



HAL
open science

Phenotypic heterogeneity in a model of tumor growth: existence of solutions and incompressible limit

Noemi David

► **To cite this version:**

Noemi David. Phenotypic heterogeneity in a model of tumor growth: existence of solutions and incompressible limit. 2022. hal-03636939v1

HAL Id: hal-03636939

<https://hal.science/hal-03636939v1>

Preprint submitted on 11 Apr 2022 (v1), last revised 31 Mar 2023 (v2)

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Phenotypic heterogeneity in a model of tumor growth: existence of solutions and incompressible limit

Noemi David^{*†}

April 11, 2022

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 recover 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.

2010 *Mathematics Subject Classification.* 35B45; 35K57; 35K65; 35Q92; 76N10; 76T99;
Keywords and phrases. Structured model, porous medium, incompressible limit, free boundary, Aronson-Bénilan estimate, tumor growth

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

$$p(x, t) = (\varrho(x, t))^\gamma, \quad \gamma > 1. \quad (1)$$

The model is the following

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

^{*}Sorbonne Université, Inria, CNRS, Laboratoire Jacques-Louis Lions UMR7598, Paris, France, email: noemi.david@sorbonne-universite.fr

[†]Dipartimento di Matematica, Università di Bologna, Italy.

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

$$\partial_t \varrho - \frac{\gamma}{\gamma + 1} \Delta \varrho^{\gamma+1} = \varrho \mathcal{R}, \quad \mathcal{R} = \int_0^1 \sigma(y) R(y, p) dy, \quad (3)$$

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, [7], as well as divergence terms with respect to the phenotypic state to account for mutations, see for instance [6]. 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 [6], the acceleration of invasion fronts has been further studied in [8, 10] in the case of unbounded mobility, see also [2–4] and references therein for applications of structured PDEs models to tumor growth.

In [28], 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 [19–22], 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 [28], 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. (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.(3). Indeed, the invasion of cancer cells can be seen as the motion of a fluid through a porous medium (the extra-cellular matrix) [12].

The power law was first adopted for one-species models of tumor growth, see for instance [30, 32] and references therein. Furthermore, this pressure law is of particular interest since

passing to the limit $\gamma \rightarrow \infty$, 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.* [30]. For an overview on the single-species case, we refer the reader to [1, 14–16, 18, 23, 26, 30, 31] and references therein.

Multi-species extensions. Lately, multi-phase extensions of the model introduced in [30] 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 [13]. Their result, which was achieved in one spatial dimension, was later extended in 2019 by Gwiazda *et al.* in multiple dimensions [24]. Here, the authors consider a two-species system which is the analogous of our model, *i.e.* Eq. (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 [5] for the classical result. The same problem was then approached in [33], 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 [33] the authors recover the strong convergence of $\nabla(n_1 + n_2)^{\gamma+1}$ without using the Aronson-Bénilan estimate of [24], 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, [9], where the authors use an approach based on a L^2 -Aronson-Bénilan estimate in the spirit of [24]. 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 [27], where the authors consider a cross-reaction-diffusion system in a bounded domain with Neumann boundary conditions. Rather than dealing with the pressure, $p_\gamma = \rho_\gamma^\gamma$, the authors focus on the quantity $\rho_\gamma^{\gamma+1}$, 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 an 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 [16, 17, 25].

Our contribution. In this paper, we aim to study the existence and regularity of solutions to System (2) and their incompressible limit. This problem can be seen as an infinitely-many-species extension of the models studied in [24, 27, 33]. At first, we extend the method by [33] to the structured case. Adapting the same argument, we are able to prove the existence of global

weak solutions, *cf.* Theorem 3.7.

The second main result of the paper, *cf.* Theorem 4.1 and Theorem 4.2, concerns the incompressible limit of System (2). As $\gamma \rightarrow \infty$ 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 [27], 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 [27], 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 5.2, which has been introduced in the context of one-species porous medium models, see for instance [15, 16, 29], 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 5.4. Moreover, we are able to recover it removing the technical assumption on the reaction terms required in [24] 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 3 is devoted to the proof of the existence of weak solutions: in Section 3.1 we introduce the regularised problem, obtained performing a viscosity perturbation, and we infer uniform a priori estimates, while in Section 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 4, we study the asymptotics of Problem (2) as $\gamma \rightarrow \infty$. The additional regularity estimates are deduced in Section 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 $n(t) := n(y, x, t)$, $n(y) := n(y, x, t)$, $\varrho(t) := \varrho(x, t)$. Given a function f , we denote

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

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

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

2 Assumptions and main results

Now let us state the main results, *i.e.* the existence of weak solutions to System (2), the incompressible limit and the additional regularity estimates, and for each of them the related assumptions.

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

$$\partial_p R(\cdot, \cdot) \leq 0, \quad R(\cdot, 0) > 0, \quad R(\cdot, p_M) \leq 0, \quad (4)$$

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 $0 < \varepsilon \leq \varepsilon_0$ the following holds

$$0 \leq \varrho_{0,\varepsilon_0} \leq (p_M)^{1/\gamma} \text{ a.e. in } \mathbb{R}^d, \quad \left\| \sup_{y \in [0,1]} \frac{n_{0,\varepsilon}(y)}{\varrho_{0,\varepsilon}} \right\|_{L^\infty(\mathbb{R}^d)} \leq C. \quad (5)$$

To show the existence of weak solutions, we extend the method developed in [33] to the structured case and we prove the following result.

Theorem 2.1 (Theorem 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 (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 $\varphi \in C([0, 1]; C^1_{comp}([0, T] \times \mathbb{R}^d))$*

$$\begin{aligned} & - \int_0^1 \int_{\mathbb{R}^d} n(y, x, t) \frac{\partial \varphi(y, x, t)}{\partial t} dx dy + \int_0^1 \int_0^T \int_{\mathbb{R}^d} n(y, x, t) \nabla p(x, t) \cdot \nabla \varphi(y, x, t) dx dt dy \\ & = \int_0^1 \int_0^T \int_{\mathbb{R}^d} n(y, x, t) R(y, p(x, t)) \varphi(y, x, t) dx dt dy + \int_0^1 \int_{\mathbb{R}^d} n_0(y, x) \varphi(y, x, 0) dx dy, \end{aligned}$$

with

$$\varrho(x, t) = \int_0^1 n(y, x, t) dy, \text{ and } p(x, t) = (\varrho(x, t))^\gamma.$$

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 [27] to our problem, namely focusing on the quantity $v_\gamma = \varrho_\gamma^{\gamma+1}$.

Unlike [27], 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 [27] 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

$$\text{supp}(n_{\gamma,0}(y)) \subset \Omega_0, \text{ for a.e. } y \in [0, 1], \forall \gamma > 1.$$

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

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

Moreover, we assume there exists $\varrho_0, p_0 \in L^{\infty}_+(\Omega)$ such that

$$\|\varrho_{\gamma,0} - \varrho_0\|_{L^1(\Omega)} \rightarrow 0 \quad \|p_{\gamma,0} - p_0\|_{L^1(\Omega)} \rightarrow 0$$

and

$$0 \leq \varrho_{\gamma,0} \leq (p_M)^\gamma, \quad 0 \leq p_{\gamma,0} \leq p_M.$$

Let us denote $v_\gamma = \varrho_\gamma^{\gamma+1}$. We can rewrite Eq. (3) as follows

$$\frac{\partial \varrho_\gamma}{\partial t} - \frac{\gamma}{\gamma+1} \Delta v_\gamma = \int_0^1 n_\gamma R(y, p_\gamma) dy. \quad (6)$$

We can pass to the incompressible limit $\gamma \rightarrow \infty$ and recover a Hele-Shaw problem, as stated in the following theorems.

Theorem 2.2 (Theorem 4.1). *Let $(n_\gamma, \varrho_\gamma, p_\gamma)$ be a solution given by Theorem 3.7. For all $T > 0$, up to the extraction of a subsequence we have*

$$\begin{aligned} n_\gamma(y, x, t) &\rightharpoonup n_\infty(y, x, t) && \text{weakly* in } L^\infty((0, 1) \times \Omega_T), \\ \varrho_\gamma(x, t) &\rightharpoonup \varrho_\infty(x, t) && \text{weakly* in } L^\infty(\Omega_T), \\ p_\gamma(x, t) &\rightharpoonup p_\infty(x, t) && \text{weakly* in } L^\infty(\Omega_T), \\ \nabla v_\gamma &\rightharpoonup \nabla v_\infty && \text{weakly in } L^2(\Omega_T), \end{aligned}$$

as $\gamma \rightarrow \infty$. Moreover, the limit satisfies the following relation

$$p_\infty(1 - \varrho_\infty) = 0 \quad \text{almost everywhere in } \Omega_T, \quad (7)$$

as well as

$$\frac{\partial \varrho_\infty}{\partial t} = \Delta v_\infty + \int_0^1 n_\infty R(y, p_\infty) dy, \quad \text{in } \mathcal{D}'(\mathbb{R}^d \times (0, \infty)).$$

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 4.8.

Theorem 2.3 (Theorem 4.2). *The limit solution ϱ_∞, p_∞ satisfies*

$$\begin{aligned} \frac{\partial n_\infty}{\partial t} &= \nabla \cdot (n_\infty \nabla p_\infty) + n_\infty R(y, p_\infty), && \text{in } \mathcal{D}'((0, 1) \times \mathbb{R}^d \times (0, \infty)), \\ p_\infty \left(\Delta p_\infty + \int_0^1 n_\infty R(y, p_\infty) dy \right) &= 0, && \text{in } \mathcal{D}'(\mathbb{R}^d \times (0, \infty)). \end{aligned} \quad (8)$$

Relation (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* (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.

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 [11, 24]. Here, we not only extend it to our structured problem, but we are able to remove the constraint on the reaction term used in [24]. 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 [29].

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)

$$\nabla p_{\gamma,0} \in L^2(\Omega), \quad (\Delta p_{\gamma,0})_- \in L^2(\Omega).$$

Moreover, we assume

$$\gamma > \max\left(\frac{3}{2}, 2 - \frac{4}{d}\right).$$

Theorem 2.4 (Theorem 5.2). *There exists a positive constant $C(T)$ such that for any $0 \leq \alpha < \frac{1}{\gamma}$ the following estimate holds true*

$$\kappa(\alpha) \int_0^T \int_{\Omega} \frac{|\nabla p|^4}{p^{1-\alpha}} dx dt \leq C(T),$$

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

Theorem 2.5 (Theorem 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*

$$\int_{\Omega} (\Delta p(t))_-^2 dx \leq C(T), \quad \int_0^T \int_{\Omega} (\Delta p)_-^3 dx dt \leq C(T).$$

3 Existence of solutions

3.1 Regularised problem

In order to prove the existence of weak solutions of Problem (2), we regularise the system introducing a viscosity term. Let $0 < \varepsilon < \varepsilon_0$, and consider the following uniformly parabolic system

$$\begin{cases} \frac{\partial n_{\varepsilon}}{\partial t} - \nabla \cdot (n_{\varepsilon} \nabla p_{\varepsilon}) - \varepsilon \Delta n_{\varepsilon} = n_{\varepsilon} R(y, p_{\varepsilon}), & y \in [0, 1], \quad (x, t) \in \Omega_T, \\ \varrho_{\varepsilon}(x, t) = \int_0^1 n_{\varepsilon}(y, x, t) dy. \end{cases} \quad (9)$$

The equation on ϱ_{ε} reads

$$\frac{\partial \varrho_{\varepsilon}}{\partial t} - \frac{\gamma}{\gamma + 1} \Delta \varrho_{\varepsilon}^{\gamma+1} - \varepsilon \Delta \varrho_{\varepsilon} = \int_0^1 n_{\varepsilon} R(y, p_{\varepsilon}) dy. \quad (10)$$

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. (9) by $\text{sign}_-(n_\varepsilon)$ we obtain

$$\frac{\partial}{\partial t}(n_\varepsilon)_- - \nabla \cdot ((n_\varepsilon)_- \nabla p_\varepsilon) - \varepsilon \Delta(n_\varepsilon)_- \leq (n_\varepsilon)_- \|R\|_\infty,$$

where we denote $\|R\|_\infty = \sup_{y \in [0,1]} R(y, 0)$. Integrating in space, we have

$$\frac{d}{dt} \int_{\mathbb{R}^d} (n_\varepsilon)_- dx - \int_{\mathbb{R}^d} \nabla \cdot ((n_\varepsilon)_- \nabla p_\varepsilon) dx - \varepsilon \int_{\mathbb{R}^d} \Delta(n_\varepsilon)_- dx \leq \|R\|_\infty \int_{\mathbb{R}^d} (n_\varepsilon)_- dx,$$

By Gronwall's lemma we infer

$$\int_0^1 \int_{\mathbb{R}^d} (n_\varepsilon(y, x, t))_- dx dy \leq e^{\|R\|_\infty t} \int_0^1 \int_{\mathbb{R}^d} (n_\varepsilon(y, x, 0))_- dx dy,$$

which implies that almost everywhere $n_\varepsilon(t) \geq 0$ 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

$$\frac{\partial \underline{\varrho}}{\partial t} = \frac{\gamma}{\gamma + 1} \Delta \underline{\varrho}^{\gamma+1} + \varepsilon \Delta \underline{\varrho} - \underline{\varrho} \|R\|_\infty.$$

In fact, we have

$$\begin{aligned} \frac{\gamma}{\gamma + 1} \Delta \underline{\varrho}^{\gamma+1} + \varepsilon \Delta \underline{\varrho} - \underline{\varrho} \|R\|_\infty &= 2\gamma \underline{\varrho}^{\gamma+1} (2(\gamma + 1)|x|^2 - 1) + 2\varepsilon (2|x|^2 - 1) \underline{\varrho} - \underline{\varrho} \|R\|_\infty \\ &\geq -2\varepsilon \underline{\varrho} - 2\gamma \underline{\varrho}^{\gamma+1} - \underline{\varrho} \|R\|_\infty \\ &\geq (-2\varepsilon - 2\gamma - \|R\|_\infty) \underline{\varrho} \\ &= -K \underline{\varrho} \\ &= \frac{\partial \underline{\varrho}}{\partial t}. \end{aligned}$$

Therefore, since by (10) ϱ_ε is a supersolution to the same equation and $\varrho_\varepsilon(0) \geq \underline{\varrho}(0)$, by the comparison principle we have

$$\varrho_\varepsilon(t) \geq \underline{\varrho}(t) > 0, \quad \forall t \in [0, T].$$

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

$$\frac{\partial \sigma_\varepsilon}{\partial t} = \nabla \sigma_\varepsilon \cdot \nabla p_\varepsilon + \sigma_\varepsilon R(y, p_\varepsilon) - \sigma_\varepsilon \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta, \quad (11)$$

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

$$\mathcal{R}_\varepsilon := \mathcal{R}(\sigma_\varepsilon, p_\varepsilon) = \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta. \quad (12)$$

Let us notice that, from (12), \mathcal{R}_ε is also uniformly bounded in $L^\infty(Q_T)$ and

$$\|\mathcal{R}_\varepsilon\|_{L^\infty(Q_T)} \leq \sup_{y \in [0,1]} |R(y, 0)| \int_0^1 \sigma_\varepsilon(\eta) d\eta = \|R\|_\infty.$$

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 (10) by $\text{sign}(\varrho_\varepsilon)$ and integrating in space we obtain

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}^d} |\varrho_\varepsilon| dx &\leq \int_{\mathbb{R}^d} \Delta |\varrho_\varepsilon|^{\gamma+1} dx + \varepsilon \int_{\mathbb{R}^d} \Delta |\varrho_\varepsilon| dx + \int_{\mathbb{R}^d} \int_0^1 \text{sign}(\varrho_\varepsilon) n_\varepsilon R(y, p_\varepsilon) dy dx \\ &\leq \|R\|_\infty \int_{\mathbb{R}^d} |\varrho_\varepsilon| dx. \end{aligned}$$

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 $\mathcal{R}_M = \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_M) d\eta$, which is negative by the definition of p_M . From Eq. (10) we have

$$\frac{\partial}{\partial t} (\varrho_\varepsilon - \varrho_M) - \frac{\gamma}{\gamma+1} \Delta (\varrho_\varepsilon^{\gamma+1} - \varrho_M^{\gamma+1}) - \varepsilon \Delta (\varrho_\varepsilon - \varrho_M) \leq (\varrho_\varepsilon - \varrho_M) \mathcal{R}_\varepsilon + \varrho_M (\mathcal{R}_\varepsilon - \mathcal{R}_M).$$

Multiplying by $\text{sign}_+(\varrho_\varepsilon - \varrho_M)$ we obtain

$$\begin{aligned} \frac{\partial}{\partial t} (\varrho_\varepsilon - \varrho_M)_+ - \frac{\gamma}{\gamma+1} \Delta (\varrho_\varepsilon^{\gamma+1} - \varrho_M^{\gamma+1})_+ - \varepsilon \Delta (\varrho_\varepsilon - \varrho_M)_+ \\ \leq (\varrho_\varepsilon - \varrho_M)_+ \mathcal{R}_\varepsilon + \varrho_M (\mathcal{R}_\varepsilon - \mathcal{R}_M) \text{sign}_+(\varrho_\varepsilon - \varrho_M) \\ \leq \|\mathcal{R}_\varepsilon\|_\infty (\varrho_\varepsilon - \varrho_M)_+, \end{aligned}$$

where in the last inequality we used $\partial_p R \leq 0$. Integrating over \mathbb{R}^d and applying Gronwall's lemma we obtain

$$\frac{d}{dt} \int_{\mathbb{R}^d} (\varrho_\varepsilon - \varrho_M)_+ dx \leq e^{\|\mathcal{R}\|_\infty t} \int_{\mathbb{R}^d} (\varrho_{0,\varepsilon} - \varrho_M)_+ dx.$$

For all $0 < \varepsilon \leq \varepsilon_0$, thanks to Assumption (5), we finally have

$$0 \leq \varrho_\varepsilon \leq \varrho_M, \quad 0 \leq p_\varepsilon \leq p_M. \quad (13)$$

Let us consider the equation on the fraction density, Eq. (11). By the assumptions on the reaction term, σ_ε satisfies

$$\frac{\partial \sigma_\varepsilon}{\partial t} \leq \nabla \sigma_\varepsilon \cdot \nabla p_\varepsilon + \sigma_\varepsilon 2\|R_\varepsilon\|_\infty.$$

Hence, by the comparison principle we obtain

$$\sigma_\varepsilon \leq e^{2\|R_\varepsilon\|_\infty t} \sigma_{0,\varepsilon}.$$

Since by Assumption (5) $\sigma_{0,\varepsilon}$ is uniformly bounded in $[0, 1] \times \mathbb{R}^d$, we have

$$\sigma_\varepsilon \in L^\infty([0, 1] \times Q_T), \quad (14)$$

and by consequence

$$n_\varepsilon \in L^\infty([0, 1] \times Q_T). \quad (15)$$

3.3 Passing to the limit $\varepsilon \rightarrow 0$

Extending the method by Price and Xu [33], in this section we prove the existence of solutions to Problem (2), by showing the convergence of the solution of the regularised problem as $\varepsilon \rightarrow 0$. 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 [24], this strategy focuses on the quantity $\varrho_\varepsilon^{\gamma+1}$ rather than on the pressure $p_\varepsilon = \varrho_\varepsilon^\gamma$.

Lemma 3.1. *There exists a positive constant $C(T)$ independent of ε such that the following holds*

$$\iint_{Q_T} \left| \nabla \varrho_\varepsilon^{\frac{\gamma+1}{2}} \right|^2 dx dt + \varepsilon \iint_{Q_T} \int_0^1 |\nabla \sqrt{n_\varepsilon}(y)|^2 dy dx dt \leq C(T).$$

Proof. Let ν be a positive constant. We multiply Eq. (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

$$\begin{aligned} \frac{d}{dt} \int_{\mathbb{R}^d} \int_0^1 ((n_\varepsilon + \nu) \ln(n_\varepsilon + \nu) - n_\varepsilon) dy dx + \int_{\mathbb{R}^d} \int_0^1 \frac{n_\varepsilon}{n_\varepsilon + \nu} \nabla p_\varepsilon \cdot \nabla n_\varepsilon dy dx + \varepsilon \int_{\mathbb{R}^d} \int_0^1 \frac{|\nabla n_\varepsilon|^2}{n_\varepsilon + \nu} dy dx \\ = \int_{\mathbb{R}^d} \int_0^1 n_\varepsilon R(y, p_\varepsilon) \ln(n_\varepsilon + \nu) dy dx \\ \leq \|R\|_\infty \int_{\mathbb{R}^d} \int_0^1 n_\varepsilon \ln(n_\varepsilon + \nu) dy dx. \end{aligned}$$

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 $t \leq T$. Upon integration in time for $\tau \in [0, t]$, we obtain

$$\begin{aligned} \int_0^t \int_{\mathbb{R}^d} \nabla p_\varepsilon \cdot \left(\int_0^1 \frac{n_\varepsilon}{n_\varepsilon + \nu} \nabla n_\varepsilon dy \right) dx d\tau + \varepsilon \int_0^t \int_{\mathbb{R}^d} \int_0^1 \frac{|\nabla n_\varepsilon|^2}{n_\varepsilon + \nu} dy dx d\tau \\ \leq \int_{\mathbb{R}^d} \int_0^1 (n_\varepsilon(t) - (n_\varepsilon(t) + \nu) \ln(n_\varepsilon(t) + \nu)) dy dx + \int_{\mathbb{R}^d} \int_0^1 (n_{0,\varepsilon} + \nu) \ln(n_{0,\varepsilon} + \nu) dy dx + C(T), \end{aligned}$$

Letting $\nu \rightarrow 0$, thanks to the L^∞ -bound of n_ε , we have

$$\int_0^t \int_{\mathbb{R}^d} \nabla \varrho_\varepsilon^\gamma \cdot \nabla \varrho_\varepsilon dx d\tau + 4\varepsilon \int_0^t \int_{\mathbb{R}^d} \int_0^1 |\nabla \sqrt{n_\varepsilon}|^2 dy dx d\tau \leq C(T),$$

for all $0 \leq t \leq T$, and this concludes the proof. \square

Lemma 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 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.

$$\begin{aligned}
\frac{\partial}{\partial t} \varrho_\varepsilon^{\frac{\gamma+1}{2}} &= \frac{\gamma+1}{2} \varrho_\varepsilon^{\frac{\gamma-1}{2}} \left(\nabla \cdot (\varrho_\varepsilon \nabla p_\varepsilon) + \varepsilon \Delta \varrho_\varepsilon + \int_0^1 n_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta \right) \\
&= \frac{\gamma+1}{2} \varrho_\varepsilon^{\frac{\gamma-1}{2}} \nabla \cdot (\varrho_\varepsilon \nabla \varrho_\varepsilon^\gamma) + \frac{\gamma+1}{2} \varepsilon \varrho_\varepsilon^{\frac{\gamma-1}{2}} \Delta \varrho_\varepsilon + \frac{\gamma+1}{2} \varrho_\varepsilon^{\frac{\gamma-1}{2}} \int_0^1 n_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta \\
&= \frac{\gamma+1}{2} \nabla \cdot \left(\varrho_\varepsilon^{\frac{\gamma+1}{2}} \nabla \varrho_\varepsilon^\gamma \right) - \frac{\gamma^2-1}{4} \varrho_\varepsilon^{\frac{\gamma-1}{2}} \nabla \varrho_\varepsilon \cdot \nabla \varrho_\varepsilon^\gamma + \frac{\gamma+1}{2} \varepsilon \nabla \cdot \left(\varrho_\varepsilon^{\frac{\gamma-1}{2}} \nabla \varrho_\varepsilon \right) \\
&\quad - \frac{\gamma^2-1}{4} \varepsilon \varrho_\varepsilon^{\frac{\gamma-3}{2}} |\nabla \varrho_\varepsilon|^2 + \frac{\gamma+1}{2} \varrho_\varepsilon^{\frac{\gamma-1}{2}} \int_0^1 n_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta \\
&= \gamma \nabla \cdot \left(\varrho_\varepsilon^\gamma \nabla \varrho_\varepsilon^{\frac{\gamma+1}{2}} \right) - \gamma \frac{\gamma-1}{\gamma+1} \varrho_\varepsilon^{\frac{\gamma-1}{2}} \left| \nabla \varrho_\varepsilon^{\frac{\gamma+1}{2}} \right|^2 + \varepsilon \Delta \varrho_\varepsilon^{\frac{\gamma+1}{2}} \\
&\quad - \varepsilon (\gamma^2-1) \varrho_\varepsilon^{\frac{\gamma-1}{2}} |\nabla \sqrt{\varrho_\varepsilon}|^2 + \frac{\gamma+1}{2} \varrho_\varepsilon^{\frac{\gamma-1}{2}} \int_0^1 n_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta.
\end{aligned}$$

Let us notice that Lemma 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 $L^2(Q_T)$. \square

Remark 3.3. The sequence ϱ_ε is precompact in any L^q -space, for $1 \leq q < \infty$. 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 3.4. Let us recall the results already proven. Up to a subsequence, we have

$$\begin{aligned}
\sigma_\varepsilon &\rightharpoonup \sigma && \text{weak}^* \text{ in } L^\infty([0, 1] \times Q_T), \\
n_\varepsilon &\rightharpoonup n && \text{weak}^* \text{ in } L^\infty([0, 1] \times Q_T), \\
\varrho_\varepsilon &\rightarrow \varrho && \text{strongly in } L^q(Q_T), \text{ for each } 1 \leq q < \infty, \\
\varrho_\varepsilon^{\frac{\gamma+1}{2}} &\rightharpoonup \varrho_\varepsilon^{\frac{\gamma+1}{2}} && \text{weakly in } L^2(0, T; H^1(\mathbb{R}^d)), \\
\frac{\partial \varrho_\varepsilon}{\partial t} &\rightharpoonup \frac{\partial \varrho}{\partial t} && \text{weakly in } L^2(0, T; H^{-1}(\mathbb{R}^d)).
\end{aligned}$$

Let us recall the notation $\mathcal{R} = \int_0^1 \sigma(\eta) R(\eta, p) d\eta$. Then

$$\mathcal{R}_\varepsilon \rightharpoonup \mathcal{R} \quad \text{weak}^* \text{ in } L^\infty(Q_T) \quad (16)$$

$$n_\varepsilon R(y, p_\varepsilon) \rightharpoonup n R(y, p) \quad \text{weak}^* \text{ in } L^\infty([0, 1] \times Q_T). \quad (17)$$

The convergences of (16) and (17) are shown in detail in Appendix B.

Lemma 3.5. *For all $q \geq \gamma + 1$ and all $t \in [0, T]$, we have*

$$\int_{\mathbb{R}^d} (\varrho_\varepsilon(x, t))^q dx \xrightarrow{\varepsilon \rightarrow 0} \int_{\mathbb{R}^d} (\varrho(x, t))^q dx.$$

Proof. Let us define

$$w_\varepsilon := \varrho_\varepsilon^{\gamma+1} + \varepsilon \frac{\gamma+1}{\gamma} \varrho_\varepsilon.$$

Hence, we rewrite Eq. (3) as

$$\frac{\partial \varrho_\varepsilon}{\partial t} - \frac{\gamma}{\gamma+1} \Delta w_\varepsilon = \varrho_\varepsilon \mathcal{R}_\varepsilon, \quad (18)$$

where we recall that $\mathcal{R}_\varepsilon = \int_0^1 \sigma_\varepsilon R(\eta, p_\varepsilon) d\eta$. We test Eq. (18) against $\partial_t w_\varepsilon$ to obtain

$$\int_{\mathbb{R}^d} \frac{\partial \varrho_\varepsilon}{\partial t} \frac{\partial w_\varepsilon}{\partial t} dx - \frac{\gamma}{\gamma+1} \int_{\mathbb{R}^d} \Delta w_\varepsilon \frac{\partial w_\varepsilon}{\partial t} dx = \int_{\mathbb{R}^d} \varrho_\varepsilon \mathcal{R}_\varepsilon \frac{\partial w_\varepsilon}{\partial t} dx.$$

Now we treat each term individually, to obtain

$$\begin{aligned} \int_{\mathbb{R}^d} \frac{\partial \varrho_\varepsilon}{\partial t} \frac{\partial w_\varepsilon}{\partial t} dx &= \int_{\mathbb{R}^d} \frac{\partial \varrho_\varepsilon}{\partial t} \frac{\partial \varrho_\varepsilon^{\gamma+1}}{\partial t} dx + \varepsilon \frac{\gamma+1}{\gamma} \int_{\mathbb{R}^d} \left| \frac{\partial \varrho_\varepsilon}{\partial t} \right|^2 dx \\ &= (\gamma+1) \int_{\mathbb{R}^d} \varrho_\varepsilon^\gamma \left| \frac{\partial \varrho_\varepsilon}{\partial t} \right|^2 dx + \varepsilon \frac{\gamma+1}{\gamma} \int_{\mathbb{R}^d} \left| \frac{\partial \varrho_\varepsilon}{\partial t} \right|^2 dx, \\ -\frac{\gamma}{\gamma+1} \int_{\mathbb{R}^d} \Delta w_\varepsilon \frac{\partial w_\varepsilon}{\partial t} dx &= \frac{\gamma}{\gamma+1} \frac{d}{dt} \int_{\mathbb{R}^d} \frac{|\nabla w_\varepsilon|^2}{2} dx, \\ \int_{\mathbb{R}^d} \varrho_\varepsilon \mathcal{R}_\varepsilon \frac{\partial w_\varepsilon}{\partial t} dx &= \int_{\mathbb{R}^d} \varrho_\varepsilon \mathcal{R}_\varepsilon \frac{\partial \varrho_\varepsilon^{\gamma+1}}{\partial t} dx + \varepsilon \frac{\gamma+1}{\gamma} \int_{\mathbb{R}^d} \varrho_\varepsilon \mathcal{R}_\varepsilon \frac{\partial \varrho_\varepsilon}{\partial t} dx \\ &\leq \frac{\gamma+1}{2} \int_{\mathbb{R}^d} \varrho_\varepsilon^\gamma \left| \frac{\partial \varrho_\varepsilon}{\partial t} \right|^2 dx + \frac{\gamma+1}{2} \int_{\mathbb{R}^d} \varrho_\varepsilon^{\gamma+2} \mathcal{R}_\varepsilon^2 dx \\ &\quad + \frac{\varepsilon}{2} \frac{\gamma+1}{\gamma} \int_{\mathbb{R}^d} \varrho_\varepsilon^2 \mathcal{R}_\varepsilon^2 dx + \frac{\varepsilon}{2} \frac{\gamma+1}{\gamma} \int_{\mathbb{R}^d} \left| \frac{\partial \varrho_\varepsilon}{\partial t} \right|^2 dx. \end{aligned}$$

Therefore, we obtain

$$\sup_{t \in [0, T]} \int_{\mathbb{R}^d} |\nabla w_\varepsilon(t)|^2 dx + \frac{\varepsilon}{2} \frac{\gamma+1}{\gamma} \iint_{Q_T} \left| \frac{\partial \varrho_\varepsilon}{\partial t} \right|^2 dx dt + \frac{\gamma+1}{2} \iint_{Q_T} \varrho_\varepsilon^\gamma \left| \frac{\partial \varrho_\varepsilon}{\partial t} \right|^2 dx dt \leq C, \quad (19)$$

where C depends on $\|\varrho_\varepsilon\|_\infty$ and $\|\mathcal{R}_\varepsilon\|_\infty$. Since $|\partial_t \varrho_\varepsilon^{\frac{\gamma+2}{2}}|^2 = \frac{(\gamma+2)^2}{4} \varrho_\varepsilon^\gamma |\partial_t \varrho_\varepsilon|^2$, from Eq. (19) we have

$$\partial_t \varrho_\varepsilon^{\frac{\gamma+2}{2}} \in L^2(Q_T), \quad \sqrt{\varepsilon} \partial_t \varrho_\varepsilon \in L^2(Q_T), \quad \nabla w_\varepsilon \in L^\infty(0, T; L^2(\mathbb{R}^d)).$$

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

$$\int_{\mathbb{R}^d} |\varrho_\varepsilon^{\gamma+1}(t) - \varrho^{\gamma+1}(t)|^2 dx \leq \int_{\mathbb{R}^d} |w_\varepsilon(t) - \varrho^{\gamma+1}(t)|^2 dx + \int_{\mathbb{R}^d} \left| \varepsilon \frac{\gamma+1}{\gamma} \varrho_\varepsilon(t) \right|^2 dx \rightarrow 0, \text{ as } \varepsilon \rightarrow 0.$$

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 $q \geq \gamma+1$. Therefore

$$\int_{\mathbb{R}^d} (\varrho_\varepsilon(x, t))^q dx \xrightarrow{\varepsilon \rightarrow 0} \int_{\mathbb{R}^d} (\varrho(x, t))^q dx, \quad \forall q \geq \gamma+1,$$

and thus the proof is completed. \square

As already mentioned above, when dealing with cross-diffusion systems as (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 3.6. *Upon the extraction of a subsequence, we have*

$$\nabla \varrho_\varepsilon^{\gamma+1} \xrightarrow{\varepsilon \rightarrow 0} \nabla \varrho^{\gamma+1} \quad \text{strongly in } L^2(Q_T).$$

Proof. For the sake of simplicity, when integrating, we now neglect the symbols dx, dt . 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. (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

$$\begin{aligned} \frac{\gamma}{\gamma+1} \iint_{Q_T} |\nabla (\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1})|^2 &= -\varepsilon \iint_{Q_T} \nabla \varrho_\varepsilon \cdot \nabla (\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}) + \int_0^T \langle \partial_t (\varrho_\varepsilon - \varrho), \varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1} \rangle \\ &\quad - \iint_{Q_T} (\varrho_\varepsilon \mathcal{R}_\varepsilon - \varrho \mathcal{R}) (\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}). \end{aligned}$$

Let us consider the three terms on the right-hand side individually. From the strong compactness of ϱ_ε in any L^p -space and the weak* compactness of \mathcal{R}_ε , it directly follows that

$$\iint_{Q_T} (\varrho_\varepsilon \mathcal{R}_\varepsilon - \varrho \mathcal{R}) (\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}) \rightarrow 0.$$

Recalling Lemma 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

$$\begin{aligned} \int_0^T \langle \partial_t (\varrho_\varepsilon - \varrho), \varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1} \rangle &= \iint_{Q_T} \frac{\partial_t \varrho_\varepsilon^{\gamma+2}}{\gamma+2} + \iint_{Q_T} \frac{\partial_t \varrho^{\gamma+2}}{\gamma+2} - \int_0^T \langle \partial_t \varrho, \varrho_\varepsilon^{\gamma+1} \rangle - \int_0^T \langle \partial_t \varrho_\varepsilon, \varrho^{\gamma+1} \rangle \\ &= \int_{\mathbb{R}^d} \frac{\varrho_\varepsilon^{\gamma+2}(T)}{\gamma+2} + \int_{\mathbb{R}^d} \frac{\varrho^{\gamma+2}(T)}{\gamma+2} - \int_{\mathbb{R}^d} \frac{\varrho_\varepsilon^{\gamma+2}(0)}{\gamma+2} - \int_{\mathbb{R}^d} \frac{\varrho^{\gamma+2}(0)}{\gamma+2} \\ &\quad - \int_0^T \langle \partial_t \varrho, \varrho_\varepsilon^{\gamma+1} \rangle - \int_0^T \langle \partial_t \varrho_\varepsilon, \varrho^{\gamma+1} \rangle \\ &\rightarrow 2 \int_{\mathbb{R}^d} \frac{\varrho^{\gamma+2}(T)}{\gamma+2} - 2 \int_{\mathbb{R}^d} \frac{\varrho^{\gamma+2}(0)}{\gamma+2} - 2 \int_0^T \langle \partial_t \varrho, \varrho^{\gamma+1} \rangle = 0. \end{aligned}$$

Since from Lemma 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

$$\varepsilon \iint_{Q_T} \nabla \varrho_\varepsilon \cdot \nabla (\varrho_\varepsilon^{\gamma+1} - \varrho^{\gamma+1}) = 4\varepsilon \iint_{Q_T} \sqrt{\varrho_\varepsilon} \nabla \sqrt{\varrho_\varepsilon} \cdot \left(\varrho_\varepsilon^{\frac{\gamma+1}{2}} \nabla \varrho_\varepsilon^{\frac{\gamma+1}{2}} - \varrho^{\frac{\gamma+1}{2}} \nabla \varrho^{\frac{\gamma+1}{2}} \right) \leq \sqrt{\varepsilon} C \rightarrow 0,$$

and this concludes the proof. \square

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 (2).

Theorem 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 (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 $\varphi \in C([0, 1]; C^1_{comp}([0, T] \times \mathbb{R}^d))$*

$$\begin{aligned} & - \int_0^1 \int_{\mathbb{R}^d} n(y, x, t) \frac{\partial \varphi(y, x, t)}{\partial t} dx dy + \int_0^1 \iint_{Q_T} n(y, x, t) \nabla p(x, t) \cdot \nabla \varphi(y, x, t) dx dt dy \\ & = \int_0^1 \iint_{Q_T} n(y, x, t) R(y, p(x, t)) \varphi(y, x, t) dx dt dy + \int_0^1 \int_{\mathbb{R}^d} n_0(y, x, t) \varphi(y, x, 0) dx dy, \end{aligned} \quad (20)$$

with

$$\varrho(x, t) = \int_0^1 n(y, x, t) dy, \quad p(x, t) = (\varrho(x, t))^\gamma.$$

Proof. For all $\varphi \in C([0, 1]; C^1_{comp}([0, T] \times \mathbb{R}^d))$, the variational formulation of Problem (9) can be written as

$$\begin{aligned} & - \int_0^1 \int_{\mathbb{R}^d} n_\varepsilon(y, x, t) \frac{\partial \varphi(y, x, t)}{\partial t} dx dy + \int_0^1 \iint_{Q_T} n_\varepsilon(y, x, t) \nabla p_\varepsilon(x, t) \cdot \nabla \varphi(y, x, t) dx dt dy \\ & = -\varepsilon \int_0^1 \iint_{Q_T} \nabla n_\varepsilon(y, x, t) \cdot \nabla \varphi(y, x, t) dx dt dy \\ & \quad + \int_0^1 \iint_{Q_T} n_\varepsilon(y, x, t) R(y, p_\varepsilon) \varphi(y, x, t) dx dt dy + \int_0^1 \int_{\mathbb{R}^d} n_{0,\varepsilon}(y, x, t) \varphi(y, x, 0) dx dy. \end{aligned} \quad (21)$$

As we already proved, there exists a bounded non-negative function $\sigma = \sigma(y, x, t)$ such that

$$\sigma_\varepsilon \rightarrow \sigma \quad \text{weakly}^* \text{ in } L^\infty([0, 1] \times Q_T).$$

Therefore, from Lemma 3.6 we infer

$$\begin{aligned} n_\varepsilon \nabla p_\varepsilon &= n_\varepsilon \nabla \varrho_\varepsilon^\gamma \\ &= \sigma_\varepsilon \varrho_\varepsilon \nabla \varrho_\varepsilon^\gamma \\ &= \sigma_\varepsilon \frac{\gamma}{\gamma+1} \nabla \varrho_\varepsilon^{\gamma+1} \xrightarrow{\varepsilon \rightarrow 0} \sigma \frac{\gamma}{\gamma+1} \nabla \varrho^{\gamma+1}, \quad \text{weakly in } L^2([0, 1] \times Q_T). \end{aligned} \quad (22)$$

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

$$\sigma_\varepsilon (\varrho_\varepsilon - \delta)_+ \rightarrow \sigma (\varrho - \delta)_+, \quad \text{weakly}^* \text{ in } L^\infty([0, 1] \times Q_T).$$

On the other hand

$$\sigma_\varepsilon (\varrho_\varepsilon - \delta)_+ = n_\varepsilon \frac{(\varrho_\varepsilon - \delta)_+}{\varrho_\varepsilon} \rightarrow n \frac{(\varrho - \delta)_+}{\varrho}, \quad \text{weakly}^* \text{ in } L^\infty([0, 1] \times Q_T),$$

by the following argument. Since $0 \leq \frac{(\varrho - \delta)_+}{\varrho} \leq 1$, we obtain

$$\begin{aligned} & \int_0^1 \iint_{Q_T} \left(n_\varepsilon \frac{(\varrho_\varepsilon - \delta)_+}{\varrho_\varepsilon} - n \frac{(\varrho - \delta)_+}{\varrho} \right) \varphi dx dt dy \\ & = \int_0^1 \iint_{Q_T} (n_\varepsilon - n) \frac{(\varrho - \delta)_+}{\varrho} \varphi dx dt dy + \int_0^1 \iint_{Q_T} n_\varepsilon \left(\frac{(\varrho_\varepsilon - \delta)_+}{\varrho_\varepsilon} - \frac{(\varrho - \delta)_+}{\varrho} \right) \varphi dx dt dy \rightarrow 0, \end{aligned}$$

as $\varepsilon \rightarrow 0$ 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. (22), Remark 3.4 and passing to the limit in Eq. (21) we obtain Eq. (20) and the proof is completed. \square

4 Incompressible limit

Thanks to the result proven in the previous section, *cf.* Theorem 3.7, we know that for each $\gamma > 1$ there exists $(n_\gamma, \varrho_\gamma, p_\gamma)$ that satisfies following equations

$$\begin{aligned} & - \int_0^1 \int_\Omega n_\gamma(y, x, t) \frac{\partial \varphi(y, x, t)}{\partial t} dx dy + \int_0^1 \iint_{\Omega_T} n_\gamma(y, x, t) \nabla p_\gamma(x, t) \cdot \nabla \varphi(y, x, t) dx dt dy \\ & = \int_0^1 \iint_{\Omega_T} n_\gamma(y, x, t) R(y, p_\gamma) \varphi(y, x, t) dx dt dy + \int_0^1 \int_\Omega n_{\gamma,0}(y, x, t) \varphi(y, x, 0) dx dy, \end{aligned} \quad (23)$$

for all $\varphi \in C([0, 1]; C_{comp}^1([0, T] \times \Omega))$

$$\begin{aligned} & - \iint_{\Omega_T} \varrho_\gamma(x, t) \frac{\partial \psi}{\partial t}(x, t) dx dt + \frac{\gamma}{\gamma + 1} \iint_{\Omega_T} \nabla v_\gamma(x, t) \cdot \nabla \psi(x, t) dx dt = \\ & \iint_{\Omega_T} \left(\int_0^1 n_\gamma(x, t) R(y, p_\gamma(x, t)) dy \right) \psi(x, t) dx dt + \int_\Omega \varrho_{\gamma,0}(x) \psi(x, 0) dx, \end{aligned} \quad (24)$$

for all test functions $\psi \in C_{comp}^1([0, T] \times \Omega)$, where $v_\gamma = \varrho^{\gamma+1}$.

The goal of this section is to study the incompressible limit $\gamma \rightarrow \infty$ 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 (23, 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 (24), as stated in the following theorem.

Theorem 4.1 (Weak Hele-Shaw problem). *Let $(n_\gamma, \varrho_\gamma, p_\gamma)$ be a solution given by Theorem 3.7. For all $T > 0$, up to the extraction of a subsequence we have*

$$n_\gamma(y, x, t) \rightharpoonup n_\infty(y, x, t) \quad \text{weakly}^* \text{ in } L^\infty((0, 1) \times \Omega_T), \quad (25)$$

$$\varrho_\gamma(x, t) \rightharpoonup \varrho_\infty(x, t) \quad \text{weakly}^* \text{ in } L^\infty(\Omega_T), \quad (26)$$

$$p_\gamma(x, t) \rightharpoonup p_\infty(x, t) \quad \text{weakly}^* \text{ in } L^\infty(\Omega_T), \quad (27)$$

$$\nabla v_\gamma \rightharpoonup \nabla v_\infty \quad \text{weakly in } L^2(\Omega_T), \quad (28)$$

as $\gamma \rightarrow \infty$. Moreover the limit satisfies

$$0 \leq \varrho_\infty \leq 1, \quad p_\infty(1 - \varrho_\infty) = 0 \quad \text{almost everywhere in } \Omega_T. \quad (29)$$

as well as

$$\begin{aligned}
-\iint_{\Omega_T} \varrho_\infty \frac{\partial \psi}{\partial t} dx dt + \iint_{\Omega_T} \nabla v_\infty \cdot \nabla \psi dx dt &= \iint_{\Omega_T} \left(\int_0^1 n_\infty R(y, p_\infty) dy \right) \psi dx dt \\
&+ \int_\Omega \varrho_0(x) \psi(x, 0) dx,
\end{aligned} \tag{30}$$

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. (23).

Theorem 4.2 (Complementarity relation). *The limit solution satisfies*

$$v_\infty \left(\Delta v_\infty + \int_0^1 n_\infty(y) R(y, p_\infty) \right) = 0, \quad \text{in } \mathcal{D}'(\Omega \times (0, \infty)), \tag{31}$$

as well as

$$\begin{aligned}
-\int_0^1 \iint_{\Omega_T} n_\infty \frac{\partial \varphi}{\partial t} dx dt dy + \int_0^1 \iint_{\Omega_T} n_\infty \nabla p_\infty \cdot \nabla \varphi dx dt dy \\
= \int_0^1 \iint_{\Omega_T} n_\infty R(y, p_\infty) \varphi dx dt dy + \int_\Omega n_0(y, x) \varphi(y, x, 0) dx dy,
\end{aligned} \tag{32}$$

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 4.1 and Theorem 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 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 4.8).

4.1 Proof of Theorem 4.1

Remark 4.3 (Weak* convergence as $\gamma \rightarrow \infty$). Let us point out that the L^∞ -bounds (13), (14) and (15) proven in Subsection 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. (25)-(27) hold. Moreover, there exists \mathcal{H}_∞ such that

$$n_\gamma R(y, p_\gamma) \rightharpoonup \mathcal{H}_\infty \text{ weakly* in } L^\infty((0, 1) \times \Omega_T). \tag{33}$$

Remark 4.4 (H^1 -bounds of p_γ and v_γ). Multiplying the equation on the density, Eq. (3), by $\gamma \varrho_\gamma^{\gamma-1}$, it is immediate to see that the pressure satisfies

$$\frac{\partial p_\gamma}{\partial t} = \gamma p_\gamma (\Delta p_\gamma + \mathcal{R}_\gamma) + |\nabla p_\gamma|^2. \tag{34}$$

Hence, the pressure gradient is bounded in $L^2(\Omega_T)$ as shown by integrating by parts in space to get

$$\frac{d}{dt} \int_\Omega p_\gamma dx = (1 - \gamma) \int_\Omega |\nabla p_\gamma|^2 dx + \gamma \int_\Omega p_\gamma \mathcal{R}_\gamma dx,$$

which implies

$$(\gamma - 1) \iint_{\Omega_T} |\nabla p_\gamma|^2 dx dt \leq \gamma \|\mathcal{R}_\gamma\|_{L^\infty(\Omega_T)} \|p_\gamma\|_{L^1(\Omega_T)} + \|p_0\|_{L^1(\Omega)}.$$

Therefore, for all $\gamma > 1$, it holds

$$p_\gamma \in L^2(0, T; H^1(\Omega)). \quad (35)$$

By the definition of v_γ , we have

$$\nabla v_\gamma = \frac{\gamma + 1}{\gamma} p_\gamma^{\frac{1}{\gamma}} \nabla p_\gamma = \frac{\gamma + 1}{\gamma} \varrho_\gamma \nabla p_\gamma \in L^2(\Omega_T), \quad (36)$$

uniformly in γ , and therefore Eq. (28) is proven.

Corollary 4.5. *The limit triplet $(n_\infty, \varrho_\infty, p_\infty)$ satisfies*

$$\frac{\partial \varrho_\infty}{\partial t} = \Delta v_\infty + \int_0^1 \mathcal{H}_\infty(y) dy, \text{ in } \mathcal{D}'(\mathbb{R}^d \times (0, \infty)), \quad (37)$$

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. (24) using the convergence results (26), (28), and (33). □

As mentioned above, in order to conclude the proof of (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. (46). At this moment, we are not able to identify the limit since we do not have the strong compactness of p_γ .

Remark 4.6 (H^{-1} -bound of the density time-derivative). From the previous bounds and Eq. (6), we have

$$\frac{\partial \varrho_\gamma}{\partial t} \in L^2(0, T; H^{-1}(\Omega)). \quad (38)$$

Corollary 4.7. *The limit solution satisfies Eq. (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 $\varrho_\gamma \leq \varrho_M = (p_M)^{1/\gamma}$ we have $0 \leq \varrho_\infty \leq 1$.

By definition we have $v_\gamma = \varrho_\gamma p_\gamma$. Thanks to Eqs. (35) and (38) we can apply the compensated compactness theorem stated in Appendix A, cf. Theorem A.1, and infer

$$\int_{\Omega_T} v_\gamma \varphi dx dt \rightarrow \int_{\Omega_T} \varrho_\infty p_\infty \varphi dx dt,$$

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

$$\lim_{\gamma \rightarrow \infty} v_\gamma = \liminf_{\gamma \rightarrow \infty} p_\gamma^{\frac{\gamma+1}{\gamma}} \geq p_\infty.$$

For the sake of completeness, we include here the full argument. Let $\psi_\delta = \psi_\delta(x)$ be a convex function such that $\psi_\delta(x) \rightarrow x$ as $\delta \rightarrow 0$. Let us denote $\Psi_\gamma(x) = x^{\frac{\gamma+1}{\gamma}}$, $\gamma > 1$. Let us take $\delta > 0$ small enough such that

$$\psi_\delta(x) \leq \Psi_\gamma(x).$$

Therefore, we have

$$\psi_\delta(p_\infty) \leq \liminf_{\gamma \rightarrow \infty} \psi_\delta(p_\gamma) \leq \liminf_{\gamma \rightarrow \infty} \Psi_\gamma(p_\gamma) = \liminf_{\gamma \rightarrow \infty} p_\gamma^{\frac{\gamma+1}{\gamma}}.$$

Since we chose $\delta > 0$ arbitrarily, we take $\delta \rightarrow 0$ to obtain

$$p_\infty \leq \liminf_{\gamma \rightarrow \infty} p_\gamma^{\frac{\gamma+1}{\gamma}}.$$

Hence $\varrho_\infty p_\infty = v_\infty \geq p_\infty$, which implies $\varrho_\infty p_\infty = p_\infty$. □

4.2 Proof of Theorem 4.2

In order to prove the complementarity relation, *cf.* Theorem 4.2, the usual strategy is to prove the strong convergence of ∇p_γ , see for instance [11, 15, 16]. 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 [27], directly proving the strong compactness of ∇v_γ . The core of the proof is given by the following lemma.

Lemma 4.8. *Up to a subsequence, as $\gamma \rightarrow \infty$, we have*

$$\nabla v_\gamma \rightarrow \nabla v_\infty \quad \text{strongly in } L^2(\Omega_T). \quad (39)$$

Proof. Let us use $v_\gamma - v_\infty$ as a test function in Eq. (6) to obtain

$$\int_{\Omega} \frac{\partial \varrho_\gamma}{\partial t} (v_\gamma - v_\infty) dx + \frac{\gamma}{\gamma+1} \int_{\Omega} \nabla v_\gamma \cdot \nabla (v_\gamma - v_\infty) dx = \int_{\Omega} \left(\int_0^1 n_\gamma R(y, p_\gamma) dy \right) (v_\gamma - v_\infty) dx. \quad (40)$$

We note that

$$\int_{\Omega} \frac{\partial \varrho_\gamma}{\partial t} v_\gamma dx = \frac{1}{\gamma+2} \int_{\Omega} \frac{\partial \varrho_\gamma^{\gamma+2}}{\partial t} dx = \frac{1}{\gamma+2} \frac{d}{dt} \int_{\Omega} \varrho_\gamma^{\gamma+2} dx.$$

Integrating in time we get

$$\iint_{\Omega_T} \frac{\partial \varrho_\gamma}{\partial t} v_\gamma dx dt = \frac{1}{\gamma+2} \int_{\Omega} \varrho_\gamma^{\gamma+2}(T) dx - \frac{1}{\gamma+2} \int_{\Omega} \varrho_\gamma^{\gamma+2}(0) dx \rightarrow 0,$$

as $\gamma \rightarrow \infty$. Now we compute

$$\begin{aligned} & \limsup_{\gamma \rightarrow \infty} \iint_{\Omega_T} |\nabla (v_\gamma - v_\infty)|^2 dx dt \\ & \leq \limsup_{\gamma \rightarrow \infty} \left(\iint_{\Omega_T} \nabla v_\gamma \cdot \nabla (v_\gamma - v_\infty) dx dt - \iint_{\Omega_T} \nabla v_\infty \cdot \nabla (v_\gamma - v_\infty) dx dt \right) \quad (41) \\ & \leq \limsup_{\gamma \rightarrow \infty} \iint_{\Omega_T} \nabla v_\gamma \cdot \nabla (v_\gamma - v_\infty) dx dt, \end{aligned}$$

where in the last inequality we use the fact that ∇v_γ is weakly compact in $L^2(\Omega_T)$. From Eq. (40) we obtain

$$\begin{aligned} & \limsup_{\gamma \rightarrow \infty} \iint_{\Omega_T} \nabla v_\gamma \cdot \nabla (v_\gamma - v_\infty) dx dt \\ & \leq \limsup_{\gamma \rightarrow \infty} \iint_{\Omega_T} \left(\int_0^1 n_\gamma R(y, p_\gamma) dy \right) (v_\gamma - v_\infty) dx dt + \limsup_{\gamma \rightarrow \infty} \iint_{\Omega_T} \frac{\partial \varrho_\gamma}{\partial t} v_\infty dx dt \quad (42) \\ & \leq \limsup_{\gamma \rightarrow \infty} \iint_{\Omega_T} \left(\int_0^1 n_\gamma R(y, p_\gamma) dy \right) (v_\gamma - v_\infty) dx dt + \iint_{\Omega_T} \frac{\partial \varrho_\infty}{\partial t} v_\infty dx dt, \end{aligned}$$

where we used the weak compactness of the density in $L^2(0, T; H^{-1}(\Omega))$ given by Eq. (38). We now treat the first term in the right-hand side of Eq. (42). We add and subtract the same quantity to get

$$\begin{aligned} \iint_{\Omega_T} \left(\int_0^1 n_\gamma R(y, p_\gamma) dy \right) (v_\gamma - v_\infty) dx dt &= \underbrace{\iint_{\Omega_T} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) (v_\gamma - v_\infty) dx dt}_{\mathcal{A}} \\ &\quad + \underbrace{\iint_{\Omega_T} \left(\int_0^1 n_\gamma R(y, p_\infty) dy \right) (v_\gamma - v_\infty) dx dt}_{\mathcal{B}}. \end{aligned}$$

Our goal is to prove that the right hand side is bounded by some quantity that converges to zero as $\gamma \rightarrow \infty$. 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

$$\begin{aligned} \mathcal{A} &= \iint_{\Omega_T} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) (p_\gamma \varrho_\gamma - v_\infty) dx dt \\ &= \iint_{\Omega_T} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) (p_\gamma (\varrho_\gamma - 1) + p_\gamma - p_\infty) dx dt \\ &= \iint_{\Omega_T} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) p_\gamma (\varrho_\gamma - 1) dx dt \\ &\quad + \iint_{\Omega_T} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) (p_\gamma - p_\infty) dx dt, \end{aligned}$$

where the last integral is non-positive by the monotonicity of R . Let $\varepsilon > 0$, we split the remaining term as follows

$$\begin{aligned} &\iint_{\Omega_T} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) p_\gamma (\varrho_\gamma - 1) dx dt \\ &= \iint_{\Omega_T \cap \{\varrho_\gamma \leq 1 - \varepsilon\}} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) \varrho_\gamma^\gamma (\varrho_\gamma - 1) dx dt \\ &\quad + \iint_{\Omega_T \cap \{\varrho_\gamma > 1 - \varepsilon\}} \left(\int_0^1 n_\gamma (R(y, p_\gamma) - R(y, p_\infty)) dy \right) p_\gamma (\varrho_\gamma - 1) dx dt \\ &\leq 2\|R\|_\infty \varrho_M (1 - \varepsilon)^\gamma + 2\|R\|_\infty \varrho_M p_M \max\left(\varepsilon, \frac{1}{\gamma} |\ln p_M| + o\left(\frac{1}{\gamma}\right)\right). \end{aligned}$$

Choosing $\varepsilon = 1/\sqrt{\gamma}$, we infer that the right-hand side converges to zero as $\gamma \rightarrow \infty$.

Now we show that, after the extraction of a subsequence, the term

$$\mathcal{B} = \int_0^1 \left(\iint_{\Omega_T} n_\gamma R(y, p_\infty) (v_\gamma - v_\infty) dx dt \right) dy,$$

converges to zero as $\gamma \rightarrow \infty$. 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 A.1. For all indexes γ_{k_j} there exist $\gamma_{k_{j_i}}$ such that

$$\iint_{\Omega_T} n_{\gamma_{k_{j_i}}}(y) R(y, p_\infty)(v_{\gamma_{k_{j_i}}} - v_\infty) dx dt \rightarrow 0,$$

as $i \rightarrow \infty$, which implies

$$\iint_{\Omega_T} n_{\gamma_k}(y) R(y, p_\infty)(v_{\gamma_k} - v_\infty) dx dt \rightarrow 0,$$

as $k \rightarrow \infty$. 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

$$\mathcal{B} = \int_0^1 \left(\iint_{\Omega_T} n_{\gamma_k} R(y, p_\infty)(v_{\gamma_k} - v_\infty) dx dt \right) dy \rightarrow 0,$$

as $k \rightarrow \infty$.

Now, we can finally come back to Eqs.(41)-(42)

$$\limsup_{\gamma \rightarrow \infty} \iint_{\Omega_T} |\nabla(v_\gamma - v_\infty)|^2 dx dt \leq \iint_{\Omega_T} \frac{\partial \varrho_\infty}{\partial t} v_\infty dx dt. \quad (43)$$

To conclude the proof we will show that the right-hand side is actually equal to zero. Let us notice that for any $\varepsilon > 0$

$$\iint_{\Omega_T} (\varrho_\infty(x, t + \varepsilon) - \varrho_\infty(x, t)) v_\infty dx dt = \iint_{\Omega_T} (\varrho_\infty(x, t + \varepsilon) - 1 + 1 - \varrho_\infty(x, t)) v_\infty dx dt \leq 0,$$

where in the last inequality we used Eq. (29). In a similar fashion we have

$$\iint_{\Omega_T} (\varrho_\infty(x, t) - \varrho_\infty(x, t - \varepsilon)) v_\infty dx dt \geq 0.$$

Now it remains to prove that

$$\lim_{\varepsilon \rightarrow 0} \iint_{\Omega_T} (\varrho_\infty(x, t + \varepsilon) - \varrho_\infty(x, t)) v_\infty dx dt = \iint_{\Omega_T} \frac{\partial \varrho_\infty}{\partial t} v_\infty dx dt. \quad (44)$$

We integrate Eq. (37) between t and $t + \varepsilon$ to obtain

$$\varrho_\infty(t + \varepsilon) - \varrho_\infty(t) = \int_t^{t+\varepsilon} \Delta v_\infty ds + \int_t^{t+\varepsilon} \int_0^1 \mathcal{H}_\infty dy ds.$$

We test the above equation against $\frac{1}{\varepsilon} v_\infty(\cdot, t)$ to get

$$\begin{aligned} \int_{\Omega} \left(\frac{\varrho_\infty(x, t + \varepsilon) - \varrho_\infty(x, t)}{\varepsilon} \right) v_\infty(x, t) dx &= - \int_{\Omega} \frac{1}{\varepsilon} \int_t^{t+\varepsilon} \nabla v_\infty(x, s) ds \cdot \nabla v_\infty(x, t) dx \\ &\quad + \int_{\Omega} \frac{1}{\varepsilon} \int_t^{t+\varepsilon} \int_0^1 \mathcal{H}_\infty(y, x, s) dy ds v_\infty(x, t) dx. \end{aligned} \quad (45)$$

We have

$$\frac{1}{\varepsilon} \int_t^{t+\varepsilon} \nabla v_\infty(x, s) ds \rightarrow \nabla v_\infty(x, t), \quad \text{a.e. in } \Omega_T.$$

From Eq. (36) we have

$$\begin{aligned}
\iint_{\Omega_T} \left| \frac{1}{\varepsilon} \int_t^{t+\varepsilon} \nabla v_\infty(x, s) \, ds \right|^2 dx \, dt &\leq \frac{1}{\varepsilon} \iint_{\Omega_T} \int_t^{t+\varepsilon} |\nabla v_\infty(x, s)|^2 ds \, dx \, dt \\
&= \frac{1}{\varepsilon} \int_0^{T+\varepsilon} \int_{\max(0, s-\varepsilon)}^{\min(T, s)} \int_\Omega |\nabla v_\infty(x, s)|^2 dx \, dt \, ds \\
&\leq \frac{1}{\varepsilon} \int_0^{T+\varepsilon} |\min(T, s) - \max(0, s - \varepsilon)| \int_\Omega |\nabla v_\infty(x, s)|^2 dx \, ds \\
&\leq C(T).
\end{aligned}$$

Therefore we have

$$\frac{1}{\varepsilon} \int_t^{t+\varepsilon} \nabla v_\infty(x, s) \, ds \rightarrow \nabla v_\infty(x, t), \quad \text{weakly in } L^2(\Omega_T).$$

In an analogous way we can prove that

$$\frac{1}{\varepsilon} \int_t^{t+\varepsilon} \int_0^1 \mathcal{H}_\infty(y, x, s) \, dy \, ds \rightarrow \int_0^1 \mathcal{H}_\infty(y, x, t) \, dy, \quad \text{weakly in } L^2(\Omega_T).$$

Combining Eq. (45) and Eq. (37) we have

$$\begin{aligned}
&\lim_{\varepsilon \rightarrow 0} \iint_{\Omega_T} \left(\frac{\varrho_\infty(t+\varepsilon) - \varrho(t)}{\varepsilon} \right) v_\infty(x, t) \, dx \, dt \\
&= - \iint_{\Omega_T} |\nabla v_\infty|^2 \, dx \, dt + \iint_{\Omega_T} \left(\int_0^1 \mathcal{H}_\infty(y, x, t) \, dy \right) v_\infty(x, t) \, dx \, dt \\
&= \iint_{\Omega_T} \frac{\partial \varrho_\infty}{\partial t} v_\infty \, dx \, dt.
\end{aligned}$$

Hence Eq. (44) is proven. As a consequence, Eq. (43) concludes the proof. \square

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 4.9 (Strong compactness of p_γ). *Up to the extraction of a subsequence, we have*

$$p_\gamma \rightarrow p_\infty, \quad \text{strongly in } L^2(\Omega_T).$$

Proof. Since we assumed the solutions to be compactly supported for all times $0 \leq t \leq T$, by Lemma 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. \square

Thanks to this result, we can finally identify the limit of the reaction term, *i.e.* the following equality holds almost everywhere in $[0, 1] \times \Omega_T$

$$\mathcal{H}_\infty(y, x, t) = n_\infty(y, x, t) R(y, p_\infty(x, t)). \quad (46)$$

Thanks to the strong compactness of the pressure gradient, we can pass to the limit in Eq. (23) to obtain Eq. (32).

Finally, to complete the proof of Theorem 4.2, we show that the complementarity relation (31) holds true. Let us multiply Eq. (6) by v_γ to get

$$\frac{1}{\gamma+2} \frac{\partial \varrho_\gamma^{\gamma+2}}{\partial t} = \frac{\gamma}{\gamma+1} v_\gamma \Delta v_\gamma + v_\gamma \int_0^1 n_\gamma R(y, p_\gamma) dy.$$

As already proven, v_γ, p_γ and ∇v_γ are strongly compact in $L^2(\Omega_T)$. Therefore, passing to the limit $\gamma \rightarrow \infty$ we obtain

$$v_\infty \left(\Delta v_\infty + \int_0^1 n_\infty(y) R(y, p_\infty) dy \right) = 0, \quad \text{in } \mathcal{D}'(\Omega \times (0, \infty)),$$

which concludes the proof.

5 Additional regularity estimates

Here we present some regularity estimates on the pressure $p = \varrho^\gamma$, where ϱ is a solution of Eq. (10). In particular, we extend a result already proved in [29] 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 [9, 11, 15, 16, 24] for a comprehensive overview.

Before presenting the proof of the main results, cf. Theorem 5.2 and Theorem 5.4, we point out that as a consequence the following corollary holds.

Corollary 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*

$$\int_\Omega |\Delta p(t)| dx \leq C(T), \quad (47)$$

for all $t \in [0, T]$.

Let us stress the fact that this estimate, together with a regularisation argument on Eq. (2) and Eq. (3), implies the existence of weak solutions. In fact, considering the equations

$$\begin{aligned} \partial_t n &= \nabla \cdot (n \nabla p) + n R(y, p), \\ \partial_t \varrho &= \nabla \cdot (\varrho \nabla p) + \varrho \mathcal{R}, \end{aligned}$$

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. (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 $1 \leq q \leq \frac{d}{d-2}$, as $\mu \rightarrow 0$. Hence, combining this result with the compactness of n , σ and ϱ stated in Remark 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 [24], 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 [24] 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 [33]. However, to recover the bound (47) on the Laplacian removing the condition on the reaction terms was still an open question.

Theorem 5.2 (L^4 -estimate). *There exists a constant $C(T)$ such that for any $0 \leq \alpha < \frac{1}{\gamma}$ the following estimate holds true*

$$\kappa(\alpha) \iint_{\Omega_T} \frac{|\nabla p|^4}{p^{1-\alpha}} dx dt \leq C(T),$$

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

Proof. First of all, let us recall that $\mathcal{R} = \int_0^1 \sigma(\eta)R(\eta, p) d\eta$, hence $\partial_p \mathcal{R} \leq 0$.

We multiply Eq. (34) by $-p^\alpha(\Delta p + \mathcal{R})$ to obtain

$$-p^\alpha \frac{\partial p}{\partial t} (\Delta p + \mathcal{R}) = -\gamma p^{\alpha+1} (\Delta p + \mathcal{R})^2 - p^\alpha |\nabla p|^2 (\Delta p + \mathcal{R}). \quad (48)$$

Now we integrate in space and we split the left-hand side treating each term individually.

$$\begin{aligned} - \int_{\Omega} p^\alpha \frac{\partial p}{\partial t} \Delta p dx &= \frac{1}{2} \int_{\Omega} p^\alpha \frac{\partial}{\partial t} |\nabla p|^2 dx + \alpha \int_{\Omega} p^{\alpha-1} \frac{\partial p}{\partial t} |\nabla p|^2 dx \\ &= \frac{1}{2} \frac{d}{dt} \int_{\Omega} p^\alpha |\nabla p|^2 dx + \frac{\alpha}{2} \int_{\Omega} p^{\alpha-1} \frac{\partial p}{\partial t} |\nabla p|^2 dx \\ &= \frac{1}{2} \frac{d}{dt} \int_{\Omega} p^\alpha |\nabla p|^2 dx + \frac{\alpha\gamma}{2} \int_{\Omega} p^\alpha (\Delta p + \mathcal{R}) |\nabla p|^2 dx + \frac{\alpha}{2} \int_{\Omega} p^{\alpha-1} |\nabla p|^4 dx. \end{aligned}$$

Let us define the following function

$$\bar{\mathcal{R}}(p, \sigma) = \int_0^p q^\alpha \mathcal{R}(q, \sigma) dq.$$

It immediately follows

$$p^\alpha \frac{\partial p}{\partial t} \mathcal{R} = \frac{\partial \bar{\mathcal{R}}}{\partial t} - \int_0^1 \left(\int_0^p q^\alpha R(\eta, q) dq \right) \partial_t \sigma d\eta.$$

Now using the equation on the fraction density σ , Eq. (11), we have

$$\begin{aligned} - \int_{\Omega} p^\alpha \frac{\partial p}{\partial t} \mathcal{R} dx &= - \frac{d}{dt} \int_{\Omega} \bar{\mathcal{R}} dx + \int_{\Omega} \int_0^1 \left(\int_0^p q^\alpha R(\eta, q) dq \right) \nabla \sigma \cdot \nabla p d\eta dx \\ &\quad + \int_{\Omega} \int_0^1 \left(\int_0^p q^\alpha R(\eta, q) dq \right) (R(\eta, p) - \mathcal{R}(p)) \sigma d\eta dx \\ &= - \frac{d}{dt} \int_{\Omega} \bar{\mathcal{R}} dx + \int_{\Omega} \int_0^1 \left(\int_0^p q^\alpha R(\eta, q) dq \right) \nabla \sigma \cdot \nabla p d\eta dx + Bdd, \end{aligned}$$

where we use Bdd to denote the bounded term

$$\int_{\Omega} \int_0^1 \left(\int_0^p q^{\alpha} R(\eta, q) dq \right) (R(\eta, p) - \mathcal{R}) \sigma d\eta dx \leq \frac{C}{\alpha + 1} \int_{\Omega} p^{\alpha+1} dx \leq C \|p\|_{L^2}^2,$$

where C is a positive constant that depends on $\|\mathcal{R}\|_{\infty}$. Now let us come back to Eq. (48) and integrate on Ω

$$\begin{aligned} & \frac{\alpha}{2} \int_{\Omega} p^{\alpha-1} |\nabla p|^4 dx + \gamma \int_{\Omega} p^{\alpha+1} (\Delta p + \mathcal{R})^2 dx \\ &= - \left(1 + \frac{\alpha\gamma}{2} \right) \int_{\Omega} p^{\alpha} (\Delta p + \mathcal{R}) |\nabla p|^2 dx + \frac{d}{dt} \int_{\Omega} \left(\overline{\mathcal{R}} - p^{\alpha} \frac{|\nabla p|^2}{2} \right) dx \\ & \quad - \underbrace{\int_{\Omega} \int_0^1 \left(\int_0^p q^{\alpha} R(\eta, q) dq \right) \nabla \sigma \cdot \nabla p d\eta dx}_{\mathcal{A}} - Bdd. \end{aligned} \quad (49)$$

Let us integrate by parts the term \mathcal{A} . We obtain

$$\begin{aligned} -\mathcal{A} &= - \int_0^1 \int_{\Omega} \left(\int_0^p q^{\alpha} R(\eta, q) dq \right) \nabla \sigma \cdot \nabla p d\eta dx \\ &= \int_{\Omega} p^{\alpha} |\nabla p|^2 \left(\int_0^1 R(\eta, p) \sigma d\eta \right) dx + \int_0^1 \int_{\Omega} \left(\int_0^p q^{\alpha} R(\eta, q) dq \right) \sigma \Delta p d\eta dx \\ &\leq \|\mathcal{R}\|_{\infty} p_M^{\alpha} \int_{\Omega} |\nabla p|^2 dx + \frac{1}{2} \int_{\Omega} \frac{\left(\int_0^1 \left(\int_0^p q^{\alpha} R(\eta, q) dq \right) \sigma d\eta \right)^2}{p^{\alpha+1}} dx + \frac{1}{2} \int_{\Omega} p^{\alpha+1} |\Delta p|^2 dx, \end{aligned}$$

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. (49) and integrating in time, we obtain

$$\begin{aligned} & \frac{\alpha}{2} \iint_{\Omega_T} p^{\alpha-1} |\nabla p|^4 dx dt + \gamma \iint_{\Omega_T} p^{\alpha+1} (\Delta p + \mathcal{R})^2 dx dt \\ & \leq - \underbrace{\left(1 + \frac{\alpha\gamma}{2} \right) \iint_{\Omega_T} p^{\alpha} (\Delta p + \mathcal{R}) |\nabla p|^2 dx dt}_{\mathcal{B}} + \int_{\Omega} \overline{\mathcal{R}}(T) dx \\ & \quad + \int_{\Omega} (p_0)^{\alpha} \frac{|\nabla p_0|^2}{2} dx + \frac{1}{2} \iint_{\Omega_T} p^{\alpha+1} |\Delta p|^2 dx dt + Bdd, \end{aligned} \quad (50)$$

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 [29], 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

$$\iint_{\Omega_T} p^{\alpha} \mathcal{R} |\nabla p|^2 dx dt \leq p_M^{\alpha} \|\mathcal{R}\|_{\infty} \|\nabla p\|_2^2 \leq \max(1, p_M) \|\mathcal{R}\|_{\infty} \|\nabla p\|_2^2. \quad (51)$$

The term with Δp is instead more involved. We refer the reader to [15] 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

$$\begin{aligned} \int_{\Omega} p^{\alpha} \Delta p |\nabla p|^2 dx &= \int_{\Omega} \Delta(p^{\alpha} |\nabla p|^2) p dx \\ &= \int_{\Omega} \Delta p^{\alpha} |\nabla p|^2 p dx + 2\alpha \int_{\Omega} \nabla p \cdot \nabla(|\nabla p|^2) p^{\alpha} dx + \int_{\Omega} p^{\alpha+1} \Delta(|\nabla p|^2) dx. \end{aligned} \quad (52)$$

Computing the sum of the first two terms of the right-hand side, we find

$$\begin{aligned} &\int_{\Omega} \Delta p^{\alpha} |\nabla p|^2 p dx + 2\alpha \int_{\Omega} \nabla p \cdot \nabla(|\nabla p|^2) p^{\alpha} dx \\ &= \alpha(\alpha-1) \int_{\Omega} p^{\alpha-1} |\nabla p|^4 dx + \alpha \int_{\Omega} p^{\alpha} \Delta p |\nabla p|^2 dx - 2\alpha \int_{\Omega} p^{\alpha} \Delta p |\nabla p|^2 dx - 2\alpha^2 \int_{\Omega} p^{\alpha-1} |\nabla p|^4 dx \\ &= -\alpha(\alpha+1) \int_{\Omega} p^{\alpha-1} |\nabla p|^4 dx - \alpha \int_{\Omega} p^{\alpha} \Delta p |\nabla p|^2 dx, \end{aligned}$$

where we used integration by parts on the second term.

We compute the last term in Eq. (52) as follows

$$\begin{aligned} \int_{\Omega} p^{\alpha+1} \Delta(|\nabla p|^2) dx &= 2 \int_{\Omega} p^{\alpha+1} \nabla p \cdot \nabla(\Delta p) dx + 2 \int_{\Omega} p^{\alpha+1} (D_{i,j}^2 p)^2 dx \\ &= -2(\alpha+1) \int_{\Omega} p^{\alpha} |\nabla p|^2 \Delta p dx - 2 \int_{\Omega} p^{\alpha+1} |\Delta p|^2 dx + 2 \int_{\Omega} p^{\alpha+1} (D_{i,j}^2 p)^2 dx, \end{aligned}$$

where in the last equality we used integration by parts and we denoted $(D_{i,j}^2 p)^2 = \sum_{i,j} (\partial_{i,j}^2 p)^2$. By consequence, Eq. (52) now reads

$$\begin{aligned} \int_{\Omega} p^{\alpha} \Delta p |\nabla p|^2 dx &= -\alpha(\alpha+1) \int_{\Omega} p^{\alpha-1} |\nabla p|^4 dx - (3\alpha+2) \int_{\Omega} p^{\alpha} \Delta p |\nabla p|^2 dx \\ &\quad - 2 \int_{\Omega} p^{\alpha+1} |\Delta p|^2 dx + 2 \int_{\Omega} p^{\alpha+1} (D_{i,j}^2 p)^2 dx, \end{aligned}$$

and thus

$$\begin{aligned} \int_{\Omega} p^{\alpha} \Delta p |\nabla p|^2 dx &= -\frac{\alpha}{3} \int_{\Omega} p^{\alpha-1} |\nabla p|^4 dx - \frac{2}{3(\alpha+1)} \int_{\Omega} p^{\alpha+1} |\Delta p|^2 dx \\ &\quad + \frac{2}{3(\alpha+1)} \int_{\Omega} p^{\alpha+1} (D_{i,j}^2 p)^2 dx. \end{aligned} \quad (53)$$

Using Eq. (53) in Eq. (50), we finally find

$$\begin{aligned} &\frac{\alpha}{2} \iint_{\Omega_T} p^{\alpha-1} |\nabla p|^4 dx dt + \gamma \iint_{\Omega_T} p^{\alpha+1} (\Delta p + \mathcal{R})^2 dx dt + \frac{2+\alpha\gamma}{3(\alpha+1)} \iint_{\Omega_T} p^{\alpha+1} (D_{i,j}^2 p)^2 dx dt \\ &\leq \frac{\alpha}{3} \left(1 + \frac{\alpha\gamma}{2}\right) \iint_{\Omega_T} p^{\alpha-1} |\nabla p|^4 dx dt + \left(\frac{2+\alpha\gamma}{3(\alpha+1)} + \frac{1}{2}\right) \iint_{\Omega_T} p^{\alpha+1} |\Delta p|^2 dx dt + Bdd, \end{aligned}$$

where Bdd includes also the bound in Eq. (51). By Young's inequality, we have

$$\iint_{\Omega_T} p^{\alpha+1} |\Delta p|^2 dx dt \leq \frac{3}{2} \iint_{\Omega_T} p^{\alpha+1} |\Delta p + \mathcal{R}|^2 dx dt + 3 \iint_{\Omega_T} p^{\alpha+1} |\mathcal{R}|^2 dx dt.$$

Then, we finally have

$$\begin{aligned} \kappa(\alpha) \iint_{\Omega_T} p^{\alpha-1} |\nabla p|^4 dx dt + \left(\gamma - \frac{3}{2} \right) \iint_{\Omega_T} p^{\alpha+1} (\Delta p + \mathcal{R})^2 dx dt \\ + \frac{2 + \alpha\gamma}{3(\alpha + 1)} \iint_{\Omega_T} p^{\alpha+1} (D_{i,j}^2 p)^2 dx dt \leq C(T), \end{aligned} \quad (54)$$

with $\kappa(\alpha) := \frac{\alpha}{6}(1 - \alpha\gamma)$. Since we assumed $0 < \alpha < \frac{1}{\gamma}$, this concludes the proof. \square

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 [15], where the authors prove its sharpness.

Corollary 5.3. *The following estimate holds uniformly in γ ,*

$$\iint_{\Omega_T} |\nabla p|^4 dx dt \leq C(T).$$

Proof. Let us take $\alpha = 0$ in Eq. (54). Then, we infer the following bounds

$$\iint_{\Omega_T} p(\Delta p + \mathcal{R})^2 dx dt \leq C(T), \quad \iint_{\Omega_T} p(D_{i,j}^2 p)^2 dx dt \leq C(T),$$

and both hold uniformly with respect to γ . Since both p and \mathcal{R} are uniformly bounded in L^∞ , this implies

$$\iint_{\Omega_T} p^2 |\Delta p|^2 dx dt \leq C(T), \quad \iint_{\Omega_T} p^2 (D_{i,j}^2 p)^2 dx dt \leq C(T).$$

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 [15] for the detailed proof. \square

Theorem 5.4 (L^2 -Aronson-Bénilan estimate). *With the assumptions of Section 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*

$$\int_{\Omega} (\Delta p(t))_-^2 dx \leq C(T), \quad \iint_{\Omega_T} (\Delta p)_-^3 dx dt \leq C(T).$$

Proof. We define $w = \Delta p + \mathcal{R}$. Hence, Eq. (34) reads

$$\partial_t p = \gamma p w + |\nabla p|^2.$$

Let us recall again the definition of \mathcal{R}

$$\mathcal{R}(p, \sigma) = \int_0^1 R(\eta, p(x, t)) \sigma(\eta, x, t) d\eta.$$

Now we compute $\partial_t w$

$$\begin{aligned}
\frac{\partial w}{\partial t} &= \Delta(\gamma p w + |\nabla p|^2) + \frac{\partial \mathcal{R}}{\partial t} \\
&= \gamma \Delta(p w) + 2 \nabla p \cdot \nabla(\Delta p) + 2 \sum_{i,j} (\partial_{i,j}^2 p)^2 + \frac{\partial \mathcal{R}}{\partial t} \\
&\geq \gamma \Delta(p w) + 2 \nabla p \cdot \nabla w - 2 \nabla p \cdot \nabla \mathcal{R} + \frac{2}{d} (w - \mathcal{R})^2 + \frac{\partial \mathcal{R}}{\partial t} \\
&= \gamma \Delta(p w) + 2 \nabla p \cdot \nabla w - 2 \mathcal{R}_p |\nabla p|^2 - 2 \int_0^1 R(\eta, p) \nabla \sigma \cdot \nabla p \, d\eta + \frac{2}{d} (w - \mathcal{R})^2 + \frac{\partial \mathcal{R}}{\partial t} \\
&= \gamma \Delta(p w) + 2 \nabla p \cdot \nabla w - 2 \mathcal{R}_p |\nabla p|^2 - 2 \int_0^1 R(\eta, p) \nabla \sigma \cdot \nabla p \, d\eta + \frac{2}{d} (w - \mathcal{R})^2 \\
&\quad + \int_0^1 \frac{\partial \sigma}{\partial t} R(\eta, p) \, d\eta + \mathcal{R}_p (\gamma p w + |\nabla p|^2) \\
&= \gamma \Delta(p w) + 2 \nabla p \cdot \nabla w - \mathcal{R}_p |\nabla p|^2 - 2 \int_0^1 R(\eta, p) \nabla \sigma \cdot \nabla p \, d\eta + \frac{2}{d} (w - \mathcal{R})^2 \\
&\quad + \int_0^1 \frac{\partial \sigma}{\partial t} R(\eta, p) \, d\eta + \mathcal{R}_p \gamma p w \\
&\geq \gamma \Delta(p w) + 2 \nabla p \cdot \nabla w - 2 \int_0^1 R(\eta, p) \nabla \sigma \cdot \nabla p + \frac{2}{d} (w - \mathcal{R})^2 + \int_0^1 \frac{\partial \sigma}{\partial t} R(\eta, p) \, d\eta + \mathcal{R}_p \gamma p w,
\end{aligned}$$

where in the last inequality we used that $\mathcal{R}_p \leq 0$. We recall that

$$\frac{\partial \sigma}{\partial t} = \nabla \sigma \cdot \nabla p + \sigma R(y, p) - \sigma \int_0^1 \sigma(\eta) R(\eta, p) \, d\eta.$$

We multiply by $\text{sign}_-(w)$ to obtain

$$\begin{aligned}
\frac{\partial(w)_-}{\partial t} &\leq \gamma \Delta(p(w)_-) + 2 \nabla p \cdot \nabla(w)_- - 2 \text{sign}_-(w) \int_0^1 R(\eta, p) \nabla \sigma \cdot \nabla p \, d\eta + \frac{2}{d} (w - \mathcal{R})^2 \text{sign}_-(w) \\
&\quad + \text{sign}_-(w) \int_0^1 \nabla \sigma \cdot \nabla p R(\eta, p) \, d\eta + C + \mathcal{R}_p \gamma p(w)_-,
\end{aligned}$$

where C is a constant depending on $\|R\|_\infty$.

Firstly, we multiply by $(w)_-$ and use again that $\mathcal{R}_p \leq 0$ to obtain

$$\begin{aligned}
\frac{1}{2} \frac{d}{dt} \int_\Omega (w)_-^2 \, dx &\leq \gamma \int_\Omega \Delta(p(w)_-)(w)_- \, dx + 2 \int_\Omega \nabla p \cdot \nabla(w)_- (w)_- \, dx \\
&\quad + \int_\Omega \left(\int_0^1 R(\eta, p) \nabla \sigma \cdot \nabla p \, d\eta \right) (w)_- \, dx \\
&\quad - \int_\Omega \frac{2}{d} (w)_-^3 \, dx - \frac{2}{d} \int_\Omega \mathcal{R}^2 (w)_- \, dx - \frac{4}{d} \int_\Omega (w)_-^2 \mathcal{R} \, dx + C \int_\Omega (w)_- \, dx.
\end{aligned} \tag{55}$$

We estimate the sum of the first two terms of the right-hand side.

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

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

$$\begin{aligned}
\int_0^1 \left(\int_{\Omega} R(\eta, p) \nabla \sigma \cdot \nabla p(w)_- dx \right) d\eta &= - \underbrace{\int_0^1 \int_{\Omega} R(\eta, p) \sigma \Delta p(w)_- dx d\eta}_{\mathcal{A}} \\
&\quad - \underbrace{\int_0^1 \int_{\Omega} R(\eta, p) \sigma \nabla p \cdot \nabla(w)_- dx d\eta}_{\mathcal{B}} \\
&\quad - \underbrace{\int_0^1 \int_{\Omega} R_p(\eta, p) \sigma |\nabla p|^2(w)_- dx d\eta}_{\mathcal{C}}.
\end{aligned} \tag{56}$$

Using $\Delta p = w - \mathcal{R}$ we find

$$\begin{aligned}
\mathcal{A} &= \int_{\Omega} (w)_-^2 \left(\int_0^1 R(\eta, p) \sigma d\eta \right) dx + \int_{\Omega} \mathcal{R}(w)_- \left(\int_0^1 R(\eta, p) \sigma d\eta \right) dx \\
&\leq \|\mathcal{R}\|_{\infty} \int_{\Omega} (w)_-^2 dx + \|\mathcal{R}\|_{\infty}^2 \int_{\Omega} (w)_- dx.
\end{aligned} \tag{57}$$

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 [24]. 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 5.2. Applying Young's inequality with exponents 4 and 4/3, we have

$$\mathcal{B} \leq \frac{\|\mathcal{R}\|_{\infty}}{4} \int_{\Omega} \frac{|\nabla p|^4}{p^{1-\alpha}} dx + \frac{3}{4} \int_{\Omega} p^{1-\alpha} |\nabla(w)_-|^{4/3} dx.$$

Taking $\alpha = 1/(\gamma+2)$, we know by Theorem 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

$$\frac{3}{4} \int_{\Omega} p^{1-\alpha} |\nabla(w)_-|^{4/3} dx \leq \frac{1}{2} \int_{\Omega} p^{(1-\alpha-\beta)\frac{3}{2}} |\nabla(w)_-|^2 dx + \frac{1}{4} \int_{\Omega} p^{3\beta} dx.$$

Thanks to the choices of α and β , we have

$$\mathcal{B} \leq \frac{\|\mathcal{R}\|_{\infty}}{4} \int_{\Omega} \frac{|\nabla p|^4}{p^{1-\alpha}} dx + \frac{1}{2} \int_{\Omega} p |\nabla(w)_-|^2 dx + \frac{1}{4} \int_{\Omega} p^{(\gamma-1)/(\gamma+2)} dx \leq \frac{1}{2} \int_{\Omega} p |\nabla(w)_-|^2 dx + C. \tag{58}$$

Coming back to Eq. (56) and recalling that R_p is bounded and non-positive, we obtain

$$\begin{aligned}
\mathcal{C} &\leq \|\mathcal{R}_p\|_\infty \int_\Omega (w)_- \nabla p \cdot \nabla p \, dx \\
&= -\|\mathcal{R}_p\|_\infty \int_\Omega p \nabla(w)_- \cdot \nabla p \, dx - \|\mathcal{R}_p\|_\infty \int_\Omega (w)_- p \Delta p \, dx \\
&\leq \frac{1}{2} \int_\Omega p |\nabla(w)_-|^2 \, dx + C \int_\Omega p |\nabla p|^2 \, dx + \|\mathcal{R}_p\|_\infty \int_\Omega p (w)_-^2 \, dx + \|\mathcal{R}_p\|_\infty \int_\Omega \mathcal{R}_p (w)_- \, dx \\
&\leq \frac{1}{2} \int_\Omega p |\nabla(w)_-|^2 \, dx + C.
\end{aligned} \tag{59}$$

Finally, combining Eq. (56), Eq. (57), Eq. (58) and Eq. (59) we find

$$\int_0^1 \left(\int_\Omega R(\eta, p) \nabla \sigma \cdot \nabla p (w)_- \, dx \right) d\eta \leq C \int_\Omega (w)_-^2 \, dx + C \int_\Omega (w)_- \, dx + \int_\Omega p |\nabla(w)_-|^2 \, dx + C.$$

We can finally come back to Eq. (55) to obtain

$$\begin{aligned}
\frac{1}{2} \frac{d}{dt} \int_\Omega (w)_-^2 \, dx + (\gamma - 1) \int_\Omega p |\nabla(w)_-|^2 \, dx \\
\leq C(\gamma, d) \int_\Omega (w)_-^3 \, dx + C \int_\Omega (w)_-^2 \, dx + C \int_\Omega (w)_- \, dx + C.
\end{aligned} \tag{60}$$

with $C(\gamma, d) = (1 - \frac{\gamma}{2} - \frac{2}{d})$ being negative thanks to the assumption on γ . Since we are on a compact support, by Young's inequality we have

$$C \int_\Omega (w)_- \, dx \leq \frac{C^2}{2} |\Omega| + \frac{1}{2} \int_\Omega (w)_-^2 \, dx.$$

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 [24] for the detailed proof in the two species case. Then we obtain

$$\frac{1}{2} \frac{d}{dt} \int_\Omega (w)_-^2 \, dx \leq C \int_\Omega (w)_-^2 \, dx + C,$$

and hence by Gronwall's inequality, we have

$$\sup_{0 \leq t \leq T} \int_\Omega (w(t))_-^2 \, dx \leq C \int_\Omega (w_0)_-^2 \, dx + C \leq C.$$

Finally, from Eq. (60) we also obtain

$$\iint_{\Omega_T} |\Delta p + \mathcal{R}|_-^3 \, dx \, dt \leq C(T),$$

and this concludes the proof. □

Proof of Corollary 5.1. Thanks to the Aronson-Bénilan estimate in L^2 proven above we have

$$\int_\Omega |\Delta p(t)| \, dx = \int_\Omega \Delta p(t) \, dx + 2 \int_\Omega (\Delta p(t))_- \, dx \leq C \left(\int_\Omega (\Delta p(t))_-^2 \, dx \right)^{1/2} \leq C$$

for all $t \in [0, T]$, and this completes the proof. □

Acknowledgements

This project has received funding from the European Union's Horizon 2020 research and innovation program under the Marie Skłodowska-Curie (grant agreement No 754362).

The author would like to thank Benoît Perthame for his valuable comments and suggestions throughout the preparation of this paper.

Appendix A Compensated compactness

Theorem 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 $\gamma \rightarrow \infty$, respectively. We assume that*

$$\frac{\partial u_\gamma}{\partial t} \in L^2(0, T; H^{-1}(\Omega)), \quad w_\gamma \in L^2(0, T; H^1(\Omega)).$$

Then, up a subsequence, we have

$$\iint_{\Omega_T} u_\gamma w_\gamma \varphi \, dx \, dt \xrightarrow{\gamma \rightarrow \infty} \iint_{\Omega_T} u_\infty w_\infty \varphi \, dx \, dt,$$

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

$$\begin{aligned} \iint_{\Omega_T} u_\gamma w_\gamma \varphi \, dx \, dt &= \iint_{\Omega_T} u_\gamma (w_\gamma \varphi - (w_\gamma \varphi) \star_x \psi_\varepsilon) \, dx \, dt + \iint_{\Omega_T} u_\gamma (w_\gamma \varphi) \star_x \psi_\varepsilon \, dx \, dt \\ &= \iint_{\Omega_T} \left(\int_{\mathbb{R}^d} (w_\gamma(x) \varphi(x) - w_\gamma(x - \varepsilon z) \varphi(x - \varepsilon z)) \psi(z) \, dz \right) u_\gamma \, dx \, dt \\ &\quad + \iint_{\Omega_T} (u_\gamma - u_\gamma \star_t \zeta_\sigma) (w_\gamma \varphi) \star_x \psi_\varepsilon \, dx \, dt + \iint_{\Omega_T} (u_\gamma \star_t \zeta_\sigma) (w_\gamma \varphi) \star_x \psi_\varepsilon \, dx \, dt. \end{aligned}$$

As $\gamma \rightarrow \infty$, we have

$$\iint_{\Omega_T} (u_\gamma \star_t \zeta_\sigma) (w_\gamma \varphi) \star_x \psi_\varepsilon \, dx \, dt \rightarrow \iint_{\Omega_T} u_\infty w_\infty \varphi \, dx \, dt.$$

It now remains to prove that the other terms converge to zero as $\varepsilon \rightarrow 0$ and $\sigma \rightarrow 0$. By the Fréchet-Kolmogorov theorem, we know that

$$\begin{aligned} &\int_{\Omega} |(w_\gamma \varphi)(x) - (w_\gamma \varphi)(x + k)|^2 \, dx \\ &\leq \int_{\Omega} |w_\gamma(x) (\varphi(x) - \varphi(x + k))|^2 \, dx + \int_{\Omega} |\varphi(x + k) (w_\gamma(x) - w_\gamma(x + k))|^2 \, dx \\ &\leq \omega(|k|), \end{aligned}$$

where $\omega(|k|) \rightarrow 0$ as $k \rightarrow 0$. Hence

$$\begin{aligned} &\iint_{\Omega_T} \left(\int_{\mathbb{R}^d} (w_\gamma(x) \varphi(x) - w_\gamma(x - \varepsilon z) \varphi(x - \varepsilon z)) \psi(z) \, dz \right) u_\gamma(x, t) \, dx \, dt \\ &= \int_0^T \int_{\mathbb{R}^d} \left(\int_{\Omega} (w_\gamma(x) \varphi(x) - w_\gamma(x - \varepsilon z) \varphi(x - \varepsilon z)) u_\gamma(x, t) \, dx \right) \psi(z) \, dz \, dt \\ &\leq \int_0^T \int_{\mathbb{R}^d} (\omega(\varepsilon|z|))^{1/2} \|u_\gamma(t)\|_{L^2(\Omega)} \psi(z) \, dz \, dt \rightarrow 0. \end{aligned}$$

Now we treat the last term. For the sake of brevity, let us denote $(w_\gamma\varphi)_\varepsilon := (w_\gamma\varphi) \star_x \psi_\varepsilon$

$$\begin{aligned}
\iint_{\Omega_T} (u_\gamma - u_\gamma \star_t \zeta_\sigma)(w_\gamma\varphi)_\varepsilon dx dt &= \iint_{\Omega_T} \left(\int_{\mathbb{R}} (u_\gamma(t) - u_\gamma(t - \sigma s)) \zeta(s) ds \right) (w_\gamma\varphi)_\varepsilon dx dt \\
&= \iint_{\Omega_T} \left[\int_{\mathbb{R}} \left(\int_{t-\sigma s}^t \frac{\partial u_\gamma(\tau)}{\partial t} d\tau \right) \right] (w_\gamma\varphi)_\varepsilon dx dt \\
&= \int_{\mathbb{R}} \zeta(s) \left(\int_0^T \int_{t-\sigma s}^t \int_{\Omega} \frac{\partial u_\gamma(\tau)}{\partial t} (w_\gamma\varphi)_\varepsilon dx d\tau dt \right) ds \\
&\leq \int_{\mathbb{R}} \zeta(s) \int_0^T \left(\int_{t-\sigma s}^t \left\| \frac{\partial u_\gamma(\tau)}{\partial t} \right\|_{H^{-1}(\Omega)} d\tau \right) \|(w_\gamma\varphi)_\varepsilon\|_{H^1(\Omega)} dt ds \\
&\leq C\sigma \int_{\mathbb{R}} \zeta(s) |s| \int_0^T \|(w_\gamma\varphi)_\varepsilon\|_{H^1(\Omega)} dt ds \leq C\sigma \rightarrow 0,
\end{aligned}$$

as $\sigma \rightarrow 0$.

□

Appendix B Convergence of the reaction terms

Now we prove that (16) and (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

$$\left\| R(y, p_\varepsilon) - \sum_{i=1}^N a_i(y) G_i(p_\varepsilon) \right\|_{L^\infty} \leq \delta. \quad (61)$$

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 $p_\varepsilon \rightarrow p$ strongly in $L^2(Q_T)$ as $\varepsilon \rightarrow 0$, we have

$$\begin{aligned}
\iint_{Q_T} \left(\sum_{i=1}^N \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon) d\eta \right) \varphi(x, t) dx dt &= \sum_{i=1}^N \int_0^1 \iint_{Q_T} \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon) \varphi(x, t) dx dt d\eta \\
&\xrightarrow{\varepsilon \rightarrow 0} \sum_{i=1}^N \int_0^1 \iint_{Q_T} \sigma(\eta) a_i(\eta) G_i(p) \varphi(x, t) dx dt d\eta.
\end{aligned}$$

Therefore, there exists ε_0 such that for all $\varepsilon < \varepsilon_0$

$$\iint_{Q_T} \left(\sum_{i=1}^N \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon) d\eta - \sum_{i=1}^N \int_0^1 \sigma(\eta) a_i(\eta) G_i(p) d\eta \right) \varphi dx dt \leq \delta. \quad (62)$$

We compute

$$\begin{aligned}
&\iint_{Q_T} \left(\int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta - \int_0^1 \sigma(\eta) R(\eta, p) d\eta \right) \varphi(x, t) dx dt \\
&\leq \left\| \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta - \sum_{i=1}^N \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon) d\eta \right\|_{L^\infty} \|\varphi\|_{L^1} \\
&\quad + \iint_{Q_T} \left(\sum_{i=1}^N \int_0^1 \sigma_\varepsilon(\eta) a_i(\eta) G_i(p_\varepsilon) d\eta - \sum_{i=1}^N \int_0^1 \sigma(\eta) a_i(\eta) G_i(p) d\eta \right) \varphi dx dt \\
&\quad + \left\| \sum_{i=1}^N \int_0^1 \sigma(\eta) a_i(\eta) G_i(p) d\eta - \int_0^1 \sigma(\eta) R(\eta, p) d\eta \right\|_{L^\infty} \|\varphi\|_{L^1} \leq 3\delta,
\end{aligned}$$

for $\varepsilon \leq \varepsilon_0$. Since δ was chosen arbitrarily, we conclude that

$$\mathcal{R}_\varepsilon := \int_0^1 \sigma_\varepsilon(\eta) R(\eta, p_\varepsilon) d\eta \rightharpoonup \int_0^1 \sigma(\eta) R(\eta, p) d\eta := \mathcal{R}, \quad \text{weakly}^* \text{ in } L^\infty(Q_T).$$

i.e. (16) is proven. By an analogous argument, we have

$$n_\varepsilon R(y, p_\varepsilon) \rightharpoonup nR(y, p), \quad \text{weakly}^* \text{ in } L^\infty((0, 1) \times Q_T),$$

and this concludes the proof of (17).

References

- [1] D. Alexander, I. Kim, and Y. Yao. Quasi-static evolution and congested crowd transport. *Nonlinearity*, 27(4):823–858, 2014.
- [2] L. Almeida, P. Bagnerini, G. Fabrini, B. D. Hughes, and T. Lorenzi. Evolution of cancer cell populations under cytotoxic therapy and treatment optimisation: insight from a phenotype-structured model. *ESAIM: M2AN*, 53(4):1157–1190, 2019.
- [3] A. Ardaševa, A. R. A. Anderson, R. A. Gatenby, H. M. Byrne, P. K. Maini, and T. Lorenzi. Comparative study between discrete and continuum models for the evolution of competing phenotype-structured cell populations in dynamical environments. *Phys. Rev. E*, 102(042404), 2020.
- [4] A. Ardaševa, R. A. Gatenby, A. R. A. Anderson, H. M. Byrne, P. K. Maini, and T. Lorenzi. Evolutionary dynamics of competing phenotype-structured populations in periodically fluctuating environments. *J. Math. Biol.*, 80:775–807, 2020.
- [5] D. G. Aronson and P. Bénéilan. Régularité des solutions de l’équation des milieux poreux dans \mathbf{R}^N . *C. R. Acad. Sci. Paris Sér. A-B*, 288(2):A103–A105, 1979.
- [6] O. Bénichou, V. Calvez, N. Meunier, and R. Voituriez. Front acceleration by dynamic selection in Fisher population waves. *Physical Review E*, 86:041908, 2012.
- [7] H. Berestycki, G. Nadin, B. Perthame, and L. Ryzhik. The non-local fisher-KPP equation: travelling waves and steady states. *Nonlinearity*, 22:2813, 2009.
- [8] N. Berestycki, C. Mouhot, and G. Raoul. Existence of self-accelerating fronts for a non-local reaction-diffusion equations. *ArXiv Preprint*, arXiv:1512.00903, 2015.
- [9] G. Bevilacqua, B. Perthame, and M. Schmidtchen. The Aronson-Bénéilan Estimate in Lebesgue Spaces. *Preprint*, hal-02909140, 2020.
- [10] E. Bouin, V. Calvez, N. Meunier, S. Mirrahimi, B. Perthame, G. Raoul, and R. Voituriez. Invasion fronts with variable motility: phenotype selection, spatial sorting and wave acceleration. *Comptes Rendus Mathématique*, 350:761–766, 2012.
- [11] F. Bubba, B. Perthame, C. Pouchol, and M. Schmidtchen. Hele-Shaw limit for a system of two reaction-(cross-)diffusion equations for living tissues. *Arch. Rational. Mech. Anal.*, 236:735–766, 2020.
- [12] H. M. Byrne and M. A. J. Chaplain. Growth of necrotic tumours in the presence and absence of inhibitors. *Mathematical biosciences*, 135(2):187–216, 1996.

- [13] J. A. Carrillo, S. Fagioli, F. Santambrogio, and M. Schmidtchen. Splitting schemes and segregation in reaction cross-diffusion systems. *SIAM J. Math. Anal.*, 50(5):5695–5718, 2018.
- [14] N. David, T. Dębiec, and B. Perthame. Convergence rate for the incompressible limit of nonlinear diffusion-advection equations. *arXiv:2108.00787, Accepted for publication in Annales de l’Institut Henri Poincaré C*, 2021.
- [15] N. David and B. Perthame. Free boundary limit of a tumor growth model with nutrient. *Journal de Mathématiques Pures et Appliquées*, 155:62–82, 2021.
- [16] N. David and M. Schmidtchen. On the incompressible limit for a tumour growth model incorporating convective effects. *arXiv:2103.02564, Accepted for publication in Communications on Pure and Applied Mathematics*, 2021.
- [17] T. Dębiec, B. Perthame, M. Schmidtchen, and N. Vauchelet. Incompressible limit for a two-species model with coupling through brinkman’s law in any dimension. *Journal de Mathématiques Pures et Appliquées*, 145:204–239, 2020.
- [18] T. Dębiec and M. Schmidtchen. Incompressible limit for a two-species tumour model with coupling through brinkman’s law in one dimension. *Acta Applicandae Mathematicae*, 169:593–611, 2020.
- [19] P. Gerlee and A. Anderson. Evolution of cell motility in an individual-based model of tumour growth. *Journal of Theoretical Biology*, 259:67–83, 2009.
- [20] P. Gerlee and S. Nelander. The impact of phenotypic switching on glioblastoma growth and invasion. *PLoS computational biology*, 8:e1002556, 2012.
- [21] A. Giese, R. Bjerkvig, M. Berens, and M. Westphal. Cost of migration: invasion of malignant gliomas and implications for treatment. *Journal of Clinical oncology*, 21:1624–1636, 2003.
- [22] A. Giese, M. A. Loo, N. Tran, D. Haskett, S. W. Coons, and M. E. Berens. Dichotomy of astrocytoma migration and proliferation. *International journal of cancer*, 67:275–282, 1996.
- [23] N. Guillen, I. Kim, and A. Mellet. A hele-shaw limit without monotonicity. *ArXiv preprint arXiv: 2012.02365*, 2020.
- [24] P. Gwiazda, B. Perthame, and A. Świerczewska Gwiazda. A two-species hyperbolic–parabolic model of tissue growth. *Communications in Partial Differential Equations*, 44(12):1605–1618, 2019.
- [25] I. Kim and A. R. Mészáros. On nonlinear cross-diffusion systems: an optimal transport approach. *Calc. Var. Partial Differential Equations*, 57(3):1–40, 2018.
- [26] I. Kim and N. Požár. Porous medium equation to Hele-Shaw flow with general initial density. *Trans. Amer. Math. Soc.*, 370(2):873–909, 2018.
- [27] J.-G. Liu and X. Xu. Existence and incompressible limit of a tissue growth model with autophagy. *ArXiv preprint arXiv: 2102.03844*, 2021.
- [28] T. Lorenzi, B. Perthame, and X. Ruan. Invasion fronts and adaptive dynamics in a model for the growth of cell populations with heterogeneous mobility. *European Journal of Applied Mathematics*, page 1–18, 2021.

- [29] A. Mellet, B. Perthame, and F. Quirós. A Hele-Shaw problem for tumor growth. *J. Funct. Anal.*, 273(10):3061–3093, 2017.
- [30] B. Perthame, F. Quirós, and J. L. Vázquez. The Hele-Shaw asymptotics for mechanical models of tumor growth. *Arch. Ration. Mech. Anal.*, 212(1):93–127, 2014.
- [31] B. Perthame, F. Quirós, M. Tang, and N. Vauchelet. Derivation of a Hele-Shaw type system from a cell model with active motion. *Interfaces Free Bound.*, 16(4):489–508, 2014.
- [32] B. Perthame and N. Vauchelet. Incompressible limit of a mechanical model of tumour growth with viscosity. *Philos. Trans. Roy. Soc. A*, 373(2050):20140283, 16, 2015.
- [33] B. C. Price and X. Xu. Global existence theorem for a model governing the motion of two cell populations. *arXiv preprint arXiv:2004.05939*, 2020.