Nonlocal models in cell migration

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Abstract

Experimental evidence suggests that cells can perceive signals not only at their actual location but also within a large neighborhood compared to the cell size. These biochemical and biophysical cues influence the migration, proliferation, and differentiation of cells. In this work, we examine four nonlocal models describing the movement of cell populations. These models are represented by reaction-diffusion(-advection) equations containing nonlocal spatial integral terms that describe the influence of the surroundings on the development of the cell population. Our focus is on the mathematical analysis of these models. Numerical simulations are performed to illustrate the solution behavior.

First, we consider two models, in which the gradient in the advection term of the respective local model is replaced by a nonlocal integral. For the first adhesion or nonlocal chemotaxis model, we show convergence of the weak solution to the weak solution of the corresponding local haptotaxis or chemotaxis model, respectively, as the sensing radius decreases. Then, we show the existence of a very weak solution for the second cell-cell-adhesion model with degenerated myopic diffusion.

Furthermore, we consider two models with a nonlocality in the reaction term. Specifically, for a model for cancer invasion with myopic diffusion, repellent pH-taxis, and nonlocal intraspecific interaction, we show the global existence of a bounded unique weak solution and visualize its behavior with numerical simulations. Additionally, we perform a 1D pattern analysis. Finally, we show the global existence of a bounded weak solution for a model with two nonlocal interaction terms and perform numerical simulations.

Zusammenfassung

Experimente haben nachgewiesen, dass Zellen Signale nicht nur an ihrer Position empfangen können, sondern innerhalb eines im Vergleich zur Zellgröße großen Wahrnehmungsradius. Diese biochemischen und biophysischen Signale beeinflussen die Bewegung, Proliferation und Differenzierung von Zellen. In dieser Arbeit betrachten wir vier nichtlokale Modelle, die die Bewegung von Zellpopulationen beschreiben. Die Nichtlokalität wird mittels eines nichtlokalen Raumintegrals modelliert, das in verschiedenen Termen der betrachteten Reaktions-Diffusions-(Advektions-) Gleichungen enthalten ist. Der Fokus liegt dabei auf der mathematischen Analyse dieser Modelle. Auch numerische Simulationen werden durchgeführt, um das Verhalten der Lösung zu veranschaulichen.

Wir betrachten zwei Modelle, in denen der Gradient im Advektionsterm durch ein nichtlokales Integral ersetzt wird. Zuerst zeigen wir die Konvergenz der schwachen Lösung eines Modells, das Adhesion oder nichtlokale Chemotaxis beschreibt, gegen die schwache Lösung des jeweils entsprechenden lokalen Haptoxis- oder Chemotaxismodells für einen verschwindenden Wahrnehmungsradius. Anschließend zeigen wir die Existenz einer sehr schwachen Lösung eines Modells für Zell-Zell-Adhesion mit degenerierter myopischer Diffusion.

Darüber hinaus betrachten wir zwei Modelle mit Nichtlokalität im Reaktionsterm. Wir zeigen die globale Existenz einer eindeutigen beschränkten Lösung eines Modells für Krebsinvasion mit myopischer Diffusion, abstoßender pH-Taxis und einem nichtlokalen innerartlichen Interaktionsterm und eines Modells mit zwei nichtlokalen Interaktionstermen. Das Verhalten der jeweiligen Lösung wird mithilfe von numerischen Simulationen veranschaulicht. Darüber hinaus analysieren wir für eines der Modelle das Auftreten von Mustern in 1D.

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CHAPTER 1

Introduction

In this dissertation, we investigate nonlocal models in cell migration. In recent decades these models have attracted increasing interest, see the review [28]. They reflect the ability of cells to receive environmental signals within a sensing region surrounding their current position. These signals can impact multiple processes, including cell migration. The nonlocal approach is suggested by experimental evidence and appears more realistic, as cells are surrounded by other cells and tissue. In certain contexts, the reduced consideration of these effects by local models could be oversimplifying and can lead to analytical and modeling problems. While there are many studies of local models, nonlocal models have been considered far less often, especially from an analytical point of view. However, the nonlocal models provide a biologically plausible description of certain processes involved in cell migration and, as we discuss later, can avoid in certain situations analytical problems of local models, such as finite-time blow-up of the solution.

The orientation of directional migration of cells is largely influenced by the extracellular environment and primarily determined by protrusions (e.g., filopodia, lamellipodia) which are outward extensions of the cell membrane. Cells respond to external diffusible and non-diffusible signals by extending protrusions in the direction of movement [86]. The main functions of protrusions include sampling the cell's environment and establishing initial dynamic adhesions to the extracellular matrix (ECM) or other cells within a sensing region that can be large compared to the cell size [1, 71, 90, 130]. Furthermore, protrusions are involved in the communication of cells over long distances, thereby transmitting signals [17, 57, 87]. The information obtained via protrusions influences the subsequent behavior of the cell, e.g., the choice of the following direction of migration [1, 122]. In areas with hard borders, such as bones, cartilage, or the walls of a Petri dish, cells receive hardly any information from outside, as the ability of cells to stretch their protrusions outwards is limited there [28].

After sampling their environment cells form cell-matrix or cell-cell adhesions to move [35, 86, 152]. The adhesion of cells to the ECM is facilitated by the attachment of specific cell receptors (e.g., integrins) to tissue fibers [38, 152]. Besides, cells adhere to other cells by binding specific cell adhesion molecules (cadherins) on the cell surface [96], which also enables the formation of cell clusters. This process is essential in organizing cells into tissue, organs, and organisms [5, 66]. The strength and number of bindings depend on chemical signals [68]. Both adhesion structures are often dynamic to allow cells to react to changes in environmental cues [34]. In addition to their role in cell movement, they are essential for embryonic development, homeostasis, immune responses, wound healing, and cell sorting [5, 34, 152]. Hence, nonlocal models align with many biological observations and empirically collected data [97].

Apart from this, nonlocal models can solve mathematical inconsistencies present in some local models, such as a finite-time blow-up that is unrealistic from a biological point of view. For example, in [79], the authors show that the considered nonlocal model has a bounded global solution, while a finite-time blow-up occurs in the corresponding local model. Thereby, the solutions of the nonlocal models have increasingly larger peaks in numerical simulations for diminishing sensing regions. It is assumed that the behavior of nonlocal models with a parameter whose reduction leads to a vanishing sensing region can be approximated by the corresponding local model [68, 79]. Related local and nonlocal models include chemotaxis, which refers to migration in response to differences in the concentration of a soluble signal, and nonlocal chemotaxis, which takes into account that migrating cells can detect this signal within a sensing region. Besides, haptotaxis referring to the migration of cells in response to different concentrations of a bound signal is the local counterpart to cell-matrix (and cell-cell) adhesion. Nonlocal and local models can also exhibit different behavior in other contexts, e.g., in the occurrence of Turing patterns [111]. Continuous local models are often incompatible with biological effects such as sorting, while nonlocal models can replicate this effect [5].

Typically, nonlocal models include a spatial integral that increases the regularity of the equation; however, nonlocalities can also be introduced with respect to other variables (e.g., time, speed). Nevertheless, these models are mathematically challenging, as comparison principles to show the biologically important boundedness of solutions do not hold for this type of equation. Further challenges arise if the nonlocal equation is coupled with other differential equations, especially if the involved equations have a different type. A numerical simulation of the integral terms is numerically costly and requires efficient numerical methods to deal with them. Additionally, a unifying analytical framework that could deal with different kinds of nonlocal terms could be advantageous. Up to our knowledge, no such framework exists, as the analysis strongly depends on the specific form of the nonlocality.

Moreover, spatially nonlocal (and local) models describing the migration of a cell population u are usually of reaction-diffusion-advection (RDA) type, i.e., of the form

$$u_t = \underbrace{\nabla \cdot (D\nabla u)}_{\text{diffusion}} - \underbrace{\nabla \cdot (vu)}_{\text{advection}} + \underbrace{f(u)}_{\text{reaction}},$$

possibly coupled with further dynamics. Here, D denotes the diffusion coefficient, v the advection velocity, and $f(u)$ a reaction function. Most nonlocal models consider RDA-equations with nonlocality in the advection term describing cell-cell or cell-matrix adhesion or nonlocal chemotaxis. Examples of such adhesion models can be found in [5, 21, 23, 68, 80, 156] and for nonlocal chemotaxis in [21, 79]. The solvability of models with nonlocal advection term was studied in [45, 46, 56, 79, 80, 82, 128]. Moreover, there are few studies on the existence and long-time behavior of solutions to local models including potentially degenerating myopic diffusion and taxis. Most studies feature haptotaxis and consider only the one-dimensional case [77, 149–151].

Less studied models contain nonlocalities in the source term. This term impacts cell movement indirectly since the evolving cell density leads to modified density-dependent coefficients. Possible applications are competition for resources, differentiation, proliferation, and growth; see [28, 99] and references therein. Examples of the modeling and analysis of this kind of problems can be found in [12–14, 99, 103, 104, 113, 136] but even for comparatively easy settings there are no complete results involving existence, boundedness, pattern formation, numerical simulations, etc. of solutions. We refer to [28, 51, 87] for more detailed reviews on these and other types of nonlocal models.

In the present work, we examine four nonlocal models with no-flux boundary conditions in bounded domains and describing the movement of cell populations. The nonlocality is modeled via a density-dependent spatial integral included in the advection (*Chapters 3* and *4*) or reaction term (*Chapters 5* and *6*) of a reaction-diffusion(-advection) equation. Our focus is on the mathematical analysis of the models. Additionally we perform a 1D pattern analysis in *Chapter 5* and numerical simulations in *Chapters 3*, *5*, and *6* to visualize the results.

The convergence of the nonlocal operators to the local gradient presented in *Chapter 3* was shown heuristically via Taylor expansion in [68, 81]. In [79], the question of convergence of nonlocal models to its local counterpart was raised. However, up to our knowledge, a rigorous proof of convergence has not been established before. Moreover, the combination of myopic diffusion and adhesion has not been analyzed so far. Therefore, our existence proof for a solution to the degenerated PDE in *Chapter 4* significantly contributes to this new field. Notably, our assumptions regarding the degeneracy set seem new in the context of degenerated diffusion. Furthermore, the existence proof and the analysis of the long-time behavior and pattern formation of solutions to the model in *Chapter 5* contribute to the rarely studied field of models that feature nonlocality in the source term and models involving myopic diffusion and advection. There, we add to the existing literature the analysis of a PDE-PDE-system, one of the PDEs combining myopic diffusion and advection with a nonlocality in the source term. Also, considering a PDE with (two) nonlocalities in the source term coupled with an ODE from *Chapter 6* is novel.

Outline

The first part of this thesis deals with nonlocal models with nonlocality in the advection term describing cell-cell or cell-matrix adhesion or nonlocal chemotaxis. Thereby, we consider models with adhesion velocity of the form

$$\mathcal{A}_r u(x) = \frac{1}{r}\int_{B_r} u(x+\xi)\frac{\xi}{|\xi|}F_r(|\xi|)\,d\xi,$$

where u denotes some interaction function taking into account cell-cell and cell-matrix interactions and depends on the cell and tissue density. The magnitude of the interaction force F_r depends on the distance within the sensing region B_r, where r is called sensing radius. In the case of nonlocal chemotaxis, we consider a similar integral (over a sphere), where the interaction function depends on the concentration of some dissolved chemical signal.

This part consists of two chapters:

- *Chapter 3* considers a PDE-ODE-system describing adhesion and a PDE-PDE-system for nonlocal chemotaxis including the aforementioned operators. The adhesion model is related to its local counterpart characterizing haptotaxis by replacing the gradient of the cell-cell and cell-matrix interaction function u by $\mathcal{A}_r u$. Similarly, we relate nonlocal chemotaxis to chemotaxis. We show the existence of a global weak-strong solution to each of the nonlocal models and link it via a limit procedure for a diminishing sensing radius to the weak solution of the corresponding local model. Our proof relies on a reformulation of the involved nonlocal operator as an integral operator that is applied directly to the gradient of the interaction function. Both types of models are treated in a unified framework. Numerical simulations in 1D are cited for completeness reasons. This chapter is largely based on [47].

· *Chapter 4* shows the existence of a global very weak solution to a nonlocal reaction-diffusion-advection equation including degenerated myopic diffusion, cell-cell adhesion, and a generalized logistic-type growth term in dimensions $n \geqslant 3$. Thereby, the degeneracy set is sufficiently low-dimensional (in terms of upper box fractal dimension) and has a positive distance to the boundary of the domain. We deal with the nonlocal operator upon rewriting it to a convolution with a bounded function. The corresponding equation without growth term was derived in [156]. Besides its biological foundation, we included the growth term to deal with analytical challenges arising especially from the degeneracy of the diffusion tensor. This chapter is largely based on [50].

The second part of this dissertation deals with models involving nonlocality in the reaction term. The nonlocal terms are of the form

$$u^\alpha(1 - J_1 * u^\beta - J_2 * w^\gamma)(x) = u^\alpha(x)\left(1 - \int_\Omega J_1(x-y)u^\beta(y)\,\mathrm{d}y - \int_\Omega J_2(x-y)w^\gamma(y)\,\mathrm{d}y\right)$$

with $J_1 > 0$ and $J_2 \geqslant 0$, where u and w denote the density of two cell populations. Such terms describe intra- and interspecific competition between cells for available resources in their surrounding, e.g., to prevent overcrowding. The assumption of strict positivity of J_1 and the integration over the whole domain indicate that the sensing region of a cell corresponds to the whole domain independent from its position.

This part consists of two chapters:

· *Chapter 5* shows the existence of a unique global bounded weak solution to a PDE-PDE-model for tumor cell migration with myopic diffusion, repellent pH-taxis, and a nonlocal source term of the above form. Moreover, we analyze the asymptotic behavior of the solution. In 1D we perform a pattern analysis for constant diffusion and numerical simulations to illustrate the behavior of the solution. The model deduction based on a mesoscopic description of cell migration with a kinetic transport equation is included for completeness. Our results extend [99], where a Fischer-KPP-equation with nonlocal intraspecific competition (but in an unbounded domain) was examined. This chapter is largely based on [49].

· In *Chapter 6* we prove the existence of a global bounded weak solution to a PDE-ODE-PDE-system describing the dynamics of active and inactive cells and a repellent signal. It has two nonlocalities in an equation, one of them depending on another cell population. Moreover, both nonlocalities depend on the signal produced by both cell populations. Also numerical simulations are performed. This chapter is largely based on [48].

The dissertation is structured as follows. *Chapter 2* contains the mathematical preliminaries of this work and introduces the relevant function spaces, convolutions in bounded domains, and notation. The notation may differ slightly from chapter to chapter, as this work consists of four independently considered models. *Chapters 3–6* begin each with a motivation, in which the biological context and the underlying literature of the concrete model are mentioned. Finally, *Chapter 7* provides a brief summary of this work along with some perspectives.

CHAPTER 2

Preliminaries

In this chapter, we introduce the notation and recall mostly without proof some facts concerning matrices, the relevant function spaces and convolutions in bounded domains. More details on these topics can be found e.g., in [20, 58, 84, 94]. Relevant results on different types of differential equations, fixed-point theorems, convergence theorems and functional analysis and the proofs of some lemmas from this chapter can be found in Appendix A.

Notation:

- Throughout this work we consider a bounded domain $\Omega \subset \mathbb{R}^n$, $n \in \mathbb{N}$, with sufficiently smooth boundary $\partial\Omega$ and outer unit normal ν.
- For $r > 0$ we introduce the subdomain $\Omega_r := \{x \in \Omega \ : \ \operatorname{dist}(x, \partial\Omega) > r\}$ of Ω.
- For a function $u : \Omega \to \mathbb{R}$ we assume, by convention, that $u \equiv 0$ on $\mathbb{R}^n \backslash \overline{\Omega}$. This allows for an obvious meaning to be given to the convolution $u * v$ for any $u \in L^1(\Omega)$ and $v \in L^1(\mathbb{R}^n)$. This extends componentwise to any vector-/matrix-valued function u.
- We denote by e_i, $i \in \mathbb{N}$, the ith canonical vector in $\mathbb{R}^n$ and by $I_n \in \mathbb{R}^{n\times n}$ the identity matrix.
- By $|\cdot|$ and $|\cdot|_\infty$ we denote the Euclidean and infinity norms in $\mathbb{R}^n$, respectively, and by $|A|$ the Lebesgue measure of a set A.
- For $x \in \mathbb{R}^n, n \geqslant 2$ we denote $x = (x', x_n)$, where $x' \in \mathbb{R}^{n-1}$ and $x_n \in \mathbb{R}$.
- For $A, B \subset \mathbb{R}^n$, $a \in \mathbb{R}^n$, and $s > 0$ we use the set notations

$$\begin{aligned} A + B &:= \{x + y : \ x \in A, \ y \in B\}, \\ a + B &:= B + a := \{a\} + B, \\ O_s(A) &:= \{x \in \mathbb{R}^n : \ \operatorname{dist}(x, A) < s\}. \end{aligned}$$

- By B_r and S_r, $r > 0$, we denote the open r-ball and the r-sphere in $\mathbb{R}^n$, both centred at the origin, and define the mean values of a function u over B_r and S_r, respectively, as

$$\begin{aligned} \fint_{B_r} u(\xi)\, d\xi &:= \frac{1}{|B_r|} \int_{B_r} u(\xi)\, d\xi, \\ \fint_{S_r} u(\xi)\, d\xi &:= \frac{1}{|S_r|} \int_{S_r} u(\xi)\, d\sigma(\xi), \end{aligned}$$

where $\sigma(\cdot)$ denotes the surface measure corresponding to the Lebesgue measure on $\mathbb{R}^n$.

- For all indices $i \in \mathbb{N}$, the quantities C_i, K_i, ε_i denote a positive constant or, alternatively, a positive function of its arguments. The constants C_i and ε_i are numbered chapter by chapter, while K_i denotes the constants from Appendix A. Dependencies upon such parameters as the space dimension n, domain Ω, the norms of the initial data, norms and bounds for the coefficient functions and parameters are mostly **not** indicated in an explicit way.

2.1 Matrices

In this section we summarize some definitions and properties of matrices.

Definition 2.1.1. *Let $P = (p_{ij})_{i,j=1,\ldots,n}, Q = (q_{ij})_{i,j=1,\ldots,n} \in \mathbb{R}^{n\times n}$. We define the following norms and inner product:*

- *the spectral norm $|P|_2 := |P| := \max_{|x|=1} |Px| = \sqrt{\lambda_{\max}(P^T P)}$, where $\lambda_{\max}$ denotes the maximal eigenvalue of a matrix,*
- $|P|_\infty := \max_{|x|_\infty=1} |Px|_\infty = \max_{i=1,\ldots,n} \sum_{j=1}^n |p_{ij}|$,
- *the Frobenius inner product*

$$P : Q = \sum_{i,j=1}^{n} p_{ij} q_{ij}.$$

If not states otherwise we will use the $|\cdot|_2$-norm for matrices.

These norms obviously satisfy the following lemma.

Lemma 2.1.2. *(i) The norms $|\cdot|_2$ and $|\cdot|_\infty$ are equivalent on $\mathbb{R}^{n\times n}$.*

(ii) Let $P = (p_{ij})_{i,j=1,\ldots,n} \in \mathbb{R}^{n\times n}$. Then, $|p_{ij}| \leqslant |P|_2$ for all $i, j = 1, \ldots, n$.

Further, we recall some facts on orthogonal matrices.

Lemma 2.1.3. *Consider an orthogonal matrix $O \in \mathbb{R}^{n\times n}$, i.e., satisfying $OO^T = O^T O = I_n$. Then, $|Ox| = |x|$ for all $x \in \mathbb{R}^n$ and $|det(O)| = 1$.*

Moreover, we introduce the following two definitions on matrix functions (see *Definition 2.2.1* for the definition of the involved spaces).

Definition 2.1.4. *For a matrix function $\mathbb{D} = (d_{ij})_{i,j=1,\ldots,n} \in C(\overline{\Omega}; \mathbb{R}^{n\times n})$ we write $\mathbb{D} > c$ if $y^T \mathbb{D}(x) y > c$ for all $x \in \overline{\Omega}$ and $y \in \mathbb{R}^n$ (analogously for $\geqslant, <, \leqslant$). Further, for $\mathbb{D} \geqslant 0$ we define the set*

$$\{\mathbb{D} \not> 0\} := \{x \in \overline{\Omega} : \exists y \in \mathbb{R}^n \text{ s.t. } y^T \mathbb{D}(x) y = 0\}.$$

Definition 2.1.5. *For a matrix function $\mathbb{D} = (d_{ij})_{i,j=1,\ldots,n} \in C(\overline{\Omega}; \mathbb{R}^{n\times n})$ and a function $u \in C^2(\overline{\Omega})$ we define*

· *the divergence*

$$\nabla \cdot \mathbb{D}(x) = \sum_{i,j=1}^{n} (d_{ij})_{x_j}(x) e_i$$

· *and the myopic diffusion*

$$\nabla\nabla : (\mathbb{D}(x)u) = \nabla \cdot (\mathbb{D}(x)\nabla u + \nabla \cdot \mathbb{D}(x)u).$$

2.2 Function spaces

In this section we recall the definitions of certain spaces of continuous functions and Lebesgue and Sobolev spaces in x and t and some of their properties.

First, we define several spaces of continuous and Hölder continuous functions.

Definition 2.2.1. *Let $k \in \mathbb{N}$, $j \in \mathbb{N} \cup \{\infty\}$, $l, m \in \mathbb{N}_0 \cup \{\infty\}$, $T > 0$, $S \subset \mathbb{R}^k$ nonempty and compact, $I \subset \mathbb{R}$ a nonempty interval and X a normed vector space with norm $\|\cdot\|_X$. We define the spaces*

· *$C(S; X)$ of continuous functions $u : S \to X$,*

· *$C^j(S; X)$ of j-times continuously differentiable functions $u : S \to X$,*

· *$C^{l,m}(S \times I; X)$ of functions $u : S \times I \to X$ that are l-times continuously differentiable in $x \in S$ and m-times continuously differentiable in $t \in I$,*

· *$C_c^j(S)$ of functions from $C^j(S; \mathbb{R})$ with compact support,*

· *$C_b(S)$ of functions from $C(S; \mathbb{R})$ that are bounded,*

· *$C_w([0, T]; X)$ of functions $u : [0, T] \to X$ which are continuous w.r.t. the weak topology of X.*

If $X = \mathbb{R}$ we leave out the dependence on $\mathbb{R}$ in the notation of the space. If S is closed and $j < \infty$, we define the norms

$$\|u\|_{C(S;X)} := \max_{x \in S} \|u(x)\|_X,$$
$$\|u\|_{C^j(S;X)} := \sum_{|\alpha| \leqslant j} \|D^\alpha u\|_X.$$

Definition 2.2.2. *Let $\vartheta \in (0, 1]$, $k \in \mathbb{N}_0$ and $T > 0$. We define the seminorms*

$$\langle u \rangle_{\Omega}^{\vartheta} := \sup_{x,y \in \overline{\Omega}, x \neq y} \frac{|u(x) - u(y)|}{|x - y|^\vartheta},$$
$$\langle u \rangle_{x,\overline{\Omega} \times [0,T]}^{\vartheta} := \sup_{(x,t),(y,t) \in \overline{\Omega} \times [0,T], x \neq y} \frac{|u(x, t) - u(y, t)|}{|x - y|^\vartheta},$$
$$\langle u \rangle_{t,\overline{\Omega} \times [0,T]}^{\vartheta} := \sup_{(x,t),(x,s) \in \overline{\Omega} \times [0,T], t \neq s} \frac{|u(x, t) - u(x, s)|}{|t - s|^\vartheta}.$$

and the following Hölder spaces

- $C^{k+\vartheta}(\overline{\Omega})$ *as the space of functions* $u \in C^k(\overline{\Omega})$ *with finite norm*

$$||u||_{C^{k+\vartheta}(\overline{\Omega})} := \sum_{|\alpha|\leqslant k} ||D^\alpha u||_{C(\overline{\Omega})} + \sum_{|\alpha|=k} \langle D^\alpha u\rangle_{\overline{\Omega}}^{\vartheta},$$

- $C^{k+\vartheta}(\Omega)$ *as the space*

$$C^{k+\vartheta}(\Omega) := \left\{u : \Omega \to \mathbb{R} : u\big|_K \in C^{k+\vartheta}(K)\, \forall K \subset \Omega \text{ compact}\right\}. \tag{2.2.1}$$

- $C^{\vartheta,\frac{\vartheta}{2}}\left(\overline{\Omega}\times[0,T]\right)$ *as the space of functions* $u \in C\left(\overline{\Omega}\times[0,T]\right)$ *that are* ϑ*-Hölder continuous in* x *and* $\frac{\vartheta}{2}$*-Hölder continuous in* t*, i.e., with finite norm*

$$||u||_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} := ||u\|_{C(\overline{\Omega}\times[0,T])} + \langle u\rangle_{x,\overline{\Omega}\times[0,T]}^{\vartheta} + \langle u\rangle_{t,\overline{\Omega}\times[0,T]}^{\frac{\vartheta}{2}},$$

- $C^{1+\vartheta,\frac{1+\vartheta}{2}}(\overline{\Omega}\times[0,T])$ *as the space of functions* $u \in C^{1,0}(\overline{\Omega}\times[0,T])$ *with finite norm*

$$\begin{aligned}||u||_{C^{1+\vartheta,\frac{1+\vartheta}{2}}(\overline{\Omega}\times[0,T])} &:= ||u\|_{C(\overline{\Omega}\times[0,T])} + \langle u\rangle_{t,\overline{\Omega}\times[0,T]}^{\frac{1+\vartheta}{2}} \\ &\quad + \sum_{i=1}^{n}\left(||u_{x_i}\|_{C(\overline{\Omega}\times[0,T])} + \langle u_{x_i}\rangle_{x,\overline{\Omega}\times[0,T]}^{\vartheta} + \langle u_{x_i}\rangle_{t,\overline{\Omega}\times[0,T]}^{\frac{\vartheta}{2}}\right),\end{aligned}$$

- $C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])$ *as the space of functions* $u \in C^{2,1}\left(\overline{\Omega}\times[0,T]\right)$ *with finite norm*

$$\begin{aligned}&||u||_{C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} \\ :=&||u\|_{C(\overline{\Omega}\times[0,T])} + ||u_t\|_{C(\overline{\Omega}\times[0,T])} + \langle u_t\rangle_{x,\overline{\Omega}\times[0,T]}^{\vartheta} + \langle u_t\rangle_{t,\overline{\Omega}\times[0,T]}^{\frac{\vartheta}{2}} \\ &+ \sum_{i=1}^{n}\left(||u_{x_i}\|_{C(\overline{\Omega}\times[0,T])} + \langle u_{x_i}\rangle_{t,\overline{\Omega}\times[0,T]}^{\frac{1+\vartheta}{2}}\right) \\ &+ \sum_{i,j=1}^{n}\left(||u_{x_ix_j}\|_{C(\overline{\Omega}\times[0,T])} + \langle u_{x_ix_j}\rangle_{x,\overline{\Omega}\times[0,T]}^{\vartheta} + \langle u_{x_ix_j}\rangle_{t,\overline{\Omega}\times[0,T]}^{\frac{\vartheta}{2}}\right).\end{aligned}$$

- *For* $k = 0, 1, 2$ *we define* $C^{k+\vartheta,\frac{k+\vartheta}{2}}(\Omega\times(0,T))$ *and* $C^{k+\vartheta,\frac{k+\vartheta}{2}}(\overline{\Omega}\times(0,T))$ *analogously to* (2.2.1).

The lemmas below will be proved in the appendix.

Lemma 2.2.3. *Let* $\vartheta, \kappa \in (0,1)$*,* $u \in C^{\vartheta}(\overline{\Omega})$ *and* $v \in C^{\kappa}(\overline{\Omega})$*. Then,*

(i) $uv \in C^{\min\{\vartheta,\kappa\}}(\overline{\Omega})$,

(ii) if $u \geqslant 0$ *then* $u^r \in C^{\vartheta r}(\overline{\Omega})$ *if* $r \in (0,1)$,

(iii) if $u \geqslant 0$ *then* $u^r \in C^{\vartheta}(\overline{\Omega})$ *if* $r > 1$,

(iv) $\frac{1}{u} \in C^{\vartheta}(\overline{\Omega})$ *if* $u \neq 0$ *in* $\overline{\Omega}$.

Next, we define Lebesgue and Sobolev spaces and introduce dual pairings.

Definition 2.2.4. *Let* $p \in [1,\infty]$*. We define* $L^p(\Omega)$ *as the space of functions* $u : \Omega \to \mathbb{R}$ *with finite norm*

$$\|u\|_{L^p(\Omega)} := \begin{cases} \left(\int_\Omega |u|^p \, dx\right)^{\frac{1}{p}}, & \text{if } p \in [1,\infty), \\ \operatorname{ess\,sup}_{x\in\Omega} |u|, & \text{if } p = \infty. \end{cases}$$

Further, we define $(L^p(\Omega))^n$ and $(L^p(\Omega))^{n\times n}$, respectively, as the space of vector-valued functions $f : \Omega \to \mathbb{R}^n$ or matrix-valued functions $\mathbb{D} : \Omega \to \mathbb{R}^{n\times n}$ with finite norms

$$\begin{aligned}\|f\|_{(L^p(\Omega))^n} &:= \||f|\|_{L^p(\Omega)},\\ \|\mathbb{D}\|_{(L^p(\Omega))^{n\times n}} &:= \||\mathbb{D}|_2\|_{L^p(\Omega)},\end{aligned}$$

and for $T > 0$ and a Banach space X with norm $\|\cdot\|_X$ we define the Bochner space $L^p(0, T; X)$ as the space of functions $g : (0, T) \to X$ with finite norm

$$\|g\|_{L^p(0,T;X)} := \begin{cases} \left(\int_0^T \|g(t)\|_X^p \, dt\right)^{\frac{1}{p}}, & \text{if } p \in [1, \infty),\\ \operatorname{ess\,sup}_{t\in(0,T)} \|g(t)\|_X, & \text{if } p = \infty.\end{cases}$$

Definition 2.2.5. *Let X a Banach space with dual space X^*. We denote the duality pairing of $x \in X$ and $x^* \in X^*$ as*

$$\langle x^*, x\rangle_{X^*,X} := x^*(x) \in \mathbb{R}.$$

A sequence $(x_k)_{k\in\mathbb{N}} \subset X$ converges weakly to $x \in X$ in X if

$$\langle x^*, x_k\rangle_{X^*,X} \underset{k\to\infty}{\to} \langle x^*, x\rangle_{X^*,X}$$

for all $x^* \in X^*$. We denote this by $x_k \underset{k\to\infty}{\rightharpoonup} x$.
A sequence $(x_k^*)_{k\in\mathbb{N}} \subset X^*$ converges weakly- to $x^* \in X^*$ in X^* if*

$$\langle x_k^*, x\rangle_{X^*,X} \underset{k\to\infty}{\to} \langle x^*, x\rangle_{X^*,X}$$

for all $x \in X$. We denote this by $x_k^* \overset{*}{\underset{k\to\infty}{\rightharpoonup}} x^*$.

Definition 2.2.6. *Let $k \in \mathbb{N}$ and $p \in [1, \infty]$. The Sobolev space $W_p^k(\Omega)$ is given by*

$$\begin{aligned}W_p^k(\Omega) := \{u \in L^p(\Omega) :\ & \text{the weak derivative } D^\alpha u \text{ exists for all } \alpha \in \mathbb{N}_0^n \text{ s.t. } |\alpha| \leqslant k\\ & \text{and } D^\alpha u \in L^p(\Omega)\}\end{aligned}$$

with norm

$$||u||_{W_p^k(\Omega)} := \sum_{|\alpha|\leqslant k} ||D^\alpha u||_{L^p(\Omega)}.$$

Moreover, we set

$$\overset{\circ}{W}{}_p^k(\Omega) := \left\{u \in W_p^k(\Omega) : \exists (u_m)_m \subset C_c^\infty(\Omega) \text{ s.t. } u_m \underset{m\to\infty}{\to} u \text{ in } W_p^k(\Omega)\right\}$$

with dual space

$$W_q^{-k}(\Omega) := \left(\overset{\circ}{W}{}_p^k(\Omega)\right)^*$$

for $q \in [1, \infty]$ s.t. $\frac{1}{p} + \frac{1}{q} = 1$.

For $p = 2$ we set $H^k(\Omega) := W_2^k(\Omega)$, $H_0^k(\Omega) := \overset{\circ}{W}{}_2^k(\Omega)$ and $H^{-1} := (H_0^1(\Omega))^*$.

Further, we define the spaces

$$
\begin{aligned}
W_p^{1,1}(\Omega \times (0,T)) &:= \{u \in L^p(\Omega \times (0,T)) : u_{x_i}, u_t \in L^p(\Omega \times (0,T))\ \forall i \in \{1,\dots,n\}\} \\
W_p^{2,1}(\Omega \times (0,T)) &:= \{u \in L^p(\Omega \times (0,T)) : u_{x_i}, u_{x_ix_j}, u_t \in L^p(\Omega \times (0,T)) \\
&\qquad\qquad \forall i,j \in \{1,\dots,n\}\}
\end{aligned}
$$

with norm

$$
\begin{aligned}
||u||_{W_p^{1,1}(\Omega\times(0,T))} :=& ||u||_{L^p(\Omega\times(0,T))} + ||u_t||_{L^p(\Omega\times(0,T))} + \sum_{i=1}^n ||u_{x_i}||_{L^p(\Omega\times(0,T))}, \\
||u||_{W_p^{2,1}(\Omega\times(0,T))} :=& ||u||_{L^p(\Omega\times(0,T))} + ||u_t||_{L^p(\Omega\times(0,T))} + \sum_{i=1}^n ||u_{x_i}||_{L^p(\Omega\times(0,T))} \\
&+ \sum_{i,j=1}^n ||u_{x_ix_j}||_{L^p(\Omega\times(0,T))}.
\end{aligned}
$$

We define continuous and compact embeddings and state some embeddings concerning Sobolev spaces.

Definition 2.2.7. *Let X, Y be Banach spaces s.t. $X \subset Y$. We say that X is continuously embedded in Y (denoted by $X \hookrightarrow Y$) if there is a constant $C_1 > 0$ s.t. for all $u \in X$ the estimate $||u||_Y \leqslant C_1||u||_X$ holds. A continuous embedding is called compact (denoted by $X \hookrightarrow\hookrightarrow Y$) if each bounded sequence $(u_m)_{m\in\mathbb{N}} \subset X$ has a subsequence that converges in Y.*

Lemma 2.2.8. *(i) The space $H^1(\Omega)$ is continuously embedded in $L^p(\Omega)$, where $p \in [1,\infty]$ if $n = 1$, $p \in [1,\infty)$ if $n = 2$ and $p \in [1, \frac{2n}{n-2}]$ if $n > 2$. For such p there is a constant $K_S(p) > 0$ s.t. for all $u \in H^1(\Omega)$ it holds that*

$$\|u\|_{L^p(\Omega)} \leqslant K_S(p)\|u\|_{H^1(\Omega)}.$$

(ii) If $p > n$ then $W_p^1(\Omega)$ is continuously embedded in $C^\vartheta(\overline{\Omega})$ (up to the choice of a continuous version) for $\vartheta = \left\lfloor \frac{n}{p} \right\rfloor + 1 - \frac{n}{p}$.

(iii) If $p > n$ then $W_p^2(\Omega) \hookrightarrow C^1(\overline{\Omega})$ and $u = 0$ and $\nabla u = 0$ on $\partial\Omega$ for $u \in \overset{\circ}{W}{}_p^2(\Omega)$.

(iv) For $p \in (1,\infty)$ the compact embedding $W_p^1(\Omega) \hookrightarrow\hookrightarrow L^p(\Omega)$ holds.

Proof. For *(i)* and *(ii)* see Theorem 6 in Section 5.6 in [58] and for *(iv)* see the remark at the end of Section 5.7 in [58].

If $p > n$ by Theorem 6 in Section 5.6 in [58] the space $\overset{\circ}{W}{}_p^2(\Omega)$ is continuously embedded in $C^1(\overline{\Omega})$. By definition, for $u \in \overset{\circ}{W}{}_p^2(\Omega)$ there is a sequence $(u_m)_m \in C_c^\infty(\Omega)$ that converges to u in the W_p^2-norm. Due to the continuous embedding $(u_m)_m$ also converges in the C^1-norm. Hence, $u = 0$ and $\nabla u = 0$ on $\partial\Omega$. □

Lemma 2.2.9. *Let $\vartheta, \kappa \in (0,1)$, $T \in (0,1)$ and $K_I(\vartheta) > 0$ denote the constant from the continuous embedding of $W_\infty^1(\Omega)$ into $C^\vartheta(\overline{\Omega})$ from Lemma 2.2.8(ii).*

(i) If $u \in C^{1+\vartheta,\frac{1+\vartheta}{2}}(\overline{\Omega} \times [0,T])$, then it holds that

$$\|u - u(\cdot,0)\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} \leqslant \max\{1, K_I(\vartheta)\} T^{\frac{\vartheta}{2}} \|u\|_{C^{1+\vartheta,\frac{1+\vartheta}{2}}(\overline{\Omega}\times[0,T])}. \tag{2.2.2}$$

(ii) If $u \in C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega} \times [0,T])$, then it holds that

$$\|u - u(\cdot,0)\|_{C^{1+\vartheta,\frac{1+\vartheta}{2}}(\overline{\Omega}\times[0,T])} \leqslant 2\max\{1, K_I(\vartheta)\}T^{\frac{1}{2}\min\{\vartheta,1-\vartheta\}}\|u\|_{C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])}. \tag{2.2.3}$$

(iii) If $u \in C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega} \times [0,T])$, then it holds that

$$\|u - u(\cdot,0)\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} \leqslant 2\max\{1, K_I(\vartheta)\}T^{\frac{1}{2}\min\{2-\vartheta,1+\kappa\}}\|u\|_{C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])}. \tag{2.2.4}$$

2.3 Convolutions on bounded domains

In this section we will consider convolutions on bounded domains Ω. The definition is obtained from the definition of a convolution over $\mathbb{R}^n$ using our convention that a function defined on a domain Ω is zero outside.

Definition 2.3.1. *Let $p, q \in [1,\infty]$ s.t. $\frac{1}{p} + \frac{1}{q} = 1$ and $u \in L^q(\Omega)$. Set $S := \{x - y : x, y \in \Omega\}$ and consider $J \in L^p(S)$. For $x \in \Omega$ we define the convolution over the bounded domain Ω as*

$$(J * u)(x) = \int_\Omega J(x-y)u(y)\,dy.$$

For a function $h \in L^\infty(\Omega)$ and an h-dependent kernel $J(\cdot,h)$ that satisfies $J(\cdot,0) \in L^p(S)$ and is Lipschitz continuous in the second argument with Lipschitz constant $L \in L^p(S)$ the convolution is defined as

$$(J(\cdot,h) * u)(x) := \int_\Omega J(x-y, h(y))u(y)\,dy. \tag{2.3.1}$$

for $x \in \Omega$. For vector- or matrix-valued kernels J or functions u the convolution is defined componentwise.

The following lemma will be proved in the appendix.

Lemma 2.3.2. *Let $T > 0$, $\vartheta \in (0,1)$, $p \in (1,\infty)$, $\beta \geqslant 1$, $S := \{x - y : x, y \in \Omega\}$, $J(x,h)$ a kernel that satisfies $J(\cdot,0) \in L^p(S)$ and is Lipschitz continuous in the second argument with Lipschitz constant $L \in L^p(S)$.*

(i) *If $u, h \in L^\infty(\Omega \times (0,T))$ then, $J(\cdot,h) * u^\beta \in L^\infty(\Omega \times (0,T))$ and satisfies*

$$\|J(\cdot,h) * u^\beta\|_{L^\infty(\Omega\times(0,T))} \leqslant \|u\|^\beta_{L^\infty(\Omega\times(0,T))}\left(\|L\|_{L^1(S)}\|h\|_{L^\infty(\Omega\times(0,T))} + \|J(x,0)\|_{L^1(S)}\right).$$

(ii) *If $u, h \in C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega} \times [0,T])$ and $u \geqslant 0$ then, for $\kappa := \min\{\vartheta, \frac{p-1}{p}\}$ it holds that $J(\cdot,h) * u^\beta \in C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega} \times [0,T])$.*

If J is independent from h this holds setting $J(x,h) := J(x)$ for $x \in S$ and $h = 0$ in the above estimate.

Definition 2.3.3. *We define the standard mollifier $\varsigma \in C^\infty(\mathbb{R}^n)$ as*

$$\varsigma(x) := \begin{cases} C_2 e^{\frac{1}{|x|^2-1}} & \text{if } |x| < 1, \\ 0 & \text{if } |x| \geqslant 1, \end{cases}$$

where $C_2 > 0$ is chosen s.t. $\int_{\mathbb{R}^n} \varsigma\,dx = 1$. For $\varepsilon > 0$ we set $\varsigma_\varepsilon(x) := \frac{1}{\varepsilon^n}\varsigma\left(\frac{x}{\varepsilon}\right)$ with $supp(\varsigma_\varepsilon) \subset \overline{B_\varepsilon}$ and $\int_{B_\varepsilon} \varsigma_\varepsilon\,dx = 1$.

Lemma 2.3.4. *([58, Appendix C, Theorem 6(i) + (iii)]) Let* $u \in L^1_{loc}(\Omega)$*. Then,* $\varsigma_\varepsilon * u \in C^\infty(\Omega_\varepsilon)$*. If* $u \in C(\Omega)$*, then* $\varsigma_\varepsilon * u \to u$ *for* $\varepsilon \to 0$ *uniformly on compact subsets of* Ω*.*

Part I

Nonlocal models with nonlocality in the advection term

CHAPTER 3

Nonlocal and local models for taxis in cell migration: a rigorous limit procedure

This chapter was first published in Volume 81 of Journal of Mathematical Biology in 2020.[1] The presentation has been adapted for use in this dissertation to clarify the details of the proofs and guarantee consistency of the notation.

3.1 Motivation

Macroscopic equations and systems describing the evolution of populations in response to soluble and insoluble environmental cues have been intensively studied and the palette of such reaction-diffusion-taxis models is continuously expanding. Models of such form are motivated by problems arising in various contexts, a large part related to cell migration and proliferation connected to tumor invasion, embryonal development, wound healing, biofilm formation, insect behavior in response to chemical cues, etc. We refer, e.g., to [9] for a recent review also containing some deduction methods for taxis equations based on kinetic transport equations.

Apart from such purely local PDE systems with taxis, several spatially nonlocal models have been introduced over the last two decades and are attracting ever increasing interest. They involve integro-differential operators in one or several terms of the featured reaction-diffusion-advection equations. Their aim is to characterize interactions between individuals or signal perception happening not only at a specific location, but over a whole set (usually a ball) containing (centered at) that location. In the context of cell populations, for instance, this seems to be a more realistic modeling assumption, as cells are able to extend various protrusions (such as lamellipodia, filopodia, cytonemes, etc.) into their surroundings, which can reach across long distances compared against cell size, see [71, 130] and references therein. Moreover, the cells are able to relay signals they perceive and thus transmit them to cells with which they are not in direct contact, thereby influencing their motility, see e.g., [57, 65]. Cell-cell and cell-tissue adhesion are essential for mutual communication, homeostasis, migration, proliferation, sorting, and many other biological processes. A large variety of models for adhesive behavior at the cellular level have been developed to account for the dynamics of focal contacts, e.g., [6, 7, 146] and to assess their influence on cytoskeleton restructuring and cell migration, e.g., [40, 41, 93,

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143]. Continuous, spatially nonlocal models involving adhesion were introduced more recently [5] and are attracting increasing interest from the modeling [16, 21, 23, 43, 68, 69, 109, 118], analytical [26, 45, 46, 80, 132], and numerical [67] viewpoints. Yet more recent models [44, 56] also take into account subcellular level dynamics, thus involving further nonlocalities (besides adhesion), with respect to some structure variable referring to individual cell state. Thereby, multiscale mathematical settings are obtained, which lead to challenging problems for analysis and numerics. Another essential aspect of cell migration is the directional bias in response to a diffusing signal, commonly termed chemotaxis. A model of cell migration with finite sensing radius, thus featuring nonlocal chemotaxis has been introduced in [117] and readdressed in [79] from the perspective of well-posedness, long time behaviour, and patterning. We also refer to [105] for further spatially nonlocal models and their formal deduction.

For adhesion and nonlocal chemotaxis models, a gradient of some nondiffusing or diffusing signal is replaced by a nonlocal integral term. Here we are only interested in this type of model, and refer to [28, 51, 87] for reviews on settings involving other types of nonlocality. Specifically, following [5, 68, 79, 117], we consider the subsequent systems, whose precise mathematical formulations will be specified further below:

1. a prototypical nonlocal model for adhesion

$$\partial_t c_r = \nabla \cdot (D_c(c_r, v_r)\nabla c_r - c_r\chi(c_r, v_r)\mathcal{A}_r(g(c_r, v_r))) + f_c(c_r, v_r), \tag{3.1.1a}$$

$$\partial_t v_r = f_v(c_r, v_r), \tag{3.1.1b}$$

where

$$\mathcal{A}_r u(x) := \frac{1}{r}\int_{B_r} u(x+\xi)\frac{\xi}{|\xi|}F_r(|\xi|)\,\mathrm{d}\xi \tag{3.1.2}$$

is referred to as the adhesion velocity, and the function F_r describes how the magnitude of the interaction force depends on the interaction range $|\xi|$ within the sensing radius r. We require this function to satisfy

Assumptions 3.1.1. *(Assumptions on F_r)*

(a) $(r, \rho) \mapsto F_r(\rho)$ *is continuous and positive in* $[0, r_0]^2$ *for some* $r_0 > 0$*;*

(b) $F_0(0) = n + 1$. [2]

The quantity

$$\mathbb{F}(c_r, v_r) = c_r\chi(c_r, v_r)\mathcal{A}_r(g(c_r, v_r))$$

is often referred to as the total adhesion flux, possibly scaled by some constant involving the typical cell size or the sensing radius, see e.g., [5, 21]. Here we also include a coefficient $\chi(c_r, v_r)$ that depends on cell and tissue (extracellular matrix, ECM) densities, which can be seen as characterizing the sensitivity of cells towards their neighbours and the surrounding tissue. It will, moreover, help provide in a rather general framework a unified presentation of this and the subsequent local and nonlocal model classes for adhesion, haptotactic, and chemotactic behavior of moving cells.

[2] In *Section 3.2* we will see that this is, indeed, the 'right' normalisation. If we assume, as in [5], that this function is a constant involving some viscosity related proportionality, then this choice provides the value of that constant.

System (3.1.1) is a simplification of the integro-differential system (4) in [68]. The main difference between the two settings is that in our case we ignore the so-called matrix-degrading enzymes (MDEs). Instead, we assume cells directly degrade the tissue: this fairly standard simplification (e.g., [118]) effectively assumes that proteolytic enzymes remain localised to the cells, and helps simplify the analysis. On the other hand, (3.1.1) can also be viewed as a nonlocal version of the haptotaxis model with nonlinear diffusion:

$$\partial_t c = \nabla \cdot (D_c(c,v)\nabla c - c\chi(c,v)\nabla g(c,v)) + f_c(c,v), \tag{3.1.3a}$$

$$\partial_t v = f_v(c,v); \tag{3.1.3b}$$

2. a prototypical nonlocal chemotaxis-growth model

$$\partial_t c_r = \nabla \cdot \left(D_c(c_r,v_r)\nabla c_r - c_r\chi(c_r,v_r)\mathring{\nabla}_r v_r\right) + f_c(c_r,v_r), \tag{3.1.4a}$$

$$\partial_t v_r = D_v \Delta v_r + f_v(c_r,v_r) \tag{3.1.4b}$$

with the nonlocal gradient

$$\mathring{\nabla}_r u(x) := \frac{n}{r^2}\int_{S_r} u(x+\xi)\xi \, \mathrm{d}\sigma(\xi) = \frac{n}{r}\int_{S_r} u(x+\xi)\frac{\xi}{|\xi|}\, \mathrm{d}\sigma(\xi). \tag{3.1.5}$$

System (3.1.4) can be seen as a nonlocal version of the chemotaxis-growth model

$$\partial_t c = \nabla \cdot (D_c(c,v)\nabla c - c\chi(c,v)\nabla v) + f_c(c,v), \tag{3.1.6a}$$

$$\partial_t v = D_v \Delta v + f_v(c,v), \tag{3.1.6b}$$

where $\chi(c,v)$ is the chemotactic sensitivity function. As mentioned above, in order to have a unified description of our systems (3.1.3) and (3.1.6) and of their respective nonlocal counterparts (3.1.1) and (3.1.4), we later introduce a more general version of the nonlocal chemotaxis flux, similar to the above adhesion velocity $\mathcal{A}_r$.

The nonlocal systems (3.1.3) and (3.1.6) are stated for

$$t > 0, \qquad x \in \Omega \subset \mathbb{R}^n.$$

Unless the spatial domain Ω is the whole $\mathbb{R}^n$, suitable boundary conditions are required. In the latter case, usually periodicity is assumed, which is not biologically realistic in general. Still, this offers the easiest way to properly define the output of the nonlocal operator in the boundary layer where the sensing region is not fully contained in Ω. Very recently various other boundary conditions have been derived and compared in the context of a single equation modeling cell-cell adhesion in 1D [82].

Few previous works focus on solvability for models with nonlocality in a taxis term. Some of them deal with single equations that only involve cell-cell adhesion [45, 46, 82], others study nonlocal systems of the sort considered here for two [79] or more components [56]. The global solvability and boundedness study in [80] is obtained for the case of a nonlocal operator with integration over a set of sampling directions being an open, not necessarily strict subset of $\mathbb{R}^n$. The systems studied there include settings with a third equation for the dynamics of diffusing MDEs. Conditions which secure uniform boundedness of solutions to such cell-cell and cell-tissue adhesion models in 1D were elaborated in [132].

Some heuristic analysis via local Taylor expansions was performed in [68] and [81] showing that as $r \to 0$ the outputs $\mathcal{A}_r u$ and $\mathring{\nabla}_r u$, respectively, converge pointwise to ∇u for a fixed and sufficiently smooth u. In [79] it was observed that it would be interesting to study rigorously the limiting behaviour of solutions of the nonlocal problems involving $\mathring{\nabla}_r u$. The authors ask in which sense, if at all, do these solutions converge to solutions of the corresponding local problem as $r \to 0$. Numerical results appeared to confirm that, in certain cases, the answer is positive. Still, to the best of our knowledge, no rigorous analytical study of this issue has as yet been performed. Clearly, any approach based on representations using Taylor polynomials requires a rather high order regularity of solution components and a suitable control on the approximation errors, and that uniformly in r. This is difficult or even impossible to obtain in most cases, particularly when dealing with weak solutions. In this chapter we propose a different approach based on the representation of the input u in terms of an integral of ∇u over line segments. This leads to a new description of the nonlocal operators $\mathcal{A}_r$ and $\mathring{\nabla}_r$ in terms of nonlocal operators applied to gradients (see *Section 3.2* below). Moreover, it turns out that redefining their outputs inside the vanishing boundary layer in a suitable way allows one to perform a rigorous proof of convergence: Under suitable assumptions on the system coefficients and other parameters, appropriately defined sequences of solutions to nonlocal problems involving the mentioned modified nonlocal operators converge for $r \to 0$ to those of the corresponding local models (3.1.3) and (3.1.6), respectively. Our convergence proof is based on estimates on c_r and v_r which are uniform in r and on a compactness argument. The two models (3.1.1) and (3.1.4) are chosen as illustrations, however our idea can be further applied to other integro-differential systems with similar properties.

The rest of the chapter is organised as follows. In *Section 3.2* we introduce the aforementioned adaptations of the nonlocal operators $\mathcal{A}_r$ and $\mathring{\nabla}_r$ and study their limiting properties as r becomes infinitesimally small. This turns out to be useful for our convergence proof later. We also establish in *Section 3.3* the well-posedness for a certain class of equations including such operators. In the subsequent *Section 3.4* we introduce a couple of nonlocal models that involve the previously considered averaging operators, prove the global existence of solutions of the respective systems, and investigate their limit behaviour as $r \to 0$. *Section 3.5* provides some numerical simulations comparing various nonlocal and local models considered in this work in the 1D case. Finally, *Section 3.6* contains a discussion of the results and a short outlook on open issues.

3.2 Operators $\mathcal{A}_r$ and $\mathring{\nabla}_r$ and averages of ∇

In this section we study the applications of the nonlocal operators $\mathcal{A}_r$ and $\mathring{\nabla}_r$ to fixed, i.e., independent of r, functions u. Our focus is on the limiting behaviour as $r \to 0$. Formal Taylor expansions performed in [68, 79] anticipate that the limit is the gradient operator in both cases. This we prove here rigorously under rather mild regularity assumptions on u. To be more precise, we replace $\mathcal{A}_r$ and $\mathring{\nabla}_r$ by certain integral operators $\mathcal{T}_r$ and $\mathcal{S}_r$ (see (3.2.2) and (3.2.7) below) applied to ∇u and show that these operators are pointwise approximations of the identity operator in the L^p spaces.

Recall that $\Omega \subset \mathbb{R}^n$ is a bounded domain with smooth enough boundary. Unless explicitly stated, the constants C_i in this chapter **do not** depend upon r.

We start with the operator $\mathcal{A}_r$. For $r \in (0, r_0]$, $u \in C^1(\Omega)$, and $x \in \Omega_r$ we compute using the mean value and Fubini's theorem that

$$\begin{aligned}
\mathcal{A}_r u(x) =& \frac{1}{r} \fint_{B_r} u(x+\xi) \frac{\xi}{|\xi|} F_r(|\xi|) \, \mathrm{d}\xi \\
=& \frac{1}{r} \fint_{B_r} (u(x+\xi) - u(x)) \frac{\xi}{|\xi|} F_r(|\xi|) \, \mathrm{d}\xi \\
=& \frac{1}{r} \fint_{B_r} \int_0^1 (\nabla u(x+s\xi) \cdot \xi) \, \mathrm{d}s \, \frac{\xi}{|\xi|} F_r(|\xi|) \, \mathrm{d}\xi \\
=& \frac{1}{r} \int_0^1 \fint_{B_r} (\nabla u(x+s\xi) \cdot \xi) \frac{\xi}{|\xi|} F_r(|\xi|) \, \mathrm{d}\xi \, \mathrm{d}s \\
=& \int_0^1 \fint_{B_1} (\nabla u(x+rsy) \cdot y) \frac{y}{|y|} F_r(r|y|) \, \mathrm{d}y \, \mathrm{d}s. \qquad (3.2.1)
\end{aligned}$$

Formula (3.2.1) extends to arbitrary $u \in W_1^1(\Omega)$ by means of a density argument. Motivated by (3.2.1) we introduce the averaging operator

$$\mathcal{T}_r w(x) := \int_0^1 \fint_{B_1} (w(x+rsy) \cdot y) \frac{y}{|y|} F_r(r|y|) \, \mathrm{d}y \, \mathrm{d}s. \qquad (3.2.2)$$

In *Subsection 3.2.1* we check that $\mathcal{T}_r w(x)$ is well-defined for all $w \in (L^1(\Omega))^n$ and a.e. $x \in \Omega$. In this notation, for all $r \in (0, r_0]$ and $u \in W_1^1(\Omega)$ identity (3.2.1) takes the form

$$\mathcal{A}_r u = \mathcal{T}_r(\nabla u) \qquad \text{a.e. in } \Omega_r.$$

In the limiting case $r = 0$ we have for $x \in \Omega$ that

$$\begin{aligned}
\mathcal{T}_0 w(x) =& \int_0^1 \fint_{B_1} (w(x) \cdot y) \frac{y}{|y|} F_0(0) \, \mathrm{d}y \, \mathrm{d}s, \\
=& F_0(0) \sum_{i,j=1}^n w_i(x) e_j \fint_{B_1} \frac{y_i y_j}{|y|} \, \mathrm{d}y \\
=& F_0(0) \sum_{i,j=1}^n w_i(x) e_j \delta_{ij} \fint_{B_1} \frac{y_i^2}{|y|} \, \mathrm{d}y \\
=& F_0(0) \sum_{i=1}^n w_i(x) e_i \fint_{B_1} \frac{y_i^2}{|y|} \, \mathrm{d}y \\
=& F_0(0) \sum_{i=1}^n w_i(x) e_i \frac{1}{n} \fint_{B_1} \frac{|y|^2}{|y|} \, \mathrm{d}y \\
=& F_0(0) \frac{1}{n} \fint_{B_1} |y| \, \mathrm{d}y \, w(x) \\
=& w(x). \qquad (3.2.3)
\end{aligned}$$

In the final step we used *Assumptions 3.1.1(b)* which says that $F_0(0) = n + 1$ (this explains our choice) and the trivial identity

$$\fint_{B_1} |y| \, \mathrm{d}y = \frac{n}{n+1}. \qquad (3.2.4)$$

Thus, we have just proved the following lemma:

Lemma 3.2.1. *(Adhesion velocity vs. $\mathcal{T}_r$) Let $u \in W_1^1(\Omega)$. Then for $r \in (0, r_0]$ it holds that*

$$\mathcal{A}_r u = \mathcal{T}_r(\nabla u) \qquad \textit{a.e. in } \Omega_r. \qquad (3.2.5)$$

Moreover, if $F_0(0) = n+1$, *then*

$$\nabla u = \mathcal{T}_0(\nabla u) \qquad a.e.\ in\ \Omega. \tag{3.2.6}$$

In a very similar manner one can establish a representation for $\mathring{\nabla}_r$. For this purpose we define for $r \in (0, r_0]$ the averaging operator

$$\mathcal{S}_r w(x) := n \int_0^1 \fint_{S_1} (w(x+rsy)\cdot y) y \,\mathrm{d}\sigma(y)\,\mathrm{d}s. \tag{3.2.7}$$

The corresponding result then reads:

Lemma 3.2.2. *(Nonlocal gradient vs.* $\mathcal{S}_r$*) Let* $u \in W_1^1(\Omega)$. *Then for* $r \in (0, r_0]$ *it holds that*

$$\mathring{\nabla}_r u = \mathcal{S}_r(\nabla u) \qquad a.e.\ in\ \Omega_r, \tag{3.2.8}$$

$$\nabla u = \mathcal{S}_0(\nabla u) \qquad a.e.\ in\ \Omega. \tag{3.2.9}$$

The proof of *Lemma 3.2.2* is very similar to that of *Lemma 3.2.1* and we omit it here.

Next, we observe that identity (3.2.5) was established for Ω_r. In the boundary layer $\Omega\backslash\Omega_r$ the definition (3.1.2) of the adhesion velocity allows various extensions. For example, one could keep (3.1.2) by assuming (as done here and, e.g., in [56]) that $u := 0$ in $\mathbb{R}^n\backslash\Omega$. An alternative would be to average over the part of the r-ball that lies inside the domain. Let us have a closer look at the first option (the second can be handled similarly). Consider the following example:

Example 3.2.3. ($\mathcal{A}_r$ vs. $\mathcal{T}_r(\nabla\cdot)$ in 1D) Let $\Omega = (-1,1)$, $r_0 = 1$, $F_r \equiv 2$, and $u \equiv 1$. In this case, $u' \equiv 0$, hence

$$\mathcal{T}_r(u') \equiv 0 \equiv u'.$$

For $\mathcal{A}_r$ one readily computes by assuming $u = 0$ in $\mathbb{R}\backslash(-1,1)$ that for $x \in (-1,1)$

$$\begin{aligned}\mathcal{A}_r u(x) =& \frac{2}{r}\frac{1}{2r}\int_{(-1-x,1-x)\cap(-r,r)} \operatorname{sign}(\xi)\,\mathrm{d}\xi \\ =& \begin{cases} \frac{1}{r^2}(-1+r-x) & \text{in } [-1,-1+r], \\ 0 & \text{in } (-1+r,1-r) = \Omega_r, \\ \frac{1}{r^2}(1-r-x) & \text{in } [1-r,1], \end{cases}\end{aligned}$$

so that

$$\begin{aligned}\|\mathcal{A}_r u\|_{L^1(-1,1)} =& \|\mathcal{A}_r u\|_{L^1(\Omega\backslash\Omega_r)} \\ =& \frac{1}{r^2}\int_{-1}^{-1+r} |-1+r-x|\,\mathrm{d}x + \frac{1}{r^2}\int_{1-r}^{1} |1-r-x|\,\mathrm{d}x \\ =& 1,\end{aligned}$$

although

$$|\Omega\backslash\Omega_r| = 2r \underset{r\to0}{\to} 0.$$

Thus,

$$\mathcal{A}_r u \underset{r\to0}{\to} 0 \equiv u'$$

in the measure but not in $L^1(\Omega)$.

Example 3.2.3 supports our idea to average ∇u instead of u itself. The same applies to $\mathring{\nabla}_r u$ vs. $\mathcal{S}_r(\nabla u)$.

Averaging w.r.t. $y \in B_1$ and then also w.r.t. $s \in (0,1)$ might appear superfluous in the definition of the operator $\mathcal{T}_r$. The following example compares the effect of $\mathcal{T}_r$ with that of an operator which averages w.r.t. to y only.

Example 3.2.4. Let $\Omega = \mathbb{R}^n$, $n \geqslant 2$, and $r > 0$, $F_r \equiv n+1$. In this case

$$\mathcal{T}_r w(x) := (n+1) \int_0^1 ⨍_{B_1} (w(x+rsy) \cdot y) \frac{y}{|y|} \, \mathrm{d}y \, \mathrm{d}s.$$

Consider also the operator

$$\widetilde{\mathcal{T}}_r w(x) := (n+1) ⨍_{B_1} (w(x+ry) \cdot y) \frac{y}{|y|} \, \mathrm{d}y.$$

It is easy to see that both operators are well-defined, linear, continuous, and self-adjoint in the space $(L^2(\mathbb{R}^n))^n$ (see *Lemma 3.2.5* below). Moreover, they map the dense subspace $C_c(\mathbb{R}^n;\mathbb{R}^n)$ into itself. This suggests the following natural extension to $(C_c(\mathbb{R}^n;\mathbb{R}^n))^*$:

$$\begin{aligned}
\langle \mathcal{T}_r \mu, \varphi \rangle_{(C_c(\mathbb{R}^n;\mathbb{R}^n))^*, C_c(\mathbb{R}^n;\mathbb{R}^n)} &:= \langle \mu, \mathcal{T}_r \varphi \rangle_{(C_c(\mathbb{R}^n;\mathbb{R}^n))^*, C_c(\mathbb{R}^n;\mathbb{R}^n)}, \\
\left\langle \widetilde{\mathcal{T}}_r \mu, \varphi \right\rangle_{(C_c(\mathbb{R}^n;\mathbb{R}^n))^*, C_c(\mathbb{R}^n;\mathbb{R}^n)} &:= \left\langle \mu, \widetilde{\mathcal{T}}_r \varphi \right\rangle_{(C_c(\mathbb{R}^n;\mathbb{R}^n))^*, C_c(\mathbb{R}^n;\mathbb{R}^n)}.
\end{aligned}$$

Let, for instance,

$$w := \delta_0 e_1,$$

where δ_0 means the usual Dirac delta. One readily computes that

$$\widetilde{\mathcal{T}}_r(\delta_0 e_1)(x) = \frac{n+1}{|B_r|} \chi_{B_r}(x) \frac{x_1}{r} \frac{x}{|x|},$$

whereas

$$\begin{aligned}
\mathcal{T}_r(\delta_0 e_1)(x) =& \frac{n+1}{|B_r|} \int_0^1 s^{-n-1} \chi_{B_{rs}}(x) \, \mathrm{d}s \frac{x_1}{r} \frac{x}{|x|} \\
=& \frac{n+1}{n|B_r|} \left(\left(\frac{r}{|x|} \right)^n - 1 \right)_+ \frac{x_1}{r} \frac{x}{|x|}.
\end{aligned}$$

For $n \geqslant 2$, the operator $\mathcal{T}_r$ retains the singularity at the origin, however making it less concentrated, while $\widetilde{\mathcal{T}}_r$ eliminates that singularity entirely and produces instead jump discontinuities all over S_r.

3.2.1 Properties of the averaging operators $\mathcal{T}_r$ and $\mathcal{S}_r$

In this section we collect some properties of the averaging operators $\mathcal{T}_r$ and $\mathcal{S}_r$.

Lemma 3.2.5. *(Properties of $\mathcal{T}_r$) Let F_r satisfy Assumptions 3.1.1 and let $r \in (0, r_0]$. Then:*

(i) $\mathcal{T}_r$ is a well-defined continuous linear operator in $(L^p(\Omega))^n$ for all $p \in [1,\infty]$. The corresponding operator norm satisfies

$$\|\mathcal{T}_r\|_{L((L^p(\Omega))^n)} \leqslant C_1(r,p), \tag{3.2.10}$$

where

$$C_1(r,p) := \begin{cases} \left(n \int\limits_0^1 \rho^{n-1+p^*} (F_r(r\rho))^{p^*} \, d\rho \right)^{\frac{1}{p^*}} & \textit{for } p \in (1,\infty],\ p^* = \frac{p}{p-1}, \\ \max\limits_{\rho\in[0,1]} \rho F_r(r\rho) & \textit{for } p = 1. \end{cases}$$

(ii) Let $p, p^* \in [1,\infty]$ be such that $p^* = \frac{p}{p-1}$. For all $w_1 \in (L^p(\Omega))^n$ and $w_2 \in \left(L^{p^*}(\Omega)\right)^n$ it holds:

$$\int_\Omega (\mathcal{T}_r w_1(x) \cdot w_2(x)) \, dx = \int_\Omega (w_1(x) \cdot \mathcal{T}_r w_2(x)) \, dx. \tag{3.2.11}$$

(iii) Let $p \in [1,\infty)$. For all $w \in (L^p(\Omega))^n$ it holds that

$$\mathcal{T}_r w \underset{r\to 0}{\to} \mathcal{T}_0 w = w \qquad \textit{in } (L^p(\Omega))^n. \tag{3.2.12}$$

(iv) For $p = 2$ it holds that

$$\|\mathcal{T}_r\|_{L((L^2(\Omega))^n)} \underset{r\to 0}{\to} 1. \tag{3.2.13}$$

Remark 3.2.6. Due to the assumptions on F_r we have in the limit that

$$C_1(r,p) \underset{r\to 0}{\to} C_2(p) := \begin{cases} (n+1)\left(\frac{n}{n+p^*}\right)^{\frac{1}{p^*}} & \text{for } p \in (1,\infty], \quad p^* = \frac{p}{p-1}, \\ n+1 & \text{for } p = 1. \end{cases} \tag{3.2.14}$$

Proof of Lemma 3.2.5. (i) Since w is measurable and $\rho \mapsto F_r(\rho)$, $(x,s,y) \mapsto x + rsy$, $(y,z) \mapsto (z\cdot y)\frac{y}{|y|}$ are continuous, we have that

$$(x,y,s) \mapsto (w(x+rsy)\cdot y)\frac{y}{|y|}F_r(r|y|)$$

is well-defined a.e. in $\Omega \times B_1 \times (0,1)$ and is measurable. Let $p \in (1,\infty)$ and $p^* = \frac{p}{p-1}$. We compute

$$\begin{aligned} \fint_{B_1} (|y|F_r(r|y|))^{p^*} \, \mathrm{d}y &= \frac{1}{|B_1|}\int_0^1 \rho^{n-1+p^*}(F_r(r\rho))^{p^*} \, \mathrm{d}\rho \cdot 2\pi \prod_{k=2}^{n-1} \int_0^\pi \sin(\phi_{n-k})^{k-1} \, \mathrm{d}\phi_{n-k} \\ &= n \int\limits_0^1 \rho^{n-1+p^*}(F_r(r\rho))^{p^*} \, \mathrm{d}\rho \end{aligned}$$

using spherical coordinates and the properties of the Gamma function. With the help of this equality, Hölder's inequality, Fubini's theorem, and our convention that w vanishes outside Ω, we deduce for all $w \in (L^p(\Omega))^n$ that

$$\begin{aligned} &\|\mathcal{T}_r w\|^p_{(L^p(\Omega))^n} \\ =&\int_\Omega \left| \int_0^1 \fint_{B_1} (w(x+rsy)\cdot y)\frac{y}{|y|}F_r(r|y|) \, \mathrm{d}y \, \mathrm{d}s \right|^p \mathrm{d}x \\ \leqslant& \int_\Omega \int_0^1 \fint_{B_1} |w(x+rsy)|^p \, \mathrm{d}y \left(\fint_{B_1} (|y|F_r(r|y|))^{p^*} \, \mathrm{d}y \right)^{\frac{p}{p^*}} \mathrm{d}s \, \mathrm{d}x \\ =& C_1^p(r,p) \int_0^1 \fint_{B_1} \int_\Omega |w(x+rsy)|^p \, \mathrm{d}x \, \mathrm{d}y \, \mathrm{d}s, \end{aligned}$$

$$\leqslant C_1^p(r,p)\int_0^1 \fint_{B_1}\int_\Omega |w(z)|^p \,\mathrm{d}z\,\mathrm{d}y\,\mathrm{d}s$$
$$= C_1^p(r,p)\|w\|^p_{(L^p(\Omega))^n}.$$

This implies that for all $p \in (1,\infty)$ the operator $\mathcal{T}_r$ is well-defined in $(L^p(\Omega))^n$. It is also clearly linear. Taken together we then have that $\mathcal{T}_r \in L((L^p(\Omega))^n)$ and (3.2.10) holds. The cases $p = 1$ and $p = \infty$ can be treated similarly.

(ii) Let $w_1 \in (L^p(\Omega))^n$ and $w_2 \in \left(L^{p^*}(\Omega)\right)^n$. We compute by using Fubini's theorem, the symmetry of B_1, and simple variable transformations that

$$\begin{aligned}
&\int_\Omega (\mathcal{T}_r w_1(x)\cdot w_2(x))\,\mathrm{d}x\\
=&\int_\Omega\int_0^1\fint_{B_1}(w_1(x+rsy)\cdot y)\frac{y}{|y|}F_r(r|y|)\,\mathrm{d}y\,\mathrm{d}s\cdot w_2(x)\,\mathrm{d}x\\
=&\int_0^1\fint_{B_1}|y|F_r(r|y|)\\
&\quad\cdot\int_\Omega\left(w_1(x+rsy)\cdot\frac{y}{|y|}\right)\left(w_2(x)\cdot\frac{y}{|y|}\right)\mathrm{d}x\,\mathrm{d}y\,\mathrm{d}s\\
=&\int_0^1\fint_{B_1}|y|F_r(r|y|)\\
&\quad\cdot\int_{\Omega\cap(-rsy+\Omega)}\left(w_1(x+rsy)\cdot\frac{y}{|y|}\right)\left(w_2(x)\cdot\frac{y}{|y|}\right)\mathrm{d}x\,\mathrm{d}y\,\mathrm{d}s
\end{aligned}\tag{3.2.15}$$

$$\begin{aligned}
=&\int_0^1\fint_{B_1}|y|F_r(r|y|)\\
&\quad\cdot\int_{(rsy+\Omega)\cap\Omega}\left(w_1(z)\cdot\frac{y}{|y|}\right)\left(w_2(z-rsy)\cdot\frac{y}{|y|}\right)\mathrm{d}z\,\mathrm{d}y\,\mathrm{d}s\\
=&\int_0^1\fint_{B_1}|y|F_r(r|y|)\\
&\quad\cdot\int_{(-rsy+\Omega)\cap\Omega}\left(w_1(z)\cdot\frac{y}{|y|}\right)\left(w_2(z+rsy)\cdot\frac{y}{|y|}\right)\mathrm{d}z\,\mathrm{d}y\,\mathrm{d}s.
\end{aligned}\tag{3.2.16}$$

Thereby we used our convention that each function defined in Ω is assumed to be prolonged by zero outside Ω. Comparing (3.2.15) and (3.2.16) we obtain (3.2.11).

(iii) We apply the Banach-Steinhaus theorem. Due to *(i)* and (3.2.14), $\{\mathcal{T}_r\}_{r\in(0,r_0]}$ is a family of uniformly bounded linear operators in the Banach space $(L^p(\Omega))^n$. Thus, as $C_c(\Omega;\mathbb{R}^n)$ is dense in $(L^p(\Omega))^n$ for $p < \infty$, we only need to check (3.2.12) for $w \in C_c(\Omega;\mathbb{R}^n)$. But for such w we can directly pass to the limit under the integral and thus obtain using (3.2.3) and the dominated convergence theorem that

$$\mathcal{T}_r w \underset{r\to 0}{\to} \mathcal{T}_0 w = w \qquad \text{for all } x \in \Omega \text{ and in } (L^p(\Omega))^n.$$

(iv) Here we make use of the Fourier transform, which we denote by the hat symbol. A straightforward calculation using Fubini's theorem and a variable transformation shows that for $w \in (L^p(\Omega))^n$ and $\xi \in \mathbb{R}^n$ it holds that

$$\widehat{\mathcal{T}_r w}(\xi) = \frac{1}{(2\pi)^{\frac{n}{2}}}\int_{\mathbb{R}^n}\mathcal{T}_r w(x)e^{-ix\cdot\xi}\,\mathrm{d}x$$

$$
\begin{aligned}
&= \frac{1}{(2\pi)^{\frac{n}{2}}} \int_{\mathbb{R}^n} \int_0^1 \fint_{B_1} (w(x+rsy)\cdot y)\,\frac{y}{|y|} F_r(r|y|)\,\mathrm{d}y\,\mathrm{d}s\, e^{-ix\cdot\xi}\,\mathrm{d}x \\
&= \frac{1}{(2\pi)^{\frac{n}{2}}} \int_{\mathbb{R}^n} \int_0^1 \fint_{B_1} (w(z)\cdot y)\,\frac{y}{|y|} F_r(r|y|)\,\mathrm{d}y\,\mathrm{d}s\, e^{-i(z-rsy)\cdot\xi}\,\mathrm{d}z \\
&= \frac{1}{(2\pi)^{\frac{n}{2}}} \int_0^1 \fint_{B_1} \left(\int_{\mathbb{R}^n} w(z) e^{-iz\cdot\xi}\,\mathrm{d}z\right)\cdot y\,\frac{y}{|y|} F_r(r|y|) e^{irsy\cdot\xi}\,\mathrm{d}y\,\mathrm{d}s \\
&= \Phi_r(\xi)\widehat{w}(\xi),
\end{aligned}
$$

where

$$
\Phi_r(\xi) := \int_0^1 \fint_{B_1} \frac{yy^T}{|y|} F_r(r|y|) e^{irsy\cdot\xi}\,\mathrm{d}y\,\mathrm{d}s. \tag{3.2.17}
$$

Combining (3.2.17) with the Plancherel theorem and using our convention that w vanishes outside Ω, we can estimate as follows:

$$
\begin{aligned}
\|\mathcal{T}_r\|_{L((L^2(\Omega))^n)} &= \sup_{\|w\|_{(L^2(\Omega))^n}=1} \|\mathcal{T}_r w\|_{(L^2(\Omega))^n} \\
&\leqslant \sup_{\|w\|_{(L^2(\Omega))^n}=1} \|\widehat{\mathcal{T}_r w}\|_{(L^2(\mathbb{R}^n))^n} \\
&\leqslant \|\Phi_r\|_{(L^\infty(\mathbb{R}^n))^n} \sup_{\|w\|_{(L^2(\Omega))^n}=1} \|\widehat{w}\|_{(L^2(\mathbb{R}^n))^n} \\
&= \|\Phi_r\|_{(L^\infty(\mathbb{R}^n))^n} \sup_{\|w\|_{(L^2(\Omega))^n}=1} \|w\|_{(L^2(\Omega))^n} \\
&= \|\Phi_r\|_{(L^\infty(\mathbb{R}^n))^n}.
\end{aligned} \tag{3.2.18}
$$

Further, consider an arbitrary orthogonal matrix $O \in \mathbb{R}^{n\times n}$ and $\xi \in \mathbb{R}^n$. With a variable transformation using the properties of orthogonal matrices from *Lemma 2.1.3* we observe that

$$
\begin{aligned}
\Phi_r(O\xi) &= \int_0^1 \fint_{B_1} \frac{yy^T}{|y|} F_r(r|y|) e^{irsy^T O\xi}\,\mathrm{d}y\,\mathrm{d}s \\
&= O \int_0^1 \fint_{B_1} \frac{O^T y (O^T y)^T}{|O^T y|} F_r(r|O^T y|) e^{irs(O^T y)^T \xi}\,\mathrm{d}y\,\mathrm{d}s\, O^T \\
&= O\Phi_r(\xi)O^T.
\end{aligned} \tag{3.2.19}
$$

Consequently, we construct an orthogonal matrix O out of an orthonormal basis containing $\frac{\xi}{|\xi|}$ in order for $O\xi = |\xi|e_1$ to hold and obtain that

$$
|\Phi_r(\xi)|_2 = |\Phi_r(|\xi|e_1)|_2 \qquad \text{for all } \xi \in \mathbb{R}^n. \tag{3.2.20}
$$

Since

$$
\Phi_r(|\xi|e_1) = \int_0^1 \fint_{B_1} \frac{yy^T}{|y|} F_r(r|y|) e^{irs|\xi|y_1}\,\mathrm{d}y\,\mathrm{d}s \tag{3.2.21}
$$

is a diagonal matrix, its spectral norm is given by the spectral radius (see *Definition 2.1.1*). Estimating the right-hand side of (3.2.21) we then conclude that

$$
|\Phi_r(|\xi|e_1)|_2 \leqslant \fint_{B_1} \frac{y_1^2}{|y|} F_r(r|y|)\,\mathrm{d}y = \frac{1}{n}\fint_{B_1} |y| F_r(r|y|)\,\mathrm{d}y \underset{r\to 0}{\longrightarrow} 1 \qquad \text{for all } \xi \in \mathbb{R}^n \tag{3.2.22}
$$

due to $F_0(0) = n+1$ and (3.2.4). Combining (3.2.18), (3.2.20), and (3.2.22) we arrive at

$$\limsup_{r\to 0} \|\mathcal{T}_r\|_{L((L^2(\Omega))^n)} \leqslant 1. \tag{3.2.23}$$

Finally, the pointwise convergence (3.2.12) and the Banach-Steinhaus theorem imply that

$$\liminf_{r\to 0} \|\mathcal{T}_r\|_{L((L^2(\Omega))^n)} \geqslant 1,$$

concluding the proof.

□

A similar result holds for $\mathcal{S}_r$:

Lemma 3.2.7. *(Operator $\mathcal{S}_r$) Let $r \in (0, r_0]$. Then:*

(i) $\mathcal{S}_r$ is a well-defined continuous linear operator in $(L^p(\Omega))^n$ for all $p \in [1,\infty]$. The corresponding operator norm satisfies

$$\|\mathcal{S}_r\|_{L((L^p(\Omega))^n)} \leqslant n. \tag{3.2.24}$$

(ii) Let $p, p^* \in [1,\infty]$ be such that $p^* = \frac{p}{p-1}$. For all $w_1 \in (L^p(\Omega))^n$ and $w_2 \in \left(L^{p^*}(\Omega)\right)^n$ it holds:

$$\int_\Omega (\mathcal{S}_r w_1(x) \cdot w_2(x))\, dx = \int_\Omega (w_1(x) \cdot \mathcal{S}_r w_2(x))\, dx.$$

(iii) Let $p \in [1,\infty)$. For all $w \in (L^p(\Omega))^n$ it holds that

$$\mathcal{S}_r w \underset{r\to 0}{\to} \mathcal{S}_0 w = w \qquad \text{in } (L^p(\Omega))^n.$$

(iv) For $p = 2$ it holds that

$$\|\mathcal{S}_r\|_{L((L^2(\Omega))^n)} \underset{r\to 0}{\to} 1.$$

Proof. The proof almost repeats that of *Lemma 3.2.5*. Therefore, we only check (3.2.24) and omit further details. Let $p \in [1,\infty)$ and $p^* = \frac{p}{p-1}$. Using Hölder's inequality, Fubini's theorem, and our convention that w vanishes outside Ω we deduce for all $w \in (L^p(\Omega))^n$ that

$$\begin{aligned}
\|\mathcal{S}_r w\|^p_{(L^p(\Omega))^n} =& n^p \int_\Omega \left| \int_0^1 \fint_{S_1} (w(x+rsy)\cdot y) y \,\mathrm{d}\sigma(y)\,\mathrm{d}s \right|^p \mathrm{d}x \\
\leqslant& n^p \int_\Omega \int_0^1 \fint_{S_1} |w(x+rsy)|^p \,\mathrm{d}\sigma(y)\,\mathrm{d}s\,\mathrm{d}x \\
=& n^p \int_0^1 \fint_{S_1} \int_\Omega |w(x+rsy)|^p \,\mathrm{d}x\,\mathrm{d}\sigma(y)\,\mathrm{d}s, \\
\leqslant& n^p \int_0^1 \fint_{S_1} \int_\Omega |w(z)|^p \,\mathrm{d}z\,\mathrm{d}\sigma(y)\,\mathrm{d}s \\
=& n^p \|w\|^p_{(L^p(\Omega))^n},
\end{aligned}$$

which means that

$$\|\mathcal{S}_r\|_{L((L^p(\Omega))^n)} \leqslant n. \tag{3.2.25}$$

The proof in the case $p = \infty$ follows the same steps, or, alternatively, one passes to the limit as $p \to \infty$ in (3.2.25).

□

Remark 3.2.8. The constants in (3.2.10) for any $n \geqslant 1$ and in (3.2.24) for $n \geqslant 2$ are not necessarily optimal. For $p \neq 2$ it remains open whether or not

$$\liminf_{r\to 0} \|\mathcal{T}_r\|_{L((L^p(\Omega))^n)} = 1,$$
$$\liminf_{r\to 0} \|\mathcal{S}_r\|_{L((L^p(\Omega))^n)} = 1.$$

The answer may depend upon Ω and p.

3.3 Well-posedness for a class of evolution equations involving $\mathcal{T}_r$ or $\mathcal{S}_r$

In this section we establish the existence and uniqueness of solutions to a certain class of single evolution equations involving $\mathcal{T}_r$ or $\mathcal{S}_r$. This result is an important ingredient for our analysis of nonlocal systems in *Section 3.4*. Thus, we consider the following initial boundary value problem:

$$\partial_t c_r = \nabla \cdot (a_1 \nabla c_r - a_2 G_\varepsilon(\mathcal{R}_r(a_3 \nabla c_r))) + f \qquad \text{in } \Omega \times (0,T), \tag{3.3.1a}$$
$$(a_1 \nabla c_r - a_2 G_\varepsilon(\mathcal{R}_r(a_3 \nabla c_r))) \cdot \nu = 0 \qquad \text{on } \partial\Omega \times (0,T), \tag{3.3.1b}$$
$$c_r(\cdot, 0) = c_0 \qquad \text{in } \Omega \tag{3.3.1c}$$

for $T \in (0,\infty)$. Here

$$\mathcal{R}_r \in \{\mathcal{T}_r, \mathcal{S}_r\},$$

and for $\varepsilon \geqslant 0$ we set

$$G_\varepsilon : \mathbb{R}^n \to \mathbb{R}^n, \quad x \mapsto \frac{x}{1+\varepsilon|x|}. \tag{3.3.2}$$

The following lemma shows that G_ε is globally Lipschitz.

Lemma 3.3.1. *The function G_ε is globally Lipschitz continuous with Lipschitz constant 1 for $\varepsilon \geqslant 0$.*

Proof. Let $i \in \{1, \dots, n\}$. For fixed $x_j \in \mathbb{R}$, $j \in \{1,\dots,n\}\backslash\{i\}$ we set $f_i(x_i) := \frac{x_i}{1+\varepsilon|x|} = G_i(x)$. We can estimate the derivative

$$|\partial_{x_i} f_i| = \frac{|1+\varepsilon|x| - \varepsilon\frac{x_i^2}{|x|}|}{(1+\varepsilon|x|)^2} \leqslant \frac{1}{1+\varepsilon|x|} \leqslant 1.$$

The one-dimensional mean value theorem implies that for fixed $x, y \in \mathbb{R}^n$ it holds that

$$|G_i(x) - G_i(y)| = |f_i(x_i) - f_i(y_i)| \leqslant \|\partial_{x_i} f_i\|_{L^\infty(\mathbb{R})}|x_i - y_i| \leqslant |x_i - y_i|.$$

Consequently,

$$|G(x) - G(y)|^2 = \sum_{i=1}^n |f_i(x_i) - f_i(y_i)|^2 \leqslant \sum_{i=1}^n |x_i - y_i|^2 = |x-y|^2.$$

□

Remark 3.3.2. Observe that for $\varepsilon = 0$ equation (3.3.1a) is linear, whereas for $\varepsilon > 0$ the nonlocal part of the flux is a priori bounded. The latter helps us to construct nonnegative solutions in *Section 3.4.*

We make the following assumptions:

$$a_1, a_2, a_3 \in L^\infty(\Omega \times (0,T)), \tag{3.3.3}$$

$$a_1 > 0 \text{ and } a_1^{-1} \in L^\infty(\Omega \times (0,T)), \tag{3.3.4}$$

$$\left\|a_1^{-\frac{1}{2}} a_2\right\|_{L^\infty(\Omega\times(0,T))} \left\|a_1^{-\frac{1}{2}} a_3\right\|_{L^\infty(\Omega\times(0,T))} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} < 1, \tag{3.3.5}$$

$$f \in L^2(0,T;(H^1(\Omega))^*), \tag{3.3.6}$$

$$c_0 \in L^2(\Omega). \tag{3.3.7}$$

To shorten the notation, we introduce a pair of constants

$$\begin{aligned} \alpha_r :=& \|a_1^{-1}\|^{-1}_{L^\infty(\Omega\times(0,T))} \left(1 - \left\|a_1^{-\frac{1}{2}} a_2\right\|_{L^\infty(\Omega\times(0,T))} \left\|a_1^{-\frac{1}{2}} a_3\right\|_{L^\infty(\Omega\times(0,T))} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}\right), \\ M_r :=& \|a_1\|_{L^\infty(\Omega\times(0,T))} + \|a_2\|_{L^\infty(\Omega\times(0,T))} \|a_3\|_{L^\infty(\Omega\times(0,T))} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}. \end{aligned} \tag{3.3.8}$$

Due to assumptions (3.3.3)–(3.3.5) it is clear that

$$0 < \alpha_r, M_r < \infty.$$

We introduce a family of operators

$$\begin{aligned} \langle \mathcal{M}(t,u), \varphi \rangle_{(H^1(\Omega))^*, H^1(\Omega)} &:= \int_\Omega a_1(\cdot,t)\nabla u \cdot \nabla\varphi \,\mathrm{d}x - \int_\Omega a_2(\cdot,t) G_\varepsilon(\mathcal{R}_r(a_3(\cdot,t)\nabla u)) \cdot \nabla\varphi \,\mathrm{d}x, \\ \langle \mathcal{M}(u), \varphi \rangle_{L^2(0,T;(H^1(\Omega))^*), L^2(0,T;H^1(\Omega))} &:= \int_0^T \langle \mathcal{M}(t,u), \varphi(t) \rangle_{(H^1(\Omega))^*, H^1(\Omega)} \,\mathrm{d}t. \end{aligned}$$

Lemma 3.3.3. *Let* (3.3.3)*–*(3.3.5) *be satisfied. Then:*

(i) For a.e. $t \in [0,T]$ *the operator*

$$\mathcal{M}(t,\cdot) : H^1(\Omega) \to (H^1(\Omega))^*$$

is well-defined, monotone, hemicontinuous, and satisfies the bounds

$$\langle \mathcal{M}(t,u), u \rangle_{(H^1(\Omega))^*, H^1(\Omega)} \geqslant \alpha_r ||\nabla u||^2_{(L^2(\Omega))^n}, \tag{3.3.9}$$

$$||\mathcal{M}(t,u)||_{(H^1(\Omega))^*} \leqslant M_r ||\nabla u||_{(L^2(\Omega))^n} \tag{3.3.10}$$

for all $u \in H^1(\Omega)$*. Moreover, for all* $u \in H^1(\Omega)$ *the function* $\mathcal{M}(\cdot,u) : [0,T] \to (H^1(\Omega))^*$ *is measurable.*

(ii) The operator

$$\mathcal{M} : L^2(0,T;H^1(\Omega)) \to L^2(0,T;(H^1(\Omega))^*)$$

is well-defined, monotone, hemicontinuous, and satisfies the bounds

$$\begin{aligned} &\langle \mathcal{M}(u), u \rangle_{L^2(0,T;(H^1(\Omega))^*), L^2(0,T;H^1(\Omega))} \geqslant \alpha_r ||\nabla u||^2_{L^2(0,T;(L^2(\Omega))^n)}, \\ &||\mathcal{M}(u)||_{L^2(0,T;(H^1(\Omega))^*)} \leqslant M_r ||\nabla u||_{L^2(0,T;(L^2(\Omega))^n)} \end{aligned}$$

for all $u \in L^2(0,T;H^1(\Omega))$*.*

Proof. The assumptions on the coefficients a_i together with the Lipschitz continuity of G_ε readily imply that for a.e. $t \in [0,T]$ the operator $\mathcal{M}(t,\cdot)$ is well-defined and satisfies (3.3.10). Moreover, due to (3.3.3) and G_ε Lipschitz, it is also clear that $\mathcal{M}(\cdot,u) : [0,T] \to (H^1(\Omega))^*$ is measurable on $[0,T]$ for all $u \in H^1(\Omega)$, whereas for a.e. t the mapping $\lambda \mapsto \langle \mathcal{M}(t,u+\lambda v), w\rangle_{(H^1(\Omega))^*,H^1(\Omega)}$ is continuous on $\mathbb{R}$ for all $u,v,w \in H^1(\Omega)$, the latter meaning that $\mathcal{M}(t,\cdot)$ is hemicontinuous. Using Hölder's inequality, the facts that G_ε is Lipschitz with Lipschitz constant 1 and $G_\varepsilon(0) = 0$, the assumptions on the a_i's, and the properties of $\mathcal{R}_r$, we compute that

$$\begin{aligned}
&\langle \mathcal{M}(t,u) - \mathcal{M}(t,v), u-v\rangle_{(H^1(\Omega))^*,H^1(\Omega)} \\
=&\int_\Omega \nabla(u-v)\cdot a_1(\cdot,t)\nabla(u-v)\,\mathrm{d}x \\
&-\int_\Omega (G_\varepsilon(\mathcal{R}_r(a_3(\cdot,t)\nabla u)) - G_\varepsilon(\mathcal{R}_r(a_3(\cdot,t)\nabla v)))\cdot a_2(\cdot,t)\nabla(u-v)\,\mathrm{d}x \\
\geqslant&\left\| a_1^{\frac{1}{2}}\nabla(u-v)\right\|^2_{(L^2(\Omega))^n} \\
&-\int_\Omega \left|\mathcal{R}_r\left(a_1^{-\frac{1}{2}}a_3(\cdot,t)\left(a_1^{\frac{1}{2}}\nabla(u-v)\right)\right)\right|\left|a_1^{-\frac{1}{2}}a_2(\cdot,t)\left(a_1^{\frac{1}{2}}\nabla(u-v)\right)\right|\,\mathrm{d}x \\
\geqslant&\left(1-\left\|a_1^{-\frac{1}{2}}a_2\right\|_{L^\infty(\Omega\times(0,T))}\left\|a_1^{-\frac{1}{2}}a_3\right\|_{L^\infty(\Omega\times(0,T))}\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}\right)\left\|a_1^{\frac{1}{2}}\nabla(u-v)\right\|^2_{(L^2(\Omega))^n} \\
\geqslant&\alpha_r\left\|\nabla(u-v)\right\|^2_{(L^2(\Omega))^n} \geqslant 0
\end{aligned} \tag{3.3.11}$$

for $u,v \in H^1(\Omega)$, which proves monotonicity. Further, taking $v = 0$ in (3.3.11) and using $\mathcal{M}(t,0) = 0$ yields (3.3.9). Part *(i)* is thus proved. A proof of *(ii)* can be done similarly; we omit further details.

□

Using the properties of the averaging operators proved in *Subsection 3.2.1* we can define weak solutions to (3.3.1) in a manner very similar to that for the classical, purely local case (i.e., when $a_2 \equiv 0$):

Definition 3.3.4. *Let* (3.3.3)-(3.3.7) *hold. We call the function* $c_r : \overline{\Omega}\times[0,T] \to \mathbb{R}$ *a weak solution of* (3.3.1) *if:*

(i) $c_r \in L^2(0,T;H^1(\Omega)) \cap C([0,T];L^2(\Omega))$, $\partial_t c_r \in L^2(0,T;(H^1(\Omega))^*)$;

(ii) c_r *satisfies* (3.3.1a)-(3.3.1b) *in the following sense: for all* $\varphi \in H^1(\Omega)$ *and a.e.* $t \in (0,T)$

$$\begin{aligned}
\langle \partial_t c_r, \varphi\rangle_{(H^1(\Omega))^*,H^1(\Omega)} =& -\int_\Omega a_1\nabla c_r\cdot\nabla\varphi\,dx \\
&+\int_\Omega a_2 G_\varepsilon(\mathcal{R}_r(a_3\nabla c_r))\cdot\nabla\varphi\,dx + \langle f,\varphi\rangle_{(H^1(\Omega))^*,H^1(\Omega)};
\end{aligned} \tag{3.3.12}$$

(iii) $c_r(\cdot,0) = c_0$ *in* $L^2(\Omega)$.

Using standard theory one readily proves the following existence result:

Lemma 3.3.5. *Let* (3.3.3)-(3.3.7) *hold. Then there exists a unique weak solution to* (3.3.1) *in terms of Definition 3.3.4. The solution satisfies the following estimates:*

$$\|c_r\|^2_{C([0,T];L^2(\Omega))} + \alpha_r\|\nabla c_r\|^2_{L^2(0,T;(L^2(\Omega))^n)} \leqslant C_3(\alpha_r,T)\left(\|c_0\|^2_{L^2(\Omega)} + \|f\|^2_{L^2(0,T;(H^1(\Omega))^*)}\right), \tag{3.3.13}$$

$$\|\partial_t c_r\|^2_{L^2(0,T;(H^1(\Omega))^*)} \leqslant C_4(\alpha_r, M_r, T)\left(\|c_0\|^2_{L^2(\Omega)} + \|f\|^2_{L^2(0,T;(H^1(\Omega))^*)}\right). \tag{3.3.14}$$

Proof. The existence of a unique weak solution to (3.3.1) is a direct consequence of *Lemma 3.3.3(i)* and the standard theory of evolution equations with monotone operators, see *Theorem A.1.17*. It remains to check the bounds (3.3.13) and (3.3.14). Taking $\varphi := c_r$ in the weak formulation (3.3.12) and using *Lemma A.3.8*, (3.3.9), and the Young inequality, we obtain that

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|c_r\|^2_{L^2(\Omega)} \leqslant& -\alpha_r\|\nabla c_r\|^2_{(L^2(\Omega))^n} + \|c_r\|_{H^1(\Omega)}\|f\|_{(H^1(\Omega))^*}\\
=& -\alpha_r\|c_r\|^2_{H^1(\Omega)} + \alpha_r\|c_r\|^2_{L^2(\Omega)} + \|c_r\|_{H^1(\Omega)}\|f\|_{(H^1(\Omega))^*}\\
\leqslant& -\frac{1}{2}\alpha_r\|c_r\|^2_{H^1(\Omega)} + \alpha_r\|c_r\|^2_{L^2(\Omega)} + \frac{1}{2}\alpha_r^{-1}\|f\|^2_{(H^1(\Omega))^*},
\end{aligned}$$

which yields (3.3.13) due to Gronwall's inequality. Finally, using (3.3.10), we obtain from the weak formulation (3.3.12) that

$$\|\partial_t c_r\|_{(H^1(\Omega))^*} \leqslant M_r\|\nabla c_r\|_{(L^2(\Omega))^n} + \|f\|_{(H^1(\Omega))^*}$$

and consequently,

$$\|\partial_t c_r\|^2_{L^2(0,T;(H^1(\Omega))^*)} \leqslant 2M_r^2\|\nabla c_r\|^2_{L^2(0,T;(L^2(\Omega))^n)} + 2\|f\|^2_{L^2(0,T;(H^1(\Omega))^*)}.$$

Together with (3.3.13) this implies (3.3.14). □

3.4 Nonlocal models involving averaging operators $\mathcal{T}_r$ and $\mathcal{S}_r$

In this section we study the following model IBVP:

$$\partial_t c_r = \nabla\cdot(D_c(c_r,v_r)\nabla c_r - c_r\chi(c_r,v_r)\mathcal{R}_r(\nabla g(c_r,v_r))) + f_c(c_r,v_r) \quad \text{in } \Omega\times(0,\infty), \tag{3.4.1a}$$

$$\partial_t v_r = D_v\Delta v_r + f_v(c_r,v_r) \quad \text{in } \Omega\times(0,\infty), \tag{3.4.1b}$$

$$D_c(c_r,v_r)\partial_\nu c_r - c_r\chi(c_r,v_r)\mathcal{R}_r(\nabla g(c_r,v_r))\cdot\nu = D_v\partial_\nu v_r = 0 \quad \text{on } \partial\Omega\times(0,\infty), \tag{3.4.1c}$$

$$c_r(\cdot,0) = c_0,\ v_r(\cdot,0) = v_0 \quad \text{in } \Omega. \tag{3.4.1d}$$

Here, as in the previous section, $\mathcal{R}_r$ stands for any of the two averaging operators:

$$\mathcal{R}_r \in \{\mathcal{T}_r, \mathcal{S}_r\}.$$

We assume that the diffusion coefficient D_v is either a positive number, or it is zero.

Equations (3.4.1a)-(3.4.1b) are closely related to (3.1.1) and (3.1.4) in *Section 3.1*, the difference being that the terms involving the adhesion velocity/nonlocal gradient are now replaced by those including the averaging operators $\mathcal{T}_r/\mathcal{S}_r$ from *Section 3.2*. Our motivation for introducing this change is twofold. First of all, due to (3.2.5) and (3.2.8) it affects the points in the boundary layer $\Omega\backslash\Omega_r$, at the most. On the other hand, *Example 3.2.3* indicates that including, e.g., $\mathcal{A}_r$ can lead to limits with unexpected blow-ups on the boundary of Ω.

System (3.4.1) is a nonlocal version of the hapto-/chemotaxis system

$$\partial_t c = \nabla \cdot (D_c(c,v)\nabla c - c\chi(c,v)\nabla g(c,v)) + f_c(c,v) \qquad \text{in } \Omega \times (0,\infty), \tag{3.4.2a}$$
$$\partial_t v = D_v \Delta v + f_v(c,v) \qquad \text{in } \Omega \times (0,\infty), \tag{3.4.2b}$$
$$D_c(c,v)\partial_\nu c_r - c\chi(c,v)\partial_\nu g(c,v) = D_v \partial_\nu v = 0 \qquad \text{on } \partial\Omega \times (0,\infty), \tag{3.4.2c}$$
$$c(\cdot,0) = c_0,\ v(\cdot,0) = v_0 \qquad \text{in } \Omega. \tag{3.4.2d}$$

In this case, the actual diffusion and haptotactic sensitivity coefficients are

$$\widetilde{D}_c(c,v) = D_c(c,v) - c\chi(c,v)\partial_c g(c,v),$$
$$\widetilde{\chi}(c,v) = \chi(c,v)\partial_v g(c,v),$$

so that in the classical formulation (3.4.2a) takes the form

$$\partial_t c = \nabla \cdot \left(\widetilde{D}_c(c,v)\nabla c - c\widetilde{\chi}(c,v)\nabla v\right) + f_c(c,v) \qquad \text{in } \Omega \times (0,\infty).$$

The main goal of this section is to establish, under suitable assumptions on the system coefficients which are introduced in *Subsection 3.4.1*, a rigorous convergence as $r \to 0$ of solutions of the nonlocal model family (3.4.1) to those of the local model (3.4.2), see *Theorem 3.4.8*. This is accomplished in the final *Subsection 3.4.4*. Since we are dealing here with a new type of nonlocal system, we establish for (3.4.1) the existence of nonnegative solutions in *Subsections 3.4.2* and *3.4.3*.

3.4.1 Problem setting and main result of the section

We begin with several general assumptions about the coefficients of system (3.4.1).

Assumptions 3.4.1. *Let $D_v \in \mathbb{R}_0^+$, $D_c, \chi \in C_b(\mathbb{R}_0^+ \times \mathbb{R}_0^+)$, and $g, f_c, f_v \in C^1(\mathbb{R}_0^+ \times \mathbb{R}_0^+)$ satisfy*

$$C_5 \leqslant D_c \leqslant C_6 \quad \text{in } \mathbb{R}_0^+ \times \mathbb{R}_0^+ \quad \text{for some } C_5, C_6 > 0,$$
$$\nabla_{(c,v)} g,\ \nabla_{(c,v)} f_v \in (L^\infty(\mathbb{R}_0^+ \times \mathbb{R}_0^+))^2,$$
$$f_c(0,\cdot) \equiv 0,$$
$$f_v(\cdot,0) \equiv 0.$$

Assume that the coefficients satisfy the following bounds:

$$C_7 := \sup_{c,v \geqslant 0} c|\chi(c,v)| < \infty, \tag{3.4.3}$$
$$C_8 := \sup_{c,v \geqslant 0} |\partial_c g(c,v)| < \infty. \tag{3.4.4}$$

Further, we assume that the initial values satisfy

$$0 \leqslant c_0 \in L^2(\Omega),$$
$$0 \leqslant v_0 \in H^1(\Omega). \tag{3.4.5}$$

Remark 3.4.2. If $D_v > 0$, then assumption (3.4.5) can be replaced by a weaker one, such as

$$v_0 \in L^2(\Omega).$$

We keep (3.4.5) in order to simplify the exposition.

In addition, we will later choose one of the following assumptions on f_c and the nonlocal operator:

Assumptions 3.4.3. *(Further assumptions on f_c) One of the following conditions holds:*

(a)

$$\nabla_{(c,v)} f_c \in \left(L^\infty(\mathbb{R}_0^+ \times \mathbb{R}_0^+)\right)^2$$

(b) there exists $s \geqslant 0$ such that

$$|f_c(c,v)| \leqslant C_9(1+|c|^s) \qquad \text{in } \mathbb{R}_0^+ \times \mathbb{R}_0^+ \qquad \text{for some } C_9 \geqslant 0, \tag{3.4.6}$$

$$cf_c(c,v) \leqslant C_{10} - C_{11}c^{s+1} \qquad \text{in } \mathbb{R}_0^+ \times \mathbb{R}_0^+ \qquad \text{for some } C_{10} \geqslant 0,\ C_{11} > 0. \tag{3.4.7}$$

Assumptions 3.4.4 (Assumptions on $\mathcal{R}_r$)**.** *One of the following holds:*

(a) for a given fixed $r \in (0, r_0]$

$$C_{12}(\|\mathcal{R}_r\|) := 1 - \frac{C_7 C_8}{C_5} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} > 0$$

(b)

$$C_{13} := \frac{C_7 C_8}{C_5} < 1. \tag{3.4.8}$$

Example 3.4.5. Let

$$\begin{aligned}
&D_v = 0,\\
&F_r(\rho) := (n+1)e^{-r\rho},\\
&g(c,v) := \frac{S_{cc}c + S_{cv}v}{1+c+v} \qquad \text{for some constants } S_{cc}, S_{cv} > 0,\\
&D_c(c,v) := \frac{1+c}{1+c+v},\\
&\chi(c,v) := \frac{b}{1+c+v}, \quad b > 0,\\
&f_c(c,v) := \mu_c \frac{c}{1+c^2}(K_c - c - \eta_c v) \quad \text{for some constants } K_c, \eta_c, \mu_c > 0,\\
&f_v(c,v) := \mu_v v(K_v - v) - \lambda_v v \frac{c}{1+c} \quad \text{for some constants } K_v, \lambda_v > 0,\ \mu_v \geqslant 0,
\end{aligned}$$

and assume that

$$0 \leqslant v_0 \leqslant K_v.$$

Then, it holds a priori that

$$0 \leqslant v \leqslant K_v$$

for any v which solves (3.4.1b) due to the form of f_v. Therefore it suffices to consider the coefficient functions in $\mathbb{R}_0^+ \times [0, K_v]$.

For D_c it holds on $\mathbb{R}_0^+ \times [0, K_v]$ that

$$D_c(c,v) \geqslant \frac{1+c}{1+c+K_v} \geqslant \frac{1}{1+K_v} =: C_5$$

and

$$D_c(c,v) \leqslant 1 =: C_6.$$

Obviously, $f_c(0,\cdot) = f_v(\cdot,0) = 0$. Moreover, $\nabla_{(c,v)}g,\ \nabla_{(c,v)}f_v \in (L^\infty(\mathbb{R}_0^+ \times \mathbb{R}_0^+))^2$, due to

$$\begin{aligned}
C_8 = \sup_{c,v\geqslant 0} |\partial_c g(c,v)| &= \max_{0\leqslant v\leqslant K_v} \max_{c\geqslant 0} \frac{|S_{cc}(1+v) - S_{cv}v|}{(1+c+v)^2} \\
&= \max\left\{S_{cc}, \left|\frac{S_{cc}}{1+K_v} - \frac{S_{cv}K_v}{(1+K_v)^2}\right|\right\}, \\
\sup_{c,v\geqslant 0} |\partial_v g(c,v)| &= \max_{0\leqslant v\leqslant K_v} \max_{c\geqslant 0} \frac{|S_{cv}(1+c) - S_{cc}c|}{(1+c+v)^2} \\
&= \max_{c\geqslant 0} \frac{|S_{cv}(1+c) - S_{cc}c|}{(1+c)^2} < \infty, \\
\sup_{c,v\geqslant 0} |\partial_c f_v(c,v)| &= \max_{0\leqslant v\leqslant K_v} \max_{c\geqslant 0} \frac{\lambda_v v}{(1+c)^2} = \lambda_v K_v
\end{aligned}$$

and

$$\sup_{c,v\geqslant 0} |\partial_v f_v(c,v)| = \max_{0\leqslant v\leqslant K_v} \max_{c\geqslant 0} \left|\mu_v(K_v - 2v) - \lambda_v \frac{c}{1+c}\right| < \infty.$$

For $C_9 := \mu_c(K_c + 1 + \eta_c K_v)$, $C_{10} := \mu_c(K_c + 1)$ and $C_{11} := \mu_c$ we can estimate on $\mathbb{R}_0^+ \times \mathbb{R}_0^+$ that

$$\begin{aligned}
&|f_c(c,v)| \leqslant C_9, \\
&c f_c(c,v) = \mu_c \frac{c^2}{1+c^2}(K_c - c - \eta_c v) \leqslant C_{10} - C_{11}c.
\end{aligned}$$

Further,

$$C_7 = \sup_{c,v\geqslant 0} c\chi(c,v) = \sup_{c,v\geqslant 0} \frac{bc}{1+c+v} = \sup_{c\geqslant 0} \frac{bc}{1+c} = b$$

holds.

Thus, *Assumptions 3.1.1, 3.4.1, 3.4.3(b)* and *3.4.4(b)* are fulfilled if

$$(1+K_v)b \max\left\{S_{cc}, \left|\frac{S_{cc}}{1+K_v} - \frac{S_{cv}K_v}{(1+K_v)^2}\right|\right\} < 1.$$

This choice of coefficient functions can be used to describe a population of cancer cells which interact among themselves and with the surrounding extracellular matrix (ECM) tissue. Both interaction types are due to adhesion, whether to other cells (cell-cell adhesion) or to the matrix (cell-matrix adhesion). The interaction force $F_r(\rho)$ is taken to diminish with increasing interaction range ρ and/or of the sensing radius r: cells too far apart/out of reach hardly interact in a direct way. Function $g(c,v)$ characterises effective interactions. Here the coefficients S_{cc} and S_{cv} represent cell-cell and cell-matrix adhesion strengths, respectively. Our choice of g accounts for some adhesiveness limitation imposed by high local cell and tissue densities. It is motivated by the fact that overcrowding may preclude further adhesive bonds, e.g., due to saturation of receptors. The diffusion coefficient $D_c(c,v)$ is chosen to be everywhere positive and increase with a growing population density, thus enhancing diffusivity under population pressure, but, further, limited by excessive cell-tissue interaction. The latter also applies to the choice of the sensitivity function χ. Indeed, there is evidence that tight packing of cells and ECM limits diffusivity and the advective effects of haptotaxis [106]. Thereby the constant $b > 0$ is assumed to be rather small. Finally, f_c and f_v describe growth of cells and tissue limited by concurrence for resources.

Next, we introduce weak-strong solutions to our problem. The definition is as follows:

Definition 3.4.6. *Let Assumptions 3.4.1 hold. Let $r \in [0, r_0]$. We call a pair of functions $(c_r, v_r) : \overline{\Omega} \times \mathbb{R}_0^+ \to \mathbb{R}_0^+ \times \mathbb{R}_0^+$ a global weak-strong solution of (3.4.1) if for all $T > 0$:*

(i) $c_r \in L^2(0,T;H^1(\Omega)) \cap C_w([0,T];L^2(\Omega))$, $\partial_t c_r \in L^1(0,T;(W^1_\infty(\Omega))^*)$;

(ii) $v_r \in W_2^{2,1}(\Omega\times(0,T)) \cap C([0,T];H^1(\Omega))$ *if* $D_v > 0$ *and* $v_r \in L^\infty(0,T;H^1(\Omega)) \cap C([0,T];L^2(\Omega))$ *with* $\partial_t v_r \in L^2(\Omega \times (0,T))$ *if* $D_v = 0$;

(iii) $f_c(c_r, v_r) \in L^1(\Omega \times (0,T))$, $f_v(c_r, v_r) \in L^2(\Omega \times (0,T))$;

(iv) (c_r, v_r) *satisfies* (3.4.1) *in the following weak-strong sense: for all* $\varphi \in C^1(\overline{\Omega})$ *and a.e.* $t \in (0,T)$

$$\langle \partial_t c_r, \varphi \rangle_{(W^1_\infty(\Omega))^*, W^1_\infty(\Omega)} = -\int_\Omega (D_c(c_r,v_r)\nabla c_r - c_r\chi(c_r,v_r)\mathcal{R}_r(\nabla g(c_r,v_r))) \cdot \nabla\varphi \, dx + \int_\Omega f_c(c_r,v_r)\varphi \, dx, \tag{3.4.9a}$$

$$c_r(\cdot,0) = c_0 \qquad \text{in } L^2(\Omega), \tag{3.4.9b}$$

and

$$\partial_t v_r = D_v \Delta v_r + f_v(c_r,v_r) \qquad \text{a.e. in } \Omega \times (0,T), \tag{3.4.9c}$$

$$D_v \partial_\nu v_r = 0 \qquad \text{a.e. on } \partial\Omega \times (0,T), \tag{3.4.9d}$$

$$v_r(\cdot,0) = v_0 \qquad \text{in } H^1(\Omega). \tag{3.4.9e}$$

Remark 3.4.7. Observe that for $r = 0$ we obtain a corresponding solution definition for the local system (3.4.2).

Our main result now reads:

Theorem 3.4.8. *Let Assumptions 3.1.1, 3.4.1, 3.4.3(b) and 3.4.4(b) hold. Then, there exists a sequence $r_m \to 0$ as $m \to \infty$ and solutions (c_{r_m}, v_{r_m}) and (c, v) in terms of Definition 3.4.6 corresponding to $r = r_m$ and $r = 0$, respectively, s.t.*

$$c_{r_m} \underset{m\to\infty}{\to} c \qquad \text{in } L^2(\Omega \times (0,T)),$$

$$v_{r_m} \underset{m\to\infty}{\to} v \qquad \text{in } L^2(\Omega \times (0,T)).$$

This Theorem is proved in *Subsection 3.4.4*.

3.4.2 Global existence of solutions to (3.4.1): the case of f_c Lipschitz

In this subsection we address the existence of solutions to the nonlocal model (3.4.1) for the case when f_c satisfies *Assumptions 3.4.3(a)*. The main result of the Subsection is as follows:

Theorem 3.4.9. *Let Assumptions 3.1.1, 3.4.1, and 3.4.3(a) hold and let r satisfy Assumptions 3.4.4(a). Then there exists a global weak-strong solution with $\partial_t c_r \in L^2(0,T;(H^1(\Omega))^*)$ to* (3.4.1) *in terms of Definition 3.4.6 for $\varphi \in H^1(\Omega)$.*

Since we aim at constructing nonnegative solutions, it turns out to be helpful to consider first the following family of approximating problems:

$$\partial_t c_{r\varepsilon} = \nabla \cdot \Big(D_c(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon} - c_{r\varepsilon}\chi(c_{r\varepsilon}, v_{r\varepsilon})\Big(G_\varepsilon(\mathcal{R}_r(\partial_c g(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon})) + G_\varepsilon(\mathcal{R}_r(\partial_v g(c_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon}))\Big)\Big) + f_c(c_{r\varepsilon}, v_{r\varepsilon}) \quad \text{in } \Omega \times (0,\infty), \tag{3.4.10a}$$

$$\partial_t v_{r\varepsilon} = D_v \Delta v_{r\varepsilon} + f_v(c_{r\varepsilon}, v_{r\varepsilon}) \quad \text{in } \Omega \times (0,\infty), \tag{3.4.10b}$$

$$D_c(c_{r\varepsilon}, v_{r\varepsilon})\partial_\nu c_{r\varepsilon} - c_{r\varepsilon}\chi(c_{r\varepsilon}, v_{r\varepsilon})\Big(G_\varepsilon(\mathcal{R}_r(\partial_c g(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon})) + G_\varepsilon(\mathcal{R}_r(\partial_v g(c_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon}))\Big) \cdot \nu = D_v \partial_\nu v_{r\varepsilon} = 0 \quad \text{on } \partial\Omega \times (0,\infty), \tag{3.4.10c}$$

$$c_{r\varepsilon}(\cdot, 0) = c_0,\ v_{r\varepsilon}(\cdot, 0) = v_0 \quad \text{in } \Omega, \tag{3.4.10d}$$

where G_ε was defined in (3.3.2). In order to obtain existence for the original problem, i.e., for $\varepsilon = 0$, we first prove existence of nonnegative solutions for the cases when $\varepsilon, D_v > 0$. This corresponds to a chemotaxis problem with a nonlocal flux-limited drift. Weak-strong solutions to (3.4.10) are understood as in *Definition 3.4.6*, with the obvious modification of the weak formulation, which now reads:

$$\begin{aligned}\langle \partial_t c_{r\varepsilon}, \varphi\rangle_{(H^1(\Omega))^*, H^1(\Omega)} = &-\int_\Omega D_c(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon} \cdot \nabla\varphi \,\mathrm{d}x \\ &+ \int_\Omega c_{r\varepsilon}\chi(c_{r\varepsilon}, v_{r\varepsilon}) G_\varepsilon(\mathcal{R}_r(\partial_c g(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon})) \cdot \nabla\varphi \,\mathrm{d}x \\ &+ \int_\Omega c_{r\varepsilon}\chi(c_{r\varepsilon}, v_{r\varepsilon}) G_\varepsilon(\mathcal{R}_r(\partial_v g(c_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon})) \cdot \nabla\varphi + f_c(c_{r\varepsilon}, v_{r\varepsilon})\varphi \,\mathrm{d}x.\end{aligned} \tag{3.4.11}$$

Lemma 3.4.10. *Let the assumptions of Theorem 3.4.9 be satisfied. Assume further that*

$$\varepsilon, D_v > 0.$$

Then there exists a global weak-strong solution to (3.4.10) *with*

$$\partial_t c_{r\varepsilon} \in L^2(0, T; (H^1(\Omega))^*)$$

for all $T > 0$.

Proof. To begin with, we extend the coefficients: for $c < 0$ we set

$$(D_c, \chi)(c, v) := (D_c, \chi)(-c, v), \quad f_c(c, v) := -f_c(-c, v), \tag{3.4.12}$$

$$g(c, v) := 2g(0, v) - g(-c, v), \quad f_v(c, v) := 2f_v(0, v) - f_v(-c, v). \tag{3.4.13}$$

These coefficients still satisfy *Assumptions* 3.4.1, *3.4.3(a)*, and *Assumptions 3.4.4(a)* if we consider all suprema over $c \in \mathbb{R}$ instead of $c \in \mathbb{R}_0^+$.

Our approach to proving existence is based on a Schaefer fixed-point argument (see *Theorem A.2.3*). In order to apply this theorem we first 'freeze' $c_{r\varepsilon}$ in the system coefficients of (3.4.10), replacing it by $\overline{c}_{r\varepsilon}$. Correspondingly, we obtain the following weak formulation in place of (3.4.11): For all $\varphi \in H^1(\Omega)$, $T > 0$ and a.e. $t \in (0, T)$

$$\langle \partial_t c_{r\varepsilon}, \varphi\rangle_{(H^1(\Omega))^*, H^1(\Omega)} = -\int_\Omega D_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon} \cdot \nabla\varphi \,\mathrm{d}x$$

$$+\int_\Omega \overline{c}_{r\varepsilon}\chi(\overline{c}_{r\varepsilon}, v_{r\varepsilon})G_\varepsilon(\mathcal{R}_r(\partial_c g(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon}))\cdot\nabla\varphi\,\mathrm{d}x$$
$$+\int_\Omega \overline{c}_{r\varepsilon}\chi(\overline{c}_{r\varepsilon}, v_{r\varepsilon})G_\varepsilon(\mathcal{R}_r(\partial_v g(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon}))\cdot\nabla\varphi + f_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\varphi\,\mathrm{d}x, \tag{3.4.14a}$$

$$c_{r\varepsilon}(0,\cdot) = c_0 \qquad \text{in } L^2(\Omega) \tag{3.4.14b}$$

and

$$\partial_t v_{r\varepsilon} = D_v\Delta v_{r\varepsilon} + f_v(\overline{c}_{r\varepsilon}, v_{r\varepsilon}) \qquad \text{a.e. in } \Omega\times(0;T), \tag{3.4.14c}$$
$$\partial_\nu v_{r\varepsilon} = 0 \qquad \text{a.e. on } \partial\Omega\times(0,T), \tag{3.4.14d}$$
$$v_{r\varepsilon}(\cdot,0) = v_0 \qquad \text{in } H^1(\Omega). \tag{3.4.14e}$$

Let $T > 0$ and let $\overline{c}_{r\varepsilon} \in L^2(\Omega\times(0,T))$.

Step 1 (Existence of $v_{r\varepsilon}$ satisfying (3.4.14c)-(3.4.14e))**.** First, we set $f_v(c,v) := -f_v(c,-v)$ for $v < 0$. We want to perform a Banach fixed-point argument in $C([0,T];L^2(\Omega))$. Therefore, we fix $\overline{v}_{r\varepsilon} \in C([0,T];L^2(\Omega))$. Then, *Theorem A.1.8* and *Lemma A.3.8* imply the existence of a unique solution $v_{r\varepsilon} \in W_2^{2,1}(\Omega\times(0,T)) \cap C([0,T];H^1(\Omega))$ satisfying

$$\partial_t v_{r\varepsilon} = D_v\Delta v_{r\varepsilon} + f_v(\overline{c}_{r\varepsilon}, \overline{v}_{r\varepsilon}) \qquad \text{a.e. in } \Omega\times(0;T),$$
$$\partial_\nu v_{r\varepsilon} = 0 \qquad \text{a.e. on } \partial\Omega\times(0,T),$$
$$v_{r\varepsilon}(\cdot,0) = v_0 \qquad \text{in } H^1(\Omega).$$

Moreover, the map $\Psi : C([0,T];L^2(\Omega)) \to C([0,T];L^2(\Omega))$, $\overline{v}_{r\varepsilon} \mapsto v_{r\varepsilon}$ satisfies

$$\|\Psi(\overline{v}_1) - \Psi(\overline{v}_2)\|_{C([0,T];L^2(\Omega))} \leqslant C_{14}(T)\|f_v\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}\|\overline{v}_1 - \overline{v}_2\|_{C([0,T];L^2(\Omega))}$$

again due to *Theorem A.1.8*, *Lemma A.3.8* and the Lipschitz continuity of f_v. Hence, for small enough T the map Ψ is a contraction and we conclude from Banach's fixed-point theorem (*Theorem A.2.1*) that the semilinear parabolic initial boundary value problem (3.4.14c)-(3.4.14e) possesses a unique strong solution $0 \leqslant v_{r\varepsilon} \in W_2^{2,1}(\Omega\times(0,T))$. The solution extends to a global solution as the choice of T only depends on fixed parameters. Multiplying (3.4.14c) by $(v_{r\varepsilon})_- := -\min\{v_{r\varepsilon}, 0\}$ and integrating over Ω implies together with the Lipschitz continuity of f_v and $f_v(\cdot,0) \equiv 0$ that

$$\frac{1}{2}\frac{d}{dt}\|(v_{r\varepsilon})_-\|^2_{L^2(\Omega)} \leqslant \|\partial_v f_v\|_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)}\|(v_{r\varepsilon})_-\|^2_{L^2(\Omega)}.$$

Due to $v_0 \geqslant 0$ and Gronwall's inequality $v_{r\varepsilon} \geqslant 0$ follows. Analogously, we conclude that

$$\|v_{r\varepsilon}\|_{L^\infty(0,T;L^2(\Omega))} \leqslant C_{15}(T)\|v_0\|_{L^2(\Omega)}.$$

Combining this with the Lipschitz continuity of f_v, $f_v(\cdot,0) \equiv 0$, *Theorem A.1.8* and *Lemma A.3.8* the estimate

$$\begin{aligned}
&\|v_{r\varepsilon}\|^2_{C([0,T];H^1(\Omega))} + \|v_{r\varepsilon}\|^2_{L^2(0,T;H^2(\Omega))} + \|\partial_t v_{r\varepsilon}\|^2_{L^2(\Omega\times(0,T))}\\
\leqslant& C_{16}(T)\left(\|v_0\|^2_{H^1(\Omega)} + \|f_v(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\|^2_{L^2(\Omega\times(0,T))}\right)\\
\leqslant& C_{16}(T)\left(\|v_0\|^2_{H^1(\Omega)} + \|\partial_v f_v\|^2_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)}\|v_{r\varepsilon}\|^2_{L^2(\Omega\times(0,T))}\right) \leqslant C_{17}(T)\|v_0\|^2_{H^1(\Omega)}
\end{aligned} \tag{3.4.15}$$

follows. Here and further in the proof we omit the dependence of constants upon D_v.

Step 2 (Existence of $c_{r\varepsilon}$ satisfying (3.4.14a) and (3.4.14b))**.** Set

$$a_1 := D_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon}), \qquad a_2 := \overline{c}_{r\varepsilon}\chi(\overline{c}_{r\varepsilon}, v_{r\varepsilon}), \qquad a_3 := \partial_c g(\overline{c}_{r\varepsilon}, v_{r\varepsilon}),$$

$$\langle f, \varphi\rangle_{(H^1(\Omega))^*, H^1(\Omega)} := \int_\Omega \overline{c}_{r\varepsilon}\chi(\overline{c}_{r\varepsilon}, v_{r\varepsilon}) G_\varepsilon(\mathcal{R}_r(\partial_v g(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon})) \cdot \nabla\varphi + f_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\varphi \,\mathrm{d}x.$$

Due to our assumptions about D_c, χ, g, and f_c, these coefficients a_i and f satisfy the requirements of *Lemma 3.3.5*. Consequently, there exists a unique global weak solution $c_{r\epsilon}$ to problem (3.3.1) with these coefficients. We estimate for the corresponding constants α_r and M_r introduced in (3.3.8):

$$\begin{aligned}
\alpha_r =& \left\| \frac{1}{D_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})} \right\|^{-1}_{L^\infty(\Omega\times(0,T))} \\
&\cdot \left(1 - \left\| \frac{\overline{c}_{r\varepsilon}\chi(\overline{c}_{r\varepsilon}, v_{r\varepsilon})}{D_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})^{\frac{1}{2}}} \right\|_{L^\infty(\Omega\times(0,T))} \left\| \frac{\partial_c g(\overline{c}_{r\varepsilon}, v_{r\varepsilon})}{D_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})^{\frac{1}{2}}} \right\|_{L^\infty(\Omega\times(0,T))} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} \right) \\
\geqslant& C_5 C_{12}(r) =: C_{18}(r), \qquad (3.4.16) \\
M_r =& \|D_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\|_{L^\infty(\Omega\times(0,T))} \\
&+ \|\overline{c}_{r\varepsilon}\chi(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\|_{L^\infty(\Omega\times(0,T))} \|\partial_c g(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\|_{L^\infty(\Omega\times(0,T))} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} \\
\leqslant& C_6 + C_7 C_8 \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} =: C_{19}(r), \qquad (3.4.17)
\end{aligned}$$

and, due to the Lipschitz continuity of G_ε and $G_\varepsilon(0) = 0$, the linearity of $\mathcal{R}_r$, the Lipschitz continuity of g and f_c and (3.4.15),

$$\begin{aligned}
&\|f\|_{L^2(0,T;(H^1(\Omega))^*)} \\
\leqslant& \|\overline{c}_{r\varepsilon}\chi(\overline{c}_{r\varepsilon}, v_{r\varepsilon}) G_\varepsilon(\mathcal{R}_r(\partial_v g(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon}))\|_{L^2(0,T;(L^2(\Omega))^n)} + \|f_c(\overline{c}_{r\varepsilon}, v_{r\varepsilon})\|_{L^2(\Omega\times(0,T))} \\
\leqslant& C_7 \|\mathcal{R}_r\|_{L(L^2(\Omega))^n)} ||\partial_v g||_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)} \|\nabla v_{r\varepsilon}\|_{L^2(0,T;(L^2(\Omega))^n)} + \|\partial_c f_c\|_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)} \|\overline{c}_{r\varepsilon}\|_{L^2(\Omega\times(0,T))} \\
\leqslant& C_{20}(r,T) \left(1 + \|\overline{c}_{r\varepsilon}\|_{L^2(\Omega\times(0,T))}\right). \qquad (3.4.18)
\end{aligned}$$

Combining (3.3.13)-(3.3.14) and (3.4.16)-(3.4.18), we obtain the following bounds for $c_{r\epsilon}$:

$$\|c_{r\varepsilon}\|^2_{C([0,T];L^2(\Omega))} + \alpha_r \|\nabla c_{r\varepsilon}\|^2_{L^2(0,T;(L^2(\Omega))^n)} \leqslant C_{21}(r,T) \left(1 + \|\overline{c}_{r\varepsilon}\|^2_{L^2(\Omega\times(0,T))}\right), \qquad (3.4.19)$$

$$\|\partial_t c_{r\varepsilon}\|^2_{L^2(0,T;(H^1(\Omega))^*)} \leqslant C_{22}(r,T) \left(1 + \|\overline{c}_{r\varepsilon}\|^2_{L^2(\Omega\times(0,T))}\right). \qquad (3.4.20)$$

Step 3 (Fixed-point argument.)**.** Now consider the mapping

$$\Phi : \overline{c}_{r\varepsilon} \mapsto c_{r\varepsilon}.$$

Thanks to (3.4.19) and (3.4.20), Φ is well-defined in $L^2(\Omega \times (0,T))$ and

$$\Phi : L^2(\Omega \times (0,T)) \to \{u \in L^2(0,T; H^1(\Omega)) : \ \partial_t u \in L^2(0,T; (H^1(\Omega))^*)\}$$
$$\text{maps bounded sets on bounded sets.} \qquad (3.4.21)$$

Due to the Lions-Aubin lemma (*Lemma A.3.9*), (3.4.21) implies that

$$\Phi : L^2(\Omega \times (0,T)) \to L^2(\Omega \times (0,T)) \text{ maps bounded sets on precompact sets.} \qquad (3.4.22)$$

Next, we verify that Φ is closed in $L^2(\Omega \times (0,T))$. Consider a sequence

$$(\overline{c}_{r\varepsilon m})_m \subset L^2(\Omega \times (0,T))$$

s.t.

$$\overline{c}_{r\varepsilon m} \underset{m\to\infty}{\to} \overline{c}_{r\varepsilon} \qquad \text{in } L^2(\Omega\times(0,T)), \tag{3.4.23}$$

$$\Phi(\overline{c}_{r\varepsilon m}) =: c_{r\varepsilon m} \underset{m\to\infty}{\to} c_{r\varepsilon} \qquad \text{in } L^2(\Omega\times(0,T)). \tag{3.4.24}$$

We need to check that

$$\Phi(\overline{c}_{r\varepsilon}) = c_{r\varepsilon}.$$

Due to (3.4.23) we have (by switching to a subsequence, if necessary) that

$$\overline{c}_{r\varepsilon m} \underset{m\to\infty}{\to} \overline{c}_{r\varepsilon} \qquad \text{a.e. in } \Omega\times(0,T). \tag{3.4.25}$$

Further, (3.4.21) and (3.4.24) together with the Banach-Alaoglu theorem and *Lemma A.3.8* imply that

$$c_{r\varepsilon m} \underset{m\to\infty}{\rightharpoonup} c_{r\varepsilon} \qquad \text{in } L^2(0,T;H^1(\Omega)), \tag{3.4.26}$$

$$\partial_t c_{r\varepsilon m} \underset{m\to\infty}{\rightharpoonup} \partial_t c_{r\varepsilon} \qquad \text{in } L^2(0,T;(H^1(\Omega))^*) \tag{3.4.27}$$

and $c_{r\varepsilon} \in C([0,T];L^2(\Omega))$. By the definition of Φ we have that $\overline{c}_{r\varepsilon m}$ and $c_{r\varepsilon m}$ satisfy: for all $\varphi \in H^1(\Omega)$ and a.e. $t \in (0,T)$

$$\begin{aligned}\langle \partial_t c_{r\varepsilon m}, \varphi\rangle_{(H^1(\Omega))^*,H^1(\Omega)} = &-\int_\Omega D_c(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\nabla c_{r\varepsilon m}\cdot\nabla\varphi\,\mathrm{d}x \\ &+\int_\Omega \overline{c}_{r\varepsilon m}\chi(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})G_\varepsilon(\mathcal{R}_r(\partial_c g(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\nabla c_{r\varepsilon m}))\cdot\nabla\varphi\,\mathrm{d}x \\ &+\int_\Omega \overline{c}_{r\varepsilon m}\chi(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})G_\varepsilon(\mathcal{R}_r(\partial_v g(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\nabla v_{r\varepsilon m}))\cdot\nabla\varphi \\ &\quad + f_c(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\varphi\,\mathrm{d}x,\end{aligned} \tag{3.4.28a}$$

$$c_{r\varepsilon m}(0,\cdot) = c_0 \qquad \text{in } L^2(\Omega) \tag{3.4.28b}$$

and

$$\partial_t v_{r\varepsilon m} = D_v\Delta v_{r\varepsilon m} + f_v(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m}) \qquad \text{a.e. in } \Omega\times(0,T), \tag{3.4.28c}$$

$$\partial_\nu v_{r\varepsilon m} = 0 \qquad \text{a.e. on } \partial\Omega\times(0,T), \tag{3.4.28d}$$

$$v_{r\varepsilon m}(\cdot,0) = v_0 \qquad \text{in } H^1(\Omega). \tag{3.4.28e}$$

From (3.4.15) and (3.4.23) we conclude that the sequence $(v_{r\varepsilon m})_m$ is uniformly bounded in $L^2(0,T;H^2(\Omega))$ and $(\partial_t v_{r\varepsilon m})_m$ in $L^2(\Omega\times(0,T))$. Hence the Lions-Aubin lemma and the Banach-Alaoglu theorem imply that there exists $v_{r\varepsilon}$ s.t. (after switching to a subsequence, if necessary)

$$\begin{aligned} v_{r\varepsilon m} &\underset{m\to\infty}{\rightharpoonup} v_{r\varepsilon} \qquad \text{in } L^2(0,T;H^2(\Omega)), \\ \partial_t v_{r\varepsilon m} &\underset{m\to\infty}{\rightharpoonup} \partial_t v_{r\varepsilon} \qquad \text{in } L^2(\Omega\times(0,T)), \\ v_{r\varepsilon m} &\underset{m\to\infty}{\to} v_{r\varepsilon} \qquad \text{in } L^2(0,T;H^1(\Omega)) \text{ and a.e. in } \Omega\times(0,T), \end{aligned} \tag{3.4.29}$$

and due to the Lipschitz continuity of f_v, the fundamental lemma of calculus of variations and the embedding $H^1(\Omega) \hookrightarrow L^2(\partial\Omega)$ this $v_{r\varepsilon}$ satisfies equation (3.4.14c) for $\overline{c}_{r\varepsilon}$ as well as the initial and boundary conditions in the required sense. Moreover, $v_{r\varepsilon} \geqslant 0$ as pointwise limit of such functions.

Further, we conclude from combining (3.4.26) and (3.4.27) with *Lemmas A.3.4* and *A.3.8* that

$$c_{r\varepsilon m}(\cdot,t) \underset{m\to\infty}{\rightharpoonup} c_{r\varepsilon}(\cdot,t) \qquad \text{in } L^2(\Omega) \tag{3.4.30}$$

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

$$c_{r\varepsilon m}(\cdot,0) = c_0,$$

i.e., the initial condition is satisfied.

It remains now to pass to the limit in (3.4.28a). For this purpose we use the Minty-Browder method. To shorten the notation, we introduce for $u \in L^2(0,T;H^1(\Omega))$ and $m \in \mathbb{N} \cup \{\infty\}$

$$\begin{aligned}
&\langle \mathcal{M}_m(u), \varphi\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))}\\
:=&\int_0^T\int_\Omega D_c(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\nabla u\cdot\nabla\varphi - G_\varepsilon(\mathcal{R}_r(\partial_c g(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\nabla u))\overline{c}_{r\varepsilon m}\chi(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\cdot\nabla\varphi\,\mathrm{d}x\,\mathrm{d}t,\\
&\langle f_m, \varphi\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))}\\
:=&\int_0^T\int_\Omega \overline{c}_{r\varepsilon m}\chi(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})G_\varepsilon(\mathcal{R}_r(\partial_v g(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\nabla v_{r\varepsilon m}))\cdot\nabla\varphi + f_c(\overline{c}_{r\varepsilon m}, v_{r\varepsilon m})\varphi\,\mathrm{d}x\,\mathrm{d}t,
\end{aligned}$$

where

$$\overline{c}_{r\varepsilon\infty} := \overline{c}_{r\varepsilon}, \qquad \overline{v}_{r\varepsilon\infty} := \overline{v}_{r\varepsilon}.$$

Due to *Lemma 3.3.3(ii)*, (3.4.17) and (3.4.26) each operator $\mathcal{M}_m$ is monotone, hemicontinuous, and satisfies

$$||\mathcal{M}_m(c_{r\varepsilon m})||_{L^2(0,T;(H^1(\Omega))^*)} \leqslant C_{19}(r)\|c_{r\varepsilon m}\|_{L^2(0,T;H^1(\Omega))} \leqslant C_{23}(r).$$

Consequently, due to weak compactness there is $\eta \in L^2(0,T;(H^1(\Omega))^*)$ s.t.

$$\mathcal{M}_m(c_{r\varepsilon m}) \rightharpoonup \eta \text{ in } L^2(0,T;(H^1(\Omega))^*). \tag{3.4.31}$$

Next, from (3.4.25) and (3.4.29), the boundedness and continuity of $(c,v) \mapsto c\chi(c,v)$, ∇g and ∇f_c over $\mathbb{R}\times\mathbb{R}_0^+$, the Lipschitz continuity of G_ε, the fact that $\mathcal{R}_r \in L((L^2(\Omega))^n)$ and the dominated convergence theorem we conclude that

$$f_m \underset{m\to\infty}{\to} f_\infty \qquad \text{in } L^2(0,T;(H^1(\Omega))^*). \tag{3.4.32}$$

A similar argument yields

$$\mathcal{M}_m(u) \underset{m\to\infty}{\to} \mathcal{M}_\infty(u), \qquad \text{in } L^2(0,T;(H^1(\Omega))^*) \tag{3.4.33}$$

for all $u \in L^2(0,T;H^1(\Omega))$ so that due to (3.4.26) and compensated compactness (*Lemma A.3.2*)

$$\langle \mathcal{M}_m(u), c_{r\varepsilon m}\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))} \underset{m\to\infty}{\to} \langle \mathcal{M}_\infty(u), c_{r\varepsilon}\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))}.$$

Observe that the weak formulation (3.4.28a) is equivalent to

$$\partial_t c_{r\varepsilon m} = -\mathcal{M}_m(c_{r\varepsilon m}) + f_m \qquad \text{in } (H^1(\Omega))^* \tag{3.4.34}$$

for a.e. $t \in (0,T)$. Combining (3.4.27), (3.4.31), and (3.4.32) we can pass to the weak limit in (3.4.34) and obtain

$$\partial_t c_{r\varepsilon} = -\eta + f_\infty \qquad \text{in } (H^1(\Omega))^* \tag{3.4.35}$$

for a.e. $t \in (0,T)$. For $u \in L^2(0,T;H^1(\Omega))$ and $m \in \mathbb{N}$ we have due to the monotonicity of $\mathcal{M}_m$ that

$$X_m := \langle \mathcal{M}_m(c_{r\varepsilon m}) - \mathcal{M}_m(u), c_{r\varepsilon m} - u\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))} \geqslant 0. \tag{3.4.36}$$

Moreover, setting $\varphi = c_{r\varepsilon m}$ in (3.4.28), integrating over $(0,T)$ and using *Lemma A.3.8* after inserting the obtained term into the definition of X_m, we conclude that

$$\begin{aligned} X_m = &- \langle \mathcal{M}_m(c_{r\varepsilon m}), u\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))} \\ &- \langle \mathcal{M}_m(u), c_{r\varepsilon m} - u\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))} \\ &+ \frac{1}{2}\|c_0\|^2_{L^2(\Omega)} - \frac{1}{2}\|c_{r\varepsilon m}(T)\|^2_{L^2(\Omega)} + \langle f_m, c_{r\varepsilon m}\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))}. \end{aligned} \tag{3.4.37}$$

From (3.4.30) for $t = T$ we conclude $\|c_{r\varepsilon}(T)\|_{L^2(\Omega)} \leqslant \liminf_{m\to\infty} \|c_{r\varepsilon m}(T)\|_{L^2(\Omega)}$. Combining this with (3.4.26), (3.4.31)–(3.4.33), (3.4.36), and (3.4.37) and compensated compactness, we obtain

$$\begin{aligned} 0 \leqslant \limsup_{m\to\infty} X_m \leqslant &- \langle \eta, u\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))} \\ &- \langle \mathcal{M}_\infty(u), c_{r\varepsilon} - u\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))} \\ &+ \frac{1}{2}\|c_0\|^2_{L^2(\Omega)} - \frac{1}{2}\|c_{r\varepsilon}(T)\|^2_{L^2(\Omega)} + \langle f_\infty, c_{r\varepsilon}\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))}. \end{aligned}$$

As $c_{r\varepsilon}$ satisfies (3.4.35), it follows again with *Lemma A.3.8* from the last inequality that

$$0 \leqslant \langle \eta - \mathcal{M}_\infty(u), c_{r\varepsilon} - u\rangle_{L^2(0,T;(H^1(\Omega))^*),L^2(0,T;H^1(\Omega))}$$

holds for all $u \in L^2(0,T;H^1(\Omega))$.

Since $\mathcal{M}_\infty$ is monotone and hemicontinuous, *Lemma A.1.16* implies that it is maximal monotone. Consequently, $\eta = \mathcal{M}_\infty(c_{r\varepsilon})$.

Altogether, we conclude that $(c_{r\varepsilon}, v_{r\varepsilon})$ satisfies (3.4.14) for $\overline{c}_{r\varepsilon}$, meaning that $\Phi(\overline{c}_{r\varepsilon}) = c_{r\varepsilon}$ holds, i.e., Φ is a closed operator. Together with (3.4.22), this implies that

$$\Phi : L^2(0,T;L^2(\Omega)) \to L^2(0,T;L^2(\Omega)) \text{ is a compact operator.} \tag{3.4.38}$$

Since we aim to apply the Schaefer's fixed-point theorem (*Theorem A.2.3*), it is necessary to consider for $\lambda \in (0,1)$ the system which corresponds to $c_{r\varepsilon} = \lambda\Phi(c_{r\varepsilon})$. The corresponding weak-strong formulation reads:

$$\begin{aligned} &\langle \partial_t c_{r\varepsilon}, \varphi\rangle_{(H^1(\Omega))^*,H^1(\Omega)} \\ &= -\int_\Omega D_c(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon} \cdot \nabla\varphi \,\mathrm{d}x \\ &\quad + \lambda\int_\Omega c_{r\varepsilon}\chi(c_{r\varepsilon}, v_{r\varepsilon})G_\varepsilon(\lambda^{-1}\mathcal{R}_r(\partial_c g(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon}))\cdot\nabla\varphi\,\mathrm{d}x \\ &\quad + \lambda\int_\Omega c_{r\varepsilon}\chi(c_{r\varepsilon}, v_{r\varepsilon})G_\varepsilon(\mathcal{R}_r(\partial_v g(c_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon}))\cdot\nabla\varphi + f_c(c_{r\varepsilon}, v_{r\varepsilon})\varphi\,\mathrm{d}x, \end{aligned} \tag{3.4.39a}$$

$$c_{r\varepsilon}(\cdot,0) = \lambda c_0 \qquad \text{in } L^2(\Omega) \tag{3.4.39b}$$

and

$$\partial_t v_{r\varepsilon} = D_v \Delta v_{r\varepsilon} + f_v(c_{r\varepsilon}, v_{r\varepsilon}) \qquad \text{a.e. in } \Omega \times (0,T), \tag{3.4.39c}$$

$$\partial_\nu v_{r\varepsilon} = 0 \qquad \text{a.e. on } \partial\Omega \times (0,T), \tag{3.4.39d}$$

$$v_{r\varepsilon}(\cdot,0) = v_0 \qquad \text{in } H^1(\Omega). \tag{3.4.39e}$$

Taking $\varphi := c_{r\varepsilon}$ in (3.4.39) and estimating the right-hand side by using *Assumptions 3.4.1* and *3.4.4(a)*, the Hölder inequality, the fact that $|G_\varepsilon(x)| \leqslant |x|$, *Lemmas 3.2.5(i)*, *3.2.7(i)* and *A.3.8* we obtain that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}||c_{r\varepsilon}||^2_{L^2(\Omega)} \\
\leqslant &- C_5 \|\nabla c_{r\varepsilon}\|^2_{(L^2(\Omega))^n} + \lambda C_7 \|G_\varepsilon(\lambda^{-1}\mathcal{R}_r(\partial_c g(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon}))\|_{(L^2(\Omega))^n} \|\nabla c_{r\varepsilon}\|_{(L^2(\Omega))^n} \\
&+ \lambda C_7 \|G_\varepsilon(\mathcal{R}_r(\partial_v g(c_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon}))\|_{(L^2(\Omega))^n} ||\nabla c_{r\varepsilon}||_{(L^2(\Omega))^n} \\
&+ \lambda \|\partial_c f_c\|_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)} ||c_{r\varepsilon}||^2_{L^2(\Omega)} \\
\leqslant &- C_5 \|\nabla c_{r\varepsilon}\|^2_{(L^2(\Omega))^n} + \lambda C_7 \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} \frac{1}{\lambda} C_8 \|\nabla c_{r\varepsilon}\|^2_{(L^2(\Omega))^n} \\
&+ C_7 ||\partial_v g||_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} \|\nabla v_{r\varepsilon}\|_{(L^2(\Omega))^n} ||\nabla c_{r\varepsilon}||_{(L^2(\Omega))^n} \\
&+ \|\partial_c f_c\|_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)} ||c_{r\varepsilon}||^2_{L^2(\Omega)} \\
\leqslant &- C_5 C_{12}(\|\mathcal{R}_r\|) \|\nabla c_{r\varepsilon}\|^2_{(L^2(\Omega))^n} \\
&+ C_7 ||\partial_v g||_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)} \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)} ||\nabla v_{r\varepsilon}||_{(L^2(\Omega))^n} \|\nabla c_{r\varepsilon}\|_{(L^2(\Omega))^n} \\
&+ \|\partial_c f_c\|_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)} ||c_{r\varepsilon}||^2_{L^2(\Omega)}
\end{aligned} \tag{3.4.40}$$

holds for a.e. $t \in (0,T)$. Hence, Young's inequality and (3.4.15) imply that

$$\frac{1}{2}\frac{d}{dt}||c_{r\varepsilon}(t)||^2_{L^2(\Omega)} \leqslant C_{24}(\|\mathcal{R}_r\|, T)\left(1 + ||c_{r\varepsilon}(t)||^2_{L^2(\Omega)}\right) \tag{3.4.41}$$

for a.e. $t \in (0,T]$ and we conclude from Gronwall's inequality that the set

$$\left\{c_{r\varepsilon} \in L^2(\Omega \times (0,T)) :\, c_{r\varepsilon} = \lambda\Phi(c_{r\varepsilon}) \text{ for } \lambda \in (0,1)\right\}$$

is uniformly bounded. Consequently, for all $\varepsilon \in (0,1)$ the Schaefer's fixed-point theorem implies that Φ has a fixed point $c_{r\varepsilon}$, which together with the corresponding $v_{r\varepsilon}$, satisfies (3.4.10) in the weak-strong sense on the interval $[0,T]$. Since $T > 0$ was arbitrary, this extends to a global solution.

Step 4 (Nonnegativity of $c_{r\varepsilon}$)**.** It remains to check that $c_{r\varepsilon}$ is nonnegative. Therefore, we take $\varphi := -(c_{r\varepsilon})_- = \min\{c_{r\varepsilon}, 0\}$ in (3.4.11) and use $f_c(0,\cdot) \equiv 0$, the boundedness of $G_\varepsilon, D_c, \partial_c f_c, \chi$, along with the Hölder and Young inequalities, which yields

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|(c_{r\varepsilon})_-\|^2_{L^2(\Omega)} = &- \int_\Omega D_c(-(c_{r\varepsilon})_-, v_{r\varepsilon}) \,|\nabla(c_{r\varepsilon})_-|^2 \,\mathrm{d}x \\
&+ \int_\Omega G_\varepsilon(\mathcal{R}_r(\partial_c g(c_{r\varepsilon}, v_{r\varepsilon})\nabla c_{r\varepsilon})) \cdot (c_{r\varepsilon})_- \chi(-(c_{r\varepsilon})_-, v_{r\varepsilon})\nabla(c_{r\varepsilon})_- \,\mathrm{d}x \\
&+ \int_\Omega G_\varepsilon(\mathcal{R}_r(\partial_v g(c_{r\varepsilon}, v_{r\varepsilon})\nabla v_{r\varepsilon})) \cdot (c_{r\varepsilon})_- \chi(-(c_{r\varepsilon})_-, v_{r\varepsilon})\nabla(c_{r\varepsilon})_- \,\mathrm{d}x
\end{aligned}$$

$$\begin{aligned}
&+\int_\Omega f_c(-(c_{r\varepsilon})_-, v_{r\varepsilon})(c_{r\varepsilon})_- \,\mathrm{d}x\\
\leqslant &-C_5\|\nabla(c_{r\varepsilon})_-\|^2_{(L^2(\Omega))^n}+\frac{2}{\varepsilon}\|\chi\|_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)}\|(c_{r\varepsilon})_-\|_{L^2(\Omega)}\|\nabla(c_{r\varepsilon})_-\|_{(L^2(\Omega))^n}\\
&+\|\partial_c f_c\|_{L^\infty(\mathbb{R}\times\mathbb{R}_0^+)}\|(c_{r\varepsilon})_-\|^2_{L^2(\Omega)}\\
\leqslant &C_{25}\|(c_{r\varepsilon})_-\|^2_{L^2(\Omega)}.
\end{aligned}$$

Since $c_{r\varepsilon}(0,\cdot)=c_0\geqslant 0$, the Gronwall inequality implies that $(c_{r\varepsilon})_-\equiv 0$, i.e., that $c_{r\varepsilon}\geqslant 0$.

□

Remark 3.4.11. Observe that $c_{r\varepsilon}$ cannot be replaced by $-(c_{r\varepsilon})_-$ inside the nonlocal operator. This is why we introduced the flux-limitation.

Now we are ready to prove *Theorem 3.4.9.*

Proof of Theorem 3.4.9. Let $T>0$.

Case $D_v>0$: We start with the case

$$D_v>0.$$

Lemma 3.4.10 gives the existence of solutions $(c_{r\varepsilon}, v_{r\varepsilon})$ to (3.4.10). Setting $\varphi=c_{r\varepsilon}$ in (3.4.11), using the fact that $|G_\varepsilon(x)|\leqslant|x|$, we obtain similarly to (3.4.15), (3.4.40), and (3.4.41) and using Gronwall's inequality that

$$\|c_{r\varepsilon}\|_{L^\infty(0,T;L^2(\Omega))}+\|\nabla c_{r\varepsilon}\|_{L^2(0,T;(L^2(\Omega))^n)}\leqslant C_{26}(\|\mathcal{R}_r\|,T), \tag{3.4.42}$$

and

$$\|v_{r\varepsilon}\|_{C([0,T];H^1(\Omega))}+\|v_{r\varepsilon}\|_{L^2(0,T;H^2(\Omega))}+\|\partial_t v_{r\varepsilon}\|_{L^2(\Omega\times(0,T))}\leqslant C_{27}(\|\mathcal{R}_r\|,T) \tag{3.4.43}$$

where all constants are especially independent from ε. Consequently, for a.e. $t\in(0,T)$ and all $\varphi\in H^1(\Omega)$ we can estimate similarly to (3.4.40) and (3.4.41) that

$$\begin{aligned}
&\langle\partial_t c_{r\varepsilon},\varphi\rangle_{(H^1(\Omega))^*,H^1(\Omega)}\\
\leqslant &C_6\|\nabla c_{r\varepsilon}\|_{(L^2(\Omega))^n}\|\nabla\varphi\|_{(L^2(\Omega))^n}+C_7\|G_\varepsilon(\mathcal{R}_r(\partial_c g(c_{r\varepsilon},v_{r\varepsilon})\nabla c_{r\varepsilon}))\|_{(L^2(\Omega))^n}\|\nabla\varphi\|_{(L^2(\Omega))^n}\\
&+C_7\|G_\varepsilon(\mathcal{R}_r(\partial_v g(c_{r\varepsilon},v_{r\varepsilon})\nabla v_{r\varepsilon}))\|_{(L^2(\Omega))^n}\|\nabla\varphi\|_{(L^2(\Omega))^n}+\|f_c(c_{r\varepsilon},v_{r\varepsilon})\|_{L^2(\Omega)}\|\varphi\|_{L^2(\Omega)}\\
\leqslant &C_{28}(\|\mathcal{R}_r\|,T)\left(1+\|\nabla c_{r\varepsilon}\|_{(L^2(\Omega))^n}\right)\|\varphi\|_{H^1(\Omega)}.
\end{aligned}$$

Integrating over $(0,T)$, we conclude from (3.4.42) that

$$\int_0^T\|\partial_t c_{r\varepsilon}\|^2_{(H^1(\Omega))^*}\,\mathrm{d}t\leqslant C_{29}(\|\mathcal{R}_r\|,T)\left(1+\int_0^T\|\nabla c_{r\varepsilon}\|^2_{(L^2(\Omega))^n}\,\mathrm{d}t\right)\leqslant C_{30}(\|\mathcal{R}_r\|,T). \tag{3.4.44}$$

Combining (3.4.42)–(3.4.44) and applying the Lions-Aubin lemma (*Lemma A.3.9*), the Banach-Alaoglu theorem and *Lemma A.3.8*, we conclude the existence of a pair of nonnegative functions $c_r\in L^2(0,T;H^1(\Omega))\cap C([0,T];L^2(\Omega))$ with $\partial_t c_r\in L^2(0,T;(H^1(\Omega))^*)$ and $v_r\in W_2^{2,1}(\Omega\times(0,T))\cap C([0,T];H^1(\Omega))$ such that for a sequence $\varepsilon_m\underset{m\to\infty}{\to}0$ it holds that

$$c_{r\varepsilon_m}\underset{m\to\infty}{\to}c_r\text{ in }L^2(\Omega\times(0,T))\text{ and a.e. in }\Omega\times(0,T), \tag{3.4.45}$$

$$c_{r\varepsilon_m} \underset{m\to\infty}{\rightharpoonup} c_r \text{ in } L^2(0,T;H^1(\Omega)), \tag{3.4.46}$$

$$\partial_t c_{r\varepsilon_m} \underset{m\to\infty}{\rightharpoonup} \partial_t c_r \text{ in } L^2(0,T;(H^1(\Omega))^*), \tag{3.4.47}$$

$$v_{r\varepsilon_m} \underset{m\to\infty}{\to} v_r \text{ in } L^2(0,T;H^1(\Omega)) \text{ and a.e. in } \Omega\times(0,T), \tag{3.4.48}$$

$$v_{r\varepsilon_m} \underset{m\to\infty}{\rightharpoonup} v_r \text{ in } L^2(0,T;H^2(\Omega)), \tag{3.4.49}$$

$$\partial_t v_{r\varepsilon_m} \underset{m\to\infty}{\rightharpoonup} \partial_t v_r \text{ in } L^2(\Omega\times(0,T)). \tag{3.4.50}$$

Consider an arbitrary measurable set $E \subset \Omega\times(0,T)$. Using $G_\varepsilon(x) - x = -\varepsilon\frac{x|x|}{1+\varepsilon|x|}$, we can estimate for every component $i \in \{1,\dots,n\}$:

$$\begin{aligned}
&\left|\int_E \left(G_{\varepsilon_m}(\mathcal{R}_r(\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m})) - \mathcal{R}_r(\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m})\right)_i \,\mathrm{d}x\,\mathrm{d}t\right| \\
\leqslant&\varepsilon_m \int_0^T\int_\Omega |\mathcal{R}_r(\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m}|^2 \,\mathrm{d}x\,\mathrm{d}t \\
\leqslant&\varepsilon_m \|\mathcal{R}_r\|^2_{L((L^2(\Omega))^n)} C_8^2 \|\nabla c_{r\varepsilon_m}\|^2_{L^2(0,T;(L^2(\Omega))^n)},
\end{aligned}$$

where the last term tends to 0 due to (3.4.42) as $\varepsilon_m \underset{m\to\infty}{\to} 0$. As the term inside the integral is moreover bounded in $L^2(\Omega\times(0,T))$ by a constant independent from ε_m, we conclude by using *Lemma A.3.3* that in $L^2(0,T;(L^2(\Omega))^n)$

$$G_{\varepsilon_m}(\mathcal{R}_r(\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m})) - \mathcal{R}_r(\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m}) \underset{m\to\infty}{\rightharpoonup} 0. \tag{3.4.51}$$

With the help of *Lemma 3.2.5(ii)* or *3.2.7(ii)* we can rewrite that

$$\begin{aligned}
&\int_0^T\int_\Omega \mathcal{R}_r(\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m}) \cdot c_{r\varepsilon_m}\chi(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla\psi \,\mathrm{d}x\,\mathrm{d}t \\
=&\int_0^T\int_\Omega \partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m} \cdot \mathcal{R}_r(c_{r\varepsilon_m}\chi(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla\psi) \,\mathrm{d}x\,\mathrm{d}t.
\end{aligned} \tag{3.4.52}$$

The pointwise convergences from (3.4.45) and (3.4.48) together with the boundedness and continuity of $(c,v) \mapsto c\chi(c,v)$ and the dominated convergence theorem imply that

$$c_{r\varepsilon_m}\chi(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla\psi \underset{m\to\infty}{\to} c_r\chi(c_r,v_r)\nabla\psi \text{ in } L^2(0,T;(L^2(\Omega))^n). \tag{3.4.53}$$

Then, we conclude from *Lemma 3.2.5(i)* or *3.2.7(i)*, (3.4.45), (3.4.48), the boundedness of $\partial_c g$ and the dominated convergence theorem that

$$\begin{aligned}
&\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\mathcal{R}_r(c_{r\varepsilon_m}\chi(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla\psi) \underset{m\to\infty}{\to} \partial_c g(c_r,v_r)\mathcal{R}_r(c_r\chi(c_r,v_r)\nabla\psi) \\
&\text{in } L^2(0,T;(L^2(\Omega))^n).
\end{aligned} \tag{3.4.54}$$

Now, combining (3.4.46) and (3.4.51)–(3.4.54) it follows due to compensated compactness (see *Lemma A.3.2*) that

$$\begin{aligned}
&\int_0^T\int_\Omega G_{\varepsilon_m}(\mathcal{R}_r(\partial_c g(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla c_{r\varepsilon_m})) \cdot c_{r\varepsilon_m}\chi(c_{r\varepsilon_m}, v_{r\varepsilon_m})\nabla\psi \,\mathrm{d}x\,\mathrm{d}t \\
\underset{m\to\infty}{\to}&\int_0^T\int_\Omega \mathcal{R}_r(\partial_c g(c_r,v_r)\nabla c_r) \cdot c_r\chi(c_r,v_r)\nabla\psi \,\mathrm{d}x\,\mathrm{d}t.
\end{aligned}$$

The convergence of the remaining terms in (3.4.9a) and the rest of (3.4.9) can be obtained from (3.4.45)-(3.4.50) in a way either completely analogous or very similar to the corresponding parts of the proof of *Lemma 3.4.10*. Consequently, (c_r, v_r) solves (3.4.1) in the required sense.

Case $D_v = 0$: In order to prove existence for the case

$$D_v = 0$$

consider a family of solutions (c_{rD_v}, v_{rD_v}) corresponding to $D_v \in (0,1)$. The existence of such solutions was shown in the first part of this proof. Multiplying (3.4.9c) for v_{rD_v} by Δv_{rD_v}, integrating over Ω and using partial integration, we can estimate for a.e. $t \in (0,T)$ with Young's inequality due to the boundedness of ∇f_v that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\|\nabla v_{rD_v}\|^2_{(L^2(\Omega))^n} + D_v\|\Delta v_{rD_v}\|^2_{L^2(\Omega)}\\
\leqslant &\int_\Omega |\nabla f_v(c_{rD_v}, v_{rD_v})||\nabla v_{rD_v}|\,\mathrm{d}x\\
\leqslant &\|\partial_c f_v\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}\int_\Omega |\nabla c_{rD_v}||\nabla v_{rD_v}|\,\mathrm{d}x + \|\partial_v f_v\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}\int_\Omega |\nabla v_{rD_v}|^2\,\mathrm{d}x\\
\leqslant &C_{31}\left(\|\nabla c_{rD_v}\|^2_{(L^2(\Omega))^n} + \|\nabla v_{rD_v}\|^2_{(L^2(\Omega))^n}\right).
\end{aligned} \tag{3.4.55}$$

Estimating $\|c_{rD_v}\|^2_{L^2(\Omega)}$ similarly to (3.4.40) and adding $\frac{C_5C_{12}}{4C_{31}}\frac{d}{dt}\|\nabla v_{rD_v}\|^2_{(L^2(\Omega))^n}$, we conlude using (3.4.55) with Young's inequality that for a.e. $t \in (0,T)$ it holds that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\left(\|c_{rD_v}\|^2_{L^2(\Omega)} + \frac{C_5C_{12}(\|\mathcal{R}_r\|)}{2C_{31}}\|\nabla v_{rD_v}\|^2_{(L^2(\Omega))^n}\right)\\
&+\frac{C_5C_{12}(\|\mathcal{R}_r\|)}{4}\|\nabla c_{rD_v}\|^2_{(L^2(\Omega))^n} + D_v\frac{C_5C_{12}(\|\mathcal{R}_r\|)}{2C_{31}}\|\Delta v_{rD_v}\|^2_{L^2(\Omega)}\\
\leqslant&\|\partial_c f_c\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}||c_{rD_v}||^2_{L^2(\Omega)} + C_{32}(\|\mathcal{R}_r\|)\|\nabla v_{rD_v}\|^2_{(L^2(\Omega))^n}.
\end{aligned}$$

Then, Gronwall's inequality implies

$$\|c_{rD_v}\|_{L^\infty(0,T;L^2(\Omega))} \leqslant C_{33}(\|\mathcal{R}_r\|, T), \tag{3.4.56}$$

$$\|\nabla c_{rD_v}\|_{L^2(0,T;(L^2(\Omega))^n)} \leqslant C_{33}(\|\mathcal{R}_r\|, T), \tag{3.4.57}$$

$$\|\nabla v_{rD_v}\|_{L^\infty(0,T;(L^2(\Omega))^n)} \leqslant C_{33}(\|\mathcal{R}_r\|, T), \tag{3.4.58}$$

$$D_v\|\Delta v_{rD_v}\|_{L^2(\Omega\times(0,T))} \leqslant C_{33}(\|\mathcal{R}_r\|, T) \tag{3.4.59}$$

for a constant $C_{33}(\|\mathcal{R}_r\|, T) > 0$ that is especially independent from D_v. Multiplying (3.4.9c) by v_{rD_v} we conclude with $f_v(\cdot, 0) = 0$ and the Lipschitz continuity of f_v using partial integration the estimate

$$\frac{1}{2}\frac{d}{dt}\|v_{rD_v}\|^2_{L^2(\Omega)} \leqslant \left|\int_\Omega f_v(c_{rD_v}, v_{rD_v})v_{rD_v}\,\mathrm{d}x\right| \leqslant \|\partial_v f_v\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}||v_{rD_v}||^2_{L^2(\Omega)}$$

for a.e. $t \in (0,T)$. Consequently, Gronwall's inequality implies that

$$\|v_{rD_v}\|_{L^\infty(0,T;L^2(\Omega))} \leqslant C_{34}(\|\mathcal{R}_r\|, T). \tag{3.4.60}$$

A uniform bound on $(\partial_t c_{rD_v})_{D_v}$ in $L^2(0,T;(H^1(\Omega))^*)$ follows combining (3.4.56)–(3.4.58) and estimating as above in (3.4.44). Moreover, we conclude with (3.4.59) and (3.4.60) and the Lipschitz continuity of f_v from (3.4.9c) that $(\partial_t v_{rD_v})_{D_v}$ is uniformly bounded in $L^2(\Omega\times(0,T))$. Combining this with (3.4.56) - (3.4.60) we conclude again from Lions-Aubin and Banach-Alaoglu (*Lemmas A.3.1* and *A.3.9*) and *Lemma A.3.8* that there are $c_{r0} \in L^2(0,T;H^1(\Omega)) \cap C([0,T];L^2(\Omega))$ with $\partial_t c_{r0} \in L^2(0,T;(H^1(\Omega))^*)$ and $v_{r0} \in L^\infty(0,T;H^1(\Omega)) \cap C([0,T];L^2(\Omega))$ with time derivative $\partial_t v_{r0} \in L^2(\Omega\times(0,T))$ s.t.

$$c_{r(D_v)_m} \underset{m\to\infty}{\to} c_{r0} \text{ in } L^2(\Omega\times(0,T)) \text{ and a.e. in } \Omega\times(0,T), \tag{3.4.61}$$

$$
\begin{aligned}
c_{r(D_v)_m} &\underset{m\to\infty}{\rightharpoonup} c_{r0} \text{ in } L^2(0,T;H^1(\Omega)),\\
\partial_t c_{r(D_v)_m} &\underset{m\to\infty}{\rightharpoonup} \partial_t c_{r0} \text{ in } L^2(0,T;(H^1(\Omega))^*),\\
v_{r(D_v)_m} &\underset{m\to\infty}{\to} v_{r0} \text{ in } C([0,T];L^2(\Omega)) \text{ and a.e. in } \Omega\times(0,T), && (3.4.62)\\
\nabla v_{r(D_v)_m} &\underset{m\to\infty}{\overset{*}{\rightharpoonup}} \nabla v_{r0} \text{ in } L^\infty(0,T;(L^2(\Omega))^n), && (3.4.63)\\
\partial_t v_{r(D_v)_m} &\underset{m\to\infty}{\rightharpoonup} \partial_t v_{r0} \text{ in } L^2(\Omega\times(0,T)) && (3.4.64)
\end{aligned}
$$

for a subsequence $(D_v)_m$. Observe that this time the gradients of c and v enter linearly into our equation, so that no strong convergence and no application of *Lemma A.3.3* are required. From this we conclude with the dominated convergence theorem, compensated compactness (*Lemma A.3.2*), *Lemma 3.2.5(i)* and *(ii)* or *3.2.7(i)* and *(ii)* similarly to above that

$$
\begin{aligned}
&\int_0^T\int_\Omega \mathcal{R}_r(\nabla g(c_{r(D_v)_m},v_{r(D_v)_m}))\cdot c_{r(D_v)_m}\chi(c_{r(D_v)_m},v_{r(D_v)_m})\nabla\psi\,\mathrm{d}x\,\mathrm{d}t\\
=&\int_0^T\int_\Omega \nabla g(c_{r(D_v)_m},v_{r(D_v)_m})\cdot \mathcal{R}_r(c_{r(D_v)_m}\chi(c_{r(D_v)_m},v_{r(D_v)_m})\nabla\psi)\,\mathrm{d}x\,\mathrm{d}t\\
\underset{m\to\infty}{\to}&\int_0^T\int_\Omega \nabla g(c_{r0},v_{r0})\cdot\mathcal{R}_r(c_{r0}\chi(c_{r0},v_{r0})\nabla\psi)\,\mathrm{d}x\,\mathrm{d}t\\
=&\int_0^T\int_\Omega \mathcal{R}_r(\nabla g(c_{r0},v_{r0}))\cdot c_{r0}\chi(c_{r0},v_{r0})\nabla\psi\,\mathrm{d}x\,\mathrm{d}t
\end{aligned}
$$

holds for $\psi\in L^2(0,T;H^1(\Omega))$. The convergence of the remaining terms in the equation of $c_{r(D_v)_m}$ follow as in the proof of *Lemma 3.4.10*. Finally, we multiply (3.4.9c) by $\psi\in L^2(\Omega\times(0,T))$, integrate over $\Omega\times(0,T)$ and use partial integration to obtain

$$
\begin{aligned}
&\int_0^T\int_\Omega \partial_t v_{r(D_v)_m}\psi\,\mathrm{d}x dt + (D_v)_m\int_0^T\int_\Omega \nabla v_{r(D_v)_m}\cdot\nabla\psi\,\mathrm{d}x dt\\
=&\int_0^T\int_\Omega f_v(c_{r(D_v)_m},v_{r(D_v)_m})\psi\,\mathrm{d}x dt.
\end{aligned}
$$

Then, we conclude from (3.4.58), (3.4.61), (3.4.62), and (3.4.64), the Lipschitz continuity of f_v and the dominated convergence theorem that

$$
\int_0^T\int_\Omega \partial_t v_{r0}\psi\,\mathrm{d}x\,\mathrm{d}t = \int_0^T\int_\Omega f_v(c_{r0},v_{r0})\psi\,\mathrm{d}x\,\mathrm{d}t.
$$

Hence, the fundamental lemma of calculus of variations that (c_{r0},v_{r0}) solves (3.4.1) for $D_v=0$ in the required sense.

□

3.4.3 Global existence of solutions to (3.4.1): the case of f_c dissipative

In this subsection we provide an extension of the existence theorem *Theorem 3.4.9* from *Subsection 3.4.2*.

Theorem 3.4.12. *Let Assumptions 3.1.1, 3.4.1, and 3.4.3(b) hold and let r satisfy Assumptions 3.4.4(a). Set*

$$
q := \min\left\{2,\frac{s+1}{s}\right\}^{3}, \qquad q^* := \frac{q}{q-1} = \max\{2,s+1\}. \tag{3.4.65}
$$

[3] As usual, here and below the expression $\frac{s+1}{s}$ means infinity if $s=0$.

Then there exists a global weak-strong solution to (3.4.1) *in terms of Definition 3.4.6, with* $\partial_t c_r \in L^q(0,T;(W^1_{q*}(\Omega))^*)$ *and* $\varphi \in W^1_{q*}(\Omega)$ *satisfying for all* $T > 0$ *the estimates*

$$||c_r||_{L^\infty(0,T;L^2(\Omega))} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T), \tag{3.4.66}$$
$$||\nabla c_r||_{L^2(0,T;(L^2(\Omega))^n)} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T), \tag{3.4.67}$$
$$||\partial_t c_r||_{L^q(0,T;(W^1_{q*}(\Omega))^*)} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T), \tag{3.4.68}$$
$$||v_r||_{L^\infty(0,T;L^2(\Omega))} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T), \tag{3.4.69}$$
$$||\nabla v_r||_{L^\infty(0,T;(L^2(\Omega))^n)} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T), \tag{3.4.70}$$
$$||\partial_t v_r||_{L^2(\Omega\times(0,T))} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T), \tag{3.4.71}$$
$$\|f_c(c_r, v_r)\|_{L^q(\Omega\times(0,T))} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T), \tag{3.4.72}$$
$$\|f_v(c_r, v_r)\|_{L^2(\Omega\times(0,T))} \leqslant C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T). \tag{3.4.73}$$

Proof. Let $T > 0$. For $k \in \mathbb{N}$ set

$$f_{ck}(c, v) := f_c(c, v)\eta_k(c, v),$$

where η_k is a cut-off function:

$$\eta_k \in C_c^\infty(B_k^2) \quad \text{with} \quad \eta_k \equiv 1 \quad \text{in } B_{k-1}^2 \quad \text{and} \quad 0 \leqslant \eta_k \leqslant 1. \tag{3.4.74}$$

Here, B_k^2 denotes the two-dimensional ball with radius k centered at the origin. The continuity of ∇f_c and (3.4.6) imply that f_{ck} has bounded derivatives. Hence, it is Lipschitz continuous due to the mean value theorem and *Theorem 3.4.9* implies the existence of a solution (c_{rk}, v_{rk}) in terms of *Definition 3.4.6* with $\partial_t c_{rk} \in L^2(0,T;(H^1(\Omega))^*)$ and $\varphi \in H^1(\Omega)$, which corresponds to $f_c = f_{ck}$. Our next aim is to prove that (c_{rk}, v_{rk}) satisfies the same bounds as in the statement of the theorem with some constant $C_{35}(\|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}, T)$ which does not depend upon k.

Set

$$C_{36}(\|\mathcal{R}_r\|) := \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)}.$$

Taking $\varphi := c_{rk}$ in (3.4.9a) written for c_{rk} and using *Assumptions 3.4.1*, *3.4.3(b)*, *3.4.4(a)*, the fact that $\mathcal{R}_r \in L((L^2(\Omega))^n)$ and the Hölder and Young inequalities, we compute

$$\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|c_{rk}\|^2_{L^2(\Omega)} = &\int_\Omega \Big(-(D_c(c_{rk}, v_{rk})\nabla c_{rk} - c_{rk}\chi(c_{rk}, v_{rk})\mathcal{R}_r(\nabla g(c_{rk}, v_{rk}))) \cdot \nabla c_{rk} \\
&\quad + c_{rk} f_{ck}(c_{rk}, v_{rk})\Big)\,\mathrm{d}x \\
\leqslant &- C_5\,\|\nabla c_{rk}\|^2_{(L^2(\Omega))^n} + C_7\,\|\nabla c_{rk}\|_{(L^2(\Omega))^n}\,\|\mathcal{R}_r(\nabla g(c_{rk}, v_{rk}))\|_{(L^2(\Omega))^n} \\
&+ \int_\Omega (C_{10} - C_{11} c_{rk}^{1+s})\eta_k(c_{rk}, v_{rk})\,\mathrm{d}x \\
\leqslant &- C_5\,\|\nabla c_{rk}\|^2_{(L^2(\Omega))^n} + C_7 C_{36}(\|\mathcal{R}_r\|)\,\|\nabla c_{rk}\|_{(L^2(\Omega))^n}\,\|\nabla g(c_{rk}, v_{rk})\|_{(L^2(\Omega))^n} \\
&+ C_{37} - C_{11}\int_\Omega c_{rk}^{1+s}\eta_k(c_{rk}, v_{rk})\,\mathrm{d}x \\
\leqslant &- C_5\,\|\nabla c_{rk}\|^2_{(L^2(\Omega))^n} \\
&+ C_7 C_{36}(\|\mathcal{R}_r\|)\,\|\nabla c_{rk}\|_{(L^2(\Omega))^n}\,\|\partial_c g(c_{rk}, v_{rk})\nabla c_{rk}\|_{(L^2(\Omega))^n} \\
&+ C_7 C_{36}(\|\mathcal{R}_r\|)\,\|\nabla c_{rk}\|_{(L^2(\Omega))^n}\,\|\partial_v g(c_{rk}, v_{rk})\nabla v_{rk}\|_{(L^2(\Omega))^n} + C_{37} \\
&- C_{11}\int_\Omega c_{rk}^{1+s}\eta_k(c_{rk}, v_{rk})\,\mathrm{d}x
\end{aligned}$$

$$
\begin{aligned}
\leqslant &- C_5C_{12}(\|\mathcal{R}_r\|)\,\|\nabla c_{rk}\|^2_{(L^2(\Omega))^n}\\
&+ C_7C_{36}(\|\mathcal{R}_r\|)\,\|\partial_v g\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}\,\|\nabla c_{rk}\|_{(L^2(\Omega))^n}\,\|\nabla v_{rk}\|_{(L^2(\Omega))^n}\\
&+ C_{37} - C_{11}\int_\Omega c_{rk}^{1+s}\eta_k(c_{rk},v_{rk})\,\mathrm{d}x\\
\leqslant &- \frac{C_5C_{12}(\|\mathcal{R}_r\|)}{2}\,\|\nabla c_{rk}\|^2_{(L^2(\Omega))^n} + C_{38}(\|\mathcal{R}_r\|)\,\|\nabla v_{rk}\|^2_{(L^2(\Omega))^n} + C_{37}\\
&- C_{11}\int_\Omega c_{rk}^{1+s}\eta_k(c_{rk},v_{rk})\,\mathrm{d}x. \qquad (3.4.75)
\end{aligned}
$$

Next, we estimate v_{rk}. If $D_v > 0$, then *Theorem A.1.8* and *Lemma A.3.8* yield as in the proof of *Lemma 3.4.10* that

$$
\|v_{rk}\|^2_{L^\infty(0,T;H^1(\Omega))} + \|v_{rk}\|^2_{L^2(0,T;H^2(\Omega))} + \|\partial_t v_{rk}\|^2_{L^2(\Omega\times(0,T))} \leqslant C_{39}(T)\|v_0\|^2_{H^1(\Omega)}. \qquad (3.4.76)
$$

Here and further in the proof we omit the dependence of constants upon D_v. If $D_v = 0$, then we get the ODE

$$
\partial_t v_{rk} = f_v(c_{rk}, v_{rk}). \qquad (3.4.77)
$$

Hence, the assumptions on f_v and the solution components together with the chain rule imply that

$$
\partial_t v_{rk} \in L^2(0,T;H^1(\Omega)).
$$

Computing the gradient on both sides of (3.4.77), multiplying by ∇v_{rk} throughout, integrating over Ω, and using *Assumptions 3.4.1* and the Young inequality, we obtain for a.e. $t \in (0,T)$ the estimate

$$
\begin{aligned}
\frac{1}{2}\frac{d}{dt}\|\nabla v_{rk}\|^2_{(L^2(\Omega))^n} =& \int_\Omega \left(\partial_v f_v(c_{rk},v_{rk})|\nabla v_{rk}|^2 + \partial_c f_v(c_{rk},v_{rk})\nabla c_{rk}\cdot\nabla v_{rk}\right)\,\mathrm{d}x\\
\leqslant& \|\partial_v f_v\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}\,\|\nabla v_{rk}\|^2_{(L^2(\Omega))^n}\\
&+ \|\partial_c f_v\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}\,\|\nabla c_{rk}\|_{(L^2(\Omega))^n}\|\nabla v_{rk}\|_{(L^2(\Omega))^n}\\
\leqslant& C_{40}\|\nabla v_{rk}\|^2_{(L^2(\Omega))^n} + C_{41}\,\|\nabla c_{rk}\|^2_{(L^2(\Omega))^n}. \qquad (3.4.78)
\end{aligned}
$$

Proceeding as for estimate (3.4.41) if $D_v > 0$ and as in the second case of the proof of *Theorem 3.4.9* if $D_v = 0$ and using the Gronwall inequality yields that c_{rk} and v_{rk} satisfy estimates as (3.4.66), (3.4.67), and (3.4.69)–(3.4.71) for a constant independent from k as this is the case for all constants involved in (3.4.75), (3.4.76), and (3.4.78). Hence, the estimate

$$
\int_0^T\int_\Omega c_{rk}^{1+s}\eta_k(c_{rk},v_{rk})\,\mathrm{d}x\,\mathrm{d}t \leqslant C_{42}(\|\mathcal{R}_r\|,T). \qquad (3.4.79)
$$

follows after integrating (3.4.75).

From (3.4.6) and (3.4.79), the embedding of Lebesgue spaces, and $\eta_k \in [0,1]$ we conclude using Hölder's inequality if necessary that

$$
\begin{aligned}
\|f_{ck}(c_{rk},v_{rk})\|_{L^q(\Omega\times(0,T))} \leqslant& C_9\,\|(1+c_{rk}^s)\,\eta_k(c_{rk},v_{rk})\|_{L^q(\Omega\times(0,T))}\\
\leqslant& C_{43}(T) + C_{44}||c_{rk}^s\eta_k(c_{rk},v_{rk})||_{L^{\frac{s+1}{s}}(\Omega\times(0,T))}\\
\leqslant& C_{43}(T) + C_{44}\left(\int_0^T\int_\Omega c_{rk}^{1+s}\eta_k(c_{rk},v_{rk})\,\mathrm{d}x\,\mathrm{d}t\right)^{\frac{s}{s+1}} \leqslant C_{45}(\|\mathcal{R}_r\|,T).
\end{aligned}
$$

so that (3.4.72) holds for $f_{ck}(c_{rk}, v_{rk})$. An estimate as (3.4.73) for $f_v(c_{rk}, v_{rk})$ follows from the Lipschitz continuity of f_v, $f_v(\cdot, 0) = 0$ and the uniform in k bound on (v_{rk}). Finally, combining *Assumptions 3.4.1* with the fact that $\mathcal{R}_r \in L((L^2(\Omega))^n)$, the uniform in k bound on (∇v_{rk}), the weak formulation (3.4.9a) for $\varphi \in W^1_{q^*}(\Omega)$, Hölder's and Young's inequality and the embedding of Lebesgue spaces yield

$$\begin{aligned}
&|\langle \partial_t c_{rk}, \varphi\rangle_{(W^1_{q^*}(\Omega))^*, W^1_{q^*}(\Omega)}| \\
\leqslant &\left|\int_\Omega (D_c(c_{rk}, v_{rk})\nabla c_{rk} - c_{rk}\chi(c_{rk}, v_{rk})\mathcal{R}_r(\nabla g(c_{rk}, v_{rk}))) \cdot \nabla\varphi \, \mathrm{d}x\right| + \left|\int_\Omega f_{ck}(c_{rk}, v_{rk})\varphi \, \mathrm{d}x\right| \\
\leqslant &C_{46}(\|\mathcal{R}_r\|)\left(\|\nabla c_{rk}\|_{(L^2(\Omega))^n} + \|\nabla v_{rk}\|_{(L^2(\Omega))^n}\right)\|\nabla\varphi\|_{(L^2(\Omega))^n} + \|f_{ck}(c_{rk}, v_{rk})\|_{L^q(\Omega)}\|\varphi\|_{L^{q^*}(\Omega)} \\
\leqslant &C_{47}(\|\mathcal{R}_r\|, T)\left(1 + \|\nabla c_{rk}\|_{(L^2(\Omega))^n} + \|f_{ck}(c_{rk}, v_{rk})\|_{L^q(\Omega)}\right)\|\varphi\|_{W^1_{q^*}(\Omega)}
\end{aligned}$$

Taking the supremum over $\|\varphi\|_{W^1_{q^*}(\Omega)} \leqslant 1$ and integrating the qth-potence over $(0, T)$ we conclude that (3.4.68) holds for $\partial_t c_{rk}$ due to the uniform in k bounds on (∇c_{rk}), and $(f_{ck}(c_{rk}, v_{rk}))$. Since (c_{rk}, v_{rk}) satisfy (3.4.66)-(3.4.73) uniformly in k, the Lions-Aubin lemma, Banach-Alaoglu theorem (*Lemmas A.3.1* and *A.3.9*) and *Lemma A.3.8* imply that there are $c_r \in L^2(0, T; H^1(\Omega))$ with $\partial_t c_r \in L^q(0, T; (W^1_{q^*}(\Omega))^*)$ and $v_r \in W^{2,1}_2(\Omega \times (0, T)) \cap C([0, T]; H^1(\Omega))$ if $D_v > 0$ or $v_r \in L^\infty(0, T; H^1(\Omega)) \cap C([0, T]; L^2(\Omega))$ with $\partial_t v_r \in L^2(\Omega \times (0, T))$ if $D_v = 0$ s.t. for a subsequence

$$c_{rk_m} \underset{m\to\infty}{\to} c_r \quad \text{in } L^2(\Omega \times (0, T)) \text{ and a.e. in } \Omega \times (0, T), \tag{3.4.80}$$

$$c_{rk_m} \underset{m\to\infty}{\overset{*}{\rightharpoonup}} c_r \quad \text{in } L^\infty(0, T; L^2(\Omega)), \tag{3.4.81}$$

$$\nabla c_{rk_m} \underset{m\to\infty}{\rightharpoonup} \nabla c_r \quad \text{in } L^2(0, T; (L^2(\Omega))^n), \tag{3.4.82}$$

$$\partial_t c_{rk_m} \underset{m\to\infty}{\rightharpoonup} \partial_t c_r \quad \text{in } L^q(0, T; (W^1_{q^*}(\Omega))^*), \tag{3.4.83}$$

$$v_{rk_m} \underset{m\to\infty}{\to} v_r \quad \text{in } C([0, T]; L^2(\Omega)) \text{ and a.e. in } \Omega \times (0, T), \tag{3.4.84}$$

$$\nabla v_{rk_m} \underset{m\to\infty}{\overset{*}{\rightharpoonup}} \nabla v_r \quad \text{in } L^\infty(0, T; (L^2(\Omega))^n), \tag{3.4.85}$$

$$\partial_t v_{rk_m} \underset{m\to\infty}{\rightharpoonup} \partial_t v_r \quad \text{in } L^2(\Omega \times (0, T)) \tag{3.4.86}$$

and additionally

$$v_{rk_m} \underset{m\to\infty}{\rightharpoonup} v_r \text{ in } L^2(0, T; H^2(\Omega)). \tag{3.4.87}$$

if $D_v > 0$. Then, due to (3.4.80) and (3.4.84), the continuity of f_c and f_v, the definition of η_k and the uniform in k bound on $(f_{ck}(c_{rk}, v_{rk}))$, the Lions lemma (*Lemma A.3.4*) implies

$$f_{ck_m}(c_{rk_m}, v_{rk_m}) \underset{m\to\infty}{\rightharpoonup} f_c(c_r, v_r) \text{ in } L^q(\Omega \times (0, T)),$$

$$f_v(c_{rk_m}, v_{rk_m}) \underset{m\to\infty}{\rightharpoonup} f_v(c_r, v_r) \text{ in } L^2(\Omega \times (0, T)).$$

Consequently, c_r and v_r satisfy (3.4.66)-(3.4.73) as (weak) limits of functions satisfying these inequalities and setting $X = L^2(\Omega)$ and $Y = \left(W^1_{q^*}(\Omega)\right)^*$ in *Lemma A.3.5* we conclude that $c_r \in C_w([0, T]; L^2(\Omega))$ with $c_r(\cdot, 0) = c_0$ in $L^2(\Omega)$. Finally, we conclude similarly to the proof of *Theorem 3.4.9* that (c_r, v_r) solve (3.4.1) in the required sense.

□

3.4.4 Limiting behaviour of the nonlocal model (3.4.1) as $r \to 0$

In this subsection we finally prove our main result concerning convergence for $r \to 0$.

Proof of Theorem 3.4.8. Due to (3.4.8) and *Lemma 3.2.5(iv)* or *3.2.7(iv)*, respectively, there exists a sequence $r_m \to 0$ as $m \to \infty$ such that

$$\sup_{m \in \mathbb{N}} \|\mathcal{R}_{r_m}\|_{L((L^2(\Omega))^n)} < \frac{1}{C_{13}}. \tag{3.4.88}$$

Since for each such r_m the *Assumptions 3.4.4(a)* are satisfied, *Theorem 3.4.12* is applicable and yields the existence of solutions (c_{r_m}, v_{r_m}) which satisfy (3.4.66)-(3.4.73). Replacing $\|\mathcal{R}_r\|$ by C_{13} in $C_{35}(T, \|\mathcal{R}_r\|_{L((L^2(\Omega))^n)})$ makes the constant in (3.4.66)-(3.4.73) independent of m. Using Lions-Aubin, Banach-Alaoglu (*Lemmas A.3.1* and *A.3.9*) and *Lemma A.3.5* we conclude (by possibly switching to a subsequence) that there are $c \in L^2(0,T;H^1(\Omega)) \cap C_w([0,T];L^2(\Omega))$ with $\partial_t c \in L^q(0,T;(W^1_{q*}(\Omega))^*)$ and $v \in W^{2,1}_2(\Omega \times (0,T)) \cap C([0,T];H^1(\Omega))$ if $D_v > 0$ or $v \in L^\infty(0,T;H^1(\Omega)) \cap C([0,T];L^2(\Omega))$ with $\partial_t v \in L^2(\Omega \times (0,T))$ if $D_v = 0$ s.t. (c_r) and (v_r) converge to c and v, respectively, in the sense of (3.4.80)-(3.4.87), i.e., especially

$$c_{r_m} \underset{m\to\infty}{\to} c, \quad v_{r_m} \underset{m\to\infty}{\to} v \qquad \text{in } L^2(\Omega \times (0,T)) \text{ and a.e. in } \Omega \times (0,T), \tag{3.4.89}$$

$$\nabla c_{r_m} \underset{m\to\infty}{\rightharpoonup} \nabla c, \quad \nabla v_{r_m} \underset{m\to\infty}{\rightharpoonup} \nabla v \qquad \text{in } L^2(0,T;(L^2(\Omega))^n). \tag{3.4.90}$$

We conclude from (3.4.89), the continuity of χ and ∇g and the dominated convergence theorem that

$$c_{r_m}\chi(c_{r_m}, v_{r_m}) \underset{m\to\infty}{\to} c\chi(c,v) \qquad \text{in } L^2(\Omega \times (0,T)), \tag{3.4.91}$$

$$\partial_c g(c_{r_m}, v_{r_m}) \underset{m\to\infty}{\to} \partial_c g(c,v), \quad \partial_v g(c_{r_m}, v_{r_m}) \underset{m\to\infty}{\to} \partial_v g(c,v) \qquad \text{in } L^2(\Omega \times (0,T)). \tag{3.4.92}$$

Observe that for any $\psi \in L^\infty(0,T;W^1_\infty(\Omega))$ the following estimate holds:

$$\begin{aligned}
&\int_0^T \int_\Omega \left|\partial_c g(c_{r_m}, v_{r_m})\mathcal{R}_{r_m}(c_{r_m}\chi(c_{r_m}, v_{r_m})\nabla\psi) - \partial_c g(c,v)c\chi(c,v)\nabla\psi\right|^2 \,\mathrm{d}x\,\mathrm{d}t \\
\leqslant 9 &\Bigg(\int_0^T \int_\Omega |(\partial_c g(c_{r_m}, v_{r_m}) - \partial_c g(c,v))\mathcal{R}_{r_m}(c_{r_m}\chi(c_{r_m}, v_{r_m})\nabla\psi)|^2 \,\mathrm{d}x\,\mathrm{d}t \\
&+ \int_0^T \int_\Omega \left|\partial_c g(c,v)\mathcal{R}_{r_m}\left((c_{r_m}\chi(c_{r_m}, v_{r_m}) - c\chi(c,v))\nabla\psi\right)\right|^2 \,\mathrm{d}x\,\mathrm{d}t \\
&+ \int_0^T \int_\Omega \left|\partial_c g(c,v)\left(\mathcal{R}_{r_m}(c\chi(c,v)\nabla\psi) - c\chi(c,v)\nabla\psi\right)\right|^2 \,\mathrm{d}x\,\mathrm{d}t \Bigg).
\end{aligned} \tag{3.4.93}$$

Now, using (3.4.88), (3.4.91), and (3.4.92) together with *Lemma 3.2.5(i)* and *(iii)* or *Lemma 3.2.7(i)* and *(iii)*, respectively, we conclude that the right-hand side of (3.4.93) tends to zero, hence

$$\partial_c g(c_{r_m}, v_{r_m})\mathcal{R}_{r_m}(c_{r_m}\chi(c_{r_m}, v_{r_m})\nabla\psi) \underset{m\to\infty}{\to} \partial_c g(c,v)c\chi(c,v)\nabla\psi \qquad \text{in } L^2(0,T;(L^2(\Omega))^n). \tag{3.4.94}$$

An analogous convergence holds for the corresponding term involving $\partial_v g$. Finally, we obtain using *Lemma 3.2.5(ii)* or *Lemma 3.2.7(ii)*, respectively, compensated compactness (*Lemma A.3.2*), (3.4.90) and (3.4.94) that

$$\begin{aligned}
&\int_0^T \int_\Omega c_{r_m}\chi(c_{r_m}, v_{r_m})\mathcal{R}_{r_m}(\nabla g(c_{r_m}, v_{r_m})) \cdot \nabla\psi \,\mathrm{d}x\,\mathrm{d}t \\
=&\int_0^T \int_\Omega \nabla g(c_{r_m}, v_{r_m}) \cdot \mathcal{R}_{r_m}(c_{r_m}\chi(c_{r_m}, v_{r_m})\nabla\psi) \,\mathrm{d}x\,\mathrm{d}t
\end{aligned}$$

$$\underset{m\to\infty}{\rightarrow} \int_0^T \int_\Omega \nabla g(c,v)\cdot c\chi(c,v)\nabla\psi \,\mathrm{d}x\,\mathrm{d}t.$$

The convergence of the remaining terms follows similarly to the proof of *Theorem 3.4.9*. Hence, (c, v) solves the local system (3.4.2) in the sense of *Definition 3.4.6*. □

3.5 Numerical simulations in 1D

This section is the sole work of Kevin Painter and is included for the sake of completeness.

We perform numerical simulations to investigate on the one hand the effect of differences between hitherto choices of nonlocal operators and our novel ones proposed in *Section 3.2*, and on the other hand convergence between nonlocal and local formulations. For compactness, our current study restricts to the prototypical nonlocal model for cellular adhesion (3.1.1), its reformulation as (3.4.1), and the corresponding local model (3.4.2). Thus, for (3.4.1) we take the operator form $\mathcal{R}_r = \mathcal{T}_r$, with $\mathcal{T}_r$ as in (3.2.2). These models can be interpreted in the context of a population of cells invading an adhesion-laden ECM/tissue environment and, with this in mind, we initially concentrate cells at the centre of a one-dimensional domain $\Omega = [0, L]$ and impose an initially homogeneous ECM. Specifically, we set for the ECM

$$v_0(x) = 1, \quad x \in \Omega \tag{3.5.1}$$

and consider for the cell population a Gaussian-shaped aggregate

$$c_0(x) = \exp\left(-\alpha(x - x_c)^2\right), \quad x \in \Omega, \tag{3.5.2}$$

where we set $x_c = L/2$ or $x_c = 0$.

The numerical scheme follows that described in [67], which we refer to for details. Briefly, a Method of Lines approach is invoked whereby equations are first discretised in space (in conservative form, via a finite volume method) to yield a high-dimensional system of ODEs, which are subsequently integrated in time. Discretisation of advective terms follows a third order upwinding scheme, augmented by flux limiting to preserve positivity of solutions and the resulting scheme is (approximately) second-order accurate in space. Time integration has been performed with standard Matlab ODE solvers: our default is "ode45" with absolute and relative error tolerances set at 10^{-6}, but simulations have been compared for varying space discretisation step, ODE solver, and error tolerances. To measure the difference between two distinct solutions over time we define a distance function as follows:

$$d(u_1(x,t), u_2(x,t))(t) = \int_\Omega |u_1(x,t) - u_2(x,t)| \,\mathrm{d}x\,,$$

where u_1 and u_2 denote the two solutions that are being compared.

3.5.1 Comparison of nonlocal operator representations

We first explore the correspondence between forms of nonlocal operator representation: we choose the prototypical nonlocal model for cell/matrix adhesion (3.1.1) and its reformulation (3.4.1), therefore taking for the latter the operator form $\mathcal{R}_r = \mathcal{T}_r$ with $\mathcal{T}_r$ as in (3.2.2). In what follows,

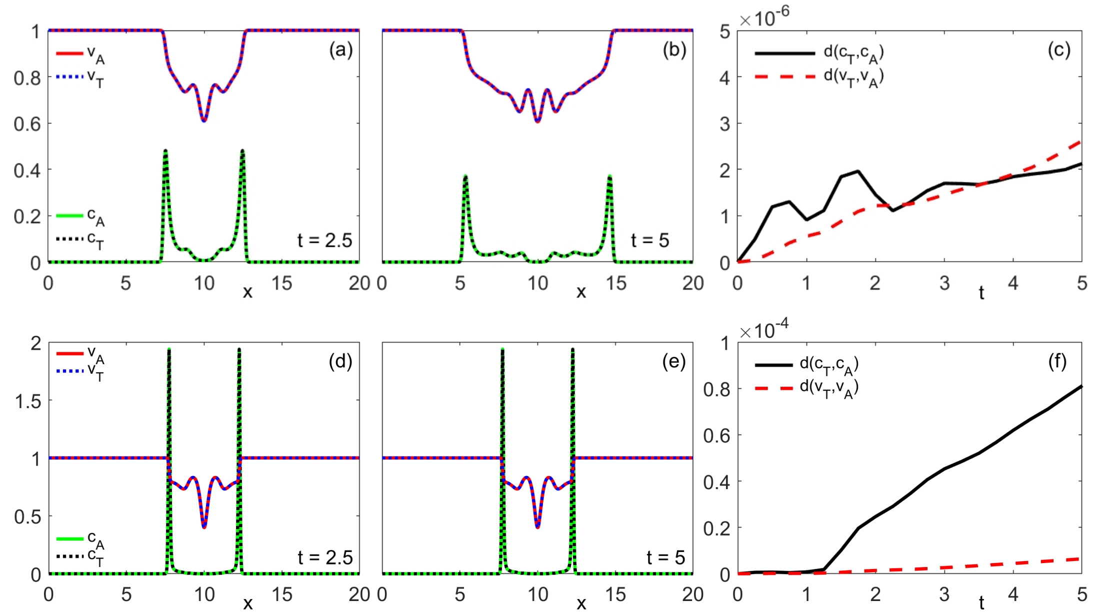

Figure 3.1: Comparison between nonlocal formulations (3.1.1) and (3.4.1). (a-b) Cell and matrix densities for the models (3.1.1) and (3.4.1) at $t = 2.5$ and $t = 5$. (c) Difference between the solutions. For these simulations we take $\alpha = 10$, $r = 1$, $D_c = 0.01$, $\chi = 1$, $F_r = 2$, $f_c = 0$ and $f_v(c, v) = -cv$, along with (a-c) $g(c, v) = 10v$, (d-f) $g(c, v) = 2.5c + 10v$.

solutions to (3.1.1) are denoted c_A and v_A and those for (3.4.1) denoted c_T and v_T. For simplicity we restrict in this section to a minimalist formulation in which D_c = constant, $\chi = 1$, $f_c = 0$. Cell-matrix interactions are defined by $g(c, v) = S_{cc}c + S_{cv}v$ and $f_v(c, v) = -\mu cv$, where S_{cc} and S_{cv} respectively represent cell-to-cell and cell-to-matrix adhesion strengths and f_v simplistically describes (direct) proteolytic degradation of matrix by cells parametrised by degradation rate μ.

Figure 3.1 shows the computed solutions under (a-c) negligible cell-cell adhesion ($S_{cc} = 0$) and (d-f) moderate cell-cell adhesion ($S_{cc} = S_{cv}/4$). The equivalence of the two formulations is revealed through the negligible difference between solutions, with the distance magnitude attributable to the subtly distinct numerical implementation. Both simulations describe an invasion/infiltration process, in which matrix degradation by the cells generates an adhesive gradient that pulls cells into the acellular surroundings. The impact of cell-cell adhesion is manifested in the compaction of cells at the leading edge into a tight aggregate.

However, as pointed out in *Section 3.2*, differences in the nonlocal formulations can emerge in the vicinity of boundaries. To highlight this we consider an equivalent formulation to *Figure 3.1* (a-c), but with the cells initially placed at the left boundary ($x_c = 0$ in (3.5.2)), e.g., suggesting a tumor mass which is concentrated there and whose cells are expected to detach and migrate into the considered 1D domain, travelling from left to right. As stated earlier we impose zero-flux boundary conditions at $x = 0$ (and $x = L$), and further suppose $c = v = 0$ and $\nabla c = \nabla v$ in the extradomain region ($\mathbb{R}\backslash\Omega$). Representative simulations are shown in *Figure 3.2*. They are in agreement with our observation in *Example 3.2.3*. Indeed, for this scenario, in the prototypical nonlocal model (3.1.1)-(3.1.2) there is a very large adhesion velocity modulus at $x = 0$; the cells

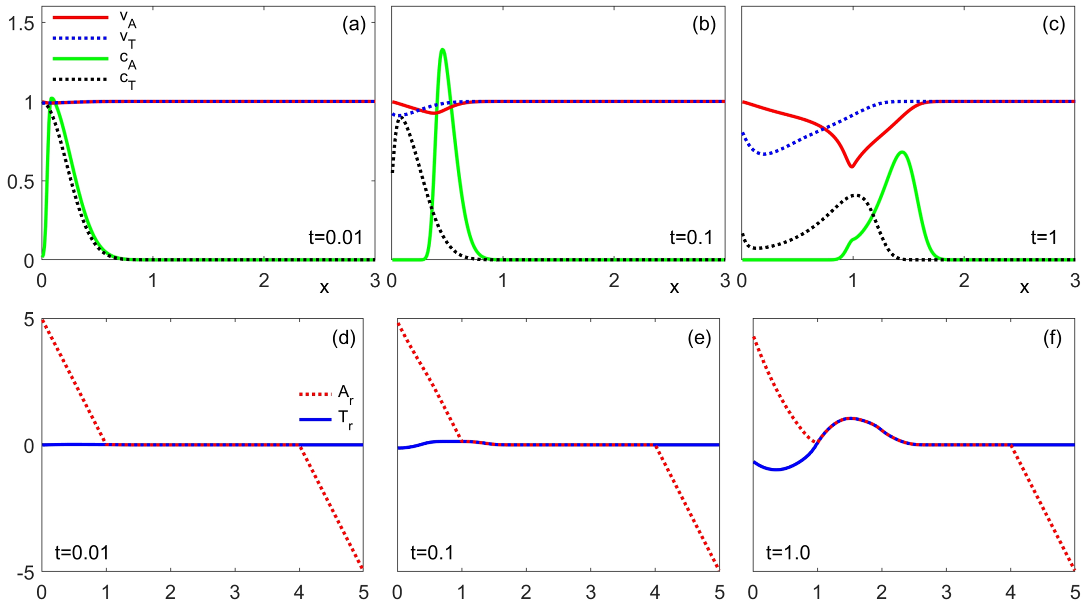

Figure 3.2: (a-c) Comparison between nonlocal formulations (3.1.1) and (3.4.1) near boundaries. Model as in *Figure 3.1* (a-c), but with the cells initially concentrated at the boundary. (d-f) Comparison of the two forms of nonlocal operator corresponding to the simulations represented in (a-c). The operators are practically identical sufficiently far from the boundary, but can diverge significantly for distances $< r$ from the boundaries.

are crowded within the tumor mass and their mutual interactions are maintained during the invasion process in a sufficiently strong manner to ensure a collective shift of the still concentrated cell aggregate, with a correspondingly strong tissue degradation in its wake. In the reformulation (3.4.1a)-(3.4.1b), rather, the adhesion magnitude at $x = 0$ is for the same initial condition much lower - suggesting a tumor whose cells are readier to detach and migrate individually. This results in a more diffusive spread, with accordingly less degradation of tissue, and with cell mass remaining available at the original site over a larger time span. The latter scenario is different from the former one, but it seems nevertheless reasonable, as a tumor mass would very often not move as a whole from its original location to another in a relatively short time; moreover, the active cells in a sufficiently large tumor (releasing substantial amounts of acidity) are known to preferentially adopt a migratory phenotype and perform EMT (epithelial-mesenchymal transition), see e.g., [73, 120, 125], which supports the idea of cells moving in a loose way rather than in compact, highly aggregated assemblies [4]. As such, our simulations suggest that, within this particular function- and parameter setting, choosing the adhesion operator in the form (3.1.2) instead of (3.2.2) might possibly overestimate the tumor invasion speed and associated healthy tissue degradation, thereby predicting a spatially concentrated tumor and neglecting regions with lower cell densities which can nevertheless trigger tumor recurrence if untreated.

[4] unless environmental influences dictate conversion to a collective type of motion

3.5.2 Comparison between nonlocal and local formulation

Having compared together the original, (3.1.1), and the new, (3.4.1), nonlocal formulations, we next consider the extent to which their dynamics can be captured by the classical local formulation (3.4.2). Note that for nonlocal model simulations we will restrict to the original formulation (3.1.1), so that we can avail ourselves of an already well-established efficient (in terms of computational time) numerical scheme [67]. Here we use c_L and v_L to denote solutions to the local formulation and c_{Ar} and v_{Ar} to denote solutions to the nonlocal model with sensing radius r. We remark that a large number of related local and nonlocal models have been numerically studied to describe the invasion-type process considered here (e.g., [3, 68, 118, 121]): here the specific focus is to explore the convergence of nonlocal to local form as $r \to 0$, which, as far as we are aware, has not been systematically investigated.

As in the first test we use the initial values (3.5.1) and (3.5.2), choosing $x_c = L/2$, $\alpha = 10$ in the latter, and consider the coefficients and functions as proposed in *Example 3.4.5.* Under these choices the resultant nonlinear diffusion coefficient for the c-equation in the classical local formulation (compare (3.4.2a)) becomes

$$\tilde{D}_c(c,v) = \frac{a^2(1+c)^2(1+c+v)^2 - bc(1+cv)(S_{cc} + (S_{cc} - S_{cv})v)}{(1+cv)^2(1+c+v)^2}. \tag{3.5.3}$$

Notably, this potentially becomes negative under an injudicious combination of adhesive strengths S_{cc}, S_{cv}, and of a, b. Likewise, the actual haptotaxis sensitivity function takes the form

$$\tilde{\chi}(c,v) = b\frac{S_{cv} + (S_{cv} - S_{cc})c}{(1+cv)(1+c+v)^2}. \tag{3.5.4}$$

Again, depending on the relationship between S_{cc} and S_{cv}, this can become negative, which would lead to repellent haptotaxis: cells effectively moving away from regions with large ECM gradients, a rather unexpected behaviour. This suggests that cell-tissue adhesions should dominate over cell-cell adhesions,[5] as 'usual' haptotaxis, i.e., towards the increasing tissue gradient, is known to be an essential component of cell migration, this applying to several types of cells moving through the ECM (tumor cells, mesenchymal stem cells, fibroblasts, endothelial cells, etc.) see e.g., [95, 123, 147] and references therein.

Simulations are plotted in *Figure 3.3* where we show cell densities for the local model (c_L) and nonlocal model under three sensing radii:

$$c_{Ar=0.1}, c_{Ar=0.3}, c_{Ar=1.0}.$$

In this first set of simulations we assume negligible cell-cell adhesion ($S_{cc} = 0$), which automatically ensures positivity for the diffusion coefficient of the equivalent local model, $\tilde{D}_c(c,v)$. We note that matrix renewal is absent ($\mu_v = 0$) in the left-hand column and present ($\mu_v > 0$) in the central column. In the right-hand column we show the greater generality of the results under vastly simplified kinetics, specifically setting $f_c(c,v) = 0$ and $f_v(c,v) = -cv$ (with the other functional forms as in *Example 3.4.5*). Simulations highlight the convergence between local and nonlocal models as $r \to 0$: for $r = 0.1$, the solution differences become negligible. However, distinctions emerge for large r, where we can expect significant discrepancy between the solutions.

[5] An analogous behaviour was suggested by the two-scale structured population model with adhesion introduced in [56].

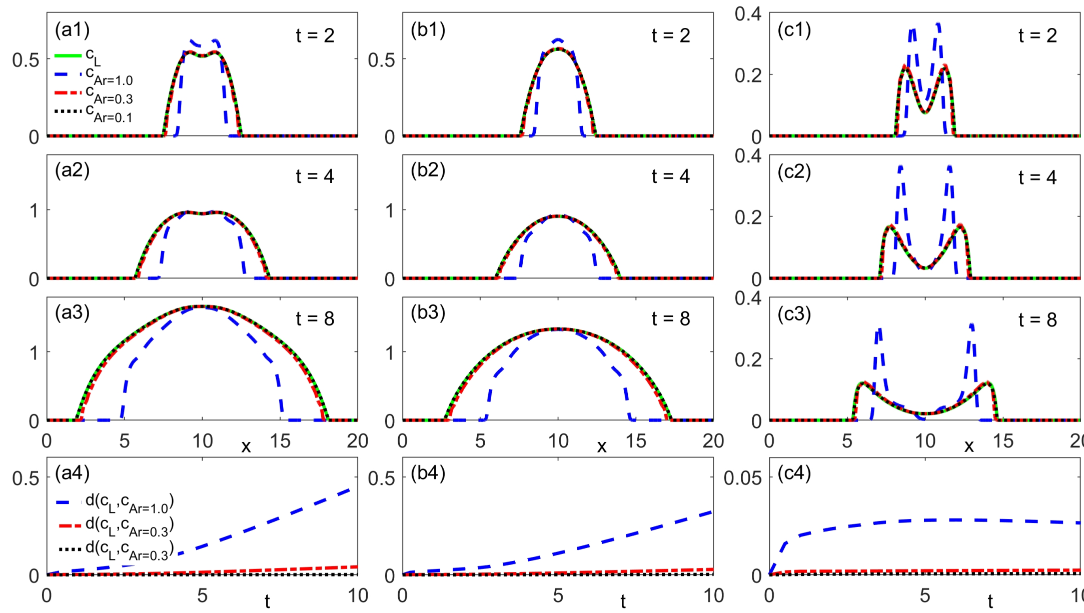

Figure 3.3: Convergence between nonlocal and local/classical formulations under negligible cell-cell adhesion, $S_{cc} = 0$, $S_{cv} = 10$. Functional forms as proposed in *Example 3.4.5*, with modifications specified in the subfigures. (a) Solutions for $r = 0.1, 0.3, 1.0$ at (a1) $t = 2$, (a2) $t = 4$ and (a3) $t = 8$; (a4) Distance between local/nonlocal solutions as a function of time. For these simulations, we take $a = 0.01$, $b = 1$, $\mu_c = 0.01$, $K_c = 2$, $\eta_c = 1$, $\mu_v = 0$, $\lambda_v = 1$. (b) Solutions for $r = 0.1, 0.3, 1.0$ at (b1) $t = 2$, (b2) $t = 4$ and (b3) $t = 8$; (b4) Distance between local/nonlocal solutions as a function of time. Parameters as in (a) except $\mu_v = 1$, $K_v = 1$. (c) Solutions for $f_c = 0$ and $f_v(c, v) = -cv$, with the other parameters as in (a).

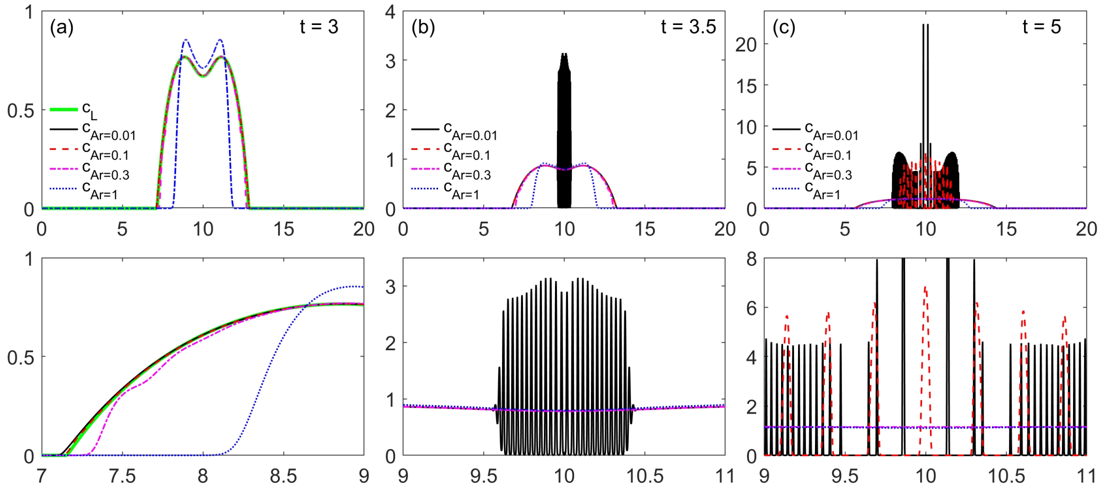

Figure 3.4: Time restricted convergence under moderate cell-cell adhesion, $S_{cc} = 2.5$, $S_{cv} = 10$. Top row shows solutions across the full spatial region ($[0, 20]$), the bottom row magnifies a relevant portion for clarity. Solutions to local and nonlocal models under the functional forms proposed in *Example 3.4.5* for $r = 0.01, 0.1, 0.3, 1.0$ at (a) $t = 3$, (b) $t = 3.5$ and (c) $t = 5$. In (a) solutions to the local model continue to exist and we observe convergence between local and nonlocal formulations. In (b-c) the solutions to the local model are noncomputable. Nonlocal models, however, can destabilise into a pattern of aggregates. Parameters: $a = 0.01$, $b = 1$, $\mu_c = 0.01$, $K_c = 2$, $\eta_c = 1$, $\mu_v = 0$, $\lambda_v = 1$ and adhesion parameters as above.

This suggests that the local model fails to accurately predict the behaviour in cases where cells sample over relatively large regions of their local environment.

Next, we extend to include a degree of cell-cell adhesion, setting functions and parameters as in *Figure 3.3*, except now $S_{cc} > 0$. Notably this raises the possibility of a negative diffusion coefficient in the classical formulation and subsequent illposedness. Solutions under a representative set of parameters are shown in Figure 3.4. For t below some critical time we observe convergence as before, with the nonlocal formulation converging to solutions of the local model as $r \to 0$. However, continued matrix degradation further depletes v, with the result that (3.5.3) can become negative. At this point (in this case $t \approx 3.2\ldots$) the local model becomes illposed and its solutions become incomputable (implying nonexistence of solutions). However, the nonlocal formulation appears to preserve wellposedness, consistent with previous theoretical studies where extending to a nonlocal formulation regularises a singular local model (e.g., [79]). Solutions to the nonlocal model instead destabilise into a quasi-periodic pattern of cell aggregations, maintained through the cell-cell adhesion, and with a wavelength shrinking as $r \to 0$.

Finally, we remark that convergence of solutions extends beyond the specific functional forms and, as a representative example, we consider a minimalist setting based on linear/constant forms. Specifically, we set $D_c = a$ (constant), $\chi = 1$, $f_c = 0$, $g(c, v) = S_{cc}c + S_{cv}v$ and $f_v(c, v) = -\mu cv$. In this scenario, the diffusion and haptotaxis coefficients for the classical local formulation (3.4.2) reduce to

$$\tilde{D}_c(c, v) = a - S_{cc}c \quad \text{and} \quad \tilde{\chi}(c, v) = S_{cv}. \tag{3.5.5}$$

Positivity is only guaranteed under appropriate parameter selection. Such a case is illustrated

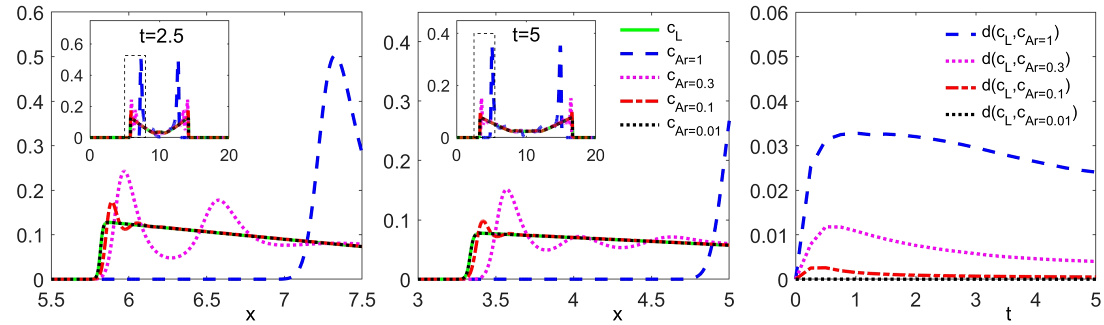

Figure 3.5: Convergence between nonlocal and local/classical formulations under a set of minimalistic linear functional forms ($D_c = 0.01,\ \chi = 1,\ f_c = 0,\ g(c,v) = S_{cc}c + S_{cv}v,\ f_v(c,v) = -\mu cv$). Negligible cell-cell adhesion, $S_{cc} = 0$, $S_{cv} = 10$: solutions shown at (left) $t = 2.5$ and (middle) $t = 5$, with the distance between solutions to the nonlocal and local model shown in the right panel.

in *Figure 3.5* where we assume negligible cell-cell adhesion ($S_{cc} = 0$). Clearly, we observe convergence between the nonlocal and local formulations as $r \to 0$. Inappropriate parameter selection, however, generates backward diffusion in the local model and solutions are consequently incomputable. In all cases considered in this test the cells do not reach the boundary region where the difference between the nonlocal formulations (3.1.1) and (3.4.1) can play a role. Thus, we expect the same solution if reformulation (3.4.1) is applied instead.

3.6 Discussion

In this chapter we provide a rigorous limit procedure which links nonlocal models involving adhesion or a nonlocal form of chemotaxis gradient to their local counterparts featuring haptotaxis, respectively chemotaxis in the usual sense. As such, it closes a gap in the existing literature. Moreover, it offers a unified treatment of the two types of models and extends the previous mathematical framework to settings allowing for more general, solution dependent, coefficient functions (diffusion, tactic sensitivity, adhesion velocity, nonlocal taxis gradient, etc.). Finally, we provide simulations illustrating some of our theoretical findings in 1D.

Our reformulations in terms of $\mathcal{T}_r$ and $\mathcal{S}_r$ reveal the tight relationship between the nonlocal operators $\mathcal{A}_r$ and $\mathring{\nabla}_r$ and the (local) gradient. This suggests that both nonlocal descriptions (adhesion, chemotaxis) actually encompass the dependence on the signal gradients rather than on the signal concentration/density itself, which is in line with the biological phenomenon. Indeed, through their transmembrane elements (e.g., receptors, ion channels etc.) the cells are mainly able to perceive and respond to differences in the signal at various locations or within more or less confined areas rather than measure effective signal concentrations. Along with the mentioned solution dependency of the nonlocal model coefficients, the influence of the gradient possibly reflects into contributions of the adhesion/nonlocal chemotaxis to the (nonlinear) diffusion in the local setting obtained through the limiting procedure.

The set Ω_r can be regarded as the 'domain of restricted sensing', meaning that there cells a priori sense only what happens inside Ω, the domain of interest. The measure of this subdomain is a decreasing function of the sensing radius r. When $r \to 0$ the set Ω_r tends to cover the whole domain Ω, whereas as r increases the cells can sense at increasingly larger distances; correspondingly, Ω_r shrinks. For $r > \operatorname{diam}(\Omega)$ the restricted sensing domain is empty: everywhere in Ω the cells can perceive signals not only from any point within Ω but potentially also from the outside. In this work, however, we look at models with no-flux boundary conditions. This corresponds, e.g., to the impenetrability of the walls of a Petri dish or that of comparatively hard barriers limiting the areas populated by migrating cells, e.g., bones or cartilage material. As a result, the cells in the boundary layer $\Omega\backslash\Omega_r$ have a much reduced ability to stretch their protrusions outside Ω and thus gain little information from without. To simplify matters, we assume in this work that there is no such information or it is insufficient to trigger any change in their behaviour. In the definitions of $\mathcal{T}_r$ and $\mathcal{S}_r$ this corresponds to the integrands being set to zero in $\Omega\backslash\overline{\Omega}_r$.

It is important to note that for points $x \in \Omega\backslash\overline{\Omega}_r$ the influence of a signal p in a direction $y \in S_1$ is not taken into account by $\mathring{\nabla}_r$ at all if $x + ry \notin \overline{\Omega}$. If $\mathcal{S}_r$ is used instead, then its contribution to the average is given by

$$\tilde{y} := n \left(\int_0^1 \chi_\Omega \nabla p(x + rsy)\, \mathrm{d}s \cdot y \right) y.$$

Thus, thanks to integration w.r.t. s, the resulting vector $\tilde{y}$ assembles the impact of those parts of the segment connecting x and $x + ry$ which are contained in Ω. It is parallel to y, and it may have the same or the opposite orientation. In particular this means that although for a certain range of directions large parts of the sensing region of a cell are actually outside Ω, this may still strongly influence the speed and actual direction of the drift. The effect of integration w.r.t. s in $\mathcal{T}_r$ is less obvious, since in this case the average w.r.t. y is computed over the ball B_1. This already achieves the covering of the whole sensing region by allowing a cell to gather information about the signal not only in any direction $y/|y|$, but also at any distance less than r. The additional integration over the path $x + rsy$, $s \in [0, 1]$, appears to mean that cells at $x \in \Omega_r$ are able to measure the average of the signal gradient all along such line segment rather than its value directly at the ending point. Indeed, from a biological viewpoint this description seems to make more sense, as cells do not jump from one position to another, nor do they send out their protrusions in a discontinuous way bypassing certain space points along a chosen direction. Averages over cell paths are then averaged w.r.t. y, which finally determines the direction of population movement. *Example 3.2.4* indicates that the effect of even an extremely concentrated signal gradient is mollified by averaging. This agrees with our expectations from using nonlocality. In higher dimensions $n \geqslant 2$, the two-stage averaging in $\mathcal{T}_r$ (w.r.t. s and y) produces a direction field which is smooth away from the concentration point and also weakens but still keeps the singularity there. In contrast, averaging only w.r.t. y leads instead to jump discontinuities at a unit distance from the accumulation point. Moreover, we remark that without integrating w.r.t. s in $\mathcal{T}_r(\nabla\cdot)$ one cannot regain $\mathcal{A}_r$.

The effect observed in *Example 3.2.3* further supports the conjecture that the nonlocal operators which act directly on the signal gradients might actually be a more appropriate modelling tool. While inside the subdomain Ω_r there is no difference (recall *Lemmas 3.2.1* and *3.2.2*), inside the boundary layer $\Omega\backslash\overline{\Omega}_r$ the limiting behaviour as $r \to 0$ is qualitatively distinct. Indeed, *Example 3.2.3* shows that using, e.g., $\mathcal{A}_r$, leads, for $r \to 0$, to unnatural sharp singularities at the boundary of Ω even in the absence of signal gradients, whereas this does not happen if $\mathcal{T}_r$ is used instead. Simulations in *Subsection 3.5.1* (see *Figure 3.2*) confirm our theoretical findings and show a substantial difference between the solutions obtained with the two nonlocal formulations involving (3.1.2) and (3.2.2), respectively. The choice (3.2.2) is motivated above all from a mathematical viewpoint (as it enables a rigorous, well-justified passage to the limit for $r \to 0$), but it also seems to make sense biologically, as our above comments and the simulations performed for the particular setting in *Subsection 3.5.1* suggest.

In this chapter we have only dealt with models that include a nonlocality in the chemotaxis or cell-cell and/or cell-tissue adhesion terms and assumed the diffusion to be local. This is in line with most of the previously developed nonlocal models for cell migration, albeit they usually cover just linear diffusion. If cell-cell adhesion is present, this means that the cell flux contains the local cell gradient, as well as some averaging of it. The latter is described in our case by a suitably chosen operator $\mathcal{T}_r$. A possible model extension could involve a diffusion flux which is also nonlocal and has a similar form. This would mean that the cell flux is completely devoid of the local gradient. From the modelling point of view this could be seen as a population pressure acting[6] in a nonlocal manner: each cell is sensing the population mass not only at its current position, but over a whole region (of radius r) around that location. This is actually true in vivo, where cells sample their biological environment by extending protrusions as far as several cell lengths. While cell-cell adhesions certainly play a role in this process and contribute to self-diffusion (as in the example handled in *Subsection 3.5.2*), there might be yet other ways of interaction by which the cells are able to perceive smaller or larger aggregates of their own kind. In this context one could think about replacing the local gradient by a nonlocal operator, e.g., of the form $\mathcal{T}_r(\nabla)$. However, the analysis of such a model would be considerably more involved and it is to expect that existence of solutions can be established only under rather restrictive assumptions.

[6] unlike Fick's classical law which typically connects the flux over the domain boundary with the diffusion inside the domain

CHAPTER 4

Global existence of solutions to a nonlocal equation with degenerate anisotropic diffusion

This chapter was first published in Volume 543 of Journal of Mathematical Analysis and Applications in 2025.[1] The presentation has been adapted for use in this dissertation to clarify the details of the proofs and guarantee consistency of the notation.

4.1 Motivation

In this chapter we study the initial boundary value problem (IBVP)

$$\partial_t c = \nabla\nabla : (\mathbb{D}c) - \nabla \cdot (c\mathcal{A}c) + \mu c(1 - c^{r-1}) \qquad \text{in } \Omega \times (0, \infty), \tag{4.1.1a}$$

$$(\nabla \cdot (\mathbb{D}c) - c\mathcal{A}c) \cdot \nu = 0 \qquad \text{on } \partial\Omega \times (0, \infty), \tag{4.1.1b}$$

$$c(\cdot, 0) = c_0 \qquad \text{in } \Omega, \tag{4.1.1c}$$

where $\mathcal{A}$ is the standard adhesion operator [5], see *Definition 4.2.1* below, $\nabla\nabla : (\mathbb{D}c)$ is the myopic diffusion [83], see *Definition 2.1.5*, driven by a symmetric non-negative definite diffusion tensor $\mathbb{D} = \mathbb{D}(x)$, $\mu > 0$ and $r \geqslant 2$ are positive constants, and Ω is a smooth bounded domain in $\mathbb{R}^n$, $n \in \mathbb{N}$. The nonlocal reaction-diffusion-advection equation (4.1.1a) is an extension of an equation that was recently derived in [156] using a multiscale approach and corresponds to the case $\mu = 0$. It can describe the evolution of density $c = c(t, x)$ of a cell population that disperses due to a potentially anisotropic diffusion and nonlocal adhesion, thus upgrading the original model from [5] where the diffusion term is $D\Delta c$ with $D > 0$ a constant. We refer to [156] for further details regarding the modelling and derivation approaches.

While the combination of adhesion with a Fickian-type diffusion has received much attention, see, e.g., [28] and references therein, the case of myopic diffusion has not been analysed so far. The few papers [77, 149–151] that have dealt with existence and long-time behaviour of solutions to problems that include both myopic diffusion and advection are restricted to versions of the model derived in [54]. It features haptotaxis, i.e., the directed movement along the local gradient of an external immovable signal, rather than the spatially nonlocal intrapopulational adhesion as in (4.1.1a). Apart from that, as a result of somewhat different underlying derivation approaches in [54] compared to [156], the advection velocity in the aforementioned haptotaxis model is

[1] [50] The paper is licensed under a CC BY license.

multiplied by the diffusion tensor, whereas in (4.1.1a) this is not the case. Thus, here it is in no way 'subordinate' to the diffusion and, in particular, the adhesion term need not vanish in those areas where diffusion is absent. Finally, we observe that apart from [77] where dimensions two and three were treated, other works [149–151] only considered the one-dimensional case.

The goal of this chapter is to establish a result on global existence of solutions to (4.1.1a) equipped with no-flux boundary and initial conditions. Our approach works for $\mu > 0$, i.e., in the presence of the generalised logistic-type growth term. While it describes a biologically relevant effect (e.g., cell growth/death), our main motivation for including the source term stems from the analytical challenges that arise in the case of $\mu = 0$. In the latter scenario, since the diffusion is non-Fickian and degenerate, only mass preservation is a priori guaranteed, indicating that generally solutions need not be functions but could be measure-valued. Here we chose to avoid this possibility by including the growth term. While our analysis allows for degenerate diffusion tensors, we require the degeneracy set, i.e., the set of points where $\mathbb{D}$ is not positive definite, to have a positive distance to the boundary of Ω and to be sufficiently low-dimensional, see condition (4.3.2f) below. This condition seems to be new in the context of degenerate diffusion. It arises from *Lemma 4.2.4* in *Subsection 4.2.2* and provides a certain balance between the degenerate diffusion and the nonlinear growth term.

The remainder of the chapter is organised in the following way. After recalling the definition of the adhesion operator $\mathcal{A}$ in *Section 4.2*, we fully set-up our model and formulate our main result on existence of very weak solutions, *Theorem 4.3.4*, in *Section 4.3*. We then analyse suitably constructed approximation problems in *Section 4.4*. The uniform estimates that we establish there allow to apply the compactness method and prove *Theorem 4.3.4* in *Section 4.5*. Finally, in *Section 4.6* we provide a justification of our solution concept proving that regular solutions of this sort are classical.

4.2 Preliminaries

4.2.1 The adhesion operator

Recall that throughout this dissertation $\Omega \subset \mathbb{R}^n$ is a domain with smooth enough boundary (C^3 in this chapter). We recall the definition of the adhesion operator $\mathcal{A}$ between two functional spaces from *Chapter 3* in the way that suits our needs, i.e., for a sensing radius equal to 1 in (3.1.2). This is no restriction of generality since this value can be always achieved through a suitable rescaling of the spatial variable.

Definition 4.2.1. *Consider a continuous function $F : [0, 1] \to [0, \infty)$. The adhesion operator is given by*

$$\mathcal{A} : L^1(\Omega) \to (L^\infty(\Omega))^n, \quad \mathcal{A}u(x) := \frac{1}{|B_1|} \int_{B_1} u(x + \xi) \frac{\xi}{|\xi|} F(|\xi|) \, d\xi. \tag{4.2.1}$$

By convention $u(x+\xi) = 0$ if $x+\xi \notin \overline{\Omega}$. The operator is well-defined and bounded, see *Chapter 3*, but in contrast to *Chapter 3* we will use here the reformulation

$$\mathcal{A}u = -\nabla H * u,$$

that was observed in [156], where H is the interaction potential given by

$$H : \mathbb{R} \to [0, \infty], \quad H(x) := \frac{1}{|B_1|} \int_{\min\{|x|,1\}}^{1} F(z)\,\mathrm{d}z,$$

so that its gradient is the L^∞ function

$$\nabla H(x) := \begin{cases} -\frac{1}{|B_1|}\frac{x}{|x|}F(|x|) & \text{if } x \in B_1 \backslash \{0\}, \\ 0 & \text{if } x \in \mathbb{R}^n \backslash \overline{B_1}. \end{cases}$$

Consequently, the operator $\mathcal{A}$ satisfies the lemma below.

Lemma 4.2.2. *Let $k \in \mathbb{N}_0$ and $\alpha \in [0, 1]$. Then, $\mathcal{A}$ is a continuous operator on $C^{k,\alpha}(\overline{\Omega})$.*

Proof. For $k = 0$ this follows from *Lemma 2.3.2.* Moreover, for $k \geqslant 1$ we conclude this combining *Theorems A.3.11* and *A.3.12* and *Lemma 2.3.2.* □

4.2.2 A lemma about sets of "sufficiently small" dimension

We recall one of the (alternative) ways of defining fractional dimension from (3.5) and the subsequent discussion on p. 42 in [60].

Definition 4.2.3. *(Upper box dimension) Let $K \subset \mathbb{R}^n$ be compact. For every $\delta > 0$ we denote*

$$Z_\delta(K) := \left\{ b \in \delta\mathbb{Z}^n : \ |x - b|_\infty \leqslant \frac{\delta}{2} \text{ for some } x \in K \right\}.$$

The upper box dimension is the non-negative number

$$\overline{\dim}_{\mathcal{F}}(K) := \limsup_{\delta \to 0} \frac{\log_2 |Z_\delta(K)|}{\log_2 \delta^{-1}}.$$

Lemma 4.2.4. *Let*

$$3 \leqslant n \in \mathbb{N}, \tag{4.2.2}$$

$$r > \frac{n}{n-2}, \tag{4.2.3}$$

and $K \subset \mathbb{R}^n$ be a compact set such that

$$\overline{\dim}_{\mathcal{F}}(K) < n - \frac{2r}{r-1}. \tag{4.2.4}$$

Then, there exists a family $(\varphi_\delta)_{\delta \in (0,1)}$ of functions such that for all $\delta > 0$

$$\varphi_\delta \in C_c^\infty(\mathbb{R}^n; [0, 1]), \tag{4.2.5a}$$

$$\varphi_\delta = 1 \qquad \text{in } \overline{O_{\delta\sqrt{n}}(K)}, \tag{4.2.5b}$$

$$\mathrm{supp}(\varphi_\delta) \subset \overline{O_{5\delta\sqrt{n}}(K)}, \tag{4.2.5c}$$

$$\|\nabla\varphi_\delta\|_{(L^\infty(\mathbb{R}^n))^n} \leqslant \delta^{-1} C_1, \tag{4.2.5d}$$

$$\|D^2\varphi_\delta\|_{(L^\infty(\mathbb{R}^n))^{n\times n}} \leqslant \delta^{-2} C_1, \tag{4.2.5e}$$

$$\varphi_\delta \underset{\delta \to 0}{\to} 0 \qquad \text{a.e. in } \mathbb{R}^n, \tag{4.2.5f}$$

$$\lim_{\delta \to 0} \delta^{-\frac{2r}{r-1}} |\mathrm{supp}(\varphi_\delta)| = 0. \tag{4.2.5g}$$

Proof. Let $\eta \in C_c^\infty([0,\infty);[0,1])$ be such that

$$\eta = \begin{cases} 1 & \text{in } [0,1], \\ 0 & \text{in } [2,\infty). \end{cases}$$

Set

$$\varphi_\delta(x) := \frac{\sum_{z\in\delta\mathbb{Z}^n\cap O_{3\delta\sqrt{n}}(K)} \eta\left(\frac{|x-z|}{\delta\sqrt{n}}\right)}{\sum_{z\in\delta\mathbb{Z}^n} \eta\left(\frac{|x-z|}{\delta\sqrt{n}}\right)} \qquad \text{for } x\in\mathbb{R}^n,\ \delta\in(0,1). \tag{4.2.6}$$

We need to check that φ_δ satisfies the required properties.

1. Since

$$\max_{x\in\mathbb{R}^n}\left|B_{3\delta\sqrt{n}}(x)\cap\delta\mathbb{Z}^n\right| = \max_{y\in\mathbb{R}^n}\left|B_{3\sqrt{n}}(y)\cap\mathbb{Z}^n\right| =: C_2 < \infty$$

   for some $C_2 > 0$, and $\eta = 0$ in $[2,\infty)$, the sums in (4.2.6) contain at most C_2 non-zero summands.

2. Since $\mathbb{R}^n = O_{\delta\sqrt{n}}(\delta\mathbb{Z}^n)$ and $\eta = 1$ in $[0,1]$, the denominator in (4.2.6) is never zero, and

$$\sum_{z\in\delta\mathbb{Z}^n} \eta\left(\frac{|x-z|}{\delta\sqrt{n}}\right) \geqslant 1. \tag{4.2.7}$$

3. By *1.* and *2.* and the assumptions on η, the function φ_δ is well-defined and belongs to $C_c^\infty(\mathbb{R}^n;[0,1])$.

4. Since $\eta = 0$ in $[2,\infty)$, the numerator and the denominator coincide for $x\in O_{\delta\sqrt{n}}(K)$ both having the value

$$\sum_{z\in\delta\mathbb{Z}^n\cap O_{2\delta\sqrt{n}}(x)} \eta\left(\frac{|x-z|}{\delta\sqrt{n}}\right),$$

   hence $\varphi_\delta = 1$ there.

5. Since $\eta = 0$ in $[2,\infty)$,

$$\begin{aligned} \operatorname{supp}(\varphi_\delta) &\subset \overline{O_{2\delta\sqrt{n}}\left(\delta\mathbb{Z}^n\cap O_{3\delta\sqrt{n}}(K)\right)} \\ &\subset \overline{O_{5\delta\sqrt{n}}(K)} \\ &\subset \overline{O_{6\delta\sqrt{n}}(Z_\delta(K))}. \end{aligned} \tag{4.2.8}$$

   Combining (4.2.4) and (4.2.8), we obtain

$$\begin{aligned} \log_2\left(\delta^{-\frac{2r}{r-1}}|\operatorname{supp}(\varphi_\delta)|\right) &\leqslant \log_2\left(\delta^{-\frac{2r}{r-1}}|Z_\delta(K)|(6\delta\sqrt{n})^n|B_1|\right) \\ &\leqslant \log_2\left(C_3\delta^{n-\frac{2r}{r-1}}|Z_\delta(K)|\right) \\ &= \log_2 C_3 + \log_2\delta^{-1}\left(\frac{\log_2|Z_\delta(K)|}{\log_2\delta^{-1}} - \left(n-\frac{2r}{r-1}\right)\right) \\ &\underset{\delta\to0}{\to} -\infty, \end{aligned} \tag{4.2.9}$$

   so (4.2.5g) holds.

6. We compute

$$\nabla\varphi_\delta(x) = \frac{1}{\delta\sqrt{n}}\left(\frac{\sum_{z\in\delta\mathbb{Z}^n\cap O_{3\delta\sqrt{n}}(K)}\operatorname{sign}(x-z)\eta'\left(\frac{|x-z|}{\delta\sqrt{n}}\right)}{\sum_{z\in\delta\mathbb{Z}^n}\eta\left(\frac{|x-z|}{\delta\sqrt{n}}\right)}\right.$$
$$\left. - \frac{\sum_{z\in\delta\mathbb{Z}^n\cap O_{3\delta\sqrt{n}}(K)}\eta\left(\frac{|x-z|}{\delta\sqrt{n}}\right)\sum_{z\in\delta\mathbb{Z}^n}\operatorname{sign}(x-z)\eta'\left(\frac{|x-z|}{\delta\sqrt{n}}\right)}{\left(\sum_{z\in\delta\mathbb{Z}^n}\eta\left(\frac{|x-z|}{\delta\sqrt{n}}\right)\right)^2}\right). \tag{4.2.10}$$

Combining *1.*, *2.* and (4.2.10) and the assumptions on η, we obtain (4.2.5d). Differentiating again and using the same argument yields (4.2.5e).

7. The convergence (4.2.5f) is a direct consequence of (4.2.5b) and (4.2.5c) and $\overline{\dim}_{\mathcal{F}}(K) < n$.

□

4.3 Problem setting and main result

We make the following assumptions on the coefficients and other parameters.

Assumptions 4.3.1.

$$n \geqslant 3,\ r > \frac{n}{n-2},\ r \geqslant 2, \tag{4.3.1}$$
$$F \in C([0,1];[0,\infty)),$$
$$\mu > 0,$$
$$c_0 \in L^r(\Omega),$$

and

$$\mathbb{D} := (d_{ij})_{i,j=1,\dots,n} \in C(\overline{\Omega};\mathbb{R}^{n\times n}), \tag{4.3.2a}$$
$$\mathbb{D}(x) \text{ symmetric for } x \in \overline{\Omega}, \tag{4.3.2b}$$
$$\nabla\cdot\mathbb{D} \in \left(L^\infty_{loc}(\{\mathbb{D} > 0\})\right)^n, \tag{4.3.2c}$$
$$\mathbb{D} \geqslant 0, \tag{4.3.2d}$$
$$a := dist(\partial\Omega, \{\mathbb{D} \ngtr 0\}) > 0, \tag{4.3.2e}$$
$$\overline{\dim}_{\mathcal{F}}(\{\mathbb{D} \ngtr 0\}) < n - \frac{2r}{r-1}. \tag{4.3.2f}$$

Recall that for $\mathbb{D} \geqslant 0$ the above sets are defined as

$$\{\mathbb{D} > 0\} = \{x \in \overline{\Omega} :\ y^T\mathbb{D}(x)y > 0\ \forall y \in \mathbb{R}^n\}$$

and

$$\{\mathbb{D} \ngtr 0\} := \{x \in \overline{\Omega} :\ \exists y \in \mathbb{R}^n \text{ s.t. } y^T\mathbb{D}(x)y = 0\}.$$

To illustrate condition (4.3.2f), we consider two special cases where it is satisfied.

Example 4.3.2. 1. For a finite set $\{\mathbb{D} \not\succ 0\} = \{a_1, \dots, a_K\}$ with $K \in \mathbb{N}$ we can estimate

$$|Z_\delta(\{\mathbb{D} \not\succ 0\})| = \left|\left\{b \in \delta\mathbb{Z}^n : |a_i - b|_\infty \leqslant \frac{\delta}{2} \text{ for some } i = 1, \dots, K\right\}\right| \leqslant 2K.$$

Then,

$$\overline{\dim}_{\mathcal{F}}(\{\mathbb{D} \not\succ 0\}) = \limsup_{\delta\to 0} \frac{\log_2 |Z_\delta(\{\mathbb{D} \not\succ 0\})|}{\log_2 \delta^{-1}} \leqslant \limsup_{\delta\to 0} \frac{\log_2(2K)}{\log_2 \delta^{-1}} = 0.$$

2. Consider a sequence $(a_k)_{k\in\mathbb{N}}$ in Ω with $\lim_{k\to\infty} a_k = \tilde{a} \in \Omega$, i.e., for all $\delta > 0$ there is $K(\delta) \in \mathbb{N}$ s.t. $|a_k - \tilde{a}| < \frac{\delta}{2}$ for all $k \geqslant K(\delta)$. We assume that the sequence converges fast enough to its limit in the sense that there is $b < n - \frac{2r}{r-1}$ s.t.

$$\limsup_{\delta\to 0} \frac{\log_2(K(\delta))}{\log_2 \delta^{-1}} = b. \tag{4.3.3}$$

If $\{\mathbb{D} \not\succ 0\} = \{\tilde{a}, a_1, a_2, \dots\}$, then

$$|Z_\delta(\{\mathbb{D} \not\succ 0\})| \leqslant 2(K(\delta) + 1). \tag{4.3.4}$$

Combining (4.3.3) and (4.3.4), we arrive at (4.3.2f).

We define solutions to the IBVP (4.1.1) as follows.

Definition 4.3.3. *We call a function* $c \in L^r_{loc}(\overline{\Omega} \times [0, \infty))$ *a global very weak solution to* (4.1.1) *if it satisfies*

$$\begin{aligned} &- \int_0^\infty \int_\Omega c\partial_t\eta \, dx \, dt - \int_\Omega c_0\eta(\cdot, 0) \, dx \\ &= \int_0^\infty \int_\Omega c\mathbb{D} : D^2\eta \, dx \, dt + \int_0^\infty \int_\Omega c(\mathcal{A}c) \cdot \nabla\eta \, dx \, dt + \mu \int_0^\infty \int_\Omega c(1 - c^{r-1})\eta \, dx \, dt \end{aligned} \tag{4.3.5}$$

for all

$$\eta \in C_c^{2,1}(\overline{\Omega} \times [0, \infty)) \qquad s.t.\ \nabla\eta \cdot (\mathbb{D}\nu) \equiv 0 \ on\ \partial\Omega \times (0, \infty).$$

The main result of this chapter concerns with the existence of such solutions.

Theorem 4.3.4. *Let Assumptions 4.3.1 hold. Then, there is a very weak solution*

$$c \in L^\infty(0, \infty; L^1(\Omega)) \cap L^r_{loc}(\overline{\Omega} \times [0, \infty))$$

to (4.1.1) *in the sense of Definition 4.3.3.*

Remark 4.3.5. The very weak formulation (4.3.5) is obtained by multiple partial integration that shifts all spatial derivatives to the test function. This choice of formulation exploits the structure of the myopic diffusion. At the same time, it avoids including terms such as $\nabla \cdot (\mathbb{D}c)$ or ∇c, for which it is likely not possible to obtain a priori bounds in the whole domain Ω due to a combination of the degeneracy of the diffusion tensor $\mathbb{D}$ and the diffusion being myopic.

Furthermore, we show in *Section 4.6* that sufficiently smooth very weak solutions are classical solutions to (4.1.1). This justifies our solution concept.

4.4 Approximate problems

4.4.1 Construction of a regular matrix family $(\mathbb{D}_\varepsilon)$

We begin by constructing a family of regular matrices $\mathbb{D}_\varepsilon$ that approximate $\mathbb{D}$ in a suitable fashion. For such diffusion matrices, existence of regular solutions can be directly concluded from known results. Unlike [77], we impose uniform L^∞ boundedness of the divergence for $(\mathbb{D}_\varepsilon)$ instead of convergence in an L^p space for finite p and make no additional restrictions such as, e.g., vanishing normal trace, because our analysis does not require this.

Lemma 4.4.1. *Let Ω be Lipschitz. For $\varepsilon_1 > 0$ small enough, there is a sequence of symmetric matrices $(\mathbb{D}_\varepsilon)_{\varepsilon\in(0,\varepsilon_1)} = (((d_{ij})_\varepsilon)_{i,j=1,\dots,n})_{\varepsilon\in(0,\varepsilon_1)} \subset C^\infty(\overline{\Omega};\mathbb{R}^{n\times n})$ s.t.*

$$\|\mathbb{D}_\varepsilon\|_{(L^\infty(\Omega))^{n\times n}} \leqslant \varepsilon + \|\mathbb{D}\|_{(L^\infty(\Omega))^{n\times n}} \qquad \text{for } \varepsilon \in (0,\varepsilon_1), \tag{4.4.1}$$

$$\mathbb{D}_\varepsilon \geqslant \varepsilon \qquad \text{for } \varepsilon \in (0,\varepsilon_1), \tag{4.4.2}$$

$$\|\mathbb{D}_\varepsilon - \mathbb{D}\|_{C(\overline{\Omega};\mathbb{R}^{n\times n})} \to 0 \text{ as } \varepsilon \to 0. \tag{4.4.3}$$

Further, for every relatively open

$$B \subset\subset \{\mathbb{D} > 0\}$$

there exists some $\varepsilon_2(B) \in (0,\varepsilon_1]$ such that

$$\|\nabla\cdot\mathbb{D}_\varepsilon\|_{(L^\infty(B))^n} \leqslant C_4(B) \qquad \text{for } \varepsilon \in (0,\varepsilon_2(B)). \tag{4.4.4}$$

Proof. We take a standard approach, arguing in a manner similar to the proof of Theorem 3 in Section 5.3.3 in [58].

Step 1. We need some preparation before we can proceed with a regularisation of $\mathbb{D}$. It concerns the domain Ω. Let $x_0 \in \partial\Omega$. Since Ω has a Lipschitz boundary, there exist $\gamma \in C^{0,1}(\mathbb{R}^{n-1};\mathbb{R})$ and $\rho \in (0,a)$ s.t. (after relabeling and reorientation of the axes if necessary)

$$\Omega \cap B_\rho(x_0) = \left\{y \in B_\rho(x_0) : y_n > \gamma(y')\right\}, \tag{4.4.5}$$

$$\partial\Omega \cap B_\rho(x_0) = \left\{y \in B_\rho(x_0) : y_n = \gamma(y')\right\}. \tag{4.4.6}$$

Due to $\rho < a$, the set $\Omega \cap B_\rho(x_0)$ does not intersect $\{\mathbb{D} \ngtr 0\}$. Let us check that

$$\Omega \cap B_{\frac{\rho}{2}}(x_0) + \varepsilon(L+1)e_n + B_\varepsilon(0) \subset \Omega \cap B_\rho(x_0) \tag{4.4.7}$$

for

$$\varepsilon \leqslant \frac{\rho}{2(L+2)}, \tag{4.4.8}$$

where L is a Lipschitz constant for γ in

$$B_\rho^{n-1}(x_0') := \left\{z' \in \mathbb{R}^{n-1} :\ |z' - x_0'| < \rho\right\}.$$

Let $y \in \Omega \cap B_{\frac{\rho}{2}}(x_0)$ and $z \in B_\varepsilon(\varepsilon(L+1)e_n) = \varepsilon(L+1)e_n + B_\varepsilon(0)$. Due to (4.4.8), it holds that

$$|y + z - x_0| \leqslant |y - x_0| + |z - \varepsilon(L+1)e_n| + \varepsilon(L+1)$$

$$\begin{aligned} &< \frac{\rho}{2} + (L+2)\varepsilon \\ &\leqslant \rho. \end{aligned} \tag{4.4.9}$$

As $z \in B_\varepsilon(\varepsilon(L+1)e_n)$ implies that $|z'| < \varepsilon$ and $z_n > \varepsilon(L+1) - \varepsilon = \varepsilon L$, the Lipschitz continuity of γ and (4.4.5) together imply

$$\begin{aligned} \gamma(y' + z') \leqslant& \gamma(y') + L|z'| \\ <& y_n + \varepsilon L \\ <& y_n + z_n - \varepsilon L + \varepsilon L \\ =& y_n + z_n. \end{aligned} \tag{4.4.10}$$

Combining (4.4.5), (4.4.9), and (4.4.10), we arrive at (4.4.7).

Due to compactness of $\overline{\Omega}$, we can find some constants $\rho \in (0, a)$, $L > 0$, and $K \in \mathbb{N}$ and points $x_k \in \partial\Omega$ and $z_k \in S_1(0)$, $k \in \{1, \ldots, K\}$, such that

$$\Omega \cap B_{\frac{\rho}{2}}(x_k) + B_\varepsilon(\varepsilon(L+1)z_k) \subset \Omega \cap B_\rho(x_k) \qquad \text{for } k \in \{1, \ldots, K\},\ \varepsilon \in \left(0, \frac{\rho}{2(L+2)}\right) \tag{4.4.11}$$

and

$$\partial\Omega \subset \bigcup_{k=1}^{K} B_{\frac{\rho}{2}(x_k)}.$$

Let

$$A_0 := \overline{\Omega} \backslash \left(\bigcup_{n=1}^{K} B_{\frac{\rho}{2}(x_k)} \right).$$

This set is compact and satisfies $\rho_0 := \operatorname{dist}(A_0, \partial\Omega) > 0$. We set

$$\varepsilon_1 := \min\left\{ \frac{\rho}{2(L+2)}, \frac{\rho_0}{3} \right\}.$$

By *Lemma A.3.10*, there is a partition of unity $\{\psi_k\}_{k=0}^K$ subordinate to the open covering

$$O_{\frac{\rho_0}{2}}(A_0),\ \{B_{\frac{\rho}{2}}(x_k)\}_{k=1}^K \tag{4.4.12}$$

of $\overline{\Omega}$, i.e., a set of functions that satisfies

$$\psi_0 \in C_c^\infty(O_{\frac{\rho_0}{2}}(A_0)), \tag{4.4.13a}$$

$$\psi_k \in C_c^\infty(B_{\frac{\rho}{2}}(x_k)) \qquad \text{for } k \in \{1, \ldots, K\}, \tag{4.4.13b}$$

$$0 \leqslant \psi_k \leqslant 1 \qquad \text{for } k \in \{0, \ldots, K\}, \tag{4.4.13c}$$

$$\sum_{k=0}^{K} \psi_k = 1 \qquad \text{in } \overline{\Omega}. \tag{4.4.13d}$$

Step 2. Now we can proceed with the construction of approximations for $\mathbb{D}$. For $\varepsilon \in (0, \varepsilon_1)$ and $x \in \overline{\Omega}$ we set

$$\mathbb{D}_\varepsilon(x) := \varepsilon I_n + \psi_0(x)(\varsigma_\varepsilon * \mathbb{D})(x) + \sum_{k=1}^{K} \psi_k(x)(\varsigma_\varepsilon * \mathbb{D})(x + \varepsilon(L+1)z_k) \tag{4.4.14}$$

$$=\varepsilon I_n + \psi_0(x)\int_{B_\varepsilon(0)} \mathbb{D}(x-y)\varsigma_\varepsilon(y)\,\mathrm{d}y + \sum_{k=1}^{K}\psi_k(x)\int_{B_\varepsilon(0)} \mathbb{D}(x+\varepsilon(L+1)z_k - y)\varsigma_\varepsilon(y)\,\mathrm{d}y.$$

We set $\mathbb{D}_\varepsilon =: ((d_{ij})_\varepsilon)_{i,j=1,\dots,n}$. Obviously, $\mathbb{D}_\varepsilon \in C^\infty(\overline{\Omega},\mathbb{R}^{n\times n})$, is symmetric in $\overline{\Omega}$, and $\mathbb{D}_\varepsilon \geqslant \varepsilon$. We estimate for $w \in \mathbb{R}^n$ and $x \in \overline{\Omega}$ that

$$\begin{aligned}|\mathbb{D}_\varepsilon(x)w| \leqslant & \varepsilon|w| + \psi_0(x)\int_{B_\varepsilon(0)} |\mathbb{D}(x-y)|_2|w|\varsigma_\varepsilon(y)\,\mathrm{d}y \\ & + \sum_{k=1}^{K}\psi_k(x)\int_{B_\varepsilon(0)} |\mathbb{D}(x+\varepsilon(L+1)z_k-y)|_2|w|\varsigma_\varepsilon(y)\,\mathrm{d}y \\ \leqslant & \varepsilon|w| + \sum_{k=0}^{K}\psi_k(x)\|\mathbb{D}\|_{(L^\infty(\Omega))^{n\times n}}|w|\int_{B_\varepsilon(0)}\varsigma_\varepsilon(y)\,\mathrm{d}y\end{aligned}$$

and taking the supremum over $|w|=1$ and $x \in \overline{\Omega}$ obtain (4.4.1).
Further, thanks to (4.4.11) we can exploit uniform continuity of $\mathbb{D}$ in $\overline{\Omega}$, yielding

$$\max_{x\in\overline{\Omega\cap B_{\frac{\rho}{2}}(x_k)}} |(\varsigma_\varepsilon * d_{ij})(x+\varepsilon(L+1)z_k) - d_{ij}(x)| \tag{4.4.15}$$

$$\begin{aligned}&= \max_{x\in\overline{\Omega\cap B_{\frac{\rho}{2}}(x_k)}}\left|\int_{B_\varepsilon(0)} (d_{ij}(x+\varepsilon(L+1)z_k-y) - d_{ij}(x))\varsigma_\varepsilon(y)\,dy\right| \\ &\leqslant \max_{(x,y)\in\overline{\Omega\cap B_{\frac{\rho}{2}}(x_k)}\times\overline{B_\varepsilon(0)}} |(d_{ij}(x+\varepsilon(L+1)z_k-y)-d_{ij}(x))| \underset{\varepsilon\to 0}{\to} 0\end{aligned} \tag{4.4.16}$$

for $k \in \{1,\dots,K\}$ and $i,j \in \{1,\dots,n\}$. Since $\overline{O_{\frac{\rho_0}{2}}(A_0)} \subset \Omega$, due to *Lemma 2.3.4* we also have

$$\varsigma_\varepsilon * d_{ij} \underset{\varepsilon\to 0}{\to} d_{ij} \qquad \text{in } C\left(\overline{O_{\frac{\rho_0}{2}}(A_0)}\right). \tag{4.4.17}$$

Combining (4.4.13), (4.4.14), (4.4.16), and (4.4.17) and using the equivalence of the $|\cdot|_2$ and $|\cdot|_\infty$ matrix norms, we arrive at

$$\mathbb{D}_\varepsilon \underset{\varepsilon\to 0}{\to} \mathbb{D} \qquad \text{in } C(\overline{\Omega};\mathbb{R}^{n\times n}).$$

Step 3. It remains to verify (4.4.4). Let $B \subset\subset \{D>0\}$ relatively open. We set

$$\varepsilon_2(B) := \min\left\{\frac{\rho}{2(L+3)}, \frac{\rho_0}{4}, \frac{1}{2(L+2)}\operatorname{dist}(\overline{B},\{\mathbb{D} \not> 0\})\right\} < \varepsilon_1.$$

Assume

$$B \subset B_{\frac{\rho}{2}}(x_k) \tag{4.4.18}$$

for some $k \in \{1,\dots,K\}$. Then,

$$\overline{B} + \overline{B_\varepsilon(0)} + \varepsilon(L+1)z_k \subset \overline{O_{\varepsilon(L+2)}(B)} \cap \overline{\Omega} \subset \{\mathbb{D}>0\} \cap B_\rho(x_k) \qquad \text{for } \varepsilon \in (0,\varepsilon_2(B)). \tag{4.4.19a}$$

Let $\varphi \in C_c^\infty(B\backslash\partial\Omega)$. By the definition of weak divergence we have

$$\int_{\mathbb{R}^n} \nabla\cdot(\varsigma_\varepsilon * \mathbb{D})(x+\varepsilon(L+1)z_k)\varphi\,\mathrm{d}x = -\int_{\mathbb{R}^n}(\varsigma_\varepsilon * \mathbb{D})(x+\varepsilon(L+1)z_k)\nabla\varphi(x)\,\mathrm{d}x.$$

Now, using integration by substitution and the symmetry of ς_ε we compute

$$\int_{\mathbb{R}^n}(\varsigma_\varepsilon * \mathbb{D})(x+\varepsilon(L+1)z_k)\nabla\varphi(x)\,\mathrm{d}x = \int_{\mathbb{R}^n}\int_{B_\varepsilon(0)}\mathbb{D}(x+\varepsilon(L+1)z_k-y)\varsigma_\varepsilon(y)\nabla\varphi(x)\,\mathrm{d}y\,\mathrm{d}x$$

$$= \int_{\mathbb{R}^n} \mathbb{D}(x) \int_{B_\varepsilon(0)} \varsigma_\varepsilon(y) \nabla\varphi(x - \varepsilon(L+1)z_k - y)\,\mathrm{d}y\,\mathrm{d}x$$
$$= \int_{\mathbb{R}^n} \mathbb{D}(x)(\varsigma_\varepsilon * \nabla\varphi)(x - \varepsilon(L+1)z_k)\,\mathrm{d}x$$
$$= \int_{\mathbb{R}^n} \mathbb{D}(x)\nabla((\varsigma_\varepsilon * \varphi)(x - \varepsilon(L+1)z_k))\,\mathrm{d}x.$$

Again by the definition of weak divergence and (4.4.19a) we obtain

$$\begin{aligned}\int_{\mathbb{R}^n} \mathbb{D}(x)\nabla((\varsigma_\varepsilon * \varphi)(x - \varepsilon(L+1)z_k))\,\mathrm{d}x &= -\int_{\mathbb{R}^n} \nabla\cdot\mathbb{D}(x)(\varsigma_\varepsilon * \varphi)(x - \varepsilon(L+1)z_k)\,\mathrm{d}x \\ &= -\int_{O_{\varepsilon(L+2)}(B)\cap\Omega} \nabla\cdot\mathbb{D}(x)(\varsigma_\varepsilon * \varphi)(x - \varepsilon(L+1)z_k)\,\mathrm{d}x\end{aligned}$$

so that

$$\begin{aligned}\left|\int_{\mathbb{R}^n} \nabla\cdot(\varsigma_\varepsilon * \mathbb{D})(x + \varepsilon(L+1)z_k)\varphi\,\mathrm{d}x\right|_\infty &\leqslant \|\nabla\cdot\mathbb{D}\|_{(L^\infty(O_{\varepsilon(L+2)}(B)\cap\Omega))^n}\,\|\varphi\|_{L^1(B)} \\ &\leqslant \|\nabla\cdot\mathbb{D}\|_{(L^\infty(O_{\varepsilon_2(B)(L+2)}(B)\cap\Omega))^n}\,\|\varphi\|_{L^1(B)}.\end{aligned} \tag{4.4.20}$$

Consequently, due to the density of $C_c^\infty(B\backslash\partial\Omega)$ in $L^1(B\backslash\partial\Omega) = L^1(B)$ and as $(L^1(B))^* = L^\infty(B)$, the estimate

$$\|\nabla\cdot(\varsigma_\varepsilon * \mathbb{D})(\cdot + \varepsilon(L+1)z_k))\|_{(L^\infty(B))^n} \leqslant \sqrt{n}\,\|\nabla\cdot\mathbb{D}\|_{(L^\infty(O_{\varepsilon_2(B)(L+2)}(B)\cap\Omega))^n} \tag{4.4.21}$$

for $\varepsilon \in (0, \varepsilon_2(B))$ follows.

On the other hand, if $B \subset\subset \{\mathbb{D} > 0\}$ and $B \subset O_{\frac{\rho_0}{2}}(A_0)$, then

$$\overline{B} + \overline{B_\varepsilon(0)} \subset \overline{O_\varepsilon(B)} \subset \{\mathbb{D} > 0\} \cap O_{\frac{5\rho_0}{6}}(A_0) \text{ for } \varepsilon \in (0, \varepsilon_2(B)).$$

A similar argument as above with $\varphi \in C_c^\infty(B)$ works for $\varsigma_\varepsilon * \mathbb{D}$, yielding

$$\|\nabla\cdot(\varsigma_\varepsilon * \mathbb{D})\|_{(L^\infty(B))^n} \leqslant \sqrt{n}\,\|\nabla\cdot\mathbb{D}\|_{(L^\infty(O_{\varepsilon_2(B)}(B)))^n} \tag{4.4.22}$$

for $\varepsilon \in (0, \varepsilon_2(B))$.

Now, consider an arbitrary $B \subset\subset \{\mathbb{D} > 0\}$. Then, $B = \bigcup_{k=1}^K \Big(B \cap B_{\frac{\rho}{2}}(x_k)\Big) \bigcup \Big(B \cap O_{\frac{\rho_0}{2}}(A_0)\Big)$. Combining (4.4.1), (4.4.13), (4.4.14), (4.4.21), and (4.4.22) and using the product rule we obtain

$$\begin{aligned}\|\nabla\cdot\mathbb{D}_\varepsilon\|_{(L^\infty(B))^n} \leqslant& \sqrt{n}\|\nabla\cdot D\|_{(L^\infty(O_{\varepsilon_2(B\cap O_{\frac{\rho_0}{2}}(A_0))}(B\cap O_{\frac{\rho_0}{2}}(A_0))))^n} \\ &+ \sqrt{n}\sum_{k=1}^K \|\nabla\cdot\mathbb{D}\|_{(L^\infty(O_{\varepsilon_2(B\cap B_{\frac{\rho}{2}}(x_k))(L+2)}(B\cap B_{\frac{\rho}{2}}(x_k))\cap\Omega))^n} + C_5 =: C_4(B)\end{aligned}$$

for $\varepsilon \in (0, \varepsilon_2(B))$.

□

4.4.2 Existence of a global classical solution to the approximate problem

Let $\alpha \in (0, \frac{1}{2})$. Since $C_c^\infty(\Omega)$ is dense in $L^2(\Omega)$, there is a sequence $(c_{0\varepsilon})_{\varepsilon\in(0,\varepsilon_1)} \subset C^{2+\alpha}(\overline{\Omega})$ and a constant C_6 satisfying

$$(\nabla\cdot(\mathbb{D}_\varepsilon c_{0\varepsilon}) - c_{0\varepsilon}\mathcal{A}c_{0\varepsilon})\cdot\nu = 0 \qquad \text{on } \partial\Omega,$$

$$c_{0\varepsilon} \underset{\varepsilon\to 0}{\to} c_0 \qquad \text{in } L^2(\Omega), \tag{4.4.23}$$
$$\|c_{0\varepsilon}\|_{L^2(\Omega)} \leqslant C_6 \qquad \text{for all } \varepsilon \in (0,\varepsilon_1).$$

With the help of the diffusion tensors constructed in *Subsection 4.4.1* we formulate for $\varepsilon \in (0,\varepsilon_1)$ the approximate problems

$$\partial_t c_\varepsilon = \nabla\nabla : (\mathbb{D}_\varepsilon c_\varepsilon) - \nabla\cdot(c_\varepsilon \mathcal{A} c_\varepsilon) + \mu c_\varepsilon(1 - c_\varepsilon^{r-1}) \qquad \text{in } \Omega\times[0,\infty), \tag{4.4.24a}$$
$$(\nabla\cdot(\mathbb{D}_\varepsilon c_\varepsilon) - c_\varepsilon\mathcal{A}c_\varepsilon)\cdot\nu = 0 \qquad \text{on } \partial\Omega\times[0,\infty), \tag{4.4.24b}$$
$$c_\varepsilon(\cdot,0) = c_{0\varepsilon} \qquad \text{in } \Omega. \tag{4.4.24c}$$

The subsequent *Lemmas 4.4.2* and *4.4.3* provide local and then global existence of classical solutions to (4.4.24).

Lemma 4.4.2. *For $\varepsilon \in (0,\varepsilon_1)$ there is a maximal existence time $T_{max,\varepsilon} \in (0,\infty]$ and a nonnegative classical solution $c_\varepsilon \in C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega}\times[0,T_{max,\varepsilon}))$ of (4.4.24). It holds that either $T_{max,\varepsilon} = \infty$ or $T_{max,\varepsilon} < \infty$ and*

$$\lim_{t\nearrow T_{max,\varepsilon}} \|c_\varepsilon(\cdot,t)\|_{C^{2+\alpha}(\overline{\Omega})} = \infty. \tag{4.4.25}$$

Proof. The proof is based on a standard fixed-point argument.

Let $\varepsilon \in (0,\varepsilon_1)$ and $\alpha \in (0,\frac{1}{2})$, as above, $T \in (0,1)$ small enough (to be determined later), and

$$M := \|c_{0\varepsilon}\|_{C^{1+\alpha}(\overline{\Omega})} + 1.$$

We define the set

$$S := \left\{ \overline{c} \in C^{1+\alpha,\frac{1+\alpha}{2}}(\overline{\Omega}\times[0,T]) : \overline{c} \geqslant 0,\ \|\overline{c}\|_{C^{1+\alpha,\frac{1+\alpha}{2}}(\overline{\Omega}\times(0,T))} \leqslant M \right\}.$$

For $\overline{c} \in S$ we consider the linearised IBVP

$$\partial_t c_\varepsilon = \nabla\nabla : (\mathbb{D}_\varepsilon c_\varepsilon) - \nabla\cdot(c_\varepsilon \mathcal{A}\overline{c}) + \mu c_\varepsilon(1 - \overline{c}^{r-1}) \qquad \text{in } \Omega\times[0,\infty), \tag{4.4.26a}$$
$$(\nabla\cdot(\mathbb{D}_\varepsilon c_\varepsilon) - c_\varepsilon\mathcal{A}\overline{c})\cdot\nu = 0 \qquad \text{in } \partial\Omega\times[0,\infty), \tag{4.4.26b}$$
$$c_\varepsilon = c_{0\varepsilon} \qquad \text{in } \Omega\times\{0\}. \tag{4.4.26c}$$

Due to *Lemmas 2.2.3*, *4.2.2*, and *4.4.1*, the coefficient functions and the initial data are smooth enough and satisfy the compatibility condition, allowing us to conclude from *Theorem A.1.6* with

$$a_{ij} := (d_{ij})_\varepsilon,$$
$$a_i := -\sum_{j=1}^n ((d_{ij})_\varepsilon + (d_{ji})_\varepsilon)_{x_j} + (\mathcal{A}\overline{c})_i,$$
$$a := -\sum_{i,j=1}^n ((d_{ij})_\varepsilon)_{x_j x_i} + \nabla\cdot(\mathcal{A}\overline{c}) - \mu(1-\overline{c}^{r-1}),$$
$$b_i := \sum_{j=1}^n (d_{ji})_\varepsilon \nu_j,$$
$$b := \sum_{i,j=1}^n ((d_{ij})_\varepsilon)_{x_j}\nu_i - (\mathcal{A}\overline{c})\cdot\nu,$$
$$f := 0$$

for $i, j = 1, ..., n$ that (4.4.26) has a unique solution $c_\varepsilon \in C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$ satisfying

$$\|c_\varepsilon\|_{C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega}\times[0,T])} \leqslant C_7(M)\|c_{0\varepsilon}\|_{C^{2+\alpha}(\overline{\Omega})} =: C_8$$

for some constant $C_7(M) > 0$ independent of the choice of $\overline{c}$. From *Theorem A.1.11* we conclude that $c_\varepsilon \geqslant 0$ in $\overline{\Omega} \times [0,T]$. *Lemma 2.2.9(ii)* implies the estimate

$$\begin{aligned}\|c_\varepsilon\|_{C^{1+\alpha,\frac{1+\alpha}{2}}(\overline{\Omega}\times[0,T])} \leqslant& \|c_\varepsilon - c_{0\varepsilon}\|_{C^{1+\alpha,\frac{1+\alpha}{2}}(\overline{\Omega}\times[0,T])} + \|c_{0\varepsilon}\|_{C^{1+\alpha}(\overline{\Omega})}\\ \leqslant& 2\max\{1, K_I(\alpha)\}T^{\frac{\alpha}{2}}\|c_\varepsilon\|_{C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega}\times[0,T])} + \|c_{0\varepsilon}\|_{C^{1+\alpha}(\overline{\Omega})}\\ \leqslant& 2\max\{1, K_I(\alpha)\}T^{\frac{\alpha}{2}}C_8 + \|c_{0\varepsilon}\|_{C^{1+\alpha}(\overline{\Omega})},\end{aligned}$$

where $K_I(\alpha)$ denotes the embedding constant from $W^1_\infty(\Omega)$ into $C^\alpha(\overline{\Omega})$ from *Lemma 2.2.8(ii)*. Hence, taking

$$T \leqslant \left(\frac{1}{2\max\{1, K_I(\alpha)\}C_8}\right)^{\frac{2}{\alpha}}$$

we ensure that $c_\varepsilon \in S$. Consequently, the operator

$$F : S \to S, \qquad \overline{c} \mapsto c_\varepsilon \tag{4.4.27}$$

is well-defined and, due to $C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega} \times [0,T]) \hookrightarrow\hookrightarrow C^{1+\alpha,\frac{1+\alpha}{2}}(\overline{\Omega} \times [0,T])$, a compact self-map. Moreover, the continuous dependence of c_ε from the coefficients (that follows with *Lemma 4.2.2* and *Theorem A.1.6*) implies that F is a continuous and compact operator. Now, Schauder's fixed-point theorem (*Theorem A.2.2*) applies, providing a fixed-point $c_\varepsilon \in C^{1+\alpha,\frac{1+\alpha}{2}}(\overline{\Omega} \times [0,T])$ of F that is also in $C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$ and a classical solution to (4.4.24) on $\overline{\Omega} \times [0,T]$.

Extending the solution to its maximal existence time $T_{max,\varepsilon}$, it holds that either $T_{max,\varepsilon} = \infty$ or $T_{max,\varepsilon} < \infty$ and (4.4.25). □

Next, we verify global existence for (4.4.24).

Lemma 4.4.3. *For $\varepsilon \in (0, \varepsilon_1)$ there is a nonnegative classical solution $c_\varepsilon \in C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega} \times [0,\infty))$ of* (4.4.24).

Proof. We follow a standard approach which is based on excluding the possibility of (4.4.25). Let $\varepsilon \in (0, \varepsilon_1)$ and assume $T_{max,\varepsilon} < \infty$, so that c_ε is a solution to (4.4.24) in $\overline{\Omega} \times [0, T_{max,\varepsilon})$. Integrating the first equation in (4.4.24) over Ω and using partial integration, we conclude from Gronwall's inequality that

$$\|c_\varepsilon\|_{L^\infty(0,T_{max,\varepsilon};L^1(\Omega))} \leqslant e^{\mu T_{max,\varepsilon}}\|c_{0\varepsilon}\|_{L^1(\Omega)} =: C_9(T_{max,\varepsilon}). \tag{4.4.28}$$

Consider an arbitrary $p \in (1,\infty)$. We multiply (4.4.24a) by pc_ε^{p-1}, integrate over Ω and use partial integration to obtain

$$\begin{aligned}\frac{d}{dt}\int_\Omega c_\varepsilon^p \,\mathrm{d}x =& -p\int_\Omega (\mathbb{D}_\varepsilon\nabla c_\varepsilon + \nabla\cdot\mathbb{D}_\varepsilon c_\varepsilon - c_\varepsilon\mathcal{A}c_\varepsilon)\cdot\nabla c_\varepsilon^{p-1}\,\mathrm{d}x + \mu p\int_\Omega c_\varepsilon^p(1 - c_\varepsilon^{r-1})\,\mathrm{d}x\\ =& -p(p-1)\int_\Omega c_\varepsilon^{p-2}(\mathbb{D}_\varepsilon\nabla c_\varepsilon)\cdot\nabla c_\varepsilon + c_\varepsilon^{p-1}(\nabla\cdot\mathbb{D}_\varepsilon - \mathcal{A}c_\varepsilon)\cdot\nabla c_\varepsilon\,\mathrm{d}x\\ &+ \mu p\int_\Omega c_\varepsilon^p(1 - c_\varepsilon^{r-1})\,\mathrm{d}x.\end{aligned}$$

Due to $\mathbb{D}_\varepsilon \geqslant \varepsilon$ and the boundedness of its divergence, the fact that $\nabla c_\varepsilon^{\frac{p}{2}} = \frac{p}{2} c_\varepsilon^{\frac{p}{2}-1} \nabla c_\varepsilon$, (4.4.28) and Young's inequality we conclude that

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega c_\varepsilon^p \,\mathrm{d}x + \frac{4(p-1)}{p}\varepsilon \int_\Omega |\nabla c_\varepsilon^{\frac{p}{2}}|^2 \,\mathrm{d}x \\
\leqslant& 2(p-1)\int_\Omega |\nabla c_\varepsilon^{\frac{p}{2}}| c_\varepsilon^{\frac{p}{2}} \left(\|\nabla H\|_{(L^\infty(B_1))^n} \|c_\varepsilon\|_{L^1(\Omega)} + \|\nabla\cdot\mathbb{D}_\varepsilon\|_{(L^\infty(\Omega))^n}\right) \mathrm{d}x + \mu p \int_\Omega c_\varepsilon^p \,\mathrm{d}x \\
\leqslant& \frac{4(p-1)}{p}\varepsilon \int_\Omega |\nabla c_\varepsilon^{\frac{p}{2}}|^2 \,\mathrm{d}x + pC_{10}(p, T_{max,\varepsilon}) \int_\Omega c_\varepsilon^p \,\mathrm{d}x,
\end{aligned}$$

where

$$C_{10}(p, T_{max,\varepsilon}) := \frac{p-1}{\varepsilon}\left(\|\nabla H\|^2_{(L^\infty(B_1))^n} C_9(T_{max,\varepsilon})^2 + \|\nabla\cdot\mathbb{D}_\varepsilon\|^2_{(L^\infty(\Omega))^n}\right) + \mu.$$

Hence, it follows again from Gronwall's inequality that

$$\|c_\varepsilon\|_{L^\infty(0,T_{max,\varepsilon};L^p(\Omega))} \leqslant e^{pC_{10}(p,T_{max,\varepsilon})T_{max,\varepsilon}} \|c_{0\varepsilon}\|_{L^p(\Omega)}.$$

The coefficients of (4.4.24) are regular enough s.t. *Theorems A.1.1* and *A.1.4* and *Remark A.1.2* with

$$a_{ij} = (d_{ij})_\varepsilon,\ a_i = \sum_{j=1}^n ((d_{ij})_\varepsilon)_{x_j} - (\mathcal{A}c_\varepsilon)_i,\ a = \mu(c_\varepsilon^{r-1} - 1),\ f = 0$$

for $i, j = 1, ..., n$ imply that

$$c_\varepsilon \in L^2(0, T_{max,\varepsilon}; H^1(\Omega)) \cap C([0, T_{max,\varepsilon}]; L^2(\Omega)) \cap L^\infty(\Omega \times (0, T_{max,\varepsilon}))$$

and uniquely solves (4.4.24) on $\Omega \times (0, T_{max,\varepsilon})$ in the weak sense from *Remark A.1.2*. Now, *Theorem A.1.12* with

$$\begin{aligned}
a(x,t,c,\nabla c) &= \mathbb{D}_\varepsilon \nabla c + \nabla\cdot\mathbb{D}_\varepsilon c - c\mathcal{A}c_\varepsilon, \\
b(x,t,c) &= \mu c(c^{r-1} - 1)
\end{aligned} \tag{4.4.29}$$

applies and yields

$$c_\varepsilon \in C^{\gamma,\frac{\gamma}{2}}(\overline{\Omega} \times [0, T_{max,\varepsilon}])$$

for some $\gamma \in (0, \alpha)$. Next, using the Hölder continuity of the coefficients (which holds especially due to *Lemmas 2.2.3*, *4.2.2*, and *4.4.1*) again and the fact that the initial data are smooth enough and satisfy the compatibility condition, *Theorem A.1.13* with the coefficients from (4.4.29) implies that there are $C_{11}(\varepsilon) > 0$ and $\delta \in (0, \gamma)$ s.t.

$$\|c_\varepsilon\|_{C^{1+\delta,\frac{1+\delta}{2}}(\overline{\Omega}\times[0,T_{max,\varepsilon}])} \leqslant C_{11}(\varepsilon).$$

Hence, as above *Theorem A.1.6* implies that

$$c_\varepsilon \in C^{2+\delta,1+\frac{\delta}{2}}(\overline{\Omega} \times [0, T_{max,\varepsilon}]) \hookrightarrow C^{1+\alpha,\frac{1+\alpha}{2}}(\overline{\Omega} \times [0, T_{max,\varepsilon}]).$$

Finally, applying *Theorem A.1.6* one more time we obtain

$$c_\varepsilon \in C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega} \times [0, T_{max,\varepsilon}])$$

contradicting (4.4.25). □

4.5 Existence of a very weak solution to the original problem

In this section, we show the convergence of a suitably chosen sequence of the classical solutions to (4.4.24) to a very weak solution to (4.1.1) in the sense of *Definition 4.3.3*. We start with some basic uniform estimates of (c_ε).

Lemma 4.5.1. *For all $\varepsilon \in (0, \varepsilon_1)$ it holds that*

$$\|c_\varepsilon\|_{L^\infty(0,\infty;L^1(\Omega))} \leqslant C_{12}, \tag{4.5.1}$$

$$\|c_\varepsilon\|_{L^r(\Omega\times(0,T))} \leqslant C_{13} + T\mu C_{12} \qquad \text{for } T > 0. \tag{4.5.2}$$

Proof. Consider a constant $C_{14} > 0$ and

$$C_{15} := \max_{x\in[0,\ \sqrt[r-1]{\frac{C_{14}}{r\mu}+\frac{1}{r}}]} \left|\mu x^r - (C_{14}+\mu)x\right|.$$

Then, $C_{15} - C_{14}x - (\mu x - \mu x^r) \geqslant 0$ holds for $x \geqslant 0$. Integrating (4.4.24a) over Ω, by parts where necessary, using the boundary condition, the assumption $r \geqslant 2$, and the boundedness of Ω, we obtain

$$\begin{aligned}\frac{d}{dt}\int_\Omega c_\varepsilon \,\mathrm{d}x =& \mu \int_\Omega c_\varepsilon - c_\varepsilon^r \,\mathrm{d}x \\ \leqslant& C_{15}|\Omega| - C_{14}\int_\Omega c_\varepsilon \,\mathrm{d}x.\end{aligned} \tag{4.5.3}$$

Consequently, *Lemma A.1.20* implies (4.5.1). Integrating (4.5.3) over $(0, T)$ and using (4.5.1) immediately yields (4.5.2). □

Next, we establish some uniform estimates for derivatives of c_ε. For the spatial gradient, the estimates hold away from the degeneracy set of $\mathbb{D}$.

Lemma 4.5.2. *For any $T > 0$ and relatively open $B \subset\subset \{\mathbb{D} > 0\}$ there is a constant $C_{16}(B,T)$ s.t.*

$$\|c_\varepsilon\|_{L^2(0,T;H^1(B))} \leqslant C_{16}(B,T), \tag{4.5.4}$$

$$\|c_\varepsilon\|_{L^{r+1}(B\times(0,T))} \leqslant C_{16}(B,T) \tag{4.5.5}$$

for all $\varepsilon \in (0, \varepsilon_2(B))$.

Furthermore, let q be a number that satisfies

$$q \in \left(1, \frac{n}{n-1}\right). \tag{4.5.6}$$

Then, for any $T > 0$ there exists some constant $C_{17}(T) > 0$ s.t.

$$\|\partial_t c_\varepsilon\|_{L^1(0,T;W_q^{-2}(\Omega))} \leqslant C_{17}(T) \tag{4.5.7}$$

for $\varepsilon \in (0, \varepsilon_1)$.

Proof. Let $T \in (0,\infty)$ and consider a relatively open set

$$B \subset\subset \{\mathbb{D} > 0\}.$$

Then, there exists a sufficiently small number $\alpha > 0$ such that

$$\hat{B} := O_\alpha(B) \subset\subset \mathbb{R}^n \backslash \{\mathbb{D} \not> 0\}.$$

Due to the uniform continuity of $\mathbb{D}$ and our choice of B,

$$\delta := \inf_{x \in \hat{B}} \min_{z \in S_1(0)} z^T \mathbb{D}(x) z > 0. \tag{4.5.8}$$

In what follows we leave out the dependence on δ and $\hat{B}$ in the constants as they are determined by B. Let $\varphi \in C_c^\infty(\mathbb{R}^n \backslash \{D \not> 0\})$ be s.t.

$$\varphi \begin{cases} = 1 & \text{on } B, \\ \in [0,1] & \text{on } \hat{B} \backslash B, \\ = 0 & \text{on } \mathbb{R}^n \backslash \hat{B}. \end{cases} \tag{4.5.9}$$

Let $\varepsilon \in (0, \varepsilon_2(B))$, where $\varepsilon_2(B)$ is from *Lemma 4.4.1.* We multiply (4.4.24a) by $c_\varepsilon \varphi^2$, integrate over Ω by parts where necessary, use the no-flux boundary condition, and obtain

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega c_\varepsilon^2 \varphi^2 \,\mathrm{d}x \\
=& -\int_\Omega (\mathbb{D}_\varepsilon \nabla c_\varepsilon + \nabla \cdot \mathbb{D}_\varepsilon c_\varepsilon - c_\varepsilon \mathcal{A} c_\varepsilon) \cdot \left(\varphi^2 \nabla c_\varepsilon + 2 c_\varepsilon \varphi \nabla \varphi\right) \mathrm{d}x + \mu \int_\Omega c_\varepsilon^2 \varphi^2 (1 - c_\varepsilon^{r-1}) \,\mathrm{d}x \\
\leqslant& -\int_\Omega (\nabla c_\varepsilon)^T \mathbb{D}_\varepsilon \varphi^2 \nabla c_\varepsilon \,\mathrm{d}x + 2\left|\int_\Omega (\varphi \nabla c_\varepsilon)^T \mathbb{D}_\varepsilon (c_\varepsilon \nabla \varphi) \,\mathrm{d}x\right| \\
&+ \left|\int_\Omega (\nabla \cdot \mathbb{D}_\varepsilon - \mathcal{A} c_\varepsilon) \cdot \left(c_\varepsilon \varphi^2 \nabla c_\varepsilon + 2 c_\varepsilon^2 \varphi \nabla \varphi\right) \mathrm{d}x\right| + \mu \int_\Omega c_\varepsilon^2 \varphi^2 \,\mathrm{d}x - \mu \int_\Omega c_\varepsilon^{r+1} \varphi^2 \,\mathrm{d}x.
\end{aligned} \tag{4.5.10}$$

The matrix $\mathbb{D}_\varepsilon$ is symmetric and positive-definite. Hence, it defines a scalar product on $\mathbb{R}^n$, and with the Cauchy-Schwartz and Young's inequalities and (4.4.1) we obtain

$$\begin{aligned}
2\left|\int_\Omega (\varphi \nabla c_\varepsilon)^T \mathbb{D}_\varepsilon (c_\varepsilon \nabla \varphi) \,\mathrm{d}x\right| \leqslant& 2\sqrt{\int_\Omega (\varphi \nabla c_\varepsilon)^T \mathbb{D}_\varepsilon \varphi \nabla c_\varepsilon \,\mathrm{d}x}\sqrt{\int_\Omega (c_\varepsilon \nabla \varphi)^T \mathbb{D}_\varepsilon c_\varepsilon \nabla \varphi \,\mathrm{d}x} \\
\leqslant& \frac{1}{4}\int_\Omega (\nabla c_\varepsilon)^T \mathbb{D}_\varepsilon \varphi^2 \nabla c_\varepsilon \,\mathrm{d}x + 4 \|\nabla \varphi\|^2_{(L^\infty(\mathbb{R}^n))^n} C_{18} \int_\Omega c_\varepsilon^2 \,\mathrm{d}x,
\end{aligned} \tag{4.5.11}$$

where $C_{18} := \varepsilon_1 + \|\mathbb{D}\|_{(L^\infty(\Omega))^{n\times n}}$ is some uniform upper bound on $\|\mathbb{D}_\varepsilon\|_{(L^\infty(\Omega))^{n\times n}}$ for $\varepsilon \in (0, \varepsilon_1)$ that exists due to (4.4.1). Moreover, combining (4.4.4), *Lemma 4.5.1*, and Hölder's and Young's inequalities, we can estimate

$$\begin{aligned}
&\left|\int_\Omega (\nabla \cdot \mathbb{D}_\varepsilon - \mathcal{A} c_\varepsilon) \cdot \left(c_\varepsilon \varphi^2 \nabla c_\varepsilon + 2 c_\varepsilon^2 \varphi \nabla \varphi\right) \mathrm{d}x\right| \\
\leqslant& \left(\|\nabla \cdot \mathbb{D}_\varepsilon\|_{(L^\infty(\hat{B}))^n} + \|\nabla H\|_{(L^\infty(B_1))^n} \|c_\varepsilon\|_{L^\infty(0,\infty;L^1(\Omega))}\right) \int_\Omega \left|c_\varepsilon \varphi^2 \nabla c_\varepsilon\right| + 2\left|c_\varepsilon^2 \varphi \nabla \varphi\right| \,\mathrm{d}x \\
\leqslant& \frac{\delta}{2}\int_\Omega |\varphi \nabla c_\varepsilon|^2 \,\mathrm{d}x + C_{19}(B) \int_\Omega c_\varepsilon^2 \,\mathrm{d}x.
\end{aligned} \tag{4.5.12}$$

Combining (4.5.10)–(4.5.12) and rearranging the terms leads due to (4.5.8) and (4.5.9) to

$$\frac{1}{2}\frac{d}{dt}\int_\Omega c_\varepsilon^2 \varphi^2 \,\mathrm{d}x + \frac{\delta}{4}\int_\Omega |\nabla c_\varepsilon|^2 \varphi^2 \,\mathrm{d}x + \mu \int_\Omega c_\varepsilon^{r+1} \varphi^2 \,\mathrm{d}x \leqslant C_{20}(B) \int_\Omega c_\varepsilon^2 \,\mathrm{d}x. \tag{4.5.13}$$

We integrate (4.5.13) over $(0,T)$ and obtain due to $r \geqslant 2$, *Lemma 4.5.1*, (4.5.9), the uniform boundedness of the initial values, and using Hölder's inequality that

$$\frac{1}{2}\|c_\varepsilon\varphi\|^2_{L^\infty(0,T;L^2(\Omega))} + \frac{\delta}{4}\|\varphi\nabla c_\varepsilon\|^2_{L^2(0,T;(L^2(\Omega))^n)} + \mu\|c_\varepsilon\|^{r+1}_{L^{r+1}(B\times(0,T))} \leqslant C_{21}(B,T), \qquad (4.5.14)$$

which yields (4.5.4) and (4.5.5).

Let $\psi \in \overset{\circ}{W}{}^2_{\frac{q}{q-1}}(\Omega)$. Due to our choice of q *Lemma 2.2.8(iii)* implies that

$$\psi \in \overset{\circ}{W}{}^2_{\frac{q}{q-1}}(\Omega) \subset \left\{\psi \in C^1(\overline{\Omega}) : \psi = 0,\ \nabla\psi = 0 \text{ on } \partial\Omega\right\}. \qquad (4.5.15)$$

Hence, multiplying (4.4.24a) by ψ and using partial integration once or twice where necessary we arrive at

$$\int_\Omega \partial_t c_\varepsilon \psi \,\mathrm{d}x = \int_\Omega c_\varepsilon \mathbb{D}_\varepsilon : D^2\psi \,\mathrm{d}x + \int_\Omega c_\varepsilon(\mathcal{A}c_\varepsilon)\cdot\nabla\psi \,\mathrm{d}x + \mu\int_\Omega c_\varepsilon(1-c_\varepsilon^{r-1})\psi \,\mathrm{d}x.$$

Using *Lemmas 2.1.2* and *2.2.8* and (4.3.1), (4.4.1), (4.5.1), (4.5.2), (4.5.6), and (4.5.15), Hölder's inequality and the embedding of Lebesgue spaces we obtain the estimate

$$\begin{aligned}\left|\int_\Omega \partial_t c_\varepsilon\psi\,\mathrm{d}x\right| \leqslant &\|\mathbb{D}_\varepsilon\|_{(L^\infty(\Omega))^{n\times n}} \sum_{i,j=1}^n \int_\Omega |c_\varepsilon||\psi_{x_ix_j}|\,\mathrm{d}x + \|\nabla H\|_{(L^\infty(B_1))^n}\|c_\varepsilon\|_{L^1(\Omega)}\int_\Omega |c_\varepsilon\nabla\psi|\,\mathrm{d}x\\ &+ \mu\int_\Omega (c_\varepsilon + c_\varepsilon^r)||\psi|\,\mathrm{d}x\\ \leqslant &C_{18}\sum_{i,j=1}^n \|\psi_{x_ix_j}\|_{L^{\frac{q}{q-1}}(\Omega)}\|c_\varepsilon\|_{L^q(\Omega)} + \|\nabla H\|_{(L^\infty(B_1))^n} C_{12}^2\|\nabla\psi\|_{(L^\infty(\Omega))^n}\\ &+ \mu(C_{12} + \|c_\varepsilon\|^r_{L^r(\Omega)})\|\psi\|_{L^\infty(\Omega)}\\ \leqslant &C_{22}\left(\|c_\varepsilon\|^r_{L^r(\Omega)} + \|c_\varepsilon\|_{L^r(\Omega)} + 1\right)\|\psi\|_{W^2_{\frac{q}{q-1}}(\Omega)}.\end{aligned}$$

We conclude

$$\|\partial_t c_\varepsilon\|_{W_q^{-2}(\Omega)} \leqslant C_{22}\left(\|c_\varepsilon\|^r_{L^r(\Omega)} + \|c_\varepsilon\|_{L^r(\Omega)} + 1\right) \qquad (4.5.16)$$

Integration over $(0,T)$ together with (4.5.2) yield (4.5.7). □

With the obtained estimates at hand we can now proceed to establishing convergence.

Lemma 4.5.3. *There exist $c \in L^\infty(0,\infty;L^1(\Omega))$ and a sequence $(\varepsilon_k) \subset (0,\varepsilon_1)$, $\varepsilon_k \to 0$, s.t.*

$$c_{\varepsilon_k} \underset{k\to\infty}{\to} c \qquad \text{in } L^1_{loc}(\overline{\Omega}\times[0,\infty)), \qquad (4.5.17)$$

$$\text{a.e. in } \Omega\times(0,\infty). \qquad (4.5.18)$$

Proof. Let $T > 0$, $q \in (1, \frac{n}{n-1})$ and consider a relatively open set $B \subset\subset \{D > 0\}$. Thanks to estimates (4.5.4) and (4.5.7), the dense embeddings

$$H^1(B) \hookrightarrow\hookrightarrow L^2(B) \hookrightarrow W_q^{-2}(\Omega),$$

where the latter holds due to our choice of q, and the Lions-Aubin lemma (*Lemma A.3.9*), every subsequence $(c_{\varepsilon_j})_{j\in\mathbb{N}}$ has a subsequence that converges in $L^2(B\times(0,T))$, and it can be chosen such that it converges a.e. in $B\times(0,T)$.

Observe that since $\{\mathbb{D} > 0\}$ is relatively open in the compact set $\overline{\Omega}$, there exists a sequence $(B_i)_{i\in\mathbb{N}}$ with $B_i \subset B_{i+1}$ of relatively open sets such that $B_i \subset\subset \{\mathbb{D} > 0\}$ and $\{\mathbb{D} > 0\} = \bigcup_{i=1}^{\infty} B_i$. In view of this, we have

$$\{\mathbb{D} > 0\} \times (0,\infty) = \bigcup_{i=1}^{\infty} B_i \times (0,i).$$

Together with a diagonal argument this description in the form of a countable union allows to conclude from the above that there exist some $c \in L^2_{loc}(\{\mathbb{D} > 0\} \times [0,\infty))$ and a sequence $(\varepsilon_k) \subset (0,\varepsilon_1)$ that converges to zero and is such that

$$c_{\varepsilon_k} \underset{k\to\infty}{\to} c \qquad \text{a.e. in } \{\mathbb{D} > 0\} \times (0,\infty). \tag{4.5.19}$$

Since by (4.3.2f) the degeneracy set $\{\mathbb{D} \not> 0\}$ has the n-dimensional Lebesgue measure zero, (4.5.19) is equivalent to

$$c_{\varepsilon_k} \underset{k\to\infty}{\to} c \qquad \text{a.e. in } \Omega \times (0,\infty). \tag{4.5.20}$$

Furthermore, due to (4.5.2) and $r \geqslant 2$, the sequence $(c_{\varepsilon_k})_{k\in\mathbb{N}}$ is uniformly integrable on $\Omega \times (0,T)$ for all $T > 0$ by the de la Vallée-Poussin theorem (*Theorem A.3.6*). Now

$$c_{\varepsilon_k} \underset{k\to\infty}{\to} c \text{ in } L^1(\Omega \times (0,T)) \qquad \text{for all } T > 0$$

and $c \in L^1_{loc}(\overline{\Omega} \times [0,\infty))$ follow with (4.5.20) and Vitali's lemma (*Lemma A.3.7*). This implies that for a.e. $t \in (0,\infty)$ we have

$$c_{\varepsilon_k} \underset{k\to\infty}{\to} c \text{ in } L^1(\Omega).$$

Hence, $c \in L^\infty(0,\infty; L^1(\Omega))$ due to (4.5.1). □

In preparation for the proof of existence of a very weak solution to (4.1.1) we still need one more lemma that allows us to handle the nonlinear part of the reaction term in (4.4.24).

Lemma 4.5.4. *Let $(\varepsilon_k)_{k\in\mathbb{N}}$ be as in Lemma 4.5.3. Then, for all $T \in (0,\infty)$ it holds that*

$$c^r_{\varepsilon_k} \underset{k\to\infty}{\to} c^r \qquad \text{in } L^1(\Omega \times (0,T)) \tag{4.5.21}$$

and $c \in L^r_{loc}(\overline{\Omega} \times [0,\infty))$.

Proof. Let $T \in (0,\infty)$ and consider the sequence $(c_{\varepsilon_k})_{k\in\mathbb{N}}$ from *Lemma 4.5.3*. Fatou's lemma together with estimate (4.5.2) from *Lemma 4.5.1* imply that

$$\int_0^T \int_\Omega c^r \,\mathrm{d}x\,\mathrm{d}t \leqslant \liminf_{k\to\infty} \int_0^T \int_\Omega c^r_{\varepsilon_k} \,\mathrm{d}x\,\mathrm{d}t \leqslant C_{23}(T),$$

and so $c \in L^r(\Omega \times (0,T))$.

Due to *Lemma 4.2.4* and assumption (4.3.2f), there exists a family of functions $(\varphi_\delta)_{\delta\in(0,1)} \subset C^\infty_c(\mathbb{R}^n;[0,1])$ satisfying (4.2.5) for $K = \{\mathbb{D} \not> 0\}$. We adopt the splitting

$$c^r_{\varepsilon_k} = c^r_{\varepsilon_k}(1-\varphi_\delta) + c^r_{\varepsilon_k}\varphi_\delta \tag{4.5.22}$$

and next study the convergence of each of the terms separately.

Step 1 (Convergence of the first term)**.** For $\delta \in (0,1)$ we set

$$B_\delta := \{\mathbb{D} > 0\} \backslash \overline{O_{\delta\sqrt{n}}(\{\mathbb{D} \not> 0\})}.$$

Obviously, B_δ is relatively open and satisfies $B_\delta \subset\subset \{\mathbb{D} > 0\}$. Arguing similar to the proof of *Lemma 4.5.3*, we conclude with (4.5.5) in *Lemma 4.5.2*, (4.5.18) in *Lemma 4.5.3*, the de la Vallée-Poussin theorem and Vitali's lemma (*Theorem A.3.6* and *Lemma A.3.7*) that

$$c^r_{\varepsilon_k} \underset{k\to\infty}{\to} c^r \qquad \text{in } L^1(B_\delta \times (0,T)). \tag{4.5.23}$$

Since $\varphi_\delta = 1$ outside of B_δ due to (4.2.5b), (4.5.23) yields

$$c^r_{\varepsilon_k}(1-\varphi_\delta) \underset{k\to\infty}{\to} c^r(1-\varphi_\delta) \qquad \text{in } L^1(\Omega \times (0,T)) \text{ for all } \delta \in (0,1). \tag{4.5.24}$$

Furthermore, the integrability of c^r together with (4.2.5f) and the uniform boundedness of (φ_δ) allow to conclude using the dominated convergence theorem that

$$c^r(1-\varphi_\delta) \underset{\delta\to 0}{\to} c^r \qquad \text{in } L^1(\Omega \times (0,T)). \tag{4.5.25}$$

Step 2 (Convergence of the second term and conclusion)**.** Due to (4.3.2e) and (4.2.5c), we have

$$\operatorname{supp}(\varphi_\delta) \subset O_{5\delta\sqrt{n}}(\{\mathbb{D} \not> 0\}) \subset\subset \Omega$$

for $\delta \in (0,1)$ sufficiently small. For such δ, we multiply (4.4.24a) by φ_δ and integrate over Ω, once/twice by parts where necessary, so as to shift all spatial derivatives to φ_δ. Using *Lemmas 2.1.2*, *4.2.4*, and *4.5.1* and (4.4.1) and Hoelder's inequality, we estimate as follows:

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega c_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x + \mu \int_\Omega c^r_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x \\
\leqslant&\mu \int_\Omega c_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x + \int_\Omega |c_{\varepsilon_k}\mathbb{D}_{\varepsilon_k} : D^2\varphi_\delta| \,\mathrm{d}x + \int_\Omega |c_{\varepsilon_k}\mathcal{A}c_{\varepsilon_k} \cdot \nabla\varphi_\delta| \,\mathrm{d}x \\
\leqslant&\mu \int_\Omega c_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x + n^2 \|\mathbb{D}_{\varepsilon_k}\|_{(L^\infty(\Omega))^{n\times n}} \|D^2\varphi_\delta\|_{(L^\infty(\Omega))^{n\times n}} \int_{\{D^2\varphi_\delta \neq 0\}} c_{\varepsilon_k} \,\mathrm{d}x \\
&+ \|c_{\varepsilon_k}\|_{L^\infty(0,\infty;L^1(\Omega))} \|\nabla H\|_{(L^\infty(B_1))^n} \|\nabla\varphi_\delta\|_{(L^\infty(\Omega))^n} \int_{\{\nabla\varphi_\delta \neq 0\}} c_{\varepsilon_k} \,\mathrm{d}x \\
\leqslant&\mu \int_\Omega c_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x + \left(\|D^2\varphi_\delta\|_{(L^\infty(\Omega))^{n\times n}} + \|\nabla\varphi_\delta\|_{(L^\infty(\Omega))^n}\right) C_{24} \int_{\operatorname{supp}(\varphi_\delta)} c_{\varepsilon_k} \,\mathrm{d}x \\
\leqslant&\mu \int_\Omega c_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x + \delta^{-2} |\operatorname{supp}(\varphi_\delta)|^{1-\frac{1}{r}} C_{25} \|c_{\varepsilon_k}\|_{L^r(\Omega)}.
\end{aligned}$$

We conclude from Gronwall's and Hölder's inequalities and *Lemma 4.5.1* that

$$\begin{aligned}
&\int_\Omega c_{\varepsilon_k}(\cdot,T)\varphi_\delta \,\mathrm{d}x + \mu \int_0^T \int_\Omega c^r_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x\,\mathrm{d}t \\
\leqslant& e^{\mu T}\left(\int_\Omega c_{0\varepsilon_k}\varphi_\delta \,\mathrm{d}x + \delta^{-2}|\operatorname{supp}(\varphi_\delta)|^{1-\frac{1}{r}} C_{25} \int_0^T \|c_{\varepsilon_k}\|_{L^r(\Omega)} \,\mathrm{d}t\right) \\
\leqslant& e^{\mu T}\left(\int_\Omega c_{0\varepsilon_k}\varphi_\delta \,\mathrm{d}x + \delta^{-2}|\operatorname{supp}(\varphi_\delta)|^{1-\frac{1}{r}} T^{1-\frac{1}{r}} C_{25} \|c_{\varepsilon_k}\|_{L^r(\Omega\times(0,T))}\right) \\
\leqslant& e^{\mu T}\left(\int_\Omega c_{0\varepsilon_k}\varphi_\delta \,\mathrm{d}x + \delta^{-2}|\operatorname{supp}(\varphi_\delta)|^{1-\frac{1}{r}} C_{26}(T)\right) \quad \text{for } t \in (0,T).
\end{aligned} \tag{4.5.26}$$

Combining (4.4.23) and (4.5.26), we find that

$$\limsup_{k\to\infty} \int_0^T \int_\Omega c^r_{\varepsilon_k}\varphi_\delta \,\mathrm{d}x\,\mathrm{d}t \leqslant \mu^{-1} e^{\mu T}\left(\int_\Omega c_0\varphi_\delta \,\mathrm{d}x + \delta^{-2}|\operatorname{supp}(\varphi_\delta)|^{1-\frac{1}{r}} C_{26}(T)\right) \tag{4.5.27}$$

for $\delta \in (0,1)$. Due to the integrability of c_0, (4.2.5f), the uniform boundedness of (φ_δ), and the dominated convergence theorem we have

$$\lim_{\delta\to 0}\int_\Omega c_0\varphi_\delta \,\mathrm{d}x = 0. \tag{4.5.28}$$

Together, (4.2.5g), (4.5.27), and (4.5.28) yield

$$c_{\varepsilon_k}^r\varphi_\delta \underset{k\to\infty}{\to}\underset{\delta\to 0}{\to} 0 \qquad \text{in } L^1(\Omega\times(0,T)). \tag{4.5.29}$$

Finally, combining (4.5.22), (4.5.24), (4.5.25), and (4.5.29), we arrive at (4.5.21).

□

Remark 4.5.5. The assumptions $n \geqslant 3$ and $r > \frac{n}{n-2}$ from (4.3.1) are only required in the proof of *Lemma 4.5.4*. Together with (4.3.2f), they ensure the existence of the φ_δs due to *Lemma 4.2.4*.

Finally, we can prove our main result on the existence of a very weak solution to the original IBVP (4.1.1).

Proof of Theorem 4.3.4. Consider the sequence $(c_{\varepsilon_k})_{k\in\mathbb{N}}$ from *Lemmas 4.5.3* and *4.5.4* and let $\eta \in C_c^{2,1}(\overline{\Omega}\times[0,\infty))$ with $\nabla\eta\cdot(\mathbb{D}\nu) = 0$ on $\partial\Omega\times(0,\infty)$. Then, there is $T\in(0,\infty)$ s.t. $\eta\equiv 0$ for $t \geqslant T$. We multiply (4.4.24a) by η and integrate over $\Omega\times(0,\infty)$, once or twice by parts where necessary, using the boundary condition on η as well as (4.4.24b), and for all $k\in\mathbb{N}$ conclude that

$$\begin{aligned} &-\int_0^\infty\int_\Omega c_{\varepsilon_k}\partial_t\eta \,\mathrm{d}x\,\mathrm{d}t - \int_\Omega c_{0\varepsilon_k}\eta(\cdot,0)\,\mathrm{d}x \\ =&\int_0^\infty\int_\Omega c_{\varepsilon_k}\mathbb{D}_{\varepsilon_k} : D^2\eta \,\mathrm{d}x\,\mathrm{d}t - \int_0^\infty\int_{\partial\Omega} c_{\varepsilon_k}\nabla\eta\cdot(\mathbb{D}_{\varepsilon_k}\nu)\,\mathrm{d}\sigma(x)\,\mathrm{d}t \\ &+\int_0^\infty\int_\Omega c_{\varepsilon_k}(\mathcal{A}c_{\varepsilon_k})\cdot\nabla\eta\,\mathrm{d}x\,\mathrm{d}t + \mu\int_0^\infty\int_\Omega c_{\varepsilon_k}(1-c_{\varepsilon_k}^{r-1})\eta\,\mathrm{d}x\,\mathrm{d}t. \end{aligned} \tag{4.5.30}$$

We first address convergence of (c_{ε_k}) on $\partial\Omega\times(0,T)$. Observe that since $O_{a/2}(\partial\Omega)\cap\Omega$ is open and precompact in $\{\mathbb{D} > 0\}$, we can make use of the uniform boundedness of $(c_{\varepsilon_k})_{k\in\mathbb{N}}$ in $L^2(0,T;H^1(O_{a/2}(\partial\Omega)\cap\Omega))$ due to (4.5.4) and convergence (4.5.17) and the Banach-Alaoglu theorem, yielding

$$c_{\varepsilon_k} \underset{k\to\infty}{\rightharpoonup} c \qquad \text{in } L^2(0,T;H^1(O_{a/2}(\partial\Omega)\cap\Omega)). \tag{4.5.31}$$

Using the continuity of the trace operator, we conclude with (4.5.31) that

$$c_{\varepsilon_k} \underset{k\to\infty}{\rightharpoonup} c \qquad \text{in } L^2(\partial\Omega\times(0,T)). \tag{4.5.32}$$

Now convergences (4.4.3), (4.4.23), (4.5.17), (4.5.21), and (4.5.32) and continuity of the operator $\mathcal{A} : L^1(\Omega) \to (L^\infty(\Omega))^n$ together with compensated compactness (*Lemma A.3.2*) allow to pass to the limit in each term in (4.5.30), yielding (4.3.5). □

4.6 Smooth very weak solutions are classical

In this final section we provide a justification for the very weak formulation (4.3.5). We show that as in the case of Neumann boundary conditions for elliptic equations (see e.g., Theorem 2.2.2.5 in [72]) it holds for smooth $\mathbb{D}$ that any sufficiently smooth very weak solution in terms of *Definition 4.3.3* is also a classical solution to (4.1.1).

Theorem 4.6.1. *In addition to Assumptions 4.3.1, let*

$$\begin{aligned}
&\mathbb{D} \in C^2(\overline{\Omega}; \mathbb{R}^{n\times n}),\\
&c \in C^{2,1}(\overline{\Omega} \times (0,\infty)) \cap C(\overline{\Omega} \times [0,\infty)),\\
&c_0 \in C(\overline{\Omega}).
\end{aligned} \tag{4.6.1}$$

Then, if c is a solution to (4.1.1) *in the sense of Definition 4.3.3, then it solves this IBVP in the classical sense.*

Proof. Let

$$\eta \in C_c^{2,1}(\overline{\Omega} \times [0,\infty)) \qquad \text{s.t. } \nabla\eta \cdot (\mathbb{D}\nu) = 0 \text{ on } \partial\Omega \times (0,\infty). \tag{4.6.2}$$

Then, there is $T \in (0,\infty)$ s.t. $\eta \equiv 0$ for $t \geqslant T$. Integrating by parts on both sides of (4.3.5), once or twice where necessary, using the information about η on $\partial\Omega \times (0,\infty)$, yields

$$\begin{aligned}
&\int_0^\infty \int_\Omega \partial_t c\eta \,\mathrm{d}x \,\mathrm{d}t + \int_\Omega (c(\cdot,0) - c_0)\eta(0) \,\mathrm{d}x\\
=& -\int_0^\infty \int_\Omega \nabla\cdot(c\mathbb{D})\cdot\nabla\eta \,\mathrm{d}x \,\mathrm{d}t - \int_0^\infty \int_\Omega \nabla\cdot(c(\mathcal{A}c))\eta \,\mathrm{d}x \,\mathrm{d}t\\
&+ \mu \int_0^\infty \int_\Omega c(1-c^{r-1})\eta \,\mathrm{d}x \,\mathrm{d}t + \int_0^\infty \int_{\partial\Omega} c(\mathcal{A}c)\cdot\nu\eta \,\mathrm{d}\sigma(x) \,\mathrm{d}t\\
=& \int_0^\infty \int_\Omega \left(\nabla\nabla : (c\mathbb{D}) - \nabla\cdot(c(\mathcal{A}c)) + \mu c(1-c^{r-1})\right)\eta \,\mathrm{d}x \,\mathrm{d}t\\
&- \int_0^\infty \int_{\partial\Omega} (\nabla\cdot(\mathbb{D}c) - c(\mathcal{A}c))\cdot\nu\eta \,\mathrm{d}\sigma(x) \,\mathrm{d}t.
\end{aligned} \tag{4.6.3}$$

For the subset of $\eta \in C_c^{2,1}(\Omega \times (0,\infty))$ it holds that $\eta(0) = 0$. Moreover, for such η the boundary integral in (4.6.3) vanishes. Thus, the fundamental lemma of calculus of variations applies and yields that c satisfies

$$\partial_t c = \nabla\nabla : (\mathbb{D}(x)c) - \nabla\cdot(c\mathcal{A}c) + \mu c(1-c^{r-1})$$

pointwise in $\Omega \times (0,\infty)$. Considering the subset of $\eta \in C_c^{2,1}(\Omega \times [0,\infty))$ again the fundamental lemma of calculus of variations that c satisfies the initial condition (4.1.1c) in $\overline{\Omega}$. Now we can conclude from (4.6.3) that for all η satisfying (4.6.2) it holds that

$$\int_0^\infty \int_{\partial\Omega} (\nabla\cdot(\mathbb{D}c) - c(\mathcal{A}c))\cdot\nu\eta \,\mathrm{d}\sigma(x) \,\mathrm{d}t = 0. \tag{4.6.4}$$

Finally, we consider η of the form $\eta(x,t) = \eta_1(x)\eta_2(t)$, where $\eta_1 \in C^2(\overline{\Omega})$ satisfies $\nabla\eta_1 \cdot (\mathbb{D}\nu) = 0$ on $\partial\Omega$ and $\eta_2 \in C_c^1([0,\infty))$. Applying the fundamental lemma of calculus of variations w.r.t. to time integration in (4.6.4) yields

$$\int_{\partial\Omega} (\nabla\cdot(\mathbb{D}c) - c(\mathcal{A}c))\cdot\nu\eta_1 \,\mathrm{d}\sigma(x) = 0 \qquad \text{for all } t \in (0,T). \tag{4.6.5}$$

The boundary condition (4.1.1b) now follows with (4.6.5), *Lemma 4.6.2* below and the embedding $H^1(\Omega) \hookrightarrow L^2(\partial\Omega)$. □

Lemma 4.6.2. *Let* $\mathbb{D} \in C^2(\overline{\Omega}; \mathbb{R}^{n\times n})$ *symmetric,* $\mathbb{D} \geqslant 0$ *with* $\{\mathbb{D} \ngtr 0\} \cap \partial\Omega = \varnothing$*. Then, the set*

$$\{\eta \in C^2(\overline{\Omega}) : \nabla\eta\cdot(\mathbb{D}\nu) = 0 \text{ on } \partial\Omega\}$$

is dense in $H^1(\Omega)$.

Proof. Since $\mathbb{D}$ is continuous and positive definite on $\partial\Omega$, it is positive definite in some open neighbourhood of $\partial\Omega$. Choose some symmetric $\mathbb{B} \in C_c^\infty(\Omega; \mathbb{R}^{n\times n})$, $\mathbb{B} \geqslant 0$, and positive definite in an open neighbourhood of $\{\mathbb{D} \not> 0\}$. Then,

$$\tilde{\mathbb{D}} := \mathbb{D} + \mathbb{B}$$

satisfies

$$\mathbb{D} = \tilde{\mathbb{D}}$$

in some open neighbourhood of $\partial\Omega$, is symmetric and there is some $\delta > 0$ s.t.

$$y^T \tilde{\mathbb{D}}(x) y \geqslant \delta |y|^2 \qquad \text{for all } x \in \overline{\Omega},\ y \in \mathbb{R}^n.$$

On $H^1(\Omega)$, consider the scalar product

$$\langle f, g\rangle := \lambda \int_\Omega fg\,\mathrm{d}x + \int_\Omega (\nabla f)^T \tilde{\mathbb{D}} \nabla g\,\mathrm{d}x \tag{4.6.6}$$

for some $\lambda > 0$. Since $\tilde{D}$ is smooth and positive definite in $\overline{\Omega}$, the norm induced by (4.6.6) is equivalent to the standard norm on $H^1(\Omega)$. Set

$$\begin{aligned} E :=& \{\eta \in C^2(\overline{\Omega}) : \quad \nabla\eta \cdot (\mathbb{D}\nu) = 0 \text{ on } \partial\Omega\} \\ =& \{\eta \in C^2(\overline{\Omega}) : \quad \nabla\eta \cdot (\tilde{\mathbb{D}}\nu) = 0 \text{ on } \partial\Omega\}. \end{aligned}$$

We thus need to verify that the orthogonal complement of E w.r.t. the above scalar product in $H^1(\Omega)$ only contains the zero vector. Assume the contrary, i.e., that

$$\overline{E}^\perp = \{\xi \in H^1(\Omega) : \quad \langle \xi, \eta\rangle = 0 \text{ for all } \eta \in \overline{E}\} \neq \{0\}.$$

Let $\xi \in \overline{E}^\perp$ and $\xi \neq 0$. Then, as $\partial\Omega$ is sufficiently smooth, there is a sequence $(\xi_n)_{n\in\mathbb{N}} \subset C^\infty(\overline{\Omega})$ s.t.

$$\xi_n \underset{n\to\infty}{\to} \xi \text{ in } H^1(\Omega). \tag{4.6.7}$$

Consider the sequence of elliptic BVPs

$$-\nabla \cdot (\tilde{\mathbb{D}} \nabla u_n) + \lambda u_n = \xi_n \qquad \text{in } \Omega, \tag{4.6.8a}$$

$$\nabla u_n \cdot (\tilde{\mathbb{D}}\nu) = 0 \qquad \text{on } \partial\Omega. \tag{4.6.8b}$$

Lemma A.1.19 implies that for sufficiently large $\lambda > 0$ there exists a unique solution $u_n \in C^2(\overline{\Omega})$ to (4.6.8) for all $n \in \mathbb{N}$, and $(u_n)_{n\in\mathbb{N}}$ is uniformly bounded in $H^2(\Omega)$. Consequently, due to the continuity of the trace operator, the embeddings $H^2(\Omega) \hookrightarrow\hookrightarrow H^1(\Omega)$, $H^2(\Omega) \hookrightarrow H^1(\partial\Omega)$ and the Banach-Alaoglu theorem there exist a sequence $(n_l)_{l\in\mathbb{N}}$ and some $u \in H^2(\Omega)$ s.t.

$$u_{n_l} \underset{l\to\infty}{\rightharpoonup} u \qquad \text{in } H^2(\Omega), \tag{4.6.9}$$

$$u_{n_l} \underset{l\to\infty}{\to} u \qquad \text{in } H^1(\Omega), \tag{4.6.10}$$

$$u_{n_l} \underset{l\to\infty}{\rightharpoonup} u \qquad \text{in } H^1(\partial\Omega). \tag{4.6.11}$$

From (4.6.7) and (4.6.9)–(4.6.11) and as $(u_n) \subset E$ it follows that $u \in \overline{E}$ and is a strong L^2 solution to the BVP

$$-\nabla \cdot (\tilde{\mathbb{D}}\nabla u) + \lambda u = \xi \qquad \text{in } \Omega \tag{4.6.12a}$$

$$\nabla u \cdot (\tilde{\mathbb{D}}\nu) = 0 \qquad \text{on } \partial\Omega. \tag{4.6.12b}$$

Multiplying (4.6.12a) by ξ and integrating by parts using (4.6.12b) and the symmetry of $\tilde{\mathbb{D}}$ then yields

$$0 = \langle u, \xi \rangle = \lambda \int_\Omega u\xi \,\mathrm{d}x + \int_\Omega (\nabla u)^T \tilde{\mathbb{D}} \nabla \xi \,\mathrm{d}x = \int_\Omega \xi^2 \,\mathrm{d}x.$$

This shows that $\xi \equiv 0$, contradicting the above assumption. Therefore, $\overline{E} = H^1(\Omega)$, as required. □

Part II

Nonlocal models with nonlocality in the reaction term

CHAPTER 5

On a mathematical model for cancer invasion with repellent pH-taxis and nonlocal intraspecific interaction

This chapter was first published in Volume 75 of Zeitschrift für Angewandte Mathematik und Physik in 2024.[1] The presentation has been adapted for use in this dissertation to clarify the details of the proofs and guarantee consistency of the notation.

5.1 Motivation

Migration, proliferation, and differentiation of cells are influenced by biochemical and biophysical characteristics of their surroundings, which they perceive by way of transmembrane units like ion channels, receptors, etc. Increasing experimental evidence suggests that cells are able to sense such cues not only where they are, but also at larger distances, up to several cell diameters around their current position [71, 90, 130]. This led to mathematical models accounting for various types of nonlocalities, most of them addressing cell-cell and/or cell-matrix adhesions; we refer to the review article [28] and references therein. The settings typically involve reaction, diffusion and drift terms, whereby the latter contain an integral operator to characterize the so-called adhesion velocity over the interaction range. In *Chapter 3* was performed a rigorous passage from a cell-matrix adhesion model to a reaction-diffusion-haptotaxis equation when the sensing radius is becoming infinitesimally small, thus recovering the local PDE formulation from that featuring the mentioned nonlocality. The remote sensing of signals by cells affects, however, not only motility, but also proliferation, growth, and phenotypic switch, either directly - by occupancy of transmembrane units on cellular extensions like cytonemes and folopodia and subsequently initiated signaling pathways, or in an indirect manner - as effects of altered migratory and aggregation behavior. Models involving reaction-diffusion equations with nonlocal source terms have been proposed in various contexts, including biological and ecological ones, see e.g., [87, 145] and references therein for rather generic settings, [13, 15, 129] for chemotaxis systems, and [113, 136, 137] for equations dedicated to tumor growth. We refer to [28, 87, 145] for some reviews of model classes addressing this type of nonlocality.

As far as growth and migration of cell populations are concerned, the reaction-diffusion models with nonlocal source terms

$$u_t = \nabla \cdot (D\nabla u) + F(u) \tag{5.1.1}$$

[1] [49]

typically feature $F(u) = \mu J * u(1-u)$ to describe nonlocal stimulation of growth (see e.g., [137, 145]), or $F(u) = \mu u^{\alpha}(1 - J * u^{\beta})$, which characterizes competition between (bunches of) cells for available resources in their surroundings, attempting, e.g., to prevent overcrowding. In the context of (tumor) cell migration such models have been handled e.g., in [136], where intra- and interspecific nonlocal interactions led to an ODE-PDE system for the interplay between cancer cells peforming linear diffusion and haptotaxis with the extracellular matrix being (nonlocally) degraded by the cells and remodeled with the mentioned growth limitation. We also refer to [28, 99] for short reviews of models with source terms of this type and therewith associated mathematical challenges.

In this chapter we propose and analyze a model for tumor cell migration involving myopic diffusion, repellent pH-taxis, and a nonlocal source term of the competition type mentioned above. The cross-diffusion system is obtained upon starting from the mesoscopic description of cell migration via a kinetic transport equation for the space-time distribution function of cells sharing some velocity regime. An appropriate upscaling relying on diffusion dominance then leads to the effective macroscopic equation for the cancer cell density, with precisely specified diffusion and drift coefficients. The remaining of this chapter is structured as follows: *Section 5.2* contains the model deduction with the mentioned upscaling. *Section 5.3* is dedicated to the mathematical analysis of the obtained nonlocal macroscopic system, in terms of global existence, uniqueness, and boundedness of a solution to a simplified version of the problem. In *Section 5.4* we study the asymptotic behavior. *Section 5.5* offers a 1D study of pattern formation for the equations handled in *Section 5.3*, but only involving constant motility coefficients. In *Section 5.6* we provide numerical simulations to illustrate the qualitative behavior of solutions to the investigated nonlocal problem. *Section 5.7* contains a discussion of the results.

5.2 Modeling

In this section we start from a mesoscopic description of cell migration and intrapopulation interactions and deduce (in a non-rigorous way) effective equations on the macroscopic scale of cell population dynamics. The deduction closely follows that in [99], however extends it, by accounting here for the repellent effects of acidity eventually leading on the population scale to chemorepellent pH-taxis.

Tumor migration and spread are typically assessed on the macroscopic scale of the cancer cell population via biomedical imaging. The involved processes are, however, highly complex and originate at the lower levels of cell aggregates sharing -beside time-space dynamics- one or several further traits (e.g., velocity, phenotypic state or other so called 'activity variables'), down to microscopic events on individual cells. This multiscale character of cell migration can be captured (at least partially) by models within the kinetic theory of active particles (KTAP) framework formulated by Bellomo et al. (see e.g., [8, 11] and references therein). Starting from kinetic transport equations (KTEs), a large variety of (spatially) local and nonlocal models have been proposed and various kinds of upscaling and moment closure methods have been performed in order to deduce their macroscopic limits which enable a mathematically more efficient handling, see e.g., [25, 27, 29–33, 42, 53–55, 78, 91, 92, 105, 155]. The obtained macroscopic equations carry in the coefficients of their motility and source terms some of the traits from the mesoscale on which KTEs were formulated. Those coefficients are no longer 'guessed' as in the case of stating reaction-diffusion-taxis directly on the population level and the diffusion is often of the 'myopic' type, involving a drift correction. We will perform here a diffusion-dominated upscaling of mesoscale dynamics.

We will use the following notations:

- $p = p(t, x, v)$: distribution function of cells having at time t and position $x \in \mathbb{R}^n$ the velocity $v \in V$;
- $V = [s_1, s_2] \times \mathbb{S}^{n-1}$: velocity space. Thereby, s_1, s_2 denote the minimum, respectively the maximum speed of a cell, $\theta \in \mathbb{S}^{n-1}$ represents the cell direction;
- $u(t, x) = \int_V p(t, x, v)\,\mathrm{d}v$: macroscopic cell density;
- $h(t, x)$: concentration of protons. This is a macroscopic quantity throughout this note.

The kinetic transport equation (KTE)

$$p_t + v \cdot \nabla_x p = \mathcal{L}[h]p + \tilde{\mu}\mathcal{I}[p, p] \tag{5.2.1}$$

characterizes the mesoscopic dynamics of the considered cell population. This is the framework set in [116], which assumes that changes in p are due to velocity jumps accompanied by reorientations dictated by a turning kernel contained in the operator $\mathcal{L}[h]$.

The first term on the right-hand side of (5.2.1) represents the so-called turning operator. The second term describes growth/decay of cells due to intraspecific proliferative/competitive interactions, while $\tilde{\mu} > 0$ is the constant interaction rate.[2] With a small constant $\varepsilon > 0$ relating to the cell size and to the distance at which cells can sense signals in their proximity, we will assume that $\tilde{\mu} = \varepsilon^2\mu$. This means that cells have a much higher preference to motility (in particular, to changing direction) than to interaction and crowding.

We assume that the turning operator is of the form

$$\mathcal{L}[h](p) = \int_V \Big(T[h](v, v')p(t, x, v') - T[h](v', v)p(t, x, v)\Big)\,\mathrm{d}v', \tag{5.2.2}$$

with the turning rate $T[h](v, v') \geqslant 0$ chosen such that the reorientation is a Poisson process with rate

$$\lambda[h] = \int_V T[h](v, v')\,\mathrm{d}v,$$

hence such that $T[h]/\lambda[h]$ is a kernel giving the probability density for a change of the velocity regime of a cell from v' to v. In particular, this means that $\mathcal{L}[h]$ is preserving mass. The reorientation of cells depends on the acidity of their environment (expressed by the concentration h of protons).

In the following we assume that the turning rate has an asymptotic expansion of the form

$$T[h] = T_0[h] + \varepsilon T_1[h] + O(\varepsilon^2), \tag{5.2.3}$$

[2] We could actually consider $\tilde{\mu}$ to be a function of x and/or t (but not of derivatives w.r.t. these variables) and even of h. The latter would allow us to account e.g., for the unfavorable effect of acidity on the proliferation of tumor cells. The deduction done here works then exactly in the same way. In fact, our analysis in *Section 5.3* is performed in the case where such h-dependence is considered.

thus the turning operator admits itself an expansion

$$\mathcal{L}[h](p) := L_0[h](p) + \varepsilon L_1[h](p) + O(\varepsilon^2), \tag{5.2.4}$$

where $L_0[h]$ and $L_1[h]$ are linear operators,

$$L_i[h](p)(t,x,v) = \int_V [T_i[h](v,v')p(t,x,v') - T_i[h](v',v)p(t,x,v)]\,\mathrm{d}v', \qquad i = 0,1. \tag{5.2.5}$$

For $\mathcal{I}$ we consider as in [99] the form

$$\mathcal{I}[p,p](t,x,v) = \frac{p^\alpha(t,x,v)}{\int_V M^\alpha(x,v)\,\mathrm{d}v} - \frac{1}{\int_V M^{\alpha+\beta}(x,v)\,\mathrm{d}v} p^\alpha(t,x,v) \int_\Omega J(x,x')p^\beta(t,x',v)\,\mathrm{d}x', \tag{5.2.6}$$

where: $\alpha, \beta > 0$ are constants, $J(x,x')$ is a function weighting the interactions between (bunches of) cells sharing the same velocity regime within a bounded domain $\Omega \subset \mathbb{R}^n$. We assume that J depends on the distance between interacting (clusters of) cells and take $J(x,x') = J(x-x')$, also requiring J to satisfy

$$\int_V J(x)\,\mathrm{d}x = 1, \tag{5.2.7}$$

$$\inf_{B_{\mathrm{diam}(\Omega)}(0)} J \geqslant \eta \quad \text{for some } \eta > 0. \tag{5.2.8}$$

We also assume that there exists a bounded velocity distribution $M(x,v) > 0$ such that:

1. $\int_V M(x,v)\,\mathrm{d}v = 1$, i.e., M is a kernel w.r.t. v.
2. $\int_V vM(x,v)\,\mathrm{d}v = 0$, i.e., the flow produced by the equilibrium distribution $M(v)$ vanishes.
3. The rate $T_0[h](v,v')$ satisfies the detailed balance equation

$$T_0[h](v,v')M(v') = T_0[h](v',v)M(v).$$

4. The turning rate $T_0[h](v,v')$ is bounded and there exists $\sigma > 0$ such that

$$T_0[h](v,v') \geqslant \sigma M(x,v), \quad \text{for all } (v,v') \in V \times V,\ x \in \mathbb{R}^n,\ t > 0.$$

The following lemma summarizing the properties of the operator $-L_0$ can be easily verified (see e.g., [10, 25]).

Lemma 5.2.1. *Let $L_0[h]$ be the operator defined in (5.2.5). Then $-L_0[h]$ has the following properties:*

(i) $-L_0[h]$ is positive definite w.r.t. the scalar product and the associated norm in the weighted space $L^2(V, \frac{dv}{M(x,v)})$, and self-adjoint: for all $p, \zeta \in L^2(V, \frac{dv}{M(x,v)})$ it holds that

$$\int_V L_0[h](p)(v)\frac{\zeta(v)}{M(v)}\,dv = \int_V L_0[h](\zeta)(v)\frac{p(v)}{M(v)}\,dv.$$

(ii) For $\phi \in L^2(V, \frac{dv}{M(x,v)})$, the equation $L_0[h](\zeta) = \phi$ has a unique solution $\zeta \in L^2(V, \frac{dv}{M(x,v)})$ satisfying[3] $\bar{\zeta} = 0$ if and only if $\bar{\phi} = 0$.

[3] Here and in the remaining of this section we use the notation $\bar{\zeta} := \int_V \zeta(v)\,\mathrm{d}v$ for any V-integrable function ζ (hence also $u = \bar{p}$).

(iii) *Ker* $L_0[h] = span\ (M(v))$.

(iv) *The equation* $L_0[h](\psi) = vM(v)$ *has a unique solution* $\psi(v) =: L_0[h]^{-1}(vM(v))$ *(this is actually a pseudoinverse).*

Example 5.2.2. Consider $T_0[h](v, v') := \lambda_0[h]M(v)$, with $\lambda[h] \geqslant \lambda_0[h] > 0$ for any h. This obviously satisfies the properties 3. and 4. in our above assumption. With this choice,

$$L_0[h](p) = \lambda_0[h](M(v)u - p) \tag{5.2.9}$$

and it is straightforward to see that this operator satisfies the properties in *Lemma 5.2.1* and the function ψ in *(iv)* becomes $\psi(v) = -vM(v)/\lambda_0[h]$ if $\psi \in (\text{span } (M(v)))^{\perp}$.[4]

Equation (5.2.1) is supplemented with the macroscopic PDE for proton concentration:

$$h_t = D_H \Delta h + g(u, h), \tag{5.2.10}$$

where $D_H > 0$ is the diffusion constant and $g(u, h)$ represents production by tumor cells and uptake (e.g., by blood capillaries - not explicitly modeled in this note) or decay. As such, g will have to be bounded; moreover, when there is no or very less acid its production is turned on and sustained, whereas a high proton concentration exceeding some upper threshold level H is leading to a drop in h, by enhanced (more or less passive) uptake by surrounding tissues and vasculature and/or by ceased expression, due to hypoxia-induced apoptosis of (too crowded) tumor cells. More details on the concrete assumptions made about $g(u, h)$ are provided at the beginning of *Sections 5.3* and *5.5*. A concrete choice of g is given at the beginning of *Section 5.6*.

We also consider initial conditions for p and h:

$$p(0, x, v) = p_0(x, v), \qquad h(0, x) = h_0(x), \quad x \in \Omega \subseteq \mathbb{R}^n, \ v \in V. \tag{5.2.11}$$

Together with these, equations (5.2.1) and (5.2.10) form a meso-macro system describing the dynamics of the (mesoscopic) cell distribution in response to acidity in the extracellular space.

We perform a parabolic scaling to obtain the diffusion limit of the KTE (5.2.1). This means that we rescale the time and space variables as follows:

$$\hat{t} = \varepsilon^2 t, \quad \hat{x} = \varepsilon x.$$

Subsequently we will drop the '$\hat{\ }$' symbol and the ε-dependency of the solution p^{ε} to the resulting KTE, in order not to complicate the writing. Then, (5.2.1) becomes

$$\varepsilon p_t + v \cdot \nabla_x p = \frac{1}{\varepsilon}\mathcal{L}[h]p + \mu\varepsilon\mathcal{I}[p, p]. \tag{5.2.12}$$

Now consider the decomposition (Chapman-Enskog expansion)

$$p(t, x, v) = F(u)(t, x, v) + \varepsilon p^{\perp}(t, x, v), \tag{5.2.13}$$

with $\int_V p^{\perp}(t, x, v)\, dv = 0$, thus $p^{\perp} \in (\text{span } (M(v)))^{\perp}$, and $F(u) \in \text{span } (M(v))$ such that $\int_V F(u)\, dv = u$. A natural choice is $F(u)(t, x, v) := M(x, v)u(t, x)$, which we will subsequently adopt.

[4] This is actually the case even if T_0 has a more general form (depending only on v and not on v') without having to satisfy condition 2.

Then observe that

$$\mathcal{I}[p,p] = \mathcal{I}[M(v)u + \varepsilon p^{\perp}, M(v)u + \varepsilon p^{\perp}] = \mathcal{I}[M(v)u, M(v)u] + O(\varepsilon)$$

and (5.2.12) becomes

$$\begin{aligned}&\partial_t(M(v)u) + \varepsilon\partial_t p^{\perp} + \frac{1}{\varepsilon} v\cdot\nabla_x(M(v)u) + v\cdot\nabla_x p^{\perp}\\ =&\frac{1}{\varepsilon}L_0[h](p^{\perp}) + \frac{1}{\varepsilon}L_1[h](M(v)u) + L_1[h](p^{\perp}) + \mu\mathcal{I}[M(v)u, M(v)u] + O(\varepsilon).\end{aligned} \tag{5.2.14}$$

Let $P : L^2(V, \frac{\mathrm{d}v}{M(v)}) \to \mathrm{Ker}\ L_0[h]$ be the projection operator. Then

$$P(\phi) = M(v)\bar{\phi}, \qquad \phi \in L^2(V, \frac{\mathrm{d}v}{M(v)}).$$

It is easy to verify that the following lemma holds (see, e.g., [10]).

Lemma 5.2.3. *The projection operator P has the following properties:*

(i) $(I - P)(M(v)u) = P(p^{\perp}) = 0.$

(ii) $(I - P)(v\cdot\nabla_x(M(v)u)) = v\cdot\nabla_x(M(v)u).$

(iii) $(I - P)(L_0[h](M(v)u)) = L_0[h](M(v)u)$ *and* $(I - P)(L_1[h](M(v)u)) = L_1[h](M(v)u).$

(iv) $(I - P)(L_1[h](p^{\perp})) = L_1[h](p^{\perp}).$

If we now apply $I - P$ to (5.2.14) we get

$$\begin{aligned}&\varepsilon\partial_t p^{\perp} + \frac{1}{\varepsilon} v\cdot\nabla_x(Mu) + (I-P)(v\cdot\nabla_x p^{\perp})\\ =&\frac{1}{\varepsilon}L_0[h](p^{\perp}) + \frac{1}{\varepsilon}L_1[h](Mu) + L_1[h](p^{\perp}) + \mu\mathcal{I}[Mu, Mu] + O(\varepsilon).\end{aligned} \tag{5.2.15}$$

Integrating (5.2.14) w.r.t. v gives (at leading order) the macroscopic PDE[5]

$$u_t + \int_V v\cdot\nabla_x p^{\perp}\,\mathrm{d}v = \mu\int_V \mathcal{I}[Mu, Mu]\,\mathrm{d}v. \tag{5.2.16}$$

On the other hand, from (5.2.15) we obtain (again at leading order)

$$L_0[h](p^{\perp}) = v\cdot\nabla_x(Mu) - L_1[h](Mu). \tag{5.2.17}$$

Since $\int_V L_1[h](Mu)\,\mathrm{d}v = 0$, we see that the integral w.r.t. v of the right-hand side in (5.2.17) vanishes, so we can pseudo-invert $L_0[h]$ to obtain

$$p^{\perp} = L_0[h]^{-1}\Big(v\cdot\nabla_x(Mu) - L_1[h](Mu)\Big). \tag{5.2.18}$$

Plugging this into (5.2.16) gives

$$u_t + \int_V v\cdot\nabla_x\Big(L_0[h]^{-1}(v\cdot\nabla_x(Mu)) - L_0[h]^{-1}(L_1[h](Mu))\Big) = \mu\int_V \mathcal{I}[Mu, Mu]\,\mathrm{d}v. \tag{5.2.19}$$

[5]involving nonlocalities w.r.t. velocity

For the right-hand side in (5.2.19) we have

$$\mu \int_V \mathcal{I}[Mu, Mu]\,\mathrm{d}v = \mu u^\alpha (1 - J * u^\beta).$$

For the first transport term on the left-hand side we compute

$$\begin{aligned}\int_V v \cdot \nabla_x \Big(L_0[h]^{-1}(v \cdot \nabla_x (Mu)) \Big)\,\mathrm{d}v &= \nabla_x \cdot \Big(\frac{1}{\lambda_0[h]} \nabla_x \cdot \Big(\int_V v \otimes v M(v)\,\mathrm{d}v\; u \Big)\Big) \\ &= -\nabla_x \cdot \Big(\frac{1}{\lambda_0[h]} \nabla_x \cdot (\mathbb{D}\; u)\Big),\end{aligned}$$

where we applied the observations made at the end of *Example 5.2.2* and denoted by

$$\mathbb{D}(x) := \int_V v \otimes v M(x, v)\,\mathrm{d}v$$

the diffusion tensor of tumor cells.

For the second transport term on the left-hand side of (5.2.19) we have

$$\begin{aligned}&- \int_V v \cdot \nabla_x \Big(L_0[h]^{-1}(L_1[h](M(v)u)) \Big)\,\mathrm{d}v \\ =& - \nabla_x \cdot \int_V v L_0[h]^{-1}(L_1[h](M(v)u))\,\mathrm{d}v \\ =& - \nabla_x \cdot \int_V v M(v) \frac{1}{M(v)} L_0[h]^{-1}(L_1[h](M(v)u))\,\mathrm{d}v \\ =& - \nabla_x \cdot \int_V L_0[h](\psi(v)) \frac{1}{M(v)} L_0[h]^{-1}(L_1[h](M(v)u))\,\mathrm{d}v \\ =& - \nabla_x \cdot \Big(\int_V \frac{\psi(v)}{M(v)} L_1[h](M(v))\,\mathrm{d}v\; u \Big) \\ =& \nabla_x \cdot \Big(u\Gamma[h] \Big),\end{aligned}$$

where we used the fact that L_0 is self-adjoint, $\psi(v) = -vM(v)$ is its pseudo-inverse, and the notation

$$\Gamma[h](x) := \frac{1}{\lambda_0[h]} \int_V v L_1[h](M(x, v))\,\mathrm{d}v.$$

With the above calculations (5.2.19) becomes

$$u_t - \nabla_x \cdot \Big(\frac{1}{\lambda_0[h]} \nabla_x \cdot (\mathbb{D}\; u)\Big) + \nabla_x \cdot \Big(u\Gamma[h] \Big) = \mu u^\alpha (1 - J * u^\beta). \tag{5.2.20}$$

To specify $\Gamma[h]$ we consider[6] $T_1[h](v, v') := -a(h)v \cdot \nabla h + b(h)v' \cdot \nabla h$ with $a, b \geqslant 0$. Then we compute

$$\int_V v L_1[h](M(x, v))\,\mathrm{d}v = -a(h) \frac{s_2^{n+2} - s_1^{n+2}}{n(n+2)} |\mathbb{S}^{n-1}| I_n \nabla h - \frac{b(h)}{|V|} \mathbb{D} \nabla h,$$

recalling that $V = [s_1, s_2] \times \mathbb{S}^{n-1}$, thus $|V| = \frac{s_2^n - s_1^n}{n} |\mathbb{S}^{n-1}|$. With the notation

$$\mathbb{T}(x) := a(h) \frac{s_2^{n+2} - s_1^{n+2}}{n(n+2)} |\mathbb{S}^{n-1}|\; I_n + \frac{b(h)}{|V|} \mathbb{D}$$

we obtain

$$\Gamma[h](x) = -\frac{1}{\lambda_0[h]} \mathbb{T}(x) \nabla h,$$

[6] a similar choice has been proposed in [25]

which leads to the macroscopic PDE

$$u_t = \nabla_x \cdot \Big(\frac{1}{\lambda_0[h]} \nabla_x \cdot (\mathbb{D}(x)u)\Big) + \nabla_x \cdot \Big(\frac{u}{\lambda_0[h]} \mathbb{T}(x)\nabla h\Big) + \mu u^\alpha (1 - J * u^\beta). \tag{5.2.21}$$

The particular choice $\lambda_0[h] := 1$, $a(h) := 0$, $b(h) := |V|$ leads to the first equation in (5.3.1).

The first term on the right-hand side of (5.2.21) represents (myopic) diffusion, the second one characterizes repellent chemotaxis, away from increasing gradients of proton concentration,[7] while the last is a source term accounting for tumor cell growth enhanced or limited by intraspecific interactions. Thereby, the growth rate μ can also depend on the proton concentration h, as will actually be the case in the subsequent sections. The requirements it has to satisfy are biologically motivated: cancer cells are able to survive and divide at far lower pH than normal cells and tissue; this gives them an advantage in using resources, thus enabling and even enhancing proliferation under mildly acidic conditions. However, when the proton concentration surpasses a certain critical level[8] the environmental conditions for cell division are so unfavorable, that tumor cells are arrested in their cycle and cease proliferation. As growth rates cannot be negative we account for an enviromental-mediated decay by way of the (nonlocal) competition term, as the crowded tumor environment is the main source of acidity.

The above deduction of a macroscopic reaction-diffusion-taxis is merely formal; the nonlinear source term prevents applying the proof of the rigorous derivation from [25]. The following section will be dedicated to proving global existence and boundedness of nonnegative solutions to the coupled PDE system for u and h obtained on the macrolevel by considering the above much simplified forms of the coefficient functions λ_0, a, b. The previous calculations were made for $x \in \mathbb{R}^n$, however we can restrict to a bounded domain $\Omega \subset \mathbb{R}^n$ upon proceeding as in [33, 42, 124] and assuming no-flux of cells or protons through the boundary.

5.3 Mathematical analysis

Let $\Omega \subset \mathbb{R}^n$ be a bounded domain with smooth enough boundary and outer unit normal ν. We consider the model

$$\begin{cases} u_t = \nabla\nabla : (\mathbb{D}(x)u) + \nabla \cdot (\mathbb{D}(x)u\nabla h) + \mu(h)u^\alpha(1 - J * u^\beta) & \text{in } \Omega \times (0,\infty), \\ h_t = D_H \Delta h + g(u,h) & \text{in } \Omega \times (0,\infty), \\ (\mathbb{D}(x)\nabla u + \nabla \cdot \mathbb{D}(x)u + \mathbb{D}(x)u\nabla h) \cdot \nu = \nabla h \cdot \nu = 0 & \text{on } \partial\Omega \times (0,\infty), \\ u(\cdot,0) = u_0,\ h(\cdot,0) = h_0 & \text{in } \Omega, \end{cases} \tag{5.3.1}$$

where u denotes the cell density and h the acid concentration. We assume that our diffusion tensor $\mathbb{D} = (d_{ij})_{i,j=1,\dots,n}$ satisfies $d_{ij} \in C^1(\overline{\Omega})$. Moreover, $\mathbb{D}$ satisfies the uniform parabolicity and boundedness condition, i.e., there are B_1, $B_2 > 0$ such that for all $\xi \in \mathbb{R}^n$ and $x \in \overline{\Omega}$ it holds that

$$B_1|\xi|^2 \leqslant \sum_{i,j=1}^n d_{ij}(x)\xi_j\xi_i \leqslant B_2|\xi|^2. \tag{5.3.2}$$

[7] as in [31, 33, 89, 91, 92] we call this a repellent pH-taxis

[8] denoted by H in the assumptions at the beginning of *Section 5.3*

The exponents $\alpha, \beta \geqslant 1$ satisfy (as in [99])

$$\alpha < \begin{cases} 1+\beta, & n = 1, 2, \\ 1+\frac{2\beta}{n}, & n > 2. \end{cases} \tag{5.3.3}$$

On the remaining functions and parameters we make the subsequent assumptions:

- $u_0 \in C(\overline{\Omega})$ and $u_0 \geqslant 0$,
- $h_0 \in W^1_\infty(\Omega)$ and $0 \leqslant h_0 \leqslant H$, $h_0 \not\equiv H$, where H is a positive constant,
- μ is Lipschitz-continuous with constant L_μ, satisfying $0 \leqslant \mu$ and $0 < \delta \leqslant \mu(h)$ for $h \leqslant H$,
- $g \in C^1(\mathbb{R}^+_0 \times \mathbb{R}^+_0)$ with $\nabla g \in (L^\infty(\mathbb{R}^+_0 \times \mathbb{R}^+_0))^2$, $0 \leqslant g(u, 0) \leqslant G$ and $g(u, H) \leqslant 0$ for $u \in \mathbb{R}^+_0$,
- $J \in L^p(B)$ for $B := B_{\text{diam}(\Omega)}(0)$ and some $p \in (1, \infty)$ and $0 < \eta \leqslant J$,
- $D_H > 0$.

5.3.1 Local existence in an approximate problem

The Stone-Weierstraß theorem implies that there is a sequence $(u_{0l})_{k\in\mathbb{N}} \subset C^{0,1}(\overline{\Omega})$, $u_{0l} \geqslant 0$ and

$$u_{0l} \underset{l\to\infty}{\to} u_0 \text{ in } C(\overline{\Omega}) \tag{5.3.4}$$

and a sequence of diffusion tensors $(\mathbb{D}_l)_{l\in\mathbb{N}}$ with $\mathbb{D}_l = (d_{lij})_{i,j=1,\dots,n}$ s.t. $d_{lij} \in C^{2+\vartheta}(\overline{\Omega})$ for $\vartheta \in (0, 1)$ and

$$\mathbb{D}_l \underset{l\to\infty}{\to} \mathbb{D} \text{ in } C^1(\overline{\Omega}; \mathbb{R}^{n\times n}). \tag{5.3.5}$$

Moreover, $\mathbb{D}_l$ satisfies the uniform parabolicity condition for all $l \in \mathbb{N}$, i.e., there are $D_1 \in (0, B_1)$ and $D_2 \in (B_2, \infty)$ such that for all $\xi \in \mathbb{R}^n$, $x \in \overline{\Omega}$ and $l \in \mathbb{N}$ it holds that

$$D_1|\xi|^2 \leqslant \sum_{i,j=1}^n d_{lij}(x)\xi_j\xi_i \leqslant D_2|\xi|^2. \tag{5.3.6}$$

For $l \in \mathbb{N}$ we consider the approximate problem

$$\begin{cases} \partial_t u_l = \nabla\nabla : (\mathbb{D}_l(x)u_l) + \nabla \cdot (\mathbb{D}_l(x)u_l\nabla h_l) + \mu(h_l)u_l^\alpha(1 - J * u_l^\beta) & \text{in } \Omega \times (0, \infty), \\ \partial_t h_l = D_H\Delta h_l + g(u_l, h_l) & \text{in } \Omega \times (0, \infty), \\ (\mathbb{D}_l(x)\nabla u_l + \nabla \cdot \mathbb{D}_l(x)u_l + \mathbb{D}_l(x)u_l\nabla h_l) \cdot \nu = \nabla h_l \cdot \nu = 0 & \text{on } \partial\Omega \times (0, \infty), \\ u_l(\cdot, 0) = u_{0l},\ h(\cdot, 0) = h_0 & \text{in } \Omega. \end{cases} \tag{5.3.7}$$

Lemma 5.3.1. *For all $l \in \mathbb{N}$ there are $T_{max} > 0$ and a weak solution (u_l, h_l) of (5.3.7) with $u_l \geqslant 0$ s.t. $u_l \in C(\overline{\Omega} \times [0, T])) \cap L^2(0, T; H^1(\Omega))$ and $h_l \in L^\infty(0, T; W^1_\infty(\Omega)) \cap W^{2,1}_2(\Omega \times (0, T))$ for all $T \in (0, T_{max})$ and (u_l, h_l) satisfies*

$$\begin{aligned} &-\int_0^T\int_\Omega u_l\eta_t\,dx\,dt + \int_0^T\int_\Omega (\nabla \cdot \mathbb{D}_l u_l + \mathbb{D}_l\nabla u_l + \mathbb{D}_l u_l\nabla h_l) \cdot \nabla\eta\,dx\,dt \\ &= \int_0^T\int_\Omega \mu(h_l)u_l^\alpha(1 - J * u_l^\beta)\eta\,dx\,dt + \int_\Omega u_{0l}(x)\eta(x, 0)\,dx, \end{aligned} \tag{5.3.8}$$

for all $\eta \in W_2^{1,1}(\Omega \times (0,T))$ *with* $\eta(T) = 0$ *and*

$$\partial_t h_l = D_H \Delta h_l + g(u_l, h_l) \quad \text{a.e. in } \Omega \times (0, T_{max}), \tag{5.3.9a}$$

$$\nabla h_l \cdot \nu = 0 \quad \text{a.e. on } \partial\Omega \times (0, T_{max}), \tag{5.3.9b}$$

$$h_l(0) = h_0 \quad \text{in } H^1(\Omega). \tag{5.3.9c}$$

Moreover, it holds either $T_{max} = \infty$ *or* $T_{max} < \infty$ *and*

$$\lim_{t \nearrow T_{max}} \left(\|u_l(\cdot, t)\|_{L^\infty(\Omega)} + \|h_l(\cdot, t)\|_{W^1_\infty(\Omega)} \right) = \infty. \tag{5.3.10}$$

Proof. Fix $l \in \mathbb{N}$. We set $M := \|u_{0l}\|_{L^\infty(\Omega)} < \infty$. For $h < 0$ and $\overline{u} \geqslant 0$ extend the coefficients by

$$g(\overline{u}, h) := 2g(\overline{u}, 0) - g(\overline{u}, -h) \text{ and } \mu(h) := \mu(-h).$$

We show the existence of a solution (u_l, h_l) of (5.3.7) in the sense of (5.3.8) and (5.3.9a)-(5.3.9c) by showing the existence of a fixed-point of the operator F introduced below similarly to [138]. Namely, we define for some small enough $T \in (0,1)$ the set

$$S := \{\overline{u} \in L^\infty(\Omega \times (0,T)) \ : \ 0 \leqslant \overline{u} \leqslant M + 1 \text{ a.e. in } \Omega \times (0,T)\}.$$

For $\overline{u} \in S$ we consider the IBVPs

$$\begin{cases} \partial_t u_l = \nabla\nabla : (\mathbb{D}_l(x) u_l) + \nabla \cdot (\mathbb{D}_l(x) u_l \nabla h_l) + \mu(h_l)\overline{u}^{\alpha-1}(1 - J * \overline{u}^\beta) u_l & \text{in } \Omega \times (0,T), \\ (\mathbb{D}_l(x)\nabla u_l + \nabla \cdot \mathbb{D}_l(x) u_l + \mathbb{D}_l(x) u_l \nabla h_l) \cdot \nu = 0 & \text{on } \partial\Omega \times (0,T), \\ u_l(\cdot, 0) = u_{0l} & \text{in } \Omega, \end{cases} \tag{5.3.11}$$

and

$$\begin{cases} \partial_t h_l = D_H \Delta h_l + g(\overline{u}, h_l) & \text{in } \Omega \times (0,T), \\ \nabla h_l \cdot \nu = 0 & \text{on } \partial\Omega \times (0,T), \\ h_l(\cdot, 0) = h_0 & \text{in } \Omega. \end{cases} \tag{5.3.12}$$

Here, T can be chosen independent of $\overline{u}$.

Let $q > \max\{2, n\}$. Consider the space

$$X := \left\{ \overline{h} \in L^\infty(0, T; W_q^1(\Omega)) : |\overline{h}| \leqslant C_1 \|h_0\|_{W_q^1(\Omega)} + 1 \right\},$$

where C_1 depends on the Sobolev embedding constant from *Lemma 2.2.8(ii)*, the constant from Poincaré inequality and from the constants in *Lemma A.1.18(ii)* and *(iii)*. For $\overline{h} \in X$ we set

$$\Psi(\overline{h})(t) := e^{tD_H\Delta} h_0 + \int_0^t e^{(t-s)D_H\Delta} g(\overline{u}, \overline{h}) \, \mathrm{d}s.$$

Using estimates from *Lemma A.1.18* it follows that Ψ defines a contraction on X for small enough T. With a Banach fixed-point argument in X similar to [85] we conclude that there is a unique $h_l \in X$ that satisfies

$$h_l(t) = \Psi(h_l)(t) = e^{tD_H\Delta} h_0 + \int_0^t e^{(t-s)D_H\Delta} g(\overline{u}, h_l) \, \mathrm{d}s. \tag{5.3.13}$$

Moreover, h_l is the unique weak solution of (5.3.12) in the sense of *Theorem A.1.1*, i.e., for all $\eta \in W_2^{1,1}(\Omega \times (0,T))$ with $\eta(T) = 0$ it holds that

$$-\int_0^T \int_\Omega h_l \eta_t \,\mathrm{d}x\,\mathrm{d}t + D_H \int_0^T \int_\Omega \nabla h_l \cdot \nabla \eta \,\mathrm{d}x\,\mathrm{d}t = \int_0^T \int_\Omega g(\bar{u}, h_l)\eta \,\mathrm{d}x\,\mathrm{d}t + \int_\Omega h_0(x)\eta(x,0)\,\mathrm{d}x. \tag{5.3.14}$$

Estimating as in *Lemma 5.3.3* below it follows from *Lemma A.1.18(ii)* and *(iii)* that

$$\|\nabla h_l\|_{L^\infty(0,T;(L^\infty(\Omega))^n)} \leqslant C_2. \tag{5.3.15}$$

Moreover, from *Theorem A.1.8* applied to the equation in non-divergence form we conclude that

$$\|h_l\|_{W_2^{2,1}(\Omega\times(0,T))} \leqslant C_3 \tag{5.3.16}$$

and solves (5.3.12) in the sense of (5.3.9a) - (5.3.9c). Moreover, the continuity of h_l follows from *Remark A.1.2* and *Theorem A.1.12* with

$$a(\nabla h_l) := D_H \nabla h_l,\; b(x,t,h_l) := -g(\overline{u}, h_l) \tag{5.3.17}$$

due the embedding of $W^1_\infty(\Omega)$ into some Hölder space on $\overline{\Omega}$ from *Lemma 2.2.8(ii)*. Now, *Theorems A.1.1* and *A.1.4* with

$$\begin{aligned} a_{ij}(x) &:= d_{lij}(x),\\ a_i(x,t) &:= \sum_{j=1}^n \left((d_{lij})_{x_j} + d_{lij}(h_l)_{x_j}\right),\\ a(x,t) &:= -\mu(h_l)\overline{u}^{\alpha-1}(1 - J * \overline{u}^\beta),\\ f &:= 0 \end{aligned} \tag{5.3.18}$$

(that are due to (5.3.5), (5.3.15), *Lemma 2.3.2* and the Lipschitz continuity of μ all bounded in $L^\infty(\Omega \times (0,T))$ by constants independent from $\overline{u}$) imply that there is a unique weak solution $u_l \in C([0,T]; L^2(\Omega)) \cap L^2(0,T; H^1(\Omega))$ of (5.3.11) satisfying

$$\begin{aligned} &-\int_0^T \int_\Omega u_l \eta_t \,\mathrm{d}x\,\mathrm{d}t + \int_0^T \int_\Omega (\nabla \cdot \mathbb{D}_l u_l + \mathbb{D}_l \nabla u_l + \mathbb{D}_l u_l \nabla h_l) \cdot \nabla \eta \,\mathrm{d}x\,\mathrm{d}t\\ &= \int_0^T \int_\Omega \mu(h_l)\overline{u}^{\alpha-1}(1 - J * \overline{u}^\beta)u_l \eta \,\mathrm{d}x\,\mathrm{d}t + \int_\Omega u_{0l}(x)\eta(x,0)\,\mathrm{d}x \end{aligned} \tag{5.3.19}$$

for all $\eta \in W_2^{1,1}(\Omega \times (0,T))$ with $\eta(T) = 0$ and $\|u_l\|_{L^\infty(\Omega\times(0,T))} \leqslant C_4$. Moreover, we conclude from *Remark A.1.2* and *Theorem A.1.12* with

$$\begin{aligned} a(x,t,u,\nabla u) &:= \mathbb{D}_l \nabla u + \nabla \cdot \mathbb{D}_l u + \mathbb{D}_l u \nabla h_l,\\ b(x,t,u) &:= -\mu(h_l)\overline{u}^{\alpha-1}(1 - J * \overline{u}^\beta)u \end{aligned} \tag{5.3.20}$$

requiring the conditions of the theorem especially due to (5.3.6) and the boundedness of the coefficients that

$$\|u_l\|_{C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])} \leqslant C_5 \tag{5.3.21}$$

for some $\kappa \in (0,1)$ and C_5 depending on l. Hence, we can estimate for $x \in \Omega$ and $t \in (0,T)$ that

$$u_l(x,t) = u_{0l}(x) + t^{\frac{\kappa}{2}} \frac{u_l(x,t) - u_{0l}(x)}{t^{\frac{\kappa}{2}}} \leqslant M + T^{\frac{\kappa}{2}} C_5 \leqslant M + 1$$

holds for a small enough T. We conclude as for (5.3.26) below with $(u_l)_- := \max\{0, -u_l\}$ that for $t \in (0,T)$ it holds that

$$\frac{1}{2}\|(u_l)_-(t)\|^2_{L^2(\Omega)} + \frac{D_1}{2}\int_0^t \|\nabla (u_l)_-\|^2_{(L^2(\Omega))^n}\,\mathrm{d}s \leqslant C_6 \int_0^t \|(u_l)_-\|^2_{L^2(\Omega)}\,\mathrm{d}s.$$

Then, Gronwall's inequality implies that $u_l \geqslant 0$ and $u_l \in S \cap C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])$. Note that C_2, C_3, C_4 and C_5 and consequently also the choice of T are independent from $\overline{u}$ and k. Hence, the operator

$$F : S \mapsto S, \quad \overline{u} \mapsto u_l,$$

where u_l solves (5.3.11) for $\overline{u}$ in the sense of (5.3.19), is well-defined. Moreover, due to the compact embedding $C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega}\times[0,T]) \hookrightarrow\hookrightarrow C(\overline{\Omega}\times[0,T])$ that is a consequence of the Arzelà-Ascoli theorem, F maps bounded sets on precompact ones. To apply Schauder's fixed-point theorem (*Theorem A.2.2*) it remains to show that F is closed and, consequently, a compact operator. Consider a sequence $(\overline{u}_m)_{m\in\mathbb{N}}$ s.t.

$$\overline{u}_m \underset{m\to\infty}{\to} \overline{u} \text{ in } L^\infty(\Omega\times(0,T)), \tag{5.3.22}$$

$$u_{lm} := F(\overline{u}_m) \underset{m\to\infty}{\to} u_l \text{ in } L^\infty(\Omega\times(0,T)). \tag{5.3.23}$$

We want to show that $F(\overline{u}) = u_l$.

Let h_{lm} be the solution of (5.3.12) that corresponds to $\overline{u}_m$ for $m \in \mathbb{N}$. From the equation of form (5.3.19) for u_{lm} we conclude with *Lemma A.1.3* that for a.e. $t \in (0,T)$ it holds that

$$\begin{aligned}&\frac{1}{2}\|u_{lm}(\cdot,t)\|^2_{L^2(\Omega)} + \int_0^t\int_\Omega (\nabla\cdot\mathbb{D}_l u_{lm} + \mathbb{D}_l\nabla u_{lm} + \mathbb{D}_l u_{lm}\nabla h_{lm})\cdot\nabla u_{lm}\,\mathrm{d}x\,\mathrm{d}s\\ &= \int_0^t\int_\Omega \mu(h_{lm})\overline{u}_m^{\alpha-1}(1 - J * \overline{u}_m^\beta)u_{lm}^2\,\mathrm{d}x\,\mathrm{d}s + \frac{1}{2}\|u_{0l}\|^2_{L^2(\Omega)}.\end{aligned} \tag{5.3.24}$$

Using Hölder's and Young's inequalities, (5.3.5) and (5.3.15), we estimate

$$\begin{aligned}\left|\int_\Omega \mathbb{D}_l u_{lm}\nabla h_{lm}\cdot\nabla u_{lm}\,\mathrm{d}x\right| &\leqslant C_2\|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}}\|u_{lm}\|_{L^2(\Omega)}\|\nabla u_{lm}\|_{(L^2(\Omega))^n}\\ &\leqslant C_7\|u_{lm}\|^2_{L^2(\Omega)} + \frac{D_1}{2}\|\nabla u_{lm}\|^2_{(L^2(\Omega))^n}.\end{aligned} \tag{5.3.25}$$

Inserting this into (5.3.24) and using (5.3.5) and (5.3.6), *Lemma 2.3.2*, Young's inequality, the boundedness of h_l and the Lipschitz-continuity of μ, we conclude that for a.e. $t \in (0,T)$ it holds

$$\frac{1}{2}\|u_{lm}(\cdot,t)\|^2_{L^2(\Omega)} + \frac{D_1}{4}\int_0^t \|\nabla u_{lm}\|^2_{(L^2(\Omega))^n}\,\mathrm{d}s \leqslant C_8\int_0^t \|u_{lm}\|^2_{L^2(\Omega)} + C_9. \tag{5.3.26}$$

From Gronwall's inequality it follows that $\|\nabla u_{lm}\|_{L^2(0,T;(L^2(\Omega))^n)} \leqslant C_{10}(T)$ for all $m \in \mathbb{N}$. Combining this with the fact that $h_{lm} \in X$, (5.3.15) and (5.3.16) we conclude from the Lions-Aubin lemma (*Lemma A.3.9*) and the Banach-Alaoglu theorem (*Lemma A.3.1*) that there is $h_l \in L^\infty(0,T;W^1_\infty(\Omega)) \cap W^{2,1}_2(\Omega\times(0,T))$ s.t. for a subsequence

$$\nabla u_{lm_o} \underset{o\to\infty}{\rightharpoonup} \nabla u_l \text{ in } L^2(0,T;(L^2(\Omega))^n), \tag{5.3.27}$$

$$h_{lm_o} \underset{o\to\infty}{\rightharpoonup} h_l \text{ in } L^2(0,T;H^2(\Omega)), \tag{5.3.28}$$

$$h_{lm_o} \underset{o\to\infty}{\to} h_l \text{ in } L^2(0,T;H^1(\Omega)) \text{ and a.e. in } \Omega\times(0,T), \tag{5.3.29}$$

$$\partial_t h_{lm_o} \underset{o\to\infty}{\rightharpoonup} \partial_t h_l \text{ in } L^2(\Omega \times (0,T)). \tag{5.3.30}$$

Therefore, due to (5.3.22) and (5.3.28)–(5.3.30), the Lipschitz-continuity of g, the dominated convergence theorem and the fundamental lemma of calculus of variations it follows that h_l is a solution of (5.3.12) in the sense of (5.3.9a)-(5.3.9c). Moreover, (5.3.5), (5.3.22), (5.3.23), (5.3.27), and (5.3.29), the Lipschitz-continuity of μ and the dominated convergence theorem imply that u_l is a solution of (5.3.11) in the sense of (5.3.8), and therefore, $F(\overline{u}) = u_l$ and F is a compact operator. Consequently, by Schauder's fixed-point theorem we obtain the existence of a fixed-point u_l of F, that satisfies for all $\eta \in W_2^{1,1}(\Omega \times (0,T))$ with $\eta(T) = 0$ the weak formulation (5.3.8).

Finally, for such pair property (5.3.10) follows from a standard extensibility argument. □

Theorem 5.3.2. *There is $T_{max} \in (0,\infty]$ and a solution (u_l, h_l) of (5.3.7) with $0 \leqslant u_l$ and $0 \leqslant h_l < H$ and*

$$u_l, h_l \in C(\overline{\Omega} \times [0, T_{max})) \cap C^{2,1}(\overline{\Omega} \times (0, T_{max})). \tag{5.3.31}$$

The solution is unique if $p \geqslant \frac{2n}{n+2}$ for $n \geqslant 3$ and $p \in (1,\infty)$ for $n = 1, 2$.

Proof. 1. *Regularity:* Let $l \in \mathbb{N}$, $0 < T_1 < T_{max}$ and consider the weak solution (u_l, h_l) from *Lemma 5.3.1*. Again from *Remark A.1.2* and *Theorem A.1.12* with a and b as in (5.3.17) and (5.3.20), respectively, it follows that $u_l \in C^{\lambda,\frac{\lambda}{2}}(\overline{\Omega} \times (0, T_1])$ and $h_l \in C^{\lambda,\frac{\lambda}{2}}(\overline{\Omega} \times [0, T_1])$ for some $\lambda \in (0,1)$. Combining this with the Lipschitz continuity of g, *Theorem A.1.5* with $a_{ii} := D_H$ and $f := -g(u,h)$ and all other coefficients equal to zero implies $h_l \in C^{2+\lambda,1+\frac{\lambda}{2}}(\Omega \times (0,T_1))$.

Let $t_0 \in (0, T_1)$. We consider $\xi \in C^\infty(\mathbb{R}, [0,1])$ satisfying $\xi \equiv 0$ on $(-\infty, \frac{t_0}{2}]$ and $\xi \equiv 1$ on $[t_0, \infty)$. Then, $\tilde{h}(x,t) := h_l(x,t)\xi(t) \in W_2^{2,1}(\Omega \times (0,T_1))$ is a strong solution of the IBVP

$$\begin{cases} \partial_t \tilde{h} = D_H \Delta \tilde{h} + g(u_l, h_l)\xi + h_l \xi' & \text{in } \Omega \times (0, T_1), \\ \partial_\nu \tilde{h} = 0 & \text{on } \partial\Omega \times (0, T_1), \\ \tilde{h}(\cdot, 0) = 0 & \text{in } \Omega. \end{cases}$$

Due to the Lipschitz continuity of g and the boundedness of u_l on $\overline{\Omega} \times [0, T_1]$, *Theorem A.1.13* with

$$a(\nabla h_{lk}) := D_H \nabla h_{lk},$$
$$b(x,t) := -g(u_l(x,t), h_l(x,t))\xi(t) - h_l(x,t)\xi'(t)$$

especially implies that $\nabla \tilde{h} \in C(\overline{\Omega} \times [0, T_1], \mathbb{R}^n)$ and consequently, h_l is a classical solution of the nonhomogeneous heat equation in (5.3.7) on $\Omega \times (0, T_1)$. Finally, using again the Lipschitz continuity of g and the Hölder continuity of u_l and h_l, *Theorem A.1.7* implies that $\tilde{h}$ is also in $C^{2,1}(\overline{\Omega} \times [0, T_1])$ which leads to $h_l \in C^{2,1}(\overline{\Omega} \times (0, T_{max}))$. Analogously, $u_l \in C^{2,1}(\overline{\Omega} \times (0, T_{max}))$ follows.

The boundedness by H of h_l follows applying *Proposition A.1.14* on $\Omega \times (0, T_1)$ using the boundedness of h_l on the closure of this set, the fact that $h \in W_2^{2,1}(\Omega \times (0,T_1))$, our assumptions on g and the estimate

$$\partial_t(h_l - H) - D_H \Delta(h_l - H) = g(u_l, h_l) = \partial_h g(\zeta)(h_l - H) + g(u_l, H) \leqslant \partial_h g(\zeta)(h_l - H)$$

that holds for all $(x,t) \in \Omega \times (0,T_1)$ for some $\zeta(x,t) \in (h_l(x,t),H)$ due to the mean value theorem. Analogously, the nonnegativity of h follows.

2. *Uniqueness:* Let $p \geqslant \frac{2n}{n+2}$ for $n \geqslant 3$ or $p \in (1,\infty)$ for $n = 1,2$. With an ansatz similar to [13] we want to show the uniqueness of the solution. Assume that there are two solutions (u_1,h_1), (u_2,h_2) of (5.3.7) for $l \in \mathbb{N}$ with the regularity from (5.3.31). The functions h_1 and h_2 satisfy

$$\partial_t(h_1 - h_2) = D_H\Delta(h_1 - h_2) + g(u_1,h_1) - g(u_2,h_2)$$

in $\Omega \times (0,T_1)$. We multiply this equation by $h_1 - h_2$ and integrate over Ω. Then, using partial integration, the Lipschitz continuity of g, and Young's inequality we conclude from Gronwall's inequality that

$$\|h_1 - h_2\|_{L^\infty(0,t;L^2(\Omega))},\ \|\nabla(h_1 - h_2)\|_{L^2(0,t;(L^2(\Omega))^n)} \leqslant C_{11}(T_1)\|u_1 - u_2\|_{L^2(\Omega\times(0,t))} \tag{5.3.32}$$

for $t \in (0,T_1)$. Moreover, we can rewrite

$$\begin{aligned}\partial_t(u_1 - u_2) =&\nabla\nabla : (\mathbb{D}_l(u_1 - u_2)) + \nabla\cdot(\mathbb{D}_l(u_1\nabla h_1 - u_2\nabla h_2))\\ &+ \mu(h_1)u_1^\alpha(1 - J * u_1^\beta) - \mu(h_2)u_2^\alpha(1 - J * u_2^\beta)\\ =&\nabla\nabla : (\mathbb{D}_l(u_1 - u_2)) + \nabla\cdot(\mathbb{D}_l(u_1 - u_2)\nabla h_1) + \nabla\cdot(\mathbb{D}_l u_2\nabla(h_1 - h_2))\\ &+ (\mu(h_1) - \mu(h_2))u_1^\alpha(1 - J * u_1^\beta) + \mu(h_2)(u_1^\alpha - u_2^\alpha)(1 - J * u_1^\beta)\\ &+ \mu(h_2)u_2^\alpha J * (u_2^\beta - u_1^\beta).\end{aligned} \tag{5.3.33}$$

With the boundedness of u_2 on $\Omega \times (0,T_1)$ by some $C_{12}(T_1,l) > 0$, Hölder's inequality, the mean value theorem and the Sobolev embedding from *Lemma 2.2.8(i)* we estimate

$$\begin{aligned}|J * (u_2^\beta - u_1^\beta)| \leqslant&\beta C_{12}^{\beta-1}(T_1,l)\int_\Omega |J(x-y)||u_1(y) - u_2(y)|\,\mathrm{d}y\\ \leqslant&\beta C_{12}^{\beta-1}(T_1,l)\|J\|_{L^p(B)}\|u_1 - u_2\|_{L^{\frac{p}{p-1}}(\Omega)} \leqslant C_{13}(T_1,l)\|u_1 - u_2\|_{H^1(\Omega)}.\end{aligned} \tag{5.3.34}$$

Again, we multiply (5.3.33) by $u_1 - u_2$ and integrate over Ω for $t \in (0,T_1)$. Then, using partial integration together with Young's and Hölder's inequality, the mean value theorem, the Lipschitz continuity of μ, *Lemma 2.3.2(i)*, the boundedness of u_1 and u_2, the boundedness of ∇h_1 by some $C_{14}(T_1,l) > 0$ and (5.3.6) and (5.3.34), it follows that

$$\begin{aligned}&\frac{1}{2}\frac{d}{dt}\|u_1 - u_2\|_{L^2(\Omega)}^2 + D_1\|\nabla(u_1 - u_2)\|_{(L^2(\Omega))^n}^2\\ \leqslant& -\int_\Omega \nabla\cdot\mathbb{D}_l(u_1 - u_2)\nabla(u_1 - u_2) + (u_1 - u_2)(\mathbb{D}_l\nabla h_1)\cdot\nabla(u_1 - u_2)\\ &\qquad + u_2(\mathbb{D}_l\nabla(h_1 - h_2))\cdot\nabla(u_1 - u_2)\,\mathrm{d}x\\ &+ \int_\Omega [(\mu(h_1) - \mu(h_2))u_1^\alpha(1 - J * u_1^\beta) + \mu(h_2)(u_1^\alpha - u_2^\alpha)(1 - J * u_1^\beta)\\ &\qquad + \mu(h_2)u_2^\alpha J * (u_2^\beta - u_1^\beta)](u_1 - u_2)\,\mathrm{d}x\\ \leqslant&(\|\nabla\cdot\mathbb{D}_l\|_{(L^\infty(\Omega))^n} + \|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}}\|\nabla h_1\|_{(L^\infty(\Omega))^n})\int_\Omega |u_1 - u_2||\nabla(u_1 - u_2)|\,\mathrm{d}x\\ &+ \|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}}C_{12}(T_1,l)\int_\Omega |\nabla(h_1 - h_2)||\nabla(u_1 - u_2)|\,\mathrm{d}x\\ &+ L_\mu C_{12}^\alpha(T_1,l)(1 + \|J\|_{L^1(B)}C_{12}^\beta(T_1,l))\int_\Omega |h_1 - h_2||u_1 - u_2|\,\mathrm{d}x\end{aligned}$$

$$
\begin{aligned}
&+\|\mu\|_{L^\infty(0,H)}\alpha C_{12}^{\alpha-1}(T_1,l)(1+\|J\|_{L^1(B)}C_{12}^{\beta}(T_1,l))\int_\Omega |u_1-u_2|^2\,\mathrm{d}x\\
&+\|\mu\|_{L^\infty(0,H)}C_{12}^{\alpha}(T_1,l)C_{13}(T_1,l)\|u_1-u_2\|_{H^1(\Omega)}\int_\Omega |u_1-u_2|\,\mathrm{d}x\\
\leqslant& C_{15}(T_1,l)\left(\|u_1-u_2\|_{L^2(\Omega)}^2+\|h_1-h_2\|_{L^2(\Omega)}^2+\|\nabla(h_1-h_2)\|_{(L^2(\Omega))^n}^2\right)\\
&+D_1\|\nabla(u_1-u_2)\|_{(L^2(\Omega))^n}^2.
\end{aligned}
$$

Integrating over $(0,t)$ for $t\in(0,T_1)$ and using (5.3.32) we conclude that for a.e. $t\in(0,T_1)$ it holds that

$$
\begin{aligned}
\|u_1-u_2\|_{L^2(\Omega)}^2 \leqslant& C_{16}(T_1,l)\left(\int_0^t \|u_1-u_2\|_{L^2(\Omega)}^2+\|\nabla(h_1-h_2)\|_{(L^2(\Omega))^n}^2+\|h_1-h_2\|_{L^2(\Omega)}^2\right)\\
\leqslant& C_{17}(T_1,l)\int_0^t \|u_1-u_2\|_{L^2(\Omega)}^2\,\mathrm{d}t.
\end{aligned}
$$

Consequently, combining this with Gronwall's inequality and (5.3.32) implies that $u_1\equiv u_2$ and $h_1\equiv h_2$ a.e. on $\Omega\times(0,T_1)$. □

5.3.2 Global existence and boundedness of u in the approximate problem

Lemma 5.3.3. *There is a positive constant C_{18} independent from l s.t.*

$$\|\nabla h_l\|_{L^\infty(0,T_{max};(L^\infty(\Omega))^n)}\leqslant C_{18}$$

holds for all $l\in\mathbb{N}$.

Proof. Let $l\in\mathbb{N}$. We have shown in *Lemma 5.3.1* that h_l satisfies

$$h_l(t)=\Psi(h_l)(t)=e^{tD_H\Delta}h_0+\int_0^t e^{(t-s)D_H\Delta}g(u_l,h_l)\,\mathrm{d}s$$

for $t\in(0,T_{max})$. With *Lemma A.1.18(ii)* and *(iii)* and (5.3.13) we estimate that

$$
\begin{aligned}
\|\nabla h_l(t)\|_{(L^q(\Omega))^n}\leqslant& K_{12}e^{-\lambda_1 D_H t}\|\nabla h_0\|_{(L^q(\Omega))^n}\\
&+K_{11}|\Omega|^{\frac{1}{q}}\int_0^t\left(1+\frac{1}{(D_H(t-s))^{\frac{1}{2}}}\right)e^{-\lambda_1 D_H(t-s)}\|g(u_l,h_l)\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}\,\mathrm{d}s
\end{aligned}
$$

holds for all $q\in(1,\infty)$, where λ_1 is the first positive eigenvalue of $-\Delta$ on Ω with Neumann boundary condition. Using the properties of g, the uniform boundedness of (h_l) and Hölder's inequality, we conclude that

$$
\begin{aligned}
\|\nabla h_l(t)\|_{(L^q(\Omega))^n}\leqslant& K_{12}|\Omega|^{\frac{1}{q}}\|\nabla h_0\|_{(L^\infty(\Omega))^n}\\
&+K_{11}|\Omega|^{\frac{1}{q}}(\|\partial_h g\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}H+G)\int_0^t\left(1+\frac{1}{(D_H(t-s))^{\frac{1}{2}}}\right)e^{-\lambda_1 D_H(t-s)}\,\mathrm{d}s\\
\leqslant& K_{12}|\Omega|^{\frac{1}{q}}\|\nabla h_0\|_{(L^\infty(\Omega))^n}+\frac{K_{11}|\Omega|^{\frac{1}{q}}(\|\partial_h g\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}H+G)}{D_H}\left(\frac{1}{\lambda_1}+\frac{\sqrt{\pi}}{\sqrt{\lambda_1}}\right).
\end{aligned}
$$

Consequently,

$$\|\nabla h_l\|_{(L^\infty(\Omega))^n}=\lim_{q\to\infty}\|\nabla h_l\|_{(L^q(\Omega))^n}$$

$$\leqslant K_{12}\|\nabla h_0\|_{(L^\infty(\Omega))^n} + \frac{K_{11}(\|\partial_h g\|_{L^\infty(\mathbb{R}_0^+\times\mathbb{R}_0^+)}H + G)}{D_H}\left(\frac{1}{\lambda_1} + \frac{\sqrt{\pi}}{\sqrt{\lambda_1}}\right) =: C_{18}$$

□

We will show the global boundedness of u_l as in the proof of Theorem 1.1 in [99]. For a more detailed proof of the boundedness of the corresponding solution see *Chapter 6*, where the same method will be used.

Lemma 5.3.4. *For all $l \in \mathbb{N}$ and $q \in [1,\infty)$ it holds that $u_l \in L^\infty(0,T_{max};L^q(\Omega))$.*

Proof. Let $l \in \mathbb{N}$ and $q > \max\{1, \beta+\alpha-1\}$. Due to (5.3.31) the terms in the estimates below are well-defined for a.e. $t \in (0,T_{max})$. Multiplying the first equation of (5.3.7) by qu_l^{q-1}, integrating over Ω and using partial integration, we obtain

$$\begin{aligned}\frac{d}{dt}\int_\Omega u_l^q\,\mathrm{d}x =& q\int_\Omega \nabla\cdot(\mathbb{D}_l\nabla u_l + (\nabla\cdot\mathbb{D}_l)u_l + \mathbb{D}_l u_l\nabla h_l)\,u_l^{q-1} + \mu(h_l)u_l^{q-1+\alpha}(1-J*u_l^\beta)\,\mathrm{d}x\\ =& -q(q-1)\int_\Omega u_l^{q-2}(\mathbb{D}_l\nabla u_l)\cdot\nabla u_l + u_l^{q-1}(\nabla\cdot\mathbb{D}_l)\cdot\nabla u_l + u_l^{q-1}(\mathbb{D}_l\nabla h_l)\cdot\nabla u_l\,\mathrm{d}x\\ &+ q\int_\Omega \mu(h_l)u_l^{q-1+\alpha}(1-J*u_l^\beta)\,\mathrm{d}x. \end{aligned} \tag{5.3.35}$$

Using the uniform parabolicity of $\mathbb{D}_l$ and $\nabla u^{\frac{q}{2}} = \frac{q}{2}u^{\frac{q}{2}-1}\nabla u$, we estimate

$$\begin{aligned}q(q-1)\int_\Omega u_l^{q-2}(\mathbb{D}_l\nabla u_l)\cdot\nabla u_l\,\mathrm{d}x =& \frac{4(q-1)}{q}\sum_{i,j=1}^n\int_\Omega d_{lij}\left(u_l^{\frac{q}{2}}\right)_{x_i}\left(u_l^{\frac{q}{2}}\right)_{x_j}\mathrm{d}x\\ \geqslant& \frac{4(q-1)}{q}D_1\int_\Omega|\nabla u_l^{\frac{q}{2}}|^2\,\mathrm{d}x.\end{aligned}$$

Further, due to Young's inequality and *Lemma 5.3.3* we obtain the estimate

$$\begin{aligned}&q(q-1)\left|\int_\Omega u_l^{q-1}(\nabla\cdot\mathbb{D}_l)\cdot\nabla u_l + u_l^{q-1}(\mathbb{D}_l\nabla h_l)\cdot\nabla u_l\,\mathrm{d}x\right|\\ \leqslant& 2(q-1)\left(\|\nabla\cdot\mathbb{D}_l\|_{(L^\infty(\Omega))^n} + \|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}}\|\nabla h_l\|_{(L^\infty(\Omega))^n}\right)\int_\Omega u_l^{\frac{q}{2}}|\nabla u_l^{\frac{q}{2}}|\,\mathrm{d}x\\ \leqslant& \frac{2(q-1)}{q}D_1\int_\Omega|\nabla u_l^{\frac{q}{2}}|^2\,\mathrm{d}x\\ &+\frac{q(q-1)}{D_1}\left(\|\nabla\cdot\mathbb{D}_l\|^2_{(L^\infty(\Omega))^{n\times n}} + \|\mathbb{D}_l\|^2_{(L^\infty(\Omega))^{n\times n}}C_{18}^2\right)\int_\Omega u_l^q\,\mathrm{d}x.\end{aligned}$$

Inserting these estimates into (5.3.35) and using our assumptions on μ and J, the boundedness of h_l, and

$$\int_\Omega u_l^q\,\mathrm{d}x \leqslant \int_\Omega u_l^{q+\alpha-1}\,\mathrm{d}x + |\Omega|, \tag{5.3.36}$$

it follows that

$$\begin{aligned}&\frac{d}{dt}\int_\Omega u_l^q\,\mathrm{d}x + \frac{2(q-1)}{q}D_1\int_\Omega|\nabla u_l^{\frac{q}{2}}|^2\,\mathrm{d}x + q\eta\delta\int_\Omega u_l^{q-1+\alpha}\,\mathrm{d}x\int_\Omega u_l^\beta\,\mathrm{d}x\\ \leqslant& qC_{19}(q,l)\left(\int_\Omega u_l^{q-1+\alpha}\,\mathrm{d}x + |\Omega|\right),\end{aligned} \tag{5.3.37}$$

where

$$C_{19}(q,l) := \frac{q-1}{D_1}\left(\|\nabla\cdot\mathbb{D}_l\|^2_{(L^\infty(\Omega))^n} + \|\mathbb{D}_l\|^2_{(L^\infty(\Omega))^{n\times n}} C_{18}^2\right) + \|\mu\|_{L^\infty(0,H)}.$$

Adding $qC_{19}(q,l)\|u_l\|^q_{L^q}$ on both sides of (5.3.37) and using (5.3.36) one more time, we obtain

$$\begin{aligned}&\frac{d}{dt}\int_\Omega u_l^q \,\mathrm{d}x + qC_{19}(q,l)\int_\Omega u_l^q \,\mathrm{d}x + 2\frac{q-1}{q}D_1\int_\Omega |\nabla u_l^{\frac{q}{2}}|^2 \,\mathrm{d}x + q\delta\eta\int_\Omega u_l^{q-1+\alpha}\,\mathrm{d}x\int_\Omega u_l^\beta \,\mathrm{d}x\\ \leqslant& 2qC_{19}(q,l)\left(\int_\Omega u_l^{q-1+\alpha}\,\mathrm{d}x + |\Omega|\right). \end{aligned}\tag{5.3.38}$$

It follows from *Lemma A.4.1* with $K_{18} = \frac{2C_{19}}{D_1}$ and $K_{22} = \frac{2C_{19}}{\delta\eta}$ that

$$\begin{aligned}2qC_{19}(q,l)\int_\Omega u_l^{q-1+\alpha} \leqslant& 2\frac{q-1}{q}D_1\int_\Omega |\nabla u_l^{\frac{q}{2}}|^2\,\mathrm{d}x + q\delta\eta\int_\Omega u_l^{q-1+\alpha}\,\mathrm{d}x\int_\Omega u_l^\beta\,\mathrm{d}x\\ &+ 2qC_{19}(q,l)K_{23}(q,l),\end{aligned}$$

where

$$\begin{aligned}K_{23}(q,l) :=& \left(2\left(\frac{2K_{21}^2 q^2 C_{19}(q,l)}{(q-1)D_1}\right)^{\frac{q+\alpha-1-\beta}{q-\alpha+1+\beta-2\frac{q+\alpha-1+\beta}{s}}} + K_{24}(q)^{\frac{q+\alpha-1-\beta}{q-\frac{q+\alpha-1+\beta}{s}}}\right)^{\frac{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\\ &\cdot\left(\frac{2C_{19}(q,l)}{\delta\eta}\right)^{\frac{q-\frac{2(q+\alpha-1)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}} K_{24}(q)^{\frac{q+\alpha-1-\beta}{q-\frac{q+\alpha-1+\beta}{s}}}\end{aligned}$$

with

$$\begin{aligned}K_{21} &:= 2K_S(s)(1+2K_P),\\ K_{24}(q) &:= 4K_S(s)|\Omega|^{\frac{1}{2}-\frac{q}{q+\alpha-1+\beta}}.\end{aligned}$$

Here, $K_S(s) > 0$ denotes the Sobolev embedding constant from $H^1(\Omega)$ into $L^s(\Omega)$ from *Lemma 2.2.8(i)*, $K_P > 0$ the constant from the Poincaré inequality, and

$$s\begin{cases} = \infty, & n=1,\\ \in\left(\frac{2(q+\alpha-1+\beta)}{q-\alpha+1+\beta},\infty\right), & n=2,\\ = \frac{2n}{n-2}, & n>2.\end{cases}\tag{5.3.39}$$

Hence, for $t \in (0, T_{max})$ we conclude that

$$\frac{d}{dt}\|u_l\|^q_{L^q(\Omega)} + qC_{19}(q,l)\|u_l\|^q_{L^q(\Omega)} \leqslant 2qC_{19}(q,l)(K_{23}(q,l)+|\Omega|)\tag{5.3.40}$$

and obtain for $t \in (0, T_{max})$ from (5.3.40) and setting $K_{14} = qC_{19}$ and $K_{15} = 2(K_{23} + |\Omega|)$ in *Lemma A.1.20* the upper bound

$$\|u_l(\cdot,t)\|_{L^q(\Omega)} \leqslant \sqrt[q]{2K_{23}(q,l)+2|\Omega| + \|u_{0l}\|^q_{L^q(\Omega)}} \leqslant \sqrt[q]{2K_{23}(q,l)+|\Omega|\left(2+\|u_{0l}\|^q_{L^\infty(\Omega)}\right)}.\tag{5.3.41}$$

□

Remark 5.3.5. As in [99] we cannot directly conclude from *Lemma 5.3.4* that u_l is bounded on $\Omega\times(0,T_{max})$ as

$$\lim_{q\to\infty}\sqrt[q]{2K_{23}(q,l)+|\Omega|\left(2+\|u_{0l}\|^q_{L^\infty(\Omega)}\right)} = \infty$$

due to

$$\left(\left(\frac{q^2C_{19}(q,l)}{q-1}\right)^{\frac{q+\alpha-1-\beta}{q-\alpha+1+\beta-2\frac{q+\alpha-1+\beta}{s}}\cdot\frac{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right)^{\frac{1}{q}}$$
$$\geqslant(\|\mu\|_{L^\infty(0,H)}q)^{\frac{1}{q}\cdot\frac{q+\alpha-1-\beta}{\beta+1-\alpha-\frac{2\beta}{s}}}=\left((\|\mu\|_{L^\infty(0,H)}q)^{1+\frac{\alpha-1-\beta}{q}}\right)^{\frac{1}{\beta+1-\alpha-\frac{2\beta}{s}}}\underset{q\to\infty}{\to}\infty.$$

Theorem 5.3.6. *For all $l\in\mathbb{N}$ there is a unique bounded and nonnegative solution (u_l,h_l) of (5.3.7) consisting of nonnegative functions*

$$u_l,h_l\in C(\overline{\Omega}\times[0,\infty))\cap C^{2,1}(\overline{\Omega}\times(0,\infty)).$$

Thereby, $h_l<H$ and there is some $C_{20}(u_{0l})>0$ s.t. $u_l\leqslant C_{20}(u_{0l})$ and

$$C_{20}(u_{0l})\underset{l\to\infty}{\to}C_{21}. \tag{5.3.42}$$

Moreover, for $K>1$ and some 'small' enough choice of parameters of type (5.3.47) and (5.3.48) below, it holds that

$$\|u_l\|_{L^\infty(\Omega\times(0,\infty))}\leqslant K\max\left\{1,\|u_{0l}\|_{L^\infty(\Omega)},\left(4K_S(s)|\Omega|^{-\frac{1}{2}}\right)^{\frac{1-\frac{2}{s}}{(1-\frac{1}{s})(\beta+1-\alpha-\frac{2\beta}{s})}}\left(\frac{2}{\delta\eta}\right)^{\frac{1-\frac{2}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right\}. \tag{5.3.43}$$

If Ω is convex, the constant $K_S(s)$ is explicitely given in Remark 6.3.4 in Chapter 6.

Proof. Let $l\in\mathbb{N}$. We proceed with a Moser iteration as in Step 2 of the proof of Theorem 1.1. in [99].

Set $q_k:=2^k+a$ with $a:=\frac{2(s-1)(\alpha-1)}{s-2}$ for $k\in\mathbb{N}$ large enough s.t. $q_k>\max\{1,\beta+\alpha-1\}$ holds. As in Step 2 of *Lemma 6.3.2* we obtain for $t\in(0,T_{max})$ the estimate

$$\frac{d}{dt}\|u_l\|^{q_k}_{L^{q_k}(\Omega)}+q_kC_{19}(q_k,l)\|u_l\|^{q_k}_{L^{q_k}(\Omega)}\leqslant 2q_kC_{19}(q_k,l)C_{22}(q_k,l)\max\left\{1,\|u_l\|^{2q_{k-1}}_{L^{q_{k-1}}}\right\}, \tag{5.3.44}$$

where

$$C_{22}(q_k,l):=2\left(\frac{2K_{21}^2q_k^2C_{19}(q_k,l)}{(q_k-1)D_1}\right)^{\frac{s}{s-2}}+2\left(\max\{4K_S(s),1\}\max\{1,|\Omega|^{-\frac{1}{2}}\}\right)^{\alpha+1}+|\Omega|.$$

Due to (5.3.5), there is $C_{23}>0$ s.t. $\|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}},\|\nabla\cdot\mathbb{D}_l\|_{(L^\infty(\Omega))^n}\leqslant C_{23}$ for all $l\in\mathbb{N}$. We can further estimate using the definition of q_k that

$$\begin{aligned}C_{19}(q_k,l)&\leqslant\frac{q_k-1}{D_1}C_{23}^2(1+C_{18}^2)+\|\mu\|_{L^\infty(0,H)},\\&\leqslant\left(\frac{1+a}{D_1}C_{23}^2(1+C_{18}^2)+\|\mu\|_{L^\infty(0,H)}\right)2^k\end{aligned} \tag{5.3.45}$$

and consequently,

$$\begin{aligned}C_{22}(q_k,l)\leqslant&2\left(\frac{2K_{21}^2}{D_1}2^k(1+a)\left(\frac{1+a}{D_1}C_{23}^2(1+C_{18}^2)+\|\mu\|_{L^\infty(0,H)}\right)2^k\right)^{\frac{s}{s-2}}\\&+2\left(\max\{4K_S(s),1\}\max\{1,|\Omega|^{-\frac{1}{2}}\}\right)^{\alpha+1}+|\Omega|\end{aligned}$$

$$\leqslant 2^{2k\frac{s}{s-2}} C_{24}$$

for

$$C_{24} := 2\left(2\frac{K_{21}^2}{D_1}(1+a)\left(\frac{1+a}{D_1}C_{23}^2\left(1+C_{18}^2\right)+\|\mu\|_{L^\infty(0,H)}\right)\right)^{\frac{s}{s-2}} + 2\left(\max\{4K_S(s),1\}\max\{1,|\Omega|^{-\frac{1}{2}}\}\right)^{\alpha+1} + |\Omega|.$$

For $k \in \mathbb{N}$ and $t \in (0, T_{max})$ we set

$$y_k(t) := \|u_l(\cdot,t)\|_{L^{q_k}(\Omega)}^{q_k}.$$

Inserting this into (5.3.44) we obtain

$$y_k'(t) + q_k C_{19}(q_k,l) y_k(t) \leqslant 2q_k C_{19}(q_k,l) 2^{2k\frac{s}{s-2}} C_{24} \max\left\{1, \left(\int_\Omega u_l^{q_{k-1}}\right)^2\right\}.$$

Moreover, we estimate that

$$\|u_{0l}\|_{L^{q_k}(\Omega)}^{q_k} \leqslant \|u_{0l}\|_{L^\infty(\Omega)}^{q_k}|\Omega| = \|u_{0l}\|_{L^\infty(\Omega)}^{2^k}\|u_{0l}\|_{L^\infty(\Omega)}^{a}|\Omega|.$$

Hence, from *Lemma A.4.3* with $c_k = q_k C_{19}(q_k,l)$, $\bar{a} = 2C_{24}$ and $D = 2\frac{s}{s-2}$ it follows that for $k \geqslant m \geqslant 1$ large enough (s.t. $2C_{24}2^{2\frac{s}{s-2}m} \geqslant 1$) and $t \in (0, T_{max})$ it holds that

$$\int_\Omega u_l^{q_k}\,\mathrm{d}x \leqslant (4C_{24})^{2^{k-m+1}} 2^{\frac{2s}{s-2}\left(2(2^{k-m}-1)+m2^{k-m+1}-k\right)} \cdot \max\left\{\sup_{t\geqslant 0}\left(\int_\Omega u_l^{q_{m-1}}\right)^{2^{k-m+1}}, \|u_{0l}\|_{L^\infty(\Omega)}^{2^k}(\|u_{0l}\|_{L^\infty(\Omega)}^{a}|\Omega|)^{2^{k-m}}, 1\right\}.$$

Consequently, for $t \in (0, T_{max})$ and $m \geqslant 1$ large enough it holds that

$$\begin{aligned}\|u_l\|_{L^\infty(\Omega)} &= \lim_{k\to\infty}\|u_l\|_{L^{q_k}(\Omega)} \\ &\leqslant (4C_{24})^{2^{-m+1}} 2^{\frac{2s(1+m)}{(s-2)2^{m-1}}} \max\left\{\sup_{t\geqslant 0}\left(\int_\Omega u_l^{q_{m-1}}\right)^{2^{-m+1}}, \|u_{0l}\|_{L^\infty(\Omega)}(\|u_{0l}\|_{L^\infty(\Omega)}^{a}|\Omega|)^{2^{-m}}, 1\right\} \\ &=: C_{25}(m,l).\end{aligned} \tag{5.3.46}$$

Due to (5.3.41) and (5.3.45) there is $C_{20}(m,u_{0l}) > 0$ s.t. $\|u_l\|_{L^\infty(\Omega\times(0,T_{max}))} \leqslant C_{20}(m,u_{0l})$ for all $l \in \mathbb{N}$. Together with (5.3.4) this implies the existence of $C_{21}(m)$ s.t. $C_{20}(m,u_{0l}) \to C_{21}(m)$ for $l \to \infty$.

Consequently, u_l is bounded on $\overline{\Omega} \times [0, T_{max})$. Combining this with the boundedness of h_l, *Lemma 5.3.3* and (5.3.10) in *Theorem 5.3.2*, $T_{max} = \infty$ follows.

We proceed as in Step 3 of the proof of Theorem 1.1 in [99]. First, we fix some m and choose our parameters sufficiently 'small' s.t.

$$\begin{aligned}&\frac{2K_{21}^2}{D_1}\left(\frac{q_{m-1}}{D_1}\left(\|\nabla\cdot\mathbb{D}_l\|_{(L^\infty(\Omega))^n}^2 + \|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}}^2 C_{18}^2\right) + \|\mu\|_{L^\infty(0,H)}\right) \\ \leqslant &\frac{2K_{21}^2}{D_1}\left(\frac{q_{m-1}}{D_1}C_{23}^2\left(1+C_{18}^2\right) + \|\mu\|_{L^\infty(0,H)}\right) < \frac{1}{q_{m-1}^2}\end{aligned} \tag{5.3.47}$$

and

$$C_{19}(q_{m-1}) \leqslant \frac{q_{m-1}-1}{D_1}C_{23}^2\left(1+C_{18}^2\right) + \|\mu\|_{L^\infty(0,H)} \leqslant 1 \tag{5.3.48}$$

are satisfied. This depends on our choice of $\mathbb{D}$, μ, g, h_0, and D_H. Consequently, we conclude again from (5.3.41) that

$$\begin{aligned}
&\int_\Omega u_l^{q_{m-1}}\,\mathrm{d}x\\
\leqslant& 5\max\Bigg\{\Bigg(2\left(\frac{1}{q_{m-1}-1}\right)^{\frac{q_{m-1}+\alpha-1-\beta}{q_{m-1}-\alpha+\beta+1-\frac{2(q_{m-1}+\alpha-1+\beta)}{s}}}\\
&\qquad +K_{24}(q_{m-1})^{\frac{q_{m-1}+\alpha-1-\beta}{q_{m-1}-\frac{q_{m-1}+\alpha-1+\beta}{s}}}\Bigg)^{\frac{q_{m-1}-\alpha+1+\beta-\frac{2(q_{m-1}+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\\
&\qquad\cdot\left(\frac{2}{\delta\eta}\right)^{\frac{q_{m-1}-\frac{2(q_{m-1}+\alpha-1)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}, K_{24}(q_{m-1})^{\frac{q_{m-1}+\alpha-1-\beta}{q_{m-1}-\frac{q_{m-1}+\alpha-1+\beta}{s}}}, |\Omega|\left(2+\|u_{0l}\|_{L^\infty(\Omega)}^{q_{m-1}}\right)\Bigg\}\\
=:& H(m).
\end{aligned}$$

With $(4C_{24})^{2^{-m+1}}2^{\frac{2s(1+m)}{(s-2)2^{m-1}}}\to 1$ and $\left(\|u_{0l}\|^a_{L^\infty(\Omega)}|\Omega|\right)^{2^{-m}}\to 1$ for $m\to\infty$ and

$$\lim_{m\to\infty}H(m)^{\frac{1}{2^{m-1}}}=\max\left\{\left(4K_S(s)|\Omega|^{-\frac12}\right)^{\frac{1-\frac{2}{s}}{(1-\frac{1}{s})(\beta+1-\alpha-\frac{2\beta}{s})}}\left(\frac{2}{\delta\eta}\right)^{\frac{1-\frac{2}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}, \|u_{0l}\|_{L^\infty(\Omega)}, 1\right\}$$

we conclude from (5.3.46) that

$$\|u_l\|_{L^\infty(\Omega\times(0,\infty))}\leqslant\max\left\{1, \|u_{0l}\|_{L^\infty(\Omega)}, \left(4K_S(s)|\Omega|^{-\frac12}\right)^{\frac{1-\frac{2}{s}}{(1-\frac{1}{s})(\beta+1-\alpha-\frac{2\beta}{s})}}\left(\frac{2}{\delta\eta}\right)^{\frac{1-\frac{2}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right\}.$$

There are obviously no parameters satisfying (5.3.47) and (5.3.48) for all m. But for any $K>1$ we find 'small' enough parameters (satisfying (5.3.47) and (5.3.48) for some large enough m) such that (5.3.43) holds. □

5.3.3 Global existence and boundedness in the original problem

Theorem 5.3.7. *There is a bounded and nonnegative weak solution (u,h) of (5.3.1) s.t. for all $T>0$ it holds that $u\in C([0,T];L^2(\Omega))\cap L^2(0,T;H^1(\Omega))$ with $\partial_t u\in L^2(0,T;H^{-1}(\Omega))$ and $h\in C([0,T];H^1(\Omega))\cap W_2^{2,1}(\Omega\times(0,T))\cap L^\infty(0,T;W^1_\infty(\Omega))$ and for all $\eta\in W_2^{1,1}(\Omega\times(0,T))$ with $\eta(T)=0$ the functions u and h satisfy*

$$\begin{aligned}
&-\int_0^T\int_\Omega u\eta_t\,dx\,dt+\int_0^T\int_\Omega(\nabla\cdot\mathbb{D}u+\mathbb{D}\nabla u+\mathbb{D}u\nabla h)\cdot\nabla\eta\,dx\,dt\\
=&\int_0^T\int_\Omega\mu(h)u^\alpha(1-J*u^\beta)\eta\,dx\,dt+\int_\Omega u_0(x)\eta(x,0)\,dx, \qquad (5.3.49)
\end{aligned}$$

and

$$\begin{aligned}
&\partial_t h=D_H\Delta h+g(u,h) && \textit{a.e. in } \Omega\times(0,T) && (5.3.50)\\
&\nabla h\cdot\nu=0 && \textit{a.e. in } \partial\Omega\times(0,T), && (5.3.51)\\
&h(0)=h_0 && \textit{in } H^1(\Omega). && (5.3.52)
\end{aligned}$$

Moreover, $u \leqslant C_{21}$, $h \leqslant H$ *in* $\Omega \times (0,\infty)$. *For* $t_0 \in (0,\infty)$ *there are constants* $\gamma(t_0) \in (0,1)$ *and* $C_{26}(t_0) > 0$ *s.t.* $u, h \in C^{\gamma,\frac{\gamma}{2}}(\overline{\Omega} \times [t_0,\infty))$ *and for all* $t \in [t_0,\infty)$ *it holds that*

$$\|u\|_{C^{\gamma,\frac{\gamma}{2}}(\overline{\Omega}\times[t,t+1])}, \|h\|_{C^{\gamma,\frac{\gamma}{2}}(\overline{\Omega}\times[t,t+1])} \leqslant C_{26}. \tag{5.3.53}$$

For the parameter choice from Theorem 5.3.6 u satisfies (5.3.43).

The solution (u,h) *is unique for* $p \geqslant \frac{2n}{n+2}$ *for* $n \geqslant 3$ *and* $p \in (1,\infty)$ *for* $n = 1,2$.

Proof. Let $\varphi \in H^1(\Omega)$ and $T > 0$. Obviously, for each $l \in \mathbb{N}$ the function u_l satisfies

$$\int_\Omega \partial_t u_l \varphi \,\mathrm{d}x = -\int_\Omega (\mathbb{D}_l \nabla u_l + \nabla \cdot \mathbb{D}_l u_l + \mathbb{D}_l u_l \nabla h_l) \cdot \nabla\varphi \,\mathrm{d}x + \int_\Omega \mu(h_l) u_l^\alpha (1 - J * u_l^\beta) \,\mathrm{d}x, \tag{5.3.54}$$

for $t \in (0,\infty)$ as it is a classical solution. Due to *Theorem A.1.8*, h_l satisfies

$$\|h_l\|_{W_2^{2,1}(\Omega\times(0,T))} \leqslant C_{27}(T), \tag{5.3.55}$$

where $C_{27}(T) > 0$ is independent from l due to the properties of g and the uniform boundedness of $(h_l)_l$ and $(u_l)_l$.

There is a constant C_{23} independent from l s.t. $\|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}}, \|\nabla\cdot\mathbb{D}_l\|_{(L^\infty(\Omega))^n} \leqslant C_{23}$ for all $l \in \mathbb{N}$ due to (5.3.5). Setting $\varphi = u_l$ in (5.3.54) and using (5.3.6), Hölder's inequality, the continuity of μ and the uniform boundedness of $(h_l)_l, (u_l)_l$ from *Theorem 5.3.6*, we can estimate that

$$\frac{1}{2}\frac{d}{dt}\|u_l\|^2_{L^2(\Omega)} + D_1\|\nabla u_l\|^2_{(L^2(\Omega))^n} \leqslant C_{23}\|u_l\|_{L^2(\Omega)}(1 + C_{18})\|\nabla u_l\|_{(L^2(\Omega))^n} + C_{28}.$$

Consequently, Young's inequality and integration over $(0,T)$ lead

$$\|\nabla u_l\|_{L^2(0,T;(L^2(\Omega))^n)} \leqslant C_{29}(T)$$

for all $l \in \mathbb{N}$. Similarly (from (5.3.54) for $\varphi \in H_0^1(\Omega)$) it follows that

$$\|\partial_t u_l\|_{L^2(0,T;H^{-1}(\Omega))} \leqslant C_{30}(T)$$

for all $l \in \mathbb{N}$. Putting this together with the uniform boundedness of $(h_l)_l, (u_l)_l$, (5.3.55), *Lemma 5.3.3*, the Lions-Aubin lemma (respectively, with $H^1(\Omega) \hookrightarrow\hookrightarrow L^2(\Omega) \hookrightarrow H^{-1}(\Omega)$ and $H^2(\Omega) \hookrightarrow\hookrightarrow H^1(\Omega) \hookrightarrow L^2(\Omega)$), the Banach-Alaoglu theorem, *Lemma A.3.8* and *Lemma A.3.1* with $L^\infty(0,T;(L^\infty(\Omega))^n) = (L^1(0,T;(L^1(\Omega))^n))^*$ we conclude that there are $u \in C([0,T];L^2(\Omega)) \cap L^2(0,T;H^1(\Omega))$ with $\partial_t u \in L^2(0,T;H^{-1}(\Omega))$ and $h \in C([0,T];H^1(\Omega)) \cap W_2^{2,1}(\Omega\times(0,T)) \cap L^\infty(0,T;W^1_\infty(\Omega))$ s.t. (after switching to a subsequence if necessary)

$$u_l \underset{l\to\infty}{\to} u \quad \text{in } L^2(\Omega\times(0,T)) \text{ and pointwise a.e.,} \tag{5.3.56}$$

$$u_l \underset{l\to\infty}{\rightharpoonup} u \quad \text{in } L^2(0,T;H^1(\Omega)),$$

$$\partial_t u_l \underset{l\to\infty}{\rightharpoonup} \partial_t u \text{ in } L^2(0,T;H^{-1}(\Omega)),$$

$$h_l \underset{l\to\infty}{\to} h \quad \text{in } L^2(0,T;H^1(\Omega)) \text{ and pointwise a.e.,} \tag{5.3.57}$$

$$h_l \underset{l\to\infty}{\rightharpoonup} h \quad \text{in } L^2(0,T;H^2(\Omega)),$$

$$\partial_t h_l \underset{l\to\infty}{\rightharpoonup} \partial_t h \text{ in } L^2(\Omega\times(0,T)),$$

$$\nabla h_l \underset{l\to\infty}{\overset{*}{\rightharpoonup}} \nabla h \text{ in } L^\infty(0,T;(L^\infty(\Omega))^n). \tag{5.3.58}$$

The uniform boundedness of $(u_l)_l$ from (5.3.42) together with (5.3.56) and the dominated convergence theorem imply

$$J * u_l^\beta \underset{l\to\infty}{\to} J * u^\beta \text{ a.e. in } \Omega \times (0,T).$$

From this using the above convergences, the dominated convergence theorem, the uniform boundedness of $(u_l)_l$, $(h_l)_l$ and $(\nabla h_l)_l$ from *Lemma 5.3.3* and *Theorem 5.3.6*, the Lipschitz-continuity of μ and g, compensated compactness (*Lemma A.3.2*) and (5.3.5) and the fundamental lemma of variational calculus, it follows as in *Theorem 6.4.4* that (u,h) solves (5.3.1) in the required sense. Moreover, $u \in C([0,T];L^2(\Omega))$ holds due to *Theorem A.1.1.*

The a.e. boundedness and nonnegativity of u and h follow from the pointwise convergence and the uniform boundedness and nonnegativity of $(u_l)_l$ and $(h_l)_l$. Uniqueness follows similarly to *Theorem 5.3.2* using *Lemma A.1.3.*

Finally, the global boundedness of u, h, (5.3.5), *Lemmas 2.3.2* and *5.3.3* and the Lipschitz continuity of μ and g, *Theorem A.1.12* and *Remark A.1.2* with a and b, respectively, chosen similar to *Lemma 5.3.1* imply (5.3.53). □

5.4 Long time behavior

We consider the long time behavior of our solution under the additional assumptions that we make from now on:

- the domain Ω is convex,
- there are $h^* \in [0,H]$ and constants $C_H > 0$ and $C_U \geqslant 0$ s.t.

$$g(u,h)(h-h^*) \leqslant -C_H(h-h^*)^2 + C_U u^{\alpha-1}(u^\beta - U)^2 \tag{5.4.1}$$

  for $0 \leqslant h \leqslant H$ and $0 \leqslant u \leqslant U^{\frac{1}{\beta}}$, where $U^{\frac{1}{\beta}}$ is some upper bound on u_l for all $l \in \mathbb{N}$ (that exists and is independent from l, due to *Theorem 5.3.6*),
- we extend J by 0 to $\mathbb{R}^n \backslash B$ and assume $J = \frac{1}{U}\tilde{J}$ for a kernel $\tilde{J} \in L^1(\mathbb{R}^n)$ with norm $\|\tilde{J}\|_{L^1(\mathbb{R}^n)} = 1$,
- the parameters

$$C_B := \frac{1}{4D_1}\|\mu\|_{L^\infty(0,H)} \left(\operatorname{diam}(\Omega)\beta\right)^2 U^{\frac{\alpha-1}{\beta}}, \tag{5.4.2}$$

$$C_A := \frac{C_U C_{23}^2 \beta^2 U}{4\delta\eta|\Omega| D_H D_1} - 1 - C_B, \tag{5.4.3}$$

  where $\|\mathbb{D}_l\|_{(L^\infty(\Omega))^{n\times n}} \leqslant C_{23}$ for all $l \in \mathbb{N}$ (due to (5.3.5)), satisfy $C_A^2 > 4C_B$, $C_A < 0$, $C_B \in (0,1)$ and

$$C_B < -\frac{C_A}{2} + \sqrt{\frac{C_A^2}{4} - C_B}, \tag{5.4.4}$$

- $u_0 \not\equiv 0$, $u_0 \leqslant U^{\frac{1}{\beta}}$ and $\int_\Omega \ln(u_0)\,\mathrm{d}x < \infty$.

Moreover, let

$$M := \left\{\mathbb{D} \in \left(C^{2+\vartheta}(\bar{\Omega})\right)^{n\times n} : (\nabla\cdot\mathbb{D})\cdot\nu = 0 \text{ on } \partial\Omega,\, \nabla\cdot(\nabla\cdot\mathbb{D}) = 0 \text{ on } \Omega\right\}.$$

We assume that $\mathbb{D}$ is in the closure of M in the $C^1(\bar{\Omega},\mathbb{R}^{n\times n})$-norm and that the sequence $(\mathbb{D}_l)_{l\in\mathbb{N}}$ from *Section 5.3* is the sequence in M that approaches $\mathbb{D}$.

Remark 5.4.1. The inequality (5.4.1) implies that such h^* is unique and $g(U^{\frac{1}{\beta}}, h^*) = 0$ holds.

We proceed by combining the methods from [91, 99].

Lemma 5.4.2. *It holds that*

$$\int_0^\infty\int_\Omega u^{\alpha-1}(u^\beta - U)^2\,dx\,dt,\ \int_0^\infty\int_\Omega |h-h^*|^2\,dx\,dt < \infty. \tag{5.4.5}$$

Proof. Let $l\in\mathbb{N}$ and consider the global classical solution to (5.3.7) from *Theorem 5.3.6*. We conclude from *Proposition A.1.10* and the assumption $u_0 \not\equiv 0$ that $u_l > 0$ holds in $\Omega\times(0,\infty)$.

As in [99] we define $a(s) := \frac{s}{\beta} - \frac{U}{\beta}\ln(s) + \frac{U}{\beta}(\ln(U)-1)$ with $a(s)\geqslant 0$ for $s\in(0,\infty)$. By multiplying the equation for u_l in (5.3.7) by $u_l^{\beta-1} - Uu_l^{-1}$, integrating over Ω and using partial integration, we obtain

$$\begin{aligned}
\frac{d}{dt}\int_\Omega a(u_l^\beta)\,\mathrm{d}x &= \int_\Omega \partial_t u_l(u_l^{\beta-1} - Uu_l^{-1})\,\mathrm{d}x\\
&= \int_\Omega \nabla\cdot(\mathbb{D}_l\nabla u_l + \nabla\cdot\mathbb{D}_l u_l + \mathbb{D}_l u_l\nabla h_l)\left(u_l^{\beta-1} - Uu_l^{-1}\right)\mathrm{d}x\\
&\quad + \int_\Omega \mu(h_l)u_l^\alpha(1 - J * u_l^\beta)(u_l^{\beta-1} - Uu_l^{-1})\,\mathrm{d}x\\
&= -\int_\Omega (\mathbb{D}_l\nabla u_l + \nabla\cdot\mathbb{D}_l u_l + \mathbb{D}_l u_l\nabla h_l)\left((\beta-1)u_l^\beta + U\right)\cdot\frac{\nabla u_l}{u_l^2}\,\mathrm{d}x\\
&\quad + \frac{1}{U}\int_\Omega \mu(h_l)u_l^{\alpha-1}\left(U - \tilde{J} * u_l^\beta\right)\left(u_l^\beta - U\right)\mathrm{d}x.
\end{aligned}$$

Due to $\mathbb{D}_l\in M$ using partial integration again leads to

$$\begin{aligned}
&\int_\Omega \nabla\cdot\mathbb{D}_l u_l((\beta-1)u_l^\beta + U)\cdot\frac{\nabla u_l}{u_l^2}\,\mathrm{d}x\\
&= \int_\Omega \nabla\cdot\mathbb{D}_l((\beta-1)u_l^{\beta-1} + Uu_l^{-1})\cdot\nabla u_l\,\mathrm{d}x\\
&= \int_\Omega (\nabla\cdot\mathbb{D}_l)\cdot\nabla\left(\frac{\beta-1}{\beta}u_l^\beta + U\ln(u_l)\right)\mathrm{d}x\\
&= -\int_\Omega \nabla\cdot(\nabla\cdot\mathbb{D}_l)\left(\frac{\beta-1}{\beta}u_l^\beta + U\ln(u_l)\right)\mathrm{d}x + \int_{\partial\Omega}\left(\frac{\beta-1}{\beta}u_l^\beta + U\ln(u_l)\right)(\nabla\cdot\mathbb{D}_l)\cdot\nu\,\mathrm{d}\sigma(x) = 0.
\end{aligned}$$

Hence, we can estimate using the positivity of u_l and (5.3.6) that

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega a(u_l^\beta)\,\mathrm{d}x + U\int_\Omega\left(\frac{\nabla u_l}{u_l}\right)^T\mathbb{D}_l\frac{\nabla u_l}{u_l}\,\mathrm{d}x\\
&\leqslant \int_\Omega\left((\beta-1)u_l^\beta + U\right)\left|(\nabla h_l)^T\mathbb{D}_l\frac{\nabla u_l}{u_l}\right|\mathrm{d}x + \frac{1}{U}\int_\Omega \mu(h_l)u_l^{\alpha-1}\left(U - \tilde{J} * u_l^\beta\right)\left(u_l^\beta - U\right)\mathrm{d}x.
\end{aligned} \tag{5.4.6}$$

Then, we proceed similarly to the proof of Proposition 3.1 in [99] and obtain using $u_l \leqslant U^{\frac{1}{\beta}}$ and Young's inequality that

$$\begin{aligned}
&\int_\Omega \mu(h_l(x))u_l^{\alpha-1}(x)(U - \tilde{J} * u_l^\beta(x))(u_l^\beta(x) - U)\,\mathrm{d}x \\
=&\int_\Omega \mu(h_l(x))u_l^{\alpha-1}(x)\left(U\int_{\mathbb{R}^n}\tilde{J}(y)\,\mathrm{d}y - \int_\Omega \tilde{J}(x-y)u_l^\beta(y)\,\mathrm{d}y\right)\left(u_l^\beta(x) - U\right)\,\mathrm{d}x \\
\leqslant&\int_\Omega \mu(h_l(x))u_l^{\alpha-1}(x)\left(\int_\Omega \tilde{J}(x-y)(U - u_l^\beta(y))\,\mathrm{d}y\right)\left(u_l^\beta(x) - U\right)\,\mathrm{d}x \\
\leqslant&-\int_\Omega \mu(h_l(x))u_l^{\alpha-1}(x)\int_\Omega \tilde{J}(x-y)(u_l^\beta(x) - U)^2\,\mathrm{d}y\,\mathrm{d}x \\
&+\int_\Omega \mu(h_l(x))u_l^{\alpha-1}(x)\int_\Omega \tilde{J}(x-y)(u_l^\beta(x) - u_l^\beta(y))(u_l^\beta(x) - U)\,\mathrm{d}y\,\mathrm{d}x \\
\leqslant&-(1-\varepsilon)\int_\Omega\int_\Omega \mu(h_l(x))u_l^{\alpha-1}(x)\tilde{J}(x-y)(u_l^\beta(x) - U)^2\,\mathrm{d}y\,\mathrm{d}x \\
&+\frac{1}{4\varepsilon}\|\mu\|_{L^\infty(0,H)}U^{\frac{\alpha-1}{\beta}}\int_\Omega\int_\Omega \tilde{J}(x-y)(u_l^\beta(x) - u_l^\beta(y))^2\,\mathrm{d}y\,\mathrm{d}x
\end{aligned} \tag{5.4.7}$$

for

$$\varepsilon \in \left(\max\left\{-\frac{C_A}{2} - \sqrt{\frac{C_A^2}{4} - C_B}; C_B\right\}, \min\left\{-\frac{C_A}{2} + \sqrt{\frac{C_A^2}{4} - C_B}; 1\right\}\right) \subset (C_B, 1),$$

where the interval on the right-hand side is nonempty due to our assumptions on C_A and C_B.

Moreover, due to the convexity of Ω and using the uniform boundedness of $(u_l)_l$ by $U^{\frac{1}{\beta}}$ we conclude from *Lemma A.4.5* the estimate

$$\begin{aligned}
\int_\Omega\int_\Omega \tilde{J}(x-y)(u_l^\beta(x) - u_l^\beta(y))^2\,\mathrm{d}y\,\mathrm{d}x &\leqslant \mathrm{diam}(\Omega)^2\int_\Omega |\nabla(u_l^\beta)|^2\,\mathrm{d}x \\
&\leqslant (\mathrm{diam}(\Omega)\beta U)^2\int_\Omega \frac{|\nabla u_l|^2}{u_l^2}\,\mathrm{d}x.
\end{aligned}$$

Now, inserting this in (5.4.7), using our assumptions on J and μ, and the uniform boundedness of $(u_l)_l$, we conclude

$$\begin{aligned}
&\frac{1}{U}\int_\Omega \mu(h_l(x))u_l^{\alpha-1}(x)(U - \tilde{J} * u_l^\beta(x))(u_l^\beta(x) - U)\,\mathrm{d}x \\
\leqslant&\frac{1}{\varepsilon}D_1UC_B\int_\Omega \frac{|\nabla u_l|^2}{u_l^2}\,\mathrm{d}x - (1-\varepsilon)\delta\eta|\Omega|\int_\Omega u_l^{\alpha-1}(u_l^\beta - U)^2\,\mathrm{d}x
\end{aligned}$$

Inserting this into (5.4.6) and using (5.3.6) and Young's inequality, it follows that

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega a(u_l^\beta)\,\mathrm{d}x + D_1U\frac{\varepsilon - C_B}{\varepsilon}\int_\Omega \frac{|\nabla u_l|^2}{u_l^2}\,\mathrm{d}x + (1-\varepsilon)\delta\eta|\Omega|\int_\Omega u_l^{\alpha-1}(u_l^\beta - U)^2\,\mathrm{d}x \\
\leqslant&\int_\Omega \left((\beta-1)u_l^\beta + U\right)\left|(\nabla h_l)^T\,\mathbb{D}_l\frac{\nabla u_l}{u_l}\right|\,\mathrm{d}x \\
\leqslant&D_1U\frac{\varepsilon - C_B}{\varepsilon}\int_\Omega \frac{|\nabla u_l|^2}{u_l^2}\,\mathrm{d}x + \frac{\varepsilon C_{23}^2\beta^2U}{4D_1(\varepsilon - C_B)}\int_\Omega |\nabla h_l|^2\,\mathrm{d}x.
\end{aligned} \tag{5.4.8}$$

Multiplying the equation for h_l by $h_l - h^*$, integrating over Ω and using (5.4.1), we obtain

$$\frac{1}{2}\frac{d}{dt}\int_\Omega (h_l - h^*)^2\,\mathrm{d}x + D_H\int_\Omega |\nabla h_l|^2\,\mathrm{d}x \leqslant -C_H\int_\Omega (h - h^*)^2\,\mathrm{d}x + C_U\int_\Omega u_l^{\alpha-1}(u_l^\beta - U)^2\,\mathrm{d}x.$$

Further, we multiply this by $C_{31} := \frac{\varepsilon C_{23}^2 \beta^2 U}{4D_1 D_H(\varepsilon - C_B)}$ and add it to (5.4.8) to obtain

$$\frac{d}{dt}\left(\int_\Omega a(u_l^\beta)\,\mathrm{d}x + \frac{1}{2}C_{31}\int_\Omega (h_l - h^*)^2\,\mathrm{d}x\right) \tag{5.4.9}$$

$$+C_H C_{31}\int_\Omega (h_l - h^*)^2\,\mathrm{d}x + ((1-\varepsilon)\delta\eta|\Omega| - C_U C_{31})\int_\Omega u_l^{\alpha-1}(u_l^\beta - U)^2\,\mathrm{d}x \leqslant 0. \tag{5.4.10}$$

Due to our assumptions on C_A, C_B and our choice of ε it holds that $(1-\varepsilon)\delta\eta|\Omega| - C_U C_{31} > 0$. Consequently, for $T \in (0,\infty)$ it holds that

$$\begin{aligned}
&\int_\Omega a(u_l^\beta(T))\,\mathrm{d}x + \frac{1}{2}C_{31}\int_\Omega (h_l(T) - h^*)^2\,\mathrm{d}x + C_H C_{31}\int_0^T\int_\Omega (h_l - h^*)^2\,\mathrm{d}x\,\mathrm{d}t \\
&+ ((1-\varepsilon)\delta\eta|\Omega| - C_U C_{31})\int_0^T\int_\Omega u_l^{\alpha-1}(u_l^\beta - U)^2\,\mathrm{d}x\,\mathrm{d}t \\
\leqslant &\int_\Omega a(u_0^\beta) + \frac{1}{2}C_{31}\int_\Omega (h_0 - h^*)^2\,\mathrm{d}x,
\end{aligned}$$

where the right-hand side is finite due to our additional assumption on u_0. Hence, using the uniform boundedness of $(u_l)_l$ and $(h_l)_l$, their pointwise a.e. convergences from (5.3.56) and (5.3.57) and the dominated convergence theorem we conclude

$$\begin{aligned}
&C_H C_{31}\int_0^T\int_\Omega (h - h^*)^2\,\mathrm{d}x\,\mathrm{d}t + ((1-\varepsilon)\delta\eta|\Omega| - C_U C_{31})\int_0^T\int_\Omega u^{\alpha-1}(u^\beta - U)^2\,\mathrm{d}x\,\mathrm{d}t \\
\leqslant &\int_\Omega a(u_0^\beta) + \frac{1}{2}C_{31}\int_\Omega (h_0 - h^*)^2\,\mathrm{d}x
\end{aligned}$$

and (5.4.5) follows. □

Now we can conclude uniform convergence as in Lemma 3.10 in [139]:

Theorem 5.4.3. *It holds that*

$$\lim_{t\to\infty}\|u(\cdot,t) - c\|_{L^\infty(\Omega)} = \lim_{t\to\infty}\|h(\cdot,t) - h^*\|_{L^\infty(\Omega)} = 0, \tag{5.4.11}$$

where $c \in \{0, U^{\frac{1}{\beta}}\}$ *if* $\alpha > 1$ *and* $c = U^{\frac{1}{\beta}}$ *if* $\alpha = 1$.

Proof. Due to (5.3.53) in *Theorem 5.3.7*, u and h are uniformly continuous in $\overline{\Omega} \times (1,\infty)$ and we can conclude from *Lemmas 2.2.3*, *5.4.2*, and *A.4.6* that

$$\lim_{t\to\infty}\|u(\cdot,t)^{\frac{\alpha-1}{2}}(u^\beta(\cdot,t) - U)\|_{L^\infty(\Omega)} = \lim_{t\to\infty}\|h(\cdot,t) - h^*\|_{L^\infty(\Omega)} = 0. \tag{5.4.12}$$

Consider $\alpha > 1$ and set

$$\varepsilon := \min\left\{\frac{U^{\frac{1}{\beta}}}{8}, \left(1 - \left(\frac{7}{8}\right)^\beta\right)\left(\frac{U^{\frac{1}{\beta}}}{8}\right)^{\beta + \frac{\alpha-1}{2}}\right\}.$$

Due to the uniform continuity of u we can consider w.l.o.g. a sequence $(t_k)_{k\in\mathbb{N}} \subset (1,\infty)$ with $\lim_{k\to\infty} t_k = \infty$ satisfying for all $x \in \overline{\Omega}$ and $k \in \mathbb{N}$ the estimate

$$|u(x, t_{k+1}) - u(x, t_k)| < \varepsilon. \tag{5.4.13}$$

Moreover, (5.4.12) implies that there is $K(\varepsilon) \in \mathbb{N}$ s.t.

$$\|u(\cdot,t_k)^{\frac{\alpha-1}{2}}(u^\beta(\cdot,t_k) - U)\|_{L^\infty(\Omega)} < \varepsilon$$

and consequently, due to our choice of ε above $u(x,t_k) \in [0, \frac{1}{8}U^{\frac{1}{\beta}}) \cup (\frac{7}{8}U^{\frac{1}{\beta}}, U^{\frac{1}{\beta}}]$ for $k \geqslant K(\varepsilon)$. Hence, either $u(x,t_k) \in [0, \frac{1}{8}U^{\frac{1}{\beta}})$ for all $x \in \Omega$ and $k \geqslant K(\varepsilon)$ or $u(x,t_k) \in (\frac{7}{8}U^{\frac{1}{\beta}}, U^{\frac{1}{\beta}}]$ for all $x \in \Omega$ and $k \geqslant K(\varepsilon)$ due to (5.4.13). If $u(x,t_k) \in [0, \frac{1}{8}U^{\frac{1}{\beta}})$ for all $x \in \Omega$ and $k \geqslant K(\varepsilon)$ then (5.4.12) implies that

$$\|u(\cdot,t_k)\|_{L^\infty(\Omega)} \leqslant \left(\frac{\|u(\cdot,t_k)^{\frac{\alpha-1}{2}}(u^\beta(\cdot,t_k) - U)\|_{L^\infty(\Omega)}}{U\left(1 - \left(\frac{1}{8}\right)^\beta\right)} \right)^{\frac{2}{\alpha-1}} \underset{k\to\infty}{\to} 0.$$

Analogously, the other convergence in the case $u(x,t_k) \in (\frac{7}{8}U^{\frac{1}{\beta}}, U^{\frac{1}{\beta}}]$ follows. □

5.5 Pattern formation: a 1D study

We want to investigate pattern formation in our model in 1D (see [110]). For this aim we adapt some of the assumptions on our functions and parameters:

- $J \in L^1(\mathbb{R})$, $J(x) = J(-x)$ for $x \in \mathbb{R}$ and $\int_{\mathbb{R}} J(x)\,\mathrm{d}x = 1$, whereas we drop the condition that $0 < \eta \leqslant J$;
- $d \in \mathbb{R}$ constant;
- there is exactly one $h^* > 0$ with $g(1,h^*) = 0$, moreover, $\mu(h^*) > 0$, $\partial_u g(1,h^*) \geqslant 0$ and $\partial_h g(1,h^*) < 0$ for this h^*. This means that when the cancer cells are at their carrying capacity (corresponding to an acidity level h^*), the production of protons is increasing with the cell mass and decreasing with enhancing proton concentration. Indeed, crowded tumor cells are highly hypoxic, and a too acidic environment leads to quiescence or necrosis, thus reducing proton expression. Moreover, we assume that $\mu'(h^*) < 0$, thus the growth rate is decreasing with the proton concentration in the neighborhood of the critical value h^*.
- w.l.o.g. we consider $\Omega = (-a,a)$ for $a \in \mathbb{R}$.

We define the convolution over $\mathbb{R}$ as $J \circledast u(x) := \int_{\mathbb{R}} J(x-y)u(y)\,dy$. Hence, we consider the model

$$\begin{cases} u_t = du_{xx} + d(uh_x)_x + \mu(h)u^\alpha(1 - J \circledast u^\beta) & \text{in } \Omega \times (0,\infty), \\ h_t = D_H h_{xx} + g(u,h) & \text{in } \Omega \times (0,\infty), \\ u_x = h_x = 0 & \text{on } \partial\Omega \times (0,\infty), \\ u(\cdot,0) = u_0,\ h(\cdot,0) = h_0 & \text{in } \Omega. \end{cases} \tag{5.5.1}$$

5.5.1 Stability in the local model without diffusion and taxis

We start by establishing the equilibria of the non-spatial local model that corresponds to (5.5.1), i.e.,

$$\begin{cases} \partial_t u &= \mu(h)u^\alpha(1 - u^\beta), \\ \partial_t h &= g(u,h). \end{cases} \tag{5.5.2}$$

The biologically more interesting one is given by $(u^*, h^*) = (1, h^*)$, where h^* is the unique solution of $g(1, h) = 0$. The corresponding characteristic equation of the Jacobian in $(1, h^*)$ is given by

$$\lambda^2 + (\beta\mu(h^*) - \partial_h g(1, h^*))\lambda - \beta\mu(h^*)\partial_h g(1, h^*) = 0.$$

The corresponding eigenvalues are

$$\lambda_1 = -\beta\mu(h^*) \text{ and } \lambda_2 = \partial_h g(1, h^*)$$

and both have negative real parts due to the assumption $\partial_h g(1, h^*) < 0$. Hence, the steady state $(1, h^*)$ is stable in this case.

5.5.2 Stability in the local model with diffusion and taxis

We continue by adding again the diffusion and taxis terms to the local model (5.5.2), i.e.,

$$\begin{cases} \partial_t u &= du_{xx} + d(uh_x)_x + \mu(h)u^\alpha(1 - u^\beta), \\ \partial_t h &= D_H h_{xx} + g(u, h). \end{cases}$$

Adapting the ansatz from [119] we consider perturbations of $(1, h^*)$ of the form $u = 1 + \varepsilon\bar{u}(k)$ and $h = h^* + \varepsilon\bar{h}(k)$, where $\bar{u}(k) = \tilde{u}e^{\lambda(k)t}\cos(kx)$ and $\bar{h}(k) = \tilde{h}e^{\lambda(k)t}\cos(kx)$ for $\tilde{u}, \tilde{h} \in \mathbb{R}$, wavenumber $k \in \mathbb{N}$ and $|\varepsilon| << 1$. Here, $\lambda(k)$ denotes some eigenvalue of the corresponding characteristic equation. As in [115] we use the fact that $\frac{e^{ikx}+e^{-ikx}}{2} = \cos(kx)$ to ensure that our perturbations are real for real λ.

Inserting these u and h into our model and linearizing about the steady state $(1, h^*)$, we obtain

$$\begin{cases} \lambda(k)\bar{u} &= -dk^2\bar{u} - dk^2\bar{h} - \beta\mu(h^*)\bar{u}, \\ \lambda(k)\bar{h} &= -D_H k^2\bar{h} + \partial_u g(1, h^*)\bar{u} + \partial_h g(1, h^*)\bar{h}. \end{cases} \tag{5.5.3}$$

The corresponding eigenvalues are given by

$$\lambda_{1,2}(k) = \frac{\operatorname{tr}(J_{u,h}(k)) \pm \sqrt{\operatorname{tr}(J_{u,h}(k))^2 - 4\det(J_{u,h}(k))}}{2},$$

where we denote by $J_{u,h}$ the Jacobian of the right-hand side of system (5.5.3) at $(1, h^*)$ and its determinant and trace are, respectively, given by

$$\begin{aligned} \operatorname{tr}(J_{u,h}(k)) &= -(d + D_H)k^2 - \beta\mu(h^*) + \partial_h g(1, h^*) < 0, \\ \det(J_{u,h}(k)) &= dD_H k^4 + (d(\partial_u g(1, h^*) - \partial_h g(1, h^*)) + \beta\mu(h^*)D_H)k^2 - \beta\mu(h^*)\partial_h g(1, h^*) > 0. \end{aligned}$$

Hence, the equilibrium $(1, h^*)$ is stable. The local model does not lead to any Turing type patterns.

5.5.3 Stability in the nonlocal model

We consider u and h as in the previous section and linearize the convolution term about $(1, h^*)$ similarly to [119]. Hence, inserting u in the convolution term and using the symmetry of J, we compute that

$$J \circledast u^\beta(x) \approx \int_{\mathbb{R}} J(x - y)(1 + \beta\varepsilon\tilde{u}e^{\lambda(k)t}\cos(ky))\, dy$$

$$\begin{aligned}&= 1 + \beta\varepsilon\tilde{u}e^{\lambda(k)t}\frac{1}{2}\int_{\mathbb{R}} J(z)e^{ik(x-z)} + J(-z)e^{-ik(x-z)}\,\mathrm{d}z\\&= 1 + \beta\varepsilon\tilde{u}e^{\lambda(k)t}\cos(kx)\int_{\mathbb{R}} J(z)e^{-ikz}\,\mathrm{d}z\\&= 1 + \varepsilon\beta\bar{u}(2\pi)^{\frac{1}{2}}\hat{J}(k).\end{aligned}$$

Here, $\hat{J}$ denotes the Fourier transform of J. Hence, linearizing system (5.5.1), we obtain

$$\begin{cases}\lambda(k)\bar{u} &= -dk^2\bar{u} - dk^2\bar{h} - \beta\mu(h^*)(2\pi)^{\frac{1}{2}}\hat{J}(k)\bar{u},\\ \lambda(k)\bar{h} &= -D_Hk^2\bar{h} + \partial_u g(1,h^*)\bar{u} + \partial_h g(1,h^*)\bar{h}.\end{cases} \tag{5.5.4}$$

The corresponding eigenvalues are as above given by

$$\lambda_{1,2}(k) = \frac{\mathrm{tr}(J_{u,h}(k)) \pm \sqrt{\mathrm{tr}(J_{u,h}(k))^2 - 4\det(J_{u,h}(k))}}{2},$$

where we denote by $J_{u,h}$ the Jacobian of the right-hand side in (5.5.4) at $(1,h^*)$ and its trace and determinant are given by

$$\begin{aligned}\mathrm{tr}(J_{u,h})(k) =& -(d+D_H)k^2 - \beta\mu(h^*)(2\pi)^{\frac{1}{2}}\hat{J}(k) + \partial_h g(1,h^*),\\ \det(J_{u,h})(k) =& dD_Hk^4 + (d(\partial_u g(1,h^*) - \partial_h g(1,h^*)) + \beta\mu(h^*)(2\pi)^{\frac{1}{2}}\hat{J}(k)D_H)k^2\\ &- \beta\mu(h^*)(2\pi)^{\frac{1}{2}}\hat{J}(k)\partial_h g(1,h^*).\end{aligned}$$

The sign of the real part of the eigenvalues is ambiguous here and depends especially on the sign of $\hat{J}(k)$, which depends on k. As above, we have stability here if

$$\mathrm{tr}J_{u,h}(k) < 0 \text{ and } \det J_{u,h}(k) > 0 \tag{5.5.5}$$

for all $k = \frac{\pi}{a}z$, where $z \in \mathbb{Z}$. We make this restriction due to our boundary condition $u_x = h_x = 0$.

Now, we are looking for a critical k_c (that is not necessarily of the form $\frac{\pi}{a}z$) depending on our choice of parameters, where we distinguish as in [115] the occurrence of Turing instabilities in the case $\mathrm{Im}(\lambda(k_c)) = 0$ for some arbitrary critical k_c, Hopf instabilities in the case $\mathrm{Im}(\lambda(0)) \neq 0$, and wave instabilities in the case $\mathrm{Im}(\lambda(k_c)) \neq 0$ for some critical $k_c \neq 0$. If $\hat{J}$ is symmetric it suffices to consider only positive k_c.

A Turing bifurcation can occur if we find k_c such that

$$\det(J_{u,h})(k_c) = 0 \text{ and } \mathrm{tr}(J_{u,h})(k_c) < 0.$$

Now, rewriting these conditions we conclude that the equality

$$\hat{J}(k_c) = -d\frac{k_c^2}{\beta(2\pi)^{\frac{1}{2}}\mu(h^*)}\left(1 + \frac{\partial_u g(1,h^*)}{D_Hk_c^2 - \partial_h g(1,h^*)}\right) \tag{5.5.6}$$

and the inequality

$$\frac{\partial_h g(1,h^*) - (d+D_H)k_c^2}{\beta\mu(h^*)(2\pi)^{\frac{1}{2}}} < \hat{J}(k_c) \tag{5.5.7}$$

have to hold for one or several critical k_c in a set K_c, whereas (5.5.5) holds for all $k \notin K_c$ that are of the form $\frac{\pi}{a}z$. Such k_c exist depending on the choice of parameters, on the functions μ and g, and especially on the sign of the Fourier transform of J. Moreover, due to our assumptions the terms on the right-hand side of (5.5.6) and on the left-hand side of (5.5.7) are negative and tend to $-\infty$ for $k \to \pm\infty$. On the other hand, a Hopf or a wave instability can occur if we find k_c such that

$$\mathrm{tr}(J_{u,h})(k_c) = 0 \text{ and } \det J_{u,h}(k_c) > 0,$$

whereas (5.5.5) holds for all k that do not satisfy this and are of the form $\frac{\pi}{a}z$. Hence, a Hopf instability occurs if

$$\frac{\partial_h g(1, h^*)}{\mu(h^*)\beta(2\pi)^{\frac{1}{2}}} = \hat{J}(0) \text{ and } \hat{J}(0) > 0, \tag{5.5.8}$$

whereas (5.5.5) holds for all $k \neq 0$. On the other hand, a wave instability occurs if

$$\frac{\partial_h g(1, h^*) - (d + D_H)k_c^2}{\mu(h^*)\beta(2\pi)^{\frac{1}{2}}} = \hat{J}(k_c) \tag{5.5.9}$$

and

$$-d\frac{k_c^2}{\beta(2\pi)^{\frac{1}{2}}\mu(h^*)}\left(1 + \frac{\partial_u g(1, h^*)}{D_H k_c^2 - \partial_h g(1, h^*)}\right) < \hat{J}(k_c) \tag{5.5.10}$$

holds for one or several $k_c \neq 0$, whereas (5.5.5) holds for all other k that are of the form $\frac{\pi}{a}z$ and do not satisfy the above equality and inequality.

From the above considerations we conclude that the occurrence of a Turing, Hopf or wave instability depends on the concrete choice of J, as we need to find suitable k of the form $\frac{\pi}{a}z$. If the Fourier transform $\hat{J}$ is nonnegative, no Turing patterns occur due to (5.5.6). More precisely, the determined patterns are only of Turing-like type as they are induced by the nonlocality and not the diffusion.

Example 5.5.1. We explore the occurrence of Turing-like patterns in the nonlocal model (5.5.1) for the uniform kernel $J_U(x) = \frac{1}{2}\chi_{[-1,1]}(x)$ and the logistic kernel $J_L(x) = \frac{1}{2+e^x+e^{-x}}$ in the domain $\Omega = (-5, 5)$ for the parameters and functions $g(u, h) = u(1 - h)$, $\mu(h) = \frac{\mu}{1+h}$, with a constant $\mu > 0$ and $d = D_H = 1$. The steady state is given by $(u^*, h^*) = (1, 1)$ with $\partial_u g(1, 1) = 0$, $\partial_h g(1, 1) = -1 < 0$ and $\mu(1) = \frac{\mu}{2}$.

The Fourier transform of the uniform kernel J_U is given by

$$\hat{J}_U(k) = \frac{\sin(k)}{\sqrt{2\pi}k} \tag{5.5.11}$$

for $k \in \mathbb{R}$. Its sign is ambiguous. Inserting this into (5.5.6) and (5.5.7) we conclude that

$$-\frac{2k_c^2}{\beta\mu} = \frac{\sin(k_c)}{k_c} \tag{5.5.12}$$

and

$$-\frac{2 + 4k_c^2}{\beta\mu} < \frac{\sin(k_c)}{k_c}$$

have to be satisfied for some k_c for the occurrence of Turing-like patterns, where the second condition is a direct consequence of the first. Equation (5.5.12) has a solution if $\beta\mu$ are larger than approximately 168,4. Hence, for such $\beta\mu$ Turing-like patterns occur.

Moreover, the Fourier transform of the logistic kernel J_L is given by

$$\hat{J}_L(k) = \frac{\sqrt{\pi}k}{\sqrt{2}\sinh(k\pi)} > 0 \tag{5.5.13}$$

for $k \in \mathbb{R}$. Consequently, no Turing-like patterns occur for this kernel

In *Section 5.6* we will perform numerical simulations for this choice of functions and kernels.

Remark 5.5.2. If there is a steady state of the form $(0, h^{**})$ for some $h^{**} > 0$ and $\partial_h g(0, h^{**}) \leqslant 0$, then this equilibrium is stable in the case with diffusion, taxis and nonlocal term. If, on the other hand, $\partial_h g(0, h^{**}) > 0$, this steady state is unstable already in the case without diffusion and taxis. This case is, however, unrealistic for the biological problem investigated here. Indeed, the proton expression by hypoxic cells is much reduced and there must be at least some very weak acid buffering, lest all cells (and surrounding tissue) become apoptotic.

Likewise, the steady state $(1, h^*)$ is unstable already in the case without diffusion and taxis if $\partial_h g(1, h^*) > 0$. This situation may occur at least in a transient manner, e.g., when the cells can still extrude protons while their environment is quite acidic and if the cells are at their carrying capacity and the proton buffering is relatively low. That can lead, e.g., to a choice of the form $g(u, h) = u + uh - \gamma h^2$ with $\gamma \leqslant 4/5$.

5.6 Numerical simulations

In this section we perform numerical simulations of system (5.5.1), in order to illustrate the solution behavior. The equations are discretized by using the algorithm in [111] similarly to *Section 6.5*; the motility terms were discretized with finite differences (centered for the diffusion, upwind for the drift). The initial conditions are as in [99]:

$$u_0(x) = \begin{cases} e^{-(x-x_l)^2}, & \text{for } x_l < x \leqslant 0 \\ e^{-x_l^2}(1 - \frac{x}{x_r}), & \text{for } 0 < x \leqslant x_r \end{cases}, \qquad \text{with } x_l = -5,\ x_r = 5.$$

Unless otherwise stated we take $g(u, h) = u(1 - h)$, $\mu(h) = \frac{\mu}{1+h}$, with $\mu > 0$ a constant and $d = D_H = 1$.

In a first test we took $\beta = \mu = 1$, along with the logistic kernel $J_L(x) = \frac{1}{2+e^x+e^{-x}}$ (see, e.g., [98]) and the uniform kernel $J_U(x; \rho) = \frac{1}{2\rho}\chi_{[-\rho,\rho]}$. The first two columns of *Figure 5.1* show simulation results for $\alpha = 2$, which is the 'limit value' in (5.3.3). The solution ceased (in finite time) to exist for sufficiently large α in each of these situations ($\alpha \sim 6.25$ and $\alpha \sim 8.2$, respectively), u exhibiting strong aggregation near the initial bulk of cells, cf. last two columns in *Figure 5.1*. This behavior was also observed for increasing values of μ, with the difference of singularities already occuring for smaller α values.

Increasing the values of μ and β leads to patterns, the shape of which depends decisively on the interaction kernel J and also on the values of α and d. *Figure 5.2* shows 1D space-time patterns of the cell density u for $\beta = 20$, $\mu = 100$, and several combinations of α and J. The results for the proton concentration h are not shown, as there are only small quantitative differences between the respective cases. *Figure 5.2* suggests that, irrespective of the chosen kernel[9], higher cooperative intraspecific interactions (larger α values) or slower diffusion delay the invasion of cells in the whole region, leading instead to enhanced proliferation. On the long run the cells

[9] We performed simulations with several other kernels, including the so-called 'Mexican hat' (also known as Ricker wavelet, see e.g., [52, 153] for its use in related, but different contexts), cosine, and Epanechnikov.

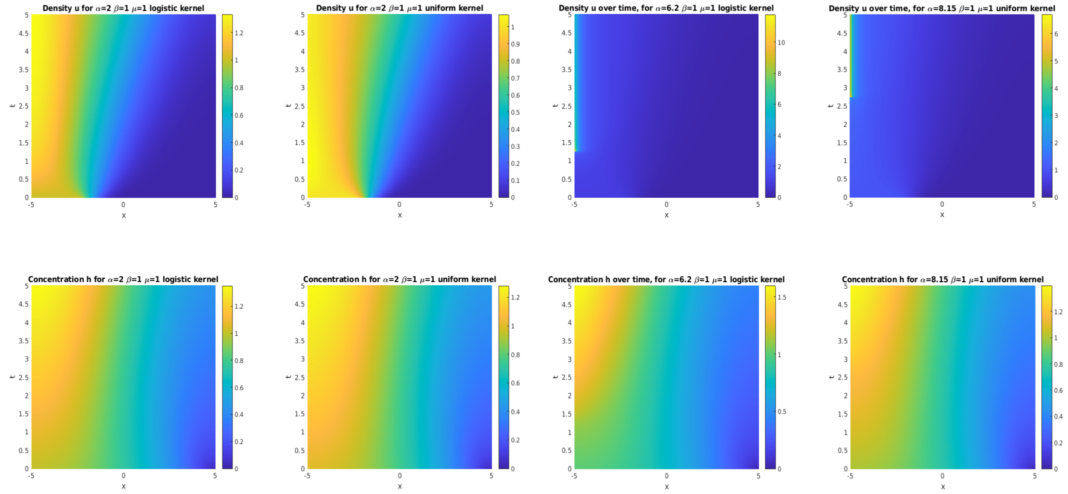

Figure 5.1: Simulation results for (5.5.1) with $\beta = \mu = 1$. First two columns: $\alpha = 2$, 3rd column: $\alpha = 6.2$, last column: $\alpha = 8.15$. Uniform kernel used with $\rho = 1$.

tend to fill the whole space and remain at their carrying capacity. This behavior endorses the results in *Section 5.4* and is particularly well visible for the logistic kernel, which satisfies all conditions in the proofs of the theoretical results of *Sections 5.3* and *5.4*; the process is much slower when a uniform kernel is used, however it has eventually the same outcome. The last row in *Figure 5.2* exhibits the situation of a cell diffusion which is much slower than that of protons. The effect is a delayed filling of the space with cells (and produced protons) and a later formation of the patterns observed in the upper rows. The asymptotic behavior is similar, only it takes longer for the solution to reach the respective states.

To assess the effect of nonlocality we performed simulations with the source term in the u-equation of (5.5.1) replaced by $\mu(h)u^\alpha(1-u^\beta)$. The results are shown in *Figure 5.3*. The first two columns illustrate the case with the same source term for proton concentration as above, namely $g(u,h) = u(1-h)$, for which no patterns seem to develop (we tried several combinations of parameters, including those used for the patterns in *Figure 5.2*). In fact, decreasing the value of ρ in the uniform kernel $J_U(x;\rho)$ eventually leads to the local version of the system. The plots in the leftmost column were produced with $d = D_H$, while those in the middle column used $d \ll D_H$. The behavior of u and h is the same, with the difference of the second case inferring a slower spread of cells and protons. The last column in *Figure 5.2* already shows the tendency of disappearing patterns when approaching the local case. The last column of *Figure 5.3* shows the case where the source term in the h-equation is replaced by $g(u,h) = u + uh - \gamma h^2$, as proposed in *Remark 5.5.2*.[10]

No patterns for u were observed for the local model, which, together with the simulations performed for intermediary values of ρ, suggests that the patterns are driven by the nonlocality of cell-cell interactions, more precisely by intraspecific competition. The simulations also confirm the long time behavior of the system, even in the local case.

[10]We tried several other source terms satisfying the conditions in *Remark 5.5.2*, e.g., $g(u,h) = uh/(1+uh+h)$, all resulting in the same qualitative behavior.

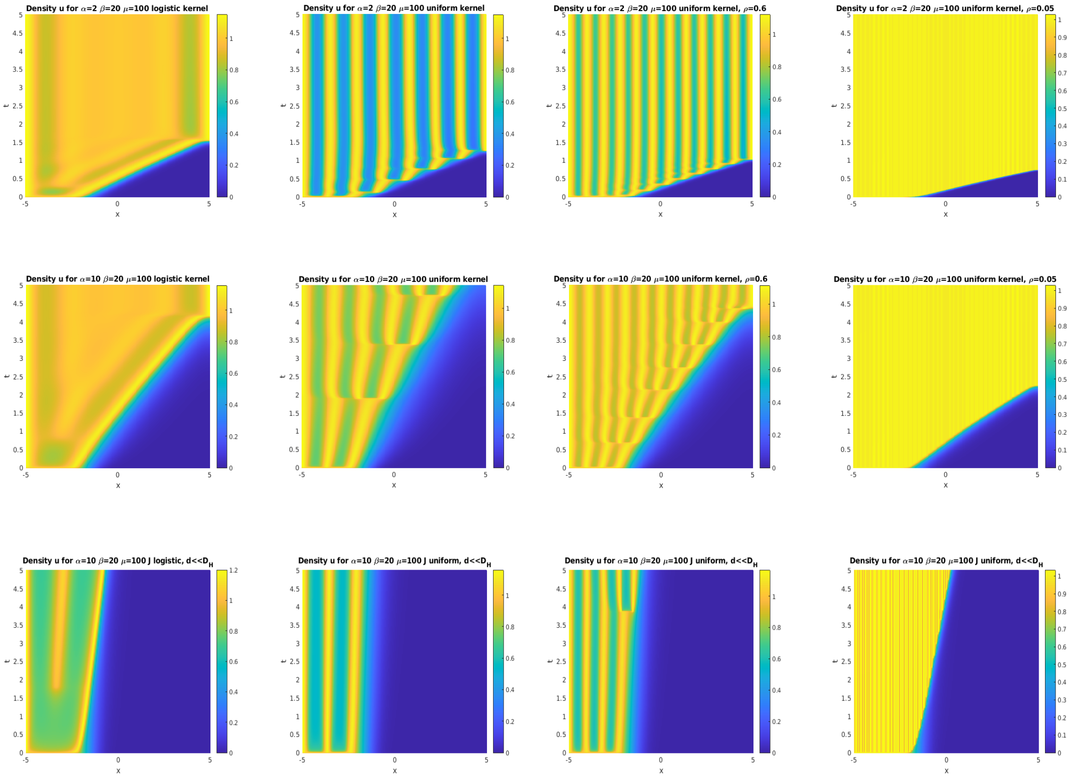

Figure 5.2: Simulation results for (5.5.1) with $\beta = 20$ and $\mu = 100$. Upper row: $\alpha = 2$, lower row: $\alpha = 10$. First column J logistic, other columns J uniform: 2nd column: $\rho = 1$, 3rd column: $\rho = 0.6$, 4th column: $\rho = 0.05$. Upper rows: $d = D_H = 1$, last row: $d \ll D_H$.

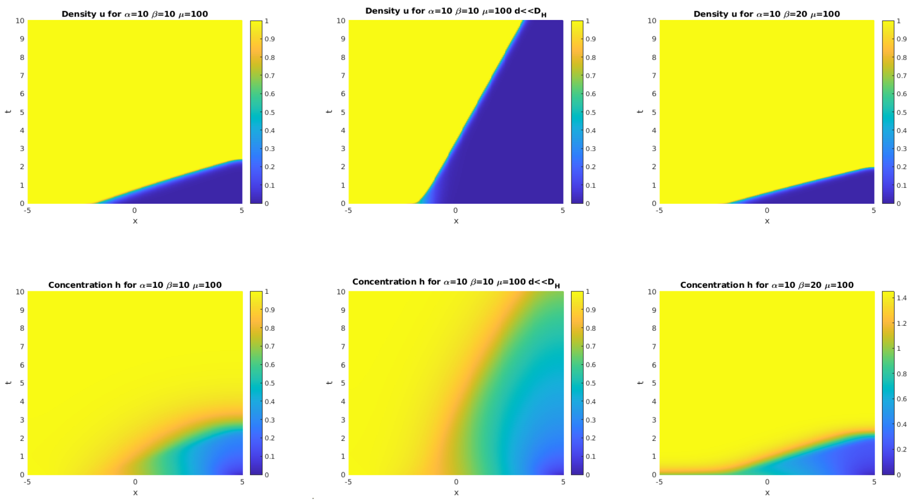

Figure 5.3: Simulation results for (5.5.1) with local source term $\mu(h)u^{\alpha}(1-u^{\beta})$ replacing the one in the equation for u. Left and middle column: $g(u,h) = u(1-h)$ with $d = D_H$ and $d \ll D_H$, respectively. Right column: $g(u,h) = u + uh - \gamma h^2$, $d = D_H$.

5.7 Discussion

In this chapter we investigated a model describing pH-tactic behavior of cells with nonlocal source terms. As such, it extends the one in [99], which studied the Fisher-KPP equation with nonlocal intraspecific competition with various powers of the solution. In contrast to [99] we handled here a problem in a bounded domain, and the population dynamics was coupled to that of the proton concentration, which also led to a taxis term. The proof of our results concerning global well-posedness and long time behavior relied, however, to a substantial extent on the methods in [99]. We also dealt here with space-dependent tensor coefficients in the motility terms, which involve myopic rather than Fickian diffusion. The dissipative effect of the repellent pH-taxis contributed to reducing some of the difficulties in the analysis - as long as the required conditions on the functions involved in the system are satisfied.

Among the relatively few existing models with nonlocal source terms, the one in [136] is closely related, however it features several differences: the cells perform attractive haptotaxis towards gradients of extracellular matrix (ECM), the nonlocal source terms are contained in both equations, do not involve any powers, and the Fickian diffusion of cells has a constant coefficient. Our model requires less regularity for the interaction kernel and the motility coefficients involve a tensor and are more general. On the other hand, the nonexploding solution behavior is favorized in our case by repellent chemotaxis. We also provided an informal model deduction and an assessment of the long time solution behavior. The analysis done in [113] for a model with standard motility and with nonlocal source terms as in [136], but with one or two species performing chemotaxis towards the same attractant imposes certain requirements on the forcing term of the latter, mainly in order to obtain the asymptotic behavior of the cell-related solution components. Our condition (5.4.1) imposed for similar purposes on the source term of the tactic signal looks rather differently. The attraction-repulsion chemotaxis models considered in [129] have closer similarities with our setting, as far as the nonlocal intraspecific interactions are concerned. Major differences occur through our system only featuring two equations, in the source terms of the chemical cues, and in the motility terms: the latter involve in our case the space-dependent tensor $\mathbb{D}(x)$ and myopic diffusion, while the nonlocal reaction term in the proton dynamics is more general. We also prove an explicit long time behavior of both solution components and provide a short analysis of space-time patterns (in 1D), along with numerical simulations.

Our preliminary analysis in *Section 5.5* and the simulation results in *Section 5.6* suggest that patterns occur only in the nonlocal model, are not of Turing type, and seem to be driven by the nonlocal source terms and influenced by the chosen kernel and the combination of parameters in the nonlocal term. This is in line with the pattern behavior observed in [99] and with other works concerning reaction-diffusion problems with nonlocal intra- and/or interspecific competition, cf. e.g., [64, 74, 119, 131, 142, 153]. Those works involved more or less similar source terms and no taxis, however the repellent pH-taxis contained in our model does not seem to have a relevant influence on the patterns.

Open problems relate to a thorough study of patterns depending on the interplay between the parameters α, β, μ and the influence of the kernel J. Moreover, the well-posedness, asymptotic and blow-up behavior, along with patterning are largely unknown in the case of a degenerating motility tensor - the less so in combination with myopic diffusion and/or other types of taxis.

Indeed, these can lead in the local case to very complex issues even in 1D, as shown e.g., in [149, 151].

CHAPTER 6

On a PDE-ODE-PDE model for two interacting cell populations under the influence of an acidic environment and with nonlocal intra- and interspecific growth limitation

This chapter is based on the article „On a PDE-ODE-PDE model for two interacting cell populations under the influence of an acidic environment and with nonlocal intra- and interspecific growth limitation“.[1] The presentation has been adapted for use in this dissertation to clarify the details of the proofs and guarantee consistency of the notation.

6.1 Motivation

Tumor heterogeneity is a well established fact [75]. The neoplastic tissue is -among others- composed of several cell phenotypes, all of which are related to the stage within the cell cycle. To simply, of this vast variety we only consider here two phenotypes: active and quiescent cells. The former are supposed to be motile and proliferate, while the latter just infer transitions toward or from activity. While competing with their active counterparts, quiescent cells can also be degraded. Furthermore, the advancement through the cell cycle and the corresponding phenotypic switch is influenced, inter alia, by biochemical factors in the peritumoral space, see [75] and references therein. In particular, pH regulation is a key feature in tumor cell cycle progression, which it can delay or even inhibit [18, 61, 62, 126].

The interactions of cells with their environment occur not only locally, but cells can perceive their surroundings in a far more extensive manner, by way of protrusions like cytonemes/filopodia/invadopodia, tunneling nanotubes etc. [24, 112, 130, 144]. This motivated the introduction of mathematical models for cell migration, proliferation, and spread. Most of them are of the reaction-diffusion-transport type, with spatial nonlocalities occuring in the advection terms, mainly to model cell-cell and/or cell-tissue adhesions, or nonlocal taxis see e.g., *Chapters 3* and *4* and [5, 23, 43, 81, 117, 156], or in the source terms, to describe intraspecific interactions over a whole sensing range as in *Chapter 5* and [99]. We refer to e.g., [4, 114, 135] for settings also involving nonlocal interspecific competition in different, but related contexts, where the focus is on global stability and pattern issues. The work [136] also considered spatially nonlocal interspecific interactions, but of cancer cells with extracellular matrix and both species featured such

[1] [48] The article is available online under `https://doi.org/10.48550/arXiv.2409.12657`.

terms. For a recent review on nonlocal models for cell migration see [28]; for more comprehensive reviews of nonlocal models in a broader context refer to [51, 87].

Nonlocal models can be obtained, thus far still in a non-rigorous manner, from space- or velocity-jump descriptions on the mesoscopic level (also including the kinetic theory of active particles framework [11]), possibly also accounting for microscale dynamics like binding of transmembrane units to soluble or unsoluble ligands. We refer to *Chapter 5* and [21, 44, 99, 156] for such deductions.

The remainder of this chapter is structured as follows: in *Section 6.2* we present the model consisting of a PDE-ODE-PDE system, along with requirements for the involved parameters and functions. *Sections 6.3* and *6.4* are dedicated to proving global existence of a nonnegative weak solution to the system, in the sense specified therein. In *Section 6.5* we perform numerical simulations in 1D within various scenarios, to get some insight into boundedness and patterning behavior under the influence of different choices of relevant parameters, interaction kernels, and phenotypic switch triggered by acidity. Finally, *Section 6.6* provides some concluding remarks and an outlook.

6.2 Model

In the following u and w represent the densities of active and of quiescent cells, respectively, whereas h is the concentration of protons in the extracellular space. By 'active' we mean here cells which are migrating and proliferating. On the other hand, 'quiescent' means cells which only interact with their active counterparts and with the environment, without moving nor being able to proliferate. We consider the IBVP in a bounded domain $\Omega \subset \mathbb{R}^n$ having a sufficiently regular boundary $\partial\Omega$ with no-flux boundary conditions

$$\begin{cases} \partial_t u = \nabla \cdot (\psi(w,h)\nabla u) + \mu_1 u^\alpha \left(1 - J_1(x,h) * u^\beta - J_2(x,h) * w^\gamma\right) & \\ \qquad + \tilde{\mu}_3(h)F(w) & \text{in } \Omega \times (0,\infty), \\ \partial_t w = \mu_2(h)(1-w)u - \mu_3(h)F(w) & \text{in } \Omega \times (0,\infty), \\ \partial_t h = D_H \Delta h + g(u,w) - \lambda h & \text{in } \Omega \times (0,\infty), \\ \partial_\nu u = \partial_\nu h = 0 & \text{on } \partial\Omega \times (0,\infty), \\ u(\cdot,0) = u_0,\ w(\cdot,0) = w_0,\ h(\cdot,0) = h_0 & \text{in } \Omega. \end{cases} \tag{6.2.1}$$

The first term on the right-hand side of the first PDE in (6.2.1) describes nonlinear diffusion of active cells. The diffusion coefficient ψ can thereby depend on w and h: a large amount of w-cells can increase the population pressure, thus leading to faster diffusion; too many quiescent cells would, however, impede migration (e.g., due to lack of space). Large h-values are also supposed to enhance motility, as the active cells tend to leave such areas faster than more favorable places. The next term describes proliferation of active cells, which is limited by spatially nonlocal intra- and interspecific interactions. As in *Chapter 5* and [99] we consider the exponents α, β, γ in the weak Allee effect and the competition/crowding terms with the interaction kernels J_1 and J_2. The latter can be seen as weighting the influence of either interactions on the dynamics of u and over a whole region. This description enables a more flexible characterization of the interaction strengths and is related to the size of u- and w-cell clusters exchanging information with (bunches of) active cells. Eventually, the last term describes phenotypic switch from quiescent to active cells; this transition is happening with a certain saturation and its rate $\tilde{\mu}_3$ depends on the concentration h of protons. Indeed, less acidic environments favor exit from the quiescent phase and advancement towards activity [22, 140].

The second equation in (6.2.1) is an ODE describing the dynamics of quiescent cells. These are supposed to be non-motile, to be produced by active cells with a rate μ_2 which depends on the acidity in the peritumoral space, and to infer a transition to activity, again with an acidity-dependent rate μ_3, which might differ from $\tilde{\mu}_3$. We also include a kind of acidity-triggered competition between active and quiescent cells; it might have an own rate, but to keep the number of model coefficients as low as possible we take it to be $\mu_2(h)$, too.

The third equation in system (6.2.1) is again a reaction-diffusion PDE and models the dynamics of proton concentration h. Protons are very small in comparison with cells and accordingly able to diffuse quite fastly. They are produced by both tumor cell phenotypes (primarily by active cells and to a lesser amount by quiescent ones) and infer natural decay (e.g., by proton buffering). Concrete choices of motility, transition, and proliferation coefficients will be provided in *Section 6.5*.

This setting extends our macroscopic model from *Chapter 5* in the sense that we consider here two interacting populations, the dynamics of both being influenced by that of the acidity in their surroundings. Instead of the tumor diffusion tensor depending only on space we have here a dependency on two of the solution components, however we do not include any repellent pH-taxis, but focus instead on the nonlocal interactions and on the phenotypic switch. It also extends the model in [136], where the two interacting species are not influenced by a third one, the diffusion of cells is of the linear type, and there are no transitions from one species to the other, although all interactions therein are nonlocal in space.

The model can be obtained in a way similar to the meso-to-macro deduction performed in *Chapter 5*, if the dynamics of w and h is given as in the second and third equations of (6.2.1), respectively. Although it is not clear how to obtain nonlinear diffusion in general, this can be achieved if the diffusion coefficient is only depending on macroscopic quantities other than u. If only linear diffusion is considered, then the method provides a space-dependent (myopic) diffusion tensor of u-cells, which by an adequate choice of the cell velocity distribution leads to classical Fickian diffusion.

Moreover, we make the following assumptions on involved parameters and functions:

- $\alpha, \beta, \gamma \geqslant 1$ satisfy

$$\alpha < \begin{cases} 1+\beta, & n = 1,2, \\ 1+\frac{2\beta}{n}, & n > 2, \end{cases} \tag{6.2.2}$$

- $\mu_1, D_H, \lambda > 0$,

- $\psi \in C^1(\mathbb{R}_0^+ \times \mathbb{R}_0^+)$ with derivatives $\partial_w \psi,\ \partial_h \psi$ that are Lipschitz continuous on $[0,1]^2$ and

$$\psi(w,h) \geqslant \delta > 0 \text{ for } h, w \in [0,1], \tag{6.2.3}$$

- $\mu_2, \mu_3 \in C^1(\mathbb{R}_0^+)$ with $\partial_h\mu_2, \partial_h\mu_3 \in L^\infty(\mathbb{R}_0^+)$, $\tilde{\mu}_3$ Lipschitz with Lipschitz constant $L_{\tilde{\mu}_3} \geqslant 0$, $\mu_2, \mu_3, \tilde{\mu}_3 \geqslant 0$,
- $F(w) = w$ or $F(w) = \frac{w}{1+w}$ and set $\tilde{F}(w) = 1$ if $F(w) = w$ and $\tilde{F}(w) = \frac{1}{1+w}$ if $F(w) = \frac{w}{1+w}$,
- g is Lipschitz continuous on $\mathbb{R}_0^+ \times \mathbb{R}_0^+$ with constant $L_g > 0$ and satisfies
$$0 \leqslant g(u,w) \leqslant G \tag{6.2.4}$$
for $G \in (0,\infty)$ s.t. $\frac{G}{\lambda} \leqslant 1$,
- for $i = 1, 2$ and $B := B_{\operatorname{diam}(\Omega)}(0)$ it holds that
$$J_i(x,\cdot) \text{ is Lipschitz continuous on } \mathbb{R}_0^+ \text{ for } x \in B \text{ with constant } L_{J_i}(x) \geqslant 0, \tag{6.2.5a}$$
$$L_{J_i},\ J_i(\cdot,0) \in L^{p_i}(B) \text{ for some } p_i \in (1,\infty), \tag{6.2.5b}$$
$$J_2 \geqslant 0,\ J_1 \geqslant \eta > 0 \text{ for } 0 \leqslant h \leqslant 1, \tag{6.2.5c}$$
- $u_0 \in C(\overline{\Omega})$, $w_0, h_0 \in H^1(\Omega)$ and $0 \leqslant u_0, h_0, w_0 \leqslant 1$.

These assumptions are primarily made out of technical reasons, in order to support the analysis in *Sections 6.3* and *6.4*, however most of them are reasonable from the application viewpoint: all parameters should be nonnegative and the interactions should involve at least one cell on either side; the diffusion of active and motile cells should be nondegenerate; there should be an effective, but uniformly limited production of protons, which should not dominate the natural decay in a too substantial manner; the interaction kernels should be nonnegative and there should be genuine intraspecific interactions, while the proton concentration remains reasonably bounded, and the initial conditions should be nonnegative and uniformly bounded.

6.3 Global existence of a classical solution to an approximate problem

Let $\vartheta \in (0,1)$. There are sequences of initial values $(u_{0\varepsilon})_{\varepsilon\in(0,1)}$, $(w_{0\varepsilon})_{\varepsilon\in(0,1)}$, $(h_{0\varepsilon})_{\varepsilon\in(0,1)}$ in $C^{2+\vartheta}(\overline{\Omega})$ s.t.
$$0 \leqslant u_{0\varepsilon}, w_{0\varepsilon}, h_{0\varepsilon} \leqslant 1, \tag{6.3.1a}$$
$$\partial_\nu u_{0\varepsilon} = \partial_\nu w_{0\varepsilon} = \partial_\nu h_{0\varepsilon} = 0 \text{ on } \partial\Omega,$$
$$u_{0\varepsilon} \underset{\varepsilon\to 0}{\to} u_0 \text{ in } C(\overline{\Omega}), \tag{6.3.1b}$$
$$w_{0\varepsilon} \underset{\varepsilon\to 0}{\to} w_0,\ h_{0\varepsilon} \underset{\varepsilon\to 0}{\to} h_0 \text{ in } H^1(\Omega). \tag{6.3.1c}$$
Throughout this chapter we consider for $\varepsilon \in (0,1)$ the approximate IBVP
$$\begin{cases} \partial_t u_\varepsilon = \nabla\cdot(\psi(w_\varepsilon,h_\varepsilon)\nabla u_\varepsilon) + \mu_1 u_\varepsilon^\alpha\left(1 - J_1(x,h_\varepsilon) * u_\varepsilon^\beta - J_2(x,h_\varepsilon) * w_\varepsilon^\gamma\right) & \\ \qquad + \tilde{\mu}_3(h_\varepsilon)F(w_\varepsilon) & \text{in } \Omega\times(0,\infty), \\ \partial_t w_\varepsilon = \varepsilon\Delta w_\varepsilon + \mu_2(h_\varepsilon)(1-w_\varepsilon)u_\varepsilon - \mu_3(h_\varepsilon)F(w_\varepsilon) & \text{in } \Omega\times(0,\infty), \\ \partial_t h_\varepsilon = D_H\Delta h_\varepsilon + g(u_\varepsilon,w_\varepsilon) - \lambda h_\varepsilon & \text{in } \Omega\times(0,\infty), \\ \partial_\nu u_\varepsilon = \partial_\nu w_\varepsilon = \partial_\nu h_\varepsilon = 0 & \text{on } \partial\Omega\times(0,\infty), \\ u_\varepsilon(\cdot,0) = u_{0\varepsilon},\ w_\varepsilon(\cdot,0) = w_{0\varepsilon},\ h_\varepsilon(\cdot,0) = h_{0\varepsilon} & \text{in } \Omega. \end{cases} \tag{6.3.2}$$

We show local existence of a solution with a fixed-point argument.

Lemma 6.3.1. *For all* $\varepsilon \in (0,1)$ *there is* $T_{max,\varepsilon} \in (0,\infty]$ *and a solution* $(u_\varepsilon, w_\varepsilon, h_\varepsilon)$ *of* (6.3.2) *in* $\left(C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T_{max,\varepsilon}))\right)^3$ *with* $0 \leqslant u_\varepsilon$ *and* $0 \leqslant w_\varepsilon, h_\varepsilon \leqslant 1$ *s.t. either* $T_{max,\varepsilon} = \infty$ *or* $T_{max,\varepsilon} < \infty$ *and*

$$\lim_{t\nearrow T_{max,\varepsilon}} \left(\|u_\varepsilon(\cdot,t)\|_{C^{2+\vartheta}(\overline{\Omega})} + \|w_\varepsilon(\cdot,t)\|_{C^{2+\vartheta}(\overline{\Omega})} + \|h_\varepsilon(\cdot,t)\|_{C^{2+\vartheta}(\overline{\Omega})}\right) = \infty. \tag{6.3.3}$$

Proof. Let $\varepsilon \in (0,1)$ and $T \in (0,1)$ small enough. For $h < 0$ we set

$$\mu_2(h) := \mu_2(-h),\ \mu_3(h) := \mu_3(-h),\ \tilde{\mu}_3(h) := \tilde{\mu}_3(-h).$$

We will perform a fixed-point argument in

$$S := \left\{(\overline{u},\overline{w}) \in \left(C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])\right)^2 : \overline{u},\overline{w} \geqslant 0,\ \|\overline{u}\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} + \|\overline{w}\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} \leqslant M+1\right\}$$

for $M := \|u_{0\varepsilon}\|_{C^\vartheta(\overline{\Omega})} + \|w_{0\varepsilon}\|_{C^\vartheta(\overline{\Omega})} + 1$. For $(\overline{u},\overline{w}) \in S$, we consider the three decoupled IBVPs

$$\begin{cases} \partial_t u_\varepsilon = \nabla\cdot(\psi(w_\varepsilon,h_\varepsilon)\nabla u_\varepsilon) - \mu_1\overline{u}^{\alpha-1}\left(J_1(x,h_\varepsilon) * \overline{u}^\beta + J_2(x,h_\varepsilon) * w_\varepsilon^\gamma\right)u_\varepsilon & \\ \qquad\quad + \mu_1\overline{u}^\alpha + \tilde{\mu}_3(h_\varepsilon)\tilde{F}(\overline{w})w_\varepsilon & \text{in } \Omega\times(0,\infty), \\ \partial_\nu u_\varepsilon = 0 & \text{on } \partial\Omega\times(0,\infty)0, \\ u_\varepsilon(\cdot,0) = u_{0\varepsilon} & \text{in } \Omega, \end{cases} \tag{6.3.4}$$

$$\begin{cases} \partial_t w_\varepsilon = \varepsilon\Delta w_\varepsilon + \mu_2(h_\varepsilon)(1-w_\varepsilon)\overline{u} - \mu_3(h_\varepsilon)\tilde{F}(\overline{w})w_\varepsilon & \text{in } \Omega\times(0,\infty), \\ \partial_\nu w_\varepsilon = 0 & \text{on } \partial\Omega\times(0,\infty), \\ w_\varepsilon(\cdot,0) = w_{0\varepsilon} & \text{in } \Omega, \end{cases} \tag{6.3.5}$$

and

$$\begin{cases} \partial_t h_\varepsilon = D_H\Delta h_\varepsilon + g(\overline{u},\overline{w}) - \lambda h_\varepsilon & \text{in } \Omega\times(0,\infty), \\ \partial_\nu h_\varepsilon = 0 & \text{on } \partial\Omega\times(0,\infty), \\ h_\varepsilon(\cdot,0) = h_{0\varepsilon} & \text{in } \Omega. \end{cases} \tag{6.3.6}$$

We start with (6.3.6). Due to the Hölder continuity of $\overline{u}$ and $\overline{w}$ and the Lipschitz continuity of g we can apply *Theorem A.1.6* with coefficients

$$a_{ii} := D_H,\ a_i := 0,\ a := \lambda,\ b_i := \nu_i,\ b := 0,\ f := g(\overline{u},\overline{w})$$

for $i \in \{1,\dots,n\}$ to (6.3.6) and obtain a unique solution $h_\varepsilon \in C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])$ satisfying

$$\|h_\varepsilon\|_{C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} \leqslant C_1\left(\|g(\overline{u},\overline{w})\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} + \|h_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})}\right) \leqslant C_2\left(M, \|h_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})}\right).$$

Moreover, due to the Lipschitz continuity of μ_2, μ_3, the Hölder continuity of $\overline{u},\overline{w}$ and *Lemma 2.2.3* we conclude again from *Theorem A.1.6* with the coefficients

$$a_{ii} := \varepsilon,\ a_i := 0,\ a := \mu_2(h_\varepsilon)\overline{u} + \mu_3(h_\varepsilon)\tilde{F}(\overline{w}),\ b_i := \nu_i,\ b := 0,\ f := \mu_2(h_\varepsilon)\overline{u}$$

for $i \in \{1, \ldots, n\}$ that there is a unique solution $w_\varepsilon \in C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega} \times [0,T])$ to (6.3.5) satisfying

$$\begin{aligned} \|w_\varepsilon\|_{C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} &\leqslant C_3 \left(\|\mu_2(h_\varepsilon)\overline{u}\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} + \|w_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})} \right) \\ &\leqslant C_4 \left(M, \|w_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})}, \|h_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})} \right). \end{aligned} \tag{6.3.7}$$

Then, we can estimate

$$0 \leqslant \mu_2(h_\varepsilon)\bar{u} = (w_\varepsilon)_t - \varepsilon\Delta w_\varepsilon + \left(\mu_2(h_\varepsilon)\overline{u} + \mu_3(h_\varepsilon)\tilde{F}(\overline{w}) \right) w_\varepsilon$$

and

$$0 \leqslant g(\bar{u}, \overline{w}) = (h_\varepsilon)_t - D_H\Delta h_\varepsilon + \lambda h_\varepsilon \leqslant G \leqslant \lambda$$

due to (6.2.4). Hence, from a parabolic comparison principle (*Theorem A.1.9*) and due to (6.3.1a) it follows that $0 \leqslant w_\varepsilon$ and $0 \leqslant h_\varepsilon \leqslant 1$. Further, we set $v_\varepsilon := 1 - w_\varepsilon$ and estimate

$$0 \leqslant \mu_3(h_\varepsilon)\tilde{F}(\overline{w})w_\varepsilon = (v_\varepsilon)_t - \varepsilon\Delta v_\varepsilon + \mu_2(h_\varepsilon)\overline{u}v_\varepsilon$$

and combining this with (6.3.1a) we conclude that $v_\varepsilon \geqslant 0$ and consequently, $w_\varepsilon \leqslant 1$. Now, we set

$$\begin{aligned} a_{ii} &:= \psi(w_\varepsilon, h_\varepsilon), \\ a_i &:= -\partial_w\psi(w_\varepsilon, h_\varepsilon)(w_\varepsilon)_{x_i} - \partial_h\psi(w_\varepsilon, h_\varepsilon)(h_\varepsilon)_{x_i}, \\ a &:= \mu_1\overline{u}^{\alpha-1} \left(J_1(x, h_\varepsilon) * \overline{u}^\beta + J_2(x, h_\varepsilon) * w_\varepsilon^\gamma \right), \\ b_i &:= \nu_i,\ b := 0, \\ f &:= \mu_1\overline{u}^\alpha + \tilde{\mu}_3(h_\varepsilon)\tilde{F}(\overline{w})w_\varepsilon \end{aligned}$$

for $i \in \{1, \ldots, n\}$ to apply again *Theorem A.1.6* to the equation corresponding to (6.3.4) in nondivergence form. From this theorem due to the Lipschitz continuity of $\partial_h\psi$ and $\partial_w\psi$ together with the bounds and the Hölder continuity of w_ε and h_ε and its gradients, the Lipschitz continuity of $\tilde{\mu}_3$ and *Lemmas 2.2.3* and *2.3.2* it follows that for $\kappa := \min\{1, \alpha-1\}\vartheta$ there is a unique solution $u_\varepsilon \in C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega} \times [0,T])$ to (6.3.4) that satisfies

$$\begin{aligned} \|u_\varepsilon\|_{C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])} \leqslant & C_5 \left(\|a_{ii}\|_{C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])}, \|a_i\|_{C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])}, \|a\|_{C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])}, \|b_i\|_{C^{1+\kappa,\frac{1+\kappa}{2}}} \right) \\ & \cdot \left(\|f\|_{C^{\kappa,\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])} + \|u_{0\varepsilon}\|_{C^{2+\kappa}(\overline{\Omega})} \right) \\ \leqslant & C_6 \left(M, \|u_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})}, \|w_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})}, \|h_{0\varepsilon}\|_{C^{2+\vartheta}(\overline{\Omega})} \right) \end{aligned} \tag{6.3.8}$$

due to the embedding of Hölder spaces. Further, we estimate

$$\begin{aligned} &(u_\varepsilon)_t - \psi(w_\varepsilon, h_\varepsilon)\Delta u_\varepsilon - (\partial_h\psi(w_\varepsilon, h_\varepsilon)\nabla h_\varepsilon + \partial_w\psi(w_\varepsilon, h_\varepsilon)\nabla w_\varepsilon) \cdot \nabla u_\varepsilon \\ &+ \mu_1\overline{u}^{\alpha-1} \left(J_1(x, h_\varepsilon) * \overline{u}^\beta + J_2(x, h_\varepsilon) * w_\varepsilon^\gamma \right) u_\varepsilon \\ =& \mu_1\overline{u}^\alpha + \tilde{\mu}_3(h_\varepsilon)\tilde{F}(\overline{w})w_\varepsilon \geqslant 0 \end{aligned}$$

and conclude from the comparison principle in *Theorem A.1.9* that $u_\varepsilon \geqslant 0$. Now, we estimate with (6.3.7) and (6.3.8) and *Lemma 2.2.9(iii)*:

$$\begin{aligned} &\|u_\varepsilon\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} + \|w_\varepsilon\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} \\ \leqslant& \|u_\varepsilon - u_{0\varepsilon}\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} + \|w_\varepsilon - w_{0\varepsilon}\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} + \|u_{0\varepsilon}\|_{C^{\vartheta}(\overline{\Omega})} + \|w_{0\varepsilon}\|_{C^{\vartheta}(\overline{\Omega})} \end{aligned}$$

$$\begin{aligned}
&\leqslant 2\max\{1,K_I(\vartheta)\}T^{\frac{1}{2}\min\{2-\vartheta,1+\kappa\}}\|u_\varepsilon\|_{C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])}\\
&\quad+2\max\{1,K_I(\vartheta)\}T^{\frac{1}{2}\min\{2-\vartheta,1+\vartheta\}}\|w_\varepsilon\|_{C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])}+\|u_{0\varepsilon}\|_{C^\vartheta(\overline{\Omega})}+\|h_{0\varepsilon}\|_{C^\vartheta(\overline{\Omega})}\\
&\leqslant 2\max\{1,K_I(\vartheta)\}T^{\frac{1}{2}}(C_6+C_4)+\|u_{0\varepsilon}\|_{C^\vartheta(\overline{\Omega})}+\|w_{0\varepsilon}\|_{C^\vartheta(\overline{\Omega})}\leqslant M+1
\end{aligned}$$

for

$$T\leqslant\left(\frac{1}{2\max\{1,K_I(\vartheta)\}(C_6+C_4)}\right)^2,$$

where $K_I(\vartheta)>0$ denotes the constant from the continuous embedding of $W^1_\infty(\Omega)$ into $C^\vartheta(\overline{\Omega})$ from *Lemma 2.2.8(ii)*. Hence, $(u_\varepsilon,w_\varepsilon)\in S$ and the operator

$$K:S\to S,\ (\overline{u},\overline{w})\mapsto(u_\varepsilon,w_\varepsilon)$$

is well-defined. Due to the continuous dependence of the solution on the coefficients in *Theorem A.1.6* the operator K is continuous. Moreover, (6.3.7) and (6.3.8) imply that K maps bounded subsets of $(C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T]))^2$ on bounded subsets of $(C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega}\times[0,T]))^2$. Hence, from the compact embedding $C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])\hookrightarrow\hookrightarrow C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])$ we conclude that K is a compact operator. Schauder's fixed-point theorem (*Theorem A.2.2*) implies that K has a fixed-point $(u_\varepsilon,w_\varepsilon)$ in $(C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T]))^2$, where additionally $u_\varepsilon\in C^{2+\kappa,1+\frac{\kappa}{2}}(\overline{\Omega}\times[0,T])$ and $w_\varepsilon\in C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])$ as was shown above. Applying *Theorem A.1.6* to u_ε again but with

$$a:=0,\ f:=\mu_1u_\varepsilon^\alpha\left(1-J_1(x,h_\varepsilon)*u_\varepsilon^\beta(x,t)-J_2(x,h_\varepsilon)*w_\varepsilon^\gamma\right)+\tilde{\mu}_3(h_\varepsilon)F(w_\varepsilon)$$

we conclude that also $u_\varepsilon\in C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])$. Finally, (6.3.3) follows extending the solution to its maximal existence time $T_{max,\varepsilon}$. □

We show the global boundedness of our solution by adapting the estimates from Step 1 and 2 of the proof of Theorem 1.1 in [99] similar to *Chapter 5.*

Lemma 6.3.2. *There is $C_7>0$ s.t. $\|u_\varepsilon\|_{L^\infty(\Omega\times(0,T_{max,\varepsilon}))}\leqslant C_7$ for all $\varepsilon\in(0,1)$.*

Proof.

Step 1. Let $\varepsilon\in(0,1)$ and $q>\max\{1,\beta+\alpha-1\}$. Consider $t\in(0,T_{max,\varepsilon})$. We multiply the first equation of (6.3.2) by qu_ε^{q-1} and integrate over Ω to obtain

$$\begin{aligned}
\frac{d}{dt}\int_\Omega u_\varepsilon^q\,\mathrm{d}x=&-q(q-1)\int_\Omega\psi(w_\varepsilon,h_\varepsilon)\left|\nabla u_\varepsilon\right|^2u_\varepsilon^{q-2}\,\mathrm{d}x\\
&+q\mu_1\int_\Omega u_\varepsilon^{q+\alpha-1}\left(1-J_1(x,h_\varepsilon)*u_\varepsilon^\beta-J_2(x,h_\varepsilon)*w_\varepsilon^\gamma\right)\mathrm{d}x\\
&+q\int_\Omega\tilde{\mu}_3(h_\varepsilon)F(w_\varepsilon)u_\varepsilon^{q-1}\,\mathrm{d}x
\end{aligned}$$

using partial integration. Hence, we conclude from (6.2.3) and (6.2.5c), the continuity of $\tilde{\mu}_3$, the boundedness of h_ε, the fact that $F(w_\varepsilon)\leqslant 1$ for $w_\varepsilon\leqslant 1$ and Young's inequality that

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega u_\varepsilon^q\,\mathrm{d}x+\frac{4(q-1)}{q}\delta\int_\Omega\left|\nabla u_\varepsilon^{\frac{q}{2}}\right|^2\mathrm{d}x+q\mu_1\eta\int_\Omega u_\varepsilon^\beta\,\mathrm{d}x\int_\Omega u_\varepsilon^{q+\alpha-1}\,\mathrm{d}x\\
\leqslant&q\mu_1\int_\Omega u_\varepsilon^{q+\alpha-1}\,\mathrm{d}x+q\|\tilde{\mu}_3\|_{L^\infty(0,1)}\int_\Omega u_\varepsilon^{q-1}\,\mathrm{d}x.
\end{aligned}$$

Setting $C_8 := \mu_1 + \|\tilde{\mu}_3\|_{L^\infty(0,1)}$ and adding $qC_8\|u_\varepsilon\|^q_{L^q(\Omega)}$ on both sides of the above equation and using Young's inequality we arrive at

$$\begin{aligned}&\frac{d}{dt}\int_\Omega u_\varepsilon^q \,\mathrm{d}x + \frac{4(q-1)}{q}\delta\int_\Omega \left|\nabla u^{\frac{q}{2}}\right|^2 \mathrm{d}x + q\mu_1\eta\int_\Omega u_\varepsilon^\beta \,\mathrm{d}x\int_\Omega u_\varepsilon^{q+\alpha-1}\,\mathrm{d}x + qC_8\int_\Omega u_\varepsilon^q\,\mathrm{d}x\\ \leqslant& 2qC_8\left(\int_\Omega u_\varepsilon^{q+\alpha-1}\,\mathrm{d}x + |\Omega|\right).\end{aligned} \tag{6.3.9}$$

From *Lemma A.4.1* it follows for $K_{18} = \frac{C_8}{\delta}$ and $K_{22} = \frac{2C_8}{\mu_1\eta}$ that

$$\int_\Omega u_\varepsilon^{q+\alpha-1}\,\mathrm{d}x \leqslant \frac{2(q-1)}{q^2C_8}\delta\int_\Omega |\nabla u_\varepsilon^{\frac{q}{2}}|^2\,\mathrm{d}x + \frac{\mu_1\eta}{2C_8}\int_\Omega u_\varepsilon^\beta\,\mathrm{d}x\int_\Omega u_\varepsilon^{q+\alpha-1}\,\mathrm{d}x + K_{23}(q), \tag{6.3.10}$$

where

$$s\begin{cases} = \infty, & n=1,\\ \in \left(\frac{2(q+\alpha-1+\beta)}{q-\alpha+1+\beta}, \infty\right), & n=2,\\ = \frac{2n}{n-2}, & n>2,\end{cases}$$

$$\begin{aligned}K_{23}(q) := &\left(2\left(\frac{K_{21}^2q^2C_8}{(q-1)\delta}\right)^{\frac{q+\alpha-1-\beta}{q-\alpha+1+\beta-2\frac{q+\alpha-1+\beta}{s}}} + K_{24}(q)^{\frac{q+\alpha-\beta-1}{q-\frac{q+\alpha-1+\beta}{s}}}\right)^{\frac{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\\ &\cdot\left(\frac{2C_8}{\mu_1\eta}\right)^{\frac{q-\frac{2(q+\alpha-1)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}} + K_{24}(q)^{\frac{q+\alpha-\beta-1}{q-\frac{q+\alpha-1+\beta}{s}}},\end{aligned}$$

and

$$\begin{aligned}K_{21} &:= 2K_S\left(1+2K_P\right),\\ K_{24}(q) &:= 4K_S|\Omega|^{\frac{1}{2}-\frac{q}{q+\alpha-1+\beta}}.\end{aligned}$$

Here, K_S denotes the embedding constant from $H^1(\Omega)$ into $L^s(\Omega)$ from *Lemma 2.2.8(i)* and K_P denotes the constant from the Poincaré inequality. We will leave out the dependence of the constants on s. Hence, inserting (6.3.10) into (6.3.9) we obtain

$$\frac{d}{dt}\int_\Omega u_\varepsilon^q\,\mathrm{d}x + qC_8\int_\Omega u_\varepsilon^q\,\mathrm{d}x \leqslant 2qC_8\left(K_{23}(q) + |\Omega|\right)$$

and conclude from *Lemma A.1.20* with $K_{14} = qC_8$ and $K_{15} = 2(K_{23}(q) + |\Omega|)$ that

$$\|u_\varepsilon\|_{L^q(\Omega)} \leqslant \sqrt[q]{2(K_{23}(q) + |\Omega|) + \|u_{0\varepsilon}\|^q_{L^q(\Omega)}} \leqslant \sqrt[q]{2K_{23}(q) + |\Omega|\left(2 + \|u_{0\varepsilon}\|^q_{L^\infty(\Omega)}\right)} \underset{q\to\infty}{\to} \infty \tag{6.3.11}$$

due to

$$\begin{aligned}&\left(\left(\frac{q^2}{q-1}\right)^{\frac{q+\alpha-1-\beta}{q-\alpha+1+\beta-2\frac{q+\alpha-1+\beta}{s}}\cdot\frac{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right)^{\frac{1}{q}}\\ \geqslant& q^{\frac{1}{q}\cdot\frac{q+\alpha-1-\beta}{\beta+1-\alpha-\frac{2\beta}{s}}} = \left(q^{1+\frac{\alpha-1-\beta}{q}}\right)^{\frac{1}{\beta+1-\alpha-\frac{2\beta}{s}}} \underset{q\to\infty}{\to} \infty.\end{aligned}$$

Due to (6.3.1a) we can also find an upper bound independent from ε, namely

$$\|u_\varepsilon\|_{L^q(\Omega)} \leqslant \sqrt[q]{2K_{23}(q) + 3|\Omega|}. \tag{6.3.12}$$

Step 2. We proceed with a Moser iteration. Set $a := \frac{2(s-1)(\alpha-1)}{s-2}$ and $q_k := 2^k + a$ for $k \in \mathbb{N}$ large enough s.t. $q_k > \max\{1, \beta+\alpha-1\}$. Then, using *Lemma A.4.1* with $K_{18} = \frac{C_8}{\delta}$ and $r = r_k := \frac{2q_{k-1}}{q_k}$ we conclude from (6.3.9) that

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega u_\varepsilon^{q_k}\,\mathrm{d}x + \frac{4(q_k-1)}{q_k}\delta\int_\Omega \left|\nabla u_\varepsilon^{\frac{q_k}{2}}\right|^2 \mathrm{d}x + q_k\mu_1\eta\int_\Omega u_\varepsilon^\beta\,\mathrm{d}x\int_\Omega u_\varepsilon^{q_k+\alpha-1}\,\mathrm{d}x + q_kC_8\int_\Omega u_\varepsilon^{q_k}\,\mathrm{d}x\\
\leqslant& 2q_kC_8\left(\int_\Omega u_\varepsilon^{q_k+\alpha-1}\,\mathrm{d}x + |\Omega|\right)\\
\leqslant& \frac{4(q_k-1)}{q_k^2}\delta\int_\Omega |\nabla u_\varepsilon^{\frac{q_k}{2}}|^2\,\mathrm{d}x\\
&+ 2q_kC_8\left((2C_9(k)+C_{10}(k))\,\|u_\varepsilon^{\frac{q_k}{2}}\|_{L^{r_k}(\Omega)}^{2r_k\frac{\frac{2(q_k+\alpha-1)}{s}-q_k}{2q_{k-1}(\frac{2}{s}-1)+2(\alpha-1)}} + C_{10}(k) + |\Omega|\right),
\end{aligned} \tag{6.3.13}$$

where

$$\begin{aligned}
C_9(k) &:= \left(\frac{K_{21}^2q_k^2C_8}{(q_k-1)\delta}\right)^{\frac{2q_{k-1}-2(q_k+\alpha-1)}{2q_{k-1}(\frac{2}{s}-1)+2(\alpha-1)}},\\
C_{10}(k) &:= K_{20}(k)^{\frac{2q_{k-1}-2(q_k+\alpha-1)}{\frac{2q_{k-1}}{s}-q_k}},\\
K_{20}(k) &:= 4K_S(s)|\Omega|^{\frac{q_{k-1}-q_k}{2q_{k-1}}}.
\end{aligned}$$

We know from *Lemma A.4.2* that

$$\frac{\frac{2(q_k+\alpha-1)}{s}-q_k}{2q_{k-1}\left(\frac{2}{s}-1\right)+2(\alpha-1)} = 1$$

and consequently,

$$\|u_\varepsilon^{\frac{q_k}{2}}\|_{L^{r_k}(\Omega)}^{2r_k\frac{\frac{2(q_k+\alpha-1)}{s}-q_k}{2q_{k-1}(\frac{2}{s}-1)+2(\alpha-1)}} = \left(\int_\Omega u_\varepsilon^{q_{k-1}}\,\mathrm{d}x\right)^2.$$

Inserting this into (6.3.13) we conclude that

$$\begin{aligned}
&\frac{d}{dt}\int_\Omega u_\varepsilon^{q_k}\,\mathrm{d}x + q_kC_8\int_\Omega u_\varepsilon^{q_k}\,\mathrm{d}x\\
\leqslant& 2q_kC_8\left(2C_9(k)+2C_{10}(k)+|\Omega|\right)\max\left\{1, \left(\int_\Omega u_\varepsilon^{q_{k-1}}\,\mathrm{d}x\right)^2\right\}.
\end{aligned} \tag{6.3.14}$$

Moreover, *Lemma A.4.2* implies that

$$\frac{2q_{k-1}-2(q_k+\alpha-1)}{2q_{k-1}\left(\frac{2}{s}-1\right)+2(\alpha-1)} = \frac{s}{s-2} \text{ and } \frac{2q_{k-1}-2(q_k+\alpha-1)}{\frac{2q_{k-1}}{s}-q_k} \leqslant \alpha+1.$$

Further, we can compute that

$$\frac{q_{k-1}-q_k}{2q_{k-1}} \in \left(-\frac{1}{2}, 0\right).$$

Hence, we can estimate

$$2C_9(k)+2C_{10}(k)+|\Omega| = 2\left(\frac{K_{21}^2q_k^2C_8}{(q_k-1)\delta}\right)^{\frac{s}{s-2}} + 2\left(4K_S|\Omega|^{\frac{q_{k-1}-q_k}{2q_{k-1}}}\right)^{\frac{2q_{k-1}-2(q_k+\alpha-1)}{\frac{2q_{k-1}}{s}-q_k}} + |\Omega|$$

$$\leqslant 2\left(\frac{K_{21}^2C_8}{\delta}2^k(1+a)\right)^{\frac{s}{s-2}}+2\left(4\max\{1,K_S\}\max\left\{1,|\Omega|^{-\frac{1}{2}}\right\}\right)^{\alpha+1}+|\Omega|$$
$$\leqslant \frac{\bar a}{2}2^{\frac{s}{s-2}k},$$

where

$$\bar a:=2\left(2\left(\frac{K_{21}^2C_8}{\delta}(1+a)\right)^{\frac{s}{s-2}}+2\left(4\max\{1,K_S\}\max\left\{1,|\Omega|^{-\frac{1}{2}}\right\}\right)^{\alpha+1}+|\Omega|\right).$$

Inserting this into (6.3.14) we obtain

$$\frac{d}{dt}\int_\Omega u_\varepsilon^{q_k}\,\mathrm{d}x+q_kC_8\int_\Omega u_\varepsilon^{q_k}\,\mathrm{d}x\leqslant q_kC_8\bar a2^{\frac{s}{s-2}k}\max\left\{1,\sup_{t\geqslant 0}\left(\int_\Omega u_\varepsilon^{q_{k-1}}\,\mathrm{d}x\right)^2\right\}.$$

For $k\geqslant 1$ we can estimate that $\int_\Omega u_{0\varepsilon}^{q_k}\,\mathrm{d}x\leqslant \|u_{0\varepsilon}\|_{L^\infty(\Omega)}^{q_k}|\Omega|\leqslant|\Omega|$ due to (6.3.1a). Hence, *Lemma A.4.3* with $c_k=q_kC_8$ and $D=\frac{s}{s-2}$ implies that for $k\geqslant m\geqslant 1$ large enough, i.e., s.t. $\bar a2^{\frac{s}{s-2}m}\geqslant 1$, it holds that

$$\begin{aligned}\left(\int_\Omega u_\varepsilon^{q_k}\,\mathrm{d}x\right)^{\frac{1}{q_k}}\leqslant&(2\bar a)^{\frac{2^{k-m+1}-1}{q_k}}2^{\frac{\frac{s}{s-2}\left(2(2^{k-m}-1)+m2^{k-m+1}-k\right)}{q_k}}\\&\cdot\max\left\{\sup_{t\geqslant 0}\left(\int_\Omega u_\varepsilon^{q_{m-1}}\,\mathrm{d}x\right)^{\frac{2^{k-m+1}}{q_k}},|\Omega|^{\frac{2^{k-m}}{q_k}},1\right\}.\end{aligned}$$

For $k\to\infty$ we obtain

$$\|u_\varepsilon\|_{L^\infty(\Omega)}\leqslant(2\bar a)^{\frac{1}{2^{m-1}}}2^{\frac{s(m+1)}{(s-2)2^{m-1}}}\max\left\{\sup_{t\geqslant 0}\left(\int_\Omega u_\varepsilon^{q_{m-1}}\,\mathrm{d}x\right)^{\frac{1}{2^{m-1}}},|\Omega|^{2^{-m}},1\right\}\tag{6.3.15}$$

in $(0,T_{max,\varepsilon})$. We already know from Step 1 that the right-hand side is bounded above by a constant indepent from ε. Consequently, $u_\varepsilon\in L^\infty(\Omega\times(0,T_{max,\varepsilon}))$ is bounded above by a constant independent from ε.

□

We can also perform a quasi-maximum principle as in Step 3 of the proof of Theorem 1.1 in [99].

Corollary 6.3.3. *We find $K>1$ and 'small' enough parameters s.t.*

$$\|u_\varepsilon\|_{L^\infty(\Omega\times(0,T_{max,\varepsilon}))}\leqslant K\max\left\{1,\left(\left(4K_S|\Omega|^{-\frac{1}{2}}\right)^{\frac{1}{1-\frac{1}{s}}}\frac{2}{\eta}\left(1+\frac{\|\tilde\mu_3\|_{L^\infty(0,1)}}{\mu_1}\right)\right)^{\frac{1-\frac{2}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right\}.\tag{6.3.16}$$

Proof. We want to consider the limit $m\to\infty$ in (6.3.15) for 'small' enough parameters. We already know from (6.3.12) in the proof of *Lemma 6.3.2* that for $t\in(0,T_{max,\varepsilon})$ it holds that

$$\int_\Omega u_\varepsilon^{q_{m-1}}\,\mathrm{d}x\leqslant 2K_{23}\left(q_{m-1}\right)+3|\Omega|.$$

We fix some m and assume that our parameters are 'small' enough s.t.

$$C_8=\mu_1+\|\tilde\mu_3\|_{L^\infty(0,1)}\leqslant\frac{\delta}{K_{21}^2q_{m-1}^2}\tag{6.3.17}$$

holds. Then, we can estimate

$$\begin{aligned}
&\int_\Omega u_\varepsilon^{q_{m-1}}\,\mathrm{d}x\\
\leqslant 7\max\Bigg\{&\Bigg(2\left(\frac{1}{2^{m-1}+a-1}\right)^{\frac{q_{m-1}+\alpha-1-\beta}{q_{m-1}-\alpha+1+\beta-2\frac{q_{m-1}+\alpha-1+\beta}{s}}}\\
&\qquad +K_{24}(q_{m-1})^{\frac{q_{m-1}+\alpha-\beta-1}{q_{m-1}-\frac{q_{m-1}+\alpha-1+\beta}{s}}}\Bigg)^{\frac{q_{m-1}-\alpha+1+\beta-\frac{2(q_{m-1}+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\\
&\quad\cdot\left(\frac{2}{\eta}\left(1+\frac{\|\tilde{\mu}_3\|_{L^\infty(0,1)}}{\mu_1}\right)\right)^{\frac{q_{m-1}-\frac{2(q_{m-1}+\alpha-1)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}},\\
&\quad K_{24}(q_{m-1})^{\frac{q_{m-1}+\alpha-\beta-1}{q_{m-1}-\frac{q_{m-1}+\alpha-1+\beta}{s}}},|\Omega|\Bigg\} =: H(m).
\end{aligned}$$

Finally, we conclude with

$$\begin{aligned}
&\lim_{m\to\infty}(H(m))^{\frac{1}{2^{m-1}}} = \max\left\{1,\left(\left(4K_S|\Omega|^{-\frac{1}{2}}\right)^{\frac{1}{1-\frac{1}{s}}}\frac{2}{\eta}\left(1+\frac{\|\tilde{\mu}_3\|_{L^\infty(0,1)}}{\mu_1}\right)\right)^{\frac{1-\frac{2}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right\},\\
&\lim_{m\to\infty}(2\bar{a})^{\frac{1}{2^{m-1}}}2^{\frac{s(m+1)}{(s-2)2^{m-1}}} = 1
\end{aligned}$$

and $|\Omega|^{2^{-(m+1)}} \underset{m\to\infty}{\to} 1$ from (6.3.15) that

$$\|u_\varepsilon\|_{L^\infty(\Omega\times(0,T_{max,\varepsilon}))} \leqslant \max\left\{1,\left(\left(4K_S|\Omega|^{-\frac{1}{2}}\right)^{\frac{1}{1-\frac{1}{s}}}\frac{2}{\eta}\left(1+\frac{\|\tilde{\mu}_3\|_{L^\infty(0,1)}}{\mu_1}\right)\right)^{\frac{1-\frac{2}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right\}.$$

Obviously, we do not find parameters satisfying (6.3.17) for m tending to infinity. Nevertheless, for any $K > 1$ we find an m^* depending only on K s.t. if (6.3.17) is satisfied for m^* then, (6.3.16) holds. □

In the following remark we give an exact formula for the Sobolev constant K_S from *Lemma 2.2.8(i)* that only depends on the domain Ω and the dimension n to get an impression of the upper bound of u_ε.

Remark 6.3.4. If Ω is convex the upper bound from *Corollary 6.3.3* can be given in terms of K and our parameters as due to *Lemma A.4.4* the Sobolev embedding constant $K_S(s)$ is given by

$$K_S(s) = \begin{cases} \max\left\{1, \frac{\mathrm{diam}(\Omega)|V|^{\frac{1}{2}}}{|\Omega|}\right\} & n = 1,\\ \sqrt{2}\max\left\{|\Omega|^{\frac{1}{s}-\frac{1}{2}}, \frac{\mathrm{diam}(\Omega)^{1+\frac{s+2}{s}}\pi^{\frac{s+2}{2s}}}{2|\Omega|}\frac{\Gamma\left(\frac{s-2}{2s}\right)}{\Gamma\left(\frac{s+2}{2s}\right)}\right\}\sqrt{\frac{\Gamma\left(\frac{2}{s}\right)}{\Gamma\left(2\frac{s-1}{s}\right)}}\left(\frac{\Gamma(2)}{\Gamma(1)}\right)^{\frac{s-2}{2s}} & n = 2,\\ \sqrt{2}\max\left\{|\Omega|^{-\frac{1}{n}}, \frac{\mathrm{diam}(\Omega)^n\pi^{\frac{n-1}{2}}}{n|\Omega|}\frac{\Gamma\left(\frac{1}{2}\right)}{\Gamma\left(\frac{n-1}{2}\right)}\right\}\sqrt{\frac{\Gamma\left(\frac{n-2}{2}\right)}{\Gamma\left(\frac{n+2}{2}\right)}}\left(\frac{\Gamma(n)}{\Gamma\left(\frac{n}{2}\right)}\right)^{\frac{1}{n}} & n \geqslant 3,\end{cases} \quad (6.3.18)$$

where $V := \bigcup_{x\in\Omega}\Omega_x$ and $\Omega_x := \{y - x : y \in \Omega\}$ for $x \in \Omega$, and Γ denotes the Gamma function given by $\Gamma(x) = \int_0^\infty t^{x-1}e^{-t}\,\mathrm{d}t$ for $x > 0$.

Global existence of our solution follows from the last lemma.

Theorem 6.3.5. *For* $\varepsilon \in (0,1)$ *there is a bounded global solution* $(u_\varepsilon, w_\varepsilon, h_\varepsilon)$ *of* (6.3.2) *in* $\left(C^{2+\vartheta,1+\frac{\vartheta}{2}}\left(\overline{\Omega}\times[0,\infty)\right)\right)^3$ *satisfying* $0 \leqslant u_\varepsilon \leqslant C_7$ *and* $0 \leqslant w_\varepsilon, h_\varepsilon \leqslant 1$.

Proof. Let $\varepsilon \in (0,1)$. *Lemmas 6.3.1* and *6.3.2* imply that $u_\varepsilon, w_\varepsilon, h_\varepsilon \in L^\infty(\Omega \times (0, T_{max,\varepsilon}))$. Assume $T_{max,\varepsilon} < \infty$. Then, $g(u_\varepsilon, w_\varepsilon) \in L^\infty(\Omega \times (0, T_{max}))$ follows from the Lipschitz continuity of g. Putting together *Theorem A.1.1*, the boundedness of h_ε, *Theorem A.1.12* with

$$a(\nabla h_\varepsilon) := D_H \nabla h_\varepsilon,\ b(x,t,h_\varepsilon) := \lambda h_\varepsilon - g(u_\varepsilon, w_\varepsilon)$$

we conclude that there is $\kappa_1 \in (0,1)$ s.t.

$$\|h_\varepsilon\|_{C^{\kappa_1,\frac{\kappa_1}{2}}(\overline{\Omega}\times[0,T_{max,\varepsilon}])} \leqslant C_{11}. \tag{6.3.19}$$

Analogously, setting

$$a(\nabla w_\varepsilon) := \varepsilon \nabla w_\varepsilon,\ b(x,t,w_\varepsilon) := \mu_3(h_\varepsilon)F(w_\varepsilon) + \mu_2(h_\varepsilon)(w_\varepsilon - 1)u_\varepsilon$$

in *Theorem A.1.12* we conclude using the boundedness of our solution and the Lipschitz continuity of μ_2 and μ_3 on $[0,1]$ that there is $\kappa_2 \in (0,1)$ s.t.

$$\|w_\varepsilon\|_{C^{\kappa_2,\frac{\kappa_2}{2}}(\overline{\Omega}\times[0,T_{max,\varepsilon}])} \leqslant C_{12}. \tag{6.3.20}$$

Moreover, due to the boundedness of our solution, the continuity of ψ, (6.2.3) and (6.2.5b) and setting

$$\begin{aligned} a(x,t,\nabla u_\varepsilon) &:= \psi(w_\varepsilon, h_\varepsilon)\nabla u_\varepsilon, \\ b(x,t,u_\varepsilon) &:= \mu_1 u_\varepsilon^\alpha \left(-1 + J_1(x,h_\varepsilon) * u_\varepsilon^\beta + J_2(x,h_\varepsilon) * w_\varepsilon^\gamma\right) - \tilde{\mu}_3(h_\varepsilon)F(w_\varepsilon) \end{aligned}$$

in *Theorem A.1.12* it follows analogously that there is $\kappa_3 \in (0,1)$ s.t.

$$\|u_\varepsilon\|_{C^{\kappa_3,\frac{\kappa_3}{2}}(\overline{\Omega}\times[0,T_{max,\varepsilon}])} \leqslant C_{13}. \tag{6.3.21}$$

Finally, it follows as in *Lemma 6.3.1* (applying *Theorem A.1.6* twice to every function if necessary) that $u_\varepsilon, w_\varepsilon, h_\varepsilon \in C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T_{max,\varepsilon}])$. This contradicts (6.3.3). Hence, $T_{max,\varepsilon} = \infty$ follows. □

We show the uniqueness of this solution as in *Chapter 5*, where we need to restrict p_1, p_2 in (6.2.5b) if $n \geqslant 3$.

Lemma 6.3.6. *Assume that* p_1, p_2 *from* (6.2.5b) *satisfy* $p_1, p_2 \geqslant \frac{2n}{n+2}$ *if* $n \geqslant 3$ *and* $p_1, p_2 \in (1,\infty)$ *as before if* $n = 1,2$ *then the classical solution from Theorem 6.3.5 is unique.*

Proof. Let $\varepsilon \in (0,1)$ and $T \in (0,\infty)$. Assume that there are two solutions (u_1, w_1, h_1) and (u_2, w_2, h_2) in $\left(C^{2+\vartheta,1+\frac{\vartheta}{2}}\left(\overline{\Omega}\times[0,\infty)\right)\right)^3$ to (6.3.2). Then, we obtain after subtracting the equations for h_1 and h_2 from another that

$$(h_1 - h_2)_t = D_H \Delta(h_1 - h_2) + g(u_1, w_1) - g(u_2, w_2) - \lambda(h_1 - h_2)$$

holds in $\Omega \times (0,T)$. Now, we multiply the above equation with $h_1 - h_2$, integrate over Ω and obtain for $t \in (0,T)$ using partial integration, the Lipschitz continuity of g and Young's inequality that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega |h_1-h_2|^2\,\mathrm{d}x + \lambda\int_\Omega |h_1-h_2|^2\,\mathrm{d}x + D_H\int_\Omega |\nabla(h_1-h_2)|^2\,\mathrm{d}x\\
=&\int_\Omega (g(u_1,w_1)-g(u_2,w_2))(h_1-h_2)\,\mathrm{d}x\\
\leqslant&2L_g\int_\Omega |u_1-u_2||h_1-h_2|\,\mathrm{d}x + 2L_g\int_\Omega |w_1-w_2||h_1-h_2|\,\mathrm{d}x\\
\leqslant&C_{14}\left(\int_\Omega |u_1-u_2|^2\,\mathrm{d}x + \int_\Omega |w_1-w_2|^2\,\mathrm{d}x\right) + \lambda\int_\Omega |h_1-h_2|^2\,\mathrm{d}x.
\end{aligned} \tag{6.3.22}$$

Subtracting the equations for w_1 and w_2 from another we obtain the equation

$$\begin{aligned}
(w_1-w_2)_t =&\varepsilon\Delta(w_1-w_2) + \mu_2(h_1)(1-w_1)u_1 - \mu_2(h_2)(1-w_2)u_2\\
&+ \mu_3(h_2)F(w_2) - \mu_3(h_1)F(w_1)\\
=&\varepsilon\Delta(w_1-w_2) + \mu_2(h_1)(1-w_1)(u_1-u_2) + \mu_2(h_1)(w_2-w_1)u_2\\
&+ (\mu_2(h_1)-\mu_2(h_2))(1-w_2)u_2 + \mu_3(h_2)(w_2-w_1)\tilde{F}(w_1)\tilde{F}(w_2)\\
&+ (\mu_3(h_2)-\mu_3(h_1))F(w_1)
\end{aligned}$$

that holds in $\Omega \times (0,T)$ and conclude analogously to above using the Lipschitz continuity of μ_2 and μ_3 and the boundedness of the solutions that for $t \in (0,T)$ it holds that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega |w_1-w_2|^2\,\mathrm{d}x + \varepsilon\int_\Omega |\nabla(w_1-w_2)|^2\,\mathrm{d}x\\
\leqslant&\|\mu_2\|_{L^\infty(0,1)}\int_\Omega |u_1-u_2||w_1-w_2|\,\mathrm{d}x + (\|\mu_2\|_{L^\infty(0,1)}C_7 + \|\mu_3\|_{L^\infty(0,1)})\int_\Omega |w_1-w_2|^2\,\mathrm{d}x\\
&+ (\|\mu_2'\|_{L^\infty(0,1)}C_7 + \|\mu_3'\|_{L^\infty(0,1)})\int_\Omega |h_1-h_2||w_1-w_2|\,\mathrm{d}x\\
\leqslant&C_{15}\left(\int_\Omega |u_1-u_2|^2\,\mathrm{d}x + \int_\Omega |w_1-w_2|^2\,\mathrm{d}x + \int_\Omega |h_1-h_2|^2\,\mathrm{d}x\right).
\end{aligned} \tag{6.3.23}$$

Further, we obtain by subtracting the equations for u_1 and u_2 from another that

$$\begin{aligned}
(u_1-u_2)_t =&\nabla\cdot(\psi(w_1,h_1)\nabla u_1 - \psi(w_2,h_2)\nabla u_2) + \mu_1\Big(u_1^\alpha - u_2^\alpha + u_2^\alpha J_1(x,h_2)*u_2^\beta\\
&-u_1^\alpha J_1(x,h_1)*u_1^\beta + u_2^\alpha J_2(x,h_2)*w_2^\gamma - u_1^\alpha J_2(x,h_1)*w_1^\gamma\Big)\\
&+ \tilde{\mu}_3(h_1)F(w_1) - \tilde{\mu}_3(h_2)F(w_2)\\
=&\nabla\cdot(\psi(w_1,h_1)\nabla(u_1-u_2) + (\psi(w_1,h_1)-\psi(w_2,h_2))\nabla u_2) + \mu_1(u_1^\alpha - u_2^\alpha)\\
&+ \mu_1\Big(u_2^\alpha J_1(x,h_2)*u_2^\beta - u_1^\alpha J_1(x,h_1)*u_1^\beta + u_2^\alpha J_2(x,h_2)*w_2^\gamma - u_1^\alpha J_2(x,h_1)*w_1^\gamma\Big)\\
&+ (\tilde{\mu}_3(h_1)-\tilde{\mu}_3(h_2))F(w_1) + \tilde{\mu}_3(h_2)(w_1-w_2)\tilde{F}(w_1)\tilde{F}(w_2)
\end{aligned} \tag{6.3.24}$$

holds in $\Omega \times (0,T)$. Using (6.2.5a), (6.2.5b), the boundedness of u_1, u_2, the mean value theorem and Hölder's inequality and the Sobolev embedding from *Lemma 2.2.8(i)* we can estimate on $\Omega \times (0,T)$ that

$$\begin{aligned}
&\left|J_1(x,h_2)*u_2^\beta - J_1(x,h_1)*u_1^\beta\right|\\
\leqslant&|(J_1(x,h_2)-J_1(x,h_1))*u_2^\beta| + |J_1(x,h_1)*(u_1^\beta - u_2^\beta)|
\end{aligned}$$

$$\begin{aligned}
&\leqslant C_7^{\beta}\int_\Omega L_{J_1}(x-y)|h_1(y)-h_2(y)|\,\mathrm{d}y+\beta C_7^{\beta-1}\int_\Omega J_1(x-y,h_1(y))|u_1(y)-u_2(y)|\,\mathrm{d}y\\
&\leqslant C_7^{\beta}\|L_{J_1}\|_{L^{p_1}(B)}\|h_1-h_2\|_{L^{\frac{p_1}{p_1-1}}(\Omega)}+\beta C_7^{\beta-1}(\|L_{J_1}\|_{L^{p_1}(B)}+\|J_1(\cdot,0)\|_{L^{p_1}(B)})\|u_1-u_2\|_{L^{\frac{p_1}{p_1-1}}(\Omega)}\\
&\leqslant C_{16}\left(\|h_1-h_2\|_{H^1(\Omega)}+\|u_1-u_2\|_{H^1(\Omega)}\right).
\end{aligned}$$

From this we obtain using (6.2.5a), (6.2.5b), the boundedness of u_1, u_2, the mean value theorem, *Lemma 2.3.2(i)* and Hölder's and Young's inequality that

$$\begin{aligned}
&\int_\Omega\left|u_2^\alpha J_1(x,h_2)*u_2^\beta-u_1^\alpha J_1(x,h_1)*u_1^\beta\right||u_1-u_2|\,\mathrm{d}x\\
\leqslant&\alpha C_7^{\alpha-1}\|J_1(\cdot,h_2)*u_2^\beta\|_{L^\infty(\Omega\times(0,T))}\|u_1-u_2\|^2_{L^2(\Omega)}\\
&+C_{16}C_7^{\alpha}\left(\|h_1-h_2\|_{H^1(\Omega)}+\|u_1-u_2\|_{H^1(\Omega)}\right)\|u_1-u_2\|_{L^1(\Omega)}\\
\leqslant&C_{17}\left(D_H^{-1},\delta^{-1}\right)\left(\|h_1-h_2\|^2_{L^2(\Omega)}+\|u_1-u_2\|^2_{L^2(\Omega)}\right)+\frac{D_H}{2}\|\nabla(h_1-h_2)\|^2_{(L^2(\Omega))^n}\\
&+\frac{\delta}{2}\|\nabla(u_1-u_2)\|^2_{(L^2(\Omega))^n}.
\end{aligned}\tag{6.3.25}$$

Analogously, we obtain

$$\begin{aligned}
&\int_\Omega|u_2^\alpha J_2(x,h_2)*w_2^\gamma-u_1^\alpha J_2(x,h_1)*w_1^\gamma|\,|u_1-u_2|\,\mathrm{d}x\\
\leqslant&C_{18}\left(D_H^{-1},\varepsilon^{-1}\right)\left(\|u_1-u_2\|^2_{L^2(\Omega)}+\|h_1-h_2\|^2_{L^2(\Omega)}+\|w_1-w_2\|^2_{L^2(\Omega)}\right)\\
&+\frac{D_H}{2}\|\nabla(h_1-h_2)\|^2_{(L^2(\Omega))^n}+\varepsilon\|\nabla(w_1-w_2)\|^2_{(L^2(\Omega))^n}.
\end{aligned}\tag{6.3.26}$$

Multiplying (6.3.24) by u_1-u_2, integrating over Ω, using partial integration, (6.2.3), the Lipschitz continuity of ψ and $\tilde{\mu}_3$, the boundedness of the solutions and of ∇u_2 on $\Omega\times(0,T)$, the mean value theorem, (6.3.25), (6.3.26) and Young's inequality we conclude that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega|u_1-u_2|^2\,\mathrm{d}x+\delta\int_\Omega|\nabla(u_1-u_2)|^2\,\mathrm{d}x\\
\leqslant&\|\nabla u_2\|_{L^\infty(0,T;(L^\infty(\Omega))^n)}\int_\Omega\left(\|\partial_w\psi\|_{L^\infty((0,1)^2)}|w_1-w_2|+\|\partial_h\psi\|_{L^\infty((0,1)^2)}|h_1-h_2|\right)|\nabla(u_1-u_2)|\,\mathrm{d}x\\
&+\mu_1\alpha C_7^{\alpha-1}\int_\Omega|u_1-u_2|^2\,\mathrm{d}x+\mu_1\int_\Omega|u_2^\alpha J_1(x,h_2)*u_2^\beta-u_1^\alpha J_1(x,h_1)*u_1^\beta||u_1-u_2|\,\mathrm{d}x\\
&+\mu_1\int_\Omega|u_2^\alpha J_2(x,h_2)*w_2^\gamma-u_1^\alpha J_2(x,h_1)*w_1^\gamma||u_1-u_2|\,\mathrm{d}x\\
&+L_{\tilde{\mu}_3}\int_\Omega|h_1-h_2||u_1-u_2|\,\mathrm{d}x+\|\tilde{\mu}_3\|_{L^\infty(0,1)}\int_\Omega|w_1-w_2||u_1-u_2|\,\mathrm{d}x\\
\leqslant&C_{19}(T)\left(\|u_1-u_2\|^2_{L^2(\Omega)}+\|h_1-h_2\|^2_{L^2(\Omega)}+\|w_1-w_2\|^2_{L^2(\Omega)}\right)\\
&+\delta\|\nabla(u_1-u_2)\|^2_{(L^2(\Omega))^n}+D_H\|\nabla(h_1-h_2)\|^2_{L^2(\Omega)}+\varepsilon\|\nabla(w_1-w_2)\|^2_{(L^2(\Omega))^n}.
\end{aligned}\tag{6.3.27}$$

Adding up (6.3.22), (6.3.23) and (6.3.27) we conclude that for $t\in(0,T)$ it holds that

$$\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\left(\|u_1-u_2\|^2_{L^2(\Omega)}+\|h_1-h_2\|^2_{L^2(\Omega)}+\|w_1-w_2\|^2_{L^2(\Omega)}\right)\\
\leqslant&(C_{14}+C_{15}+C_{19})\left(\|u_1-u_2\|^2_{L^2(\Omega)}+\|h_1-h_2\|^2_{L^2(\Omega)}+\|w_1-w_2\|^2_{L^2(\Omega)}\right)
\end{aligned}$$

Finally, we obtain $u_1\equiv u_2$, $h_1\equiv h_2$ and $w_1\equiv w_2$ on $\overline{\Omega}\times[0,T]$ from Gronwall's inequality. As this holds for all $T\in(0,\infty)$ uniqueness of the classical solution to (6.3.2) follows. □

6.4 Existence of a weak solution to the original problem

Definition 6.4.1. *By a weak solution to* (6.2.1) *we mean a tuple* (u, w, h) *of nonnegative bounded functions s.t. for all* $T \in (0, \infty)$ *it holds that* $u \in L^2(0, T; H^1(\Omega)) \cap C([0, T]; L^2(\Omega))$, $w \in L^\infty(0, T; H^1(\Omega)) \cap C([0, T]; L^2(\Omega))$ *with* $\partial_t w \in L^2(\Omega \times (0, T))$ *and* $h \in W_2^{2,1}(\Omega \times (0, T)) \cap C([0, T]; H^1(\Omega))$ *and they satisfy*

$$\begin{aligned} &-\int_0^T \int_\Omega u \partial_t \eta \, dx \, dt - \int_\Omega u_0 \eta(\cdot, 0) \, dx \\ =& -\int_0^T \int_\Omega \psi(w, h) \nabla u \cdot \nabla \eta \, dx \, dt + \mu_1 \int_0^T \int_\Omega u^\alpha \left(1 - J_1(x, h) * u^\beta - J_2(x, h) * w^\gamma\right) \eta \, dx \, dt \\ &+ \int_0^T \int_\Omega \tilde{\mu}_3(h) F(w) \eta \, dx \, dt, \end{aligned} \tag{6.4.1}$$

for all $\eta \in W_2^{1,1}(\Omega \times (0, T))$ *with* $\eta(T) = 0$ *and*

$$w_t = \mu_2(h)(1 - w)u - \mu_3(h)F(w) \quad \text{a.e. in } \Omega \times (0, T), \tag{6.4.2}$$

$$h_t = D_H \Delta h + g(u, w) - \lambda h \quad \text{a.e. in } \Omega \times (0, T), \tag{6.4.3}$$

$$\partial_\nu h = 0 \quad \text{a.e. on } \partial\Omega \times (0, T),$$

$$w(\cdot, 0) = w_0, \; h(\cdot, 0) = h_0 \quad \text{a.e. in } \Omega.$$

Lemma 6.4.2. *There are* u, w, h *with bounds* $0 \leqslant u \leqslant C_7$ *and* $0 \leqslant w, h \leqslant 1$ *on* $\overline{\Omega} \times [0, \infty)$ *s.t. for all* $T \in (0, T)$ *it holds that* $u \in L^2(0, T; H^1(\Omega))$, $w \in L^\infty(0, T; H^1(\Omega)) \cap C([0, T]; L^2(\Omega))$ *and* $h \in W_2^{2,1}(\Omega \times (0, T))$ *and for a subsequence*

$$u_{\varepsilon_k} \underset{k \to \infty}{\rightharpoonup} u \quad \text{in } L^2(0, T; H^1(\Omega)), \tag{6.4.4a}$$

$$u_{\varepsilon_k} \underset{k \to \infty}{\to} u \quad \text{in } L^2(\Omega \times (0, T)) \text{ and a.e. in } \Omega \times (0, T), \tag{6.4.4b}$$

$$w_{\varepsilon_k} \underset{k \to \infty}{\to} w \quad \text{in } C([0, T]; L^2(\Omega)) \text{ and a.e. in } \Omega \times (0, T),, \tag{6.4.4c}$$

$$\nabla w_{\varepsilon_k} \underset{k \to \infty}{\overset{*}{\rightharpoonup}} \nabla w \quad \text{in } L^\infty(0, T; (L^2(\Omega))^n), \tag{6.4.4d}$$

$$\partial_t w_{\varepsilon_k} \underset{k \to \infty}{\rightharpoonup} \partial_t w \quad \text{in } L^2(\Omega \times (0, T)), \tag{6.4.4e}$$

$$h_{\varepsilon_k} \underset{k \to \infty}{\rightharpoonup} h \quad \text{in } L^2(0, T; H^2(\Omega)), \tag{6.4.4f}$$

$$h_{\varepsilon_k} \underset{k \to \infty}{\to} h \quad \text{in } L^2(0, T; H^1(\Omega)) \text{ and a.e. in } \Omega \times (0, T), \tag{6.4.4g}$$

$$\partial_t h_{\varepsilon_k} \underset{k \to \infty}{\rightharpoonup} \partial_t h \quad \text{in } L^2(\Omega \times (0, T)), \tag{6.4.4h}$$

Proof. Let $T > 0$. First, *Theorem A.1.8* implies that

$$\|h_\varepsilon\|_{W_2^{2,1}(\Omega \times (0,T))} \leqslant C_{20} \left(\|g(u_\varepsilon, w_\varepsilon)\|_{L^2(\Omega \times (0,T))} + \|h_{0\varepsilon}\|_{H^1(\Omega)}\right). \tag{6.4.5}$$

Due to the Lipschitz continuity of g, the uniform boundedness of (u_ε) and (w_ε) and the convergence in (6.3.1c) the right-hand side of (6.4.5) is uniformly bounded for $\varepsilon \in (0, 1)$. Hence, Lions-Aubin (with $H^2(\Omega) \hookrightarrow\hookrightarrow H^1(\Omega) \hookrightarrow L^2(\Omega)$) and Banach-Alaoglu imply the existence of $h \in W_2^{2,1}(\Omega \times (0, T))$ and a subsequence s.t. (6.4.4f) - (6.4.4h) hold and from *Lemma 6.3.1* it follows for a.e. $(x, t) \in \Omega \times (0, T)$ that $0 \leqslant h(x, t) = \lim_{k \to \infty} h_{\varepsilon_k}(x, t) \leqslant 1$.

Next, we want to obtain a uniform estimate on the norm of ∇u_ε. Therefore, we multiply the equation for u_ε in (6.3.2) by u_ε, integrate over Ω and use partial integration to obtain

$$\frac{1}{2}\frac{d}{dt}\int_\Omega u_\varepsilon^2 \,\mathrm{d}x = -\int_\Omega \psi(w_\varepsilon,h_\varepsilon)|\nabla u_\varepsilon|^2 \,\mathrm{d}x + \mu_1 \int_\Omega u_\varepsilon^{\alpha+1}\left(1 - J_1(x,h_\varepsilon) * u_\varepsilon^\beta - J_2(x,h_\varepsilon) * w_\varepsilon^\gamma\right) \mathrm{d}x$$
$$+ \int_\Omega \tilde{\mu}_3(h_\varepsilon)F(w_\varepsilon)u_\varepsilon \,\mathrm{d}x.$$

Then, we can estimate using (6.2.3), *Lemma 2.3.2(i)*, the uniform boundedness of (u_ε), (w_ε), (h_ε), $\alpha \geqslant 1$, the continuity of $\tilde{\mu}_3$ that

$$\frac{1}{2}\frac{d}{dt}\int_\Omega u_\varepsilon^2 \,\mathrm{d}x + \delta \int_\Omega |\nabla u_\varepsilon|^2 \,\mathrm{d}x$$
$$\leqslant \mu_1 C_7^{\alpha-1}\left(1 + C_7^\beta(\|L_{J_1}\|_{L^1(B)} + \|J_1(\cdot,0)\|_{L^1(B)}) + \|\mathrm{L}_{J_2}\|_{L^1(B)} + \|J_2(\cdot,0)\|_{L^1(B)}\right)\int_\Omega u_\varepsilon^2 \,\mathrm{d}x$$
$$+ \|\tilde{\mu}_3\|_{L^\infty(0,1)}C_7|\Omega|$$

Hence, we conclude from Gronwall's inequality that for all $\varepsilon \in (0,1)$ it holds that

$$\|\nabla u_\varepsilon\|_{L^2(0,T;(L^2(\Omega))^n)} \leqslant C_{21}(T). \tag{6.4.6}$$

Further, we multiply the equation for u_ε in (6.3.2) by $\varphi \in H_0^1(\Omega)$ and obtain obtain using partial integration, the Hölder inequality, the continuity of ψ, the uniform boundedness of (u_ε), (w_ε) and (h_ε), *Lemma 2.3.2(i)* and the Lipschitz continuity of $\tilde{\mu}_3$ that

$$\left|\int_\Omega \partial_t u_\varepsilon \varphi \,\mathrm{d}x\right| \leqslant \int_\Omega |\psi(w_\varepsilon,h_\varepsilon)\nabla u_\varepsilon \cdot \nabla\varphi| \,\mathrm{d}x + \mu_1 \int_\Omega \left|u_\varepsilon^\alpha\left(1 - J_1(x,h_\varepsilon) * u_\varepsilon^\beta - J_2(x,h_\varepsilon) * w_\varepsilon^\gamma\right)\varphi\right| \mathrm{d}x$$
$$+ \int_\Omega |\tilde{\mu}_3(h_\varepsilon)F(w_\varepsilon)\varphi| \,\mathrm{d}x$$
$$\leqslant \|\psi\|_{L^\infty((0,1)^2)}\|\nabla u_\varepsilon\|_{(L^2(\Omega))^n}\|\nabla\varphi\|_{(L^2(\Omega))^n}$$
$$+ \Big(\mu_1 C_7^\alpha\left(1 + C_7^\beta(\|L_{J_1}\|_{L^1(B)} + \|J_1(\cdot,0)\|_{L^1(B)}) + \|\mathrm{L}_{J_2}\|_{L^1(B)} + \|J_2(\cdot,0)\|_{L^1(B)}\right)$$
$$+ \|\tilde{\mu}_3\|_{L^\infty(0,1)}\Big)\|\varphi\|_{L^1(\Omega)}$$
$$\leqslant C_{22}(\|\nabla u_\varepsilon\|_{(L^2(\Omega))^n} + 1)\|\varphi\|_{H^1(\Omega)}.$$

Hence,

$$\|\partial_t u_\varepsilon\|_{H^{-1}(\Omega)} \leqslant C_{22}(\|\nabla u_\varepsilon\|_{(L^2(\Omega))^n} + 1)$$

and we conclude from (6.4.6) that

$$\|\partial_t u_\varepsilon\|_{L^2(0,T;H^{-1}(\Omega))} \leqslant C_{23}(T). \tag{6.4.7}$$

Combining (6.4.6) and (6.4.7) with the uniform boundedness of (u_ε) we conclude from Lions-Aubin (*Lemma A.3.9*) with $H^1(\Omega) \hookrightarrow\hookrightarrow L^2(\Omega) \hookrightarrow H^{-1}(\Omega)$ and Banach-Alaoglu that there is $u \in L^2(0,T;H^1(\Omega))$ and a subsequence s.t. (6.4.4a) and (6.4.4b) hold. Moreover, due to the pointwise convergence it holds a.e. in $\Omega \times (0,T)$ that $0 \leqslant u(x,t) \leqslant \lim_{k\to\infty} u_{\varepsilon_k}(x,t) \leqslant C_7$.

To obtain a uniform estimate on the norm of ∇w_ε we multiply the equation for w_ε by Δw_ε and obtain after integration over Ω and partial integration due to our boundary condition on w_ε that

$$\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla w_\varepsilon|^2 \,\mathrm{d}x = \int_\Omega (\nabla w_\varepsilon)_t \cdot \nabla w_\varepsilon \,\mathrm{d}x = -\int_\Omega (w_\varepsilon)_t \Delta w_\varepsilon \,\mathrm{d}x$$

$$
\begin{aligned}
&= -\varepsilon \int_\Omega |\Delta w_\varepsilon|^2 \,\mathrm{d}x - \int_\Omega \mu_2(h_\varepsilon)(1-w_\varepsilon)u_\varepsilon \Delta w_\varepsilon \,\mathrm{d}x + \int_\Omega \mu_3(h_\varepsilon)F(w_\varepsilon)\Delta w_\varepsilon \,\mathrm{d}x \\
&= -\varepsilon \int_\Omega |\Delta w_\varepsilon|^2 \,\mathrm{d}x + \int_\Omega \big(\mu_2'(h_\varepsilon)(1-w_\varepsilon)\nabla h_\varepsilon u_\varepsilon - \mu_2(h_\varepsilon)\nabla w_\varepsilon u_\varepsilon + \mu_2(h_\varepsilon)(1-w_\varepsilon)\nabla u_\varepsilon\big)\cdot \nabla w_\varepsilon \,\mathrm{d}x \\
&\quad - \int_\Omega \Big(\mu_3'(h_\varepsilon)\nabla h_\varepsilon F(w_\varepsilon) + \mu_3(h_\varepsilon)(\tilde{F}(w_\varepsilon))^2 \nabla w_\varepsilon\Big)\cdot \nabla w_\varepsilon \,\mathrm{d}x.
\end{aligned}
$$

Hence, using the uniform boundedness of $(u_\varepsilon), (h_\varepsilon), (w_\varepsilon)$, continuity of μ_2', μ_3' and Young's inequality we obtain

$$
\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega |\nabla w_\varepsilon|^2 \,\mathrm{d}x + \varepsilon \int_\Omega |\Delta w_\varepsilon|^2 \,\mathrm{d}x \\
&\leqslant (\|\mu_2'\|_{L^\infty(0,1)} C_7 + \|\mu_3'\|_{L^\infty(0,1)}) \int_\Omega |\nabla h_\varepsilon||\nabla w_\varepsilon| \,\mathrm{d}x + \|\mu_2\|_{L^\infty(0,1)} \int_\Omega |\nabla u_\varepsilon||\nabla w_\varepsilon| \,\mathrm{d}x \\
&\quad + \big(\|\mu_2\|_{L^\infty(0,1)} C_7 + \|\mu_3\|_{L^\infty(0,1)}\big) \int_\Omega |\nabla w_\varepsilon|^2 \,\mathrm{d}x \\
&\leqslant C_{24}\left(\int_\Omega |\nabla u_\varepsilon|^2 \,\mathrm{d}x + \int_\Omega |\nabla w_\varepsilon|^2 \,\mathrm{d}x + \int_\Omega |\nabla h_\varepsilon|^2 \,\mathrm{d}x\right)
\end{aligned}
$$

Hence, Gronwall's inequality, the fact that $(\nabla w_{0\varepsilon})$ is uniformly bounded in $(L^2(\Omega))^n$ due to the convergence in (6.3.1c), (6.4.5) and (6.4.6) and imply that

$$
\begin{aligned}
&\int_\Omega |\nabla w_\varepsilon(t)|^2 \,\mathrm{d}x + \varepsilon \int_0^T \int_\Omega |\Delta w_\varepsilon|^2 \,\mathrm{d}x \,\mathrm{d}t \\
&\leqslant C_{25}(T)\left(\|\nabla w_{0\varepsilon}\|_{(L^2(\Omega))^n} + \int_0^T \int_\Omega |\nabla u_\varepsilon|^2 \,\mathrm{d}x \,\mathrm{d}t + \int_0^T \int_\Omega |\nabla h_\varepsilon|^2 \,\mathrm{d}x \,\mathrm{d}t\right) \leqslant C_{26}(T)
\end{aligned}
$$

for $t \in (0,T)$ and $\varepsilon \in (0,1)$. Consequently, for all $\varepsilon \in (0,1)$ it holds that

$$\|\nabla w_\varepsilon\|_{L^\infty(0,T;(L^2(\Omega))^n)} \leqslant C_{26}(T), \tag{6.4.8}$$

$$\varepsilon\|\Delta w_\varepsilon\|_{L^2(\Omega\times(0,T))} \leqslant C_{27}(T). \tag{6.4.9}$$

To obtain a uniform estimate on some norm of the time derivative of w_ε, we multiply the equation for w_ε from (6.3.2) by $\varphi \in L^2(\Omega)$, integrate over Ω, use the Lipschitz continuity of μ_2 and μ_3, the uniform boundedness of (u_ε), (w_ε) and (h_ε) and Hölder's inequality to conclude that

$$
\begin{aligned}
\left|\int_\Omega \partial_t w_\varepsilon \varphi \,\mathrm{d}x\right| &\leqslant \varepsilon \int_\Omega |\Delta w_\varepsilon||\varphi| \,\mathrm{d}x + \int_\Omega |\mu_2(h_\varepsilon)(1-w_\varepsilon)u_\varepsilon \varphi| \,\mathrm{d}x + \int_\Omega |\mu_3(h_\varepsilon)F(w_\varepsilon)\varphi| \,\mathrm{d}x \\
&\leqslant \left(\varepsilon\|\Delta w_\varepsilon\|_{L^2(\Omega)} + (\|\mu_2\|_{L^\infty(0,1)} C_7 + \|\mu_3\|_{L^\infty(0,1)})|\Omega|^{\frac{1}{2}}\right)\|\varphi\|_{L^2(\Omega)}.
\end{aligned}
$$

Consequently, we conclude from (6.4.9) as $(L^2(\Omega))^* = L^2(\Omega)$ that for all $\varepsilon \in (0,1)$ it holds that

$$\|\partial_t w_\varepsilon\|_{L^2(\Omega\times(0,T))} \leqslant C_{28}(T). \tag{6.4.10}$$

Combining the uniform boundedness of (w_ε) with (6.4.8) and (6.4.10) we conclude from Lions-Aubin (*Lemma A.3.9*) with $H^1(\Omega) \hookrightarrow\hookrightarrow L^2(\Omega) \hookrightarrow L^2(\Omega)$ and *Lemma A.3.1* in the space $L^\infty(0,T;(L^2(\Omega))^n) = (L^1(0,T;(L^2(\Omega))^n))^*$ that there is $w \in C([0,T];L^2(\Omega)) \cap L^\infty(0,T;H^1(\Omega))$ and a subsequence s.t. (6.4.4c) - (6.4.4e) hold. From the pointwise a.e. convergence we conclude that $0 \leqslant w(x,t) = \lim_{k\to\infty} w_{\varepsilon_k}(x,t) \leqslant 1$ holds a.e. in $\Omega \times (0,T)$. □

Due to the pointwise convergence shown in the proof of the last lemma the following corollary is a direct consequence of *Corollary 6.3.3*.

Corollary 6.4.3. *For $K > 1$ and 'small' enough parameters it holds that*

$$\|u\|_{L^\infty(\Omega\times(0,\infty))} \leqslant K \max\left\{1, \left(\left(4K_S|\Omega|^{-\frac{1}{2}}\right)^{\frac{1}{1-\frac{1}{s}}} \frac{2}{\eta}\left(1+\frac{\|\tilde{\mu}_3\|_{L^\infty(0,1)}}{\mu_1}\right)\right)^{\frac{1-\frac{2}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}\right\}.$$

Theorem 6.4.4. *There is a bounded nonnegative weak solution (u, w, h) to (6.2.1) in the sense of Definition 6.4.1 satisfying $u \leqslant C_7$ and $w, h \leqslant 1$ a.e. in $\Omega \times (0,\infty)$.*

Proof. Let $T > 0$ and $\eta \in W_2^{1,1}(\Omega\times(0,T))$ with $\eta(T) = 0$. We consider the subsequence (ε_k) from *Lemma 6.4.2*. Multiplying the equations from (6.3.2) by η, integrating over $\Omega\times(0,T)$ and using partial integration we obtain the weak formulation

$$\begin{aligned}
&-\int_0^T\int_\Omega u_{\varepsilon_k}\partial_t\eta\,\mathrm{d}x\,\mathrm{d}t - \int_\Omega u_{0\varepsilon_k}\eta(\cdot,0)\,\mathrm{d}x\\
=&-\int_0^T\int_\Omega \psi(w_{\varepsilon_k},h_{\varepsilon_k})\nabla u_{\varepsilon_k}\cdot\nabla\eta\,\mathrm{d}x\,\mathrm{d}t\\
&+\mu_1\int_0^T\int_\Omega u_{\varepsilon_k}^\alpha\left(1-J_1(x,h_{\varepsilon_k})*u_{\varepsilon_k}^\beta - J_2(x,h_{\varepsilon_k})*w_{\varepsilon_k}^\gamma\right)\eta\,\mathrm{d}x\,\mathrm{d}t\\
&+\int_0^T\int_\Omega \tilde{\mu}_3(h_{\varepsilon_k})F(w_{\varepsilon_k})\eta\,\mathrm{d}x\,\mathrm{d}t,
\end{aligned}$$

$$\begin{aligned}
\int_0^T\int_\Omega \partial_t w_{\varepsilon_k}\eta\,\mathrm{d}x\,\mathrm{d}t =& -\varepsilon_k\int_0^T\int_\Omega \nabla w_{\varepsilon_k}\cdot\nabla\eta\,\mathrm{d}x\,\mathrm{d}t\\
&+\int_0^T\int_\Omega \left(\mu_2(h_{\varepsilon_k})(1-w_{\varepsilon_k})u_{\varepsilon_k}-\mu_3(h_{\varepsilon_k})F(w_{\varepsilon_k})\right)\eta\,\mathrm{d}x\,\mathrm{d}t
\end{aligned}$$

and

$$\int_0^T\int_\Omega \partial_t h_{\varepsilon_k}\eta\,\mathrm{d}x\,\mathrm{d}t = D_H\int_0^T\int_\Omega \Delta h_{\varepsilon_k}\eta\,\mathrm{d}x\,\mathrm{d}t + \int_0^T\int_\Omega (g(u_{\varepsilon_k},w_{\varepsilon_k})-\lambda h_{\varepsilon_k})\eta\,\mathrm{d}x\,\mathrm{d}t.$$

From the continuity of ψ and $\tilde{\mu}_3$, (6.4.4c), (6.4.4g) and the dominated convergence theorem we conclude that

$$\begin{aligned}
\psi(w_{\varepsilon_k},h_{\varepsilon_k})\nabla\eta &\underset{k\to\infty}{\to} \psi(w,h)\nabla\eta \text{ in } L^2(0,T;(L^2(\Omega))^n),\\
\tilde{\mu}_3(h_{\varepsilon_k})F(w_{\varepsilon_k}) &\underset{k\to\infty}{\to} \tilde{\mu}_3(h)F(w) \text{ in } L^2(\Omega\times(0,T)).
\end{aligned} \tag{6.4.11}$$

Hence,

$$\int_0^T\int_\Omega \psi(w_{\varepsilon_k},h_{\varepsilon_k})\nabla u_{\varepsilon_k}\cdot\nabla\eta\,\mathrm{d}x\,\mathrm{d}t \underset{k\to\infty}{\to} \int_0^T\int_\Omega \psi(w,h)\nabla u\cdot\nabla\eta\,\mathrm{d}x\,\mathrm{d}t \tag{6.4.12}$$

follows from (6.4.4a) and compensated compactness (*Lemma A.3.2*). Further, due to (6.2.5a) and the uniform boundedness of (u_{ε_k}) we estimate for $(x,t)\in\Omega\times(0,T)$ that

$$\begin{aligned}
&\left|J_1(x,h_{\varepsilon_k})*u_{\varepsilon_k}^\beta(t) - J_1(x,h)*u^\beta(t)\right|\\
\leqslant&\int_\Omega |J_1(x-y,h_{\varepsilon_k}(y,t))-J_1(x-y,h(y,t))|u_{\varepsilon_k}^\beta(y,t)\,\mathrm{d}y\\
&+\int_\Omega J_1(x-y,h(y,t))|u_{\varepsilon_k}^\beta(y,t)-u^\beta(y,t)|\,\mathrm{d}y
\end{aligned}$$

$$\leqslant C_7^\beta \int_\Omega L_{J_1}(x-y)|h_{\varepsilon_k}(y,t)-h(y,t)|\,\mathrm{d}y$$
$$+\int_\Omega (L_{J_1}(x-y)h(y,t)+J_1(x-y,0))|u^\beta_{\varepsilon_k}(y,t)-u^\beta(y,t)|\,\mathrm{d}y \underset{k\to\infty}{\to} 0$$

due to the dominated convergence theorem combined with (6.4.4b), (6.4.4g), and (6.2.5b) and the uniform boundedness of (u_{ε_k}) and (h_{ε_k}). Consequently,

$$J_1(\cdot,h_{\varepsilon_k}) * u^\beta_{\varepsilon_k} \underset{k\to\infty}{\to} J_1(\cdot,h) * u^\beta \text{ pointwise a.e. in } \Omega\times(0,T) \tag{6.4.13}$$

and analogously,

$$J_2(\cdot,h_{\varepsilon_k}) * w^\gamma_{\varepsilon_k} \underset{k\to\infty}{\to} J_2(\cdot,h) * w^\gamma \text{ pointwise a.e. in } \Omega\times(0,T) \tag{6.4.14}$$

follows. Hence, we conclude combining (6.4.4b), (6.4.13), and (6.4.14) that

$$u^\alpha_{\varepsilon_k}\left(1-J_1(\cdot,h_{\varepsilon_k}) * u^\beta_{\varepsilon_k} - J_2(\cdot,h_{\varepsilon_k}) * w^\gamma_{\varepsilon_k}\right) \underset{k\to\infty}{\to} u^\alpha\left(1-J_1(\cdot,h) * u^\beta - J_2(\cdot,h) * w^\gamma\right)$$
$$\text{pointwise a.e. in } \Omega\times(0,T)$$

and from the uniform boundedness of (u_{ε_k}), (w_{ε_k}) and (h_{ε_k}) and *Lemma 2.3.2(i)* that for all $k\in\mathbb{N}$ it holds that

$$|u^\alpha_{\varepsilon_k}\left(1-J_1(x,h_{\varepsilon_k}) * u^\beta_{\varepsilon_k}(t) - J_2(x,h_{\varepsilon_k}) * w^\gamma_{\varepsilon_k}(t)\right)| \leqslant C_{29}.$$

Consequently, the dominated convergence theorem implies that

$$u^\alpha_{\varepsilon_k}\left(1-J_1(\cdot,h_{\varepsilon_k}) * u^\beta_{\varepsilon_k} - J_2(\cdot,h_{\varepsilon_k}) * w^\gamma_{\varepsilon_k}\right) \underset{k\to\infty}{\to} u^\alpha\left(1-J_1(\cdot,h) * u^\beta - J_2(\cdot,h) * w^\gamma\right)$$
$$\text{in } L^2(\Omega\times(0,T)).$$

Combining this with (6.3.1b), (6.4.4b), (6.4.11) and (6.4.12) we conclude that u satisfies (6.4.1), i.e., solves the corresponding equations of (6.2.1) in the sense of *Theorem A.1.1*. Hence, also $u\in C([0,T];L^2(\Omega))$ holds due to *Theorem A.1.1*.

With the help of Hölder's inequality and (6.4.8) we obtain

$$\varepsilon_k\left|\int_0^T\int_\Omega \nabla w_{\varepsilon_k}\cdot\nabla\eta\,\mathrm{d}x\,\mathrm{d}t\right| \leqslant \varepsilon_k\|\nabla w_{\varepsilon_k}\|_{L^2(0,T;(L^2(\Omega))^n)}\|\nabla\eta\|_{L^2(0,T;(L^2(\Omega))^n)}$$
$$\leqslant \varepsilon_k C_{26}T^{\frac{1}{2}}\|\nabla\eta\|_{L^2(0,T;(L^2(\Omega))^n)} \underset{k\to\infty}{\to} 0. \tag{6.4.15}$$

Further, we conclude from the continuity of μ_2 and μ_3, the pointwise convergences in (6.4.4b), (6.4.4c) and (6.4.4g), the uniform boundedness of (u_{ε_k}), (w_{ε_k}) and (h_{ε_k}) and the dominated convergence theorem that

$$\mu_2(h_{\varepsilon_k})(1-w_{\varepsilon_k})u_{\varepsilon_k} \underset{k\to\infty}{\to} \mu_2(h)(1-w)u \text{ in } L^2(\Omega\times(0,T)), \tag{6.4.16}$$
$$\mu_3(h_{\varepsilon_k})F(w_{\varepsilon_k}) \underset{k\to\infty}{\to} \mu_3(h)F(w) \text{ in } L^2(\Omega\times(0,T)). \tag{6.4.17}$$

Combining (6.3.1c) and (6.4.4c) with (6.4.15) - (6.4.17) we conclude that

$$\int_0^T\int_\Omega \partial_t w\eta\,\mathrm{d}x\,\mathrm{d}t = \int_0^T (\mu_2(h)(1-w)u-\mu_3(h)F(w))\,\eta\,\mathrm{d}x\,\mathrm{d}t.$$

Due to $C_c^\infty(\Omega\times(0,T)) \subset W_2^{1,1}(\Omega\times(0,T))$ the fundamental lemma of calculus of variations implies that w satisfies (6.4.2). Moreover, using partial integration we conclude due to (6.3.1c), (6.4.4c), and (6.4.4e) that (especially also for $\eta \in C_c^\infty(\overline{\Omega} \times [0,T)) \subset W_2^{1,1}(\Omega \times (0,T))$ with $\eta(T) = 0$) it holds that

$$\begin{aligned} -\int_0^T \int_\Omega w\eta_t \,\mathrm{d}x\,\mathrm{d}t - \int_\Omega w(\cdot,0)\eta(\cdot,0)\,\mathrm{d}x\,\mathrm{d}t &= \int_0^T \int_\Omega \partial_t w\eta \,\mathrm{d}x\,\mathrm{d}t \\ &= \lim_{k\to\infty} \int_0^T \int_\Omega \partial_t w_{\varepsilon_k}\eta \,\mathrm{d}x\,\mathrm{d}t \\ &= \lim_{k\to\infty} \left(-\int_0^T \int_\Omega w_{\varepsilon_k}\eta_t \,\mathrm{d}x\,\mathrm{d}t - \int_\Omega w_{0\varepsilon_k}(\cdot)\eta(\cdot,0)\,\mathrm{d}x\,\mathrm{d}t \right) \\ &= -\int_0^T \int_\Omega w\eta_t \,\mathrm{d}x\,\mathrm{d}t - \int_\Omega w_0(\cdot)\eta(\cdot,0)\,\mathrm{d}x\,\mathrm{d}t \end{aligned}$$

Hence, we conclude again from the fundamental lemma of calculus of variations that indeed $w(\cdot,0) = w_0$ a.e. in Ω.

Furthermore, we estimate with the help of Hölder's inequality and the Lipschitz continuity of g that

$$\begin{aligned} &\int_0^T \int_\Omega |g(u_{\varepsilon_k}, w_{\varepsilon_k}) - g(u,w)||\eta| \,\mathrm{d}x\,\mathrm{d}t \\ \leqslant & 2L_g \left(\|u_{\varepsilon_k} - u\|_{L^2(\Omega\times(0,T))} + \|w_{\varepsilon_k} - w\|_{L^2(\Omega\times(0,T))} \right) \|\eta\|_{L^2(\Omega\times(0,T))} \underset{k\to\infty}{\longrightarrow} 0 \end{aligned}$$

due to (6.4.4b) and (6.4.4c). Hence, it follows from (6.4.4f) - (6.4.4h) that

$$\int_0^T \int_\Omega \partial_t h\eta \,\mathrm{d}x\,\mathrm{d}t = D_H \int_0^T \int_\Omega \Delta h\eta \,\mathrm{d}x\,\mathrm{d}t + \int_0^T \int_\Omega (g(u,w) - \lambda h)\eta \,\mathrm{d}x\,\mathrm{d}t$$

for all $\eta \in W_2^{1,1}(\Omega \times (0,T))$ with $\eta(T) = 0$. We conclude again from the fundamental lemma of calculus of variations that h satisfies (6.4.3) a.e. in $\Omega \times (0,T)$. Finally, $h(\cdot,0) = h_0$ a.e. in Ω follows as for w. We conclude similary that

$$\int_0^T \int_{\partial\Omega} \nabla h \cdot \nu\eta \,\mathrm{d}\sigma(x)\,\mathrm{d}t = 0$$

which due to $H^1(\Omega) \hookrightarrow L^2(\partial\Omega)$ gives us $\nabla h \cdot \nu = 0$ a.e. on $\partial\Omega \times (0,T)$. □

6.5 1D Simulations

In this section we simulate the behavior of solutions to (6.2.1) in one dimension. Thereby, we decompose the domain $\Omega = [-5,5]$ into an equidistant mesh $x_2, \dots, x_{N-1}$ with step size $dx = 0.05$ and the time interval $[0,50]$ with step size $dt = 0.0001$. For a simulation of the no-flux boundary condition we add points $x_1 < x_2$ and $x_N > x_{N-1}$ outside of Ω and assume equality of the solutions on the neighboring points. As in *Chapter 5*, we use the method from [111] to discretize the nonlocal integral terms via a composite trapezoidal rule. Moreover, as in [156], we recompute the convolution matrices only every 40 time steps to improve the runtime. Thereby, we assume that changes in the values of the convolution matrices phi_mat_1 and phi_mat_2 (due to changes of h) are negligible within this time interval. Namely, for $i,j \in \{2,\dots,N-1\}$ the corresponding entry of the kth-convolution matrix is

$$(phi\_mat_1)_{ij}^k = J_1(x_i - x_j, h_j^{40k})$$

and with the help of this we compute the $n+1$st convolution term at x_i, $i \in \{2,\dots,N-1\}$ as:

$$\begin{aligned}(conv_1)_i^{n+1} =& dx \sum_{j=3}^{N-2} (phi\_mat_1)_{ij}^{\lfloor n/40 \rfloor} (u_j^n)^\beta \\ &+ \frac{dx}{2}\left((phi\_mat_1)_{i2}^{\lfloor n/40 \rfloor}(u_2^n)^\beta + (phi\_mat_1)_{i(N-1)}^{\lfloor n/40 \rfloor}(u_{(N-1)}^n)^\beta\right).\end{aligned}$$

Analogously we compute phi_mat_2 and $conv_2$. For the discretization of the diffusion term we use finite differences and an upwind scheme. The initial conditions are depicted in *Figure 6.1* and are given by

$$u_0(x) = \begin{cases} 0.3e^{-\frac{1}{5}(x+5)^2}, & x \in [-5,0], \\ 0.3e^{-5}\left(1-\frac{x}{5}\right), & x \in (0,5], \end{cases}$$

$$w_0(x) = \begin{cases} 0.7e^{-(x+5)^2}, & x \in [-5,0], \\ 0.7e^{-25}\left(1-\frac{x}{5}\right), & x \in (0,5] \end{cases},$$

$$h_0(x) = \begin{cases} \frac{1}{5}(0.3e^{-5}-0.05)x + 0.3e^{-5}, & x \in [-5,0], \\ 0.3e^{-5}\left(1-\frac{x}{5}\right), & x \in (0,5]. \end{cases}$$

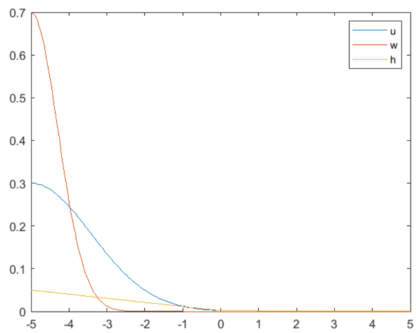

Figure 6.1: Initial conditions u_0, w_0, h_0.

We choose the functions $\psi(h,w) = 0.5$ (for simplicity), $\mu_2(h) = h$ (meaning that the net 'deactivation' of u-cells is directly proportional to the amount of protons available in the microtumor space), $\mu_3(h) = \tilde{\mu}_3(h) = \frac{h}{1+h}$ (there is no loss of w-cells when becoming u-cells, the transition - primarily to motility- is favored by acidity, but in a limited manner, quickly reaching saturation), $F(w) = \frac{w}{1+w}$, $g(u,w) = \frac{u+w}{1+u+w}$ (both phenotypes are producing acid, also in a limited way), and the constants $D_H = 0.1$ and $\lambda = 1$.

First, we took $\beta = \gamma = \mu_1 = 1$ and explored the influence of the kernels on the minimal value α^* of α for which the solution ceases to exist globally in time (with accuracy to one decimal place). Thereby, we considered as in *Chapter 5* the logistic kernel $J_L(x) = \frac{1}{2+e^x+e^{-x}}$, the uniform kernel $J_U(x) = \chi_{[-1,1]}(x)$ and, moreover, the h-dependent kernels

$$J_1(x,h) = \frac{1}{\sqrt{2\pi}} e^{-\frac{x^2}{2}}\left(\frac{h}{1+h}+\frac{1}{10}\right), \tag{6.5.1}$$

$$J_2(x,h) = \frac{h^2}{2(1+h^2)}, \tag{6.5.2}$$

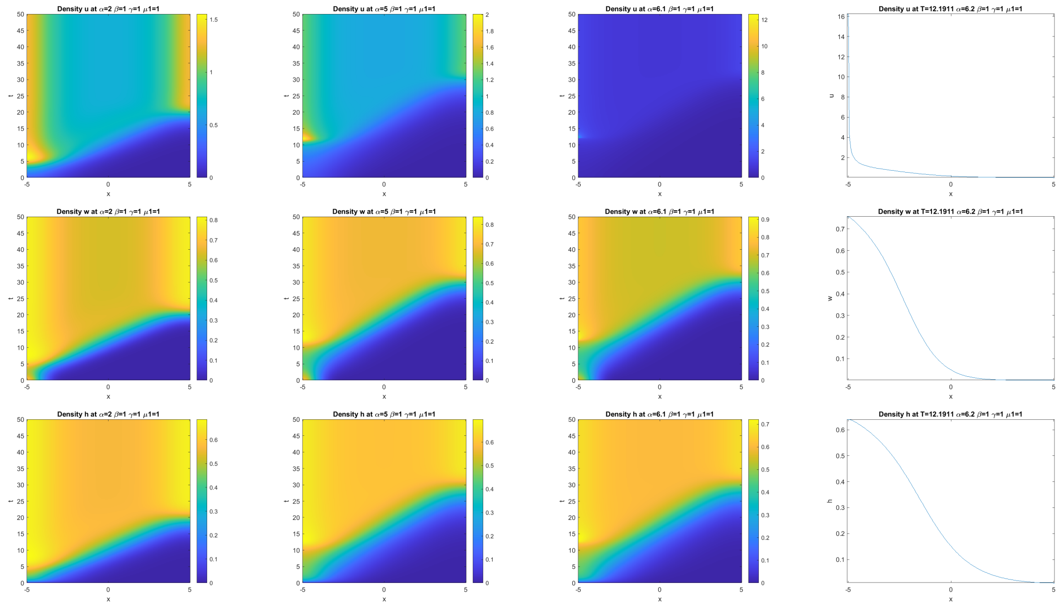

Figure 6.2: Simulation results of model (6.2.1) with $J_1 = J_2 = J_L$, i.e., logistic kernels, $\beta = \gamma = \mu_1 = 1$, $\alpha = 2, 5, 6.1, 6.2$ (columns from left to right, respectively). Component u of the solution starts to become unbounded near $\alpha = 6.2$. In the rightmost column a blow-up occurs in the next time step.

the first of which is a h-dependent shift of a Gaussian, while the latter is a Holling III-type function of h suggesting a slower increase towards saturation, with a certain 'learning effect' as far as the response to more acidity is concerned: as J_2 stands for the interaction of the two cell phenotypes, it accounts for both of them extruding protons, along with the corresponding adaptation of u-cells to interspecific cues.

The first columns of *Figures 6.2* and *6.3* show the solution for the critical α from (6.2.2), when J_1 and J_2 are both logistic or uniform, respectively. The solution u aggregates at the position of the initial accumulation of the active cells at the left boundary. In the case of two logistic kernels a stronger aggregation for increasing α values can be observed leading to a blow-up at the left boundary near $\alpha^* = 6.2$. On the other hand, in the case of two uniform kernels u invades the whole domain and aggregates at the right boundary, leading to a blow-up there for approximately $\alpha^* = 14.7$. This invasive behavior can also be observed for all combinations of kernels and parameters $\alpha, \beta, \gamma, \mu$ as long as no blow-up at the left boundary occurs. An overview of the minimal values α^* depending on the kernels can be found in *Table 6.1*.

In further tests we investigated for logistic kernels the influence of β,γ and the growth rate μ_1 on the blow-up behavior. Higher values of β lead to an increase of the minimal value α^* where blow-up occurs. In the case $\beta = 10$ and $\gamma = \mu_1 = 1$ we observed that for $\alpha = 26.9, 27.1, 27.3$ the solution ceases to exist, whereas it exists globally in time for $\alpha = 27, 27.2, 27.4$. Hence, in contrast to *Chapter 5* and [99] we cannot determine a value α^* s.t. for $\alpha < \alpha^*$ the solution is global, whereas it blows-up for $\alpha \geqslant \alpha^*$. It seems that for $\alpha \geqslant \alpha^{**} = 27.5$ blow-up occurs but

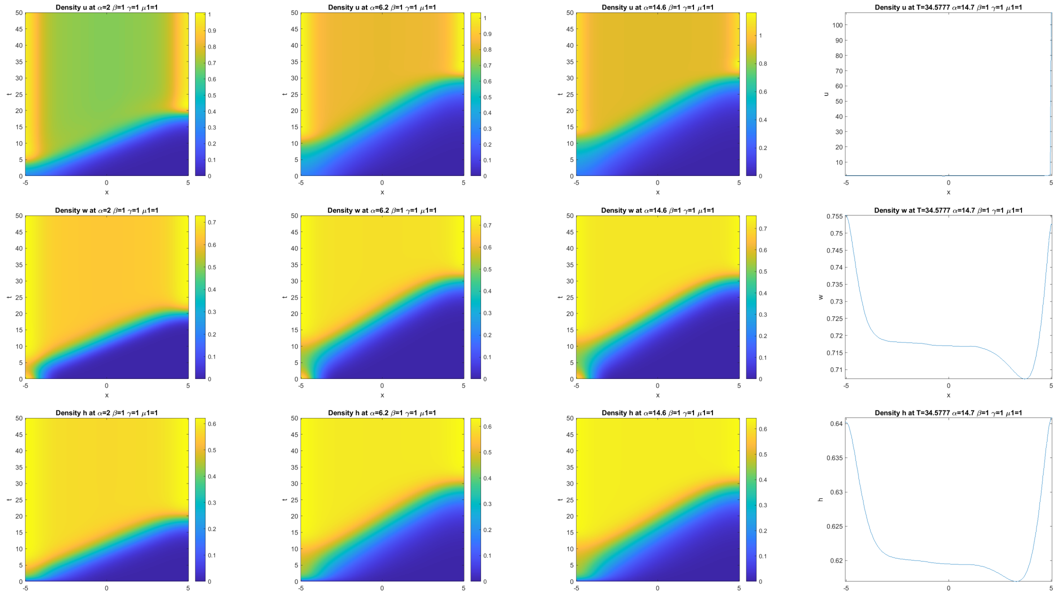

Figure 6.3: Simulation results of model (6.2.1) with $J_1 = J_2 = J_U$, i.e., uniform kernels, $\beta = \gamma = \mu_1 = 1$, $\alpha = 2, 6.2, 14.6, 14.7$ (columns from left to right, respectively). Component u of the solution starts to become unbounded near $\alpha = 14.7$. In the rightmost column a blow-up occurs in the next time step.

	α^*	Figure
J_1, J_2 logistic	6.2	*Figure 6.2*
J_1 logistic, J_2 uniform	7.4	
J_1 uniform, J_2 logistic	10.3	
J_1, J_2 uniform	14.7	*Figure 6.3*
J_1, J_2 from (6.5.1),(6.5.2)	4.1	*Figure 6.6*

Table 6.1: Minimal value α^* for which the solution ceases to exist for $\beta = \gamma = \mu_1 = 1$ depending on the kernels J_1 and J_2.

we cannot assure this. In contrast, higher values of γ and/or μ_1 lead to a blow-up for lower α's, see *Table 6.2* for an overview of the concrete values of α^* along with the respective parameter combinations.

Parameters	α^*
$\beta = 10,\ \gamma = \mu_1 = 1$	26.9
$\beta = \gamma = 10,\ \mu_1 = 1$	22.1
$\beta = 10,\ \gamma = 0.1,\ \mu_1 = 1$	33.4
$\beta = 1,\ \gamma = 10,\ \mu_1 = 1$	4.6
$\beta = 1,\ \gamma = 0.1,\ \mu_1 = 1$	25.3
$\beta = \gamma = 1,\ \mu_1 = 10$	3.6

Table 6.2: Minimal value α^* for which the solution ceases to exist, depending on parameters β, γ, μ_1. Both convolution kernels are logistic: $J_1 = J_2 = J_L$.

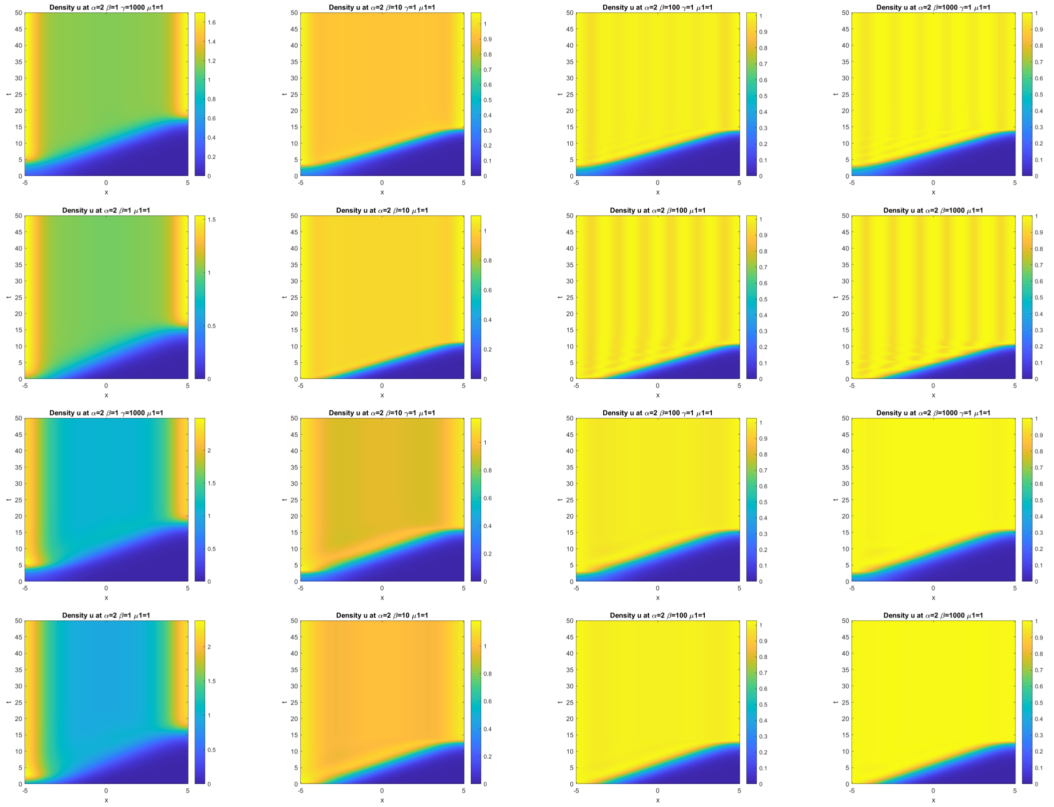

Figure 6.4: Simulations of models (6.2.1) and (6.5.3) with $\alpha = 2$, $\mu_1 = 1$, and (from left to right) $\beta = 1, 10, 100, 1000$ and $\gamma = 1000$ in column 1, $\gamma = 1$ in columns 2-4. First row: $J_1 = J_2 = J_U$; 2nd row: model without w, with $J = J_U$; 3rd row: $J_1 = J_2 = J_L$; 4th row: model without w, with $J = J_L$

Moreover, as in *Chapter 5*, increasing values of β and μ_1 in *Figure 6.4* lead to patterns depending on the kernels J_1 and J_2. A high value of γ does not seem to lead by itself to patterns, but further experiments suggest that γ influences the height of the peaks, thus leading to less pronounced u-patterns. This is due to the stronger dampening of proliferation, which hinders stronger aggregates. To illustrate the effect of γ we plot in *Figure 6.4* two situations with very different values ($\gamma = 1000$ in the first column and $\gamma = 1$ in the remaining columns).

The performed simulations are very similar to those of the reduced model

$$\begin{cases} \partial_t u = \nabla \cdot (\psi(h)\nabla u) + \mu_1 u^\alpha \left(1 - J(x,h) * u^\beta\right) & \text{in } \Omega \times (0,\infty), \\ \partial_t h = D_H \Delta h + g(u) - \lambda h & \text{in } \Omega \times (0,\infty) \end{cases} \tag{6.5.3}$$

without inactive cells w (compare rows 1 and 2 and rows 3 and 4 in *Figure 6.4*, respectively, for uniform or logistic kernels). System (6.5.3) is a simplification of the model considered in *Chapter 5* without myopic diffusion and taxis, where Turing-like patterns for large values of $\beta\mu_1$ were induced by the nonlocal term. This also seems to be the case here in model (6.2.1). However, the calculation of a strictly positive steady-state (u^*, w^*, h^*) already leads to analytical problems, since this requires even in the corresponding local model without diffusion and for $\mu_2, \mu_3, \tilde{\mu}_3$ independent from h a solution to the nonlinear system

$$
\begin{aligned}
0 &= \mu_1 (u^*)^\alpha \left(1 - (u^*)^\beta - (w^*)^\gamma\right) + \tilde{\mu}_3 F(w^*),\\
0 &= \mu_2(1-w^*)u^* - \mu_3 F(w^*).
\end{aligned}
\tag{6.5.4}
$$

Comparing the height of the peaks in columns 3 and 4 of *Figure 6.4* for uniform kernels (i.e., first two rows therein) clearly shows the dampening effect of interspecific interactions. Moreover, the solution of (6.5.3) reaches its maximum accumulation at the left boundary faster than the solution of (6.2.1), which is again due to the supplementary interspecific dampening in the latter model. *Figure 6.5* shows that in model (6.5.3) a blow-up already occurs for relatively smaller values of α.

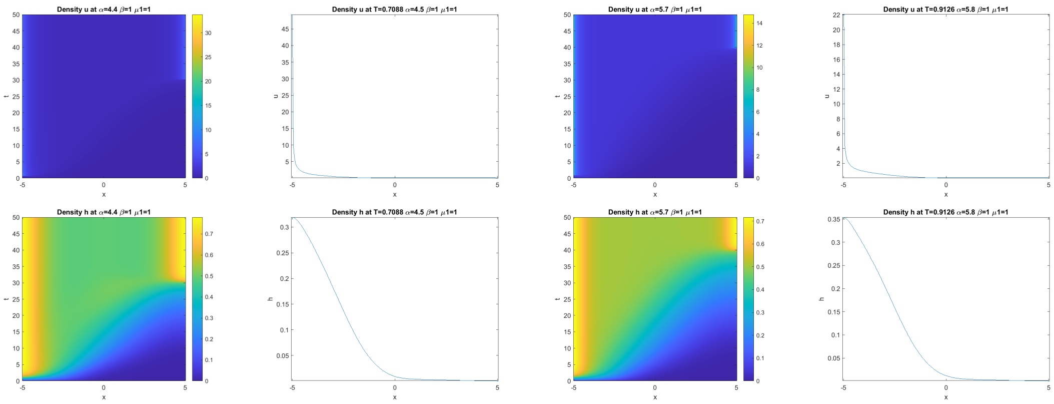

Figure 6.5: Simulations of model (6.5.3) without w with $\beta = \mu_1 = 1$. Columns 1 and 2: J logistic and $\alpha = 4.4, 4.5$. Columns 3 and 4: J uniform and $\alpha = 5.7, 5.8$. In the 2nd and 4th column a blow-up occurs in the next time step..

For the h-dependent kernels J_1 and J_2 from (6.5.1) and (6.5.2) the solution u in *Figure 6.6* rapidly accumulates at the left boundary and then invades the whole domain aggregating much less at the boundaries than in *Figures 6.2* and *6.3*. As mentioned in *Table 6.1* the blow-up already occurs for $\alpha^* = 4.1$. The 4th column in *Figure 6.6* shows one example of pattern formation for a certain choice of parameters.

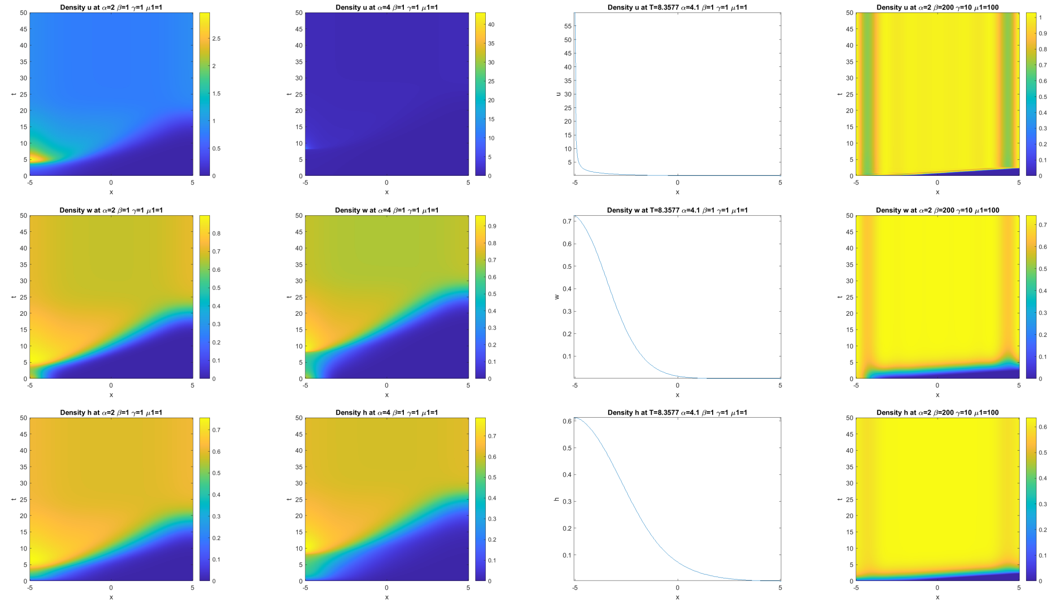

Figure 6.6: Simulations of model (6.2.1) with h-dependent kernels J_1 and J_2 from (6.5.1) and (6.5.2) for $\beta = \gamma = \mu_1 = 1$, $\alpha = 2, 4, 4.1$. In the 3rd column a blow-up occurs in the next time step. The 4th column shows patterns for $\alpha = 2$, $\beta = 200$, $\gamma = 10$, $\mu_1 = 100$.

6.6 Discussion

As mentioned in *Section 6.2*, the model introduced here extends previous settings [99] and, in a certain sense, *Chapter 5* and [136]. As in *Chapter 5* and [99], the main mathematical challenge comes from the interaction strengths $\alpha, \beta \geqslant 1$ present in the nonlocal terms; interspecific interactions did not add further difficulties as far as global existence and boundedness are concerned. In contrast to *Chapter 5* we do not have here any myopic diffusion, nor taxis terms, which saves us the efforts otherwise needed to estimate first derivatives of the tactic signal. The model with interspecific interactions from [136] involves haptotaxis, but there $\alpha = \beta = \gamma = 1$ and the lack of transitions from one population to another, along with the assumptions made on initial data, convolution kernels, and coefficient functions render the analysis therein more accessible.

The missing diffusion of w-cells required the construction of the approximate problem in *Section 6.3*. Introducing the term $-wu$ in the dynamics of w-cells helped ensure in that problem the boundedness of w_ε, with the aid of a comparison principle. Such term does have a biological motivation as well: it describes competition between active and inactive cells, which in our model is also triggered by the acidity profile, as both tumor cell phenotypes extrude protons in the interstitial space (the active ones more than their quiescent counterparts).

As in *Chapter 5* and [99], the condition (6.2.2) is not sharp: the numerical simulations suggest that the solution also exists globally for certain pairs (α, β) which do not satisfy that requirement. Interestingly, the critical value α^* for which a solution ceases to exist does not seem to be an absolute α-minimum, but can jump to higher or lower values, depending on the particular combination of the other parameters β, γ, μ_1 (even for the same choice of kernels), as seen in *Table 6.2*. Indeed, there seems to be an $\alpha^{**} > \alpha^*$ such that the solution blows up in finite time for $\alpha \geqslant \alpha^{**}$, but stays global for certain values $\alpha \in (\alpha^*, \alpha^{**})$. A thorough mathematical investigation thereof remains, however, open. As *Table 6.1* shows, α^* also depends on the choice of convolution kernels (for fixed parameter values); this greatly complicates the analysis of blow-up behavior, due to the unlimited degrees of freedom one has for such choices, notwithstanding conditions (6.2.5).

A rigorous mathematical stability and pattern analysis for this kind of PDE-ODE-PDE models seems to be out of reach with the established approaches (see, e.g., [4, 107, 114, 135]), mainly due to the nonlinearities featuring weak Allee and overcrowding/competition effects with the respective interaction strengths α, β, γ, which preclude from identifying nontrivial steady-states even in the absence of diffusion; the phenotypic switch terms only add difficulty to such attempts. The numerical simulations performed in *Section 6.5* give some insight into the long term and patterning behavior of solutions, suggesting that the solution seems to be able to approach in the long term some stable state and to exhibit patterns, depending (as in *Chapter 5*) on the choice of kernels and the parameter combination. The model extension with w-cells and interspecific interactions does not change substantially the type and shape of obtained oscillatory patterns, but does have an influence on the peaks of u-cell aggregates. The noticed dampening effect also contributes to detering solution blow-up or at least ensuring global boundedness for substantially larger α values which, again, depend on the choice of the convolution kernels and of the interaction strength γ.

Our analysis explicitly required the diffusion coefficient $\psi(w, h)$ to be nondegenerate. Alleviating this assumption leads to further mathematical challenges, when trying to obtain (as usually in such proofs) a bound on ∇u from the ODE for w. Indeed, the problem thereby relies on u being involved in the growth, instead of the decay term. On the other hand, considering such nonlinear diffusion is motivated from a biological viewpoint, in order to account e.g., for chemokinesis [63, 76, 122].

CHAPTER 7

Summary and outlook

To conclude this work, we summarize what was considered, which methods were used, and name possible continuations of this work. We looked at four models involving reaction-diffusion-advection equations with spatial nonlocality, three of them also involving couplings with an ODE and/or a PDE. The considered models describe migration of cells in different biological contexts, in bounded domains. Thereby, we showed the global existence of a weak or very weak solution for each of the considered models. Moreover, we proved the boundedness of the solutions obtained in *Chapters 5* and *6*. In *Chapters 3*, *5*, and *6* numerical simulations were performed. *Chapter 5* also contains an analysis of the long-time behavior of the solution and pattern formation to explain the oscillations in the simulations. *Chapters 3*, *5*, and *6* were already discussed in *Sections 3.6*, *5.7*, and *6.6*, respectively. Therefore, we will only deal with them briefly here and refer to the just mentioned sections for a more detailed discussion of our considerations and related literature. The corresponding assessment of related literature for the model in *Chapter 4* can be found in *Section 4.1*.

In *Chapter 3* we analyzed the PDE-PDE-/PDE-ODE-system from (3.4.1) consisting of a reaction-diffusion-advection equation with nonlinear diffusion and nonlocal advection term modeling the development of the cell density and a PDE or an ODE for a diffusible or nondiffusible signal, respectively. Thereby, we combined a prototypical cell-cell and cell-matrix adhesion model with adhesion operator $\mathcal{A}_r$ and a general form of the nonlocal chemotaxis model with nonlocal gradient $\mathring{\nabla}_r$ in the unified framework (3.4.1). This nonlocal model was related to the local unified hapto-/chemotaxis model (3.4.2) in the sense that our adhesion model was the nonlocal version of the haptotaxis model with nonlinear diffusion and our nonlocal chemotaxis-growth model was the nonlocal version of the local chemotaxis-growth model. We established the connection of these frameworks by demonstrating that the weak solution of the nonlocal model converges in L^2 to the weak solution of the corresponding local model.

The proof relied on the functionwise convergence of the integral operators $\mathcal{T}_r$ and $\mathcal{S}_r$ to the identity operator for diminishing sensing radius r (which did not hold for the original nonlocal operators) and their self-adjoint-like property shown in *Lemmas 3.2.5* and *3.2.7*. These operators were applied to the functions' gradient, and were reformulations of the adhesion and nonlocal gradient operators (on the subdomain Ω_r with distance r to the boundary), respectively. Furthermore, numerical simulations depicted in *Figure 3.1* indicated that in a minimalist model, the difference between the solutions of the models involving $\mathcal{A}_r$ and $\mathcal{T}_r$ is negligible when the cells start at the center of the domain. However, the solutions differed when the cells started near the boundary, as seen in *Figure 3.2* .

We showed the existence of a weak-strong solution to the approximate problems (3.4.10) in the case of a diffusible signal involving the functions G_ε to assure the nonnegativity of the solution with a Leray-Schauder fixed-point argument and monotone operator theory and concluded the existence of a weak-strong solution to the nonlocal problem (3.4.1) in the sense of *Definition 3.4.6* for a diffusing and nondiffusing signal with the help of several approximations. Further, we established uniform in r estimates on these solutions and proved their convergence to the solution of the local model in the sense of *Definition 3.4.6* for $r = 0$ using the properties of the reformulated operators indicated above. This convergence could also be seen in *Figures 3.3* and *3.5* for an appropriate choice of parameters that guaranteed well-posedness. Finite-time blow-up occurred in the local model (cf. *Figure 3.4*), whereas the nonlocal model exhibited pattern for large t.

A possible extension of our model would be to include a similar nonlocality in the diffusion term of the adhesion model (see *Section 3.6*).

In *Chapter 4* we considered the reaction-diffusion-advection equation from (4.1.1) that combined degenerate myopic diffusion with self-adhesion and a generalized logistic-type growth term. This extended the model derived in [156] by the term $\mu c(1 - c^{r-1})$ which allowed us to establish the uniform bound in L^r from *Lemma 4.5.1.* We showed the existence of a global very weak solution in the sense of *Definition 4.3.3.* The very weak formulation was obtained from (4.1.1) through two partial integrations that shifted all spatial derivatives to the test functions. There, the boundary integral from the first partial integration vanished due to our no-flux boundary condition, but to eliminate the other boundary integral we imposed on our test functions that their derivative in direction $\mathbb{D}\nu$ is zero on the boundary. The density of such functions in H^1 was shown in *Lemma 4.6.2*, which led to *Theorem 4.6.1*, where we checked that our very weak formulation is appropriate by showing that a $C^{2,1}$-function satisfying the very weak formulation is a classical solution to (4.1.1). To show the existence of an 'only' weak solution we lack a uniform bound on ∇c on the whole domain Ω, whose proof seems unlikely, due to the combination of myopic diffusion and degeneracy.

Our equation included the standard adhesion operator also considered in *Chapter 3* from *Definition 4.2.1* into the advection term. In contrast to the approach there, we did not use its reformulation from *Lemma 3.2.1* shifting the application of the nonlocal operator from the function itself to its gradient. Instead, we have rewritten the adhesion operator as in [156] to a convolution with the bounded gradient of an interaction potential, which (thanks to our assumptions on F) illustrated that our operator maps functions from L^1 to bounded functions, a fact that was not used in *Chapter 3*. For this reason, it was sufficient that the approximating sequence of classical solutions (c_ε) only converged in L^1 in order to conclude the convergence of the nonlocal term $c_\varepsilon \mathcal{A} c_\varepsilon$. Moreover, the adhesion operator preserved Hölder-continuity, which was necessary for the existence proof of a classical solution.

The assumptions of a positive distance to the boundary of the domain and some sufficiently low dimension of the degeneracy set of $\mathbb{D}$ and the boundedness of its divergence from (4.3.2c) were necessary for the construction of an approximating sequence of smooth and non-degenerating diffusion tensors $\mathbb{D}_\varepsilon$ in *Subsection 4.4.1* with the standard approach from Theorem 3 in Section 5.3.3 from [58]. Using this method, the diffusion tensors were uniformly bounded on Ω. Moreover, also their divergences were uniformly bounded on sets compactly contained in $\{\mathbb{D} > 0\}$, which together with the already mentioned uniform boundedness in L^r was used to show the uniform bounds established in *Lemma 4.5.2*. In contrast to [77] we did not require the convergence of its divergence or additional restrictions on $\mathbb{D}_\varepsilon$.

The existence of global classical solutions c_ε to the approximate problems involving the diffusion tensors $\mathbb{D}_\varepsilon$ was shown with a standard fixed-point argument. Thereby, the difficulty in proving their convergence to the desired weak solution lay in the convergence of the term c_ε^r shown in *Lemma 4.5.4*. This was necessary as we could not apply the de la Vallée-Poussin theorem on the whole domain to obtain L^1-convergence, but only on the already mentioned sets compactly contained in the complement of the degeneracy set. Therefore, we introduced the upper box dimension to quantify the required sufficiently low dimensionality of the degeneracy set of $\mathbb{D}$ and constructed a sequence (φ_δ) of smooth functions with diminishing support satisfying properties (4.2.5a)-(4.2.5g) and equal one in neighborhoods of $\{\mathbb{D} \not\succ 0\}$ that diminish in δ. Using them, we showed the required convergence after splitting c_ε^r in a function with support in a set with a positive distance to the degeneracy set and a function whose support contained the degeneracy set. Only there the assumptions on r from (4.3.1) and $n \geqslant 3$ were required to ensure the positivity of the term on the right-hand side of condition (4.2.4).

The next step could be an analysis of the original model from [156]. Our solution approach does not work there, because without the growth term we lack the uniform bound on the approximate solutions in L^r. Moreover, the solution there could be measure-valued rather than a function, as we can only guarantee mass preservation. In [128] local well-posedness was established for an equation of this form coupled with a nonlinear integral equation, where the myopic diffusion was replaced by a quasilinear degenerated diffusion. The model there was also derived in [156] by additionally taking into account the cadherin binding dynamics of a pair of cells. In addition, the numerical simulations are still missing. Thereby, the difficulty lies in the degeneracy of the diffusion.

Chapter 5 dealt with the PDE-PDE-system coupling an reaction-diffusion-advection equation with myopic diffusion, repellent pH-taxis, and a nonlocal intraspecific interaction for the tumor cell density with a reaction-diffusion equation for the acid concentration from (5.3.1). There, the nonlocality was of form $J * u^\beta$. Our model extended [99] by replacing the Fickian diffusion with myopic and additionally considers the effects of a soluble signal via repellent pH-taxis. The formal modeling started from a meso-macro-system describing the mesoscopic tumor cell dynamics in response to acidity in the extracellular space. It consisted of a kinetic transport equation in the framework from [116] for the mesoscopic description of cell migration and intraspecific interaction and a macroscopic PDE describing the proton concentration. We deduced the macroscopic equation for the cell population dynamics (5.2.21) by a diffusion-dominated upscaling of the mesoscopic description. Due to the nonlinear source term, we could not apply the method from [25] for a rigorous derivation here. For α and β satisfying (5.3.3), the global existence of a bounded solution was followed with a fixed-point argument and estimates from [99]. Under additional assumptions on the norm of the kernel and the parameters that required especially some 'smallness' of $\beta^2\|\mu\|_{L^\infty}$ as in [99], the tumor cell density approached on a long-term basis either some upper bound or zero, whereas the acid concentration approached some value depending on the concrete form of g from estimate (5.4.1). Thereby, the proof relied on the handling of the myopic diffusion as in [91] and the treatment of nonlocality from [99]. A 1D pattern analysis suggested that the occurrence of Turing-like, Hopf, or wave instabilities is due to the nonlocality and not due to the diffusion and depends on the concrete choice of parameters, especially on the product $\beta\mu$, and the Fourier transform of the kernel. This matched the observations in other non-local models [64, 74, 99, 119, 131, 142, 153] and was confirmed by numerical simulations depicted in *Figures 5.2* and *5.3*.

Further numerical simulations (see *Figure 5.1*) indicated that the solution exists globally for combinations of larger α compared to β not satisfying (5.3.3). Since the estimates from [99] were restricted to this case, a new approach is required to handle the nonlocal term for such α and β in the proof of global existence. Moreover, the simulations in *Figure 5.1* suggested that, as in [99], the maximum value of such α also depends on the kernel. In this context, a further step in the analysis of this model would be the determination of the α about which a blow-up occurs depending on β and the kernel.

The existence proof of a weak solution for a degenerating diffusion tensor $\mathbb{D}$ would require uniform estimates of appropriate norms of the global classical solutions from *Theorem 5.3.6* (and its gradients) that are independent from the lower bounds of the approximating diffusion tensors. This can get very difficult even in 1D (e.g., [149, 151]). Our estimates from the proof of (5.3.4) no longer work here as we lack a uniform lower bound of the diffusion tensors in contrast to *Theorem 5.3.6* and, consequently, the uniform upper bound of the approximate solutions from *Lemma 5.3.4*, which was used in particular for large α for the uniform estimate of the source term, is lost. Similarly, we would need bounds independent from the divergence of the proton concentration, in order to show the existence of a weak solution in the model with haptotaxis instead of chemotaxis. Our estimates cannot be used for this case either, because the uniform bound on the gradients of the acid concentrations from *Lemma 5.3.3* depends on D_H^{-1}.

In contrast to this, in the model presented in *Chapter 6*, we were able to use such estimates to obtain weak solutions in the PDE-ODE-PDE-system (6.2.1) describing the interactions of an active and a quiescent cell population in an acidic environment from classical solutions of the approximating PDE-PDE-PDE-system (6.3.2). Compared to *Chapter 5*, the model took into account a second inactive cell population w whose development was described by an ODE. Moreover, the reaction-diffusion equation for the active cells u did not contain a taxis term or myopic diffusion. Instead, we added a second nonlocality describing interspecific interactions between u and w to the nonlocal reaction term in the equation of u from the last chapter and a growth term of the form $\tilde{\mu}_3(h)F(w)$ that depended on w and the acid concentration h. As the model did not contain a taxis term, we did not require a uniform bound on ∇w_ε independent of the diffusion coefficient ε there to conclude the existence of a global uniform bound of the approximate solutions u_ε.

We included the term $1 - w$ into the u-dependent growth term in the equation for the quiescent cells w in order to ensure its boundedness with the help of a comparison principle in the approximate problem. Otherwise, this boundedness could not even be shown for bounded functions u. Further, the boundedness and consequent global existence of the approximate solutions u_ε followed similarly to *Chapter 5* using the estimates from [99] to handle the nonlocal intraspecific term. As in *Chapter 5*, the solution was also global for pairs of α and β that did not fulfill condition (6.2.2). In our method, the nonlocal interspecific term did not contribute to the proof of global existence for further pairs of α and β. However, a comparison of the simulations of this model from *Figures 6.2* and *6.3* with those of model (6.5.3) without w from *Figure 6.5* suggested that this term damped the blow-up behavior of the solution u. Also, the choice of the kernels, the exponents β and γ and the growth rate μ_1 influenced the minimum value of α^* for which a blow-up occurred (see *Tables 6.1* and *6.2*). Additionally, for certain combinations of parameters, the solution also existed globally for some $\alpha > \alpha^*$. In these cases there seemed to be an $\alpha^{**} > \alpha^*$, s.t. the solution blew-up in finite time for $\alpha \geqslant \alpha^{**}$, while there were α in (α^*, α^{**}), where the solution was global. A thorough mathematical investigation of this remains an open problem.

In *Figure 6.4* increasing values of β led to oscillations in the case of uniform kernels, which was not the case for increasing γ. Also, for large enough parameters, oscillations occurred for the h-dependent kernels from (6.5.1) and (6.5.2) as seen in *Figure 6.6*. Hence, we assume that as in *Chapter 5*, the formation of Turing-like patterns depends on the kernel and the product $\beta\mu_1$. We lack a pattern analysis here, as the computation of a positive steady state of the corresponding local model without diffusion led to the system of equations (6.5.4), which can only be solved numerically.

One extension of our analysis would be, again, to consider a degenerate diffusion coefficient $\psi(h, w)$. Thereby, the problem is that it is not possible to obtain a bound on ∇u from the equation of w, as is usually the case, since u is contained in the growth and not in the decay term.

Appendix A Additional Theorems

We summarize some results on different types of differential equations, fixed-point and convergence theorems and further results from functional analysis used in this work in Appendices *A.1*–*A.3*. In Appendix *A.4* we state some results, especially from [99], used in *Part II* and slightly adopted to our needs. Finally, we prove some results on Hölder continuous functions and convolutions from *Chapter 2* in Appendix *A.5*. If not stated otherwise $\Omega \subset \mathbb{R}^n$, $n \in \mathbb{N}$, denotes a bounded domain with smooth enough boundary throughout this chapter.

A.1 Differential Equations

A.1.1 Linear PDEs

Theorem A.1.1. *([94, Theorem III.5.1]) Let $T > 0$ and consider the IBVP*

$$\begin{cases} u_t - \mathcal{M}u = -f & \text{in } \Omega \times (0,T), \\ \sum_{i=1}^n \left(\sum_{j=1}^n a_{ij} u_{x_j} + a_i u \right) \nu_i = 0 & \text{on } \partial\Omega \times (0,T), \\ u(x,0) = u_0(x) & \text{in } \Omega, \end{cases} \tag{A.1.1}$$

where the operator

$$\mathcal{M}u := \sum_{i,j=1}^n \left(a_{ij} u_{x_j} + a_i u \right)_{x_i} - au.$$

satisfies the uniform ellipticity and boundedness condition, i.e., there are $\mu_1, \mu_2 > 0$ s.t. for all $\xi \in \mathbb{R}^n$, $x \in \Omega$ and $t \in (0,T)$ it holds that

$$\mu_1 |\xi|^2 \leqslant \sum_{i,j=1}^n a_{ij}(x,t) \xi_i \xi_j \leqslant \mu_2 |\xi|^2 \tag{A.1.2}$$

and $a_i, a, f \in L^\infty(\Omega \times (0,T))$ for $i = 1, \ldots, n$.

Then, for any $u_0 \in L^2(\Omega)$ there is a unique weak solution $u \in C([0,T]; L^2(\Omega)) \cap L^2(0,T; H^1(\Omega))$ in the sense that for all $\eta \in W_2^{1,1}(\Omega \times (0,T))$ with $\eta(T) = 0$ it holds that

$$-\int_0^T \int_\Omega u \eta_t \, dx \, dt + \int_0^T \int_\Omega \sum_{i=1}^n \left(\sum_{j=1}^n a_{ij} u_{x_j} + a_i u \right) \eta_{x_i} + au\eta + f\eta \, dx \, dt = \int_\Omega u_0(x) \eta(x,0) \, dx. \tag{A.1.3}$$

Moreover, any weak solution $u \in L^\infty(0,T; L^2(\Omega)) \cap L^2(0,T; H^1(\Omega))$ is also in $C([0,T]; L^2(\Omega))$.

Proof. This follows similarly to the proof of Theorem III.5.1 in [94] by adapting it to our boundary condition and is a special case for bounded coefficient functions. Then, the coefficients are in the required spaces for any suitable combination of q, r, q_1, r_1. □

Remark A.1.2. The weak formulation (A.1.3) is equivalent to

$$\int_\Omega u(x,t)\eta(x,t)\,\mathrm{d}x - \int_0^t \int_\Omega u\eta_t\,\mathrm{d}x\,\mathrm{d}s + \int_0^t \int_\Omega \sum_{i=1}^n \left(\sum_{j=1}^n a_{ij} u_{x_j} + a_i u \right) \eta_{x_i} + au\eta + f\eta\,\mathrm{d}x\,\mathrm{d}s$$
$$= \int_\Omega u_0(x)\eta(x,0)\,\mathrm{d}x. \tag{A.1.4}$$

for a.e. $t \in (0,T)$ and all $\eta \in W_2^{1,1}(\Omega \times (0,T))$.

Lemma A.1.3. *Under the assumptions of Theorem A.1.1 any weak solution* $u \in C([0,T]; L^2(\Omega)) \cap L^2(0,T; H^1(\Omega))$ *of* (A.1.1) *in the sense of* (A.1.3) *satisfies*

$$\frac{1}{2}\int_\Omega u^2(t)\,dx + \int_0^t \int_\Omega \sum_{i=1}^n \left(\sum_{j=1}^n a_{ij} u_{x_j} + a_i u \right) u_{x_i} + au^2 + fu\,dx\,dt = \frac{1}{2}\int_\Omega u_0^2\,dx$$

for a.e. $t \in (0,T)$,

Proof. This follows similarly to (2.13) in Chapter III in [94] from the corresponding weak formulation (A.1.3) of a solution. □

Theorem A.1.4. *For* $u_0 \in L^\infty(\Omega)$ *under the assumptions of Theorem A.1.1 there is a constant* $K_1 > 0$ *depending on* $\mu_1, \|a_i\|_{L^\infty(\Omega\times(0,T))}, \|a\|_{L^\infty(\Omega\times(0,T))}, \|f\|_{L^\infty(\Omega\times(0,T))}$ *s.t.* $\|u\|_{L^\infty(\Omega\times(0,T))} \leqslant K_1$ *holds for any weak solution* $u \in C([0,T]; L^2(\Omega)) \cap L^2(0,T; H^1(\Omega))$ *of* (A.1.1) *in the sense of* (A.1.3).

Proof. This follows similarly to the proof of Theorem III.7.1 in [94] by adapting it to our boundary condition and is a special case for bounded coefficients. Then, the coefficients are in the required spaces for any suitable combination of q, r. □

Theorem A.1.5. *([94, Theorem III.12.1]) Let* $\alpha \in (0,1)$ *and* $T > 0$. *If* $a_{ij}, (a_{ij})_{x_i}, a_i, (a_i)_{x_i}, a, f \in C^{\alpha,\frac{\alpha}{2}}(\Omega \times (0,T))$ *for* $i,j = 1,\dots,n$, *then* $u \in C^{2+\alpha,1+\frac{\alpha}{2}}(\Omega \times (0,T))$ *holds for any weak solution* $u \in C([0,T]; L^2(\Omega)) \cap L^2(0,T; H^1(\Omega))$ *of* (A.1.1) *in the sense of* (A.1.3)

Theorem A.1.6. *Let* $\alpha \in (0,1)$, $T > 0$ *and consider the IBVP*

$$\begin{cases} u_t + \mathcal{L}u = f & \text{in } \Omega \times (0,T), \\ \mathcal{B}u = 0 & \text{on } \partial\Omega \times (0,T), \\ u(x,0) = u_0(x) & \text{in } \Omega, \end{cases} \tag{A.1.5}$$

where

$$\mathcal{L}u := -\sum_{i,j=1}^n a_{ij} u_{x_j x_i} + \sum_{i=1}^n a_i u_{x_i} + au$$

satisfies (A.1.2) *and*

$$\mathcal{B}u = \sum_{i=1}^n b_i u_{x_i} + bu$$

satisfies

$$\left| \sum_{i=1}^n b_i \nu_i \right| \geqslant \delta > 0 \text{ on } \partial\Omega \times (0,T).$$

If $a_{ij}, a_i, a \in C^{\alpha,\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$ and $b_i, b \in C^{1+\alpha,\frac{1+\alpha}{2}}(\partial\Omega \times [0,T])$ for $i,j = 1,\dots,n$, then for any $f \in C^{\alpha,\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$ and $u_0 \in C^{2+\alpha}(\overline{\Omega})$ satisfying the compatibility condition $\mathcal{B}u_0 = 0$ on $\partial\Omega \times \{0\}$ there is a unique solution $u \in C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$ of (A.1.5) *and a constant $K_2 > 0$ depending continuously on the norms of a_{ij}, a_i, a in $C^{\alpha,\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$ and the norms of b_i, b in $C^{1+\alpha,\frac{1+\alpha}{2}}(\partial\Omega \times [0,T])$ s.t.*

$$\|u\|_{C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega}\times[0,T])} \leqslant K_2 \left(\|f\|_{C^{\alpha,\frac{\alpha}{2}}(\overline{\Omega}\times[0,T])} + \|u_0\|_{C^{2+\alpha}(\overline{\Omega})} \right). \tag{A.1.6}$$

The solution u depends continuously on the coefficients and functions.

Proof. Set $\Phi = 0$ in Theorem IV.5.3 in [94]. The continuous dependence of K_2 on the coefficients and of u on the coefficients and functions follows from the proof of this theorem. □

Theorem A.1.7. *Let $T > 0$ and consider the IBVP* (A.1.5). *Suppose that for $i,j = 1,\dots,n$, $a_{ij}, a_i, a \in C^{\alpha,\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$, $b_i, b \in C^{1+\alpha,\frac{1+\alpha}{2}}(\partial\Omega \times [0,T])$ and satisfy $\sum_{i,j=1}^n a_{ij}(x,t)\xi_j\xi_i \geqslant \mu_1|\xi|^2$ for $\mu_1 > 0$ and $\sum_{i=1}^n b_i\nu_i \geqslant \delta > 0$. Then, for any $f \in C^{\alpha,\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$ and $u_0 \in C(\overline{\Omega})$ there is a unique solution $u \in C^{2,1}(\Omega \times (0,T)) \cap C(\overline{\Omega} \times [0,T]) \cap C^{1,0}(\overline{\Omega} \times (0,T))$ of* (A.1.5). *If additionally $u_0 \in C^{2+\alpha}(\Omega)$ and satisfies the compatibility condition $\mathcal{B}u_0 = 0$ on $\partial\Omega \times \{0\}$, then $u \in C^{2+\alpha,1+\frac{\alpha}{2}}(\overline{\Omega} \times [0,T])$.*

Proof. This is a special case of Theorem 5.18 in [100]. □

Theorem A.1.8. *Let $T > 0$ and consider for a constant $D > 0$ the nonhomogeneous heat equation with Neumann boundary condition*

$$\begin{cases} u_t = D\Delta u + f & \text{in } \Omega \times (0,T), \\ \partial_\nu u = 0 & \text{on } \partial\Omega \times (0,T), \\ u(x,0) = u_0(x) & \text{in } \Omega. \end{cases} \tag{A.1.7}$$

Then, for any $f \in L^2(\Omega \times (0,T))$ and $u_0 \in H^1(\Omega)$ there is a unique solution $u \in W_2^{2,1}(\Omega \times (0,T))$ satisfying

$$\|u\|_{W_2^{2,1}(\Omega\times(0,T))} \leqslant K_3(T) \left(\|f\|_{L^2(\Omega\times(0,T))} + \|u_0\|_{H^1(\Omega)} \right).$$

Proof. This is a special case of Theorem IV.9.1 (together with the remark at the end of the chapter for Neumann boundary conditions) in [94] for a nonhomogeneous heat equation with $\Phi = 0$, $q = 2$. □

Theorem A.1.9. *([100, Theorem 2.9]) Let $T > 0$ and $u, v \in C^{2,1}(\overline{\Omega} \times (0,T)) \cap C(\overline{\Omega} \times [0,T])$. Suppose that $\mathcal{L}$ satisfies* (A.1.2), *$\sum_{i=1}^n a_{ii}, a_i, a \in L^\infty(\Omega \times (0,T))$ for $i = 1,\dots,n$, $a \geqslant 0$, $-(b_1,\dots,b_n)^T$ is a vector that points strongly inside $\Omega \times (0,T)$ on $\partial\Omega \times (0,T)$ and $b \geqslant 0$ on $\partial\Omega \times (0,T)$. If*

$$\begin{cases} u_t + \mathcal{L}u \leqslant v_t + \mathcal{L}v & \text{in } \Omega \times (0,T), \\ \mathcal{B}u \leqslant \mathcal{B}v & \text{on } \partial\Omega \times (0,T), \\ u \leqslant v & \text{in } \overline{\Omega}, \end{cases}$$

then $u \leqslant v$ holds in $\overline{\Omega} \times [0,T]$.

Proposition A.1.10. *([36, Proposition 13.1]) Let $T > 0$, $u \in W_p^{2,1}(\Omega \times (0,T))$ for $p \geqslant n+1$ and consider an operator $\mathcal{L}$ that satisfies* (A.1.2) *with coefficients that are continuous on $\overline{\Omega} \times [0,T]$. Suppose*

$$u_t + \mathcal{L}u \geqslant 0,$$

holds a.e. in $\Omega \times (0,T)$. If u attains its minimum $m \leqslant 0$ at $(x_0, t_0) \in \Omega \times (0,T]$, then $u \equiv m$ in $\overline{\Omega} \times [0, t_0]$.

Theorem A.1.11. *([36, Theorem 13.5 with the remark at the end of the chapter]) Let $T > 0$, $a_{ij}, a_i, a \in C(\overline{\Omega} \times [0,T])$, $b_i \in C^1(\partial\Omega)$ and $b \in C^1(\partial\Omega \times [0,T])$. If $u \in W_p^{2,1}(\Omega \times (0,T))$ for $p > n+2$ satisfies*

$$\begin{cases} u_t + \mathcal{L}u \geqslant 0 & \text{in } \Omega \times (0,T), \\ \mathcal{B}u \geqslant 0 & \text{on } \partial\Omega \times (0,T), \\ u(x,0) \geqslant 0 & \text{in } \Omega, \end{cases} \tag{A.1.8}$$

then $u \geqslant 0$ holds in $\overline{\Omega} \times [0,T]$.

A.1.2 Nonlinear parabolic PDEs

Theorem A.1.12. *Let $T > 0$, $p \geqslant 2$ and $a : \mathbb{R}^{2n+2} \to \mathbb{R}^n$ and $b : \mathbb{R}^{2n+2} \to \mathbb{R}$ be measurable and satisfy the estimates*

$$a(x,t,u,\nabla u) \cdot \nabla u \geqslant K_4 |\nabla u|^p - \psi_0(x,t), \tag{A.1.9}$$

$$|a(x,t,u,\nabla u)| \leqslant K_5 |\nabla u|^{p-1} + \psi_1(x,t), \tag{A.1.10}$$

$$|b(x,t,u,\nabla u)| \leqslant K_6 |\nabla u|^p + \psi_2(x,t), \tag{A.1.11}$$

where K_4, K_5, K_6 are positive constants and $\psi_j \in L^\infty(\Omega \times (0,T))$, $j = 0,1,2$, are non-negative. Besides, let $u \in C([0,T]; L^2(\Omega)) \cap L^p(0,T; W_p^1(\Omega)) \cap L^\infty(\Omega \times (0,T))$ be a weak solution of

$$\begin{cases} \partial_t u - \nabla \cdot a(x,t,u,\nabla u) + b(x,t,u,\nabla u) = 0 & \text{in } \Omega \times (0,T), \\ a(x,t,u,\nabla u) \cdot \nu(x) = 0 & \text{on } \partial\Omega \times (0,T), \\ u(x,0) = u_0(x) & \text{in } \Omega \end{cases} \tag{A.1.12}$$

in the sense that

$$\int_\Omega u\varphi \, dx \Big|_{t_1}^{t_2} + \int_{t_1}^{t_2} \int_\Omega -u\varphi_t + a(x,t,u,\nabla u) \cdot \nabla\varphi + b(x,t,u,\nabla u)\varphi \, dx \, dt = 0$$

holds for all $0 \leqslant t_1 < t_2 \leqslant T$ and for all $\varphi \in L^p((0,T), W_p^1(\Omega))$ with derivative $\varphi_t \in L^2(\Omega \times (0,T))$. Then, u is Hölder continuous on $\overline{\Omega} \times [\varepsilon, T]$ for any $\varepsilon > 0$, i.e., there are constants $K_7 > 0$ and $\alpha \in (0,1)$ depending only on the constants appearing in (A.1.9) - (A.1.11)*, the norms of the ψ_j and $||u\|_{L^\infty(\Omega \times (0,T))}$ and ε s.t. the estimate*

$$|u(x_1,t_1) - u(x_2,t_2)| \leqslant K_7(\varepsilon) \left(|x_1 - x_2|^{\alpha(\varepsilon)} + |t_1 - t_2|^{\frac{\alpha(\varepsilon)}{p}} \right) \tag{A.1.13}$$

is satisfied for any pair $(x_1,t_1), (x_2,t_2) \in \overline{\Omega} \times [\varepsilon, T]$.

If additionally $u_0 \in C^{\alpha'}(\overline{\Omega})$ for $\alpha' \in (0,1)$, then u satisfies (A.1.13) *in $\overline{\Omega} \times [0,T]$ for constants K_7 and α that can be chosen independent from ε. In this case α also depends on α'.*

Proof. This is a special case of Theorem 4 in [39] for $g = 0$ and bounded ψ_i that are in the required spaces for any suitable combination of q, r. □

Theorem A.1.13. *Let $T > 0$ and $u \in C([0,T]; L^2(\Omega)) \cap L^2(0,T; H^1(\Omega)) \cap L^\infty(\Omega \times (0,T))$ a weak solution to* (A.1.12). *Suppose that there are $\alpha \in (0,1)$ and $\lambda, \Lambda, \mu_1, \mu_2, \mu_3 > 0$ s.t. for all $(x,t,z,p) \in \Omega \times (0,T) \times \mathbb{R} \times \mathbb{R}^n$ with $|z| \leqslant M := \|u\|_{L^\infty(\Omega\times(0,T))}$ and all $(y,w) \in \Omega \times [-M, M]$ it holds that*

$$\begin{aligned} |a(x,t,z,0)| &\leqslant \mu_1, \\ |a(x,t,z,p) - a(y,t,w,p)| &\leqslant \mu_2(1+|p|)\left(|x-y|^\alpha + |z-w|^\alpha\right), \\ |b(x,t,z,p)| &\leqslant \mu_3(1+|p|^2) \end{aligned}$$

and that for all $(x,t,z,p) \in \partial\Omega \times (0,T) \times \mathbb{R} \times \mathbb{R}^n$ and all $(s,w) \in (0,T) \times \mathbb{R}$ with $|z|, |w| \leqslant M$ the estimate

$$|a(x,t,z,p) - a(x,s,w,p)| \leqslant \mu_2(1+|p|)|t-s|^{\frac{\alpha}{2}}$$

holds. Moreover, suppose that $a_{ij} := \frac{\partial a_i}{\partial p_j}$ satisfies

$$\begin{aligned} \sum_{i,j=1}^{n} a_{ij}(x,t,z,p)\xi_i\xi_j &\geqslant \lambda|\xi|^2, \\ |a_{ij}(x,t,z,p)| &\leqslant \Lambda \end{aligned}$$

for all $(x,t,z,p) \in \Omega \times (0,T) \times \mathbb{R} \times \mathbb{R}^n$ with $|z| \leqslant M$ and $\xi \in \mathbb{R}^n$ and that $u_0 \in C^{1+\alpha}(\overline{\Omega})$ satisfies the compatibility condition

$$a(x,0,u_0,\nabla u_0) \cdot \nu = 0 \text{ for } x \in \partial\Omega.$$

Then, there are $\delta(\lambda,\Lambda,\alpha) \in (0,1)$ and $K_8(\lambda,\Lambda,M,\mu_1,\mu_2,\mu_3,\|u_0\|_{C^{1+\alpha}(\overline{\Omega})},T) > 0$ s.t.

$$\|u\|_{C^{1+\delta,\frac{1+\delta}{2}}(\overline{\Omega}\times[0,T])} \leqslant K_8$$

Proof. This is a special case of Theorem 1.1 in [101] for $\psi = 0$. □

Proposition A.1.14. *Let $T > 0$ and consider a function $f(x,t,s) : \overline{\Omega} \times [0,T] \times \mathbb{R} \to \mathbb{R}$ that is continuous in x and t and continuously differentiable in s. Further, let $p > n+2$ and $u, w \in W_p^{2,1}(\Omega\times(0,T)) \cap C([0,T]; L^2(\Omega)) \cap L^\infty(\Omega\times(0,T))$ s.t. $u(\cdot,0) \leqslant w(\cdot,0)$ and $u(\cdot,0) \not\equiv w(\cdot,0)$ hold on $\overline{\Omega}$. If the estimates*

$$\partial_t u - \Delta u - f(x,t,u) \leqslant \partial_t w - \Delta w - f(x,t,w) \tag{A.1.14}$$

in $\Omega \times (0,T)$ and

$$\frac{\partial u}{\partial \nu} \leqslant \frac{\partial w}{\partial \nu} \tag{A.1.15}$$

on $\partial\Omega \times (0,T)$ are satisfied, then

$$u < w$$

holds in $\overline{\Omega} \times (0,T)$.

Proof. This is a special case of Proposition 52.7 in [127] with $b = 0$ and f independent from ξ. □

A.1.3 Monotone Operators

Definition A.1.15. *Let V be a reflexive Banach space and $\mathcal{A} : V \to V^*$. The operator $\mathcal{A}$ is called*

- *monotone if $\langle \mathcal{A}u - \mathcal{A}v, u - v\rangle_{V^*,V} \geqslant 0$ for all $u, v \in V$,*
- *maximal monotone if $\mathcal{A}$ is monotone and $\mathcal{A}u = f$ if and only if $\langle f - \mathcal{A}v, u - v\rangle_{V^*,V} \geqslant 0$ for all $u \in V$,*
- *hemicontinuous if $t \mapsto \langle \mathcal{A}(u + tv), w\rangle_{V^*,V}$ is continuous for all $u, v, w \in V$.*

Lemma A.1.16. *(Minty's lemma [133, Lemma 2.1 in Chapter II]) Let V a reflexive Banach space and consider an operator $\mathcal{A} : V \to V^*$. If $\mathcal{A}$ is monotone and hemicontinuous, then it is maximal monotone.*

Theorem A.1.17. *Let $T > 0$, $p \in (1, \infty)$, p^* s.t. $\frac{1}{p} + \frac{1}{p^*} = 1$, V a separable and reflexive Banach space and H a Hilbert space s.t. $V \hookrightarrow H$ is dense. Consider a family of operators $\mathcal{A}(t, \cdot) : V \to V^*$, $t \in [0, T]$ s.t.*

(i) *$\mathcal{A}(\cdot, v) : [0, T] \to V^*$ is measurable for all $v \in V$,*

(ii) *$\mathcal{A}(t, \cdot) : V \to V^*$ is monotone, hemicontinuous and bounded by*

$$\|\mathcal{A}(t, v)\|_{V^*} \leqslant K_9 \|v\|_V^{p-1}$$

for all $v \in V$ and a.e. $t \in [0, T]$,

(iii) *there are a seminorm $[\cdot]$ on V and $\lambda, \alpha > 0$ s.t.*

$$[v] + \|v\|_H \geqslant \alpha \|v\|_V,$$
$$\langle \mathcal{A}(t, v), v\rangle_{V^*,V} \geqslant \alpha [v]^p$$

for a.e. $t \in [0, T]$ and $v \in V$.

Then, for every $f \in L^{p^*}(0, T; V^*)$ and $u_0 \in H$ there is a unique solution $u \in L^p(0, T; V) \cap C([0, T]; H)$ with $u_t \in L^{p^*}(0, T; V^*)$ to the Cauchy Problem

$$\begin{cases} u_t(t) + \mathcal{A}(t, u(t)) = f(t) & \text{in } L^{p^*}(0, T; V^*), \\ u(0) = u_0 & \text{in } H \end{cases} \tag{A.1.16}$$

in the sense that for all $\varphi \in V$ and a.e. $t \in (0, T)$

$$\langle u_t, \varphi\rangle_{V^*,V} + \langle \mathcal{A}(t, u(t)), \varphi\rangle_{V^*,V} = \langle f, \varphi\rangle_{V^*,V}$$

and $u(0) = u_0$ in H.

Proof. This follows from Propositions 2.1 and 4.1 in Chapter III in [133]. □

A.1.4 Evolution equations

Lemma A.1.18. *([85, p.56 (iii)] and [148, Lemma 1.3 (ii) and (iii)]) Consider the Neumann heat semigroup* $(e^{t\Delta})_{t\geqslant 0}$ *in* Ω. *Let* $\lambda_1 > 0$ *the first nonzero eigenvalue of* $-\Delta$ *under Neumann boundary conditions in* Ω. *Then, there are constants* $K_{10}, K_{11}, K_{12} > 0$ *depending only on* Ω *s.t.*

(i) if $1 \leqslant q < p < \infty$ *then*
$$\|e^{t\Delta}u\|_{L^p(\Omega)} \leqslant K_{10}t^{-\frac{n}{2}\left(\frac{1}{q}-\frac{1}{p}\right)}\|u\|_{L^q(\Omega)}$$
for all $u \in L^q(\Omega)$ *and* $t \in (0,1)$,

(ii) if $1 \leqslant q \leqslant p \leqslant \infty$ *then*
$$\|\nabla e^{t\Delta}u\|_{L^p(\Omega)} \leqslant K_{11}\left(1 + t^{-\frac{1}{2}-\frac{n}{2}\left(\frac{1}{q}-\frac{1}{p}\right)}\right)e^{-\lambda_1 t}\|u\|_{L^q(\Omega)}$$
for all $u \in L^q(\Omega)$ *and* $t > 0$,

(iii) if $2 \leqslant p < \infty$ *then*
$$\|\nabla e^{t\Delta}u\|_{L^p(\Omega)} \leqslant K_{12}e^{-\lambda_1 t}\|\nabla u\|_{L^p(\Omega)}$$
for all $u \in W^1_p(\Omega)$ *and* $t > 0$.

A.1.5 Elliptic PDEs

Lemma A.1.19. *Let* $\lambda > 0$ *and* $a_{ij}, b_i \in C^2(\overline{\Omega})$. $i,j = 1,\dots,n$ *s.t.* $a_{ij} = a_{ji}$. *Assume that for some* $\alpha > 0$ *it holds that* $\sum_{i,j=1}^n a_{ij}\xi_i\xi_j \geqslant \alpha|\xi|^2$ *on* $\overline{\Omega}$ *for all* $\xi \in \mathbb{R}^n$ *and* $\sum_{i=1}^n b_i\nu_i > 0$ *on* $\partial\Omega$. *Then, for all* $f \in W^1_\infty(\Omega)$ *the elliptic problem*
$$\begin{cases} -\sum_{i,j=1}^n (a_{ij}u_{x_j})_{x_i} + \lambda u = f & \text{in } \Omega, \\ \sum_{i=1}^n b_i u_{x_i} = 0 & \text{on } \partial\Omega \end{cases} \tag{A.1.17}$$
has a unique solution $u \in C^2(\overline{\Omega})$. *Moreover, there are* λ_0 *and a constant* $K_{13} > 0$ *s.t. for all* $\lambda > \lambda_0$ *the estimate*
$$\|u\|_{H^2(\Omega)} \leqslant K_{13}\|f\|_{L^2(\Omega)} \tag{A.1.18}$$
holds

Proof. We conclude from Theorems 2.4.2.7 and 2.5.1.1 in [72] that (A.1.17) has a unique solution $u \in \bigcap_{p>1} W^3_p(\Omega) \subset C^2(\overline{\Omega})$. The estimate (A.1.18) follows from Theorem 2.3.3.6 in [72]. □

A.1.6 ODEs

Lemma A.1.20. *Let* $T > 0$. *If* $f \in C([0,T];\mathbb{R}^+_0) \cap C^1((0,T);\mathbb{R}^+_0)$ *satisfies the inequality*
$$f'(t) + K_{14}f(t) \leqslant K_{14}K_{15},$$
on $(0,T)$ *for constants* $K_{14}, K_{15} > 0$, *then for* $t \in (0,T)$ *it holds that*
$$f(t) \leqslant K_{15} + f(0).$$

Proof. Let $t \in (0, T)$. We differentiate

$$\left(f(t)e^{K_{14}t}\right)' = (f'(t) + K_{14}f(t))e^{K_{14}t} \leqslant K_{14}K_{15}e^{K_{14}t}.$$

Integrating over $[0, t]$ we obtain

$$f(t)e^{K_{14}t} \leqslant K_{14}K_{15}\int_0^t e^{K_{14}s}\,\mathrm{d}s + f(0) = K_{15}\left(e^{K_{14}t} - 1\right) + f(0).$$

Consequently,

$$f(t) \leqslant K_{15}\left(1 - e^{-K_{14}t}\right) + f(0)e^{-K_{14}t} \leqslant K_{15} + f(0).$$

□

A.2 Fixed-point theorems

Theorem A.2.1. *(Banachs's fixed-point theorem, [58, Section 9.2.1, Theorem 1]) Let X a Banach space and consider a contraction $T : X \to X$. Then, T has a unique fixed-point.*

Theorem A.2.2. *(Schauder's fixed-point theorem, [154, Section 2.6, Theorem 2.A]) Let X a Banach space and $M \subset X$ nonempty, closed, bounded and convex. Then, a compact operator $T : M \to M$ has a fixed-point.*

Theorem A.2.3. *(Schaefer's fixed-point theorem, [58, Section 9.2.2, Theorem 4]) Let X a Banach space and consider a compact operator $T : X \to X$. If the set*

$$\{u \in X : u = \lambda Tu \text{ for some } \lambda \in [0, 1]\}$$

is bounded, then T has a fixed-point.

A.3 Results from functional analysis

In this section we summarize some results from functional analysis.

Lemma A.3.1. *([20, Corollary 3.30]) Let X a separable Banach space. Then, every bounded sequence in its dual space X^* has a weakly-*-convergent subsequence.*

Lemma A.3.2. *(Compensated compactness, [20, Propositions 3.5 (iv) and 3.13 (iv)]) Let X a Banach space, $x_k \in X$ and $f_k \in X^*$ for $k \in \mathbb{N}$. If $x_k \rightharpoonup x$ in X and $f_k \to f$ in X^* or $x_k \to x$ in X and $f_k \overset{*}{\rightharpoonup} f$ in X^* for $k \to \infty$, then*

$$\langle f_k, x_k \rangle_{X^*,X} \underset{k\to\infty}{\to} \langle f, x \rangle_{X^*,X}.$$

Lemma A.3.3. *(A result from [59, p. 6]) Let $p \in (1, \infty)$ and consider a bounded sequence $(f_k)_{k\in\mathbb{N}} \subset L^p(\Omega)$. If*

$$\int_E f_k\, dx \underset{k\to\infty}{\to} \int_E f\, dx$$

for each bounded, measurable set $E \subset \Omega$, then

$$f_k \underset{k\to\infty}{\rightharpoonup} f \text{ in } L^p(\Omega).$$

Lemma A.3.4. *([102, Lemma 1.3]) Let $p \in (1,\infty)$ and $f_k, f \in L^p(\Omega)$, $k \in \mathbb{N}$. If there is a constant $K_{16} > 0$ s.t. $\|f_k\|_{L^p(\Omega)} \leqslant K_{16}$ and $f_k \to f$ for $k \to \infty$ a.e. in Ω, then*

$$f_k \underset{k\to\infty}{\rightharpoonup} f \text{ in } L^p(\Omega).$$

Lemma A.3.5. *([141, Lemma 1.4 in Chapter III]) Let X, Y Banach spaces s.t. $X \hookrightarrow Y$. If $f \in L^\infty(0,T;X) \cap C_w([0,T];Y)$, then $f \in C_w([0,T];X)$.*

Theorem A.3.6. *(**De la Vallée-Poussin theorem**, [19, Theorem 4.5.9]) Let $O \subset \mathbb{R}^n$ open and bounded and $\{f_k\}_{k\in\mathbb{N}} \subset L^1(O)$. Then, the following are equivalent:*

(i) $\{f_k\}_k$ is uniformly integrable,

(ii) there is an increasing function $G : [0,\infty) \to [0,\infty)$ satisfying $\lim_{t\to\infty} \frac{G(t)}{t} = \infty$ and

$$\sup_{k\in\mathbb{N}} \int_O G(|f_k|)\, dx < \infty.$$

Lemma A.3.7. *(**Vitali's lemma**, [37, Theorem 21]) Let $O \subset \mathbb{R}^n$ open and bounded and consider functions $f_k \in L^1(O)$, $k \in \mathbb{N}$, s.t. $f_k \to f$ for $k \to \infty$ a.e. in O. Then, the following are equivalent:*

(i) $f \in L^1(O)$ and $f_k \to f$ in $L^1(O)$ for $k \to \infty$,

(ii) $\{f_k\}_k$ is uniformly integrable.

Lemma A.3.8. *([133, Chapter III Proposition 1.2]) Let $T > 0$, $p, q \in (0,1)$ s.t. $\frac{1}{p} + \frac{1}{q} = 1$, V a Banach space and H a Hilbert spaces s.t. $V \hookrightarrow H \hookrightarrow V^*$ are dense. If $f \in L^p(0,T;V)$ and $\partial_t f \in L^q(0,T;V^*)$, then $f \in C([0,T];H)$ with*

$$\|f\|_{C([0,T];H)} \leqslant K_{17} \left(\|f\|_{L^p(0,T;V)} + \|\partial_t f\|_{L^q(0,T;V^*)} \right)$$

and

$$\frac{d}{dt}\|f\|_H^2 = 2\langle \partial_t f, f\rangle_{V^*,V}.$$

Lemma A.3.9. *(**Lions-Aubin lemma**, [134, Corollary 4]) Let X, B, Y Banach spaces s.t. $X \hookrightarrow\hookrightarrow B \hookrightarrow Y$ and $p \in [1,\infty)$, $r \in (1,\infty)$.*

(i) If $\{f_k\}_{k\in\mathbb{N}}$ is bounded in $L^p(0,T;X)$ and $\{\partial_t f_k\}_{k\in\mathbb{N}}$ is bounded in $L^1(0,T;Y)$, then $\{f_k\}_{k\in\mathbb{N}}$ is relatively compact in $L^p(0,T;B)$.

(ii) If $\{f_k\}_{k\in\mathbb{N}}$ is bounded in $L^\infty(0,T;X)$ and $\{\partial_t f_k\}_{k\in\mathbb{N}}$ is bounded in $L^r(0,T;Y)$, then $\{f_k\}_{k\in\mathbb{N}}$ is relatively compact in $C([0,T];B)$.

Lemma A.3.10. *(Partition of unity, [2, Theorem 3.15]) Let $K \subset \Omega$ compact and consider an open covering $\{O_k\}_{k=1,\ldots,N}$ of K. Then, there is a partition of unity $\{\psi_k\}_{k=1,\ldots,N}$ s.t. $0 \leqslant \psi_k \leqslant 1$, $\psi_k \in C_c^\infty(O_k)$ for $k = 1,\ldots,N$ and $\sum_{k=1}^N \psi_k = 1$ on K.*

Theorem A.3.11. *([88, Chapter 6, Theorems 6.27]) Let $S \subset \mathbb{R}^n$ open and bounded, $x_0 \in \Omega$ and $f : S \times \Omega \to \mathbb{R}$ a map s.t.*

- *for any $x \in \Omega$ the map $y \mapsto f(y,x)$ is in $L^1(S)$,*

- *for a.e.* $y \in S$, *the map* $x \mapsto f(y,x)$ *is continuous at* x_0,
- *there is* $h \in L^1(S)$, $h \geqslant 0$ *s.t.* $|f(\cdot,x)| \leqslant h$ *a.e. in* S *for all* $x \in \Omega$.

Then, the map $F : \Omega \to \mathbb{R}$, $x \mapsto \int_S f(y,x)\,dy$ *is continuous in* x_0.

Theorem A.3.12. *([88, Chapter 6, Theorems 6.28]) Let* $S \subset \mathbb{R}^n$ *open and bounded,* $I \subset \mathbb{R}$ *a nontrivial open interval and* $f : S \times I \to \mathbb{R}$ *a map with the following properties:*

- *for any* $x \in I$ *the map* $y \mapsto f(y,x)$ *is in* $L^1(I)$,
- *for a.e.* $y \in S$, *the map* $x \mapsto f(y,x)$ *is differentiable with derivative* f',
- *there is* $h \in L^1(S)$, $h \geqslant 0$ *s.t.* $|f'(\cdot,x)| \leqslant h$ *a.e. in* S *for all* $x \in \Omega$.

Then, for any $x \in I$ *it holds that* $f'(\cdot,x) \in L^1(S)$ *and* $F(x) := \int_S f(y,x)\,dy$ *is differentiable with derivative* $F'(x) = \int_S f'(y,x)\,dy$.

A.4 Results used in part II

Lemma A.4.1. *Let* $u \in C^1(\overline{\Omega})$ *and consider* $\alpha, \beta \geqslant 1$ *satisfying*

$$\alpha < \begin{cases} 1+\beta, & n = 1,2, \\ 1+\frac{2\beta}{n}, & n > 2. \end{cases} \tag{A.4.1}$$

Moreover, let $q > \max\{1, \beta+\alpha-1\}$,

$$\max\left\{\frac{n(\alpha-1)}{q}, \frac{2(\alpha-1)}{q}, 1\right\} < r \leqslant \frac{2(q+\alpha-1)}{q}$$

and

$$s \begin{cases} = \infty, & n = 1, \\ \in \left(\frac{2qr}{qr-2(\alpha-1)}, \infty\right), & n = 2, \\ = \frac{2n}{n-2}, & n > 2. \end{cases} \tag{A.4.2}$$

Then, for any $K_{18} > 0$ *it holds that*

$$\int_\Omega u^{q+\alpha-1}\,dx \leqslant \frac{2(q-1)}{q^2 K_{18}} \int_\Omega |\nabla u^{\frac{q}{2}}|^2\,dx + K_{19}(K_{18},q,r)\|u^{\frac{q}{2}}\|_{L^r(\Omega)}^{2r\frac{\frac{2(q+\alpha-1)}{s}-q}{qr(\frac{2}{s}-1)+2(\alpha-1)}} + K_{20}(r)^{\frac{qr-2(q+\alpha-1)}{\frac{qr}{s}-q}}, \tag{A.4.3}$$

where

$$\begin{aligned} K_{19}(K_{18},q,r) &:= 2\left(\frac{{K_{21}}^2 q^2 K_{18}}{q-1}\right)^{\frac{qr-2(q+\alpha-1)}{qr(\frac{2}{s}-1)+2(\alpha-1)}} + K_{20}(r)^{\frac{qr-2(q+\alpha-1)}{\frac{qr}{s}-q}}, \\ K_{20}(r) &:= 4K_S(s)|\Omega|^{\frac{r-2}{2r}}, \\ K_{21} &:= 2K_S(s)\,(1+2K_P)\,. \end{aligned}$$

Here, $K_S(s)$ *denotes the Sobolev embedding constant from* $H^1(\Omega)$ *into* $L^s(\Omega)$ *from Lemma 2.2.8 and* $K_P > 0$ *denotes the constant from the Poincaré inequality.*

Moreover, for any $K_{18}, K_{22} > 0$ *(after setting* $r = \frac{q+\alpha-1+\beta}{q}$*) the estimate*

$$\int_\Omega u^{q+\alpha-1}\,dx \leqslant \frac{2(q-1)}{q^2 K_{18}} \int_\Omega |\nabla u^{\frac{q}{2}}|^2\,dx + \frac{1}{K_{22}} \int_\Omega u^\beta\,dx \int_\Omega u^{q+\alpha-1}\,dx + K_{23}(K_{18}, K_{22}, q) \tag{A.4.4}$$

holds, where

$$K_{23}(K_{18}, K_{22}, q) := \left(2\left(\frac{K_{21}^2 q^2 K_{18}}{q-1}\right)^{\frac{q+\alpha-1-\beta}{q-\alpha+1+\beta-2\frac{q+\alpha-1+\beta}{s}}} + K_{24}(q)^{\frac{q+\alpha-\beta-1}{q-\frac{q+\alpha-1+\beta}{s}}}\right)^{\frac{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}} \cdot K_{22}^{\frac{q-\frac{2(q+\alpha-1)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}} + K_{24}(q)^{\frac{q+\alpha-\beta-1}{q-\frac{q+\alpha-1+\beta}{s}}},$$

and

$$K_{24}(q) := 4K_S(s)|\Omega|^{\frac{1}{2}-\frac{q}{q+\alpha-1+\beta}}.$$

Proof. Let

$$\lambda = \frac{\frac{q}{2(q+\alpha-1)} - \frac{1}{r}}{\frac{1}{s} - \frac{1}{r}}.$$

Then, $\lambda \in [0,1)$ and $\frac{\lambda(q+\alpha-1)}{q} \in [0,1)$ hold due to our choice of parameters. We state inequality (2.11) from the proof of Theorem 1.1 in [99] (with $B(x,\delta)$ replaced by Ω)

$$\int_\Omega u^{q+\alpha-1}\,\mathrm{d}x \leqslant 2\left(K_{21}\|\nabla u^{\frac{q}{2}}\|_{(L^2(\Omega))^n}\right)^{\frac{2\lambda(q+\alpha-1)}{q}} \|u^{\frac{q}{2}}\|_{L^r(\Omega)}^{\frac{2(1-\lambda)(q+\alpha-1)}{q}} + \left(K_{20}(r)^\lambda \|u^{\frac{q}{2}}\|_{L^r(\Omega)}\right)^{\frac{2(q+\alpha-1)}{q}},$$

where

$$K_{20}(r) := 4K_S(s)|\Omega|^{\frac{r-2}{2r}},\ K_{21} := 2K_S(s)\left(1+2K_P\right).$$

We proceed as in the proof of (2.14) in [99]. Applying Young's inequality twice and regrouping the terms we conclude that for $K_{18} > 0$ it holds that

$$\begin{aligned}\int_\Omega u^{q+\alpha-1}\,\mathrm{d}x \leqslant& \frac{2(q-1)}{q^2 K_{18}}\|\nabla u^{\frac{q}{2}}\|^2_{(L^2(\Omega))^n} \\ &+ 2\left(K_{21}^{\frac{2\lambda(q+\alpha-1)}{q}} \|u^{\frac{q}{2}}\|_{L^r(\Omega)}^{\frac{2(1-\lambda)(q+\alpha-1)}{q}} \left(\frac{q^2 K_{18}}{q-1}\right)^{\frac{\lambda(q+\alpha-1)}{q}}\right)^{\frac{q}{q-\lambda(q+\alpha-1)}} \\ &+ K_{20}(r)^{\frac{2\lambda(q+\alpha-1)}{q}}\left(\|u^{\frac{q}{2}}\|_{L^r(\Omega)}^{\frac{2(1-\lambda)(q+\alpha-1)}{q-\lambda(q+\alpha-1)}} + 1\right) \\ \leqslant& \frac{2(q-1)}{q^2 K_{18}}\|\nabla u^{\frac{q}{2}}\|^2_{(L^2(\Omega))^n} + K_{19}(K_{18}, q, r)\|u^{\frac{q}{2}}\|_{L^r(\Omega)}^{\frac{2(1-\lambda)(q+\alpha-1)}{q-\lambda(q+\alpha-1)}} + K_{20}(r)^{\frac{2\lambda(q+\alpha-1)}{q}},\end{aligned} \tag{A.4.5}$$

where

$$K_{19}(K_{18}, q, r) := 2\left(\frac{K_{21}^2 q^2 K_{18}}{q-1}\right)^{\frac{\lambda(q+\alpha-1)}{q-\lambda(q+\alpha-1)}} + K_{20}(r)^{\frac{2\lambda(q+\alpha-1)}{q}}.$$

Inserting the definition of λ we obtain inequality (A.4.3). Moreover, we state inequality (2.17) from the proof of Theorem 1.1 in [99], i.e.,

$$\|u^{\frac{q}{2}}\|_{L^{\frac{q+\alpha-1+\beta}{q}}(\Omega)}^{\frac{2(1-\lambda)(q+\alpha-1)}{q-\lambda(q+\alpha-1)}} \leqslant \left(\|u^{\frac{q}{2}}\|_{L^{\frac{2\beta}{q}}(\Omega)}^{\frac{2\beta}{q}} \|u^{\frac{q}{2}}\|_{L^{\frac{2(q+\alpha-1)}{q}}(\Omega)}^{\frac{2(q+\alpha-1)}{q}}\right)^{\frac{q-\frac{2(q+\alpha-1)}{s}}{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}}}, \tag{A.4.6}$$

where due to our choice of α, β and s in (A.4.1) and (A.4.2) it holds that

$$\frac{q-\frac{2(q+\alpha-1)}{s}}{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}} < 1.$$

Now, we estimate the term from (A.4.5) for $r = \frac{q+\alpha-1+\beta}{q}$ using (A.4.6) as in (2.19) from [99]. Young's inequality leads for any $K_{22} > 0$ to the estimate

$$\begin{aligned} &K_{19}(K_{18}, q, r)\|u^{\frac{q}{2}}\|_{L^{\frac{q+\alpha-1+\beta}{q}}(\Omega)}^{\frac{2(1-\lambda)(q+\alpha-1)}{q-\lambda(q+\alpha-1)}} \\ \leqslant &\frac{1}{K_{22}} \int_\Omega u^\beta \,\mathrm{d}x \int_\Omega u^{q+\alpha-1} \,\mathrm{d}x + K_{19}(K_{18}, q, r)^{\frac{q-\alpha+1+\beta-\frac{2(q+\alpha-1+\beta)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}} K_{22}^{\frac{q-\frac{2(q+\alpha-1)}{s}}{\beta+1-\alpha-\frac{2\beta}{s}}}. \end{aligned}$$

Inserting this estimate and our choice of r into (A.4.5) we arrive at (A.4.4). □

Lemma A.4.2. *Consider s as in Lemma A.4.1. Set $q_k := 2^k + h$ for $h := \frac{2(s-1)(\alpha-1)}{s-2}$, $k \in \mathbb{N}_0$. Then, for all k it holds that*

$$\frac{\frac{2(q_k+\alpha-1)}{s} - q_k}{2q_{k-1}\left(\frac{2}{s}-1\right) + 2(\alpha-1)} = 1, \tag{A.4.7}$$

$$\frac{2q_{k-1} - 2(q_k+\alpha-1)}{2q_{k-1}\left(\frac{2}{s}-1\right) + 2(\alpha-1)} = \frac{s}{s-2} \tag{A.4.8}$$

and

$$\frac{2q_{k-1} - 2(q_k+\alpha-1)}{\frac{2q_{k-1}}{s} - q_k} \leqslant \alpha + 1. \tag{A.4.9}$$

Proof. See part 2 of the proof of Theorem 1.1 in [99], where they show (in their notation) that $\frac{Q_k}{r_k} = 2$ in (2.28). Comparing this to the term in (A.4.7) we obtain the desired equality. Moreover, they show (in their notation) in (2.32) that $\frac{\lambda_k(q_k+\alpha-1)}{q_k-\lambda_k(q_k+\alpha-1)} = \frac{s}{s-2}$ where the left-hand side equals $\frac{2q_{k-1}-2(q_k+\alpha-1)}{2q_{k-1}\left(\frac{2}{s}-1\right)+2(\alpha-1)}$. This gives us (A.4.8). We obtain (A.4.9) from (2.33) in [99], where $\frac{2q_{k-1}-2(q_k+\alpha-1)}{\frac{2q_{k-1}}{s}-q_k} = \frac{2\lambda_k(q_k+\alpha-1)}{q_k} \leqslant \alpha+1$ was shown □

Lemma A.4.3. *Let $y_k \in C([0,\infty)) \cap C^1(0,\infty)$ nonnegative for $k \in \mathbb{N}_0$ and satisfying*

$$y_k'(t) + c_k y_k(t) \leqslant c_k A_k \max\left\{1, \sup_{t\geqslant 0} y_{k-1}^2(t)\right\},$$

where $A_k = \bar{a}2^{Dk} \geqslant 1$ and $c_k, \bar{a}, D > 0$. We assume that $y_k(0) \leqslant bK^{2^k}$ holds for some constants $b \geqslant 1$ and $K > 0$. Then, for all $m \geqslant 1$ it holds that

$$y_k(t) \leqslant (2\bar{a})^{2^{k-m+1}-1} 2^{D\left(2(2^{k-m}-1)+m2^{k-m+1}-k\right)} \max\left\{\sup_{t\geqslant 0} y_{m-1}^{2^{k-m+1}}(t), b^{2^{k-m}} K^{2^k}, 1\right\}.$$

Proof. See Lemma 2.1 in [99] and adapt the proof for $y_k(0) \leqslant bK^{2^k}$ instead of $y_k(0) \leqslant K^{2^k}$. □

Lemma A.4.4. *Let $\Omega \subset \mathbb{R}^n$ a bounded convex domain. Let $p = \infty$ if $n = 1$, $p \in (2,\infty)$ if $n = 2$ and $2 < p \leqslant \frac{2n}{n-2}$ if $n > 2$. Then, it holds that*

$$\|u\|_{L^p(\Omega)} \leqslant K_S(p)\|u\|_{H^1(\Omega)},$$

where

$$K_S(p) = \begin{cases} \max\left\{1, \frac{\operatorname{diam}(\Omega)|V|^{\frac{1}{2}}}{|\Omega|}\right\} & n = 1, \\ \sqrt{2}\max\left\{|\Omega|^{\frac{1}{p}-\frac{1}{2}}, \frac{\operatorname{diam}(\Omega)^{1+\frac{p+2}{2p}n}\pi^{\frac{p+2}{4p}n}}{n|\Omega|}\frac{\Gamma\left(\frac{p-2}{4p}n\right)}{\Gamma\left(\frac{p+2}{4p}n\right)}\right\}\sqrt{\frac{\Gamma\left(\frac{n}{p}\right)}{\Gamma\left(\frac{p-1}{p}n\right)}}\left(\frac{\Gamma(n)}{\Gamma\left(\frac{n}{2}\right)}\right)^{\frac{p-2}{2p}} & n \geqslant 2. \end{cases}$$

Here, $V := \bigcup_{x\in\Omega}\Omega_x$, where $\Omega_x := \{x - y : y \in \Omega\}$ for $x \in \Omega$, and Γ denotes the Gamma function given by $\Gamma(x) = \int_0^\infty t^{x-1}e^{-t}\,dt$ for $x > 0$.

Proof. See Theorems 2.1, 3.2 and 3.4 in [108]. □

Lemma A.4.5. *Let $\Omega \subset \mathbb{R}^n$ a bounded convex domain. Consider $J \in L^1(B_{\operatorname{diam}(\Omega)}(0))$ with $\|J\|_{L^1(B_{\operatorname{diam}(\Omega)}(0))} = 1$ and $u \in C^1(\overline{\Omega})$. Then,*

$$\int_\Omega\int_\Omega J(x-y)(u(x)-u(y))^2\,dy\,dx \leqslant |\operatorname{diam}(\Omega)|^2\int_\Omega |\nabla u(x)|^2\,dx.$$

Proof. This follows due to the convexity of Ω as in the proof of (3.6) in the proof of Proposition 3.1 in [99] with $B(x,\delta)$ replaced by Ω. □

Lemma A.4.6. *Let $t_0 \geqslant 0$, $U > 0$ and $u : \Omega \times (t_0,\infty) \to [0,U]$, $\varphi : [0,U] \to [0,\infty)$ uniformly continuous satisfying*

$$\int_{t_0}^\infty\int_\Omega (\varphi(u(x,t)))^2\,dx\,dt < \infty.$$

Then, also

$$\|\varphi(u(t))\|_{L^\infty(\Omega)} \underset{t\to\infty}{\to} 0.$$

Proof. See proof of Lemma 3.10 in [139] for φ as above. □

A.5 Proofs of some lemmas from *Chapter 2*

Proof of Lemma 2.2.3. (i) See (4.7) in [70].

(ii) For $r \in (0,1)$ and $v, w \in \mathbb{R}$ the estimate $|v + w|^r \leqslant |v|^r + |w|^r$ holds. Hence, we estimate for $x, y \in \overline{\Omega}$ with $v := u(x) - u(y)$ and $w := u(y)$ or $v := u(y) - u(x)$ and $w := u(x)$ that

$$|u(x)^r - u(y)^r| \leqslant |u(x) - u(y)|^r \leqslant K_{25}|x - y|^{\vartheta r}.$$

(iii) We estimate for $x, y \in \overline{\Omega}$ with the mean value theorem that

$$|u^r(x) - u^r(y)| \leqslant r\|u\|^{r-1}_{L^\infty(\Omega)}|u(x) - u(y)| \leqslant K_{26}|x - y|^\vartheta.$$

(iv) The function u is continuous. Hence, there is $m := \min_{x\in\overline{\Omega}} |u(x)| > 0$ and we can estimate for $x, y \in \overline{\Omega}$ that

$$\left|\frac{1}{u(x)} - \frac{1}{u(y)}\right| = \frac{|u(y)-u(x)|}{|u(y)u(x)|} \leqslant \frac{|u(y)-u(x)|}{m^2} \leqslant K_{27}|x-y|^{\vartheta}.$$

□

Proof of Lemma 2.2.9. (i) Let $u \in C^{1+\vartheta,\frac{1+\vartheta}{2}}(\overline{\Omega}\times[0,T])$. We estimate the norm of $u - u(\cdot,0)$ term by term. Let $t,t' \in [0,T]$, $t \neq t'$ and $x \in \overline{\Omega}$. First, we estimate

$$\begin{aligned}\frac{|u(x,t)-u(x,0)-(u(x,t')-u(x,0))|}{|t-t'|^{\frac{\vartheta}{2}}} &= \frac{|u(x,t)-u(x,t')|}{|t-t'|^{\frac{\vartheta}{2}}}\\ &= |t-t'|^{\frac{1}{2}}\frac{|u(x,t)-u(x,t')|}{|t-t'|^{\frac{1+\vartheta}{2}}} \leqslant T^{\frac{1}{2}}\langle u\rangle^{\frac{1+\vartheta}{2}}_{t,\overline{\Omega}\times[0,T]}.\end{aligned} \tag{A.5.1}$$

Moreover, we use the continuous embedding of $W^1_\infty(\Omega)$ into $C^{\vartheta}(\overline{\Omega})$ with constant $K_I(\vartheta)$ from *Lemma 2.2.8(ii)* to estimate that

$$\begin{aligned}&\|u-u(\cdot,0)\|_{C(\overline{\Omega}\times[0,T])} + \langle u-u(\cdot,0)\rangle^{\vartheta}_{x,\overline{\Omega}\times[0,T]}\\ \leqslant& K_I(\vartheta)\left(\|u-u(\cdot,0)\|_{C(\overline{\Omega}\times[0,T])} + \sum_{i=1}^n \|u_{x_i}-u_{x_i}(\cdot,0)\|_{C(\overline{\Omega}\times[0,T])}\right)\\ \leqslant& K_I(\vartheta)\left(T^{\frac{1+\vartheta}{2}}\langle u\rangle^{\frac{1+\vartheta}{2}}_{t,\overline{\Omega}\times[0,T]} + T^{\frac{\vartheta}{2}}\sum_{i=1}^n\langle u_{x_i}\rangle^{\frac{\vartheta}{2}}_{t,\overline{\Omega}\times[0,T]}\right)\end{aligned} \tag{A.5.2}$$

Putting this together with the supremum of (A.5.1) we obtain (2.2.2) due to $T < 1$.

(ii) Let $u \in C^{2+\vartheta,1+\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])$, $t,t' \in [0,T]$, $t \neq t'$ and $x \in \overline{\Omega}$. First, we conclude from the mean value theorem that

$$\|u(x,t)-u(x,0)\|_{C(\overline{\Omega}\times[0,T])} + \langle u-u(x,0)\rangle^{\frac{1+\vartheta}{2}}_{t,\overline{\Omega}\times[0,T]} \leqslant (T+T^{\frac{1-\vartheta}{2}})\|u_t\|_{C(\overline{\Omega}\times[0,T])}.$$

Moreover, *(i)* implies for $i = 1,\dots,n$ that

$$\|u_{x_i}-u_{x_i}(\cdot,0)\|_{C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])} \leqslant \max\{1,K_I(\vartheta)\}T^{\frac{\vartheta}{2}}\|u_{x_i}\|_{C^{1+\vartheta,\frac{1+\vartheta}{2}}(\overline{\Omega}\times[0,T])}.$$

Together with the above estimates we obtain (2.2.3).

(iii) We estimate as before with the help of the mean value theoren and the Sobolev embedding that

$$\begin{aligned}&\langle u-u(\cdot,0)\rangle^{\frac{\vartheta}{2}}_{t,\overline{\Omega}\times[0,T]} \leqslant T^{\frac{2-\vartheta}{2}}\|u_t\|_{C(\overline{\Omega}\times[0,T])},\\ &\|u-u(\cdot,0)\|_{C(\overline{\Omega}\times[0,T])} + \langle u-u(\cdot,0)\rangle^{\vartheta}_{x,\overline{\Omega}\times[0,T]}\\ \leqslant& K_I(\vartheta)\left(T\|u_t\|_{C(\overline{\Omega}\times[0,T])} + T^{\frac{1+\kappa}{2}}\sum_{i=1}^n\langle u_{x_i}\rangle^{\frac{1+\kappa}{2}}_{t,\overline{\Omega}\times[0,T]}\right).\end{aligned}$$

□

Proof of Lemma 2.3.2. (i) Let $u, h \in L^\infty(\Omega \times (0,T))$, $x \in \overline{\Omega}$ and $t \in [0,T]$. Using our assumptions on J we can estimate

$$\begin{aligned}\left|J(x,h) * u^\beta(t)\right| &\leqslant \left|\int_\Omega J(x-y, h(y,t))u^\beta(y,t)\,\mathrm{d}y\right| \\ &\leqslant \|u\|^\beta_{L^\infty(\Omega\times(0,T))}\left|\int_\Omega L(x-y)|h(y,t)| + |J(x-y,0)|\,\mathrm{d}y\right| \\ &\leqslant \|u\|^\beta_{L^\infty(\Omega\times(0,T))}\left(\|L\|_{L^1(S)}\|h\|_{L^\infty(\Omega\times(0,T))} + \|J(x,0)\|_{L^1(S)}\right).\end{aligned}$$

Taking the supremum on the left-hand side, we conclude that $J(\cdot,h) * u^\beta \in L^\infty(\Omega\times(0,T))$.

(ii) Let $u, h \in C^{\vartheta,\frac{\vartheta}{2}}(\overline{\Omega}\times[0,T])$, $u \geqslant 0$, $x \in \overline{\Omega}$ and $t_1, t_2 \in [0,T], t_1 \neq t_2$. Then, we can estimate using our assumptions on J, the Hölder continuity of u and h and the mean value theorem that

$$\begin{aligned}&|J(x,h) * u^\beta(t_1) - J(x,h) * u^\beta(t_2)| \\ =&\left|\int_\Omega J(x-y,h(y,t_1))u^\beta(y,t_1) - J(x-y,h(y,t_2))u^\beta(y,t_2)\,\mathrm{d}y\right| \\ \leqslant&\left|\int_\Omega \big(J(x-y,h(y,t_1)) - J(x-y,h(y,t_2))u^\beta(y,t_1)\big)\,\mathrm{d}y\right| \\ &+\left|\int_\Omega J(x-y,h(y,t_2))\big(u^\beta(y,t_1) - u^\beta(y,t_2)\big)\,\mathrm{d}y\right| \\ \leqslant&\|u\|^\beta_{L^\infty(\Omega\times(0,T))}\int_\Omega L(x-y)|h(y,t_1)-h(y,t_2)|\,\mathrm{d}y \\ &+\beta\|u\|^{\beta-1}_{L^\infty(\Omega\times(0,T))}\int_\Omega (L(x-y)|h(y,t_2)| + |J(x-y,0)|)\,|u(y,t_1)-u(y,t_2)|\,\mathrm{d}y \\ \leqslant&K_{28}\left(\|u\|_{L^\infty},\|h\|_{L^\infty},\|L\|_{L^1},\|J(\cdot,0)\|_{L^1},\beta\right)T^{\frac{\vartheta}{2}}\left(\langle h\rangle^{\frac{\vartheta}{2}}_{t,\overline{\Omega}\times[0,T]} + \langle u\rangle^{\frac{\vartheta}{2}}_{t,\overline{\Omega}\times[0,T]}\right).\end{aligned} \quad \text{(A.5.3)}$$

Now, let $x_1, x_2 \in \overline{\Omega}, x_1 \neq x_2$ and $t \in [0,T]$. Then, we can estimate

$$\begin{aligned}&|J(x_1,h) * u^\beta(t) - J(x_2,h) * u^\beta(t)| \\ =&\left|\int_{\mathbb{R}^n} J(x_1-y,h(y,t))u^\beta(y,t)\chi_\Omega(y) - J(x_2-y,h(y,t))u^\beta(y,t)\chi_\Omega(y)\,\mathrm{d}y\right| \\ =&\left|\int_{\mathbb{R}^n} J(z,h(x_1-z,t))u^\beta(x_1-z,t)\chi_\Omega(x_1-z)\right. \\ &\qquad\left. - J(z,h(x_2-z,t))u^\beta(x_2-z,t)\chi_\Omega(x_2-z)\,\mathrm{d}z\right| \\ \leqslant&\left|\int_{\mathbb{R}^n}\big(J(z,h(x_1-z,t))u^\beta(x_1-z,t)\right. \\ &\qquad\left.-J(z,h(x_2-z,t))u^\beta(x_2-z,t)\big)\chi_\Omega(x_1-z)\chi_\Omega(x_2-z)\,\mathrm{d}z\right| \quad \text{(A.5.4)} \\ &+\int_{\mathbb{R}^n}\left|J(z,h(x_1-z,t))u^\beta(x_1-z,t)\chi_\Omega(x_1-z)(1-\chi_\Omega(x_2-z))\right|\,\mathrm{d}y \quad \text{(A.5.5)} \\ &+\int_{\mathbb{R}^n}\left|J(z,h(x_2-z,t))u^\beta(x_2-z,t)(1-\chi_\Omega(x_1-z))\chi_\Omega(x_2-z)\right|\,\mathrm{d}z. \quad \text{(A.5.6)}\end{aligned}$$

We can estimate (A.5.4) analogously to (A.5.3). To estimate (A.5.5) we define for $x_1, x_2 \in \overline{\Omega}$ the sets

$$S_{x_1x_2} := \left\{z \in \mathbb{R}^n : x_1 - z \in \overline{\Omega},\, x_2 - z \notin \overline{\Omega}\right\},$$

$$G_{x_1x_2} := \left\{ z \in \mathbb{R}^n : x_1 - z \in \overline{\Omega},\, \operatorname{dist}(x_1 - z, \partial\Omega) \leqslant |x_1 - x_2| \right\}.$$

Let $z \in S_{x_1x_2}$. Then, $a := x_1 - z \in \overline{\Omega}$ and $x_2 - z = x_2 - x_1 + a \notin \overline{\Omega}$. Assume $\operatorname{dist}(x_1 - z, \partial\Omega) > |x_1 - x_2|$. Consequently, $\overline{B_{|x_1-x_2|}(a)} \subset \overline{\Omega}$ and $a + x_2 - x_1 \in \overline{\Omega}$ which leads to a contradiction. Hence, $S_{x_1x_2} \subset G_{x_1x_2}$ and $|S_{x_1x_2}| \leqslant |G_{x_1x_2}| \leqslant K_{29}(\Omega)|x_1 - x_2|$ holds for sufficiently smooth $\partial\Omega$. Then, we can estimate

$$\begin{aligned}
|(\mathrm{A}.5.5)| &= \left| \int_{S_{x_1x_2}} J(z, h(x_1 - z, t)) u^\beta(x_1 - z, t) \,\mathrm{d}z \right| \\
&\leqslant \|u\|^\beta_{L^\infty(\Omega\times(0,T))} \int_{G_{x_1x_2}} L(z)|h(x_1 - z, t)| + |J(z, 0)| \,\mathrm{d}z \\
&\leqslant \|u\|^\beta_{L^\infty(\Omega\times(0,T))} \max\{1, \|h\|^\beta_{L^\infty(\Omega\times(0,T))}\} \left(\|L\|_{L^p(S)} + \|J(\cdot, 0)\|_{L^p(S)} \right) |G_{x_1x_2}|^{\frac{p-1}{p}} \\
&\leqslant K_{30}|x_1 - x_2|^{\frac{p-1}{p}}.
\end{aligned}$$

We can estimate (A.5.6) analogously. Putting this together with the estimates of the other terms, we conclude $J(\cdot, h) * u^\beta \in C^{\kappa, \frac{\kappa}{2}}(\overline{\Omega} \times [0, T])$ for $\kappa := \min\{\vartheta, \frac{p-1}{p}\}$.

□

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