[1 - \Delta t G(\bar{N}_i^\gamma) + \beta_i(t)\right] W_i = 0.$$

Noticing that $W_i \geq 0$ and $1 - \Delta t G(\bar{N}_i^{\gamma}) + \beta_i(t) > 0$, we have $W_i = 0$ for all $i \in I$. In other words, for each i, there is a unique limit of $\bar{n}_i(t)$ and $\underline{n}_i(t)$ as $t \to \infty$, which is N_i^{k+1}, the unique solution of (3.22).

□

Part II

Stiff limit of a tumor growth model including convective effects: regularity and convergence rate

Chapter 4

Incompressible limit of a tumor growth model incorporating convective effects

Abstract

In this work we study a tissue growth model with applications to tumour growth. The model is based on that of Perthame, Quirós, and Vázquez proposed in 2014 but incorporates the advective effects caused, for instance, by the presence of nutrients, oxygen, or, possibly, as a result of self-propulsion. The main result of this work is the incompressible limit of this model which builds a bridge between the density-based model and a geometry free-boundary problem by passing to a singular limit in the pressure law. The limiting objects are then proven to be unique.

This chapter is taken from N. D. and M. Schmidtchen. *On the Incompressible Limit for a Tumour Growth Model incorporating Convective Effects*, Accepted for publication in CPAM, (2021).

4.1 Introduction

Modelling living tissue poses a whole range of challenges. On the one hand, it is important to identify the biomedical drivers that should be incorporated in the model, while, on the other hand there are certain modelling choices that need to be discussed. One of these choices that, in a way, separates the community is the type of model used to describe tissue growth. Roughly speaking we identify the following two types of models: those that describe the tissue as an evolving distribution in space and those that describe the tissue as an evolving domain in space. While the first type is mostly based on a partial differential equation description, the latter is known as a free-boundary or evolving boundary model.

The goal of this paper is to build a bridge between the two types of models by passing to the so-called stiff limit in the population-based model to obtain a free-boundary description. The model we propose here describes the evolution of the tissue density, $n_\gamma = n_\gamma(x,t)$, and is given by

$$\frac{\partial n_\gamma}{\partial t} - \nabla \cdot \ (n_\gamma \nabla p_\gamma) - \nabla \cdot (n_\gamma \nabla V) = n_\gamma G(p_\gamma). \tag{4.1}$$

on $\mathbb{R}^d$ and for $t > 0$. It is equipped with some non-negative initial data $n_\gamma(0,x) = n^0_\gamma(x) \in L^1_+(\mathbb{R}^d)$. Here $p_\gamma = n^\gamma_\gamma$ denotes the pressure, $G = G(p_\gamma)$ models the cell proliferation (resp. cell death), and $V = V(x,t)$ denotes a chemical concentration. In order to pass to the incompressible limit $\gamma \to \infty$ we need to study the equation satisfied by the pressure, *i.e.* , the equation

$$\frac{\partial p_\gamma}{\partial t} = \gamma p_\gamma(\Delta p_\gamma + \Delta V + G(p_\gamma)) + \nabla p_\gamma \cdot \nabla(p_\gamma + V). \tag{4.2}$$

While it is intuitive to expect

$$p_\infty(\Delta p_\infty + \Delta V + G(p_\infty)) = 0, \quad \text{as well as} \quad p_\infty(n_\infty - 1) = 0,$$

in the limit, there are technical subtleties, obtaining strong compactness of the pressure gradient to be precise, that need to be overcome. We are by no means the first to ask this question. As a matter of fact, there are already some promising results towards this rigorous limit. However, all of them are borderline and just not good enough to obtain the strong compactness of the pressure gradient. A blend of two techniques finally allows us to settle this open question. The rest of the introduction is dedicated to recall previous results on this type of models. We will also use this as an opportunity to introduce the tools necessary for the limit passage in a brief, explanatory way.

4.1.1 Previous works on the incompressible limit

The question of passing to the incompressible limit has a rich history and several variations of it have been studied in the literature. Historically, the problem has its early foundation in the work of Bénilan and Crandall on the continuous dependence on φ of solutions to the filtration equation $\partial_t n = \Delta\varphi(n)$ in 1981, *cf.* [18], see also [127, 141].
Henceforth the problem has been attracting a lot of attention. In [45] the authors consider the limit of the density of the porous equation but they can weaken the assumption on the initial data thus extending the results of [18]. Moreover, they are able to show that the limit density, n_∞, is independent of time and bounded $0 \leqslant n_\infty \leqslant 1$. Later, in 2001, Gil and Quirós revisit the study of the incompressible limit of the solution of the porous medium equation defined in $[0, +\infty) \times \Omega$, with non-trivial boundary data $g = g(x)$.
In this case, the pressure is "forced" to be positive near to the boundary, and then, since the pressure gradient is no longer zero, the motion of the free boundary $\partial\{p_\infty > 0\}$ is governed by Darcy's law $V = -\partial_\nu p_\infty$, where ν denotes the outward normal on the free boundary, see also [88].
Emanating from the early works on the mesa problem for the porous medium equation, research began branching out in different directions. The first generalisation concerns the inclusion of a pressure-dependent growth term proposed in the work of [130]. Here the authors propose a tissue-growth model where cells move according to a population pressure generated by the total density of the form $p(n) = n^\gamma$. In conjunction with Darcy's law they recover the porous-medium type degenerate diffusion. In addition, they include a proliferation term, $nG(p)$, which models cells divisions with a pressure depending rate. Thus the proliferation rate, G, is assumed to be a decreasing function accounting for the fact that cells are less "willing" to divide in packed regimes. Their paper is seminal in that they were the first to perform the rigorous stiff pressure

limit in the presence of growth terms. While strong compactness of the pressure is absolutely sufficient for the Hele-Shaw limit itself, obtaining the so-called complementarity relation which provides an equation for the pressure in the limit is much more involved. In fact, in order to obtain it strong compactness of the pressure gradient is indispensable. To this purpose, using the comparison principle, they show that the Laplacian of the pressure satisfies an Aronson-Bénilan type estimate, namely $\Delta p + G(p) \gtrsim -C/\gamma t$.
Later in [102] the authors study the same model through a viscosity solution approach. They are also able to recover the velocity law in presence of *mushy regions*, *i.e.* regions where $P_\infty = 0$ and $0 < n_\infty < 1$.
The related free boundary problem was further studied in [123], where the authors prove that the velocity law of the free boundary holds both in a weak (distributional) and in a measure theoretical sense. In the same paper, they also provide an L^4-bound of the pressure gradient that relies on the Aronson-Bénilan estimate, which we extend to our model, Eq. (4.1), through a self-contained proof in Lemma 4.3.2, independently of any estimate on Δp_γ.
In [130], the authors also study an extension of the model including the effect of a nutrient with concentration $c = c(x, t)$. While they were able to prove the strong convergence of n_γ and c_γ as $\gamma \to \infty$, they leave open the question of how to recover the compactness needed to pass to the limit in the pressure equation and obtain the complementarity relation. As presented in Chapter 2, this problem was addressed in [61], where the authors combine a weak version of the Aronson-Bénilan estimate in L^3 with a uniform bound of the pressure gradient in L^4 to infer strong compactness. Recently, interesting progress have been made in [93] in the non-monotone case.
The model by [130] was then extended by the inclusion of migratory processes, *i.e.* , drift terms given by a velocity field, $v(x, t)$, as a model extension received a lot of attention.
In [106] and [1], this problem is analysed through both viscosity solutions and optimal transportation approaches. This result was extended in 2016, by Craig, Kim, and Yao, *cf.* [57] to a model with non-local Newtonian potential, $\mathcal{N}$. The question of how to pass to the limit $\gamma \to \infty$ in the porous medium equation with a drift and a non-trivial source term has been addressed in [103]. The authors propose a model with a generic vector field $v : \mathbb{R}^d \times \mathbb{R}^+ \to \mathbb{R}^d$ as drift term, *i.e.* ,

$$\frac{\partial n_\gamma}{\partial t} - \Delta n_\gamma^\gamma + \nabla \cdot (n_\gamma \; v) = n_\gamma G,$$

with a growth rate $G = G(x, t)$. Through viscosity solutions methods, they prove that as $\gamma \to \infty$ the model converges to a free boundary model of Hele-Shaw type. Their work improves the results previously achieved in [1], extending the class of initial data from patches to any continuous and compactly supported function bounded between zero and one.
This is also where our contribution to the current discourse enters, namely the first rigorous derivation of the complementarity relation, that is, an equation governing the pressure distribution inside of the moving boundary problem.

4.1.2 Our Contribution

As set out in the introduction, there have been several promising steps towards establishing the incompressible limit and the complementarity relation for reaction-diffusion models incorporating convective effects. As a matter of fact, just like the authors of [103], we address the problem of passing to the incompressible limit in a porous medium equation with both a drift and a source term. While their approach is based on a viscosity solution approach, we use a weak (distributional) interpretation. By employing a blend of recently developed tools, *i.e.* , an L^p-version of the celebrated Aronson-Bénilan estimate, *cf.* [9], along with the optimal L^4-regularity of the pressure gradient observed in [61], we can obtain strong compactness of the pressure gradient and proceed to passing to the incompressible limit and obtain the complementarity relation in the same vein as [31]. To summarise:

- We obtain an L^3-space-time estimate on the negative part of the Laplacian of the pressure which ultimately helps us obtain strong compactness of the pressure gradient. We note that an L^∞-version has been obtain recently in [105, Theorem 3.1]. However, the lower bound on the Laplacian of the pressure that they infer, $\Delta p \geqslant -C/t - C$, does not go to zero as $\gamma \to \infty$, as in the classical Aronson-Bénilan estimate. Nonetheless, this result in conjunction with our uniform L^4-estimate on the pressure gradient would already be sufficient to obtain the complementarity relation rigorously, following [61, 31, 123].

- Here, we choose a different route by only striving for the much weaker L^3-estimate on the negative part of the Laplacian of the pressure. This, in turn, allows us to drastically relax the $C^{3,1}_{x,t}$-regularity of the velocity field, ∇V, required by [105]. In fact, our assumptions on the drift, *cf.* Eq. (A1-V) and Eq. (A2-V), in a way boil down to controlling certain third derivatives in $L^{12/5}_{\mathrm{loc}}(Q_T)$.

- Finally, to the best of our knowledge, we are the first to prove the uniqueness of the solution, (n_∞, p_∞), to the limit problem
$$\frac{\partial n_\infty}{\partial t} = \Delta p_\infty + n_\infty G(p_\infty) + \nabla \cdot (n_\infty \nabla V).$$
This result is only possible since we work with weak solutions in the classical sense which ultimately allows us to apply a variation of Hilbert's duality method. The only related results in this direction in the literature are given by [1] where the uniqueness of so-called patch solutions is shown in the drift-diffusion model with $\Delta V > 0$ in the absence of growth dynamics and the very recent preprint [98] where uniqueness of the limit equation is shown for signed solutions, linear drifts, and general growth dynamics. In the absence of drifts uniqueness was known since [130] and for a special type of growth term it can also be obtained from λ-contractivity of metric gradient flows, cf. [70, 53].

Moreover, our approach provides an answer to several open problems proposed in [103]:

- The first question the authors raise concerns the monotonicity assumption on $G(p)+\Delta V > 0$, which in our case is not necessary. An improvement in this direction has also been obtained very recently, [93]. We stress that in the growth rate in [103] does not depend on the pressure but on space and time, only.

- The next question concerns the class of initial data. In [103], the authors write "A more interesting question arises with the initial data that is larger than 1 at some points. In such cases there is a jump in the solution at $t = 0$ in the limit '$\gamma \to \infty$' which adds another challenge in the analysis."[1] This effect has already been observed at the early stages of this singular limit problem. The parts of the density that are larger than 1 are known to "collaps" immediately and a mesa-structure is obtained instantaneously, for instance, *cf.* [45]. Following our approach, we can allow for the larger class of non-negative $L^1(\mathbb{R}^d) \cap L^\infty(\mathbb{R}^d)$ functions with compact support as initial data.[2]

[1] This quote is directly taken from [103] where we only adapted the notation to that of our paper.
[2] While L^∞-data with compact support immediately implies integrability, we trust that the assumption on the support may be removed by a localising argument in the spirit of [61, 94].

- Finally, in [103], the authors postulate BV-regularity of the limiting density, also suggested by [64] based on the "five-gradients-estimate" using tools from optimal transportation. Even though our arguments do not borrow techniques from optimal transport but, instead, rely on Sobolev compactness theory, we are able to improve the regularity result in that we obtain the BV-regularity of the limit density for any initial data. What is more, we additionally have an L^4-regularity of the limit pressure gradient, which, to the best of our knowledge, is novel.

4.1.3 Problem Setting and Main Results

Before we present the main results of our paper let us introduce some notation used throughout this work. Henceforth, we call $Q_T := \mathbb{R}^d \times (0,T)$ the truncated space-time cylinder and drop the subscript T to denote the entire cylinder, *i.e.* , $Q := \mathbb{R}^d \times (0,\infty)$. Besides, for the sake of readability, we shall employ the short-hand notation

$$n_\gamma := n_\gamma(t) := n_\gamma(x,t),$$

and, similarly,

$$p_\gamma = p_\gamma(t) := p_\gamma(x,t).$$

Moreover, throughout, $C > 0$ denotes a generic positive constant independent of γ that may change from line to line.

In order to be able to establish our result we impose the following set of assumptions which, for clarity, are split into assumptions on the initial data, the growth terms, and the advective term, respectively.
We assume that for every $\gamma > 1$ the initial data are non-negative, integrable, and uniformly essentially bounded, *i.e.* ,

$$n_\gamma^0 \in BV(\mathbb{R}^d) \cap L^\infty(\mathbb{R}^d), \quad 0 \leqslant n_\gamma^0 \leqslant n_M, \quad \text{and} \quad 0 \leqslant p_\gamma^0 \leqslant p_M, \tag{A1-n_γ^0}$$

for some constants $n_M, p_M > 0$. Here BV denotes the space of functions with bounded variation. Moreover, we assume the initial population is contained in a compact set, *i.e.* , there exists a bounded set $K \subset \mathbb{R}^d$ such that

$$\operatorname{supp}(n_\gamma^0) \subset K. \tag{A2-n_γ^0}$$

Let us notice that, thanks to the finite speed of propagation property of porous medium type equations, assumption (A2-n_γ^0) implies that, for any $T > 0$, there exists a bounded domain $\Omega \subset \mathbb{R}^d$ such that the supports of $n_\gamma(\cdot,t), p_\gamma(\cdot,t)$ are contained in Ω for any $t \in [0,T]$, uniformly in γ, as proven in the next section, *cf.* Lemma 4.2.1.
In addition, we suppose that there exists a positive constant C independent of γ such that

$$\|\Delta(n_\gamma^0)^{\gamma+1}\|_{L^1(\mathbb{R}^d)} + \|\nabla p_\gamma^0\|_{L^2(\mathbb{R}^d)} + \|(\Delta p^0)_-\|_{L^2(\mathbb{R}^d)} \leqslant C. \tag{A3-n_γ^0}$$

Note, that strictly speaking, the L^2-bound on the pressure gradient is not required as it is a consequence of the L^2-control on the Laplacian of the pressure. Besides we make the biological assumption

$$G'(p) < -\alpha, \quad \text{and} \quad G(p_M) = 0, \tag{A-G}$$

for some $\alpha > 0$ and all $p \geqslant 0$, and some $p_M > 0$, to include the tendency of tissue to grow slower as the pressure increases and starts to die when the pressure exceeds the homeostatic pressure, p_M. Finally, we have to make the following regularity assumptions on the chemical distribution

$$\begin{cases} \nabla(\partial_t V) \in L^1((0,T); L^\infty_{\text{loc}}(\mathbb{R}^d)), \\ \Delta(\partial_t V) \in L^1_{\text{loc}}(Q_T), \\ D^2 V \in L^\infty_{\text{loc}}(Q_T), \\ \nabla V \in L^2_{\text{loc}}(Q_T) \cap L^\infty_{\text{loc}}(Q_T), \end{cases} \tag{A1-V}$$

and

$$\nabla(\Delta V) \in L^{12/5}_{\text{loc}}(Q_T). \tag{A2-V}$$

Note, that the additional assumption, (A2-V), is required solely for technical reasons to establish the control of the Laplacian of the pressure.
Under these hypotheses we are now able to state the two main theorems of this work. The first concerns the complementarity relation.

Theorem 4.1.1 (Complementarity relation). *We may pass to the limit in Eq. (4.2) as $\gamma \to \infty$ and establish the so-called complementarity relation*

$$p_\infty(\Delta p_\infty + \Delta V + G(p_\infty)) = 0, \tag{4.3}$$

in the distributional sense. Moreover, $0 \leqslant n_\infty \leqslant 1$ and $p_\infty \geqslant 0$ satisfy the equation

$$\frac{\partial n_\infty}{\partial t} = \Delta p_\infty + n_\infty G(p_\infty) + \nabla \cdot (n_\infty \nabla V), \tag{4.4a}$$

in $\mathcal{D}'(Q_T)$, as well as

$$p_\infty(1 - n_\infty) = 0, \tag{4.4b}$$

almost everywhere.

The complementarity relation, Eq. (4.3), is a crucial link that allows us to bridge the gap between the compressible model, Eq. (4.1), and the geometrical free boundary problem of Hele-Shaw type. Let us define the set

$$\Omega(t) := \{x \mid p_\infty(x,t) > 0\}.$$

Then, the pressure satisfies

$$\begin{cases} -\Delta p_\infty = \Delta V + G(p_\infty), & \text{in } \Omega(t), \\ \quad p_\infty = 0, & \text{on } \partial\Omega(t), \end{cases}$$

which coincides with the classical Hele-Shaw problem whenever V and G are identically equal to zero.

Theorem 4.1.2 (Uniqueness of the limit solution). *There exists at most one distributional solution such that for all $T > 0$ the couple $(n_\infty, p_\infty) \in L^\infty(Q_T) \times L^2(0,T; H^1(\Omega))$ is a solution to system (4.4a).*

The rest of the paper is organised as follows. In Section 4.2 we present straigh-forward a priori estimates necessary to derive more refined bounds on the pressure. The latter are proven in

Section 4.3. This includes both the L^3-version of the Aronson-Bénilan estimate as well as an L^4-space-time estimate on the pressure gradient. Building on the estimates derived in the previous sections, Section 4.4 is dedicated to the rigorous limit process in the pressure equation and to obtaining the complementarity relation. In the subsequent section, Section 4.5, we then proceed to proving the uniqueness of solutions to the complementarity relation.

4.2 A Priori Estimates

We state some a priori estimates on the main quantities and their derivatives, that we need to obtain the main result of the paper.

Lemma 4.2.1 (A priori estimates)**.** *For any $T > 0$, there exists a bounded domain $\Omega \subset \mathbb{R}^d$ such that the supports of $n_\gamma(\cdot,t), p_\gamma(\cdot,t)$ are contained in Ω for any $t \in [0,T]$, uniformly in γ. Moreover, the following estimates hold uniformly in γ:*

(i) $n_\gamma, p_\gamma \in L^\infty(0,T;L^\infty(\Omega))$,

(ii) $\partial_i n_\gamma, \partial_t n_\gamma \in L^\infty(0,T;L^1(\Omega))$, *for* $i = 1,\dots,d$,

(iii) $\partial_i p_\gamma, \partial_t p_\gamma \in L^1((0,T)\times\Omega)$, *for* $i = 1,\dots,d$,

(iv) $\nabla p_\gamma \in L^2(0,T;L^2(\Omega))$.

Proof. Thanks to the comparison principle, from Eq. (4.1) we immediately find $n_\gamma \geqslant 0$ and, as a consequence, $p_\gamma \geqslant 0$. In order to establish uniform essential bounds, we construct a super solution. To this end we define

$$\Pi(x,t) := C\left(R(t) - \frac{|x|^2}{2}\right)_+$$

where C is a positive constant that satisfies

$$C \geqslant \frac{2}{d}(G(0) + \|\Delta V\|_\infty), \tag{4.5}$$

and we take $R(t)$ such that

$$R'(t) \geqslant (2C+1)R(t) + \frac{\|\nabla V\|_\infty}{2}. \tag{4.6}$$

From Eq. (4.2) and the assumption on the growth term (A-G), we know that p_γ satisfies

$$\frac{\partial p_\gamma}{\partial t} - |\nabla p_\gamma|^2 - \nabla p_\gamma \cdot \nabla V - \gamma p_\gamma(\Delta p_\gamma + G(0) + \|\Delta V\|_\infty) \leqslant 0.$$

Let us show that $\Pi(x,t)$ is a super-solution to this differential inequality. We have

$$\frac{\partial \Pi}{\partial t} = CR'(t)\mathbb{1}_{\left\{R(t)\geqslant \frac{|x|^2}{2}\right\}},$$

and

$$\nabla \Pi = -Cx\mathbb{1}_{\left\{R(t)\geqslant \frac{|x|^2}{2}\right\}},$$

as well as

$$\Delta\Pi = -Cd\mathbb{1}_{\left\{R(t)\geqslant\frac{|x|^2}{2}\right\}} - C|x|\delta_{\left\{R(t)=\frac{|x|^2}{2}\right\}}.$$

Using Eq. (4.5) in conjunction with Eq. (4.6) we get

$$\begin{aligned}\frac{\partial\Pi}{\partial t} - |\nabla\Pi|^2 - &\nabla\Pi\cdot\nabla V - \gamma\Pi(\Delta\Pi + G(0) + \|\Delta V\|_\infty)\\ &\geqslant CR'(t)\mathbb{1}_{\left\{R(t)\geqslant\frac{|x|^2}{2}\right\}} - C^2|x|^2\mathbb{1}_{\left\{R(t)\geqslant\frac{|x|^2}{2}\right\}} + Cx\cdot\nabla V\mathbb{1}_{\left\{R(t)\geqslant\frac{|x|^2}{2}\right\}} + \gamma C\Pi\frac{d}{2}\\ &\geqslant\left(R'(t) - 2CR(t) - \frac{|x|^2}{2} - \frac{\|\nabla V\|_\infty}{2}\right)\mathbb{1}_{\left\{R(t)\geqslant\frac{|x|^2}{2}\right\}}\\ &\geqslant 0.\end{aligned} \tag{4.7}$$

Taking $R(0)$ such that $K\subset B_{\sqrt{2R(0)}}$ and C large enough, by the assumption on the initial data (A2-n_γ^0) we have $p_\gamma^0\leqslant\Pi(0)$. Then, this implies that $p_\gamma(t)\leqslant\Pi(t)$ for all positive times by comparison. Let us show the argument for the sake of completeness.

Setting $N(\Pi)=\Pi^{1/\gamma}$, and multiplying Eq. (4.7) by $N'(\Pi)$ we obtain

$$\frac{\partial N}{\partial t} - N'(\Pi)|\nabla\Pi|^2 - N'(\Pi)\nabla\Pi\cdot\nabla V - \gamma N'(\Pi)\Pi\Delta\Pi \geqslant \gamma N'(\Pi)\Pi(G(0)+\|\Delta V\|_\infty),$$

whence

$$\frac{\partial N}{\partial t} - \nabla\cdot(N\nabla\Pi) - \nabla N\cdot\nabla V \geqslant N(G(0)+\|\Delta V\|_\infty).$$

Since, by Eq. (4.1), we know that n_γ is a sub-solution to the same equation, we have $n_\gamma(t)\leqslant N(t)$ for all $t>0$, by the comparison principle. Therefore, we conclude that $p_\gamma(t)\leqslant\Pi(t)$ for all positive times. We take $\Omega\subset\mathbb{R}^d$ a bounded domain such that $B_{\sqrt{2R(T)}}\subset\Omega$ and then, by the definition of Π, we infer that

$$\operatorname{supp}(p_\gamma(t))\subset\Omega,$$

for all $t\in[0,T]$ and any $\gamma>1$. As consequence, both n_γ and p_γ are uniformly bounded in $L^\infty(\Omega_T)$, where $\Omega_T:=\Omega\times(0,T)$.

Now we prove the BV-estimates on the density. Differentiating Eq. (4.1) with respect to the i-th component of the space variable, x_i, and multiplying by $\operatorname{sign}(\partial_{x_i}n_\gamma)$ we get

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega\left|\frac{\partial n_\gamma}{\partial x_i}\right|\mathrm{d}x &\leqslant \int_\Omega\gamma\Delta\left(n_\gamma^\gamma\left|\frac{\partial n_\gamma}{\partial x_i}\right|\right)\mathrm{d}x + \int_\Omega\nabla\cdot\left(n_\gamma\nabla\left(\frac{\partial V}{\partial x_i}\right)\right)\operatorname{sign}\left(\frac{\partial n_\gamma}{\partial x_i}\right)\mathrm{d}x + G(0)\int_\Omega\left|\frac{\partial n_\gamma}{\partial x_i}\right|\mathrm{d}x\\ &\leqslant\sum_{j=1}^d\int_\Omega\left|\frac{\partial n_\gamma}{\partial x_j}\right|\left|\frac{\partial^2 V}{\partial x_i\partial x_j}\right|\mathrm{d}x + \sum_{j=1}^d\int_\Omega n_\gamma\left|\frac{\partial^3 V}{\partial x_i\partial x_j^2}\right|\mathrm{d}x + G(0)\int_\Omega\left|\frac{\partial n_\gamma}{\partial x_i}\right|\mathrm{d}x,\end{aligned}$$

for $i=1,\dots,d$. We sum the inequalities over all $i=1,\dots,d$, and obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\sum_{i=1}^d\int_\Omega\left|\frac{\partial n_\gamma}{\partial x_i}\right|\mathrm{d}x \leqslant C\sum_{i=1}^d\int_\Omega\left|\frac{\partial n_\gamma}{\partial x_i}\right|\mathrm{d}x + C,$$

where the constants depend on the L^∞-norm of G and the assumptions on the potential V, *cf.* Eqs. (A-G, A1-V). Using Gronwall's lemma we conclude

$$\sum_{i=1}^{d}\int_\Omega \left|\frac{\partial n_\gamma}{\partial x_i}\right| \mathrm{d}x \leqslant Ce^{Ct}\sum_{i=1}^{d}\int_\Omega \left|\frac{\partial n_\gamma^0}{\partial x_i}\right| \mathrm{d}x \leqslant C(T),$$

where, in the last inequality, we have used the uniform BV-bounds on the initial data, *cf.* assumption (A1-n_γ^0).

Following the same line of reasoning for the time derivatives we obtain

$$\begin{aligned}\frac{\partial}{\partial t}\left|\frac{\partial n_\gamma}{\partial t}\right| \leqslant &\gamma\Delta\left(p_\gamma\left|\frac{\partial n_\gamma}{\partial t}\right|\right)+\nabla\cdot\left(\left|\frac{\partial n_\gamma}{\partial t}\right|\nabla V\right)+\operatorname{sign}\left(\frac{\partial n_\gamma}{\partial t}\right)\nabla\cdot\left(n_\gamma\nabla\left(\frac{\partial V}{\partial t}\right)\right)\\ &+\left|\frac{\partial n_\gamma}{\partial t}\right|G(p_\gamma)+n_\gamma G'(p_\gamma)\left|\frac{\partial p_\gamma}{\partial t}\right|,\end{aligned} \tag{4.8}$$

due to the fact that $\operatorname{sign}(\partial_t p_\gamma)=\operatorname{sign}(\partial_t n_\gamma)$. An integration in space yields

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega\left|\frac{\partial n_\gamma}{\partial t}\right|\mathrm{d}x \leqslant G(0)\int_\Omega\left|\frac{\partial n_\gamma}{\partial t}\right|\mathrm{d}x+\underbrace{\int_\Omega\left|\nabla\cdot\left(n_\gamma\nabla\left(\frac{\partial V}{\partial t}\right)\right)\right|\mathrm{d}x}_{\mathcal{I}},$$

where we used that $G'<-\alpha$, *cf.* Eq. (A-G). We can estimate the term $\mathcal{I}$ as follows

$$\begin{aligned}\mathcal{I}=&\int_\Omega\left|\nabla n_\gamma\cdot\nabla\left(\frac{\partial V}{\partial t}\right)+n\Delta\left(\frac{\partial V}{\partial t}\right)\right|\mathrm{d}x\\ \leqslant&\int_\Omega\left|\nabla n_\gamma\cdot\nabla\left(\frac{\partial V}{\partial t}\right)\right|\mathrm{d}x+\int_\Omega\left|n\Delta\left(\frac{\partial V}{\partial t}\right)\right|\mathrm{d}x\\ \leqslant&\left\|\nabla\left(\frac{\partial V}{\partial t}\right)(\cdot,t)\right\|_{L^\infty(\Omega)}\|\nabla n_\gamma\|_{L^\infty(0,T;L^1(\Omega))}+n_H\left\|\Delta\left(\frac{\partial V}{\partial t}\right)(\cdot,t)\right\|_{L^1(\Omega)}\\ \leqslant&C\left\|\nabla\left(\frac{\partial V}{\partial t}\right)(\cdot,t)\right\|_{L^\infty(\Omega)}+C\left\|\Delta\left(\frac{\partial V}{\partial t}\right)(\cdot,t)\right\|_{L^1(\Omega)},\end{aligned}$$

where we have used the BV-space regularity of n_γ from before. Hence, we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega\left|\frac{\partial n_\gamma}{\partial t}\right|\mathrm{d}x \leqslant G(0)\int_\Omega\left|\frac{\partial n_\gamma}{\partial t}\right|\mathrm{d}x+C\left\|\nabla\left(\frac{\partial V}{\partial t}\right)(\cdot,t)\right\|_{L^\infty(\Omega)}+C\left\|\Delta\left(\frac{\partial V}{\partial t}\right)(\cdot,t)\right\|_{L^1(\Omega)}.$$

By assumption (A1-V) we know that $\|\nabla(\partial_t V)(\cdot,t)\|_{L^\infty(\Omega)}$ and $\|\Delta(\partial_t V)(\cdot,t)\|_{L^1(\Omega)}$ are L^1-integrable in time. Using Gronwall's lemma, we conclude

$$\begin{aligned}\left\|\frac{\partial n_\gamma}{\partial t}(t)\right\|_{L^1(\Omega)} &\leqslant e^{G(0)t}\left\|\left(\frac{\partial n_\gamma}{\partial t}\right)_0\right\|_{L^1(\Omega)}\\ &\qquad + \int_0^t C\left(\left\|\nabla\left(\frac{\partial V}{\partial t}\right)(\cdot,t)\right\|_{L^\infty(\Omega)} + \left\|\Delta\left(\frac{\partial V}{\partial t}\right)(s,\cdot)\right\|_{L^1(\Omega)}\right) e^{G(0)(t-s)}\,\mathrm{d}s\\ &\leqslant C(T),\end{aligned} \tag{4.9}$$

for a.e. $t\in(0,T)$, *i.e.* , $\partial_t n_\gamma \in L^\infty(0,T;L^1(\Omega))$. Let us stress that assumptions (A1-n_γ^0) and (A3-n_γ^0) imply the initial bound $\left\|(\partial_t n_\gamma)_0\right\|_{L^1(\Omega)} \leqslant C$.

Before establishing the BV-bounds on the pressure, let us notice that integrating Eq. (4.8) in space and time, we have

$$\left\|\frac{\partial n_\gamma}{\partial t}(\cdot,t)\right\|_{L^1(\Omega)} + \min_{0\leqslant p_\gamma\leqslant \Pi(0,T)}|G'(p_\gamma)|\int_0^t\int_\Omega n_\gamma\left|\frac{\partial p_\gamma}{\partial t}\right|\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

thanks to Eq. (4.9). Then, it holds

$$\left\|\frac{\partial p_\gamma}{\partial t}\right\|_{L^1(\Omega_T)} \leqslant \iint_{\Omega_T\cap\{n_\gamma\leqslant 1/2\}}\gamma n_\gamma^{\gamma-1}\left|\frac{\partial n_\gamma}{\partial t}\right|\mathrm{d}x\,\mathrm{d}t + 2\iint_{\Omega_T\cap\{n_\gamma>1/2\}} n_\gamma\left|\frac{\partial p_\gamma}{\partial t}\right|\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

The same argument can be used for the space derivatives of p_γ and it goes through without major changes.

We can actually gain more information on the pressure gradient, by integrating Eq. (4.2) in space, *i.e.* ,

$$\int_\Omega \frac{\partial p_\gamma}{\partial t}\,\mathrm{d}x = \gamma\int_\Omega p_\gamma(\Delta(p_\gamma+V)+G(p_\gamma))\,\mathrm{d}x + \int_\Omega \nabla p_\gamma\cdot\nabla(p_\gamma+V)\,\mathrm{d}x.$$

Integration by parts yields

$$\int_\Omega \frac{\partial p_\gamma}{\partial t}\,\mathrm{d}x \leqslant (1-\gamma)\int_\Omega |\nabla p_\gamma|^2\,\mathrm{d}x + \gamma\int_\Omega p_\gamma G(p_\gamma)\,\mathrm{d}x + (1-\gamma)\int_\Omega \nabla p_\gamma\cdot\nabla V\,\mathrm{d}x,$$

and using Young's inequality we obtain

$$\frac{\gamma-1}{2}\iint_{\Omega_T}|\nabla p_\gamma(t)|^2\,\mathrm{d}x\,\mathrm{d}t \leqslant \|p_\gamma^0\|_{L^1(\Omega)} + \frac{(\gamma-1)}{2}\iint_{\Omega_T}|\nabla V|^2\,\mathrm{d}x\,\mathrm{d}t + \gamma\iint_{\Omega_T}|p_\gamma G(p_\gamma)|\,\mathrm{d}x\,\mathrm{d}t.$$

Dividing by $(\gamma-1)$ we finally get

$$\iint_{\Omega_T}|\nabla p_\gamma|^2\,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

which concludes the proof. $\square$

4.3 Stronger bounds on p_γ

This section is dedicated to establishing more refined estimates on the pressure, *cf.* Lemma 4.3.2 and Lemma 4.3.3. Upon obtaining those estimates we will then be able to proceed to proving the strong compactness of the pressure gradient, *cf.* Lemma 4.3.6, which is crucial in the overall endeavour of establishing the incompressible limit.

The first result on the pressure's regularity is the L^4-boundedness of its gradient. This bound was already proved in [123], although, the authors use the L^∞-version of the Aronson-Bénilan estimate. Here we adapted the method used in [61], where a new method was employed, that does not require any estimate on Δp_γ. Unlike the model in [61], the convective term may not vanish at the boundary which leads to boundary terms to be considered in the subsequent analysis. In the following remark we shall see, however, that they do not pose any problems.

Remark 4.3.1 (Boundary Terms and Integration by Parts)**.** The subsequent technical lemmas (Lemma 4.3.2 and Lemma 4.3.3) are critical to establishing the regularity necessary for passing to the stiff limit. Due to several integrations by parts, boundary terms occur that need to be addressed. Since their treatment is purely technical and they are not even at the heart of the strategy we introduce the notation $\mathcal{O}_{\partial\Omega_T}(1)$ to indicate that the traces of the respective quantities are bounded uniformly in γ. This is possible due to the elliptic regularity result presented in [89, Theorem 9.11] which states that

$$\|u\|_{H^2(U')} \leqslant C(\|u\|_{L^2(U)} + \|\Delta u\|_{L^2(U)}),$$

for some open $U \subset \mathbb{R}^n$ containing $U' \subset$ compactly. Choosing $u = \partial_i V$, for all $i = 1, \ldots, d$, and using assumption (A2-V), it is immediate that $\nabla \Delta V \in H^2(Q_T)$. With the third-order derivatives controlled in $L^2(Q_T)$ the traces of all second order derivatives appearing in the integration by parts are bounded. Let us highlight, too, that terms involving p_γ and its derivatives vanish close to the boundary by the choice of Ω_T. We therefore collect all boundary terms in $\mathcal{O}_{\partial\Omega_T}(1)$ lest the notation blow up.

Lemma 4.3.2 (L^4-estimate of the pressure gradient.)**.** *Given $T > 0$, there exists a positive constant C, independent of γ, such that*

$$\iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 p_\gamma}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x \, \mathrm{d}t + (\gamma - 1) \iint_{\Omega_T} p_\gamma |\Delta p_\gamma + \Delta V + G|^2 \, \mathrm{d}x \, \mathrm{d}t \leqslant C(T),$$

as well as

$$\iint_{\Omega_T} |\nabla p_\gamma|^4 \, \mathrm{d}x \, \mathrm{d}t \leqslant C(T).$$

Proof. We write the equation for the pressure as follows

$$\frac{\partial p_\gamma}{\partial t} = \gamma p_\gamma (\Delta f_\gamma + G) + \nabla p_\gamma \cdot \nabla f_\gamma, \tag{4.10}$$

where $f_\gamma := p_\gamma + V$. We multiply Eq. (4.10) by $-(\Delta f_\gamma + G)$ and integrate in space and time to obtain

$$\begin{aligned}
&\int_0^T \frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \frac{|\nabla p_\gamma|^2}{2}\,\mathrm{d}x\,\mathrm{d}t - \iint_{\Omega_T} \Delta V \frac{\partial p_\gamma}{\partial t}\,\mathrm{d}x\,\mathrm{d}t - \iint_{\Omega_T} G\frac{\partial p_\gamma}{\partial t}\,\mathrm{d}x\,\mathrm{d}t \\
&\qquad = \underbrace{-\iint_{\Omega_T} \nabla p_\gamma \cdot \nabla f_\gamma(\Delta f_\gamma + G)\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{I}} - \gamma\iint_{\Omega_T} p_\gamma |\Delta f_\gamma + G|^2\,\mathrm{d}x\,\mathrm{d}t.
\end{aligned} \tag{4.11}$$

For convenience, let us define the function $\overline{G} = \overline{G}(p_\gamma) = \int_0^{p_\gamma} G(q)\,\mathrm{d}q$. Thus, we have

$$\partial_t p_\gamma\, G(p_\gamma) = \partial_t \overline{G}(p_\gamma),$$

and thus

$$\iint_{\Omega_T} \frac{\partial p_\gamma}{\partial t}\, G(p_\gamma)\,\mathrm{d}x\,\mathrm{d}t = \int_0^T \frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \overline{G}(p_\gamma)\,\mathrm{d}x\,\mathrm{d}t.$$

Now, we need to estimate the term $\mathcal{I}$ on the right-hand side of Eq. (4.11). Since $p_\gamma = f_\gamma - V$ we have

$$\begin{aligned}
\mathcal{I} &= -\iint_{\Omega_T} \nabla p_\gamma \cdot \nabla f_\gamma (\Delta f_\gamma + G)\,\mathrm{d}x\,\mathrm{d}t \\
&= -\iint_{\Omega_T} |\nabla f_\gamma|^2 \Delta f_\gamma\,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} \nabla V\cdot\nabla f_\gamma \Delta f_\gamma\,\mathrm{d}x\,\mathrm{d}t - \iint_{\Omega_T} G\nabla p_\gamma\cdot\nabla f_\gamma\,\mathrm{d}x\,\mathrm{d}t \\
&\leqslant \underbrace{-\iint_{\Omega_T} |\nabla f_\gamma|^2 \Delta f_\gamma\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{I}_1} + \underbrace{\iint_{\Omega_T} \nabla V\cdot\nabla f_\gamma \Delta f_\gamma\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{I}_2} + C,
\end{aligned}$$

thanks to the L^2-bounds of both ∇p_γ and ∇V. We integrate by parts twice in space the term $\mathcal{I}_1$ and obtain

$$\begin{aligned}
\mathcal{I}_1 &= \iint_{\Omega_T} f_\gamma \Delta(|\nabla f_\gamma|^2)\,\mathrm{d}x\,\mathrm{d}t \\
&= 2\iint_{\Omega_T} f_\gamma \nabla f_\gamma\cdot\nabla(\Delta f_\gamma)\,\mathrm{d}x\,\mathrm{d}t + 2\iint_{\Omega_T} f_\gamma \sum_{i,j=1}^d \left|\frac{\partial^2 f}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1) \\
&= -2\iint_{\Omega_T} f_\gamma |\Delta f_\gamma|^2\,\mathrm{d}x\,\mathrm{d}t - 2\iint_{\Omega_T} |\nabla f_\gamma|^2\Delta f_\gamma\,\mathrm{d}x\,\mathrm{d}t + 2\iint_{\Omega_T} f_\gamma \sum_{i,j=1}^d \left|\frac{\partial^2 f}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1).
\end{aligned}$$

Let us notice that the second term on the right-hand side is equal to $-2\mathcal{I}_1$. Hence, moving it to the left-hand side of the equation and simplifying the expression we obtain

$$\begin{aligned}
-\mathcal{I}_1 &= -\iint_{\Omega_T} |\nabla f_\gamma|^2 \Delta f_\gamma\,\mathrm{d}x\,\mathrm{d}t \\
&= \frac{2}{3}\iint_{\Omega_T} f_\gamma |\Delta f_\gamma|^2\,\mathrm{d}x\,\mathrm{d}t - \frac{2}{3}\iint_{\Omega_T} f_\gamma \sum_{i,j=1}^d \left|\frac{\partial^2 f_\gamma}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1)
\end{aligned}$$

$$
\begin{aligned}
&= \frac{2}{3}\iint_{\Omega_T} p_\gamma |\Delta f_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t - \frac{2}{3}\iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left|\frac{\partial^2 f_\gamma}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x\,\mathrm{d}t \\
&\quad + \frac{2}{3}\iint_{\Omega_T} V|\Delta f_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t - \frac{2}{3}\iint_{\Omega_T} V \sum_{i,j=1}^{d} \left|\frac{\partial^2 f_\gamma}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1).
\end{aligned}
$$

We now compute the sum of the last two integrals of the right-hand side

$$
\begin{aligned}
\frac{2}{3}\iint_{\Omega_T} V|\Delta f_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t &- \frac{2}{3}\iint_{\Omega_T} V \sum_{i,j=1}^{d} \left|\frac{\partial^2 f_\gamma}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x\,\mathrm{d}t \\
&= \frac{2}{3}\iint_{\Omega_T} \left(\sum_{i,j=1}^{d} \frac{\partial f_\gamma}{\partial x_j}\frac{\partial^2 V}{\partial x_i \partial x_j}\frac{\partial f_\gamma}{\partial x_i} \,\mathrm{d}x\,\mathrm{d}t - \Delta V |\nabla f_\gamma|^2 \right) \mathrm{d}x\,\mathrm{d}t \\
&\leqslant C(\|D^2 V\|_{L^\infty}\|\nabla f_\gamma\|_{L^2}^2 + \|\Delta V\|_{L^\infty}\|\nabla f_\gamma\|_{L^2}^2) \\
&\leqslant C,
\end{aligned}
$$

having used the assumptions on the velocity field, *cf.* (A1-V), and the information on the pressure gradient, *cf.* Lemma 4.2.1. Therefore, we can estimate the term $-\mathcal{I}_1$ as follows

$$
-\mathcal{I}_1 \leqslant \frac{2}{3}\iint_{\Omega_T} p_\gamma |\Delta f_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t - \frac{2}{3}\iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left|\frac{\partial^2 f_\gamma}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x\,\mathrm{d}t + C.
$$

Now we proceed integrating by parts and estimating the term $\mathcal{I}_2$

$$
\begin{aligned}
\mathcal{I}_2 &= \iint_{\Omega_T} \nabla V \cdot \nabla f_\gamma \Delta f_\gamma \,\mathrm{d}x\,\mathrm{d}t \\
&= -\iint_{\Omega_T} \sum_{i,j=1}^{d} \frac{\partial f_\gamma}{\partial x_j}\frac{\partial^2 V}{\partial x_i \partial x_j}\frac{\partial f_\gamma}{\partial x_i} \,\mathrm{d}x\,\mathrm{d}t - \iint_{\Omega_T} \sum_{i,j=1}^{d} \frac{\partial V}{\partial x_j}\frac{\partial^2 f_\gamma}{\partial x_i \partial x_j}\frac{\partial f_\gamma}{\partial x_i} \,\mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1) \\
&\leqslant C\|D^2 V\|_{L^\infty}\|\nabla f_\gamma\|_{L^2}^2 - \iint_{\Omega_T} \sum_{i,j=1}^{d} \frac{\partial V}{\partial x_j}\frac{\partial^2 f_\gamma}{\partial x_i \partial x_j}\frac{\partial f_\gamma}{\partial x_i} \,\mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1) \\
&\leqslant C - \frac{1}{2}\iint_{\Omega_T} \nabla V \cdot \nabla |\nabla f_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1) \\
&= C + \frac{1}{2}\iint_{\Omega_T} \Delta V \cdot |\nabla f_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t + \mathcal{O}_{\partial\Omega_T}(1) \\
&\leqslant C + \frac{1}{2}\|\Delta V\|_{L^\infty}\|\nabla f_\gamma\|_{L^2}^2 + \mathcal{O}_{\partial\Omega_T}(1) \\
&\leqslant C.
\end{aligned}
$$

Therefore, we obtain

$$
\mathcal{I} \leqslant -\mathcal{I}_1 + \mathcal{I}_2
$$

$$
\begin{aligned}
&\leqslant \frac{2}{3} \iint_{\Omega_T} p_\gamma |\Delta f_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t - \frac{2}{3} \iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 f_\gamma}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x\,\mathrm{d}t + C \\
&\leqslant \frac{2}{3} \iint_{\Omega_T} p_\gamma |\Delta f_\gamma + G|^2 \,\mathrm{d}x\,\mathrm{d}t - \frac{2}{3} \iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 f_\gamma}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x\,\mathrm{d}t + C,
\end{aligned}
$$

where in the last inequality we used the fact that G is uniformly bounded.

Gathering all the bounds we can write Eq. (4.11) as

$$
\begin{aligned}
&\frac{2}{3} \iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 f_\gamma}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x\,\mathrm{d}t + \left(\gamma - \frac{2}{3}\right) \iint_{\Omega} p_\gamma |\Delta f_\gamma + G|^2 \,\mathrm{d}x\,\mathrm{d}t \\
&\qquad \leqslant \int_0^T \frac{\mathrm{d}}{\mathrm{d}t} \int_\Omega \left(\overline{G} - \frac{|\nabla p_\gamma|^2}{2} \right) \mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} \Delta V \frac{\partial p_\gamma}{\partial t} \,\mathrm{d}x\,\mathrm{d}t + C \\
&\qquad \leqslant \; C(T),
\end{aligned}
$$

where in the last inequality we used the L^1-bound of $\partial_t p_\gamma$. Thus, we have proved the following bound

$$
\frac{2}{3} \iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 f_\gamma}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x\,\mathrm{d}t + \left(\gamma - \frac{2}{3}\right) \iint_{\Omega_T} p_\gamma |\Delta f_\gamma + G|^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).
$$

Finally, thanks to the boundedness of $\partial^2_{i,j} V$, we have

$$
\begin{aligned}
&\iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 p_\gamma}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x\,\mathrm{d}t \\
&\qquad \leqslant 2 \iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 f_\gamma}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x\,\mathrm{d}t + 2 \iint_{\Omega_T} p_\gamma \sum_{i,j=1}^{d} \left| \frac{\partial^2 V}{\partial x_i \partial x_j} \right|^2 \mathrm{d}x\,\mathrm{d}t \\
&\qquad \leqslant C(T),
\end{aligned}
\tag{4.12}
$$

and since $\gamma > 1$

$$
\begin{aligned}
\iint_{\Omega_T} p_\gamma |\Delta p_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t &\leqslant 2 \iint_{\Omega_T} p_\gamma |\Delta f_\gamma + G|^2 \,\mathrm{d}x\,\mathrm{d}t + 2 \iint_{\Omega_T} p_\gamma |\Delta V + G|^2 \,\mathrm{d}x\,\mathrm{d}t \\
&\leqslant C(T),
\end{aligned}
$$

and the first part of the lemma is proven. Now it remains to prove the L^4-bound of the pressure gradient. Integrating by parts we have

$$
\int_\Omega |\nabla p_\gamma|^4 \,\mathrm{d}x = - \int_\Omega p_\gamma \Delta p_\gamma |\nabla p_\gamma|^2 \,\mathrm{d}x - \int_\Omega p_\gamma \nabla p_\gamma \cdot \nabla(|\nabla p_\gamma|^2) \,\mathrm{d}x.
$$

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

$$\frac{1}{2}\int_\Omega |\nabla p_\gamma|^4 \,\mathrm{d}x \leqslant \frac{1}{2}\int_\Omega p_\gamma^2 |\Delta p_\gamma|^2 \,\mathrm{d}x - 2\sum_{i,j=1}^d \int_\Omega p_\gamma \frac{\partial p_\gamma}{\partial x_i}\frac{\partial p_\gamma}{\partial x_j}\frac{\partial^2 p_\gamma}{\partial x_i \partial x_j}\,\mathrm{d}x.$$

Thanks to Young's inequality, the last term can be bounded from above by

$$\left| 2\sum_{i,j=1}^d \int_\Omega p_\gamma \frac{\partial p_\gamma}{\partial x_i}\frac{\partial p_\gamma}{\partial x_j}\frac{\partial^2 p_\gamma}{\partial x_i \partial x_j}\,\mathrm{d}x \right| \leqslant \frac{1}{4}\int_\Omega |\nabla p_\gamma|^4 \,\mathrm{d}x + 4\int_\Omega p_\gamma^2 \sum_{i,j=1}^d \left|\frac{\partial^2 p_\gamma}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x.$$

Therefore, we obtain

$$\frac{1}{4}\int_\Omega |\nabla p_\gamma|^4 \,\mathrm{d}x \leqslant \frac{1}{2}\int_\Omega p_\gamma^2 |\Delta p_\gamma|^2 \,\mathrm{d}x + 4\int_\Omega p_\gamma^2 \sum_{i,j=1}^d \left|\frac{\partial^2 p_\gamma}{\partial x_i \partial x_j}\right|^2 \mathrm{d}x.$$

Since $p_\gamma \leqslant \Pi(0,T)$ and thanks to Eq. (4.12), we conclude that

$$\iint_{\Omega_T} |\nabla p_\gamma|^4 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

which completes the proof. □

Building on the L^4-estimate on the pressure gradient, we are now dedicated to an additional bound on the pressure which, by itself, yields L^1-compactness of the pressure gradient. In conjunction with the L^4-estimate the gradient is then shown to be strongly compact in any $L^p(\Omega_T)$, for $1 \leqslant p < 4$, *cf.* Lemma 4.3.6. The subsequent estimate is an L^p-version of the celebrated Aronson-Bénilan estimate, *cf.* [9, 26]. At the heart of its proof is the study of an auxiliary second-order quantity and its evolution along the flow of the pressure equation. We define $w := \Delta p_\gamma + G(p_\gamma)$ and, for the reader's convenience, recall that the pressure satisfies the equation

$$\frac{\partial p_\gamma}{\partial t} = \gamma p_\gamma w + \gamma p_\gamma \Delta V + \nabla p_\gamma \cdot (\nabla p_\gamma + \nabla V). \tag{4.13}$$

Lemma 4.3.3 (Aronson-Bénilan L^3-estimate.)**.** *For all $T > 0$ and $\gamma > \max(1, 2 - \frac{2}{d})$, there exists a positive constant $C(T)$, independent of γ, such that*

$$\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

Proof. We compute the time derivative of w

$$\begin{aligned}\frac{\partial w}{\partial t} =& \gamma\Delta(p_\gamma w) + \gamma p_\gamma \Delta(\Delta V) + \gamma(w - G)\Delta V + 2\gamma \nabla p_\gamma \cdot \nabla(\Delta V) + 2\nabla p_\gamma \cdot \nabla(w - G)\\ &+ 2\sum_{i,j=1}^d \left|\frac{\partial^2 p_\gamma}{\partial x_i \partial x_j}\right|^2 + \nabla(w - G)\cdot\nabla V + \nabla p_\gamma \cdot \nabla(\Delta V) + 2\sum_{i,j=1}^d \frac{\partial^2 p_\gamma}{\partial x_i \partial x_j}\frac{\partial^2 V}{\partial x_i \partial x_j} + G'\frac{\partial p_\gamma}{\partial t}.\end{aligned}$$

Young's inequality yields

$$\left|2\sum_{i,j=1}^{d}\partial^2_{i,j}p_\gamma\frac{\partial^2 V}{\partial x_i\partial x_j}\right|\leqslant\sum_{i,j=1}^{d}\left|\frac{\partial^2 p_\gamma}{\partial x_i\partial x_j}\right|^2+\sum_{i,j=1}^{d}\left|\frac{\partial^2 V}{\partial x_i\partial x_j}\right|^2,$$

and thus, using Eq. (4.13), we get

$$\begin{aligned}\frac{\partial w}{\partial t}\geqslant&\gamma\Delta(p_\gamma w)+\gamma p_\gamma\Delta(\Delta V)+\gamma w\Delta V-\gamma G\Delta V+(2\gamma+1)\nabla p_\gamma\cdot\nabla(\Delta V)+2\nabla p_\gamma\cdot\nabla w\\&-2|\nabla p|^2G'+\sum_{i,j=1}^{d}\left|\frac{\partial^2 p_\gamma}{\partial x_i\partial x_j}\right|^2-\sum_{i,j=1}^{d}\left|\frac{\partial^2 V}{\partial x_i\partial x_j}\right|^2+\nabla w\cdot\nabla V-G'\nabla p\cdot\nabla V\\&+\gamma G'p_\gamma w+\gamma p_\gamma G'\Delta V+G'|\nabla p_\gamma|^2+G'\nabla p_\gamma\cdot\nabla V.\end{aligned}$$

We use the fact that

$$\sum_{i,j=1}^{d}\left|\frac{\partial^2 p_\gamma}{\partial x_i\partial x_j}\right|^2\geqslant\frac{1}{d}|\Delta p_\gamma|^2=\frac{1}{d}(w-G)^2,$$

and we obtain

$$\begin{aligned}\frac{\partial w}{\partial t}\geqslant&\gamma\Delta(p_\gamma w)+\gamma p_\gamma\Delta(\Delta V)+\gamma w\Delta V-\gamma G\Delta V+(2\gamma+1)\nabla p_\gamma\cdot\nabla(\Delta V)+2\nabla p_\gamma\cdot\nabla w\\&-|\nabla p|^2G'+\frac{1}{d}w^2-\frac{2}{d}wG+\frac{1}{d}G^2-\sum_{i,j=1}^{d}\left|\frac{\partial^2 V}{\partial x_i\partial x_j}\right|^2+\nabla w\cdot\nabla V\\&+\gamma G'p_\gamma w+\gamma p_\gamma G'\Delta V.\end{aligned}$$

We multiply by $-(w)_-$, to find

$$\begin{aligned}-\frac{\partial w}{\partial t}(w)_-\leqslant&-\frac{1}{d}(w)_-^3+\gamma\Delta V(w)_-^2-\frac{2}{d}G(w)_-^2+\gamma G'p_\gamma(w)_-^2-\frac{1}{d}G^2(w)_-+\gamma G\Delta V(w)_-\\&+\sum_{i,j=1}^{d}\left|\frac{\partial^2 V}{\partial x_i\partial x_j}\right|^2(w)_--\gamma p_\gamma G'\Delta V(w)_-+|\nabla p_\gamma|^2G'(w)_-\\&+\gamma\Delta(p_\gamma(w)_-)(w)_-+2\nabla p_\gamma\cdot\nabla(w)_-(w)_-\\&-\gamma p_\gamma\Delta(\Delta V)(w)_--(2\gamma+1)\nabla p_\gamma\cdot\nabla(\Delta V)(w)_-\\&+\nabla V\cdot\nabla(w)_-(w)_-.\end{aligned}$$

Hence, using the fact that $G' < -\alpha$ and integrating in space and time, we obtain

$$\begin{aligned}
-\int_\Omega \frac{(w^0)_-^2}{2}\,\mathrm{d}x \leqslant & -\frac{1}{d}\iint_{\Omega_T} (w)_-^3\,\mathrm{d}x\,\mathrm{d}t + C\gamma\iint_{\Omega_T} |w|_-^2\,\mathrm{d}x\,\mathrm{d}t + C\gamma\iint_{\Omega_T} (w)_-\,\mathrm{d}x\,\mathrm{d}t \\
& + \underbrace{\gamma\iint_{\Omega_T} \Delta(p_\gamma(w)_-)(w)_- + 2\nabla p_\gamma\cdot\nabla(w)_-(w)_-\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{I}_1} \\
& \underbrace{-\gamma\iint_{\Omega_T} p_\gamma\Delta(\Delta V)(w)_-\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{I}_2} - \underbrace{(2\gamma+1)\iint_{\Omega_T} \nabla p_\gamma\cdot\nabla(\Delta V)(w)_-\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{I}_3} \\
& + \underbrace{\iint_{\Omega_T} \nabla V\cdot\nabla(w)_-(w)_-\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{I}_4}
\end{aligned} \tag{4.14}$$

where C represents different constants depending on the L^∞-norms of G, G' and $\partial^2_{i,j}V$, for $i,j = 1,\dots,d$.

Now, we compute each term individually. Integration by parts yields

$$\begin{aligned}
\mathcal{I}_1 =& \gamma\iint_{\Omega_T} \Delta(p_\gamma(w)_-)(w)_- + 2\nabla p_\gamma\cdot\nabla(w)_-(w)_-\,\mathrm{d}x\,\mathrm{d}t \\
=& -\frac{\gamma}{2}\iint_{\Omega_T} \nabla p_\gamma\cdot\nabla(w)_-^2\,\mathrm{d}x\,\mathrm{d}t - \gamma\iint_{\Omega_T} p\,|\nabla(w)_-|^2\,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} \nabla p_\gamma\cdot\nabla(w)_-^2\,\mathrm{d}x\,\mathrm{d}t \\
=& -\left(1-\frac{\gamma}{2}\right)\iint_{\Omega_T} (w-G)(w)_-^2\,\mathrm{d}x\,\mathrm{d}t - \gamma\iint_{\Omega_T} p_\gamma\,|\nabla(w)_-|^2\,\mathrm{d}x\,\mathrm{d}t \\
=& \left(1-\frac{\gamma}{2}\right)\iint_{\Omega_T} (w)_-^3\,\mathrm{d}x\,\mathrm{d}t + \left(1-\frac{\gamma}{2}\right)\iint_{\Omega_T} G(w)_-^2\,\mathrm{d}x\,\mathrm{d}t - \gamma\iint_{\Omega_T} p_\gamma\,|\nabla(w)_-|^2\,\mathrm{d}x\,\mathrm{d}t \\
\leqslant& \left(1-\frac{\gamma}{2}\right)\iint_{\Omega_T} (w)_-^3\,\mathrm{d}x\,\mathrm{d}t - \gamma\iint_{\Omega_T} p_\gamma\,|\nabla(w)_-|^2\,\mathrm{d}x\,\mathrm{d}t + C\gamma\iint_{\Omega_T} (w)_-^2\,\mathrm{d}x\,\mathrm{d}t.
\end{aligned}$$

We continue by using integration by parts and Young's inequality to get

$$\begin{aligned}
\mathcal{I}_2 =& -\gamma\iint_{\Omega_T} p_\gamma\Delta(\Delta V)(w)_-\,\mathrm{d}x\,\mathrm{d}t \\
=& \gamma\iint_{\Omega_T} p_\gamma\nabla(\Delta V)\cdot\nabla(w)_-\,\mathrm{d}x\,\mathrm{d}t + \gamma\iint_{\Omega_T} \nabla p_\gamma\cdot\nabla(\Delta V)(w)_-\,\mathrm{d}x\,\mathrm{d}t \\
\leqslant& \frac{\gamma}{2}\iint_{\Omega_T} p_\gamma\,|\nabla(w)_-|^2\,\mathrm{d}x\,\mathrm{d}t + \frac{\gamma}{2}\iint_{\Omega_T} p_\gamma\,|\nabla(\Delta V)|^2\,\mathrm{d}x\,\mathrm{d}t \\
& + \gamma\left(\iint_{\Omega_T} |\nabla p_\gamma|^4\right)^{1/4}\left(\iint_{\Omega_T} |\nabla(\Delta V)(w)_-|^{4/3}\,\mathrm{d}x\,\mathrm{d}t\right)^{3/4}
\end{aligned}$$

$$
\begin{aligned}
&\leqslant \frac{\gamma}{2} \iint_{\Omega_T} p_\gamma \left|\nabla (w)_-\right|^2 \,\mathrm{d}x\,\mathrm{d}t + \frac{\gamma}{2} \iint_{\Omega_T} p_\gamma \left|\nabla(\Delta V)\right|^2 \,\mathrm{d}x\,\mathrm{d}t \\
&\quad + C\gamma \left(\iint_{\Omega_T} |\nabla(\Delta V)|^{12/5} \,\mathrm{d}x\,\mathrm{d}t \right)^{5/12} \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{1/3} \\
&\leqslant \frac{\gamma}{2} \iint_{\Omega_T} p_\gamma \left|\nabla (w)_-\right|^2 \,\mathrm{d}x\,\mathrm{d}t + C\gamma + C\gamma \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{1/3},
\end{aligned}
$$

where we used Hölder's inequality, the L^4-bound of the pressure gradient of Lemma 4.3.2 and the assumption (A2-V), $\nabla(\Delta V) \in L^{12/5}_{\mathrm{loc}}(Q_T)$.
Using again Young's and Holder's inequalities we have

$$
\begin{aligned}
\mathcal{I}_3 &\leqslant (2\gamma+1) \left(\iint_{\Omega_T} |\nabla p_\gamma|^4 \,\mathrm{d}x\,\mathrm{d}t \right)^{1/4} \left(\iint_{\Omega_T} |\nabla(\Delta V)(w)_-|^{4/3} \,\mathrm{d}x\,\mathrm{d}t \right)^{3/4} \\
&\leqslant C\gamma \left(\iint_{\Omega_T} |\nabla(\Delta V)|^{12/5} \,\mathrm{d}x\,\mathrm{d}t \right)^{5/12} \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{1/3} \\
&\leqslant C\gamma \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{1/3}.
\end{aligned}
$$

The last term is

$$
\mathcal{I}_4 = \iint_{\Omega_T} \frac{1}{2} \nabla V \cdot \nabla (w)_-^2 \,\mathrm{d}x\,\mathrm{d}t = -\frac{1}{2} \iint_{\Omega_T} \Delta V (w)_-^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C \iint_{\Omega_T} (w)_-^2 \,\mathrm{d}x\,\mathrm{d}t.
$$

Here we have used the fact that Ω is a compact set which contains $\mathrm{supp}(p_\gamma)$ and large enough such that $\Delta p_\gamma = 0$ on $\partial\Omega$, then $(w)_- = 0$ on $\partial\Omega$.
Hence, gathering all the estimates and using Hölder's inequality, we can rewrite Eq. (4.14) as

$$
\left(\frac{\gamma}{2} - 1 + \frac{1}{d}\right) \iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \leqslant C\gamma \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{1/3} + C\gamma \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{2/3} + C\gamma,
$$

since we assumed $(w^0)_- \in L^2(\mathbb{R}^d)$. Finally, for $\gamma > \max(1, 2-2/d)$, we have

$$
\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \leqslant C \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{1/3} + C \left(\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \right)^{2/3} + C,
$$

which yields

$$
\iint_{\Omega_T} (w)_-^3 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),
$$

where $C(T)$ depends on T, $|\Omega|$ and previous uniform bounds, and the proof is concluded.

□

Corollary 4.3.4. *It holds*

$$
\iint_{\Omega_T} |\Delta p_\gamma| \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T). \tag{4.15}
$$

Proof. The compact support assumption yields

$$\iint_{\Omega_T} (\Delta p_\gamma + G)\,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

and then, thanks to Hölder's inequality, we have

$$\begin{aligned}\iint_{\Omega_T} |\Delta p_\gamma + G|\,\mathrm{d}x\,\mathrm{d}t &= \iint_{\Omega_T} (\Delta p_\gamma + G)\,\mathrm{d}x\,\mathrm{d}t + 2\iint_{\Omega_T} (w)_-\,\mathrm{d}x\,\mathrm{d}t\\ &\leqslant C(T) + C\left(\iint_{\Omega_T} |w|_-^3\,\mathrm{d}x\,\mathrm{d}t\right)^{1/3}\\ &\leqslant C(T).\end{aligned}$$

Finally, since G is bounded, we obtain

$$\iint_{\Omega_T} |\Delta p_\gamma|\,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

□

Remark 4.3.5. The proof of the Aronson-Bénilan estimate can be made independent of the L^4-bound on ∇p_γ imposing a stronger condition on V, namely $\nabla(\Delta V) \in L^6$ rather than $L^{12/5}$.

The bounds provided by Lemma 4.3.2 and Lemma 4.3.3 allow us to prove the strong convergence of ∇p_γ in $L^2(Q_T)$ thanks to compactness arguments, in particular the Fréchet-Kolmogorov theorem and the Aubin-Lions lemma.

Lemma 4.3.6 (Strong convergence of the pressure gradient)**.** *For any $T > 0$ it holds*

$$\nabla p_\gamma \to \nabla p_\infty,$$

strongly in $L^2(Q_T)$.

Proof. Thanks to Lemma 4.3.2, we infer the weak convergence (up to a subsequence) of the pressure gradient

$$\nabla p_\gamma \rightharpoonup \nabla p_\infty, \tag{4.16}$$

weakly in $L^4(Q_T)$. From Lemma 4.3.3, we know that Δp_γ is bounded in $L^1(Q_T)$, which is instrumental in establishing space-time compactness in any $L^r(Q_T)$, with $1 \leqslant r < 4$. The proof of this claim is an extension of [109, Theorem 1] to a space-time setting.

To this end, let us define the continuous function ψ, by setting

$$\begin{cases}\psi(s) = -\epsilon, & \text{for } s < -\epsilon,\\ \psi(s) = s, & \text{for } -\epsilon \leqslant s \leqslant \epsilon,\\ \psi(s) = \epsilon, & \text{for } s > \epsilon,\end{cases}$$

for $\epsilon > 0$. Given $\gamma, \hat{\gamma} > 1$, we compute

$$\iint_{\Omega_T} |\nabla p_\gamma - \nabla p_{\hat{\gamma}}|^2 \psi'(p_\gamma - p_{\hat{\gamma}})\,\mathrm{d}x\,\mathrm{d}t = -\iint_{\Omega_T} (\Delta p_\gamma - \Delta p_{\hat{\gamma}})\psi(p_\gamma - p_{\hat{\gamma}})\,\mathrm{d}x\,\mathrm{d}t.$$

Next we split the domain into two parts by defining the set

$$\Omega_{T,\epsilon} := \{(x,t) \in \Omega_T \mid |p_\gamma(x,t) - p_{\hat{\gamma}}(x,t)| \leqslant \epsilon\}.$$

Thus, since Δp_γ is bounded in $L^1(Q_T)$ (uniformly with respect to γ), we have

$$\iint_{\Omega_{T,\epsilon}} |\nabla p_\gamma - \nabla p_{\hat{\gamma}}|^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C\epsilon.$$

Hence

$$\begin{aligned}\iint_{\Omega_T} |\nabla p_\gamma - \nabla p_{\hat{\gamma}}| \,\mathrm{d}x\,\mathrm{d}t &= \iint_{\Omega_{T,\epsilon}} |\nabla p_\gamma - \nabla p_{\hat{\gamma}}| \,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega^c_{T,\epsilon}} |\nabla p_\gamma - \nabla p_{\hat{\gamma}}| \,\mathrm{d}x\,\mathrm{d}t \\ &\leqslant C\epsilon^{1/2} + 2\,T^{1/2} \|\nabla p_\gamma\|_{L^2(Q_T)} \cdot |\Omega^c_{T,\epsilon}|^{1/2},\end{aligned}$$

where in the last line we used Hölder's inequality. Since p_γ is compact, it is a Cauchy sequence, and there exist $\Gamma(\epsilon)$ large enough such that for $\gamma, \hat{\gamma} > \Gamma(\epsilon)$ there holds

$$\iint_{\Omega_T} |\nabla p_\gamma - \nabla p_{\hat{\gamma}}| \,\mathrm{d}x\,\mathrm{d}t \leqslant C\epsilon^{1/2} + C\epsilon.$$

This implies that ∇p_γ is a Cauchy sequence in $L^1(Q_T)$. Up to a subsequence we have a.e. convergence. Thanks to Eq. (4.16), the pressure gradient is compact in any $L^r(Q_T)$, for $1 \leqslant r < 4$.

□

Remark 4.3.7. The tumour growth rate usually depends also on the presence of nutrients, therefore one can couple Eq. (4.1), with an equation on the nutrient concentration. Then, the model reads

$$\begin{cases} \dfrac{\partial n_\gamma}{\partial t} - \nabla \cdot \left(n_\gamma \nabla p_\gamma\right) - \nabla \cdot \left(n_\gamma \nabla V\right) &= n_\gamma G(p_\gamma, c_\gamma), \\ \dfrac{\partial c_\gamma}{\partial t} - \Delta c_\gamma &= -n_\gamma H(c_\gamma), \end{cases} \tag{4.17}$$

where H is the nutrient consumption rate. Thus, system (4.17) is actually an extension of the model with nutrient studied in [130].

Let us notice that the proofs of the estimates in Lemma 4.3.2 and Lemma 4.3.3 can be adapted for system (4.17) without any particular difficulty. In fact, the boundedness of the new terms depending on $c_\gamma, \nabla c_\gamma$, and Δc_γ relies only on the L^2-regularity of c_γ and its derivatives, which comes directly from its equation in system (4.17). Therefore, the strong convergence stated in Lemma 4.3.6 still holds for this model. We refer the reader to [130] and [61] for the complete treatment of these additional terms.

4.4 The Incompressible Limit

The results obtained in Section 4.3 allow us to finally pass to the incompressible limit in Eq. (4.2) and obtain the complementarity relation, Eq. (4.3). Let us point out that, thanks to the uniform (with respect to γ) boundness of ∇p_γ in $L^2(Q_T)$ and $\partial_t p_\gamma$ in $L^1(Q_T)$, the complementarity relation turns out to be equivalent to the strong convergence of ∇p_γ in $L^2(Q_T)$, given by Lemma 4.3.6.

Theorem 4.4.1 (Complementarity relation)**.** *We may pass to the limit in Eq. (4.2), as $\gamma \to \infty$, and obtain the so-called complementarity relation*

$$p_\infty(\Delta p_\infty + \Delta V + G(p_\infty)) = 0,$$

in the distributional sense. Moreover, n_∞ and p_∞ satisfy the equations

$$\frac{\partial n_\infty}{\partial t} = \Delta p_\infty + n_\infty G(p_\infty) + \nabla \cdot (n_\infty \nabla V), \tag{4.18a}$$

in $\mathcal{D}'(Q_T)$, as well as

$$p_\infty(1 - n_\infty) = 0, \tag{4.18b}$$

almost everywhere.

Proof. Thanks to the bounds in Lemma 4.2.1,

$$\iint_{\Omega_T} \left|\frac{\partial p_\gamma}{\partial t}\right| + |\nabla p_\gamma| \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

then, by the Fréchet-Kolmogorov Theorem, p_γ is strongly compact in $L^1(Q_T)$, for all $T > 0$. We integrate Eq. (4.2) against a test function $\varphi \in C_c^\infty(Q_T)$ to obtain

$$\begin{aligned}\iint_{Q_T} \frac{\partial p_\gamma}{\partial t}\varphi \,\mathrm{d}x\,\mathrm{d}t =& (1-\gamma)\left(\iint_{Q_T} |\nabla p_\gamma|^2 \varphi \,\mathrm{d}x\,\mathrm{d}t + \iint_{Q_T} \nabla p_\gamma \cdot \nabla V \varphi \,\mathrm{d}x\,\mathrm{d}t\right)\\ &- \gamma \iint_{Q_T} p_\gamma \nabla p_\gamma \cdot \nabla \varphi \,\mathrm{d}x\,\mathrm{d}t - \gamma \iint_{Q_T} p_\gamma \nabla V \cdot \nabla \varphi \,\mathrm{d}x\,\mathrm{d}t\\ &+ \gamma \iint_{Q_T} p_\gamma G(p_\gamma) \varphi \,\mathrm{d}x\,\mathrm{d}t.\end{aligned}$$

Dividing by $\gamma - 1$ and passing to the limit $\gamma \to \infty$, we obtain

$$\begin{aligned}\lim_{\gamma\to\infty} \Bigg[&- \iint_{Q_T} \left(|\nabla p_\gamma|^2 \varphi + p_\gamma \nabla p_\gamma \cdot \nabla \varphi\right) \mathrm{d}x\,\mathrm{d}t\\ &- \iint_{Q_T} \left(\nabla p_\gamma \cdot \nabla V \varphi + p_\gamma \nabla V \cdot \nabla \varphi\right) \mathrm{d}x\,\mathrm{d}t + \iint_{Q_T} p_\gamma G(p_\gamma)\varphi \,\mathrm{d}x\,\mathrm{d}t\Bigg] = 0.\end{aligned}$$

It remains to identify the limit. By the strong convergence of p_γ and ∇p_γ in $L^2(Q_T)$ we have

$$\begin{aligned}&- \iint_{Q_T} \left(|\nabla p_\infty|^2 \varphi + p_\infty \nabla p_\infty \cdot \nabla \varphi\right) \mathrm{d}x\,\mathrm{d}t - \iint_{Q_T} \left(\nabla p_\infty \cdot \nabla V \varphi + p_\infty \nabla V \cdot \nabla \varphi\right) \mathrm{d}x\,\mathrm{d}t\\ &+ \iint_{Q_T} p_\infty G(p_\infty)\varphi \,\mathrm{d}x\,\mathrm{d}t = 0,\end{aligned}$$

i.e. ,

$$p_\infty(\Delta p_\infty + \Delta V + G(p_\infty)) = 0,$$

in the distributional sense.
Now, we prove that Eq. (4.18a) and Eq. (4.18b) are satisfied. By Lemma 4.2.1, we have

$$\iint_{\Omega_T} \left|\frac{\partial n_\gamma}{\partial t}\right| + |\nabla n_\gamma| \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

and then we infer the compactness of the density. Up to a subsequence, we also have almost everywhere convergence, both for n_γ and p_γ. Passing to the limit in the relation $p_\gamma^{(1+\gamma)/\gamma} = n_\gamma p_\gamma$, we obtain

$$p_\infty(1 - n_\infty) = 0,$$

a.e. in Q_T.

Now, we may pass to the limit in Eq. (4.1) to obtain

$$\frac{\partial n_\infty}{\partial t} = \nabla \cdot \ (n_\infty \nabla p_\infty) + n_\infty G(p_\infty) + \nabla \cdot (n_\infty \nabla V).$$

From the following relation

$$\frac{1+\gamma}{\gamma} n_\gamma \nabla p_\gamma = p_\gamma \nabla n_\gamma + n_\gamma \nabla p_\gamma,$$

we infer $p_\infty \nabla n_\infty = 0$, and thus

$$n_\infty \nabla p_\infty = \nabla p_\infty.$$

By consequence, n_∞ and p_∞ satisfy

$$\frac{\partial n_\infty}{\partial t} = \Delta p_\infty + n_\infty G(p_\infty) + \nabla \cdot (n_\infty \nabla V),$$

which completes the proof. □

4.5 Uniqueness of the Limit Pressure

This section is dedicated to proving the following statement.

Theorem 4.5.1 (Uniqueness of n_∞ and p_∞)**.** *The incompressible limit obtained in the previous section,* (n_∞, p_∞)*,* cf. *Eq.* (4.4a) *is unique.*

Proof. In order to prove uniqueness, we assume that (n_1, p_1) and (n_2, p_2) are two solutions and let Ω be a compact, simply connected Lipschitz set that contains the union of their supports. Upon subtracting the equation for n_2 from the equation for n_1 we see that difference, $n_1 - n_2$, satisfies

$$\frac{\partial(n_1 - n_2)}{\partial t} - \Delta(p_1 - p_2) - \nabla \cdot ((n_1 - n_2)\nabla V) - (n_1 G(p_1) - n_2 G(p_2)) = 0. \tag{4.19}$$

For the sake of simplicity, we shall use the short-hand notation $G_i = G(p_i)$, for $i = 1, 2$, and $u = \nabla V$. Multiplying Eq. (4.19) by a test function $\psi = \psi(x, t)$ and integrating by parts we get

$$\iint_{\Omega_T} \left[(n_1 - n_2)\frac{\partial \psi}{\partial t} + (p_1 - p_2)\Delta\psi - (n_1 - n_2)\nabla\psi \cdot u + (n_1 G_1 - n_2 G_2)\psi \right] \mathrm{d}x \, \mathrm{d}t = 0. \tag{4.20}$$

The strategy is to employ Hilbert's dual method to establish uniqueness. To this end we introduce the following notation

$$\begin{cases} \mathcal{Z} & := n_1 - n_2 + p_1 - p_2, \\ \mathcal{A} & := \dfrac{n_1 - n_2}{\mathcal{Z}}, \\ \mathcal{B} & := \dfrac{p_1 - p_2}{\mathcal{Z}}, \\ \mathcal{C} & := -n_2 \dfrac{G_1 - G_2}{p_1 - p_2}, \end{cases}$$

where we set $\mathcal{A} = \mathcal{B} = 0$, whenever $\mathcal{Z} = 0$. Using this notation we rewrite Eq. (4.20) which becomes

$$\iint_{\Omega_T} \mathcal{Z} \left[\mathcal{A} \frac{\partial \psi}{\partial t} + \mathcal{B} \Delta \psi - \mathcal{A} \nabla \psi \cdot u + (\mathcal{A} G_1 - \mathcal{B}\mathcal{C}) \psi \right] \mathrm{d}x \, \mathrm{d}t = 0. \tag{4.21}$$

Note that, by definition,

$$0 \leqslant \mathcal{A}, \mathcal{B} \leqslant 1, \quad \text{as well as} \quad 0 \leqslant \mathcal{C} \leqslant \sup_{0 \leqslant p \leqslant p_M} |G'(p)|.$$

In order to apply Hilbert's duality method, we have to find a solution, ψ, to the *dual problem*

$$\mathcal{A} \frac{\partial \psi}{\partial t} + \mathcal{B} \Delta \psi - \mathcal{A} \nabla \psi \cdot u + (\mathcal{A} G_1 - \mathcal{B}\mathcal{C}) \psi = \mathcal{A} \xi, \tag{4.22}$$

in Ω_T, and $\psi = 0$ on $\partial\Omega \times (0, T)$. The equation is complemented by the final time condition $\psi(x, T) = 0$ for $x \in \Omega$. Here, ξ is an arbitrary smooth function. If solved, substituting the solution to the dual problem, ψ, into Eq. (4.21) would yield

$$\iint_{\Omega_T} \mathcal{A} \mathcal{Z} \xi \, \mathrm{d}x \, \mathrm{d}t = \iint_{\Omega_T} (n_1 - n_2) \xi \, \mathrm{d}x \, \mathrm{d}t = 0, \tag{4.23}$$

thus proving uniqueness of the density. Subsequently, from Eq. (4.20), the uniqueness of the pressure follows.

However, since the coefficient of Eq. (4.22) are not smooth and A and B can vanish, the equation is not uniformly parabolic and we need to regularise the system first. To this end, let $\{\mathcal{A}_k\}, \{\mathcal{B}_k\}, \{\mathcal{C}_k\}, \{u_k\}, \{\mathcal{G}_{1,k}\}$ be approximating sequences of smooth and bounded functions such that

$$\|\mathcal{A} - \mathcal{A}_k\|_{L^2(\Omega_T)}, \|\mathcal{B} - \mathcal{B}_k\|_{L^2(\Omega_T)}, \|\mathcal{C} - \mathcal{C}_k\|_{L^2(\Omega_T)}, \|G_1 - \mathcal{G}_{1,k}\|_{L^2(\Omega_T)}, \|u - u_k\|_{L^2(\Omega_T)} \leqslant \frac{1}{k}, \tag{4.24a}$$

such that

$$1/k \leqslant \mathcal{A}_k, \mathcal{B}_k \leqslant 1, \quad \text{as well as} \quad 0 \leqslant \mathcal{C}_k, |\mathcal{G}_{1,k}| \leqslant C, \tag{4.24b}$$

and

$$\|\partial_t \mathcal{C}_k\|_{L^1(\Omega_T)}, \|\nabla \mathcal{G}_{1,k}\|_{L^2(\Omega_T)} \leqslant C, \tag{4.24c}$$

where $C > 0$ is some positive constant. Using the regularised quantities, we consider the regularised equation

$$\frac{\partial \psi_k}{\partial t} + \frac{\mathcal{B}_k}{\mathcal{A}_k}\Delta\psi_k - \nabla\psi_k \cdot u_k + \left(\mathcal{G}_{1,k} - \frac{\mathcal{B}_k\mathcal{C}_k}{\mathcal{A}_k}\right)\psi_k = \xi, \tag{4.25}$$

in Ω_T, and $\psi_k = 0$, on $\partial\Omega \times (0,T)$, and $\psi_k(T,x) = 0$, in Ω. Here, ξ denotes an arbitrary smooth test function which is crucial for this approach, as discussed above, *cf.* Eq. (4.23). Since the coefficient $\mathcal{B}_k/\mathcal{A}_k$ is smooth and bounded from away from zero, the equation is uniformly parabolic, whence we infer the existence of a smooth solution, ψ_k.

Using ψ_k as a test function in Eq. (4.21) and thanks to Eq. (4.25) we get

$$\begin{aligned}
0 &= \iint_{\Omega_T} \mathcal{Z}\left(\mathcal{A}\frac{\partial \psi_k}{\partial t} + \mathcal{B}\Delta\psi_k - \mathcal{A}u\cdot\nabla\psi_k + (\mathcal{A}G_1 - \mathcal{B}\mathcal{C})\psi_k\right)\mathrm{d}x\,\mathrm{d}t \\
&= \iint_{\Omega_T} \mathcal{Z}\mathcal{A}\left(-\frac{\mathcal{B}_k}{\mathcal{A}_k}\Delta\psi_k + u_k\cdot\nabla\psi_k - \left(\mathcal{G}_{1,k} - \frac{\mathcal{B}_k\mathcal{C}_k}{\mathcal{A}_k}\right)\psi_k + \xi\right)\mathrm{d}x\,\mathrm{d}t \\
&\quad + \iint_{\Omega_T} \mathcal{Z}(\mathcal{B}\Delta\psi_k - \mathcal{A}u\cdot\nabla\psi_k + (\mathcal{A}G_1 - \mathcal{B}\mathcal{C})\psi_k)\,\mathrm{d}x\,\mathrm{d}t \\
&= \iint_{\Omega_T} \mathcal{Z}\mathcal{A}\xi + \iint_{\Omega_T} \mathcal{Z}\frac{\mathcal{B}_k}{\mathcal{A}_k}(\mathcal{A} - \mathcal{A}_k)(-\Delta\psi_k + \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}t \\
&\quad + \iint_{\Omega_T} \mathcal{Z}(\mathcal{B}_k - \mathcal{B})(-\Delta\psi_k + \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} \mathcal{Z}\mathcal{B}(\Delta\psi_k - \mathcal{C}\psi_k)\,\mathrm{d}x\,\mathrm{d}t \\
&\quad + \iint_{\Omega_T} \mathcal{Z}\mathcal{B}(-\Delta\psi_k + \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} \mathcal{Z}\mathcal{A}\psi_k(G_1 - \mathcal{G}_{1,k})\,\mathrm{d}x\,\mathrm{d}t \\
&\quad + \iint_{\Omega_T} \mathcal{Z}\mathcal{A}\nabla\psi_k\cdot(u_k - u)\,\mathrm{d}x\,\mathrm{d}t.
\end{aligned}$$

Using the definition of $\mathcal{A}$, $\mathcal{B}$, and $\mathcal{Z}$, we finally obtain

$$\iint_{\Omega_T} (n_1 - n_2)\xi\,\mathrm{d}x\,\mathrm{d}t = I_k^1 - I_k^2 + I_k^3 - I_k^4 + I_k^5,$$

where

$$I_k^1 = \iint_{\Omega_T} (n_1 - n_2 + p_1 - p_2)\frac{\mathcal{B}_k}{\mathcal{A}_k}(\mathcal{A} - \mathcal{A}_k)(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}t,$$

$$I_k^2 = \iint_{\Omega_T} (n_1 - n_2 + p_1 - p_2)(\mathcal{B} - \mathcal{B}_k)(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}t,$$

$$I_k^3 = \iint_{\Omega_T} (p_1 - p_2)(\mathcal{C} - \mathcal{C}_k)\psi_k\,\mathrm{d}x\,\mathrm{d}t,$$

$$I_k^4 = \iint_{\Omega_T} (n_1 - n_2)(G_1 - \mathcal{G}_{1,k})\psi_k\,\mathrm{d}x\,\mathrm{d}t,$$

$$I_k^5 = \iint_{\Omega_T} (n_1 - n_2)\nabla\psi_k \cdot (u - u_k)\,\mathrm{d}x\,\mathrm{d}t.$$

We aim at showing that

$$\lim_{k\to\infty} I_k^i = 0,$$

for $i = 1, \ldots, 5$, in order to be able to conclude that $n_1 = n_2$. Before proving the convergence of each I_k^i, we need certain uniform bounds which we collect and state in the subsequent lemma.

Lemma 4.5.2 (Uniform bounds)**.** *There exist a positive constant $C > 0$, independent of k, such that*

$$\begin{gathered}\sup_{0\leqslant t\leqslant T} \|\psi_k(t)\|_{L^\infty(\Omega)} \leqslant C, \qquad \sup_{0\leqslant t\leqslant T} \|\nabla\psi_k(t)\|_{L^2(\Omega)} \leqslant C,\\ \|(\mathcal{B}_k/\mathcal{A}_k)^{1/2}(\Delta\psi_k - \mathcal{C}_k\psi_k)\|_{L^2(\Omega_T)} \leqslant C.\end{gathered} \tag{4.26}$$

Proof. The L^∞-bound comes directly from the maximum principle applied to Eq. (4.25), since ξ is bounded and

$$\mathcal{G}_{1,k} - \frac{\mathcal{B}_k\mathcal{C}_k}{\mathcal{A}_k} \leqslant C.$$

Now we multiply Eq. (4.25) by $(\Delta\psi_k - \mathcal{C}_k\psi_k)$ and integrate in $(t, T) \times \Omega$ to obtain

$$\begin{aligned}
-\int_t^T\int_\Omega \frac{\partial}{\partial t}\frac{|\nabla\psi_k|^2}{2}\,\mathrm{d}x\,\mathrm{d}s - \int_t^T\int_\Omega \frac{\mathcal{C}_k}{2}\frac{\partial}{\partial t}\psi_k^2\,\mathrm{d}x\,\mathrm{d}s + \int_t^T\int_\Omega \frac{\mathcal{B}_k}{\mathcal{A}_k}|\Delta\psi_k - \mathcal{C}_k\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s&\\
= \underbrace{\int_t^T\int_\Omega u\cdot\nabla\psi_k(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}s}_{\mathcal{I}_1} + \underbrace{-\int_t^T\int_\Omega \mathcal{G}_{1,k}\psi_k(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}s}_{\mathcal{I}_2}&\\
+ \underbrace{\int_t^T\int_\Omega \xi(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}s}_{\mathcal{I}_3},&
\end{aligned} \tag{4.27}$$

where we shall bound each of the terms, $\mathcal{I}_i$, for $i = 1, 2, 3$, individually. First note that

$$\begin{aligned}
\mathcal{I}_1 &= \int_t^T\int_\Omega u\cdot\nabla\psi_k\Delta\psi_k\,\mathrm{d}x\,\mathrm{d}s - \int_t^T\int_\Omega u\cdot\nabla\psi_k\mathcal{C}_k\psi_k\,\mathrm{d}x\,\mathrm{d}s\\
&= \mathcal{I}_{1,1} + \mathcal{I}_{1,2}.
\end{aligned}$$

Integrating by parts in the first term of $\mathcal{I}_1$ we get

$$\begin{aligned}
\mathcal{I}_{1,1} &= -\int_t^T\int_\Omega \sum_{i,j=1}^d \frac{\partial u^{(i)}}{\partial x_j}\frac{\partial\psi_k}{\partial x_i}\frac{\partial\psi_n}{\partial x_j}\,\mathrm{d}x\,\mathrm{d}s - \int_t^T\int_\Omega \sum_{i,j=1}^d u^{(i)}\frac{\partial^2\psi_k}{\partial x_i\partial x_j}\frac{\partial\psi_k}{\partial x_j}\,\mathrm{d}x\,\mathrm{d}s\\
&= -\int_t^T\int_\Omega \sum_{i,j=1}^d \frac{\partial u^{(i)}}{\partial x_j}\frac{\partial\psi_k}{\partial x_i}\frac{\partial\psi_n}{\partial x_j}\,\mathrm{d}x\,\mathrm{d}s + \int_t^T\int_\Omega \frac{|\nabla\psi_k|^2}{2}\nabla\cdot u\,\mathrm{d}x\,\mathrm{d}s
\end{aligned}$$

$$\leqslant \left(d\|\nabla u\|_{L^\infty} + \frac{1}{2}\|\nabla \cdot u\|_{L^\infty}\right) \int_t^T \int_\Omega |\nabla \psi_k|^2 \,\mathrm{d}x\,\mathrm{d}s,$$

where $u^{(i)}$ is the i-th component of the vector u and ∇u is the matrix with element $(\nabla u)_{i,j} = \partial_j u^{(i)}$. Similarly, we observe

$$\begin{aligned}\mathcal{I}_{1,2} &= -\int_t^T \int_\Omega u \cdot \nabla \psi_k \mathcal{C}_k \psi_k \,\mathrm{d}x\,\mathrm{d}s \\ &\leqslant \frac{1}{2}\|u\|_{L^\infty(\Omega_T)}\|\mathcal{C}_k\|_{L^\infty(\Omega_T)}\|\psi_k\|^2_{L^2(\Omega_T)} + \frac{1}{2}\|\nabla\psi_k\|^2_{L^2(\Omega_T)} \\ &\leqslant C + C\|\nabla\psi_k\|^2_{L^2(\Omega_T)},\end{aligned}$$

with $C > 0$ independent of k, after applying Young's inequality. Hence

$$\mathcal{I}_1 \leqslant C + C\|\nabla\psi_k\|^2_{L^2(\Omega_T)}.$$

Next, let us address the term $\mathcal{I}_2$. We observe that

$$\begin{aligned}\mathcal{I}_2 &= -\int_t^T \int_\Omega \mathcal{G}_{1,k}\psi_k(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}s \\ &= \int_t^T \int_\Omega \mathcal{G}_{1,k}|\nabla\psi_k|^2 \,\mathrm{d}x\,\mathrm{d}s + \int_t^T \int_\Omega \psi_k \nabla\psi_k \cdot \nabla\mathcal{G}_{1,k}\,\mathrm{d}x\,\mathrm{d}s + \int_t^T \int_\Omega \mathcal{G}_{1,k}\mathcal{C}_k\psi_k\,\mathrm{d}x\,\mathrm{d}s.\end{aligned}$$

We note that $\|\mathcal{G}_{1,k}\|_{L^\infty(\Omega_T)}$ whence we obtain bounds for the first and the last term, respectively. In addition, we recall $\|\nabla\mathcal{G}_{1,k}\|_{L^2(\Omega_T)} \leqslant C$, whence, upon using Young's inequality, we get

$$\begin{aligned}\int_t^T \int_\Omega \psi_k\nabla\psi_k \cdot \nabla\mathcal{G}_{1,k}\,\mathrm{d}x\,\mathrm{d}s &\leqslant \frac{1}{2}\|\psi_k\|_{L^\infty(\Omega_T)}\|\nabla\mathcal{G}_{1,k}\|^2_{L^2(\Omega_T)} + \frac{1}{2}\|\psi_k\|_{L^\infty(\Omega_T)}\int_t^T\int_\Omega |\nabla\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s \\ &\leqslant C + C\int_t^T\int_\Omega |\nabla\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s.\end{aligned}$$

In combination we get

$$\mathcal{I}_2 \leqslant C + C\|\nabla\psi_k\|^2_{L^2(\Omega_T)},$$

with $C > 0$ independent of k. Last, let us address the term $\mathcal{I}_3$. We readily observe

$$\begin{aligned}\mathcal{I}_3 &= \int_t^T\int_\Omega \xi(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}s \\ &\leqslant C,\end{aligned}$$

integrating by parts twice and using the L^∞-bounds. Using the bounds obtained above, the right-hand side of Eq. (4.27) can be bounded as follows

$$C + C\|\nabla\psi_k\|^2_{L^2(\Omega_T)}$$

$$\geqslant -\int_t^T \int_\Omega \frac{\partial}{\partial t}\frac{|\nabla\psi_k|^2}{2}\,\mathrm{d}x\,\mathrm{d}s - \int_t^T \int_\Omega \frac{\mathcal{C}_k}{2}\frac{\partial}{\partial t}\psi_k^2\,\mathrm{d}x\,\mathrm{d}s + \int_t^T \int_\Omega \frac{\mathcal{B}_k}{\mathcal{A}_k}|\Delta\psi_k - \mathcal{C}_n\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s$$

$$\geqslant -\int_t^T \frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \frac{|\nabla\psi_k|^2}{2}\,\mathrm{d}x\,\mathrm{d}s + \int_t^T \int_\Omega \frac{\partial\mathcal{C}_k}{\partial t}\frac{\psi_k^2}{2}\,\mathrm{d}x\,\mathrm{d}s + \int_t^T \int_\Omega \frac{\mathcal{B}_k}{\mathcal{A}_k}|\Delta\psi_k - \mathcal{C}_k\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s$$

$$+ \int_\Omega \frac{\mathcal{C}_k(t)\psi_k^2(t)}{2}\,\mathrm{d}x$$

$$\geqslant \frac{1}{2}\|\nabla\psi_k(\cdot,t)\|^2_{L^2(\Omega)} - \|\partial_t\mathcal{C}_k\|_{L^1(\Omega_T)}\|\psi_k\|^2_{L^\infty(\Omega_T)} + \int_t^T \int_\Omega \frac{\mathcal{B}_k}{\mathcal{A}_k}|\Delta\psi_k - \mathcal{C}_k\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s$$

$$- \frac{1}{2}\|\mathcal{C}_k\|_{L^\infty(\Omega_T)}\|\psi_k\|^2_{L^2(\Omega_T)}$$

$$\geqslant \frac{1}{2}\|\nabla\psi_k(\cdot,t)\|^2_{L^2(\Omega)} + \int_t^T \int_\Omega \frac{\mathcal{B}_k}{\mathcal{A}_k}|\Delta\psi_k - \mathcal{C}_k\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s - C,$$

having used the regularity assumptions on the regularised coefficients, *cf.* Eq. (4.24). Finally, since $\mathcal{C}_k$ is positive, we get

$$\frac{1}{2}\int_\Omega |\nabla\psi_k(t)|^2\,\mathrm{d}x + \int_t^T \int_\Omega \frac{\mathcal{B}_k}{\mathcal{A}_k}|\Delta\psi_k - \mathcal{C}_k\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s \leqslant C + C\int_t^T \int_\Omega |\nabla\psi_k|^2\,\mathrm{d}x\,\mathrm{d}s. \tag{4.28}$$

Introducing the notation

$$Q(s) := \int_\Omega |\nabla\psi_k(s,x)|^2\,\mathrm{d}x,$$

we observe that Eq. (4.28) now reads

$$Q(t) \leqslant C + C\int_t^T Q(s)\,\mathrm{d}s,$$

and by Gronwall's lemma we conclude that

$$\sup_{0\leqslant t\leqslant T} Q(t) = \sup_{0\leqslant t\leqslant T}\|\nabla\psi_k(t)\|^2_{L^2(\Omega)} \leqslant C.$$

The third bound of Eq. (4.26) comes a posteriori from Eq. (4.28), which completes proof. □

Thanks to these uniform bounds, we obtain

$$I_k^1 = \iint_{\Omega_T} (n_1 - n_2 + p_1 - p_2)\frac{\mathcal{B}_k}{\mathcal{A}_k}(\mathcal{A} - \mathcal{A}_k)(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}t$$

$$\leqslant C\|(\mathcal{B}_k/\mathcal{A}_k)^{1/2}(\mathcal{A} - \mathcal{A}_k)\|_{L^2(\Omega_T)}$$

$$\leqslant Ck^{1/2}\|\mathcal{A} - \mathcal{A}_k\|_{L^2(\Omega_T)}$$

$$\leqslant C/k^{1/2},$$

and, similarly,

$$\begin{aligned} I_n^2 &= \iint_{\Omega_T} (n_1 - n_2 + p_1 - p_2)(\mathcal{B} - \mathcal{B}_k)(\Delta\psi_k - \mathcal{C}_k\psi_k)\,\mathrm{d}x\,\mathrm{d}t \\ &\leqslant Ck^{1/2}\|\mathcal{B} - \mathcal{B}_k\|_{L^2(\Omega_T)} \\ &\leqslant C/k^{1/2}. \end{aligned}$$

Finally, we have

$$\begin{aligned} I_k^3 &= \iint_{\Omega_T} (p_1 - p_2)(\mathcal{C} - \mathcal{C}_n)\psi_k\,\mathrm{d}x\,\mathrm{d}t \\ &\leqslant C\|\mathcal{C} - \mathcal{C}_k\|_{L^2(\Omega_T)} \\ &\leqslant C/k, \end{aligned}$$

and

$$\begin{aligned} I_k^4 &= \iint_{\Omega_T} (n_1 - n_2)(G_1 - \mathcal{G}_{1,k})\psi_n\,\mathrm{d}x\,\mathrm{d}t \\ &\leqslant C\|G_1 - \mathcal{G}_{1,k}\|_{L^2(\Omega_T)} \\ &\leqslant C/k, \end{aligned}$$

as well as

$$\begin{aligned} I_n^5 &= \iint_{\Omega_T} (n_1 - n_2)\nabla\psi_n \cdot (u - u_k)\,\mathrm{d}x\,\mathrm{d}t \\ &\leqslant C\|u - u_k\|_{L^2(\Omega_T)} \\ &\leqslant C/k. \end{aligned}$$

In summary, we have

$$\iint_{\Omega_T} (n_1 - n_2)\xi\,\mathrm{d}x\,\mathrm{d}t = I_k^1 - I_k^2 + I_k^3 - I_k^4 + I_k^5 \longrightarrow 0,$$

as $k \to \infty$, and therefore $n_1 = n_2$. From Eq. (4.20) we have

$$\iint_{\Omega_T} ((p_1 - p_2)\Delta\psi + n_1(G(p_1) - G(p_2))\psi)\,\mathrm{d}x\,\mathrm{d}t = 0.$$

Taking a smooth approximation of $p_1 - p_2$ as test function we get

$$\iint_{\Omega_T} |\nabla(p_1 - p_2)|^2\,\mathrm{d}x\,\mathrm{d}t = \iint_{\Omega_T} n_1(G(p_1) - G(p_2))(p_1 - p_2)\,\mathrm{d}x\,\mathrm{d}t,$$

and, by the monotonicity of G, *cf.* Eq. (A-G), we conclude that $p_1 = p_2$. □

4.6 Velocity of the boundary for patches

Let us recall that the Hele-Shaw problem is given by

$$\begin{cases} -\Delta p_\infty &= \Delta V + G(p_\infty), \qquad \text{in } \Omega(t), \\ \qquad v &= -(\nabla p_\infty + \nabla V)\cdot \nu, \quad \text{on } \partial\Omega(t), \end{cases} \tag{4.29}$$

where ν indicates the outward normal to the boundary, and $\Omega(t) := \{x;\ p_\infty(x,t) > 0\}$. Here we denote v the normal velocity of the free boundary. Below we give a characterisation of patch solutions, *i.e.* , the indicator of the growing domain described by Eq. (4.29) satisfies the incompressible limit equation, *cf.* Eq. (4.4a). To this end, we suppose that the boundary $\partial\Omega(t)$ admits a Lipschitz parameterisation $\partial\Omega(t) = \{x(t,\alpha)\,|\,\alpha \in [0,1], x(t,0) = x(t,1)\}$ that satisfies

$$\frac{\mathrm{d}}{\mathrm{d}t}x(t,\alpha) = -(\nabla p_\infty(x(t,\alpha),t) + \nabla V(x(t,\alpha),t)). \tag{4.30}$$

Then the characteristic function

$$n_\infty(t) = \mathbb{1}_{\Omega(t)}. \tag{4.31}$$

satisfies the limit problem, Eq. (4.4a).

Theorem 4.6.1 (Characterisation of the Free Boundary Velocity)**.** *Let Ω_0 be a bounded and Lipschitz continuous domain. Let us consider the solution $(\Omega(t), p_\infty)$ to the free boundary problem, Eq.* (4.29)*, with initial data Ω_0. Then, the characteristic function in Eq.* (4.31)*, satisfies Eq.* (4.4a)*.*

Proof. We have to show that $n_\infty(t) = \mathbb{1}_{\Omega(t)}$ satisfies

$$\frac{\partial n_\infty}{\partial t} = \Delta p_\infty + \nabla\cdot(n_\infty \nabla V) + n_\infty G(p_\infty),$$

in the distributional sense. Given a test function $\psi = \psi(x)$, by Reynolds' transport Theorem and Eq. (4.30), we have

$$\int_{\mathbb{R}^d} \psi(x)\frac{\partial n_\infty}{\partial t}\,\mathrm{d}x = \frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}\psi(x)\mathbb{1}_{\Omega(t)}\,\mathrm{d}x = \int_{\partial\Omega(t)} v\psi(x)\,\mathrm{d}x = v\delta_{\partial\Omega(t)}.$$

On the other hand, it holds

$$\Delta p_\infty + \nabla\cdot(n_\infty\nabla V) + n_\infty G(p_\infty) = -(\partial_\nu p_\infty + \partial_\nu V)\delta_{\partial\Omega(t)} = v\delta_{\partial\Omega(t)},$$

in the sense of distributions, as can be seen by the following argument. First, by the definition of $\Omega(t)$ as the positivity set of p_∞ and the fact that $n_\infty = \mathbb{1}_{\Omega(t)}$ we observe that the weak formulation of the left-hand side can be manipulated as follows:

$$\int_{\mathbb{R}^d} -\nabla p_\infty\cdot\nabla\psi - n_\infty\nabla V\cdot\nabla\psi + n_\infty G(p_\infty)\psi\,\mathrm{d}x = \int_{\Omega(t)} -\nabla p_\infty\cdot\nabla\psi - \nabla V\cdot\nabla\psi + G(p_\infty)\psi\,\mathrm{d}x.$$

Integrating by parts the right-hand side, we obtain

$$\int_{\Omega(t)} (\Delta p_\infty + \Delta V + G(p_\infty))\psi \,\mathrm{d}x - \int_{\partial\Omega(t)} \partial_\nu p_\infty \psi \,\mathrm{d}x - \int_{\partial\Omega(t)} \partial_\nu V \psi \,\mathrm{d}x$$
$$= - \int_{\partial\Omega(t)} \partial_\nu p_\infty \psi \,\mathrm{d}x - \int_{\partial\Omega(t)} \partial_\nu V \psi \,\mathrm{d}x$$

where we used $\Delta p_\infty + \Delta V + G(p_\infty) = 0$, in $\mathcal{D}'$, by Eq. (4.29). $\square$

Chapter 5

Convergence rate for the incompressible limit of nonlinear diffusion-advection equations

Abstract

The incompressible limit of nonlinear diffusion equations of porous medium type has attracted a lot of attention in recent years, due to its ability to link the weak formulation of cell-population models to free boundary problems of Hele-Shaw type. Although vast literature is available on this singular limit, little is known on the convergence rate of the solutions. In this work, we compute the convergence rate in a negative Sobolev norm and, upon interpolating with BV-uniform bounds, we deduce a convergence rate in appropriate Lebesgue spaces.

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5.1 Introduction

We consider the following nonlinear drift-diffusion equation

$$\frac{\partial n}{\partial t} - \nabla \cdot (n \nabla p + n \nabla V) = ng, \tag{5.1}$$

posed on $\mathbb{R}^d \times (0, T)$, $d \geqslant 2$, where n describes a population density and $p = p(n)$ is the density dependent pressure. The reaction term on the right-hand side represents the population growth rate, $g = g(x, t)$, while $V = V(x, t)$ is a chemical concentration. The pressure is assumed to be a known increasing function of the density. We consider the following two representative examples:

$$p_\gamma = P_\gamma(n) := \frac{\gamma}{\gamma - 1} n^{\gamma - 1}, \ \gamma > 1, \tag{5.2}$$

and

$$p_\epsilon = P_\epsilon(n) := \epsilon \frac{n}{1-n}, \qquad \epsilon > 0. \tag{5.3}$$

We are concerned with calculating the rate at which solutions to Eq. (5.1) converge to the so-called *incompressible* (or *stiff pressure*) limit, as described below. More precisely we prove the following results.

Theorem 5.1.1 (Convergence rate in $\dot{H}^{-1}$)**.** *Assume* (A–L^1data)*,* (A–drift)*, and* (A–reaction) *(for $d=2$) and* (A–reaction') *or* (A–reaction") *(for $d \geqslant 3$). For $d=2$ assume additionally* (A–2D)*. Then, for all $T>0$, there exists a unique function $n_\infty \in C([0,T]; L^1(\mathbb{R}^d))$ such that the sequence n_γ (resp. n_ϵ) converges, as $\gamma \to \infty$ (resp. $\epsilon \to 0$) to n_∞ strongly in $L^\infty(0,T;\dot{H}^{-1}(\mathbb{R}^d))$ with the following rate*

$$\sup_{t\in[0,T]} \|n_\gamma(t) - n_\infty(t)\|_{\dot{H}^{-1}(\mathbb{R}^d)} \leqslant \frac{C(T)}{\gamma^{1/2}} + \|n_\gamma^0 - n_\infty^0\|_{\dot{H}^{-1}(\mathbb{R}^d)}. \tag{5.4}$$

Theorem 5.1.2 (Convergence rate in $L^{4/3}$)**.** *Under the assumptions of Theorem 5.1.1, and additionally* (A–BV data)*,* (A–BV drift) *and $g \in BV(\mathbb{R}^d \times (0,T))$, we also have $n_\infty \in BV(\mathbb{R}^d \times (0,T))$ and*

$$\sup_{t\in[0,T]} \|n_\gamma(t) - n_\infty(t)\|_{L^{4/3}(\mathbb{R}^d)} \leqslant \frac{C(T)}{\gamma^{1/4}} + \|n_\gamma^0 - n_\infty^0\|_{\dot{H}^{-1}(\mathbb{R}^d)}^{1/2}. \tag{5.5}$$

Theorem 5.1.3. *Under the assumptions of Theorem 5.1.1, there exists a function $p_\infty \in L^\infty(\mathbb{R}^d \times (0,T))$ such that, after extracting a subsequence, the sequence p_γ converges to p_∞ weakly* in $L^\infty((0,T)\times\mathbb{R}^d)$ and the following relation holds*

$$p_\infty(1-n_\infty) = 0, \tag{5.6}$$

almost everywhere in $(0,T)\times\mathbb{R}^d$.

The above graph relation between the limit pressure and density is well-known in the literature. In particular, when considering tumor growth models it implies that saturation holds in the region where there is a positive pressure, which is usually referred to as the region occupied by the tumor. Here we provide a new proof that does not require strong convergence of the density nor the pressure.
In fact, the limit n_∞ satisfies (together with a limit pressure, p_∞) a free boundary type problem, discussed shortly below, and the question of passing to this limiting problem has been vastly addressed in literature. Our contribution is to provide a new proof together with a convergence rate.

Motivation and previous works. Models like Eq. (5.1) are well-known and commonly employed in a variety of applications, for instance in bio-mathematical modelling of living tissue. In the case $V=0$, $g=0$, it is well-known that if the pressure satisfies the power law (5.2), then Eq. (5.1) is actually the porous medium equation

$$\frac{\partial n_\gamma}{\partial t} - \Delta n_\gamma^\gamma = 0, \tag{5.7}$$

whose well-understood properties (e.g. regularising effects) facilitate the analysis notably. The other choice of the pressure, given by Eq. (5.3), is well-known in kinetic theory of dense gases where the short-distance interactions between particles are strongly repulsive. In this spirit it has been used in models describing collective motion or congested traffic flow, see [96, 128, 68, 21, 22]. Despite having a singularity when the population density reaches its maximum value (here standardised to 1), this choice of pressure gives rise to a tissue growth model with similar properties – indeed, the crucial a-priori estimates are the same and the limiting free boundary type problem is almost identical. A difference is that the singularity in the pressure prevents the cell densities to ever rise above the maximum value 1. Taking advantage of these similarities, we shall henceforth index the solution of Eq. (5.1) by γ, $n = n_\gamma$, and consider the singular limit $\gamma \to \infty$. Each of the assumptions and properties we discuss below has its natural ϵ-analogue by putting $\epsilon = 1/\gamma$.

Let us recall that the study of the incompressible limit has a long history and it has been investigated for many different models related to Eq. (5.1). The first result on the limit $\gamma \to \infty$ has been obtained for the classical porous medium equation (5.7). The most interesting difference from the case with a non-trivial reaction term is that the free boundary problem arising in the limit turns out to be stationary. In fact, as proven in [45] the limit density, n_∞, is independent of time. This result can be intuitively explained by noticing that the degenerate diffusivity of Eq. (5.1), namely $\gamma n^{\gamma-1}$ converges to 0 if $n < 1$, while it tends to infinity in the regions where $n > 1$. Therefore, while there is no motion in the regions where the density is below 1, where the solution lies above this level it tends to collapse instantaneously, *cf.* [88]. In the absence of reaction terms and, hence, of any evolution process in the Hele-Shaw problem, the limit pressure turns out to be constantly equal to zero, $p_\infty \equiv 0$.

Introducing non-trivial Dirichlet boundary conditions changes drastically the behaviour of the limit free boundary problem. In fact, the limit pressure no longer vanishes and this triggers the evolution of the interface in accordance with Darcy's law (which states that the velocity of the free boundary is proportional to the pressure gradient). This problem was addressed in [87], where the authors study the incompressible limit of the porous medium equation defined in $[0, \infty) \times \Omega$, where Ω is a compact subset of $\mathbb{R}^d$, and the pressure satisfies $p(x, t) = f(x, t)$ on $\partial\Omega$, for some $f(x, t) \geqslant 0$. In the absence of Dirichlet boundary data, *i.e.* $f \equiv 0$, and for Ω large enough, the problem is actually the same as in [45] and it still holds that $n_\infty = n_\infty(x)$ as well as $p_\infty \equiv 0$. On the other hand, if one imposes the pressure to be strictly positive somewhere on $\partial\Omega$, *i.e.* $f \not\equiv 0$, then the pressure gradient no longer vanishes and the dynamics of the limit problem is governed by Darcy's law.

The same non-stationary effect, although due to different dynamics, is produced by a non-trivial reaction process. The incompressible limit for Eq. (5.1) without convective effects, *i.e.* $V = 0$, and with a pressure-dependent growth rate $g = G(p)$, was first addressed in the seminal paper [130] by Perthame, Quirós and Vázquez. They prove that it is possible to extract subsequences of n_γ and p_γ which converge in the L^1-norm to functions

$$n_\infty \in C([0, T]; L^1(\mathbb{R}^d)) \cap BV(\mathbb{R}^d \times (0, T)), \quad p_\infty \in L^2(0, T; H^1(\mathbb{R}^d)) \cap BV(\mathbb{R}^d \times (0, T)), \tag{5.8}$$

satisfying the following equation in the sense of distributions on $\mathbb{R}^d \times (0, T)$

$$\frac{\partial n_\infty}{\partial t} - \Delta p_\infty = n_\infty G(p_\infty), \tag{5.9}$$

and the following relations

$$(1 - n_\infty) p_\infty = 0, \tag{5.10}$$

almost everywhere, as well as

$$p_\infty(\Delta p_\infty + G(p_\infty)) = 0, \tag{5.11}$$

in the sense of distributions. The last equality is usually referred to as the *complementarity* *relation* and represents the link between the limit equation and the free boundary problem. In fact, denoting by $\Omega(t) := \{x \in \mathbb{R}^d \mid p_\infty(x,t) > 0\}$ the region occupied by the tumor, from Eq. (5.11) one can see that the pressure satisfies an elliptic equation in the evolving domain $\Omega(t)$ with homogeneous Dirichlet boundary conditions. The free boundary $\partial\Omega(t)$ is moving under Darcy's law, which finally allows to obtain the fully geometrical representation of the limit problem. A derivation of the velocity law can be found in [130] for initial data given by characteristic functions of bounded sets, although the proof relies on formal arguments. A weak (distributional) and a measure-theoretic interpretation of the free boundary condition have been recovered in [123], while in [102] the same result is achieved through the viscosity solutions approach.

An analogous result regarding the limit $\gamma \to \infty$ has been shown in [96] for the pressure law given by Eq. (5.3). The authors obtain virtually the same limiting problem, the only difference being that the complementarity relation (5.11) becomes

$$p_\infty^2(\Delta p_\infty + G(p_\infty)) = 0, \tag{5.12}$$

see [96, Theorem 2.1]. Let us point out that due to uniform estimates in L^∞ the convergence of the sequence of densities is also true in any L^p-space, $p < \infty$.

The Hele-Shaw limit for the porous medium equation including convective effects, *cf.* Eq. (5.1) with $V \not\equiv 0$, and possibly reaction terms, has attracted a lot of interest as well. Similarly as for the driftless case, when passing to the limit $\gamma \to \infty$, the model converges to a free boundary problem where, however, the interface dynamics is no longer driven only by Darcy's law, but also by the external drift, *i.e.* the normal velocity is given by $-(\nabla p_\infty + \nabla V)\cdot\nu$, where ν is the outward normal direction. The asymptotics as $\gamma \to \infty$ has been addressed both for local and non-local drift, in the absence of reactions, see for instance [1, 57], where the authors adopt techniques relying on the gradient flow structure of the equation. In [103], Kim, Požàr and Woodhouse include also a linear reaction term into the equation and are able to prove the convergence to the incompressible limit using viscosity solutions. Recently, in [63] the authors show that the complementarity condition including a drift, *i.e.*

$$p_\infty(\Delta p_\infty + \Delta V + G(p_\infty)) = 0,$$

holds in the sense of distributions.

In recent years, many other variations of the model at hand have been proposed together with the analysis of their incompressible limit. We refer the reader to [61] for a model including the effects of nutrients, [93] for the generalization of the driftless model with a non-monotone proliferation term, and [147] for the model including active motion. In order to account for visco-elastic effects, several models propose to use Brinkman's law instead of Darcy's law [132]. Moreover, cross-reaction-diffusion model using Darcy's law, Brinkman's law or singular pressure law have attracted a lot of attention as they raise challenging questions both on the existence of solutions and their incompressible limit, see [115, 31, 94, 47, 65, 66].

Our aim is to compute the rate of convergence of the solutions of Eq. (5.1) as $\epsilon \to 0$ or $\gamma \to \infty$ in Eq. (5.3) or Eq. (5.2) respectively. To the best of our knowledge the only result in this direction is given by Alexander, Kim and Yao in [1] for the porous medium equation including a space-dependent drift. Passing to the incompressible limit, the authors are able to build a link between the Hele-Shaw model and the following congested crowd motion model

$$\partial_t n + \nabla\cdot(n\nabla V) = 0, \quad \text{if} \quad n < 1,$$

with the constraint $n \leqslant 1$. To prove the equivalence of the two models, they study the convergence as $\gamma \to \infty$ of the porous medium equation with drift, *cf.* Eq. (5.1) with $G \equiv 0$. Unlike [130], their approach is based on viscosity solutions. On the one hand, they are able to prove locally uniform convergence of the viscosity solution of Eq. (5.1) to a solution of the Hele-Shaw model. On the other hand, they show the convergence of the porous medium equation with drift to the aforementioned crowd motion model in the 2-Wasserstein distance. Therefore, they prove the equivalence of the two models in the special case of initial data given by "patches", namely $n^0 = \mathbb{1}_{\Omega_0}$ for a compact set Ω_0. In fact, the locally uniform limit holds only for solutions of the form of a characteristic function, while the limit in the 2-Wasserstein metric holds for any bounded initial data, $0 \leqslant n^0 \leqslant 1$ with finite energy and second moment. Moreover, while the local uniform convergence only requires a strict subharmonicity assumption on the drift term, *i.e.* $V \in C^2(\mathbb{R}^d)$, $\Delta V > 0$, stronger regularity is needed to pass to the 2-Wasserstein limit. More precisely the authors make the following assumptions on $V = V(x)$: there exists $\lambda \in \mathbb{R}$ such that

$$\inf_{x\in\mathbb{R}^d} V(x) = 0, \qquad D^2V(x) \geqslant \lambda I_d, \quad \forall x \in \mathbb{R}^d, \qquad \|\Delta V\|_{L^\infty(\mathbb{R}^d)} \leqslant C.$$

Under these assumptions, they derive the following rate of convergence, *cf.* [1, Theorem 4.2.]

$$\sup_{t\in[0,T]} W_2(n_\gamma(t), n_\infty(t)) \leqslant \frac{C}{\gamma^{1/24}},$$

where C is a positive constant depending on $\int Vn^0$, $\|\Delta V\|_\infty$ and T.

The main result of this paper offers an improved polynomial rate of convergence in a negative Sobolev norm and the strong topology of Lebesgue spaces, see Theorems 5.1.1 and 5.1.2 above and Corollary 5.1.7 below. Let us remark that the 2-Wasserstein distance and the $\dot{H}^{-1}$-norm can be bounded by each other when the densities are uniformly bounded away from vacuum, see Appendix 5.A. We refer the reader to [144, Section 5.5.2], and references therein, for further discussion about the equivalence of the two distances.

Preliminaries and assumptions. Throughout this paper we make the following assumptions on the components of the model. Firstly, we assume that Eq. (5.1) is equipped with non-negative initial data n_γ^0 (resp. n_ϵ^0) such that there is a compact set $K \subset \mathbb{R}^d$ and a function $n_\infty^0 \in L^1(\mathbb{R}^d)$ satisfying

$$\begin{aligned} \operatorname{supp} n_\gamma^0 \subset K,\ p_\gamma^0 = P_\gamma(n_\gamma^0) \in L^\infty(\mathbb{R}^d), \quad 0 \leqslant n_\gamma^0 \in L^1(\mathbb{R}^d), \quad \|n_\gamma^0 - n_\infty^0\|_{L^1(\mathbb{R}^d)} \to 0,\\ p_\epsilon^0 = P_\epsilon(n_\epsilon^0) \in L^\infty(\mathbb{R}^d), \quad 0 \leqslant n_\epsilon^0 \in L^1(\mathbb{R}^d), \quad \|n_\epsilon^0 - n_\infty^0\|_{L^1(\mathbb{R}^d)} \to 0. \end{aligned} \tag{A–L^1data}$$

Note in particular that the compact support assumption is needed only in the power law pressure. This is because when the pressure is given by Eq. (5.3) we can achieve our main estimate without a uniform bound for the pressure in L^∞, which is not the case for the power law. Having uniformly compactly supported data allows to derive a maximum principle for the equation satisfied by the pressure. When additionally specified, we assume further

$$n_\gamma^0 \in BV(\mathbb{R}^d), \qquad \Delta\big(n_\gamma^0\big)^\gamma \in L^1(\mathbb{R}^d), \tag{A–BV data}$$

uniformly in γ. Secondly, the chemical concentration potential, V, is assumed to satisfy

$$D^2V \geqslant \left(\lambda + \frac{1}{2}\operatorname{tr}(D^2V)\right) I_d, \quad \text{for some } \lambda \in \mathbb{R}, \tag{A–drift}$$

and additionally

$$D^2V \in L^\infty(\mathbb{R}^d \times (0,T)), \quad \nabla V \in L^\infty(\mathbb{R}^d \times (0,T)), \quad \nabla\Delta V \in L^1(\mathbb{R}^d \times (0,T)). \quad \text{(A–BV drift)}$$

Thirdly, we assume the proliferation rate, $g = g(x,t)$, to be locally integrable and satisfy one of the following assumptions

$$g_+ \in L^\infty(\mathbb{R}^d \times (0,T)) \text{ and } \Delta g \geqslant 0, \quad \text{(A–reaction)}$$

where $f_+ := \max(f, 0)$ denotes the positive part of the function, or

$$g_+ \in L^\infty(\mathbb{R}^d \times (0,T)) \text{ and } (\Delta g)_- \in L^\infty(0,T; L^{d/2}(\mathbb{R}^d)), \ d \geqslant 3, \quad \text{(A–reaction')}$$

where $f_- := \max(-f, 0)$ denotes the negative part of the function, or in alternative

$$g_+ \in L^\infty(\mathbb{R}^d \times (0,T)) \text{ and } \nabla g \in L^\infty(0,T; L^d(\mathbb{R}^d)), \ d \geqslant 3. \quad \text{(A–reaction'')}$$

Under these assumptions one can derive several crucial uniform estimates for Eq. (5.1).

Lemma 5.1.4 (A-priori estimates)**.** *Under assumption (A–L^1data) the family n_γ of solutions to Eq. (5.1) satisfies the following bounds, uniformly in γ*

1. $\operatorname{supp} p_\gamma(t) \subset K(t)$ *for some compact set* $K(t)$,
2. *there exists a positive constant* $p_M = p_M(T)$ *such that* $0 \le p_\gamma \leqslant p_M$, $0 \leqslant n_\gamma \leqslant \left(\frac{\gamma-1}{\gamma} p_M\right)^{\frac{1}{\gamma-1}}$,
3. $n_\gamma \in L^\infty(0,T; L^1(\mathbb{R}^d))$.

Assuming in addition (A–BV drift) we also have $n_\gamma \in L^\infty(0,T; BV(\mathbb{R}^d))$. When the pressure is given by Eq. (5.3) points 2. and 3. still hold, and moreover $0 \leqslant n_\epsilon \leqslant 1$.

These bounds are enough for our purposes. Their proofs are fairly standard and derived in full detail in [130, 96, 93, 63], so we omit them here. Let us point out that to fully justify passing to the incompressible limit $\gamma \to \infty$ one usually needs to derive additional estimates for the time derivative of the population density and the pressure.

Remark 5.1.5 (More general drift term)**.** It is easily seen in the proof of our main results that we do not require the drift velocity to be a gradient. Indeed, one can replace the term $n\nabla V$ in Eq. (5.1) by $nU(x,t)$ with appropriate modifications to the regularity assumptions (A–drift) and (A–BV drift).

Our approach is to first obtain a rate of convergence in the homogeneous negative Sobolev norm $\dot{H}^{-1}$ and then interpolate with the uniform bound in BV to deduce a convergence rate in Lebesgue spaces. To realise this program we make use of the diffusion structure of the problem and "lift" the Laplacian. More precisely, we define the function φ to be the solution of the following Poisson equation in $\mathbb{R}^d \times (0,T)$

$$-\Delta\varphi_\gamma = n_\gamma, \tag{5.13}$$

given by the convolution $\varphi_\gamma = \mathcal{K} \star n_\gamma$, where $\mathcal{K}$ is the fundamental solution of the Laplace equation. Explicitly, for $x \neq 0$,

$$\mathcal{K}(x) = \begin{cases} -\dfrac{1}{2\pi} \ln |x|, & \text{for} \quad d = 2, \\ \dfrac{1}{d(d-2)\omega_d} |x|^{2-d}, & \text{for} \quad d \geqslant 3, \end{cases} \tag{5.14}$$

where ω_d denotes the volume of the unit ball in $\mathbb{R}^d$.
Suppose for now that $d \geqslant 3$. Then, since $n_\gamma \in L^1(\mathbb{R}^d) \cap L^\infty(\mathbb{R}^d)$, a straightforward application of Young's inequality shows that

$$\varphi_\gamma \in L^p(\mathbb{R}^d), \quad \text{for} \quad p > \frac{d}{d-2}, \tag{5.15}$$

and

$$\nabla \varphi_\gamma \in L^2(\mathbb{R}^d). \tag{5.16}$$

If $d = 2$, then we do not have $\varphi_\gamma \in L^\infty(\mathbb{R}^2)$ and we cannot apply Young's inequality to deduce square-integrability of $\nabla\varphi_\gamma$ (indeed, this is an endpoint case). However, let us point out that, for the power law case, since by Lemma 5.1.4 (point 1.) solutions are always compactly supported we can take φ_γ to be the solution of the Poisson equation on $K(T) \subset \mathbb{R}^2$ with homogeneous Dirichlet boundary conditions. In this case, we know that $\nabla\varphi_\gamma \in L^2(K)$.
Under suitable conditions it is possible to infer the L^2-integrability of $\nabla(\varphi_\epsilon - \varphi_{\epsilon'})$ in $\mathbb{R}^2$, which is needed for the singular pressure law. In this case, we impose the following additional assumptions

$$g = g(t), \quad \nabla V \in L^1((0,T) \times \mathbb{R}^2), \quad \int_{\mathbb{R}^2} |x| \, n_\epsilon^0 < \infty. \tag{A–2D}$$

The bound on the first moment is propagated in time and guarantees the well-posedness of $\mathcal{K} \star n_\epsilon$. Taking a space-independent growth rate implies that the difference $n_\epsilon - n_{\epsilon'}$ has zero mean for all times. Therefore, we have

$$\int_{\mathbb{R}^2} (n_\epsilon - n_{\epsilon'}) = 0, \qquad \int_{\mathbb{R}^2} |x||n_\epsilon - n_{\epsilon'}| < \infty,$$

from which we conclude that $\nabla(\varphi_\epsilon - \varphi_{\epsilon'}) \in L^2(\mathbb{R}^2)$.

Notice that the L^1 convergence of the initial data implies the convergence of $\nabla\varphi_\gamma^0$ to $\nabla\varphi_\infty^0$ in L^2. Moreover, the uniform bounds on n_γ together with the Hardy-Littlewood-Sobolev inequality imply that the convolution $n_\gamma \mapsto \mathcal{K} \star n_\gamma$ is a bounded linear operator from $L^{2d/d+2}$ to L^2. Therefore there is a subsequence $\nabla\varphi_{\gamma_k}$ which converges weakly in L^2 to $\nabla\varphi_\infty$.
Finally, we recall that the gradient $\nabla\varphi$ can be used to represent the $\dot{H}^{-1}$-norm of the function n as follows

$$\|n(t)\|_{\dot{H}^{-1}(\mathbb{R}^d)} = \|\nabla\varphi(t)\|_{L^2(\mathbb{R}^d)}. \tag{5.17}$$

Having obtained a convergence rate in the negative norm and assuming additionally the BV bounds provided by Lemma 5.1.4, we will use the following interpolation inequality, proved (in greater generality) by Cohen et al. [56] (see also [54]), to deduce a rate in the Lebesgue 4/3-norm:

Lemma 5.1.6 (Interpolation inequality)**.** *There exists a constant $C = C(d,T) > 0$, such that, for all $t \in [0,T]$,*

$$\|n(t)\|_{L^{4/3}(\mathbb{R}^d)} \leqslant C|n(t)|^{1/2}_{BV(\mathbb{R}^d)} \|\nabla\varphi(t)\|^{1/2}_{L^2(\mathbb{R}^d)}. \tag{5.18}$$

Thus, Theorem 5.1.2 is a simple consequence of Theorem 5.1.1, Lemma 5.1.6 and the uniform bound in BV provided by Lemma 5.1.4.
By the usual log-convex interpolation of the L^p-norms we readily obtain the following corollary to Theorem 5.1.2.

Corollary 5.1.7 (Convergence rate in L^p)**.**

$$\sup_{t\in[0,T]} \|n_\gamma(t) - n_\infty(t)\|_{L^p(\mathbb{R}^d)} \leqslant \frac{C}{\gamma^\alpha}, \tag{5.19}$$

with

$$\alpha := \begin{cases} \dfrac{p-1}{p}, & \textit{for} \quad p \in (1, 4/3], \\ \dfrac{1}{3p}, & \textit{for} \quad p \in [4/3, \infty). \end{cases} \tag{5.20}$$

Remark 5.1.8 (Finite speed of propagation)**.** When one assumes additionally that the initial data have uniformly compact support, then at any later time the support of n_γ is still uniformly contained in a bounded set (this is one of the fundamental properties of the porous medium equation, see [130, Lemma 2.6] and [96, Lemma 3.3] for the model with a non-zero right-hand side). Therefore one can consider problem (5.1) to be posed on a bounded subset of $\mathbb{R}^d$ with homogeneous Dirichlet boundary condition. Naturally our results remain true in this case with the improvement that we obtain a rate $\sim \gamma^{-1/4}$ in any L^p-norm, $1 \leqslant p \leqslant 4/3$. In particular this covers the case of "patches", *i.e.* , when the initial distribution is given by an indicator function of a compact set, as considered recently in [1].

Plan of the paper. The remainder of the paper is devoted to proving the main theorem. It turns out that the equation can be conveniently trisected and dealt with term-by-term: considering separately the pressure-driven advection, drift, and proliferation. Indeed, it is the diffusion term that governs the rate of convergence. The proof is therefore structured as follows. In Sections 5.2 and 5.3 we prove the main theorem for the choice of the singular pressure in Eq. (5.3) and the power law pressure in Eq. (5.2) in the absence of reactions and drift. Then in Section 5.4 we explain how to treat the additional terms.
Notation. Henceforth we shall usually suppress the dependence on time and space of the quantities of interest, only exhibiting the time variable in the final results. Similarly, for the sake of brevity, all space integration should be understood with respect to the d-dimensional Lebesgue measure.

5.2 Singular pressure law

In this and the following section, to explain the main idea in a simple situation, we ignore the drift and proliferation terms in Eq. (5.1) and consider only the nonlinear diffusion equation

$$\frac{\partial n_\epsilon}{\partial t} - \nabla \cdot (n_\epsilon \nabla p_\epsilon) = 0, \tag{5.21}$$

assuming now the pressure law as in Eq. (5.3). In this case we can rewrite Eq. (5.21) as

$$\frac{\partial n_\epsilon}{\partial t} - \Delta H_\epsilon(n_\epsilon) = 0, \tag{5.22}$$

with

$$H_\epsilon(n_\epsilon) := \int_0^{n_\epsilon} s p'_\epsilon(s)\,\mathrm{d}s = \epsilon \frac{n_\epsilon}{1-n_\epsilon} + \epsilon \ln(1-n_\epsilon). \tag{5.23}$$

Recall that we have the uniform bound $n_\epsilon < 1$, so that the right-hand side above is well-defined with $\ln(1-n_\epsilon) \leqslant 0$.

Let us take $\epsilon > \epsilon' > 0$. We subtract the equation for $n_{\epsilon'}$ from the equation for n_ϵ to obtain

$$\frac{\partial(n_\epsilon - n_{\epsilon'})}{\partial t} - \Delta\big(H_\epsilon(n_\epsilon) - H_{\epsilon'}(n_{\epsilon'})\big) = 0. \tag{5.24}$$

Now we pose Eq. (5.13) for both solutions n_ϵ and $n_{\epsilon'}$

$$-\Delta\varphi_\epsilon = n_\epsilon, \qquad -\Delta\varphi_{\epsilon'} = n_{\epsilon'}.$$

Then Eq. (5.24) reads

$$-\Delta\frac{\partial(\varphi_\epsilon - \varphi_{\epsilon'})}{\partial t} - \Delta\big(H_\epsilon(n_\epsilon) - H_{\epsilon'}(n_{\epsilon'})\big) = 0, \tag{5.25}$$

and we test it against $\varphi_\epsilon - \varphi_{\epsilon'}$ to derive

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} |\nabla(\varphi_\epsilon - \varphi_{\epsilon'})|^2 = \int_{\mathbb{R}^d} (n_\epsilon - n_{\epsilon'})\big(H_{\epsilon'}(n_{\epsilon'}) - H_\epsilon(n_\epsilon)\big).$$

We now proceed to estimate the right-hand side. On the set $\{n_\epsilon > n_{\epsilon'}\}$ we make use of non-negativity of $H_\epsilon(n_\epsilon)$ and non-positivity of the logarithmic term in $H_{\epsilon'}(n_{\epsilon'})$ to write

$$\int_{\{n_\epsilon > n_{\epsilon'}\}} (n_\epsilon - n_{\epsilon'})\big(H_{\epsilon'}(n_{\epsilon'}) - H_\epsilon(n_\epsilon)\big) \leqslant \epsilon' \int_{\{n_\epsilon > n_{\epsilon'}\}} (n_\epsilon - n_{\epsilon'})\frac{n_{\epsilon'}}{1-n_{\epsilon'}} \leqslant \epsilon' \int_{\{n_\epsilon > n_{\epsilon'}\}} n_{\epsilon'}.$$

Similarly, on the complementary set $\{n_\epsilon \leqslant n_{\epsilon'}\}$ we have

$$\int_{\{n_\epsilon \leqslant n_{\epsilon'}\}} (n_\epsilon - n_{\epsilon'})\big(H_{\epsilon'}(n_{\epsilon'}) - H_\epsilon(n_\epsilon)\big) \leqslant \epsilon \int_{\{n_\epsilon \leqslant n_{\epsilon'}\}} (n_{\epsilon'} - n_\epsilon)\frac{n_\epsilon}{1-n_\epsilon} \leqslant \epsilon \int_{\{n_\epsilon \leqslant n_{\epsilon'}\}} n_\epsilon.$$

Therefore we have

$$\begin{aligned}\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} |\nabla(\varphi_\epsilon - \varphi_{\epsilon'})|^2 &\leqslant \epsilon \int_{\{n_\epsilon \leqslant n_{\epsilon'}\}} n_\epsilon + \epsilon' \int_{\{n_\epsilon \geqslant n_{\epsilon'}\}} n_{\epsilon'} \\ &\leqslant \epsilon \|n_\epsilon(t)\|_{L^1(\mathbb{R}^d)} + \epsilon' \|n_{\epsilon'}(t)\|_{L^1(\mathbb{R}^d)},\end{aligned}$$

and since n_ϵ and $n_{\epsilon'}$ are uniformly bounded in $L^\infty((0,T), L^1(\mathbb{R}^d))$ with respect to ϵ and ϵ', we obtain

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} |\nabla(\varphi_\epsilon - \varphi_{\epsilon'})(t)|^2 \leqslant C(\epsilon + \epsilon'). \tag{5.26}$$

Integrating in time on $[0,t)$ we then have

$$\frac{1}{2}\int_{\mathbb{R}^d} |\nabla(\varphi_\epsilon - \varphi_{\epsilon'})(t)|^2 \leqslant Ct(\epsilon + \epsilon') + \int_{\mathbb{R}^d} |\nabla(\varphi_\epsilon - \varphi_{\epsilon'})(0)|^2. \tag{5.27}$$

It follows that the sequence $(\nabla\varphi_\epsilon)_\epsilon$ converges in the strong topology of $L^\infty((0,T),L^2(\mathbb{R}^d))$ to $\nabla\varphi_\infty$. Consequently, letting $\epsilon'\to 0$, we deduce the following rate for the convergence $n_\epsilon \to n_\infty$ in the space $\dot{H}^{-1}(\mathbb{R}^d)$

$$\|n_\epsilon(t)-n_\infty(t)\|_{\dot{H}^{-1}(\mathbb{R}^d)} \leqslant C\sqrt{t}\sqrt{\epsilon}+\|n_\epsilon^0-n_\infty^0\|_{\dot{H}^{-1}(\mathbb{R}^d)}, \tag{5.28}$$

where C is a positive constant defined as follows

$$C=\sqrt{2\sup_{\epsilon>0}\|n_\epsilon\|_{L^1(\mathbb{R}^d\times(0,T))}}.$$

Assuming the additional BV bounds for the initial data, we get from Lemma 5.1.4 that n_ϵ is uniformly bounded in $L^\infty(0,T;BV(\mathbb{R}^d))$, and we can use Eq. (5.18) to obtain the rate $\epsilon^{1/4}$, as announced in Eq. (5.5). Thus Theorems 5.1.1 and 5.1.2 are proved in this special case.

5.3 Power law

Let us now consider Eq. (5.21) with the pressure law given by Eq. (5.2) and demonstrate that the method employed in the previous section remains valid. We now have the porous medium equation

$$\frac{\partial n_\gamma}{\partial t}-\Delta n_\gamma^\gamma=0. \tag{5.29}$$

Let us recall that there exists a positive constant p_M such that

$$0\leqslant \frac{\gamma}{\gamma-1}n_\gamma^{\gamma-1}\leqslant p_M,\qquad 0\leqslant \frac{\gamma'}{\gamma'-1}n_{\gamma'}^{\gamma'-1}\leqslant p_M.$$

Let us define

$$c_\gamma:=\left(\frac{\gamma-1}{\gamma}\right)^{\frac{1}{\gamma-1}}p_M^{1/(\gamma-1)}\quad\text{and}\quad \tilde{n}_\gamma:=\frac{n_\gamma}{c_\gamma}.$$

Then it immediately follows that $\tilde{n}_\gamma\leqslant 1$ and solves the equation

$$\partial_t\tilde{n}_\gamma-\Delta(c_\gamma^{\gamma-1}\tilde{n}_\gamma^\gamma)=0.$$

Following the same argument as before, we define φ_γ and $\tilde{\varphi}_\gamma$ by

$$-\Delta\varphi_\gamma=n_\gamma,\qquad -\Delta\tilde{\varphi}_\gamma=\tilde{n}_\gamma,$$

i.e. $\tilde{\varphi}_\gamma=\varphi_\gamma/c_\gamma$.
Without loss of generality, we take $1<\gamma<\gamma'$. Now we subtract the equation for $\tilde{n}_{\gamma'}$ from the equation for $\tilde{n}_\gamma$ to obtain

$$\frac{\partial(\tilde{n}_\gamma-\tilde{n}_{\gamma'})}{\partial t}-\Delta(c_\gamma^{\gamma-1}\tilde{n}_\gamma^\gamma-c_{\gamma'}^{\gamma'-1}\tilde{n}_{\gamma'}^{\gamma'})=0. \tag{5.30}$$

Then from Eq. (5.30) we have

$$-\Delta\frac{\partial(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})}{\partial t}-\Delta(c_\gamma^{\gamma-1}\tilde{n}_\gamma^\gamma-c_{\gamma'}^{\gamma'-1}\tilde{n}_{\gamma'}^{\gamma'})=0,$$

and we test it against $\tilde{\varphi}_\gamma - \tilde{\varphi}_{\gamma'}$ to deduce

$$\begin{aligned}\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}|\nabla(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})|^2 &= \int_{\mathbb{R}^d}(c_\gamma^{\gamma-1}\tilde{n}_\gamma^\gamma - c_{\gamma'}^{\gamma'-1}\tilde{n}_{\gamma'}^{\gamma'})(\tilde{n}_{\gamma'}-\tilde{n}_\gamma)\\ &\leqslant \int_{\mathbb{R}^d}c_\gamma^{\gamma-1}\tilde{n}_\gamma^\gamma(1-\tilde{n}_\gamma) + \int_{\mathbb{R}^d}c_{\gamma'}^{\gamma'-1}\tilde{n}_{\gamma'}^{\gamma'}(1-\tilde{n}_{\gamma'}),\end{aligned} \tag{5.31}$$

where the inequality follows from the fact that $\tilde{n}_\gamma, \tilde{n}_{\gamma'} \leqslant 1$. It is easy to see that for $0 \leqslant s \leqslant 1$ it holds $s^\gamma(1-s) \leqslant \frac{s}{\gamma}$. Hence, we have

$$\begin{aligned}\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}|\nabla(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})|^2 &\leqslant c_\gamma^{\gamma-1}\frac{1}{\gamma}\int_{\mathbb{R}^d}\tilde{n}_\gamma + c_{\gamma'}^{\gamma'-1}\frac{1}{\gamma'}\int_{\mathbb{R}^d}\tilde{n}_{\gamma'}\\ &\leqslant \left(\frac{\gamma-1}{\gamma}p_M\sup_\gamma\|\tilde{n}_\gamma(t)\|_{L^1(\mathbb{R}^d)}\right)\frac{1}{\gamma} + \left(\frac{\gamma'-1}{\gamma'}p_M\sup_{\gamma'}\|\tilde{n}_{\gamma'}(t)\|_{L^1(\mathbb{R}^d)}\right)\frac{1}{\gamma'}\\ &\leqslant C\left(\frac{1}{\gamma}+\frac{1}{\gamma'}\right),\end{aligned}$$

where in the last inequality we used the fact that by Lemma 5.1.4 n_γ is uniformly bounded in $L^\infty(0,T;L^1(\mathbb{R}^d))$. Finally, we remove the scaling using the triangle inequality

$$\begin{aligned}&\frac{1}{3}\|\nabla(\varphi_\gamma-\varphi_{\gamma'})(t)\|^2_{L^2(\mathbb{R}^d)}\\ &\qquad\leqslant \|\nabla(\varphi_\gamma-\tilde{\varphi}_\gamma)(t)\|^2_{L^2(\mathbb{R}^d)} + \|\nabla(\tilde{\varphi}_{\gamma'}-\varphi_{\gamma'})(t)\|^2_{L^2(\mathbb{R}^d)} + \|\nabla(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})(t)\|^2_{L^2(\mathbb{R}^d)}\\ &\qquad\leqslant \left|1-\frac{1}{c_\gamma}\right|^2\|\nabla\varphi_\gamma(t)\|^2_{L^2(\mathbb{R}^d)} + \left|1-\frac{1}{c_{\gamma'}}\right|^2\|\nabla\varphi_{\gamma'}(t)\|^2_{L^2(\mathbb{R}^d)}\\ &\qquad\quad + Ct\left(\frac{1}{\gamma}+\frac{1}{\gamma'}\right) + \|\nabla(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})(0)\|^2_{L^2(\mathbb{R}^d)}\\ &\qquad\leqslant \frac{1}{\gamma}\left(Ct + \gamma\left|1-\frac{1}{c_\gamma}\right|^2\sup_\gamma\|n_\gamma(t)\|^2_{\dot{H}^{-1}(\mathbb{R}^d)}\right)\\ &\qquad\quad + \frac{1}{\gamma'}\left(Ct + \gamma'\left|1-\frac{1}{c_{\gamma'}}\right|^2\sup_{\gamma'}\|n_{\gamma'}(t)\|^2_{\dot{H}^{-1}(\mathbb{R}^d)}\right) + \|\nabla(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})(0)\|^2_{L^2(\mathbb{R}^d)}.\end{aligned}$$

By the definition of c_γ, $\gamma\left|1-\frac{1}{c_\gamma}\right|^2 \to 0$ as $\gamma\to\infty$. Thus, we have

$$\|\nabla(\varphi_\gamma-\varphi_{\gamma'})(t)\|^2_{L^2(\mathbb{R}^d)} \leqslant (Ct+C)\left(\frac{1}{\gamma}+\frac{1}{\gamma'}\right) + 3\|\nabla(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})(0)\|^2_{L^2(\mathbb{R}^d)}.$$

By the same argument, we find

$$\|\nabla(\tilde{\varphi}_\gamma-\tilde{\varphi}_{\gamma'})(0)\|^2_{L^2(\mathbb{R}^d)} \leqslant C\left(\frac{1}{\gamma}+\frac{1}{\gamma'}\right) + 3\|\nabla(\varphi_\gamma-\varphi_{\gamma'})(0)\|^2_{L^2(\mathbb{R}^d)}.$$

Finally, we conclude

$$\|\nabla(\varphi_\gamma-\varphi_{\gamma'})(t)\|^2_{L^2(\mathbb{R}^d)} \leqslant (Ct+C)\left(\frac{1}{\gamma}+\frac{1}{\gamma'}\right) + 9\|\nabla(\varphi_\gamma-\varphi_{\gamma'})(0)\|^2_{L^2(\mathbb{R}^d)}. \tag{5.32}$$

Consequently, arguing as before and letting $\gamma' \to \infty$, we find

$$\|n_\gamma(t) - n_\infty(t)\|_{\dot H^{-1}(\mathbb{R}^d)} \leqslant \frac{C\sqrt{t}+C}{\sqrt{\gamma}} + 9\|n_\gamma^0 - n_\infty^0\|_{\dot H^{-1}(\mathbb{R}^d)}. \tag{5.33}$$

Again, under the additional BV assumptions we obtain (5.5) thanks to the interpolation inequality in Lemma 5.1.6.

5.4 Including drift and reaction terms

Having obtained the announced rate of convergence due to the nonlinear diffusion term, we now exhibit that we can include the drift and reaction terms. In fact, due to our assumptions on the proliferation rate and the chemical potential, all the additional terms will either have an appropriate sign, or be absorbed into the L^2-norm of the potential φ. We now write Eq. (5.1) as follows

$$\frac{\partial n_\gamma}{\partial t} - \Delta A_\gamma(n_\gamma) = \nabla\cdot(n_\gamma \nabla V) + n_\gamma g, \tag{5.34}$$

where $g = g(x,t)$ and A_γ is chosen appropriately depending on the state law for the pressure. As seen before, there is no harm in assuming the uniform bound $n \leqslant 1$. Then, arguing in the same way as previously, we obtain

$$\begin{aligned}
&\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2 + \int_{\mathbb{R}^d} (n_\gamma - n_{\gamma'})(A_\gamma(n_\gamma) - A_{\gamma'}(n_{\gamma'}))\\
&\quad = -\int_{\mathbb{R}^d} (n_\gamma - n_{\gamma'})\nabla(\varphi_\gamma - \varphi_{\gamma'})\cdot\nabla V + \int_{\mathbb{R}^d} g(x,t)(n_\gamma - n_{\gamma'})(\varphi_\gamma - \varphi_{\gamma'})\\
&\quad = \int_{\mathbb{R}^d} \Delta(\varphi_\gamma - \varphi_{\gamma'})\nabla(\varphi_\gamma - \varphi_{\gamma'})\cdot\nabla V - \int_{\mathbb{R}^d} g(x,t)\Delta(\varphi_\gamma - \varphi_{\gamma'})(\varphi_\gamma - \varphi_{\gamma'}).
\end{aligned}$$

It only remains to consider the two new terms on the right-hand side. For the first one we can write

$$\begin{aligned}
&\int_{\mathbb{R}^d} \Delta(\varphi_\gamma - \varphi_{\gamma'})\nabla(\varphi_\gamma - \varphi_{\gamma'})\cdot\nabla V\\
&\quad = -\int_{\mathbb{R}^d} \nabla(\varphi_\gamma - \varphi_{\gamma'})^T D^2(\varphi_\gamma - \varphi_{\gamma'})\nabla V - \int_{\mathbb{R}^d} \nabla(\varphi_\gamma - \varphi_{\gamma'})^T D^2 V \nabla(\varphi_\gamma - \varphi_{\gamma'})\\
&\quad = -\frac{1}{2}\int_{\mathbb{R}^d} \nabla|\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2\cdot\nabla V - \int_{\mathbb{R}^d} \nabla(\varphi_\gamma - \varphi_{\gamma'})^T D^2 V \nabla(\varphi_\gamma - \varphi_{\gamma'})\\
&\quad = \frac{1}{2}\int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2\Delta V - \int_{\mathbb{R}^d} \nabla(\varphi_\gamma - \varphi_{\gamma'})^T D^2 V \nabla(\varphi_\gamma - \varphi_{\gamma'})\\
&\quad \leqslant -\lambda\int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2,
\end{aligned}$$

where we have integrated by parts and used assumptions (A–drift). For the remaining term we integrate by parts to obtain

$$\int_{\mathbb{R}^d} g|\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2 + \int_{\mathbb{R}^d} (\varphi_\gamma - \varphi_{\gamma'})\nabla(\varphi_\gamma - \varphi_{\gamma'})\cdot\nabla g$$

$$\leqslant \|g_+\|_{L^\infty(\mathbb{R}^d\times(0,T))} \int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2 + \underbrace{\int_{\mathbb{R}^d} (\varphi_\gamma - \varphi_{\gamma'})\nabla(\varphi_\gamma - \varphi_{\gamma'}) \cdot \nabla g}_{\mathcal{A}}.$$

In case of $d = 2$, we suppose that g satisfies Assumption (A–reaction). Then we can integrate by parts in the last term to obtain

$$\mathcal{A} = -\frac{1}{2}\int_{\mathbb{R}^d} |\varphi_\gamma - \varphi_{\gamma'}|^2 \Delta g \leqslant 0. \tag{5.35}$$

If instead $d \geqslant 3$, we may alternatively assume that g satisfies Assumption (A–reaction') or Assumption (A–reaction"). In the first case, using successively the inequalities of Hölder and Sobolev we obtain

$$\mathcal{A} \leqslant \frac{1}{2}\|\varphi_\gamma - \varphi_{\gamma'}\|^2_{L^{2^*}(\mathbb{R}^d)} \|(\Delta g)_-\|_{L^{d/2}(\mathbb{R}^d)} \leqslant C_S \|(\Delta g)_-\|_{L^{d/2}(\mathbb{R}^d)} \int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2,$$

where C_S denotes the constant from Sobolev inequality, and $2^* = \frac{2d}{d-2}$ is the Sobolev conjugate exponent. Otherwise, if g satisfies Eq. (A–reaction"), in order to estimate the term $\mathcal{A}$ we do not integrate it by parts and we use in turn the inequalities of Young, Hölder and Sobolev to obtain

$$\begin{aligned}
2\mathcal{A} &\leqslant \int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2 + \int_{\mathbb{R}^d} |(\varphi_\gamma - \varphi_{\gamma'})|^2 |\nabla g|^2 \\
&\leqslant \int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2 + \|\varphi_\gamma - \varphi_{\gamma'}\|^2_{L^{2^*}(\mathbb{R}^d)} \|\nabla g\|^2_{L^d(\mathbb{R}^d)} \\
&\leqslant \left(1 + C_S \|\nabla g\|^2_{L^d(\mathbb{R}^d)}\right) \int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2.
\end{aligned}$$

Therefore we have

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2 + \int_{\mathbb{R}^d} (n_\gamma - n_{\gamma'})(A_\gamma(n_\gamma) - A_{\gamma'}(n_{\gamma'})) \leqslant C \int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})|^2.$$

Assuming for concreteness the power law pressure, using inequality (5.32) and a Gronwall inequality, we deduce

$$\sup_{t\in[0,T]} \|\nabla(\varphi_\gamma - \varphi_{\gamma'})(t)\|_{L^2(\mathbb{R}^d)} \leqslant C\left(\frac{1}{\sqrt{\gamma}} + \frac{1}{\sqrt{\gamma'}}\right) + \|\nabla(\varphi_\gamma - \varphi_{\gamma'})(0)\|_{L^2(\mathbb{R}^d)}. \tag{5.36}$$

Finally, passing to the limit $\gamma' \to \infty$, we conclude the proof of Theorem 5.1.1. Using the uniform BV-bound and Eq. (5.18) we obtain Theorem 5.1.2.

5.4.1 Limit relation between n_∞ and p_∞

Here we prove relation (5.6) between the limit density and pressure, where p_∞ is defined as the weak* limit (up to a sub-sequence) of p_γ in $L^\infty(\mathbb{R}^d \times (0,T))$.

Proof of Theorem 5.1.3. The relation is a straightforward consequence of the main estimate obtained in Section 5.3. We inspect Eq. (5.31), this time not ignoring the non-positive terms. After integration in time, these terms can be bounded as follows, using Eq. (5.32)

$$\int_0^T \int_{\mathbb{R}^d} \tilde{n}_{\gamma'}^{\gamma'}(1-\tilde{n}_\gamma)c_{\gamma'}^{\gamma'-1} + \int_0^T \int_{\mathbb{R}^d} \tilde{n}_{\gamma}^{\gamma}(1-\tilde{n}_{\gamma'})c_{\gamma}^{\gamma-1} \leqslant C(T)\left(\frac{1}{\gamma}+\frac{1}{\gamma'}\right) + \int_{\mathbb{R}^d} |\nabla(\varphi_\gamma - \varphi_{\gamma'})(0)|^2 .$$

Now let ψ be a compactly supported test function and consider the quantity

$$\left|\int_0^T \int_{\mathbb{R}^d} \psi \tilde{n}_\gamma^\gamma (1-\tilde{n}_{\gamma'})\right| \leqslant \|\psi\|_\infty \int_0^T \int_{\operatorname{supp}\psi} \tilde{n}_\gamma^\gamma(1-\tilde{n}_{\gamma'}) = \|\psi\|_\infty \int_0^T \int_{\operatorname{supp}\psi} \tilde{p}_\gamma^{\frac{\gamma}{\gamma-1}}(1-\tilde{n}_{\gamma'}).$$

Using weak lower semicontinuity of convex functionals and weak* convergence of the pressure and the density, we can pass to the limit with γ' and γ in turn to obtain

$$\int_0^T \int_{\mathbb{R}^d} \psi p_\infty (1-n_\infty) = 0,$$

which concludes the proof. □

5.5 Conclusions and open problems

We computed the rate of convergence of the solutions of a reaction-advection-diffusion equation of porous medium type in the incompressible limit. Our result in a negative Sobolev's norm can be interpolated with uniform BV-estimates in order to find a rate in any L^p-space for $1 < p < \infty$. How to assess the accuracy of our estimate remains an open problem. For the pure porous medium equation it might seem tempting to attempt a calculation for the illustrious example of the Barenblatt solution (taking as initial data the solution at some time $t > 0$). However, a direct calculation shows that in this case the data is “ill prepared” in the sense that it converges (in L^1) to its limit profile with too slow a rate of $\sim \ln\gamma/\gamma$. It is unclear how to approach the question of optimality in general. We expect that the "worst" rate would be exhibited by a *focusing solution*, whose support is initially contained outside of a compact set and closes up in finite time, thus generating a singularity.
Another challenging problem is to find an estimate for the convergence rate of the pressure, for which the method used above seems inapplicable as it is not clear how to relate the quantities $p_\gamma - p_{\gamma'}$ and $\varphi_\gamma - \varphi_{\gamma'}$. Consequently, we are also currently unable to treat more general, pressure dependent, reaction terms. Finally, it would be of interest to investigate whether it is possible to strengthen the estimate of Theorem 5.1.1 to Lebesgue norms without interpolation with BV. One advantage of any such alternative approach could be to allow for passing to the incompressible limit when BV bounds are not available, as is the case for systems of equations like (5.1). Additionally, it could allow for estimating the rate of convergence in the L^1-norm rather than the seemingly arbitrary $L^{4/3}$-norm.

5.A Bounding W_2-norm by the $\dot{H}^{-1}$-norm

We consider here the conservative case of Eq. (5.1), assuming $\int n_\gamma(t) = \int n_\infty(t) = 1$. Moreover, rather than the Cauchy problem set in the whole space, we consider the boundary valued problem set in a bounded domain $\Omega \subset \mathbb{R}^d$ with homogeneous Neumann boundary conditions.
We put $\mathrm{d}\mu_\gamma = n_\gamma(x)\,\mathrm{d}x$, $\mathrm{d}\mu_\infty = n_\infty(x)\,\mathrm{d}x$, ignoring time-dependence for the sake of brevity. Furthermore we make the additional assumption that $n_\infty \geqslant \underline{n} > 0$ for some constant $\underline{n}$.

Consider the curve $\rho : [0,1] \to \mathcal{P}_2(\mathbb{R}^d)$ given by $\tau \mapsto \rho_\tau := (1-\tau)\mu_\gamma + \tau\mu_\infty$ together with the vector field

$$V_\tau(x) = \frac{1}{(1-\tau)n_\gamma(x) + \tau n_\infty(x)} \nabla(\varphi_\gamma - \varphi_\infty). \tag{5.37}$$

For any test function $\psi \in C_c^\infty((0,1)\times\Omega)$ we have

$$\int_0^1 \int_\Omega \frac{\partial\psi}{\partial\tau} \,\mathrm{d}\rho_\tau(x)\,\mathrm{d}\tau = \int_0^1 \int_\Omega \frac{\partial\psi}{\partial\tau}((1-\tau)n_\gamma(x) + \tau n_\infty(x))\,\mathrm{d}x\,\mathrm{d}\tau \tag{5.38}$$

$$= \int_0^1 \int_\Omega \psi(n_\gamma(x) - n_\infty(x))\,\mathrm{d}x\,\mathrm{d}\tau \tag{5.39}$$

$$= \int_0^1 \int_\Omega \nabla\psi \cdot \nabla(\varphi_\gamma - \varphi_\infty)\,\mathrm{d}x\,\mathrm{d}\tau \tag{5.40}$$

$$= \int_0^1 \int_\Omega \nabla\psi \cdot V_\tau \,\mathrm{d}\rho_\tau(x)\,\mathrm{d}\tau. \tag{5.41}$$

Therefore the pair (ρ, V) solves the continuity equation

$$\frac{\partial\rho_\tau}{\partial\tau} + \nabla\cdot(V_\tau(x)\rho_\tau) = 0, \tag{5.42}$$

posed on $(0,1)\times\mathbb{R}^d$ with the marginal constraints

$$\rho_0 = \mu_\gamma, \quad \rho_1 = \mu. \tag{5.43}$$

Consequently, from Theorem 5.15 in [144], we deduce that ρ is absolutely continuous and the following inequality holds

$$|\rho'|(\tau) \leqslant \|V_\tau\|_{L^2(\mathbb{R}^d, \mathrm{d}\rho_\tau)},$$

where $|\rho'|$ denotes the metric derivative of the curve ρ with respect to the Wasserstein distance. Furthermore, since $(\mathcal{P}_2(\mathbb{R}^d), W_2)$ is a length space, we have

$$W_2(\mu_\gamma, \mu_\infty) \leqslant \int_0^1 |\rho'|(\tau)\,\mathrm{d}\tau. \tag{5.44}$$

Combining these last two inequalities, we obtain the following bound

$$W_2(\mu_\gamma, \mu_\infty) \leqslant \int_0^1 \|V_\tau(x)\|_{L^2(\mathbb{R}^d, \mathrm{d}\rho_\tau)}\,\mathrm{d}\tau \tag{5.45}$$

$$\leqslant \frac{1}{\sqrt{\underline{n}}}\|\nabla(\varphi_\gamma - \varphi_\infty)\|_{L^2(\mathbb{R}^d)} \int_0^1 \frac{1}{\sqrt{\tau}}\,\mathrm{d}\tau \tag{5.46}$$

$$= \frac{2}{\sqrt{\underline{n}}}\|n_\gamma - n_\infty\|_{\dot{H}^{-1}(\mathbb{R}^d)}. \tag{5.47}$$

Interestingly, a reverse bound can also be shown. Rather than a positive lower bound, a common upper bound is now required of all the densities (which is of course the case here). Let now $\sigma : [0,1] \to \mathcal{P}_2(\mathbb{R}^d)$ be a constant-speed geodesic from μ_γ to μ_∞ and E be a vector field such that (σ, E) satisfy the continuity equation, and $\|E_\tau\|_{L^2(\mathbb{R}^d;\sigma_\tau)} = W_2(\mu_\gamma, \mu_\infty)$. Then

$$\begin{aligned}
\|\nabla\varphi_\gamma - \nabla\varphi_\infty\|_{L^2}^2 &= \int_\Omega (\varphi_\gamma - \varphi_\infty)(n_\gamma - n_\infty) \\
&= \int_0^1 \int_\Omega \nabla(\varphi_\gamma - \varphi_\infty) \cdot E_\tau \,\mathrm{d}\rho_\tau \,\mathrm{d}\tau \\
&\leqslant \frac{1}{2}\|\nabla\varphi_\gamma - \nabla\varphi_\infty\|_{L^2}^2 + \frac{1}{2} W_2(\mu_\gamma, \mu_\infty)^2.
\end{aligned}$$

We refer the reader to [144, Section 5.5.2], and references therein, for further discussion about the equivalence of the two distances.

Part III

A multi-species model structured by phenotype

Chapter 6

Phenotypic heterogeneity in a model of tumor growth: existence of solutions and incompressible limit

Abstract

We consider a cross-diffusion model of tumor growth structured by phenotypic trait. We prove the existence of weak solutions and the incompressible limit as the pressure becomes stiff extending methods recently introduced in the context of two-species cross-diffusion systems. Moreover, we prove additional regularity estimates. We show that an L^2-version of the celebrated Aronson-Bénilan estimate extends to structured models. As a consequence, we recover a sharp L^1-bound on the Laplacian of the pressure. In particular, we are able to remove a technical constraint on the reaction terms assumed by Gwiazda et al. for the two-species model, by proving a new L^4-bound on the pressure gradient.

This chapter is taken from N.D. *Phenotypic heterogeneity in a model of tumor growth: existence of solutions and incompressible limit*, Submitted, (2021).

6.1 Introduction

We consider the following model of tumor growth structured by phenotypic trait, represented by the continuous variable $y \in [0, 1]$. The cell proliferation rate depends on both the trait and the pressure inside the tissue. The motion of cells is driven by Darcy's law, since the cell movement is passively generated by the birth and death of cells which create pressure gradients. We denote by $n = n(y, x, t)$ the density of the population with phenotypic trait $y \in [0, 1]$, and with $\varrho = \varrho(x, t)$ the total density at point $x \in \mathbb{R}^d$ and time $t > 0$. The pressure is related to the total density by the following power law

$$p(x, t) = (\varrho(x, t))^\gamma, \qquad \gamma > 1. \tag{6.1}$$

The model is the following

$$\begin{cases} \dfrac{\partial n}{\partial t}(y,x,t) - \nabla \cdot (n(y,x,t)\nabla p(x,t)) = nR(y,p), & (y,x,t) \in [0,1] \times \mathbb{R}^d \times (0,\infty), \\ \varrho(x,t) = \displaystyle\int_0^1 n(y,x,t)\,\mathrm{d}y, \end{cases} \tag{6.2}$$

with initial data $n_0(y,x) \in L^\infty_+([0,1] \times \mathbb{R}^d) \cap L^1([0,1] \times \mathbb{R}^d)$.
Let us point out that the equation satisfied by $\varrho(x,t)$ is a porous medium-reaction equation with coefficient $\gamma + 1$, namely

$$\partial_t \varrho - \frac{\gamma}{\gamma+1} \Delta \varrho^{\gamma+1} = \varrho \mathcal{R}, \qquad \mathcal{R} = \int_0^1 \sigma(y) R(y,p)\,\mathrm{d}y, \tag{6.3}$$

where with $\sigma = n/\varrho$ we denote the phenotype density fractions, while $\mathcal{R}$ represents the total population growth rate.

Structured models: motivations. The mathematical modelling of living tissue has attracted increasing attention in the last decades for both its ability to describe and investigate biological phenomenon and the extremely challenging mathematical problems that arise from such models. Among them, there is a growing interest towards models where the population density is structured by a phenotypic trait. In structured models, intra-population heterogeneity is taken into account by letting the mobility rate and/or the growth rate of each phenotypic distribution be functions of the structuring variable. Most of these models are based on Fisher-KPP equations, hence they describe the random movement of the cells through a linear diffusion term, with a phenotype-dependent mobility rate, and cell proliferation through a logistic growth rate. Non-local reaction terms are also considered, as in the non-local version of the Fisher-KPP model, [19], as well as divergence terms with respect to the phenotypic state to account for mutations, see for instance [16]. In this paper, Calvez *et al.* introduce a model in which only the mobility rate depends on the phenotypic trait. In particular, they assume the mobility rate to be proportional to the structuring variable. Computing an exact asymptotic traveling wave solution, they show that phenotypic segregation occurs and leads to front acceleration. Originating from [16], the acceleration of invasion fronts has been further studied in [20, 27] in the case of unbounded mobility, see also [4, 6, 5] and references therein for applications of structured PDEs models to tumor growth.
In [118], Lorenzi *et al.* propose a model structured by phenotypic trait to study a phenomena arising in cancer development which is usually referred to as '*growth or go*', *i.e.* the dichotomy of migration and proliferation. As investigated in [85, 82, 83, 86], more mobile cells tend to divide less than cells that have a lower mobility rate. For this reason, the authors consider mobility and growth rates which are, respectively, increasing and decreasing functions of the structuring variable. Unlike the previously mentioned models, they consider a velocity field which depends on the total population, *i.e.* the integral of the distributions with respect to the phenotypic trait. In particular, they take the velocity field to be proportional to the gradient of the total density. Therefore, the diffusion in the model is degenerate and no longer linear. The authors study the creation of compactly supported invasion fronts, and show that phenotypic separation occurs in the case of bounded mobility while the front undergoes acceleration in the case of unbounded mobility.

Porous medium models. As suggested in [118], a natural generalisation of their model consists of considering a pressure p related to the density by a power law with exponent greater

than 1, as in Eq. (6.1). This pressure law has been extensively used in the modelling of tumor growth, since it can be associated to the pressure of a compressible fluid. Combining the power law with Darcy's law yields to porous medium type equations as Eq.(6.3). Indeed, the invasion of cancer cells can be seen as the motion of a fluid through a porous medium (the extra-cellular matrix) [34].
The power law was first adopted for one-species models of tumor growth, see for instance [130, 132] and references therein. Furthermore, this pressure law is of particular interest since passing to the limit $\gamma \to \infty$, it is possible to establish a link between compressible models and 'geometrical' problems. As the pressure becomes more and more stiff, porous medium models converge to Hele-Shaw free boundary problems where the density is saturated and the pressure satisfies an elliptic equation. This limit, referred to as *incompressible limit* or *stiff pressure* limit, has been studied for a lot of non-structured one-species models, starting from the seminal paper by Perthame *et al.* [130]. For an overview on the single-species case, we refer the reader to [130, 61, 63, 102, 60, 93, 1, 129] and references therein.

Multi-species extensions. Lately, multi-phase extensions of the model introduced in [130] have been studied from different perspectives. Multi-species models allow to study the interaction between different types of tissue, for instance, cancer tissue, immune cells, healthy tissue, or dead tissue. In cross-reaction-diffusion systems, the coupling of the single densities equations gives rise to new mathematical challenges, such as the loss of regularity due to internal layers, namely regions where two species get in contact. For this reason, the mathematical analysis of these models presents many involved open problems. In 2018, Carrillo *et al.* show the existence of solutions to a reaction-cross-diffusion system of two equations using methods from optimal transport [47]. Their result, which was achieved in one spatial dimension, was later extended in 2019 by Gwiazda *et al.* in multiple dimensions [94]. Here, the authors consider a two-species system which is the analogous of our model, *i.e.* Eq. (6.2) for $y \in \{1, 2\}$. In particular, the two species evolve under Darcy's law, where the pressure is given by $p = (n_1 + n_2)^\gamma$, and n_i, $i = 1, 2$ denotes the two phases. Their existence result relies on applying a uniformly parabolic regularisation to the initial data and then passing to the limit. To this end, the most involved term is the nonlinear cross-diffusion term $n_i \nabla p$. In order to pass to the limit, the authors prove an L^2-version of the Aronson-Bénilan estimate, which is a celebrated estimate in the context of porous medium equations, and provides a bound on the Laplacian of the pressure. We refer the reader to [9] for the classical result. The same problem was then approached in [135], in which the authors are able to prove convergence by focusing on the quantity $(n_1 + n_2)^{\gamma+1}$ rather than the pressure itself. Their proof is simpler, since it does not require any regularity result on the second order derivatives of p. In fact, in [135] the authors recover the strong convergence of $\nabla(n_1 + n_2)^{\gamma+1}$ without using the Aronson-Bénilan estimate of [94], for which a restrictive condition on the reaction terms was needed.
As mentioned above, the analysis of the incompressible limit for porous medium models has a long history and has been addressed by many researchers for several models. The stiff limit for systems including two different species have been firstly addressed by Bubba *et al.* in 2019, [26], where the authors use an approach based on a L^2-Aronson-Bénilan estimate in the spirit of [94]. However, due to the absence of BV controls on the single species population densities, their argument only works in dimension 1. The result in any spatial dimension has been recently achieved by Liu and Xu in [115], where the authors consider a cross-reaction-diffusion system in a bounded domain with Neumann boundary conditions. Rather than dealing with the pressure, $p_\gamma = \varrho_\gamma^\gamma$, the authors focus on the quantity $\varrho_\gamma^{\gamma+1}$, proving strong compactness of its gradient, thus being able to prove convergence of the cross-diffusion terms. However, they are not able to include pressure-dependent reaction terms, and proving strong compactness of the pressure itself

remains a open question in this setting. The stiff limit for cross-diffusion systems has also been studied for different pressure laws and in the presence of drifts, see for instance [101, 63, 66].

Our contribution. In this paper, we aim to study the existence and regularity of solutions to System (6.2) and their incompressible limit. This problem can be seen as an infinitely-many-species extension of the models studied in [135, 94, 115]. At first, we extend the method by [135] to the structured case. Adapting the same argument, we are able to prove the existence of global weak solutions, *cf.* Theorem 6.3.7.

The second main result of the paper, *cf.* Theorem 6.4.1 and Theorem 6.4.2, concerns the incompressible limit of System (6.2). As $\gamma \to \infty$ in the pressure law, the problem turns out to be a free boundary problem of Hele-Shaw type. By extending and adapting the new method used in [115], we are able to recover the compactness needed to pass to the limit. Moreover, by restricting our study to the class of compactly supported solutions, we are able to show strong compactness of the pressure p_γ which, unlike in [115], allows us to account for pressure-dependent reaction terms.

Finally, we prove higher order regularity results on the pressure. First of all, we recover an L^4-bound on the pressure gradient, *cf.* Theorem 6.5.2, which has been introduced in the context of one-species porous medium models, see for instance [123, 61, 63], and represents a novelty in the multi-species case. Thanks to this bound, we are able to prove that an L^2-version of the Aronson-Bénilan estimate also holds for structured models, *cf.* Theorem 6.5.4. Moreover, we are able to recover it removing the technical assumption on the reaction terms required in [94] for the two-species case.

Plan of the paper. In the next section, we present the assumptions and the main results of the paper. Section 6.3 is devoted to the proof of the existence of weak solutions: in Section 6.3.1 we introduce the regularised problem, obtained performing a viscosity perturbation, and we infer uniform a priori estimates, while in Section 6.3.3, we show that $\nabla(\varrho_\varepsilon)^{\gamma+1}$ is strongly precompact in L^2, which is essential in order to pass to the limit in the regularised problem. In Section 6.4, we study the asymptotics of Problem (6.2) as $\gamma \to \infty$. The additional regularity estimates are deduced in Section 6.5.

Notation. Given $T > 0$ and $\Omega \subset \mathbb{R}^d$, we denote $Q_T := \mathbb{R}^d \times (0,T), \Omega_T := \Omega \times (0,T)$. We frequently use the abbreviated forms $n(t) := n(y,x,t)$, $n(y) := n(y,x,t)$, $\varrho(t) := \varrho(x,t)$.

6.2 Assumptions and main results

Now let us state the main results, *i.e.* the existence of weak solutions to System (6.2), the incompressible limit and the additional regularity estimates, and for each of them the related assumptions.

6.2.1 Existence of weak solutions

Assumptions on the reaction term. The function $R(y,p)$ is assumed to be smooth and bounded. Moreover, since the pressure induces an inhibitory effect on cell proliferation, we suppose there exists a positive constant p_M representing the *homeostatic pressure*, such that

$$\partial_p R(\cdot,\cdot) \leqslant 0, \quad R(\cdot,0) > 0, \quad R(\cdot,p_M) \leqslant 0, \tag{6.4}$$

Assumptions on the initial data. In order for the density fractions to be well defined we need to regularize the initial data such that it is always strictly positive. Therefore we take $n_{0,\varepsilon}(y,x) = n_0(y,x) + \varepsilon e^{-|x|^2}$, *i.e.* $\varrho_{0,\varepsilon}(y,x) = \varrho_0(y,x) + \varepsilon e^{-|x|^2}$, and $p_{0,\varepsilon} = (\varrho_{0,\varepsilon})^\gamma$.
We say that the initial data are well-prepared if they satisfy the following assumptions: there exists $0 < \varepsilon_0 < 1$ and C independent of ε, such that for all $0 < \varepsilon \leqslant \varepsilon_0$ the following holds

$$0 \leqslant \varrho_{0,\varepsilon_0} \leqslant (p_M)^{1/\gamma} \text{ a.e. in } \mathbb{R}^d, \qquad \left\| \sup_{y\in[0,1]} \frac{n_{0,\varepsilon}(y)}{\varrho_{0,\varepsilon}} \right\|_{L^\infty(\mathbb{R}^d)} \leqslant C. \tag{6.5}$$

To show the existence of weak solutions, we extend the method developed in [135] to the structured case and we prove the following result.

Theorem 6.2.1 (Theorem 6.3.7)**.** *Given $n_0 \in L^\infty_+([0,1]\times\mathbb{R}^d) \cap L^1([0,1]\times\mathbb{R}^d)$, there exists a weak solution to System (6.2), namely, there exists $n(y,x,t) \in L^\infty_+([0,1]\times\mathbb{R}^d\times(0,\infty)) \cap L^1([0,1]\times\mathbb{R}^d\times(0,\infty))$ such that $\nabla p(x,t) \in L^2(\mathbb{R}^d\times(0,\infty))$ and for all $T > 0$ and $\varphi \in C([0,1]; C^1_{comp}([0,T)\times\mathbb{R}^d))$*

$$\begin{aligned}
&-\int_0^1\int_{\mathbb{R}^d} n(y,x,t)\frac{\partial\varphi(y,x,t)}{\partial t}\,\mathrm{d}x\,\mathrm{d}y + \int_0^1\int_0^T\int_{\mathbb{R}^d} n(y,x,t)\nabla p(x,t)\cdot\nabla\varphi(y,x,t)\,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y\\
&\quad= \int_0^1\int_0^T\int_{\mathbb{R}^d} n(y,x,t)R(y,p(x,t))\varphi(y,x,t)\,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y + \int_0^1\int_{\mathbb{R}^d} n_0(y,x)\varphi(y,x,0)\,\mathrm{d}x\,\mathrm{d}y,
\end{aligned}$$

with

$$\varrho(x,t) = \int_0^1 n(y,x,t)\,\mathrm{d}y, \ \textit{and} \ \ p(x,t) = (\varrho(x,t))^\gamma.$$

6.2.2 Incompressible limit

In order to pass to the incompressible limit the more involved part is to find compactness of the pressure gradient. Our approach consists in extending and adapting the methods developed in [115] to our problem, namely focusing on the quantity $v_\gamma = \varrho_\gamma^{\gamma+1}$.
Unlike [115], we consider nonlinear pressure-dependent reaction terms. Consequently, our treatment of this term is different, and involves compensated compactness results and the monotonicity of R with respect to p. Moreover, we need to assume that the solutions are compactly supported (uniformly in γ). Indeed, outside of this class of solutions we are not able to show the strong compactness of the pressure which is necessary in order to pass to the limit in the reaction terms. The problem then reduces to a boundary valued problem with Dirichlet homogeneous conditions, while in [115] the authors choose Neumann homogeneous conditions on the boundary.

Assumptions on the initial data. We assume $n_{\gamma,0} \in L^\infty([0,1]\times\mathbb{R}^d)$, $\varrho_{\gamma,0} \in L^1_+(\mathbb{R}^d)\cap L^\infty(\mathbb{R}^d)$, and that there exists $\Omega_0 \subset \mathbb{R}^d$ such that

$$\operatorname{supp}(n_{\gamma,0}(y)) \subset \Omega_0, \ \text{ for a.e. } y \in [0,1], \forall\gamma > 1.$$

Thanks to the finite speed of propagation of porous medium type equations, we can reduce the problem to the case of a bounded domain $\Omega \subset \mathbb{R}^d$, on which we have homogeneous Dirichlet boundary conditions, $\varrho_\gamma(x,t) = 0$, for almost every (x,t) on $\partial\Omega\times[0,T]$. Since $\varrho_{\gamma,0}$ is compactly supported, then for all $T > 0$ there exists $\Omega \subset \mathbb{R}^d$ such that

$$\operatorname{supp}\varrho_\gamma(t) \subset \Omega, \qquad \forall t \in [0,T], \ \forall\gamma > 1.$$

Moreover, we assume there exists $\varrho_0, p_0 \in L^\infty_+(\Omega)$ such that

$$\|\varrho_{\gamma,0} - \varrho_0\|_{L^1(\Omega)} \to 0 \qquad \|p_{\gamma,0} - p_0\|_{L^1(\Omega)} \to 0$$

and

$$0 \leqslant \varrho_{\gamma,0} \leqslant (p_M)^\gamma, \qquad 0 \leqslant p_{\gamma,0} \leqslant p_M.$$

Let us denote $v_\gamma = \varrho_\gamma^{\gamma+1}$. We can rewrite Eq. (6.3) as follows

$$\frac{\partial \varrho_\gamma}{\partial t} - \frac{\gamma}{\gamma+1}\Delta v_\gamma = \int_0^1 n_\gamma R(y, p_\gamma)\,\mathrm{d}y. \tag{6.6}$$

We can pass to the incompressible limit $\gamma \to \infty$ and recover a Hele-Shaw problem, as stated in the following theorems.

Theorem 6.2.2 (Theorem 6.4.1). *Let $(n_\gamma, \varrho_\gamma, p_\gamma)$ be a solution given by Theorem 6.3.7. For all $T > 0$, up to the extraction of a subsequence we have*

$$\begin{aligned}
n_\gamma(y,x,t) &\rightharpoonup n_\infty(y,x,t) && \textit{weakly* in } L^\infty((0,1)\times\Omega_T),\\
\varrho_\gamma(x,t) &\rightharpoonup \varrho_\infty(x,t) && \textit{weakly* in } L^\infty(\Omega_T),\\
p_\gamma(x,t) &\rightharpoonup p_\infty(x,t) && \textit{weakly* in } L^\infty(\Omega_T),\\
\nabla v_\gamma &\rightharpoonup \nabla v_\infty && \textit{weakly in } L^2(\Omega_T),
\end{aligned}$$

as $\gamma \to \infty$. Moreover, the limit satisfies the following relation

$$p_\infty(1-\varrho_\infty) = 0 \qquad \textit{almost everywhere in } \Omega_T, \tag{6.7}$$

as well as

$$\frac{\partial \varrho_\infty}{\partial t} = \Delta v_\infty + \int_0^1 n_\infty R(y, p_\infty)\,\mathrm{d}y, \;\; \textit{in} \quad \mathcal{D}'(\mathbb{R}^d \times (0,\infty)).$$

In order to pass to the limit in the equations for n_γ and p_γ we need to prove the strong compactness of ∇v_γ in $L^2(\Omega_T)$, see Lemma 6.4.8.

Theorem 6.2.3 (Theorem 6.4.2). *The limit solution ϱ_∞, p_∞ satisfies*

$$\frac{\partial n_\infty}{\partial t} = \nabla\cdot(n_\infty \nabla p_\infty) + n_\infty R(y, p_\infty), \qquad \textit{in } \; \mathcal{D}'((0,1)\times\mathbb{R}^d\times(0,\infty)),$$

$$p_\infty\left(\Delta p_\infty + \int_0^1 n_\infty R(y,p_\infty)\,\mathrm{d}y\right) = 0, \qquad \textit{in } \; \mathcal{D}'(\mathbb{R}^d\times(0,\infty)). \tag{6.8}$$

Relation (6.7) implies that the total limit density ϱ_∞ is saturated in the positivity set of the pressure $\Omega(t) := \{x;\; p_\infty(x,t) > 0\}$, which can be seen as the region occupied by the tumor. Moreover, the *complementarity relation* (6.8) tells us that in $\Omega(t)$ the limit pressure satisfies an elliptic equation, which is usually referred to as a Hele-Shaw free boundary problem.

6.2.3 Additional regularity

The last part of the paper concerns additional regularity estimates on the pressure gradient, therefore we focus on p rather than $\varrho^{\gamma+1}$. We prove an L^2-version of the Aronson-Bénilan estimate on the Laplacian of the pressure. This estimate was already obtained in the context of two-species systems, see [94, 31]. Here, we not only extend it to our structured problem, but we are able to remove the constraint on the reaction term used in [94]. To this end, we infer a bound on the quantity $p^{\alpha-1}|\nabla p|^4$, for certain values of α, in the spirit of [123].

Additional assumptions. In order to prove the following additional regularity results on the pressure, it is necessary to make stronger assumptions on the initial data. In particular, we assume that $p_{\gamma,0}$ satisfies (uniformly in γ)

$$\nabla p_{\gamma,0} \in L^2(\Omega), \qquad (\Delta p_{\gamma,0})_- \in L^2(\Omega).$$

Moreover, we assume

$$\gamma > \max\left(\frac{3}{2}, 2-\frac{4}{d}\right).$$

Theorem 6.2.4 (Theorem 6.5.2)**.** *There exists a positive constant $C(T)$ such that for any $0 \leqslant \alpha < \frac{1}{\gamma}$ the following estimate holds true*

$$\kappa(\alpha)\int_0^T\int_\Omega \frac{|\nabla p|^4}{p^{1-\alpha}}\,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

with $\kappa(\alpha) := \frac{\alpha}{6}(1-\alpha\gamma)$.

Theorem 6.2.5 (Theorem 6.5.4)**.** *For all $T>0$, there exists a positive constant $C(T)$ independent of γ such that for all $t\in[0,T]$ we have*

$$\int_\Omega (\Delta p(t))_-^2\,\mathrm{d}x \leqslant C(T), \qquad \int_0^T\int_\Omega (\Delta p)_-^3\,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

6.3 Existence of solutions

6.3.1 Regularised problem

In order to prove the existence of weak solutions of Problem (6.2), we regularise the system introducing a viscosity term. Let $0<\varepsilon<\varepsilon_0$, and consider the following uniformly parabolic system

$$\begin{cases} \dfrac{\partial n_\varepsilon}{\partial t} - \nabla\cdot(n_\varepsilon \nabla p_\varepsilon) - \varepsilon\Delta n_\varepsilon = n_\varepsilon R(y,p_\varepsilon), \qquad y\in[0,1], \quad (x,t)\in\Omega_T, \\ \varrho_\varepsilon(x,t) = \displaystyle\int_0^1 n_\varepsilon(y,x,t)\,\mathrm{d}y. \end{cases} \tag{6.9}$$

The equation on ϱ_ε reads

$$\frac{\partial \varrho_\varepsilon}{\partial t} - \frac{\gamma}{\gamma+1}\Delta\varrho_\varepsilon^{\gamma+1} - \varepsilon\Delta\varrho_\varepsilon = \int_0^1 n_\varepsilon R(y,p_\varepsilon)\,\mathrm{d}y. \tag{6.10}$$

As mentioned above, in order to define the population fraction densities $\sigma_\varepsilon = n_\varepsilon/\varrho_\varepsilon$ we have to make sure that the total population density ϱ_ε is always strictly positive. To this end, we regularise the initial data as follows

$$n_{0,\varepsilon}(y,x,t) = n_0(y,x) + \varepsilon\, e^{-|x|^2},$$

therefore

$$\varrho_{0,\varepsilon}(x,t) = \varrho_0(x) + \varepsilon\, e^{-|x|^2}.$$

Before proving that this implies strict positivity of $\varrho_\varepsilon(x,t)$ for all times, we have to prove non-negativity of solutions.

Non-negativity. Multiplying Eq. (6.9) by $\operatorname{sign}_-(n_\varepsilon)$ we obtain

$$\frac{\partial}{\partial t}(n_\varepsilon)_- - \nabla\cdot((n_\varepsilon)_-\nabla p_\varepsilon) - \varepsilon\Delta(n_\varepsilon)_- \leqslant (n_\varepsilon)_-\|R\|_\infty,$$

where we denote $\|R\|_\infty = \sup_{y\in[0,1]} R(y,0)$. Integrating in space, we have

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}(n_\varepsilon)_-\,\mathrm{d}x - \int_{\mathbb{R}^d}\nabla\cdot((n_\varepsilon)_-\nabla p_\varepsilon)\,\mathrm{d}x - \varepsilon\int_{\mathbb{R}^d}\Delta(n_\varepsilon)_-\,\mathrm{d}x \leqslant \|R\|_\infty\int_{\mathbb{R}^d}(n_\varepsilon)_-\,\mathrm{d}x,$$

By Gronwall's lemma we infer

$$\int_0^1\int_{\mathbb{R}^d}(n_\varepsilon(y,x,t))_-\,\mathrm{d}x\,\mathrm{d}y \leqslant e^{\|R\|_\infty t}\int_0^1\int_{\mathbb{R}^d}(n_\varepsilon(y,x,0))_-\,\mathrm{d}x\,\mathrm{d}y,$$

which implies that almost everywhere $n_\varepsilon(t)\geqslant 0$ for $t\in(0,T]$ and by consequence both the density ϱ_ε and the pressure p_ε are non-negative.

Positivity. Let us define the function

$$\underline{\varrho} = \varepsilon e^{-Kt}e^{-|x|^2},$$

with $K = 2(\varepsilon+\gamma)+\|R\|_\infty$. We state that $\underline{\varrho}$ is a subsolution of the following equation

$$\frac{\partial\varrho}{\partial t} = \frac{\gamma}{\gamma+1}\Delta\varrho^{\gamma+1} + \varepsilon\Delta\varrho - \varrho\|R\|_\infty.$$

In fact, we have

$$\begin{aligned}
\frac{\gamma}{\gamma+1}\Delta\underline{\varrho}^{\gamma+1} + \varepsilon\Delta\underline{\varrho} - \underline{\varrho}\|R\|_\infty &= 2\gamma\underline{\varrho}^{\gamma+1}(2(\gamma+1)|x|^2-1) + 2\varepsilon(2|x|^2-1)\underline{\varrho} - \underline{\varrho}\|R\|_\infty\\
&\geqslant -2\varepsilon\underline{\varrho} - 2\gamma\underline{\varrho}^{\gamma+1} - \underline{\varrho}\|R\|_\infty\\
&\geqslant(-2\varepsilon-2\gamma-\|R\|_\infty)\underline{\varrho}\\
&= -K\underline{\varrho}\\
&= \frac{\partial\underline{\varrho}}{\partial t}.
\end{aligned}$$

Therefore, since by (6.10) ϱ_ε is a supersolution to the same equation and $\varrho_\varepsilon(0)\geqslant\underline{\varrho}(0)$, by the comparison principle we have

$$\varrho_\varepsilon(t) \geqslant \underline{\varrho}(t) > 0, \ \forall t \in [0,T].$$

Therefore, the quantity

$$\sigma_\varepsilon(y,x,t) := \frac{n_\varepsilon(y,x,t)}{\varrho_\varepsilon(x,t)},$$

is well defined, and satisfies the following transport equation

$$\frac{\partial \sigma_\varepsilon}{\partial t} = \nabla \sigma_\varepsilon \cdot \nabla p_\varepsilon + \sigma_\varepsilon R(y,p_\varepsilon) - \sigma_\varepsilon \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon)\,\mathrm{d}\eta, \tag{6.11}$$

where we used the notation η to distinguish the variable of integration from the variable y involved in the equation.
Therefore, we rewrite the equation on ϱ_ε as

$$\frac{\partial \varrho_\varepsilon}{\partial t} - \frac{\gamma}{\gamma+1}\Delta \varrho_\varepsilon^{\gamma+1} - \varepsilon \Delta \varrho_\varepsilon = \varrho_\varepsilon \mathcal{R}_\varepsilon,$$

where we denote

$$\mathcal{R}_\varepsilon := \mathcal{R}(\sigma_\varepsilon, p_\varepsilon) = \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon)\,\mathrm{d}\eta. \tag{6.12}$$

Let us notice that, from (6.12), $\mathcal{R}_\varepsilon$ is also uniformly bounded in $L^\infty(Q_T)$ and

$$\|\mathcal{R}_\varepsilon\|_{L^\infty(Q_T)} \leqslant \sup_{y\in[0,1]} |R(y,0)| \int_0^1 \sigma_\varepsilon(\eta)\,\mathrm{d}\eta = \|R\|_\infty.$$

6.3.2 A priori estimates

Here we prove a priori estimates (uniform in ε) which are essential to prove the existence of weak solutions.

L^1-bounds. Multiplying (6.10) by $\mathrm{sign}(\varrho_\varepsilon)$ and integrating in space we obtain

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d} |\varrho_\varepsilon|\,\mathrm{d}x &\leqslant \int_{\mathbb{R}^d} \Delta|\varrho_\varepsilon|^{\gamma+1}\,\mathrm{d}x + \varepsilon\int_{\mathbb{R}^d}\Delta|\varrho_\varepsilon|\,\mathrm{d}x + \int_{\mathbb{R}^d}\int_0^1 \mathrm{sign}(\varrho_\varepsilon)\ n_\varepsilon R(y,p_\varepsilon)\,\mathrm{d}y\,\mathrm{d}x\\ &\leqslant \|R\|_\infty \int_{\mathbb{R}^d} |\varrho_\varepsilon|\,\mathrm{d}x.\end{aligned}$$

By Gronwall's lemma we have $\varrho_\varepsilon \in L^\infty(0,T,L^1(\mathbb{R}^d))$ and thus $p_\varepsilon \in L^\infty(0,T,L^1(\mathbb{R}^d))$.

L^∞-bounds. Let us denote $\varrho_M := (p_M)^{1/\gamma}$ and $\mathcal{R}_M = \int_0^1 \sigma_\varepsilon(\eta)R(\eta,p_M)\,\mathrm{d}\eta$, which is negative by the definition of p_M. From Eq. (6.10) we have

$$\frac{\partial}{\partial t}(\varrho_\varepsilon - \varrho_M) - \frac{\gamma}{\gamma+1}\Delta(\varrho_\varepsilon^{\gamma+1} - \varrho_M^{\gamma+1}) - \varepsilon\Delta(\varrho_\varepsilon - \varrho_M) \leqslant (\varrho_\varepsilon - \varrho_M)\mathcal{R}_\varepsilon + \varrho_M(\mathcal{R}_\varepsilon - \mathcal{R}_M).$$

Multiplying by $\mathrm{sign}_+(\varrho_\varepsilon - \varrho_M)$ we obtain

$$\begin{aligned}\frac{\partial}{\partial t}(\varrho_\varepsilon - \varrho_M)_+ - \frac{\gamma}{\gamma+1}\Delta(\varrho_\varepsilon^{\gamma+1} - \varrho_M^{\gamma+1})_+ - \varepsilon\Delta(\varrho_\varepsilon - \varrho_M)_+ \\ \leqslant (\varrho_\varepsilon - \varrho_M)_+\mathcal{R}_\varepsilon + \varrho_M(\mathcal{R}_\varepsilon - \mathcal{R}_M)\mathrm{sign}_+(\varrho_\varepsilon - \varrho_M) \\ \leqslant \|\mathcal{R}_\varepsilon\|_\infty(\varrho_\varepsilon - \varrho_M)_+,\end{aligned}$$

where in the last inequality we used $\partial_p R \leqslant 0$. Integrating over $\mathbb{R}^d$ and applying Gronwall's lemma we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}(\varrho_\varepsilon - \varrho_M)_+ \,\mathrm{d}x \leqslant e^{\|\mathcal{R}\|_\infty t}\int_{\mathbb{R}^d}(\varrho_{0,\varepsilon} - \varrho_M)_+ \,\mathrm{d}x.$$

For all $0 < \varepsilon \leqslant \varepsilon_0$, thanks to Assumption (6.5), we finally have

$$0 \leqslant \varrho_\varepsilon \leqslant \varrho_M, \quad 0 \leqslant p_\varepsilon \leqslant p_M. \tag{6.13}$$

Let us consider the equation on the fraction density, Eq. (6.11). By the assumptions on the reaction term, σ_ε satisfies

$$\frac{\partial \sigma_\varepsilon}{\partial t} \leqslant \nabla\sigma_\varepsilon \cdot \nabla p_\varepsilon + \sigma_\varepsilon 2\|R_\varepsilon\|_\infty.$$

Hence, by the comparison principle we obtain

$$\sigma_\varepsilon \leqslant e^{2\|R_\varepsilon\|_\infty t}\sigma_{0,\varepsilon}.$$

Since by Assumption (6.5) $\sigma_{0,\varepsilon}$ is uniformly bounded in $[0,1]\times\mathbb{R}^d$, we have

$$\sigma_\varepsilon \in L^\infty([0,1]\times Q_T), \tag{6.14}$$

and by consequence

$$n_\varepsilon \in L^\infty([0,1]\times Q_T). \tag{6.15}$$

6.3.3 Passing to the limit $\varepsilon \to 0$

Extending the method by Price and Xu [135], in this section we prove the existence of solutions to Problem (6.2), by showing the convergence of the solution of the regularised problem as $\varepsilon \to 0$. To this end, the most involved part consists in proving the strong convergence of the degenerate divergence term. Unlike the method developed by Gwiazda *et al.* in [94], this strategy focuses on the quantity $\varrho_\varepsilon^{\gamma+1}$ rather than on the pressure $p_\varepsilon = \varrho_\varepsilon^\gamma$.

Lemma 6.3.1. *There exists a positive constant $C(T)$ independent of ε such that the following holds*

$$\iint_{Q_T}\left|\nabla\varrho_\varepsilon^{\frac{\gamma+1}{2}}\right|^2 \mathrm{d}x\,\mathrm{d}t + \varepsilon\iint_{Q_T}\int_0^1 |\nabla\sqrt{n_\varepsilon}(y)|^2\,\mathrm{d}y\,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

Proof. Let ν be a positive constant. We multiply Eq. (6.9) by $\ln(n_\varepsilon+\nu)$ and we obtain

$$\frac{\partial n_\varepsilon}{\partial t}\ln(n_\varepsilon+\nu) - \nabla\cdot(n_\varepsilon\nabla p_\varepsilon)\ln(n_\varepsilon+\nu) - \varepsilon\Delta n_\varepsilon\ln(n_\varepsilon+\nu) = n_\varepsilon R(y,p_\varepsilon)\ln(n_\varepsilon+\nu).$$

Integrating in space and in y over $[0,1]$ we have

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}\int_0^1 ((n_\varepsilon+\nu)\ln(n_\varepsilon+\nu)-n_\varepsilon)\,\mathrm{d}y\,\mathrm{d}x+\int_{\mathbb{R}^d}\int_0^1 \frac{n_\varepsilon}{n_\varepsilon+\nu}\nabla p_\varepsilon\cdot\nabla n_\varepsilon\,\mathrm{d}y\,\mathrm{d}x+\varepsilon\int_{\mathbb{R}^d}\int_0^1\frac{|\nabla n_\varepsilon|^2}{n_\varepsilon+\nu}\,\mathrm{d}y\,\mathrm{d}x\\
=\int_{\mathbb{R}^d}\int_0^1 n_\varepsilon R(y,p_\varepsilon)\ln(n_\varepsilon+\nu)\,\mathrm{d}y\,\mathrm{d}x\\
\leqslant \|R\|_\infty\int_{\mathbb{R}^d}\int_0^1 n_\varepsilon\ln(n_\varepsilon+\nu)\,\mathrm{d}y\,\mathrm{d}x.\end{aligned}$$

Let us notice that, since n_ε is uniformly bounded in $L^\infty([0,1]\times Q_T)$, the right-hand side is bounded. Let $t\leqslant T$. Upon integration in time for $\tau\in[0,t]$, we obtain

$$\begin{aligned}&\int_0^t\int_{\mathbb{R}^d}\nabla p_\varepsilon\cdot\left(\int_0^1\frac{n_\varepsilon}{n_\varepsilon+\nu}\nabla n_\varepsilon\,\mathrm{d}y\right)\mathrm{d}x\,\mathrm{d}\tau+\varepsilon\int_0^t\int_{\mathbb{R}^d}\int_0^1\frac{|\nabla n_\varepsilon|^2}{n_\varepsilon+\nu}\,\mathrm{d}y\,\mathrm{d}x\,\mathrm{d}\tau\\
&\quad\leqslant\int_{\mathbb{R}^d}\int_0^1(n_\varepsilon(t)-(n_\varepsilon(t)+\nu)\ln(n_\varepsilon(t)+\nu))\,\mathrm{d}y\,\mathrm{d}x+\int_{\mathbb{R}^d}\int_0^1(n_{0,\varepsilon}+\nu)\ln(n_{0,\varepsilon}+\nu)\,\mathrm{d}y\,\mathrm{d}x+C(T),\end{aligned}$$

Letting $\nu\to0$, thanks to the L^∞-bound of n_ε, we have

$$\int_0^t\int_{\mathbb{R}^d}\nabla\varrho_\varepsilon^\gamma\cdot\nabla\varrho_\varepsilon\,\mathrm{d}x\,\mathrm{d}\tau+4\varepsilon\int_0^t\int_{\mathbb{R}^d}\int_0^1|\nabla\sqrt{n_\varepsilon}|^2\,\mathrm{d}y\,\mathrm{d}x\,\mathrm{d}\tau\leqslant C(T),$$

for all $0\leqslant t\leqslant T$, and this concludes the proof.

□

Lemma 6.3.2. *The sequence $\varrho_\varepsilon^{\frac{\gamma+1}{2}}$ is precompact in $L^2(0,T;L^2(\mathbb{R}^d))$.*

Proof. From Lemma 6.3.1 we know that the gradient of $\varrho_\varepsilon^{\frac{\gamma+1}{2}}$ is bounded in $L^2(Q_T)$. Now we compute its time derivative.

$$\begin{aligned}\frac{\partial}{\partial t}\varrho_\varepsilon^{\frac{\gamma+1}{2}}=&\frac{\gamma+1}{2}\varrho_\varepsilon^{\frac{\gamma-1}{2}}\left(\nabla\cdot(\varrho_\varepsilon\nabla p_\varepsilon)+\varepsilon\Delta\varrho_\varepsilon+\int_0^1 n_\varepsilon(\eta)R(\eta,p_\varepsilon)\,\mathrm{d}\eta\right)\\
=&\frac{\gamma+1}{2}\varrho_\varepsilon^{\frac{\gamma-1}{2}}\nabla\cdot(\varrho_\varepsilon\nabla\varrho_\varepsilon^\gamma)+\frac{\gamma+1}{2}\varepsilon\varrho_\varepsilon^{\frac{\gamma-1}{2}}\Delta\varrho_\varepsilon+\frac{\gamma+1}{2}\varrho_\varepsilon^{\frac{\gamma-1}{2}}\int_0^1 n_\varepsilon(\eta)R(\eta,p_\varepsilon)\,\mathrm{d}\eta\\
=&\frac{\gamma+1}{2}\nabla\cdot\left(\varrho_\varepsilon^{\frac{\gamma+1}{2}}\nabla\varrho_\varepsilon^\gamma\right)-\frac{\gamma^2-1}{4}\varrho_\varepsilon^{\frac{\gamma-1}{2}}\nabla\varrho_\varepsilon\cdot\nabla\varrho_\varepsilon^\gamma+\frac{\gamma+1}{2}\varepsilon\nabla\cdot\left(\varrho_\varepsilon^{\frac{\gamma-1}{2}}\nabla\varrho_\varepsilon\right)\\
&-\frac{\gamma^2-1}{4}\varepsilon\varrho_\varepsilon^{\frac{\gamma-3}{2}}|\nabla\varrho_\varepsilon|^2+\frac{\gamma+1}{2}\varrho_\varepsilon^{\frac{\gamma-1}{2}}\int_0^1 n_\varepsilon(\eta)R(\eta,p_\varepsilon)\,\mathrm{d}\eta\\
=&\gamma\nabla\cdot\left(\varrho_\varepsilon^\gamma\nabla\varrho_\varepsilon^{\frac{\gamma+1}{2}}\right)-\gamma\frac{\gamma-1}{\gamma+1}\varrho_\varepsilon^{\frac{\gamma-1}{2}}\left|\nabla\varrho_\varepsilon^{\frac{\gamma+1}{2}}\right|^2+\varepsilon\Delta\varrho_\varepsilon^{\frac{\gamma+1}{2}}\\
&-\varepsilon(\gamma^2-1)\varrho_\varepsilon^{\frac{\gamma-1}{2}}|\nabla\sqrt{\varrho_\varepsilon}|^2+\frac{\gamma+1}{2}\varrho_\varepsilon^{\frac{\gamma-1}{2}}\int_0^1 n_\varepsilon(\eta)R(\eta,p_\varepsilon)\,\mathrm{d}\eta.\end{aligned}$$

Let us notice that Lemma 6.3.1 and the uniform L^∞-bound of σ_ε imply $\varepsilon|\nabla\sqrt{\varrho_\varepsilon}|^2\in L^1(Q_T)$. Therefore, the time derivative of $\varrho_\varepsilon^{\frac{\gamma+1}{2}}$ is a sum of functions bounded in $L^2(0,T;H^{-1}(\mathbb{R}^d))$ and

L^1-functions. Applying Aubin-Lions' lemma we infer that $\varrho_\varepsilon^{\frac{\gamma+1}{2}}$ is precompact in $L^2(Q_T)$. □

Remark 6.3.3. The sequence ϱ_ε is precompact in any L^q-space, for $1 \leqslant q < \infty$. In fact, if $q < \frac{\gamma+1}{2}$, the result follows from Hölder's inequality, while if $q > \frac{\gamma+1}{2}$ it follows from the uniform boundedness of ϱ_ε in L^∞.

Remark 6.3.4. Let us recall the results already proven. Up to a subsequence, we have

$$\begin{aligned} \sigma_\varepsilon &\rightharpoonup \sigma && \text{weak}^* \text{ in } L^\infty([0,1]\times Q_T),\\ n_\varepsilon &\rightharpoonup n && \text{weak}^* \text{ in } L^\infty([0,1]\times Q_T),\\ \varrho_\varepsilon &\to \varrho && \text{strongly in } L^q(Q_T), \text{ for each } 1\leqslant q<\infty,\\ \varrho_\varepsilon^{\frac{\gamma+1}{2}} &\rightharpoonup \varrho_\varepsilon^{\frac{\gamma+1}{2}} && \text{weakly in } L^2(0,T;H^1(\mathbb{R}^d)),\\ \frac{\partial \varrho_\varepsilon}{\partial t} &\rightharpoonup \frac{\partial \varrho}{\partial t} && \text{weakly in } L^2(0,T;H^{-1}(\mathbb{R}^d)). \end{aligned}$$

Let us recall the notation $\mathcal{R} = \int_0^1 \sigma(\eta) R(\eta,p)\,\mathrm{d}\eta$. Then

$$\mathcal{R}_\varepsilon \rightharpoonup \mathcal{R} \quad \text{weak}^* \text{ in } L^\infty(Q_T) \tag{6.16}$$

$$n_\varepsilon R(y,p_\varepsilon) \rightharpoonup nR(y,p) \quad \text{weak}^* \text{ in } L^\infty([0,1]\times Q_T). \tag{6.17}$$

The convergences of (6.16) and (6.17) are shown in detail in Appendix 6.B.

Lemma 6.3.5. *For all $q \geq \gamma+1$ and all $t\in[0,T]$, we have*

$$\int_{\mathbb{R}^d} (\varrho_\varepsilon(x,t))^q\,\mathrm{d}x \xrightarrow{\varepsilon\to 0} \int_{\mathbb{R}^d} (\varrho(x,t))^q\,\mathrm{d}x.$$

Proof. Let us define

$$w_\varepsilon := \varrho_\varepsilon^{\gamma+1} + \varepsilon\frac{\gamma+1}{\gamma}\varrho_\varepsilon.$$

Hence, we rewrite Eq. (6.3) as

$$\frac{\partial \varrho_\varepsilon}{\partial t} - \frac{\gamma}{\gamma+1}\Delta w_\varepsilon = \varrho_\varepsilon \mathcal{R}_\varepsilon, \tag{6.18}$$

where we recall that $\mathcal{R}_\varepsilon = \int_0^1 \sigma_\varepsilon R(\eta,p_\varepsilon)\,\mathrm{d}\eta$. We test Eq. (6.18) against $\partial_t w_\varepsilon$ to obtain

$$\int_{\mathbb{R}^d} \frac{\partial \varrho_\varepsilon}{\partial t}\frac{\partial w_\varepsilon}{\partial t}\,\mathrm{d}x - \frac{\gamma}{\gamma+1}\int_{\mathbb{R}^d} \Delta w_\varepsilon \frac{\partial w_\varepsilon}{\partial t}\,\mathrm{d}x = \int_{\mathbb{R}^d} \varrho_\varepsilon \mathcal{R}_\varepsilon \frac{\partial w_\varepsilon}{\partial t}\,\mathrm{d}x.$$

Now we treat each term individually, to obtain

$$\begin{aligned} \int_{\mathbb{R}^d} \frac{\partial \varrho_\varepsilon}{\partial t}\frac{\partial w_\varepsilon}{\partial t}\,\mathrm{d}x =& \int_{\mathbb{R}^d} \frac{\partial \varrho_\varepsilon}{\partial t}\frac{\partial \varrho_\varepsilon^{\gamma+1}}{\partial t}\,\mathrm{d}x + \varepsilon\frac{\gamma+1}{\gamma}\int_{\mathbb{R}^d}\left|\frac{\partial \varrho_\varepsilon}{\partial t}\right|^2\mathrm{d}x\\ =&(\gamma+1)\int_{\mathbb{R}^d}\varrho_\varepsilon^\gamma\left|\frac{\partial \varrho_\varepsilon}{\partial t}\right|^2\mathrm{d}x + \varepsilon\frac{\gamma+1}{\gamma}\int_{\mathbb{R}^d}\left|\frac{\partial \varrho_\varepsilon}{\partial t}\right|^2\mathrm{d}x, \end{aligned}$$

$$-\frac{\gamma}{\gamma+1}\int_{\mathbb{R}^d}\Delta w_\varepsilon \frac{\partial w_\varepsilon}{\partial t}\,\mathrm{d}x = \frac{\gamma}{\gamma+1}\frac{\mathrm{d}}{\mathrm{d}t}\int_{\mathbb{R}^d}\frac{|\nabla w_\varepsilon|^2}{2}\,\mathrm{d}x,$$

$$\begin{aligned}\int_{\mathbb{R}^d}\varrho_\varepsilon\mathcal{R}_\varepsilon\frac{\partial w_\varepsilon}{\partial t}\,\mathrm{d}x &= \int_{\mathbb{R}^d}\varrho_\varepsilon\mathcal{R}_\varepsilon\frac{\partial \varrho_\varepsilon^{\gamma+1}}{\partial t}\,\mathrm{d}x + \varepsilon\frac{\gamma+1}{\gamma}\int_{\mathbb{R}^d}\varrho_\varepsilon\mathcal{R}_\varepsilon\frac{\partial \varrho_\varepsilon}{\partial t}\,\mathrm{d}x\\ &\leqslant \frac{\gamma+1}{2}\int_{\mathbb{R}^d}\varrho_\varepsilon^\gamma\left|\frac{\partial\varrho_\varepsilon}{\partial t}\right|^2\mathrm{d}x + \frac{\gamma+1}{2}\int_{\mathbb{R}^d}\varrho_\varepsilon^{\gamma+2}\mathcal{R}_\varepsilon^2\,\mathrm{d}x\\ &\quad + \frac{\varepsilon}{2}\frac{\gamma+1}{\gamma}\int_{\mathbb{R}^d}\varrho_\varepsilon^2\mathcal{R}_\varepsilon^2\,\mathrm{d}x + \frac{\varepsilon}{2}\frac{\gamma+1}{\gamma}\int_{\mathbb{R}^d}\left|\frac{\partial\varrho_\varepsilon}{\partial t}\right|^2\mathrm{d}x.\end{aligned}$$

Therefore, we obtain

$$\sup_{t\in[0,T]}\int_{\mathbb{R}^d}|\nabla w_\varepsilon(t)|^2\,\mathrm{d}x + \frac{\varepsilon}{2}\frac{\gamma+1}{\gamma}\iint_{Q_T}\left|\frac{\partial\varrho_\varepsilon}{\partial t}\right|^2\mathrm{d}x\,\mathrm{d}t + \frac{\gamma+1}{2}\iint_{Q_T}\varrho_\varepsilon^\gamma\left|\frac{\partial\varrho_\varepsilon}{\partial t}\right|^2\mathrm{d}x\,\mathrm{d}t \leqslant C, \tag{6.19}$$

where C depends on $\|\varrho_\varepsilon\|_\infty$ and $\|\mathcal{R}_\varepsilon\|_\infty$. Since $\left|\partial_t\varrho_\varepsilon^{\frac{\gamma+2}{2}}\right|^2 = \frac{(\gamma+2)^2}{4}\varrho_\varepsilon^\gamma|\partial_t\varrho_\varepsilon|^2$, from Eq. (6.19) we have

$$\partial_t\varrho_\varepsilon^{\frac{\gamma+2}{2}} \in L^2(Q_T), \qquad \sqrt{\varepsilon}\partial_t\varrho_\varepsilon \in L^2(Q_T), \qquad \nabla w_\varepsilon \in L^\infty(0,T;L^2(\mathbb{R}^d)).$$

It follows easily from the boundedness of ϱ_ε, that $\partial_t\varrho_\varepsilon^{\gamma+1}\in L^2(Q_T)$. Hence, $\partial_t w_\varepsilon \in L^2(Q_T)$. Thanks to the bound on ∇w_ε and the Aubin-Lions lemma, w_ε is precompact in $C([0,T],L^2(\mathbb{R}^d))$. Consequently, $\varrho_\varepsilon^{\gamma+1}$ is also precompact in $C([0,T],L^2(\mathbb{R}^d))$, since we have

$$\int_{\mathbb{R}^d}\left|\varrho_\varepsilon^{\gamma+1}(t)-\varrho^{\gamma+1}(t)\right|^2\mathrm{d}x \leqslant \int_{\mathbb{R}^d}\left|w_\varepsilon(t)-\varrho^{\gamma+1}(t)\right|^2\mathrm{d}x + \int_{\mathbb{R}^d}\left|\varepsilon\frac{\gamma+1}{\gamma}\varrho_\varepsilon(t)\right|^2\mathrm{d}x \to 0, \text{ as } \varepsilon\to 0.$$

Once again, thanks to the uniform boundedness of ϱ_ε we infer that ϱ_ε is precompact in $C([0,T],L^q(\mathbb{R}^d))$ for any $q\geqslant\gamma+1$. Therefore

$$\int_{\mathbb{R}^d}(\varrho_\varepsilon(x,t))^q\,\mathrm{d}x \xrightarrow{\varepsilon\to 0} \int_{\mathbb{R}^d}(\varrho(x,t))^q\,\mathrm{d}x, \quad \forall q\geqslant\gamma+1,$$

and thus the proof is completed.

□

As already mentioned above, when dealing with cross-diffusion systems as (6.2), the most involved part is to obtain the compactness needed to pass to the limit in the cross-diffusion term. In the absence of strong compactness of the single species densities, here being the distribution of each phenotypic trait $n_\varepsilon(y)$, it is essential to infer strong compactness of $\nabla\varrho_\varepsilon^{\gamma+1}$. For this reason, the following convergence result is the core of the proof.

Lemma 6.3.6. *Upon the extraction of a subsequence, we have*

$$\nabla\varrho_\varepsilon^{\gamma+1} \xrightarrow{\varepsilon\to 0} \nabla\varrho^{\gamma+1} \quad \textit{strongly in } L^2(Q_T).$$

Proof. For the sake of simplicity, when integrating, we now neglect the symbols $\mathrm{d}x,\mathrm{d}t$. Let us consider the limit equation

$$\frac{\partial\varrho}{\partial t} - \frac{\gamma}{\gamma+1}\Delta\varrho^{\gamma+1} = \varrho\mathcal{R},$$

and then subtract it from Eq. (6.10), to obtain

$$\frac{\partial}{\partial t}(\varrho_\varepsilon - \varrho) + \frac{\gamma}{\gamma+1}\Delta(\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}) + \varepsilon\Delta\varrho_\varepsilon = \varrho_\varepsilon\mathcal{R}_\varepsilon - \varrho\mathcal{R}.$$

We test the above equation against $\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}$ and we obtain

$$\begin{aligned}\frac{\gamma}{\gamma+1}\iint_{Q_T}|\nabla(\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1})|^2 = &-\varepsilon\iint_{Q_T}\nabla\varrho_\varepsilon\cdot\nabla(\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}) + \int_0^T\langle\partial_t(\varrho_\varepsilon - \varrho), \varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}\rangle\\ &- \iint_{Q_T}(\varrho_\varepsilon\mathcal{R}_\varepsilon - \varrho\mathcal{R})(\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}).\end{aligned}$$

Let us consider the three terms on the right-hand side individually. From to the strong compactness of ϱ_ε in any L^p-space and the weak* compactness of $\mathcal{R}_\varepsilon$, it directly follows that

$$\iint_{Q_T}(\varrho_\varepsilon\mathcal{R}_\varepsilon - \varrho\mathcal{R})(\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}) \to 0.$$

Recalling Lemma 6.3.5, the strong convergence of $\varrho_\varepsilon^{\gamma+1}$ and the weak convergence of $\partial_t\varrho_\varepsilon$ in $L^2(0,T;H^{-1}(\mathbb{R}^d))$, we have

$$\begin{aligned}\int_0^T\langle\partial_t(\varrho_\varepsilon - \varrho), \varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}\rangle &= \iint_{Q_T}\frac{\partial_t\varrho_\varepsilon^{\gamma+2}}{\gamma+2} + \iint_{Q_T}\frac{\partial_t\varrho^{\gamma+2}}{\gamma+2} - \int_0^T\langle\partial_t\varrho, \varrho_\varepsilon^{\gamma+1}\rangle - \int_0^T\langle\partial_t\varrho_\varepsilon, \varrho^{\gamma+1}\rangle\\ &= \int_{\mathbb{R}^d}\frac{\varrho_\varepsilon^{\gamma+2}(T)}{\gamma+2} + \int_{\mathbb{R}^d}\frac{\varrho^{\gamma+2}(T)}{\gamma+2} - \int_{\mathbb{R}^d}\frac{\varrho_\varepsilon^{\gamma+2}(0)}{\gamma+2} - \int_{\mathbb{R}^d}\frac{\varrho^{\gamma+2}(0)}{\gamma+2}\\ &\quad - \int_0^T\langle\partial_t\varrho, \varrho_\varepsilon^{\gamma+1}\rangle - \int_0^T\langle\partial_t\varrho_\varepsilon, \varrho^{\gamma+1}\rangle\\ &\to 2\int_{\mathbb{R}^d}\frac{\varrho^{\gamma+2}(T)}{\gamma+2} - 2\int_{\mathbb{R}^d}\frac{\varrho^{\gamma+2}(0)}{\gamma+2} - 2\int_0^T\langle\partial_t\varrho, \varrho^{\gamma+1}\rangle = 0.\end{aligned}$$

Since from Lemma 6.3.1 we have $\sqrt{\varepsilon}\nabla\sqrt{\varrho_\varepsilon} \in L^2(Q_T)$, as well as $\nabla\varrho_\varepsilon^{\frac{\gamma+1}{2}} \in L^2(Q_T)$, we finally compute

$$\varepsilon\iint_{Q_T}\nabla\varrho_\varepsilon\cdot\nabla(\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}) = 4\varepsilon\iint_{Q_T}\sqrt{\varrho_\varepsilon}\nabla\sqrt{\varrho_\varepsilon}\cdot\left(\varrho_\varepsilon^{\frac{\gamma+1}{2}}\nabla\varrho_\varepsilon^{\frac{\gamma+1}{2}} - \varrho^{\frac{\gamma+1}{2}}\nabla\varrho^{\frac{\gamma+1}{2}}\right) \leqslant \sqrt{\varepsilon}C \to 0,$$

and this concludes the proof.

□

Having proved the L^2-strong convergence of $\nabla\varrho_\varepsilon^{\gamma+1}$, we can now show that the limit of the sequence $(n_\varepsilon, \varrho_\varepsilon)$ is a solution of Problem (6.2).

Theorem 6.3.7. *Given $n_0 \in L^\infty_+([0,1]\times\mathbb{R}^d)\cap L^1([0,1]\times\mathbb{R}^d)$, there exists a weak solution to System (6.2), namely, there exists $n(y,x,t) \in L^\infty_+([0,1]\times\mathbb{R}^d\times(0,\infty))\cap L^1([0,1]\times\mathbb{R}^d\times(0,\infty))$*

such that $\nabla p(x,t) \in L^2(\mathbb{R}^d \times (0,\infty))$ *and for all* $T>0$ *and* $\varphi \in C([0,1]; C^1_{comp}([0,T) \times \mathbb{R}^d))$

$$\begin{aligned} &-\int_0^1 \int_{\mathbb{R}^d} n(y,x,t) \frac{\partial \varphi(y,x,t)}{\partial t} \,\mathrm{d}x \,\mathrm{d}y + \int_0^1 \iint_{Q_T} n(y,x,t) \nabla p(x,t) \cdot \nabla \varphi(y,x,t) \,\mathrm{d}x \,\mathrm{d}t \,\mathrm{d}y \\ &= \int_0^1 \iint_{Q_T} n(y,x,t) R(y,p(x,t)) \varphi(y,x,t) \,\mathrm{d}x \,\mathrm{d}t \,\mathrm{d}y + \int_0^1 \int_{\mathbb{R}^d} n_0(y,x,t) \varphi(y,x,0) \,\mathrm{d}x \,\mathrm{d}y, \end{aligned} \tag{6.20}$$

with

$$\varrho(x,t) = \int_0^1 n(y,x,t) \,\mathrm{d}y, \quad p(x,t) = (\varrho(x,t))^\gamma.$$

Proof. For all $\varphi \in C([0,1]; C^1_{comp}([0,T) \times \mathbb{R}^d))$, the variational formulation of Problem (6.9) can be written as

$$\begin{aligned} &-\int_0^1 \int_{\mathbb{R}^d} n_\varepsilon(y,x,t) \frac{\partial \varphi(y,x,t)}{\partial t} \,\mathrm{d}x \,\mathrm{d}y + \int_0^1 \iint_{Q_T} n_\varepsilon(y,x,t) \nabla p_\varepsilon(x,t) \cdot \nabla \varphi(y,x,t) \,\mathrm{d}x \,\mathrm{d}t \,\mathrm{d}y \\ &= -\varepsilon \int_0^1 \iint_{Q_T} \nabla n_\varepsilon(y,x,t) \cdot \nabla \varphi(y,x,t) \,\mathrm{d}x \,\mathrm{d}t \,\mathrm{d}y \\ &\quad + \int_0^1 \iint_{Q_T} n_\varepsilon(y,x,t) R(y,p_\varepsilon) \varphi(y,x,t) \,\mathrm{d}x \,\mathrm{d}t \,\mathrm{d}y + \int_0^1 \int_{\mathbb{R}^d} n_{0,\varepsilon}(y,x,t) \varphi(y,x,0) \,\mathrm{d}x \,\mathrm{d}y. \end{aligned} \tag{6.21}$$

As we already proved, there exists a bounded non-negative function $\sigma = \sigma(y,x,t)$ such that

$$\sigma_\varepsilon \to \sigma \qquad \text{weakly}^* \text{ in } L^\infty([0,1] \times Q_T).$$

Therefore, from Lemma 6.3.6 we infer

$$\begin{aligned} n_\varepsilon \nabla p_\varepsilon &= n_\varepsilon \nabla \varrho_\varepsilon^\gamma \\ &= \sigma_\varepsilon \varrho_\varepsilon \nabla \varrho_\varepsilon^\gamma \\ &= \sigma_\varepsilon \frac{\gamma}{\gamma+1} \nabla \varrho_\varepsilon^{\gamma+1} \xrightarrow{\varepsilon \to 0} \sigma \frac{\gamma}{\gamma+1} \nabla \varrho^{\gamma+1}, \quad \text{weakly in } L^2([0,1] \times Q_T). \end{aligned} \tag{6.22}$$

It remains to show that $\sigma(y,x,t) = n(y,x,t)/\varrho(x,t)$ almost everywhere in $[0,1] \times Q_T$. Let $\delta > 0$ be an arbitrary positive constant. Then, we have

$$\sigma_\varepsilon (\varrho_\varepsilon - \delta)_+ \to \sigma (\varrho - \delta)_+, \qquad \text{weakly}^* \text{ in } L^\infty([0,1] \times Q_T).$$

On the other hand

$$\sigma_\varepsilon (\varrho_\varepsilon - \delta)_+ = n_\varepsilon \frac{(\varrho_\varepsilon - \delta)_+}{\varrho_\varepsilon} \to n \frac{(\varrho - \delta)_+}{\varrho}, \qquad \text{weakly}^* \text{ in } L^\infty([0,1] \times Q_T),$$

by the following argument. Since $0 \leqslant \frac{(\varrho-\delta)_+}{\varrho} \leqslant 1$, we obtain

$$\int_0^1 \iint_{Q_T} \left(n_\varepsilon \frac{(\varrho_\varepsilon - \delta)_+}{\varrho_\varepsilon} - n \frac{(\varrho - \delta)_+}{\varrho} \right) \varphi \,\mathrm{d}x \,\mathrm{d}t \,\mathrm{d}y$$

$$= \int_0^1 \iint_{Q_T} (n_\varepsilon - n)\frac{(\varrho-\delta)_+}{\varrho}\varphi \,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y + \int_0^1 \iint_{Q_T} n_\varepsilon\left(\frac{(\varrho_\varepsilon-\delta)_+}{\varrho_\varepsilon} - \frac{(\varrho-\delta)_+}{\varrho}\right)\varphi\,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y \to 0,$$

as $\varepsilon \to 0$ for any $\varphi \in L^1([0,1]\times Q_T)$. Therefore,

$$\sigma(\varrho-\delta)_+ = n\frac{(\varrho-\delta)_+}{\varrho} \quad \text{almost everywhere in } [0,1]\times Q_T,$$

for any $\delta > 0$. Hence $\sigma\varrho = n$, almost everywhere on the set where ϱ is strictly positive. If $\varrho = 0$ then $n(y) = 0$ for almost every $y \in [0,1]$, and thus

$$\sigma(y,x,t)\varrho(x,t) = n(y,x,t) \quad \text{for almost every } (y,x,t)\in[0,1]\times Q_T.$$

Finally, using Eq. (6.22), Remark 6.3.4 and passing to the limit in Eq. (6.21) we obtain Eq. (6.20) and the proof is completed.

□

6.4 Incompressible limit

Thanks to the result proven in the previous section, *cf.* Theorem 6.3.7, we know that for each $\gamma > 1$ there exists $(n_\gamma, \varrho_\gamma, p_\gamma)$ that satisfies following equations

$$\begin{aligned}
-\int_0^1\int_\Omega n_\gamma(y,x,t)\frac{\partial\varphi(y,x,t)}{\partial t}\,\mathrm{d}x\,\mathrm{d}y + \int_0^1\iint_{\Omega_T} n_\gamma(y,x,t)\nabla p_\gamma(x,t)\cdot\nabla\varphi(y,x,t)\,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y \\
= \int_0^1\iint_{\Omega_T} n_\gamma(y,x,t)R(y,p_\gamma)\varphi(y,x,t)\,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y + \int_0^1\int_\Omega n_{\gamma,0}(y,x,t)\varphi(y,x,0)\,\mathrm{d}x\,\mathrm{d}y,
\end{aligned} \tag{6.23}$$

for all $\varphi \in C([0,1]; C^1_{comp}([0,T)\times\Omega))$

$$\begin{aligned}
-\iint_{\Omega_T}\varrho_\gamma(x,t)\frac{\partial\psi}{\partial t}(x,t)\,\mathrm{d}x\,\mathrm{d}t + \frac{\gamma}{\gamma+1}\iint_{\Omega_T}\nabla v_\gamma(x,t)\cdot\nabla\psi(x,t)\,\mathrm{d}x\,\mathrm{d}t = \\
\iint_{\Omega_T}\left(\int_0^1 n_\gamma(x,t)R(y,p_\gamma(x,t))\,\mathrm{d}y\right)\psi(x,t)\,\mathrm{d}x\,\mathrm{d}t + \int_\Omega \varrho_{\gamma,0}(x)\psi(x,0)\,\mathrm{d}x,
\end{aligned} \tag{6.24}$$

for all test functions $\psi \in C^1_{comp}([0,T)\times\Omega)$, where $v_\gamma = \varrho^{\gamma+1}$.
The goal of this section is to study the incompressible limit $\gamma\to\infty$ and recover the weak formulation of a Hele-Shaw free boundary problem. To this end, we have to infer the compactness on the main quantities needed to pass to the limit in (6.23, 6.24). While for the first equation the strong compactness of ∇p_γ is needed, weak compactness of ∇v_γ is sufficient in order to pass to the limit in equation (6.24), as stated in the following theorem.

Theorem 6.4.1 (Weak Hele-Shaw problem)**.** *Let $(n_\gamma, \varrho_\gamma, p_\gamma)$ be a solution given by Theorem 6.3.7. For all $T > 0$, up to the extraction of a subsequence we have*

$$n_\gamma(y,x,t) \rightharpoonup n_\infty(y,x,t) \quad \text{weakly* in } L^\infty((0,1)\times\Omega_T), \tag{6.25}$$

$$\varrho_\gamma(x,t) \rightharpoonup \varrho_\infty(x,t) \quad \text{weakly* in } L^\infty(\Omega_T), \tag{6.26}$$

$$p_\gamma(x,t) \rightharpoonup p_\infty(x,t) \quad \text{weakly* in } L^\infty(\Omega_T), \tag{6.27}$$

$$\nabla v_\gamma \to \nabla v_\infty \qquad \textit{weakly in } L^2(\Omega_T), \tag{6.28}$$

as $\gamma \to \infty$. *Moreover the limit satisfies*

$$0 \leqslant \varrho_\infty \leqslant 1, \qquad p_\infty(1-\varrho_\infty) = 0 \qquad \textit{almost everywhere in } \Omega_T. \tag{6.29}$$

as well as

$$\begin{aligned} -\iint_{\Omega_T} \varrho_\infty \frac{\partial \psi}{\partial t} \,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} \nabla v_\infty \cdot \nabla \psi \,\mathrm{d}x\,\mathrm{d}t = \iint_{\Omega_T} \Big(\int_0^1 n_\infty R(y,p_\infty)\,\mathrm{d}y \Big) \psi \,\mathrm{d}x\,\mathrm{d}t \\ + \int_\Omega \varrho_0(x)\psi(x,0)\,\mathrm{d}x, \end{aligned} \tag{6.30}$$

for all test functions $\psi \in C^1_{comp}([0,T)\times\Omega)$.

The second main result is the *complementarity relation* which allows to recover the limit pressure as the solution of an elliptic equation. In order to prove it we need to infer the strong compactness of ∇p_γ, which also allows us to pass to the limit in Eq. (6.23).

Theorem 6.4.2 (Complementarity relation). *The limit solution satisfies*

$$v_\infty \Big(\Delta v_\infty + \int_0^1 n_\infty(y) R(y,p_\infty) \Big) = 0, \qquad \textit{in } \mathcal{D}'(\Omega\times(0,\infty)), \tag{6.31}$$

as well as

$$\begin{aligned} -\int_0^1 \iint_{\Omega_T} n_\infty \frac{\partial \varphi}{\partial t} \,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y + \int_0^1 \iint_{\Omega_T} n_\infty \nabla p_\infty \cdot \nabla\varphi \,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y \\ = \int_0^1 \iint_{\Omega_T} n_\infty R(y,p_\infty)\varphi \,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}y + \int_\Omega n_0(y,x)\varphi(y,x,0)\,\mathrm{d}x\,\mathrm{d}y, \end{aligned} \tag{6.32}$$

for all test functions $\varphi \in C((0,1); C^1_{comp}([0,T)\times\Omega))$.

The following part of this section is devoted to the proof of Theorem 6.4.1 and Theorem 6.4.2. Since we are not able to prove any control on $\partial_t p_\gamma$, it is not possible to directly prove the strong compactness of p_γ (Corollary 6.4.9) which is necessary in order to find the limit of the reaction term. For this reason we will be able to identify the limit only after the proof of the strong compactness of ∇v_γ (Lemma 6.4.8).

6.4.1 Proof of Theorem 6.4.1

Remark 6.4.3 (Weak* convergence as $\gamma\to\infty$). Let us point out that the L^∞-bounds (6.13),(6.14) and (6.15) proven in Subsection 6.3.2 are also uniform with respect to γ. Therefore, there exist $n_\infty, \varrho_\infty, p_\infty$ and v_∞ such that, after the extraction of a subsequence Eqs. (6.25)-(6.27) hold. Moreover, there exists $\mathcal{H}_\infty$ such that

$$n_\gamma R(y,p_\gamma) \rightharpoonup \mathcal{H}_\infty \text{ weakly* in } L^\infty((0,1)\times\Omega_T). \tag{6.33}$$

Remark 6.4.4 (H^1-bounds of p_γ and v_γ)**.** Multiplying the equation on the density, Eq. (6.3), by $\gamma\varrho_\gamma^{\gamma-1}$, it is immediate to see that the pressure satisfies

$$\frac{\partial p_\gamma}{\partial t} = \gamma p_\gamma(\Delta p_\gamma + \mathcal{R}_\gamma) + |\nabla p_\gamma|^2. \tag{6.34}$$

Hence, the pressure gradient is bounded in $L^2(\Omega_T)$ as shown by integrating by parts in space to get

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega p_\gamma \,\mathrm{d}x = (1-\gamma)\int_\Omega |\nabla p_\gamma|^2 \,\mathrm{d}x + \gamma \int_\Omega p_\gamma \mathcal{R}_\gamma \,\mathrm{d}x,$$

which implies

$$(\gamma-1)\iint_{\Omega_T} |\nabla p_\gamma|^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant \gamma \|\mathcal{R}_\gamma\|_{L^\infty(\Omega_T)} \|p_\gamma\|_{L^1(\Omega_T)} + \|p_0\|_{L^1(\Omega)}.$$

Therefore, for all $\gamma > 1$, it holds

$$p_\gamma \in L^2(0,T;H^1(\Omega)). \tag{6.35}$$

By the definition of v_γ, we have

$$\nabla v_\gamma = \frac{\gamma+1}{\gamma} p_\gamma^{\frac{1}{\gamma}} \nabla p_\gamma = \frac{\gamma+1}{\gamma}\varrho_\gamma \nabla p_\gamma \in L^2(\Omega_T), \tag{6.36}$$

uniformly in γ, and therefore Eq. (6.28) is proven.

Corollary 6.4.5. *The limit triplet* $(n_\infty, \varrho_\infty, p_\infty)$ *satisfies*

$$\frac{\partial \varrho_\infty}{\partial t} = \Delta v_\infty + \int_0^1 \mathcal{H}_\infty(y)\,\mathrm{d}y, \quad in \quad \mathcal{D}'(\mathbb{R}^d \times (0,\infty)), \tag{6.37}$$

where $\mathcal{H}_\infty = \mathcal{H}_\infty(y,x,t)$ *is the weak limit of* $n_\gamma R(y,p_\gamma)$.

Proof. The result comes from passing to the limit in Eq. (6.24) using the convergence results (6.26), (6.28), and (6.33).

□

As mentioned above, in order to conclude the proof of (6.30) we have to show that $\mathcal{H}_\infty = n_\infty R(y,p_\infty)$. This will be proven in the following subsection, *cf.* Eq. (6.46). At this moment, we are not able to identify the limit since we do not have the strong compactness of p_γ.

Remark 6.4.6 (H^{-1}-bound of the density time-derivative)**.** From the previous bounds and Eq. (6.6), we have

$$\frac{\partial \varrho_\gamma}{\partial t} \in L^2(0,T;H^{-1}(\Omega)). \tag{6.38}$$

Corollary 6.4.7. *The limit solution satisfies Eq.* (6.29).

Proof. Let us recall that the non-negativity of n_γ, and consequently of ϱ_γ and p_γ, has already been proven in the previous sections. Since $\varrho_\gamma \leqslant \varrho_M = (p_M)^{1/\gamma}$ we have $0 \leqslant \varrho_\infty \leqslant 1$.
By definition we have $v_\gamma = \varrho_\gamma p_\gamma$. Thanks to Eqs. (6.35) and (6.38) we can apply the compensated compactness theorem stated in Appendix 6.A, *cf.* Theorem 6.A.1, and infer

$$\int_{\Omega_T} v_\gamma \varphi \,\mathrm{d}x\,\mathrm{d}t \to \int_{\Omega_T} \varrho_\infty p_\infty \varphi \,\mathrm{d}x\,\mathrm{d}t,$$

for every $\varphi \in C(0,T;C^1(\Omega))$. Hence $v_\infty = \varrho_\infty p_\infty$, almost everywhere. Finally, by weak lower semi-continuity of convex functionals we have

$$\lim_{\gamma\to\infty} v_\gamma = \liminf_{\gamma\to\infty} p_\gamma^{\frac{\gamma+1}{\gamma}} \geqslant p_\infty.$$

For the sake of completeness, we include here the full argument. Let $\psi_\delta = \psi_\delta(x)$ be a convex function such that $\psi_\delta(x) \to x$ as $\delta \to 0$. Let us denote $\Psi_\gamma(x) = x^{\frac{\gamma+1}{\gamma}}$, $\gamma > 1$. Let us take $\delta > 0$ small enough such that

$$\psi_\delta(x) \leqslant \Psi_\gamma(x).$$

Therefore, we have

$$\psi_\delta(p_\infty) \leqslant \liminf_{\gamma\to\infty} \psi_\delta(p_\gamma) \leqslant \liminf_{\gamma\to\infty} \Psi_\gamma(p_\gamma) = \liminf_{\gamma\to\infty} p_\gamma^{\frac{\gamma+1}{\gamma}}.$$

Since we chose $\delta > 0$ arbitrarily, we take $\delta \to 0$ to obtain

$$p_\infty \leqslant \liminf_{\gamma\to\infty} p_\gamma^{\frac{\gamma+1}{\gamma}}.$$

Hence $\varrho_\infty p_\infty = v_\infty \geqslant p_\infty$, which implies $\varrho_\infty p_\infty = p_\infty$.

□

6.4.2 Proof of Theorem 6.4.2

In order to prove the complementarity relation, *cf.* Theorem 6.4.2, the usual strategy is to prove the strong convergence of ∇p_γ, see for instance [61, 63, 31]. Although we are able to prove strong compactness in space of the gradient (thanks to the Aronson-Bénilan estimate proven in the next section) we do not have any control on $\partial_t p_\gamma$ from which to infer time compactness. Therefore, we follow the strategy of [115], directly proving the strong compactness of ∇v_γ. The core of the proof is given by the following lemma.

Lemma 6.4.8. *Up to a subsequence, as $\gamma \to \infty$, we have*

$$\nabla v_\gamma \to \nabla v_\infty \quad \textit{strongly in } L^2(\Omega_T). \tag{6.39}$$

Proof. Let us use $v_\gamma - v_\infty$ as a test function in Eq. (6.6) to obtain

$$\int_\Omega \frac{\partial \varrho_\gamma}{\partial t}(v_\gamma - v_\infty)\,\mathrm{d}x + \frac{\gamma}{\gamma+1}\int_\Omega \nabla v_\gamma \cdot \nabla(v_\gamma - v_\infty)\,\mathrm{d}x = \int_\Omega \left(\int_0^1 n_\gamma R(y,p_\gamma)\,\mathrm{d}y\right)(v_\gamma - v_\infty)\,\mathrm{d}x. \tag{6.40}$$

We note that

$$\int_\Omega \frac{\partial \varrho_\gamma}{\partial t} v_\gamma\,\mathrm{d}x = \frac{1}{\gamma+2}\int_\Omega \frac{\partial \varrho_\gamma^{\gamma+2}}{\partial t}\,\mathrm{d}x = \frac{1}{\gamma+2}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \varrho_\gamma^{\gamma+2}\,\mathrm{d}x.$$

Integrating in time we get

$$\iint_{\Omega_T} \frac{\partial \varrho_\gamma}{\partial t} v_\gamma\,\mathrm{d}x\,\mathrm{d}t = \frac{1}{\gamma+2}\int_\Omega \varrho_\gamma^{\gamma+2}(T)\,\mathrm{d}x - \frac{1}{\gamma+2}\int_\Omega \varrho_\gamma^{\gamma+2}(0)\,\mathrm{d}x \to 0,$$

as $\gamma \to \infty$. Now we compute

$$
\begin{aligned}
\limsup_{\gamma\to\infty} \iint_{\Omega_T} |\nabla(v_\gamma - v_\infty)|^2 \,\mathrm{d}x\,\mathrm{d}t \\
&\leqslant \limsup_{\gamma\to\infty}\left(\iint_{\Omega_T} \nabla v_\gamma \cdot \nabla(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t - \iint_{\Omega_T} \nabla v_\infty \cdot \nabla(v_\gamma - \nabla v_\infty)\,\mathrm{d}x\,\mathrm{d}t\right) \\
&\leqslant \limsup_{\gamma\to\infty} \iint_{\Omega_T} \nabla v_\gamma \cdot \nabla(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t,
\end{aligned}
\tag{6.41}
$$

where in the last inequality we use the fact that ∇v_γ is weakly compact in $L^2(\Omega_T)$. From Eq. (6.40) we obtain

$$
\begin{aligned}
\limsup_{\gamma\to\infty} \iint_{\Omega_T} \nabla v_\gamma \cdot \nabla(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t \\
&\leqslant \limsup_{\gamma\to\infty} \iint_{\Omega_T}\left(\int_0^1 n_\gamma R(y,p_\gamma)\,\mathrm{d}y\right)(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t + \limsup_{\gamma\to\infty}\iint_{\Omega_T} \frac{\partial \varrho_\gamma}{\partial t} v_\infty\,\mathrm{d}x\,\mathrm{d}t \\
&\leqslant \limsup_{\gamma\to\infty} \iint_{\Omega_T}\left(\int_0^1 n_\gamma R(y,p_\gamma)\,\mathrm{d}y\right)(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} \frac{\partial \varrho_\infty}{\partial t} v_\infty\,\mathrm{d}x\,\mathrm{d}t,
\end{aligned}
\tag{6.42}
$$

where we used the weak compactness of the density in $L^2(0,T;H^{-1}(\Omega))$ given by Eq. (6.38). We now treat the first term in the right-hand side of Eq. (6.42). We add and subtract the same quantity to get

$$
\begin{aligned}
\iint_{\Omega_T}\left(\int_0^1 n_\gamma R(y,p_\gamma)\,\mathrm{d}y\right)(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t &= \underbrace{\iint_{\Omega_T}\left(\int_0^1 n_\gamma (R(y,p_\gamma) - R(y,p_\infty))\,\mathrm{d}y\right)(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{A}} \\
&\quad + \underbrace{\iint_{\Omega_T}\left(\int_0^1 n_\gamma R(y,p_\infty)\,\mathrm{d}y\right)(v_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{B}}.
\end{aligned}
$$

Our goal is to prove that the right hand side is bounded by some quantity that converges to zero as $\gamma \to \infty$. To deal with $\mathcal{A}$ we use the monotonicity of $R(y,\cdot)$, which is a decreasing function of the pressure. We rewrite $\mathcal{A}$ as follows

$$
\begin{aligned}
\mathcal{A} &= \iint_{\Omega_T}\left(\int_0^1 n_\gamma (R(y,p_\gamma) - R(y,p_\infty))\,\mathrm{d}y\right)(p_\gamma\varrho_\gamma - v_\infty)\,\mathrm{d}x\,\mathrm{d}t \\
&= \iint_{\Omega_T}\left(\int_0^1 n_\gamma (R(y,p_\gamma) - R(y,p_\infty))\,\mathrm{d}y\right)(p_\gamma(\varrho_\gamma - 1) + p_\gamma - p_\infty)\,\mathrm{d}x\,\mathrm{d}t \\
&= \iint_{\Omega_T}\left(\int_0^1 n_\gamma (R(y,p_\gamma) - R(y,p_\infty))\,\mathrm{d}y\right)p_\gamma(\varrho_\gamma - 1)\,\mathrm{d}x\,\mathrm{d}t \\
&\quad + \iint_{\Omega_T}\left(\int_0^1 n_\gamma (R(y,p_\gamma) - R(y,p_\infty))\,\mathrm{d}y\right)(p_\gamma - p_\infty)\,\mathrm{d}x\,\mathrm{d}t,
\end{aligned}
$$

where the last integral is non-positive by the monotonicity of R. Let $\varepsilon > 0$, we split the remaining term as follows

$$
\begin{aligned}
&\iint_{\Omega_T}\left(\int_0^1 n_\gamma(R(y,p_\gamma)-R(y,p_\infty))\,\mathrm{d}y\right)p_\gamma(\varrho_\gamma-1)\,\mathrm{d}x\,\mathrm{d}t\\
&=\iint_{\Omega_T\cap\{\varrho_\gamma\leqslant 1-\varepsilon\}}\left(\int_0^1 n_\gamma(R(y,p_\gamma)-R(y,p_\infty))\,\mathrm{d}y\right)\varrho_\gamma^\gamma(\varrho_\gamma-1)\,\mathrm{d}x\,\mathrm{d}t\\
&\qquad+\iint_{\Omega_T\cap\{\varrho_\gamma> 1-\varepsilon\}}\left(\int_0^1 n_\gamma(R(y,p_\gamma)-R(y,p_\infty))\,\mathrm{d}y\right)p_\gamma(\varrho_\gamma-1)\,\mathrm{d}x\,\mathrm{d}t\\
&\leqslant 2\|R\|_\infty\varrho_M(1-\varepsilon)^\gamma+2\|R\|_\infty\varrho_M p_M\max\left(\varepsilon,\frac{1}{\gamma}|\ln p_M|+o\left(\frac{1}{\gamma}\right)\right).
\end{aligned}
$$

Choosing $\varepsilon=1/\sqrt{\gamma}$, we infer that the right-hand side converges to zero as $\gamma\to\infty$.

Now we show that, after the extraction of a subsequence, the term

$$
\mathcal{B}=\int_0^1\left(\iint_{\Omega_T} n_\gamma R(y,p_\infty)(v_\gamma-v_\infty)\,\mathrm{d}x\,\mathrm{d}t\right)\mathrm{d}y,
$$

converges to zero as $\gamma\to\infty$. Let us choose $y\in(0,1)$. We denote $w_\gamma:=R(y,p_\infty)(v_\gamma-v_\infty)$. First of all, there exists a subsequence γ_k independent of y such that w_{γ_k} converges to zero weakly in $L^2(\Omega_T)$. Let us recall that

$$
\partial_t n_\gamma(y)=\nabla\cdot(n_\gamma(y)\nabla p_\gamma)+n_\gamma(y)R(y,p_\gamma).
$$

Hence, $\partial_t n_\gamma(y)\in L^2(0,T;H^{-1}(\Omega))$. Therefore, we can apply the compensated compactness theorem, see Theorem 6.A.1. For all indexes γ_{k_j} there exist $\gamma_{k_{j_i}}$ such that

$$
\iint_{\Omega_T} n_{\gamma_{k_{j_i}}}(y)R(y,p_\infty)(v_{\gamma_{k_{j_i}}}-v_\infty)\,\mathrm{d}x\,\mathrm{d}t\to 0,
$$

as $i\to\infty$, which implies

$$
\iint_{\Omega_T} n_{\gamma_k}(y)R(y,p_\infty)(v_{\gamma_k}-v_\infty)\,\mathrm{d}x\,\mathrm{d}t\to 0,
$$

as $k\to\infty$. Moreover, the above function is uniformly bounded in $L^1([0,1])$. Since γ_k only depends on the convergence of v_γ we have

$$
\mathcal{B}=\int_0^1\left(\iint_{\Omega_T} n_{\gamma_k}R(y,p_\infty)(v_{\gamma_k}-v_\infty)\,\mathrm{d}x\,\mathrm{d}t\right)\mathrm{d}y\to 0,
$$

as $k\to\infty$.

Now, we can finally come back to Eqs.(6.41)-(6.42)

$$
\limsup_{\gamma\to\infty}\iint_{\Omega_T}|\nabla(v_\gamma-v_\infty)|^2\,\mathrm{d}x\,\mathrm{d}t\leqslant\iint_{\Omega_T}\frac{\partial\varrho_\infty}{\partial t}v_\infty\,\mathrm{d}x\,\mathrm{d}t. \tag{6.43}
$$

To conclude the proof we will show that the right-hand side is actually equal to zero. Let us notice that for any $\varepsilon > 0$

$$\iint_{\Omega_T} (\varrho_\infty(x,t+\varepsilon) - \varrho_\infty(x,t))v_\infty \,\mathrm{d}x\,\mathrm{d}t = \iint_{\Omega_T} (\varrho_\infty(x,t+\varepsilon) - 1 + 1 - \varrho_\infty(x,t))v_\infty \,\mathrm{d}x\,\mathrm{d}t \leqslant 0,$$

where in the last inequality we used Eq. (6.29). In a similar fashion we have

$$\iint_{\Omega_T} (\varrho_\infty(x,t) - \varrho_\infty(x,t-\varepsilon))v_\infty \,\mathrm{d}x\,\mathrm{d}t \geqslant 0.$$

Now it remains to prove that

$$\lim_{\varepsilon\to 0} \iint_{\Omega_T} \left(\frac{\varrho_\infty(x,t+\varepsilon) - \varrho_\infty(x,t)}{\varepsilon}\right) v_\infty \,\mathrm{d}x\,\mathrm{d}t = \iint_{\Omega_T} \frac{\partial \varrho_\infty}{\partial t} v_\infty \,\mathrm{d}x\,\mathrm{d}t. \tag{6.44}$$

We integrate Eq. (6.37) between t and $t+\varepsilon$ to obtain

$$\varrho_\infty(t+\varepsilon) - \varrho_\infty(t) = \int_t^{t+\varepsilon} \Delta v_\infty \,\mathrm{d}s + \int_t^{t+\varepsilon}\int_0^1 \mathcal{H}_\infty \,\mathrm{d}y\,\mathrm{d}s.$$

We test the above equation against $\frac{1}{\varepsilon} v_\infty(\cdot,t)$ to get

$$\begin{aligned} \int_\Omega \left(\frac{\varrho_\infty(x,t+\varepsilon) - \varrho_\infty(x,t)}{\varepsilon}\right) v_\infty(x,t)\,\mathrm{d}x = &-\int_\Omega \frac{1}{\varepsilon}\int_t^{t+\varepsilon} \nabla v_\infty(x,s)\,\mathrm{d}s \;\cdot \nabla v_\infty(x,t)\,\mathrm{d}x \\ &+ \int_\Omega \frac{1}{\varepsilon}\int_t^{t+\varepsilon}\int_0^1 \mathcal{H}_\infty(y,x,s)\,\mathrm{d}y\,\mathrm{d}s\; v_\infty(x,t)\,\mathrm{d}x. \end{aligned} \tag{6.45}$$

We have

$$\frac{1}{\varepsilon}\int_t^{t+\varepsilon} \nabla v_\infty(x,s)\,\mathrm{d}s \to \nabla v_\infty(x,t), \qquad \text{a.e. in } \Omega_T.$$

From Eq. (6.36) we have

$$\begin{aligned} \iint_{\Omega_T} \left|\frac{1}{\varepsilon}\int_t^{t+\varepsilon} \nabla v_\infty(x,s)\,\mathrm{d}s\right|^2 \mathrm{d}x\,\mathrm{d}t \leqslant &\frac{1}{\varepsilon}\iint_{\Omega_T}\int_t^{t+\varepsilon} |\nabla v_\infty(x,s)|^2 \,\mathrm{d}s\,\mathrm{d}x\,\mathrm{d}t \\ = &\frac{1}{\varepsilon}\int_0^{T+\varepsilon}\int_{\max(0,s-\varepsilon)}^{\min(T,s)}\int_\Omega |\nabla v_\infty(x,s)|^2 \,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}s \\ \leqslant &\frac{1}{\varepsilon}\int_0^{T+\varepsilon} |\min(T,s) - \max(0,s-\varepsilon)| \int_\Omega |\nabla v_\infty(x,s)|^2 \,\mathrm{d}x\,\mathrm{d}s \\ \leqslant &\; C(T). \end{aligned}$$

Therefore we have

$$\frac{1}{\varepsilon}\int_t^{t+\varepsilon} \nabla v_\infty(x,s)\,\mathrm{d}s \to \nabla v_\infty(x,t), \quad \text{weakly in } L^2(\Omega_T).$$

In an analogous way we can prove that

$$\frac{1}{\varepsilon}\int_t^{t+\varepsilon}\int_0^1 \mathcal{H}_\infty(y,x,s)\,\mathrm{d}y\,\mathrm{d}s \to \int_0^1 \mathcal{H}_\infty(y,x,t)\,\mathrm{d}y, \quad \text{weakly in } L^2(\Omega_T).$$

Combining Eq. (6.45) and Eq. (6.37) we have

$$\begin{aligned}
&\lim_{\varepsilon\to 0}\iint_{\Omega_T}\left(\frac{\varrho_\infty(t+\varepsilon)-\varrho(t)}{\varepsilon}\right)v_\infty(x,t)\,\mathrm{d}x\,\mathrm{d}t\\
&\quad=-\iint_{\Omega_T}|\nabla v_\infty|^2\,\mathrm{d}x\,\mathrm{d}t+\iint_{\Omega_T}\left(\int_0^1\mathcal{H}_\infty(y,x,t)\,\mathrm{d}y\right)v_\infty(x,t)\,\mathrm{d}x\,\mathrm{d}t\\
&\quad=\iint_{\Omega_T}\frac{\partial\varrho_\infty}{\partial t}v_\infty\,\mathrm{d}x\,\mathrm{d}t.
\end{aligned}$$

Hence Eq. (6.44) is proven. As a consequence, Eq. (6.43) concludes the proof. □

Having proved the strong compactness of ∇v_γ, we can finally recover the strong compactness of the pressure itself, by simply applying the Poincaré inequality, using the fact that Ω has been chosen large enough such that the pressure satisfies Dirichlet boundary conditions.

Corollary 6.4.9 (Strong compactness of p_γ)**.** *Up to the extraction of a subsequence, we have*

$$p_\gamma\to p_\infty,\qquad \textit{strongly in}\ \ L^2(\Omega_T).$$

Proof. Since we assumed the solutions to be compactly supported for all times $0\leqslant t\leqslant T$, by Lemma 6.4.8 and Poincaré's inequality we infer the strong compactness of v_γ in $L^2(\Omega_T)$. Finally, since $p_\gamma=v_\gamma^{\gamma/(\gamma+1)}$ and $p_\infty=v_\infty$, the proof is completed. □

Thanks to this result, we can finally identify the limit of the reaction term, *i.e.* the following equality holds almost everywhere in $[0,1]\times\Omega_T$

$$\mathcal{H}_\infty(y,x,t)=n_\infty(y,x,t)R(y,p_\infty(x,t)).\tag{6.46}$$

Thanks to the strong compactness of the pressure gradient, we can pass to the limit in Eq. (6.23) to obtain Eq. (6.32).
Finally, to complete the proof of Theorem 6.4.2, we show that the complementarity relation (6.31) holds true. Let us multiply Eq. (6.6) by v_γ to get

$$\frac{1}{\gamma+2}\frac{\partial\varrho_\gamma^{\gamma+2}}{\partial t}=\frac{\gamma}{\gamma+1}v_\gamma\Delta v_\gamma+v_\gamma\int_0^1 n_\gamma R(y,p_\gamma)\,\mathrm{d}y.$$

As already proven, v_γ, p_γ and ∇v_γ are strongly compact in $L^2(\Omega_T)$. Therefore, passing to the limit $\gamma\to\infty$ we obtain

$$v_\infty\left(\Delta v_\infty+\int_0^1 n_\infty(y)R(y,p_\infty)\,\mathrm{d}y\right)=0,\quad \text{in } \mathcal{D}'(\Omega\times(0,\infty)),$$

which concludes the proof.

6.5 Additional regularity estimates

Here we present some regularity estimates on the pressure $p=\varrho^\gamma$, where ϱ is a solution of Eq. (6.10). In particular, we extend a result already proved in [123] for a Hele-Shaw model of one species, which implies that $p^{\alpha-1}|\nabla p|^4$ is integrable, for certain values of α. This new

estimate allows us to prove an L^2-version of the Aronson-Bénilan estimate for the structured model at hand. The original AB estimate is a lower L^∞-bound on the Laplacian of the pressure. In recent years, several extensions in both L^1 and L^2-settings have been proposed in the context of degenerate parabolic equations and systems. We refer the reader to [26, 31, 61, 63, 94] for a comprehensive overview.
Before presenting the proof of the main results, *cf.* Theorem 6.5.2 and Theorem 6.5.4, we point out that as a consequence the following corollary holds.

Corollary 6.5.1. *With the assumptions of the previous sections, for all $T>0$ there exists a constant $C(T)$ which does not depend on γ, such that*

$$\int_\Omega |\Delta p(t)| \,\mathrm{d}x \leqslant C(T), \tag{6.47}$$

for all $t \in [0,T]$.

Let us stress the fact that this estimate, together with a regularisation argument on Eq. (6.2) and Eq. (6.3), implies the existence of weak solutions. In fact, considering the equations

$$\begin{aligned}\partial_t n &= \nabla \cdot (n \nabla p) + nR(y,p),\\ \partial_t \varrho &= \nabla \cdot (\varrho \nabla p) + \varrho \mathcal{R},\end{aligned}$$

we can replace the initial data $n_0(y)$ by $n_{0,\mu}(y) = n_0(y) + \mu e^{-|x|^2}$, with $\mu > 0$. Therefore, the equations are non degenerate and have a positive solution (n_μ, ϱ_μ) and $\sigma_\mu(y) = n_\mu(y)/\varrho_\mu$ is well defined. Since the bound on the Laplacian, Eq. (6.47), is independent of the regularisation, applying the Aubin-Lions lemma it is possible to obtain strong compactness of the pressure gradient in $L^q(\Omega_T)$ for all $1 \leqslant q \leqslant \frac{d}{d-2}$, as $\mu \to 0$. Hence, combining this result with the compactness of n, σ and ϱ stated in Remark 6.3.4 allows to pass to the limit in the model and prove existence. For the detailed proof of a particular case, we refer the reader to [94], where the authors study the same problem for two species, n_1 and n_2, rather than for an infinite set of phenotypic traits, $y \in [0,1]$. In fact, the estimate on the Laplacian of the pressure is analogous, and relies on the Aronson-Bénilan estimate in an L^2-setting. The improvement that we bring here is to prove the AB estimate removing the strong technical assumption that the authors in [94] impose on the reaction terms, namely

$$F(0) = G(0),$$

where the source term of the total density is

$$\mathcal{R}(p, \sigma_1, \sigma_2) = F(p)\sigma_1 + G(p)\sigma_2,$$

with $\sigma_i = n_i/(n_1+n_2)$, for $i = 1,2$. As shown in the previous section, the question of how to prove existence without this assumption can be achieved using the method by Price and Xu in [135]. However, to recover the bound (6.47) on the Laplacian removing the condition on the reaction terms was still an open question.

Theorem 6.5.2 (L^4-estimate)**.** *There exists a constant $C(T)$ such that for any $0 \leqslant \alpha < \frac{1}{\gamma}$ the following estimate holds true*

$$\kappa(\alpha) \iint_{\Omega_T} \frac{|\nabla p|^4}{p^{1-\alpha}} \,\mathrm{d}x \,\mathrm{d}t \leqslant C(T),$$

with $\kappa(\alpha) := \frac{\alpha}{6}(1-\alpha\gamma)$.

Proof. First of all, let us recall that $\mathcal{R} = \int_0^1 \sigma(\eta)R(\eta,p)\,\mathrm{d}\eta$, hence $\partial_p \mathcal{R} \leqslant 0$.

We multiply Eq. (6.34) by $-p^\alpha(\Delta p + \mathcal{R})$ to obtain

$$-p^\alpha \frac{\partial p}{\partial t}(\Delta p + \mathcal{R}) = -\gamma p^{\alpha+1}(\Delta p + \mathcal{R})^2 - p^\alpha |\nabla p|^2 (\Delta p + \mathcal{R}). \tag{6.48}$$

Now we integrate in space and we split the left-hand side treating each term individually.

$$\begin{aligned} -\int_\Omega p^\alpha \frac{\partial p}{\partial t}\Delta p\,\mathrm{d}x &= \frac{1}{2}\int_\Omega p^\alpha \frac{\partial}{\partial t}|\nabla p|^2\,\mathrm{d}x + \alpha\int_\Omega p^{\alpha-1}\frac{\partial p}{\partial t}|\nabla p|^2\,\mathrm{d}x \\ &= \frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega p^\alpha|\nabla p|^2\,\mathrm{d}x + \frac{\alpha}{2}\int_\Omega p^{\alpha-1}\frac{\partial p}{\partial t}|\nabla p|^2\,\mathrm{d}x \\ &= \frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega p^\alpha|\nabla p|^2\,\mathrm{d}x + \frac{\alpha\gamma}{2}\int_\Omega p^\alpha(\Delta p + \mathcal{R})|\nabla p|^2\,\mathrm{d}x + \frac{\alpha}{2}\int_\Omega p^{\alpha-1}|\nabla p|^4\,\mathrm{d}x. \end{aligned}$$

Let us define the following function

$$\overline{\mathcal{R}}(p,\sigma) = \int_0^p q^\alpha \mathcal{R}(q,\sigma)\,\mathrm{d}q.$$

It immediately follows

$$p^\alpha \frac{\partial p}{\partial t}\mathcal{R} = \frac{\partial \overline{\mathcal{R}}}{\partial t} - \int_0^1 \left(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\right)\partial_t \sigma\,\mathrm{d}\eta.$$

Now using the equation on the fraction density σ, Eq. (6.11), we have

$$\begin{aligned} -\int_\Omega p^\alpha \frac{\partial p}{\partial t}\mathcal{R}\,\mathrm{d}x &= -\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \overline{\mathcal{R}}\,\mathrm{d}x + \int_\Omega\int_0^1\left(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\right)\nabla\sigma\cdot\nabla p\,\mathrm{d}\eta\,\mathrm{d}x \\ &\quad + \int_\Omega\int_0^1\left(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\right)(R(\eta,p) - \mathcal{R}(p))\sigma\,\mathrm{d}\eta\,\mathrm{d}x \\ &= -\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \overline{\mathcal{R}}\,\mathrm{d}x + \int_\Omega\int_0^1\left(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\right)\nabla\sigma\cdot\nabla p\,\mathrm{d}\eta\,\mathrm{d}x + Bdd, \end{aligned}$$

where we use Bdd to denote the bounded term

$$\int_\Omega\int_0^1\left(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\right)(R(\eta,p) - \mathcal{R})\sigma\,\mathrm{d}\eta\,\mathrm{d}x \leqslant \frac{C}{\alpha+1}\int_\Omega p^{\alpha+1}\,\mathrm{d}x \leqslant C\|p\|_{L^2}^2,$$

where C is a positive constant that depends on $\|\mathcal{R}\|_\infty$. Now let us come back to Eq. (6.48) and integrate on Ω

$$
\begin{aligned}
&\frac{\alpha}{2}\int_\Omega p^{\alpha-1}|\nabla p|^4\,\mathrm{d}x+\gamma\int_\Omega p^{\alpha+1}(\Delta p+\mathcal{R})^2\,\mathrm{d}x\\
&\qquad=-\Big(1+\frac{\alpha\gamma}{2}\Big)\int_\Omega p^\alpha(\Delta p+\mathcal{R})|\nabla p|^2\,\mathrm{d}x+\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega\Big(\overline{\mathcal{R}}-p^\alpha\frac{|\nabla p|^2}{2}\Big)\,\mathrm{d}x\\
&\qquad\quad-\underbrace{\int_\Omega\int_0^1\Big(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\Big)\nabla\sigma\cdot\nabla p\,\mathrm{d}\eta\,\mathrm{d}x}_{\mathcal{A}}-Bdd.
\end{aligned}
\tag{6.49}
$$

Let us integrate by parts the term $\mathcal{A}$. We obtain

$$
\begin{aligned}
-\mathcal{A}&=-\int_0^1\int_\Omega\Big(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\Big)\nabla\sigma\cdot\nabla p\,\mathrm{d}\eta\,\mathrm{d}x\\
&=\int_\Omega p^\alpha|\nabla p|^2\Big(\int_0^1 R(\eta,p)\sigma\,\mathrm{d}\eta\Big)\,\mathrm{d}x+\int_0^1\int_\Omega\Big(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\Big)\sigma\Delta p\,\mathrm{d}\eta\,\mathrm{d}x\\
&\leqslant\|\mathcal{R}\|_\infty p_M^\alpha\int_\Omega|\nabla p|^2\,\mathrm{d}x+\frac{1}{2}\int_\Omega\frac{\Big(\int_0^1\big(\int_0^p q^\alpha R(\eta,q)\,\mathrm{d}q\big)\,\sigma\,\mathrm{d}\eta\Big)^2}{p^{\alpha+1}}\,\mathrm{d}x+\frac{1}{2}\int_\Omega p^{\alpha+1}|\Delta p|^2\,\mathrm{d}x,
\end{aligned}
$$

where in the last line we used Fubini's Theorem and Young's inequality. Since by assumption both $R(y,p)$ and $\partial_p R(y,p)$ are bounded, the second term in the right-hand side is bounded.

Combining the estimate on the term $-\mathcal{A}$ with Eq. (6.49) and integrating in time, we obtain

$$
\begin{aligned}
&\frac{\alpha}{2}\iint_{\Omega_T}p^{\alpha-1}|\nabla p|^4\,\mathrm{d}x\,\mathrm{d}t+\gamma\iint_{\Omega_T}p^{\alpha+1}(\Delta p+\mathcal{R})^2\,\mathrm{d}x\,\mathrm{d}t\\
&\qquad\leqslant-\Big(1+\frac{\alpha\gamma}{2}\Big)\underbrace{\iint_{\Omega_T}p^\alpha(\Delta p+\mathcal{R})|\nabla p|^2\,\mathrm{d}x\,\mathrm{d}t}_{\mathcal{B}}+\int_\Omega\overline{\mathcal{R}}(T)\,\mathrm{d}x\\
&\qquad\quad+\int_\Omega(p_0)^\alpha\frac{|\nabla p_0|^2}{2}\,\mathrm{d}x+\frac{1}{2}\iint_{\Omega_T}p^{\alpha+1}|\Delta p|^2\,\mathrm{d}x\,\mathrm{d}t+Bdd,
\end{aligned}
\tag{6.50}
$$

where Bdd now includes other bounded quantities. Now it remains to treat the term $\mathcal{B}$. Let us point out here that we cannot estimate it in the same way as in [123], since the authors make use of a lower bound of the quantity $\Delta p+\mathcal{R}$, *i.e.* the L^∞-Aronson-Bénilan estimate, which does not hold for a multi-species system like the one at hand. For this reason, we deal with the term $\mathcal{B}$ by splitting it into two parts. The one coming from the source term is easier to estimate, since it can be bounded in the following way

$$
\iint_{\Omega_T}p^\alpha\mathcal{R}|\nabla p|^2\,\mathrm{d}x\,\mathrm{d}t\leqslant p_M^\alpha\|\mathcal{R}\|_\infty\|\nabla p\|_2^2\leqslant\max(1,p_M)\|\mathcal{R}\|_\infty\|\nabla p\|_2^2.
\tag{6.51}
$$

The term with Δp is instead more involved. We refer the reader to [61] for the same method applied to the case of one species and $\alpha=0$. From now on, for the sake of simplicity, we only compute the integral in space. Integrating by parts twice we have

$$\begin{aligned}\int_\Omega p^\alpha \Delta p|\nabla p|^2 \,\mathrm{d}x &= \int_\Omega \Delta(p^\alpha |\nabla p|^2) p \,\mathrm{d}x \\ &= \int_\Omega \Delta p^\alpha |\nabla p|^2 p \,\mathrm{d}x + 2\alpha \int_\Omega \nabla p \cdot \nabla(|\nabla p|^2) p^\alpha \,\mathrm{d}x + \int_\Omega p^{\alpha+1} \Delta(|\nabla p|^2) \,\mathrm{d}x. \end{aligned} \tag{6.52}$$

Computing the sum of the first two terms of the right-hand side, we find

$$\begin{aligned}&\int_\Omega \Delta p^\alpha |\nabla p|^2 p \,\mathrm{d}x + 2\alpha \int_\Omega \nabla p \cdot \nabla(|\nabla p|^2) p^\alpha \,\mathrm{d}x \\ &\quad= \alpha(\alpha-1) \int_\Omega p^{\alpha-1} |\nabla p|^4 \,\mathrm{d}x + \alpha \int_\Omega p^\alpha \Delta p |\nabla p|^2 \,\mathrm{d}x - 2\alpha \int_\Omega p^\alpha \Delta p|\nabla p|^2 \,\mathrm{d}x - 2\alpha^2 \int_\Omega p^{\alpha-1}|\nabla p|^4 \,\mathrm{d}x \\ &\quad= -\alpha(\alpha+1) \int_\Omega p^{\alpha-1}|\nabla p|^4 \,\mathrm{d}x - \alpha \int_\Omega p^\alpha \Delta p |\nabla p|^2 \,\mathrm{d}x,\end{aligned}$$

where we used integration by parts on the second term.
We compute the last term in Eq. (6.52) as follows

$$\begin{aligned}\int_\Omega p^{\alpha+1}\Delta(|\nabla p|^2)\,\mathrm{d}x &= 2\int_\Omega p^{\alpha+1} \nabla p \cdot \nabla(\Delta p)\,\mathrm{d}x + 2\int_\Omega p^{\alpha+1}(D^2_{i,j}p)^2 \,\mathrm{d}x \\ &= -2(\alpha+1)\int_\Omega p^\alpha |\nabla p|^2 \Delta p \,\mathrm{d}x - 2\int_\Omega p^{\alpha+1}|\Delta p|^2\,\mathrm{d}x + 2\int_\Omega p^{\alpha+1}(D^2_{i,j}p)^2\,\mathrm{d}x,\end{aligned}$$

where in the last equality we used integration by parts and we denoted $(D^2_{i,j}p)^2 = \sum_{i,j}(\partial^2_{i,j}p)^2$. By consequence, Eq. (6.52) now reads

$$\begin{aligned}\int_\Omega p^\alpha \Delta p |\nabla p|^2 \,\mathrm{d}x = -\alpha(\alpha+1)\int_\Omega p^{\alpha-1}|\nabla p|^4\,\mathrm{d}x - (3\alpha+2)\int_\Omega p^\alpha \Delta p|\nabla p|^2\,\mathrm{d}x \\ - 2\int_\Omega p^{\alpha+1}|\Delta p|^2\,\mathrm{d}x + 2\int_\Omega p^{\alpha+1}(D^2_{i,j}p)^2\,\mathrm{d}x,\end{aligned}$$

and thus

$$\begin{aligned}\int_\Omega p^\alpha \Delta p|\nabla p|^2\,\mathrm{d}x = &-\frac{\alpha}{3}\int_\Omega p^{\alpha-1}|\nabla p|^4\,\mathrm{d}x - \frac{2}{3(\alpha+1)}\int_\Omega p^{\alpha+1}|\Delta p|^2\,\mathrm{d}x \\ &+ \frac{2}{3(\alpha+1)}\int_\Omega p^{\alpha+1}(D^2_{i,j}p)^2\,\mathrm{d}x.\end{aligned} \tag{6.53}$$

Using Eq. (6.53) in Eq. (6.50), we finally find

$$\begin{aligned}&\frac{\alpha}{2}\iint_{\Omega_T} p^{\alpha-1}|\nabla p|^4\,\mathrm{d}x\,\mathrm{d}t + \gamma\iint_{\Omega_T} p^{\alpha+1}(\Delta p + \mathcal{R})^2\,\mathrm{d}x\,\mathrm{d}t + \frac{2+\alpha\gamma}{3(\alpha+1)}\iint_{\Omega_T} p^{\alpha+1}(D^2_{i,j}p)^2\,\mathrm{d}x\,\mathrm{d}t \\ &\quad\leqslant \frac{\alpha}{3}\Big(1+\frac{\alpha\gamma}{2}\Big)\iint_{\Omega_T} p^{\alpha-1}|\nabla p|^4\,\mathrm{d}x\,\mathrm{d}t + \left(\frac{2+\alpha\gamma}{3(\alpha+1)} + \frac{1}{2}\right)\iint_{\Omega_T} p^{\alpha+1}|\Delta p|^2\,\mathrm{d}x\,\mathrm{d}t + Bdd,\end{aligned}$$

where Bdd includes also the bound in Eq. (6.51). By Young's inequality, we have

$$\iint_{\Omega_T} p^{\alpha+1}|\Delta p|^2\,\mathrm{d}x\,\mathrm{d}t \leqslant \frac{3}{2}\iint_{\Omega_T} p^{\alpha+1}|\Delta p + \mathcal{R}|^2\,\mathrm{d}x\,\mathrm{d}t + 3\iint_{\Omega_T} p^{\alpha+1}|\mathcal{R}|^2\,\mathrm{d}x\,\mathrm{d}t.$$

Then, we finally have

$$\kappa(\alpha) \iint_{\Omega_T} p^{\alpha-1}|\nabla p|^4 \,\mathrm{d}x\,\mathrm{d}t + \left(\gamma - \frac{3}{2}\right) \iint_{\Omega_T} p^{\alpha+1}(\Delta p + \mathcal{R})^2 \,\mathrm{d}x\,\mathrm{d}t \\ + \frac{2+\alpha\gamma}{3(\alpha+1)} \iint_{\Omega_T} p^{\alpha+1}(D^2_{i,j}p)^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T), \tag{6.54}$$

with $\kappa(\alpha) := \frac{\alpha}{6}(1-\alpha\gamma)$. Since we assumed $0 < \alpha < \frac{1}{\gamma}$, this concludes the proof.

□

Let us point out that for $\alpha = 0$ the result proved above immediately implies a bound on the pressure gradient which is uniform with respect to γ. This bound was also investigated in [61], where the authors prove its sharpness.

Corollary 6.5.3. *The following estimate holds uniformly in γ,*

$$\iint_{\Omega_T} |\nabla p|^4 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

Proof. Let us take $\alpha = 0$ in Eq. (6.54). Then, we infer the following bounds

$$\iint_{\Omega_T} p(\Delta p + \mathcal{R})^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T), \qquad \iint_{\Omega_T} p(D^2_{i,j}p)^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

and both hold uniformly with respect to γ. Since both p and $\mathcal{R}$ are uniformly bounded in L^∞, this implies

$$\iint_{\Omega_T} p^2|\Delta p|^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T), \qquad \iint_{\Omega_T} p^2(D^2_{i,j}p)^2 \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

Using integration by parts, it follows that the boundedness of these two terms implies $\nabla p \in L^4(\Omega_T)$. We refer the reader to [61] for the detailed proof.

□

Theorem 6.5.4 (L^2-Aronson-Bénilan estimate)**.** *With the assumptions of Section 6.2.3, for all $T > 0$, there exists a constant $C(T)$ independent of γ, such that for all $t \in [0, T]$ we have*

$$\int_\Omega (\Delta p(t))^2_- \,\mathrm{d}x \leqslant C(T), \qquad \iint_{\Omega_T} (\Delta p)^3_- \,\mathrm{d}x\,\mathrm{d}t \leqslant C(T).$$

Proof. We define $w = \Delta p + \mathcal{R}$. Hence, Eq. (6.34) reads

$$\partial_t p = \gamma p w + |\nabla p|^2.$$

Let us recall again the definition of $\mathcal{R}$

$$\mathcal{R}(p,\sigma) = \int_0^1 R(\eta, p(x,t))\sigma(\eta,x,t)\,\mathrm{d}\eta.$$

Now we compute $\partial_t w$

$$\begin{aligned}
\frac{\partial w}{\partial t} =& \Delta(\gamma p w + |\nabla p|^2) + \frac{\partial \mathcal{R}}{\partial t} \\
=& \gamma \Delta(pw) + 2\nabla p \cdot \nabla(\Delta p) + 2\sum_{i,j} (\partial^2_{i,j} p)^2 + \frac{\partial \mathcal{R}}{\partial t} \\
\geq& \gamma \Delta(pw) + 2\nabla p \cdot \nabla w - 2\nabla p \cdot \nabla \mathcal{R} + \frac{2}{d}(w-\mathcal{R})^2 + \frac{\partial \mathcal{R}}{\partial t} \\
=& \gamma \Delta(pw) + 2\nabla p \cdot \nabla w - 2\mathcal{R}_p |\nabla p|^2 - 2\int_0^1 R(\eta,p)\nabla\sigma\cdot\nabla p \,\mathrm{d}\eta + \frac{2}{d}(w-\mathcal{R})^2 + \frac{\partial \mathcal{R}}{\partial t} \\
=& \gamma \Delta(pw) + 2\nabla p \cdot \nabla w - 2\mathcal{R}_p |\nabla p|^2 - 2\int_0^1 R(\eta,p)\nabla\sigma\cdot\nabla p \,\mathrm{d}\eta + \frac{2}{d}(w-\mathcal{R})^2 \\
&\quad + \int_0^1 \frac{\partial \sigma}{\partial t} R(\eta,p)\,\mathrm{d}\eta + \mathcal{R}_p(\gamma p w + |\nabla p|^2) \\
=& \gamma \Delta(pw) + 2\nabla p \cdot \nabla w - \mathcal{R}_p |\nabla p|^2 - 2\int_0^1 R(\eta,p)\nabla\sigma\cdot\nabla p \,\mathrm{d}\eta + \frac{2}{d}(w-\mathcal{R})^2 \\
&+ \int_0^1 \frac{\partial \sigma}{\partial t} R(\eta,p)\,\mathrm{d}\eta + \mathcal{R}_p \gamma p w \\
\geq& \gamma \Delta(pw) + 2\nabla p \cdot \nabla w - 2\int_0^1 R(\eta,p)\nabla\sigma\cdot\nabla p + \frac{2}{d}(w-\mathcal{R})^2 + \int_0^1 \frac{\partial \sigma}{\partial t} R(\eta,p)\,\mathrm{d}\eta + \mathcal{R}_p \gamma p w,
\end{aligned}$$

where in the last inequality we used that $\mathcal{R}_p \leqslant 0$. We recall that

$$\frac{\partial \sigma}{\partial t} = \nabla\sigma\cdot\nabla p + \sigma R(y,p) - \sigma\int_0^1 \sigma(\eta)R(\eta,p)\,\mathrm{d}\eta.$$

We multiply by $\mathrm{sign}_-(w)$ to obtain

$$\begin{aligned}
\frac{\partial (w)_-}{\partial t} \leq& \gamma\Delta(p(w)_-) + 2\nabla p\cdot\nabla(w)_- - 2\ \mathrm{sign}_-(w)\int_0^1 R(\eta,p)\nabla\sigma\cdot\nabla p\,\mathrm{d}\eta + \frac{2}{d}(w-\mathcal{R})^2\mathrm{sign}_-(w) \\
&+ \mathrm{sign}_-(w)\int_0^1 \nabla\sigma\cdot\nabla p R(\eta,p)\,\mathrm{d}\eta + C + \mathcal{R}_p\gamma p(w)_-,
\end{aligned}$$

where C is a constant depending on $\|R\|_\infty$.

Firstly, we multiply by $(w)_-$ and use again that $\mathcal{R}_p \leqslant 0$ to obtain

$$\begin{aligned}
\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega (w)_-^2\,\mathrm{d}x \leq& \gamma\int_\Omega \Delta(p(w)_-)(w)_-\,\mathrm{d}x + 2\int_\Omega \nabla p\cdot\nabla(w)_-(w)_-\,\mathrm{d}x \\
&+ \int_\Omega\left(\int_0^1 R(\eta,p)\nabla\sigma\cdot\nabla p\,\mathrm{d}\eta\right)(w)_-\,\mathrm{d}x \\
&- \int_\Omega \frac{2}{d}(w)_-^3\,\mathrm{d}x - \frac{2}{d}\int_\Omega \mathcal{R}^2(w)_-\,\mathrm{d}x - \frac{4}{d}\int_\Omega (w)_-^2\mathcal{R}\,\mathrm{d}x + C\int_\Omega (w)_-\,\mathrm{d}x.
\end{aligned} \tag{6.55}$$

We estimate the sum of the first two terms of the right-hand side.

$$
\begin{aligned}
\gamma \int_\Omega \Delta(p(w)_-)(w)_- \,\mathrm{d}x + 2\int_\Omega \nabla p \cdot \nabla (w)_-(w)_- \,\mathrm{d}x =& \Big(1-\frac{\gamma}{2}\Big)\int_\Omega \nabla p \cdot \nabla \frac{(w)_-^2}{2}\,\mathrm{d}x - \gamma \int_\Omega p|\nabla (w)_-|^2\,\mathrm{d}x\\
=& \Big(\frac{\gamma}{2}-1\Big)\int_\Omega \Delta p (w)_-^2\,\mathrm{d}x - \gamma \int_\Omega p|\nabla (w)_-|^2\,\mathrm{d}x\\
\leqslant& \Big(1-\frac{\gamma}{2}\Big)\int_\Omega (w)_-^3\,\mathrm{d}x + \Big(1-\frac{\gamma}{2}\Big)\int_\Omega \mathcal{R}(w)_-^2\,\mathrm{d}x\\
&- \gamma \int_\Omega p|\nabla (w)_-|^2\,\mathrm{d}x\\
\leqslant& \Big(1-\frac{\gamma}{2}\Big)\int_\Omega (w)_-^3\,\mathrm{d}x - \gamma \int_\Omega p|\nabla (w)_-|^2\,\mathrm{d}x.
\end{aligned}
$$

Now we treat the term with $\nabla\sigma$. Since we do not have any BV-estimate on the density fraction we lift the derivative from σ

$$
\begin{aligned}
\int_0^1 \Big(\int_\Omega R(\eta,p)\nabla\sigma\cdot\nabla p(w)_-\,\mathrm{d}x\Big)\,\mathrm{d}\eta =& \underbrace{-\int_0^1\int_\Omega R(\eta,p)\sigma\Delta p(w)_-\,\mathrm{d}x\,\mathrm{d}\eta}_{\mathcal{A}}\\
&\underbrace{-\int_0^1\int_\Omega R(\eta,p)\sigma\nabla p\cdot\nabla(w)_-\,\mathrm{d}x\,\mathrm{d}\eta}_{\mathcal{B}}\\
&\underbrace{-\int_0^1\int_\Omega R_p(\eta,p)\sigma|\nabla p|^2(w)_-\,\mathrm{d}x\,\mathrm{d}\eta}_{\mathcal{C}}.
\end{aligned}
\tag{6.56}
$$

Using $\Delta p = w - \mathcal{R}$ we find

$$
\begin{aligned}
\mathcal{A} =& \int_\Omega (w)_-^2\Big(\int_0^1 R(\eta,p)\sigma\,\mathrm{d}\eta\Big)\,\mathrm{d}x + \int_\Omega \mathcal{R}(w)_-\Big(\int_0^1 R(\eta,p)\sigma\,\mathrm{d}\eta\Big)\,\mathrm{d}x\\
\leqslant& \|\mathcal{R}\|_\infty \int_\Omega (w)_-^2\,\mathrm{d}x + \|\mathcal{R}\|_\infty^2\int_\Omega (w)_-\,\mathrm{d}x.
\end{aligned}
\tag{6.57}
$$

Let us point out that it is in order to bound the term $\mathcal{B}$ that the assumption $F(0)=G(0)$ was needed in [94]. In fact, combining this assumption and Young's inequality (with exponent 2), the authors are able to estimate $\mathcal{B}$ by $\frac{1}{2}\int_\Omega p|\nabla(w)_-|^2$. In order to avoid imposing an analogous assumption on $R(y,p)$, we treat this term differently, using the estimate proven in Theorem 6.5.2. Applying Young's inequality with exponents 4 and 4/3, we have

$$
\mathcal{B} \leqslant \frac{\|\mathcal{R}\|_\infty}{4}\int_\Omega \frac{|\nabla p|^4}{p^{1-\alpha}}\,\mathrm{d}x + \frac{3}{4}\int_\Omega p^{1-\alpha}|\nabla(w)_-|^{4/3}\,\mathrm{d}x.
$$

Taking $\alpha = 1/(\gamma+2)$, we know by Theorem 6.5.2 that the first term is bounded. Let us denote $\beta = (\gamma-1)/3(\gamma+2)$. Then using Young's inequality with exponents 3/2 and 3 it is straightforward to see

$$
\frac{3}{4}\int_\Omega p^{1-\alpha}|\nabla(w)_-|^{4/3}\,\mathrm{d}x \leqslant \frac{1}{2}\int_\Omega p^{(1-\alpha-\beta)\frac{3}{2}}|\nabla(w)_-|^2\,\mathrm{d}x + \frac{1}{4}\int_\Omega p^{3\beta}\,\mathrm{d}x.
$$

Thanks to the choices of α and β, we have

$$\mathcal{B} \leqslant \frac{\|\mathcal{R}\|_\infty}{4}\int_\Omega \frac{|\nabla p|^4}{p^{1-\alpha}}\,\mathrm{d}x + \frac{1}{2}\int_\Omega p|\nabla(w)_-|^2\,\mathrm{d}x + \frac{1}{4}\int_\Omega p^{(\gamma-1)/(\gamma+2)}\,\mathrm{d}x \leqslant \frac{1}{2}\int_\Omega p|\nabla(w)_-|^2\,\mathrm{d}x + C. \tag{6.58}$$

Coming back to Eq. (6.56) and recalling that R_p is bounded and non-positive, we obtain

$$\begin{aligned}
\mathcal{C} \leqslant &\|\mathcal{R}_p\|_\infty \int_\Omega (w)_- \nabla p\cdot\nabla p\,\mathrm{d}x\\
= &-\|\mathcal{R}_p\|_\infty \int_\Omega p\nabla(w)_-\cdot\nabla p\,\mathrm{d}x - \|\mathcal{R}_p\|_\infty\int_\Omega (w)_- p\Delta p\,\mathrm{d}x\\
\leqslant &\frac{1}{2}\int_\Omega p|\nabla(w)_-|^2\,\mathrm{d}x + C\int_\Omega p|\nabla p|^2\,\mathrm{d}x + \|\mathcal{R}_p\|_\infty\int_\Omega p(w)_-^2\,\mathrm{d}x + \|\mathcal{R}_p\|_\infty\int_\Omega \mathcal{R}p(w)_-\,\mathrm{d}x\\
\leqslant &\frac{1}{2}\int_\Omega p|\nabla(w)_-|^2\,\mathrm{d}x + C.
\end{aligned} \tag{6.59}$$

Finally, combining Eq. (6.56), Eq. (6.57), Eq. (6.58) and Eq. (6.59) we find

$$\int_0^1\left(\int_\Omega R(\eta,p)\nabla\sigma\cdot\nabla p(w)_-\,\mathrm{d}x\right)\mathrm{d}\eta \leqslant C\int_\Omega (w)_-^2\,\mathrm{d}x + C\int_\Omega (w)_-\,\mathrm{d}x + \int_\Omega p|\nabla(w)_-|^2\,\mathrm{d}x + C.$$

We can finally come back to Eq. (6.55) to obtain

$$\begin{aligned}
&\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega (w)_-^2\,\mathrm{d}x + (\gamma-1)\int_\Omega p|\nabla(w)_-|^2\,\mathrm{d}x\\
&\qquad\leqslant C(\gamma,d)\int_\Omega (w)_-^3\,\mathrm{d}x + C\int_\Omega (w)_-^2\,\mathrm{d}x + C\int_\Omega (w)_-\,\mathrm{d}x + C.
\end{aligned} \tag{6.60}$$

with $C(\gamma,d) = \left(1-\frac{\gamma}{2}-\frac{2}{d}\right)$ being negative thanks to the assumption on γ. Since we are on a compact support, by Young's inequality we have

$$C\int_\Omega (w)_-\,\mathrm{d}x \leqslant \frac{C^2}{2}|\Omega| + \frac{1}{2}\int_\Omega (w)_-^2\,\mathrm{d}x.$$

Let us stress that this assumption can be removed and all the estimates can be proven in $\mathbb{R}^d$ by multiplying by a properly chosen test function, see [94] for the detailed proof in the two species case. Then we obtain

$$\frac{1}{2}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega (w)_-^2\,\mathrm{d}x \leqslant C\int_\Omega (w)_-^2\,\mathrm{d}x + C,$$

and hence by Gronwall's inequality, we have

$$\sup_{0\leqslant t\leqslant T}\int_\Omega (w(t))_-^2\,\mathrm{d}x \leqslant C\int_\Omega (w_0)_-^2\,\mathrm{d}x + C \leqslant C.$$

Finally, from Eq. (6.60) we also obtain

$$\iint_{\Omega_T} |\Delta p + \mathcal{R}|_-^3\,\mathrm{d}x\,\mathrm{d}t \leqslant C(T),$$

and this concludes the proof.

□

Proof of Corollary 6.5.1. Thanks to the Aronson-Bénilan estimate in L^2 proven above we have

$$\int_\Omega |\Delta p(t)|\,\mathrm{d}x = \int_\Omega \Delta p(t)\,\mathrm{d}x + 2\int_\Omega (\Delta p(t))_-\,\mathrm{d}x \leqslant C\left(\int_\Omega (\Delta p(t))_-^2\,\mathrm{d}x\right)^{1/2} \leqslant C$$

for all $t \in [0,T]$, and this completes the proof.

□

6.A Compensated compactness

Theorem 6.A.1. *Let $u_\gamma, w_\gamma \in L^\infty(0,T;L^2(\Omega))$, and let u_∞, w_∞ be the L^2-weak limits of u_γ, w_γ as $\gamma \to \infty$, respectively. We assume that*

$$\frac{\partial u_\gamma}{\partial t} \in L^2(0,T;H^{-1}(\Omega)), \qquad w_\gamma \in L^2(0,T;H^1(\Omega)).$$

Then, up a subsequence, we have

$$\iint_{\Omega_T} u_\gamma w_\gamma \varphi\,\mathrm{d}x\,\mathrm{d}t \xrightarrow{\gamma\to\infty} \iint_{\Omega_T} u_\infty w_\infty \varphi\,\mathrm{d}x\,\mathrm{d}t,$$

for all $\varphi \in C(0,T;C^1(\Omega))$.

Proof. Let $\psi_\varepsilon(x) := \frac{1}{\varepsilon^d}\psi(\frac{x}{\varepsilon})$ for $x \in \mathbb{R}^d$ and $\zeta_\sigma(t) := \frac{1}{\sigma}\zeta(t)$, for $t > 0$ be smooth mollifiers. Then, we compute

$$\begin{aligned}
\iint_{\Omega_T} u_\gamma w_\gamma \varphi\,\mathrm{d}x\,\mathrm{d}t &= \iint_{\Omega_T} u_\gamma (w_\gamma\varphi - (w_\gamma\varphi) \star_x \psi_\varepsilon)\,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} u_\gamma (w_\gamma\varphi) \star_x \psi_\varepsilon\,\mathrm{d}x\,\mathrm{d}t \\
&= \iint_{\Omega_T}\left(\int_{\mathbb{R}^d} (w_\gamma(x)\varphi(x) - w_\gamma(x-\varepsilon z)\varphi(x-\varepsilon z))\psi(z)\,\mathrm{d}z\right) u_\gamma\,\mathrm{d}x\,\mathrm{d}t \\
&\quad + \iint_{\Omega_T} (u_\gamma - u_\gamma \star_t \zeta_\sigma)(w_\gamma\varphi) \star_x \psi_\varepsilon\,\mathrm{d}x\,\mathrm{d}t + \iint_{\Omega_T} (u_\gamma \star_t \zeta_\sigma)(w_\gamma\varphi) \star_x \psi_\varepsilon\,\mathrm{d}x\,\mathrm{d}t.
\end{aligned}$$

As $\gamma \to \infty$, we have

$$\iint_{\Omega_T} (u_\gamma \star_t \zeta_\sigma)(w_\gamma\varphi) \star_x \psi_\varepsilon\,\mathrm{d}x\,\mathrm{d}t \to \iint_{\Omega_T} u_\infty w_\infty \varphi\,\mathrm{d}x\,\mathrm{d}t.$$

It now remains to prove that the other terms converge to zero as $\varepsilon \to 0$ and $\sigma \to 0$. By the Fréchet-Kolmogorov theorem, we know that

$$\begin{aligned}
&\int_\Omega |(w_\gamma\varphi)(x) - (w_\gamma\varphi)(x+k)|^2\,\mathrm{d}x \\
&\qquad \leqslant \int_\Omega |w_\gamma(x)(\varphi(x) - \varphi(x+k))|^2\,\mathrm{d}x + \int_\Omega |\varphi(x+k)(w_\gamma(x) - w_\gamma(x+k)|^2\,\mathrm{d}x \\
&\qquad \leqslant \omega(|k|),
\end{aligned}$$

where $\omega(|k|) \to 0$ as $k \to 0$. Hence

$$\iint_{\Omega_T} \left(\int_{\mathbb{R}^d} (w_\gamma(x)\varphi(x) - w_\gamma(x - \varepsilon z)\varphi(x - \varepsilon z))\psi(z)\,\mathrm{d}z \right) u_\gamma(x,t)\,\mathrm{d}x\,\mathrm{d}t$$
$$= \int_0^T \int_{\mathbb{R}^d} \left(\int_\Omega (w_\gamma(x)\varphi(x) - w_\gamma(x - \varepsilon z)\varphi(x - \varepsilon z))u_\gamma(x,t)\,\mathrm{d}x \right) \psi(z)\,\mathrm{d}z\,\mathrm{d}t$$
$$\leqslant \int_0^T \int_{\mathbb{R}^d} (\omega(\varepsilon|z|))^{1/2} \|u_\gamma(t)\|_{L^2(\Omega)} \psi(z)\,\mathrm{d}z\,\mathrm{d}t \to 0.$$

Now we treat the last term. For the sake of brevity, let us denote $(w_\gamma\varphi)_\varepsilon := (w_\gamma\varphi) \star_x \psi_\varepsilon$

$$\begin{aligned}
\iint_{\Omega_T} (u_\gamma - u_\gamma \star_t \zeta_\sigma)(w\varphi)_\varepsilon\,\mathrm{d}x\,\mathrm{d}t &= \iint_{\Omega_T} \left(\int_{\mathbb{R}} (u_\gamma(t) - u_\gamma(t - \sigma s))\zeta(s)\,\mathrm{d}s \right) (w_\gamma\varphi)_\varepsilon\,\mathrm{d}x\,\mathrm{d}t \\
&= \iint_{\Omega_T} \left[\int_{\mathbb{R}} \left(\int_{t-\sigma s}^t \frac{\partial u_\gamma(\tau)}{\partial t}\,\mathrm{d}\tau \right) \right] (w_\gamma\varphi)_\varepsilon\,\mathrm{d}x\,\mathrm{d}t \\
&= \int_{\mathbb{R}} \zeta(s) \left(\int_0^T \int_{t-\sigma s}^t \int_\Omega \frac{\partial u_\gamma(\tau)}{\partial t} (w_\gamma\varphi)_\varepsilon\,\mathrm{d}x\,\mathrm{d}\tau\,\mathrm{d}t \right) \mathrm{d}s \\
&\leqslant \int_{\mathbb{R}} \zeta(s) \int_0^T \left(\int_{t-\sigma s}^t \left\| \frac{\partial u_\gamma(\tau)}{\partial t} \right\|_{H^{-1}(\Omega)} \mathrm{d}\tau \right) \|(w_\gamma\varphi)_\varepsilon\|_{H^1(\Omega)}\,\mathrm{d}t\,\mathrm{d}s \\
&\leqslant C\sigma \int_{\mathbb{R}} \zeta(s)|s| \int_0^T \|(w_\gamma\varphi)_\varepsilon\|_{H^1(\Omega)}\,\mathrm{d}t\,\mathrm{d}s \leqslant C\sigma \to 0,
\end{aligned}$$

as $\sigma \to 0$.

□

6.B Convergence of the reaction terms

Now we prove that (6.16) and (6.17) hold. By the Stone-Weierstrass theorem we know that, for any $\delta > 0$, there exists $N > 0$ and $\{a_i\}_{i=1}^N$ and $\{G_i\}_{i=1}^N$ such that

$$\left\| R(y, p_\varepsilon) - \sum_{i=1}^N a_i(y) G_i(p_\varepsilon) \right\|_{L^\infty} \leqslant \delta. \tag{6.61}$$

Let $\varphi \in L^1(Q_T)$, such that $\|\varphi\|_{L^1} = 1$. Since $\sigma_\varepsilon \rightharpoonup \sigma$ weakly* in $L^\infty((0,1) \times Q_T)$ and $p_\varepsilon \to p$ strongly in $L^2(Q_T)$ as $\varepsilon \to 0$, we have

$$\begin{aligned}
\iint_{Q_T} \left(\sum_{i=1}^N \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon)\,\mathrm{d}\eta \right) \varphi(x,t)\,\mathrm{d}x\,\mathrm{d}t &= \sum_{i=1}^N \int_0^1 \iint_{Q_T} \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon) \varphi(x,t)\,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}\eta \\
&\xrightharpoonup{\varepsilon \to 0} \sum_{i=1}^N \int_0^1 \iint_{Q_T} \sigma(\eta) a_i(\eta) G_i(p) \varphi(x,t)\,\mathrm{d}x\,\mathrm{d}t\,\mathrm{d}\eta.
\end{aligned}$$

Therefore, there exists ε_0 such that for all $\varepsilon < \varepsilon_0$

$$\iint_{Q_T} \left(\sum_{i=1}^{N} \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon)\, \mathrm{d}\eta - \sum_{i=1}^{N} \int_0^1 \sigma(\eta) a_i(\eta) G_i(p)\, \mathrm{d}\eta \right) \varphi \, \mathrm{d}x \, \mathrm{d}t \leqslant \delta. \tag{6.62}$$

We compute

$$\begin{aligned}
&\iint_{Q_T} \left(\int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon)\, \mathrm{d}\eta - \int_0^1 \sigma(\eta) R(\eta, p)\, \mathrm{d}\eta \right) \varphi(x,t) \, \mathrm{d}x \, \mathrm{d}t \\
\leqslant &\left\| \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon)\, \mathrm{d}\eta - \sum_{i=1}^{N} \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon)\, \mathrm{d}\eta \right\|_{L^\infty} \|\varphi\|_{L^1} \\
&+ \iint_{Q_T} \left(\sum_{i=1}^{N} \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon)\, \mathrm{d}\eta - \sum_{i=1}^{N} \int_0^1 \sigma(\eta) a_i(\eta) G_i(p)\, \mathrm{d}\eta \right) \varphi \, \mathrm{d}x \, \mathrm{d}t \\
&+ \left\| \sum_{i=1}^{N} \int_0^1 \sigma(\eta) a_i(\eta) G_i(p)\, \mathrm{d}\eta - \int_0^1 \sigma(\eta) R(\eta, p)\, \mathrm{d}\eta \right\|_{L^\infty} \|\varphi\|_{L^1} \leqslant 3\delta,
\end{aligned}$$

for $\varepsilon \leqslant \varepsilon_0$. Since δ was chosen arbitrarily, we conclude that

$$\mathcal{R}_\varepsilon := \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon)\, \mathrm{d}\eta \rightharpoonup \int_0^1 \sigma(\eta) R(\eta, p)\, \mathrm{d}\eta := \mathcal{R}, \qquad \text{weakly}^* \text{ in } L^\infty(Q_T).$$

i.e. (6.16) is proven. By an analogous argument, we have

$$n_\varepsilon R(y, p_\varepsilon) \rightharpoonup n R(y,p), \qquad \text{weakly}^* \text{ in } L^\infty((0,1) \times Q_T),$$

and this concludes the proof of (6.17).

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Incompressible limit and well-posedness of PDE models of tissue growth

Abstract

Both compressible and incompressible porous medium models have been used in the literature to describe the mechanical aspects of living tissues, and in particular of tumor growth. Using a stiff pressure law, it is possible to build a link between these two different representations. In the incompressible limit, compressible models generate free boundary problems of Hele-Shaw type where saturation holds in the moving domain. Our work aims at investigating the stiff pressure limit of reaction-advection-porous medium equations motivated by tumor development. Our first study concerns the analysis and numerical simulation of a model including the effect of nutrients. Then, a coupled system of equations describes the cell density and the nutrient concentration. For this reason, the derivation of the pressure equation in the stiff limit was an open problem for which the strong compactness of the pressure gradient is needed. To establish it, we use two new ideas: an L^3-version of the celebrated Aronson-Bénilan estimate, also recently applied to related problems, and a sharp uniform L^4-bound on the pressure gradient. We further investigate the sharpness of this bound through a finite difference upwind scheme, which we prove to be stable and asymptotic preserving. Our second study is centered around porous medium equations including convective effects. We are able to extend the techniques developed for the nutrient case, hence finding the complementarity relation on the limit pressure. Moreover, we provide an estimate of the convergence rate at the incompressible limit. Finally, we study a multi-species system. In particular, we account for phenotypic heterogeneity, including a structured variable into the problem. In this case, a cross-(degenerate)-diffusion system describes the evolution of the phenotypic distributions. Adapting methods recently developed in the context of two-species systems, we prove existence of weak solutions and we pass to the incompressible limit. Furthermore, we prove new regularity results on the total pressure, which is related to the total density by a power law of state.

Keywords: porous medium equation, tumor growth, Aronson-Bénilan estimate, free boundary, Hele-Shaw problem

Résumé

Les modèles de milieux poreux, en régime compressible ou incompressible, sont utilisés dans la littérature pour décrire les propriétés mécaniques des tissus vivants et en particulier de la croissance tumorale. Il est possible de construire un lien entre ces deux différentes représentations en utilisant une loi de pression raide. Dans la limite incompressible, les modèles compressibles conduisent à des problèmes de frontières libres de type Hele-Shaw. Nos travaux visent à étudier la limite de pression raide des équations de type milieu poreux motivées par le développement tumoral. Notre première étude concerne l'analyse et la simulation numérique d'un modèle incluant l'effet des nutriments. Ensuite, un système d'équations, dont le couplage est délicat, décrit la densité cellulaire et la concentration en nutriments. Pour cette raison, la dérivation de l'équation de pression dans la limite incompressible était un problème ouvert qui nécessite la compacité forte du gradient de pression. Pour l'établir, nous utilisons deux nouvelles idées : une version L^3 de la célèbre estimation d'Aronson-Bénilan, également utilisée récemment pour des problèmes connexes, et une estimation L^4 sur le gradient de pression (où l'exposant 4 est optimal). Nous étudions en outre l'optimalité de cette estimation par un schéma numérique upwind aux différences finies, que nous montrons être stable et *asymptotic preserving*. Notre deuxième étude est centrée sur l'équation de milieux poreux avec effets convectifs. Nous étendons les techniques développées pour le cas avec nutriments, trouvant ainsi la relation de complémentarité sur la pression limite. De plus, nous fournissons une estimation du taux de convergence à la limite incompressible. Enfin, nous étudions un système multi-espèces. En particulier, en tenant compte de l'hétérogénéité phénotypique, nous incluons une variable structurée dans le problème. Par conséquent, un système de diffusion croisée et dégénérée décrit l'évolution des distributions phénotypiques. En adaptant des méthodes récemment développées pour des systèmes à deux équations, nous prouvons l'existence de solutions faibles et nous passons à la limite incompressible. En outre, nous prouvons de nouveaux résultats de régularité sur la pression totale, qui est liée à la densité totale par une loi de puissance.

Mots clés : équation des milieux poreux, croissance tumorale, estimation d'Aronson-Bénilan, frontière libre, problème de Hele-Shaw

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