TECHNISCHE UNIVERSITÄT DARMSTADT

Department of Mathematics

Master Thesis

Global Existence for a Tumor Invasion Model with Repellent Taxis and Therapy

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Introduction

In the treatment of cancer a major difficulty is caused by tumor invasion. It is considered to be the reason why even after a surgical removal of the visible tumor mass, gliomas recur to their original size in very short time. It is widely accepted that highly proliferating cells have lower mobility and very motile cells have a low proliferating rate. This so called go-or-grow dichotomy was first proposed by Giese et al. in [GLT+96]. As the proliferating cells are more sensitive against therapy than migrating ones (see for example [MHL12]) it is worthwhile from a therapeutical view to split the population of cancer cells. Moreover, it is known that cells can change their phenotype, i.e., proliferating cells become migrating ones and vice versa. Nevertheless, the mechanisms governing these changes are not fully understood yet. For possible explanations we refer to for example [HBS+12].

In this thesis we consider an extension, based on an idea of Christina Surulescu, of the model studied in [SSU16]. Namely, in the equation for the migrating cells we add a term which describes chemorepulsion. The aim of this thesis is to examine possible choices of the new term so that the methods presented in [SSU16] can be adapted.

This thesis is structured in the following way: In Chapter 1 we provide a detailed description of the model studied in this thesis, especially for the newly added term. In Chapter 2 we first introduce approximating problems for the original problem and show that those possess classical global-in-time solutions. Additionally, we prove an estimate for an entropy-type functional which will be the basis towards the existence of global weak solutions for the original problem. This global weak solution will then be constructed in Chapter 3 with help of the Aubin-Lions lemma together with the aforementioned entropy functional.

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1. The Model

In this section we derive the model that we want to consider in this thesis. The basis for our considerations is a simplification of the model presented in [SSU16]. We focus on the migrating (m) and proliferating cancer cells (q) as well as the tissue fibers (v) and neglect the integrins bound to ECM fibers and assume the contractivity function of cancer cells (κ) to be constant. Hence we obtain the following model:

$$\begin{cases} \partial_t m = & \nabla \cdot (D(m,q,v)\nabla m) - \nabla \cdot \left(\frac{v}{1+v} m \nabla v\right) \\ & +\lambda q - \gamma m - r_m(t)m, \\ \partial_t q = & \mu_q q(1-(m+q)-\eta_1 v) - \lambda q + \gamma m - r_q(t)q, \\ \partial_t v = & -\alpha m v - \beta q v + \mu_v v(1-v) - r_v(t)v. \end{cases} \tag{1.1}$$

Here, D is a diffusion coefficient and the second term in the first equation describes haptotaxis, i.e., cell movement along an adhesion gradient. The coefficient λ describes the rate with which proliferating cells become migrating ones and analogously γ the rate with which migrating cells stop moving and begin proliferating. Moreover, α and β describe how the tissue fibers degenerate due to interaction with the tumor cells. Additionally, μ_q and μ_v are proliferating constants while $r_m(t)$, $r_q(t)$, $r_v(t)$ model the influence of radiotherapy which affects all cells. Note that for the proliferation of both cancer cells and tissue fibers we use a logistic model. For more details on the derivation of the above model (without splitting of the cancer cells) we refer the interested reader to [MSS15].

We extend this model by introducing a term modeling chemorepulsion in the time development of the migrating cells. It is reasonable to consider migrating cells moving away from high concentrations of proliferating cancer cells. Similarly as in [CLMR06] and the references therein, this process can be modeled by adding $\nabla \cdot (g(q)m\nabla q)$ on the right hand side of the first equation in (1.1). Here, the function g describes how strong the repulsion is.

Hence, we consider

$$\begin{cases} \partial_t m = & \nabla \cdot (D(m,q,v)\nabla m) - \nabla \cdot \left(\frac{v}{1+v} m \nabla v\right) \\ & +\nabla \cdot (g(q) m \nabla q) + \lambda q - \gamma m - r_m(t) m, \\ \partial_t q = & \mu_q q(1-(m+q)-\eta_1 v) - \lambda q + \gamma m - r_q(t) q, \\ \partial_t v = & -\alpha m v - \beta q v + \mu_v v(1-v) - r_v(t) v, \end{cases} \tag{1.2}$$

with $x \in \Omega$ and $t > 0$ where $\Omega \subseteq \mathbb{R}^n$ is a bounded domain with smooth boundary, $n \in \{1,2,3\}$. Moreover, we impose no-flux boundary conditions:

$$D(m,q,v)\partial_\nu m - \frac{v}{1+v} m \partial_\nu v + g(q) m \partial_\nu q = 0, \quad x \in \partial\Omega, \quad t > 0, \tag{1.3}$$

where ν denotes the outer unit normal on $\partial\Omega$ and the initial conditions:

$$m(x,0) = m_0(x), \quad q(x,0) = q_0(x), \quad v(x,0) = v_0(x), \quad x \in \Omega, \tag{1.4}$$

where we assume that

$$m_0 \in \mathrm{C}^0(\overline{\Omega}), \quad q_0, v_0 \in \mathrm{W}^{1,2}(\Omega) \cap \mathrm{C}^0(\overline{\Omega}) \tag{1.5}$$

satisfy

$$m_0 \geq 0, \quad q_0 \geq 0, \quad v_0 \geq 0 \quad \text{in } \overline{\Omega}. \tag{1.6}$$

Furthermore, we assume that for any $A, L > 0$ there exist positive constants C_1, C_2 and C_3 such that

$$\begin{aligned} & D \in \mathrm{C}^3([0,\infty)^3) \cap \mathrm{W}^{2,\infty}([0,\infty) \times [0,A] \times [0,L]), g \in \mathrm{C}^2([0,\infty)), \\ & r_i \in \mathrm{C}^1([0,\infty)), \quad i \in \{m,q,v\}, \\ & 0 < C_2 \leq D(m,q,v) \leq C_1 \quad \text{for all } (m,q,v) \in [0,\infty) \times [0,A] \times [0,L], \\ & 0 \leq r_i(t) \leq C_3, \quad \text{for all } t \geq 0, i \in \{m,q,v\}, \; 0 \leq g(q) \quad \text{for all } q \in [0,A] \end{aligned} \tag{1.7}$$

hold. Moreover, the parameters λ, γ, μ_q, η_1, μ_v, α and β are assumed to be positive.

In this thesis we will examine for which choices of g the method proposed in [SSU16] can be adapted. We will first deal with the constant case and after that examine possible extensions.

We will prove the global existence for the following concept of weak solutions. Note that due to the intended compactness properties we formally rewrite $\nabla m = 2\sqrt{1+m} \cdot \nabla \sqrt{1+m}$ (as done in [SSU16] and [SSW14]).

Definition 1.1. Let $T \in (0, \infty)$. A weak solution to (1.2)-(1.4) consists of non-negative functions

$$m \in \mathrm{L}^1((0,T);\mathrm{L}^2(\Omega)) \text{ with } \sqrt{1+m} \in \mathrm{L}^2((0,T);\mathrm{W}^{1,2}(\Omega))$$
$$\sqrt{m}\nabla q, \sqrt{m}\nabla v \in \mathrm{L}^2(\Omega \times (0,T)),\ q, v \in \mathrm{L}^\infty(\Omega \times (0,T)) \cap \mathrm{L}^2((0,T);\mathrm{W}^{1,2}(\Omega))$$

which satisfy for all $\varphi \in \mathrm{C}_0^\infty\left(\overline{\Omega} \times [0,T)\right)$ (infinitely often differentiable with compact support in $\overline{\Omega} \times [0,T)$) the equations

$$\begin{aligned}
&-\int_0^T \int_\Omega m\partial_t\varphi - \int_\Omega m_0\varphi(\cdot,0) \\
&\quad = -2\int_0^T \int_\Omega D(m,q,v)\sqrt{1+m}\nabla\sqrt{(1+m)} \cdot \nabla\varphi \\
&\qquad + \int_0^T \int_\Omega \frac{v}{1+v} m\nabla v \cdot \nabla\varphi - \int_0^T \int_\Omega g(q) m\nabla q \cdot \nabla\varphi \\
&\qquad + \int_0^T \int_\Omega (\lambda q - \gamma m - r_m(t)m)\varphi, && (1.8) \\
&-\int_0^T \int_\Omega q\partial_t\varphi - \int_\Omega q_0\varphi(\cdot,0) \\
&\quad = \int_0^T \int_\Omega (\mu_q q(1-(m+q)-\eta_1 v) - \lambda q + \gamma m - r_q(t)q)\varphi, && (1.9) \\
&-\int_0^T \int_\Omega v\partial_t\varphi - \int_\Omega v_0\varphi(\cdot,0) \\
&\quad = \int_0^T \int_\Omega (-\alpha m v - \beta q v + \mu_v v(1-v) - r_v(t)v)\varphi. && (1.10)
\end{aligned}$$

A tuple (m, q, v) is a global weak solution to (1.2)-(1.4) if it is a weak solution in $\Omega \times (0,T)$ for all $T > 0$.

The main result of this thesis is the existence of a global weak solution.

Theorem 1.2. *Let $n \in \{1,2,3\}$ and $\Omega \subseteq \mathbb{R}^n$ be a bounded domain with smooth boundary and assume that* (1.5)-(1.7) *are satisfied. Moreover let $g \equiv c$ be either constant or of the form $\frac{c}{1+q}$ with $0 < c \leq \frac{1}{2}\left(\frac{4\gamma C_2(1-\frac{\delta}{2})}{\mu_q A^2}\right)$ where C_2 is the lower bound for D specified in* (1.7)*, $\delta \in (0,2)$ and A is the constant introduced in Lemma 2.3. Then there exists a global weak solution to* (1.2)-(1.4) *in the sense of Definition 1.1 which fulfills*

$$m \in \mathrm{L}^\infty((0,\infty);\mathrm{L}^1(\Omega))$$
$$q, v \in \mathrm{L}^\infty(\Omega \times (0,\infty)).$$

Note that the condition $n \leq 3$ is used to obtain compactness properties.

As a convention for constants we denote with C (possibly with arguments showing on what the constant depends) positive constants which change from one use to the next. In contrast, constants labeled with a number remain fixed from their first use on.

Moreover, we write $\nabla \cdot v$ for the divergence of a vector-valued function v.

2. Solution of the Approximate Problems

In this chapter we consider a sequence of approximating problems for the original PDE-ODE system. The important feature is that the equations for the migrating cells and the tissue fibers are now also (semilinear) parabolic PDEs instead of ODEs. This will allow us to find a classical solution of each approximate problem. The first part of this chapter is devoted to prove the existence of such solution and its global-in-time existence. In the second part we set, based on ε-independent estimates and an entropy-type functional, the preparations for constructing a global weak solution of the original problem.

For $\varepsilon \in (0,1)$ we consider the regularization of (1.2)-(1.4) given by

$$\begin{cases} \partial_t m_\varepsilon = \nabla \cdot (D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\nabla m_\varepsilon) - \nabla \cdot \left(\frac{v_\varepsilon}{1+v_\varepsilon} m_\varepsilon \nabla v_\varepsilon\right) & \\ \qquad\qquad +\nabla \cdot (g(q_\varepsilon) m_\varepsilon \nabla q_\varepsilon) + \lambda q_\varepsilon - \gamma m_\varepsilon - r_m(t) m_\varepsilon - \varepsilon m_\varepsilon^\theta, & x \in \Omega,\ t > 0, \\ \partial_t q_\varepsilon = \varepsilon \Delta q_\varepsilon + \mu_q q_\varepsilon (1 - (m_\varepsilon + q_\varepsilon) - \eta_1 v_\varepsilon) - \lambda q_\varepsilon + \gamma m_\varepsilon - r_q(t) q_\varepsilon, & x \in \Omega,\ t > 0, \\ \partial_t v_\varepsilon = \varepsilon \Delta v_\varepsilon - \alpha m_\varepsilon v_\varepsilon - \beta q_\varepsilon v_\varepsilon + \mu_v v_\varepsilon (1 - v_\varepsilon) - r_v(t) v_\varepsilon, & x \in \Omega,\ t > 0, \\ \partial_\nu m_\varepsilon = \partial_\nu q_\varepsilon = \partial_\nu v_\varepsilon = 0, & x \in \partial\Omega,\ t > 0, \\ m_\varepsilon(x,0) = m_{0\varepsilon}(x), \quad q_\varepsilon(x,0) = q_{0\varepsilon}(x), & \\ v_\varepsilon(x,0) = v_{0\varepsilon}(x), & x \in \Omega, \end{cases} \tag{2.1}$$

where $\theta > \max\{2, n\}$ is a fixed parameter, the functions $m_{0\varepsilon}$, $q_{0\varepsilon}$, $v_{0\varepsilon}$ satisfy

$$m_{0\varepsilon}, q_{0\varepsilon}, v_{0\varepsilon} \in \mathrm{C}^3(\overline{\Omega}), \tag{2.2}$$

$$m_{0\varepsilon} > 0, q_{0\varepsilon} > 0, v_{0\varepsilon} > 0 \text{ in } \overline{\Omega}, \tag{2.3}$$

$$\partial_\nu m_{0\varepsilon} = \partial_\nu q_{0\varepsilon} = \partial_\nu v_{0\varepsilon} = 0 \text{ on } \partial\Omega \tag{2.4}$$

for $\varepsilon \in (0,1)$ and demand

$$m_{0\varepsilon} \to m_0 \text{ in } \mathrm{C}_0(\overline{\Omega}), \quad q_{0\varepsilon} \to q_0 \text{ and } v_{0\varepsilon} \to v_0 \text{ in } \mathrm{W}^{1,2}(\Omega) \cap \mathrm{C}^0(\overline{\Omega}) \tag{2.5}$$

as $\varepsilon \searrow 0$.

2.1. Global Existence for the Approximate Problems

The aim of this section is to show global-in-time existence of classical solutions of the above system of equations. To this end, we will mainly work in the Hölder spaces $\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)$ and $\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)$. For the sake of completeness we recall the definition here.

Definition 2.1. Let $\Omega \subseteq \mathbb{R}^n$ be a bounded domain, $T > 0$ and $\beta \in (0,1)$. For $u\colon \overline{\Omega}\times[0,T]$ we define the seminorms

$$\langle u\rangle_x^\beta := \sup_{x,x'\in\overline{\Omega},t\in[0,T],x\neq x'} \frac{|u(x,t)-u(x',t)|}{|x-x'|^\beta}$$

and

$$\langle u\rangle_t^\beta := \sup_{x\in\overline{\Omega},t,t'\in[0,T],t\neq t'} \frac{|u(x,t)-u(x,t')|}{|t-t'|^\beta}.$$

We define the Hölder norms

$$\|\cdot\|_{\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} := \|\cdot\|_{\mathrm{C}^0\left(\overline{\Omega}\times[0,T]\right)} + \langle\cdot\rangle_x^\beta + \langle\cdot\rangle_t^{\frac{\beta}{2}}$$

and

$$\begin{aligned}\|\cdot\|_{\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} &:= \|\cdot\|_{\mathrm{C}^0\left(\overline{\Omega}\times[0,T]\right)} + \|\partial_t\cdot\|_{\mathrm{C}^0\left(\overline{\Omega}\times[0,T]\right)} + \langle\partial_t\cdot\rangle_x^\beta + \langle\partial_t\cdot\rangle_t^{\frac{\beta}{2}}\\ &\quad + \sum_{i=1}^n \left(\|\partial_i\cdot\|_{\mathrm{C}^0\left(\overline{\Omega}\times[0,T]\right)} + \langle\partial_i\cdot\rangle_t^{\frac{1+\beta}{2}}\right)\\ &\quad + \sum_{i,j=1}^n \left(\|\partial_{ij}\cdot\|_{\mathrm{C}^0\left(\overline{\Omega}\times[0,T]\right)} + \langle\partial_{ij}\cdot\rangle_x^\beta + \langle\partial_{ij}\cdot\rangle_t^{\frac{\beta}{2}}\right).\end{aligned}$$

Finally, we can define the Hölder spaces

$$\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right) := \{u\in\mathrm{C}^0\left(\overline{\Omega}\times[0,T]\right) : \|u\|_{\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} < \infty\}$$

and

$$\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right) := \{u\in\mathrm{C}^{2,1}\left(\overline{\Omega}\times[0,T]\right) : \|u\|_{\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} < \infty\}.$$

It is a well-known result that those spaces are Banach spaces.

First we will show local-in-time existence of solutions to (2.1) using Schauder's fixed-point theorem. We will adapt the proof presented in [SSW14] as suggested in [SSU16].

Theorem 2.2. *For any $\varepsilon \in (0,1)$ there exist $T_\varepsilon \in (0,\infty]$ and positive functions $m_\varepsilon, q_\varepsilon, v_\varepsilon \in \mathrm{C}^{2,1}(\overline{\Omega} \times [0,T_\varepsilon))$ solving (2.1) in the classical sense. Moreover, we can choose T_ε such that if $T_\varepsilon < \infty$ is satisfied, then*

$$\limsup_{t \nearrow T_\varepsilon} \left\{ \|m_\varepsilon(\cdot,t)\|_{\mathrm{C}^{2+\beta}(\overline{\Omega})} + \|q_\varepsilon(\cdot,t)\|_{\mathrm{C}^{2+\beta}(\overline{\Omega})} + \|v_\varepsilon(\cdot,t)\|_{\mathrm{C}^{2+\beta}(\overline{\Omega})} \right\} = \infty$$

holds for all $\beta \in (0,1)$.

Proof. We fix $\varepsilon \in (0,1)$ and $\beta \in (0,1)$ and define

$$A := \|m_{0\varepsilon}\|_{\mathrm{C}^{2+\beta}(\overline{\Omega})} + \|q_{0\varepsilon}\|_{\mathrm{C}^{2+\beta}(\overline{\Omega})} + \|v_{0\varepsilon}\|_{\mathrm{C}^{2+\beta}(\overline{\Omega})}.$$

This is a good choice as it will later turn out that the existence time given by Schauder's fixed-point theorem depends only on A. Consider the Banach space $Y := \mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$ as in Definition 2.1. The proof is based on a fixed-point argument in the subspace

$$X := \{(m_\varepsilon, q_\varepsilon) \in Y^2 \colon m_\varepsilon, q_\varepsilon \geq 0 \text{ s.t. } \|m_\varepsilon\|_{\mathrm{C}^{\beta,\frac{\beta}{2}}(\overline{\Omega}\times[0,T])} + \|q_\varepsilon\|_{\mathrm{C}^{\beta,\frac{\beta}{2}}(\overline{\Omega}\times[0,T])} \leq B+1\}$$

for $B := \|m_{0\varepsilon}\|_{\mathrm{C}^{\beta}(\overline{\Omega})} + \|m_{0\varepsilon t}\|_{\mathrm{C}^{0}(\overline{\Omega})} + \|q_{0\varepsilon}\|_{\mathrm{C}^{\beta}(\overline{\Omega})} + \|q_{0\varepsilon t}\|_{\mathrm{C}^{0}(\overline{\Omega})}$ and some $T \in (0,1)$ to be chosen later. Here we denote with $m_{0\varepsilon t}$ and $q_{0\varepsilon t}$ the right hand side of the first and second equation in (2.1) evaluated at $t=0$, respectively. We note that $B \leq C_4(A)$ holds with some constant $C_4(A) > 0$ depending on A. Next, we want to define a suitable self-map on X.

We choose $(\tilde{m}, \tilde{q}) \in X$ and plug them into the third equation of (2.1) to obtain the following semilinear parabolic Neumann problem for v_ε:

$$\begin{cases} \partial_t v_\varepsilon = \varepsilon \Delta v_\varepsilon - \alpha \tilde{m} v_\varepsilon - \beta \tilde{q} v_\varepsilon + \mu_v v_\varepsilon (1 - v_\varepsilon) - r_v(t) v_\varepsilon & x \in \Omega,\ t > 0, \\ v_\varepsilon(x,0) = v_{0\varepsilon}(x) & x \in \Omega, \\ \partial_\nu v_\varepsilon = 0 & x \in \partial\Omega,\ t > 0. \end{cases}$$

Assuming the existence of a classical solution v_ε, the comparison principle for the semilinear heat equation (Theorem A.3) implies $0 < v_\varepsilon \leq \max(1, \|v_{0\varepsilon}\|_{\mathrm{C}^0(\overline{\Omega})})$, as $v_{0\varepsilon} > 0$ holds by assumption. Now, we can use Theorem A.5 (the conditions in (ii) and (iii) are satisfied as $a(x,t,u)$ is constant and $b(x,t,u,p)$ is a polynomial of degree 2) to obtain a unique classical solution $v_\varepsilon \in \mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)$ of the above semilinear problem. In order to get a bound on the norm of v_ε, we note that v_ε satisfies the following linear equation in $\widetilde{v_\varepsilon}$:

$$\partial_t\widetilde{v_\varepsilon} = \varepsilon\Delta\widetilde{v_\varepsilon} - \alpha\tilde{m}\widetilde{v_\varepsilon} - \beta\tilde{q}\widetilde{v_\varepsilon} + \mu_v\widetilde{v_\varepsilon}(1-v_\varepsilon) - r_v(t)\widetilde{v_\varepsilon}, \quad x\in\Omega, t>0.$$

By Theorem A.4 (the compatibility condition is satisfied by (2.4)) we obtain the norm estimate

$$\|v_\varepsilon\|_{\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} \le C(A)\,\|v_{0\varepsilon}\|_{\mathrm{C}^{2+\beta}\left(\overline{\Omega}\right)} \le C_5(A)$$

for some $C(A)>0$ and $C_5(A)>0$. Next, we take this solution v_ε together with $\tilde{m},\tilde{q}$ such that the second equation in (2.1) becomes a linear equation in q_ε:

$$\begin{cases} \partial_t q_\varepsilon = \varepsilon\Delta q_\varepsilon + \mu_q q_\varepsilon(1-(\tilde{m}+\tilde{q})-\eta_1 v_\varepsilon) - \lambda q_\varepsilon + \gamma\tilde{m} - r_q(t)q_\varepsilon, & x\in\Omega, t>0,\\ q_\varepsilon(x,0) = q_{0\varepsilon}(x), & x\in\Omega,\\ \partial_\nu q_\varepsilon = 0, & x\in\partial\Omega, t>0, \end{cases}$$

Again, by Theorem A.4 (the compatibility condition is again satisfied by (2.4)) this equation has a unique solution $q_\varepsilon \in \mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)$ and we obtain the norm estimate

$$\begin{aligned} \|q_\varepsilon\|_{\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} &\le C(A)\left(\|\tilde{m}\|_{\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} + \|q_{0\varepsilon}\|_{\mathrm{C}^{2+\beta}\left(\overline{\Omega}\right)}\right)\\ &\le C(A)(B+1+A) \le C_6(A) \end{aligned} \tag{2.6}$$

for some $C(A)>0$ and $C_6(A)>0$ depending on A. Moreover, by the strong parabolic maximum principle (Theorem A.3) this solution is positive. Last, we consider the first equation of (2.1) and plug $\tilde{m}, q_\varepsilon, v_\varepsilon$ into this equation and obtain

$$\begin{aligned} \partial_t m_\varepsilon = \nabla\cdot(D(m_\varepsilon,q_\varepsilon,v_\varepsilon)\nabla m_\varepsilon) - \nabla\cdot\left(\frac{v_\varepsilon}{1+v_\varepsilon}m_\varepsilon\nabla v_\varepsilon\right) + \nabla\cdot(g(q_\varepsilon)m_\varepsilon\nabla q_\varepsilon) + \lambda q_\varepsilon - \gamma m_\varepsilon\\ - r_m(t)m_\varepsilon - \varepsilon m_\varepsilon\tilde{m}^{\theta-1}. \end{aligned}$$

Note that in the first term we cannot use $\tilde{m}$ as it is not regular enough. In order to show a-priori positivity, we note that any classical solution can be plugged into the above equation in such a way that it becomes a linear parabolic PDE (still satisfied by the plugged-in function).

A comparison principle (see [DKM92, Theorem 13.5]), more general than Theorem A.3, then shows that any classical solution of this linear PDE must be strictly positive. The above is a quasilinear equation in m_ε but not yet in the form as in Theorem A.5. In order to achieve this, we simplify the divergence in the above equation and obtain

$$\begin{aligned}\partial_t m_\varepsilon = {} & D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\Delta m_\varepsilon + \partial_1 D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\left|\nabla m_\varepsilon\right|^2 + \partial_2 D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\nabla q_\varepsilon \cdot \nabla m_\varepsilon \\ & + \partial_3 D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\nabla v_\varepsilon \cdot \nabla m_\varepsilon - \nabla m_\varepsilon \cdot \left(\frac{v_\varepsilon}{1+v_\varepsilon}\nabla v_\varepsilon\right) - m_\varepsilon\, \nabla \cdot \left(\frac{v_\varepsilon}{1+v_\varepsilon}\nabla v_\varepsilon\right) \\ & + \nabla \cdot (g(q_\varepsilon)\nabla q_\varepsilon)\, m_\varepsilon + g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla m_\varepsilon + \lambda q_\varepsilon - \gamma m_\varepsilon - r_m(t) m_\varepsilon - \varepsilon m_\varepsilon \tilde{m}^{\theta-1}.\end{aligned}$$

Now, we check the assumptions of Theorem A.5. (A.3) and (A.5) are satisfied by assumption on D (see (1.7)). Moreover, (A.4) holds for suitable constants by Young's inequality, the Sobolev regularity of D imposed in (1.7) and as $q_\varepsilon, v_\varepsilon$ are sufficiently regular (consequently all coefficients of m_ε and ∇m_ε are bounded).

Next, (A.6) and (A.7) are direct consequences of the continuity assumptions on D. (A.8) and (A.9) follow as b depends at most quadratically on p, the regularity of D and the (time) regularity, in particular boundedness, of q_ε and v_ε. Last, (A.10) is satisfied as we assumed $D \in \mathrm{W}^{2,\infty}([0,\infty) \times [0,A] \times [0,L])$. Hence, we can choose $\mu > 0$ large enough such that all the previous estimates are satisfied with the same μ.

Finally, the regularity conditions imposed in (iii) of Theorem A.5 are an immediate consequence of the regularity of D, q_ε and v_ε. Hence, we obtain a unique classical solution $m_\varepsilon \in \mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$.

Now, we can proceed as for v_ε to obtain a bound on the norm of m_ε in that space. To this end we want to apply again Theorem A.4. By the choice of the initial value m_ε in (2.4) the compatibility condition is satisfied.

It remains to verify that all coefficients are sufficiently smooth, i.e., are in $\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$. To this end, we note that the Hölder space $\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$ is closed under multiplication (cf. [Kra18, Lemma 2.11]) and for strictly positive functions closed under taking reciprocals (Lemma A.1). This, together with the assumption $g \in \mathrm{C}^2([0,\infty))$ (see (1.7)) implies that all coefficients have the desired regularity. Hence, we obtain by Theorem A.4

$$\|m_\varepsilon\|_{\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}(\overline{\Omega}\times[0,T])} \leq C(A)\left(\|q_\varepsilon\|_{\mathrm{C}^{\beta,\frac{\beta}{2}}(\overline{\Omega}\times[0,T])} + \|m_{0\varepsilon}\|_{\mathrm{C}^{2+\beta}(\overline{\Omega})}\right) \leq C_7(A) \qquad (2.7)$$

for some $C(A) > 0$ and $C_7(A) > 0$ depending on A in view of (2.6).

Now we consider the map

$$\begin{aligned} F\colon X &\to X \\ (\tilde{m},\tilde{q}) &\mapsto (m_\varepsilon, q_\varepsilon) \end{aligned}$$

and we want to show that it satisfies the assumption of Schauder's fixed-point theorem (see for example [PRR19, Theorem 3.2.20]). It is clear that X is a nonempty bounded, closed, convex subset of the Banach space Y^2. Hence, it remains to show that F indeed is a self-map of X and is compact. We already know that m_ε and q_ε are nonnegative and have the desired regularity. Thus, it suffices to show the norm estimate

$$\|q_\varepsilon\|_{C^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} + \|m_\varepsilon\|_{C^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} \leq B+1$$

for some suitable $T\in(0,1)$ to be chosen later. We estimate the first term in detail, the second one is done analogously. Using the triangle inequality, we obtain

$$\begin{aligned} \|q_\varepsilon\|_{C^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} \leq{}& \|q_\varepsilon - q_\varepsilon(\cdot,0)\|_{C^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} + \|q_\varepsilon(\cdot,0)\|_{C^{\beta}\left(\overline{\Omega}\right)} \\ ={}& \|q_\varepsilon - q_\varepsilon(\cdot,0)\|_{C^0\left(\overline{\Omega}\times[0,T]\right)} + \langle q_\varepsilon - q_\varepsilon(\cdot,0)\rangle^{\beta}_{x,\Omega} \\ &+ \langle q_\varepsilon - q_\varepsilon(\cdot,0)\rangle^{\frac{\beta}{2}}_{t,\Omega} + \|q_\varepsilon(\cdot,0)\|_{C^{\beta}\left(\overline{\Omega}\right)} \\ \leq{}& C_8\left(\|q_\varepsilon - q_\varepsilon(\cdot,0)\|_{C^0\left(\overline{\Omega}\times[0,T]\right)} + \sum_{i=1}^{n}\|\partial_{x_i}\left(q_\varepsilon - q_\varepsilon(\cdot,0)\right)\|_{C^0\left(\overline{\Omega}\times[0,T]\right)}\right) \\ &+ \langle q_\varepsilon - q_\varepsilon(\cdot,0)\rangle^{\frac{\beta}{2}}_{t,\Omega} + \|q_\varepsilon(\cdot,0)\|_{C^{\beta}\left(\overline{\Omega}\right)} \end{aligned}$$

for some $C_8>0$ where in the last step we used [Kra18, Lemma 2.21.1]. Now, we will examine the terms separately and note that we can already control the last part. For the first term, we use the mean value theorem in t and the proof of Lemma 3.9 in [Kra18] to obtain

$$\begin{aligned} \|q_\varepsilon - q_{0\varepsilon}\|_{C^0\left(\overline{\Omega}\times[0,T]\right)} + \sum_{i=1}^{n}\|\partial_{x_i}\left(q_\varepsilon - q_{0\varepsilon}\right)\|_{C^0\left(\overline{\Omega}\times[0,T]\right)} \leq{}& T\,\|\partial_t q_\varepsilon\|_{C^0\left(\overline{\Omega}\times[0,T]\right)} \\ &+ \sum_{i=1}^{n} T^{\frac{1+\beta}{2}}\langle \partial_{x_i} q_\varepsilon\rangle^{\frac{1+\beta}{2}}_{t,\Omega}. \end{aligned}$$

For the Hölder seminorm in t we get, using the arguments in the proof of [Kra18, Lemma 2.21.2],

$$\langle q_\varepsilon - q_{0\varepsilon}\rangle^{\frac{\beta}{2}}_{t,\Omega} \leq T^{1-\frac{\beta}{2}}\,\|\partial_t q_\varepsilon - \partial_t q_\varepsilon(\cdot,0)\|_{C^0\left(\overline{\Omega}\times[0,T]\right)}$$

$$\leq T^{1-\frac{\beta}{2}} \left(\|\partial_t q_\varepsilon\|_{C^0\left(\overline{\Omega}\times[0,T]\right)} + \|q_{0\varepsilon t}\|_{C^0\left(\overline{\Omega}\right)} \right)$$

by regularity of q_ε and the definition of $q_{0\varepsilon t}$ in the beginning of the proof. Combining the above estimates and using (2.6), we obtain that

$$\begin{aligned} \|q_\varepsilon\|_{C^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_1]\right)} \leq\ & \max\left\{T_1^{1-\frac{\beta}{2}}, C_8 T_1^{\frac{1+\beta}{2}}\right\} \|q_\varepsilon\|_{C^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_1]\right)} \\ & + \|q_{\varepsilon 0t}\|_{C^0\left(\overline{\Omega}\right)} + \|q_{0\varepsilon}\|_{C^\beta\left(\overline{\Omega}\right)} \\ \leq\ & C(A) \max\left\{T_1^{1-\frac{\beta}{2}}, T_1^{\frac{1+\beta}{2}}\right\} + \|q_{0\varepsilon t}\|_{C^0\left(\overline{\Omega}\right)} + \|q_{0\varepsilon}\|_{C^\beta\left(\overline{\Omega}\right)} \\ \leq\ & \frac{1}{2} + \|q_{0\varepsilon t}\|_{C^0\left(\overline{\Omega}\right)} + \|q_{0\varepsilon}\|_{C^\beta\left(\overline{\Omega}\right)} \end{aligned}$$

holds for some $T_1 \in (0,1)$, only depending on A, sufficiently small. Similarly for some $0 < T_2 \leq T_1$ sufficiently small (also depending on A only) we obtain for m_ε

$$\|m_\varepsilon\|_{C^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_2]\right)} \leq \frac{1}{2} + \|m_{0\varepsilon t}\|_{C^0\left(\overline{\Omega}\right)} + \|m_{0\varepsilon}\|_{C^\beta\left(\overline{\Omega}\right)}.$$

Combining these estimates, we conclude that F is well-defined. Moreover, as a map with values in $C^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_2]\right)^2$ it is continuous due (2.6) and (2.7). In view of the compact embedding $C^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_2]\right) \hookrightarrow C^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_2]\right)$ the map F is also compact. Thus, Schauder's fixed-point theorem yields the existence of a fixed-point $(m_\varepsilon, q_\varepsilon)$. Starting with this $(m_\varepsilon, q_\varepsilon)$ the above reasoning gives the existence of a classical solution to (2.1) in $\overline{\Omega}\times[0,T_2]$ where the components are all positive and belong to $C^{2,1}\left(\overline{\Omega}\times[0,T_2]\right)$.

Now, we choose $T_\varepsilon \coloneqq \sup\{T \in (0,\infty] \mid \text{there exists a solution in } C^{2,1}(\overline{\Omega}\times[0,T])\}$, the maximal existence time. We assume $T_\varepsilon < \infty$ as well as

$$\limsup_{t\nearrow T_\varepsilon} \left\{ \|m_\varepsilon(\cdot,t)\|_{C^{2+\beta}\left(\overline{\Omega}\right)} + \|q_\varepsilon(\cdot,t)\|_{C^{2+\beta}\left(\overline{\Omega}\right)} + \|v_\varepsilon(\cdot,t)\|_{C^{2+\beta}\left(\overline{\Omega}\right)} \right\} < \infty$$

for some $\beta \in (0,1)$. Hence, we can find $A' > 0$ such that

$$\|m_\varepsilon(\cdot,t)\|_{C^{2+\beta}\left(\overline{\Omega}\right)} + \|q_\varepsilon(\cdot,t)\|_{C^{2+\beta}\left(\overline{\Omega}\right)} + \|v_\varepsilon(\cdot,t)\|_{C^{2+\beta}\left(\overline{\Omega}\right)} < A'$$

is satisfied for all $t < T_\varepsilon$ and the above $\beta \in (0,1)$. Next, we choose T_3 sufficiently small such that the above procedure works in $\overline{\Omega}\times[0,T_3]$ after replacing A by A'. Now, set $T_4 \coloneqq T_\varepsilon - \frac{T_3}{2}$. As T_3 depends only on A', we may choose $m_\varepsilon(\cdot,T_4), q_\varepsilon(\cdot,T_4), v_\varepsilon(\cdot,T_4)$ as initial values (here $m_\varepsilon, q_\varepsilon$ and v_ε are solutions in $C^{2,1}\left(\overline{\Omega}\times[0,T_4]\right)$) and by the above procedure obtain a solution in $C^{2,1}\left(\overline{\Omega}\times[T_4, T_\varepsilon + \frac{T_3}{2}]\right)$. Gluing those solutions with $m_\varepsilon, q_\varepsilon$ and v_ε contradicts the maximality of T_ε. $\square$

In a next step we prove estimates for the solution of (2.1) which are uniform with respect to $\varepsilon \in (0,1)$.

Lemma 2.3. *Let q_ε and v_ε denote a solution of* (2.1) *given by the preceding theorem. For any $\varepsilon \in (0,1)$ the following estimates hold true:*

$$0 < q_\varepsilon \leq A := \max\left\{ \sup_{\varepsilon\in(0,1)} \|q_{0\varepsilon}\|_{\mathrm{L}^\infty(\Omega)}, 1 - \frac{\lambda}{\mu_q}, \frac{\gamma}{\mu_q} \right\}$$

for $x \in \overline{\Omega}$, $t \in [0, T_\varepsilon)$ as well as

$$0 < v_\varepsilon(x,t) \leq L := \max\left\{ \sup_{\varepsilon\in(0,1)} \|v_{0\varepsilon}\|_{\mathrm{L}^\infty(\Omega)}, 1 \right\}$$

for $x \in \overline{\Omega}$, $t \in [0, T_\varepsilon)$.

Proof. This is an immediate consequence of the parabolic comparison principle (Theorem A.3) while the positivity has been already shown in the existence theorem. □

Lemma 2.4. *Let m_ε denote a solution given by Theorem 2.2. For any $\varepsilon \in (0,1)$ we have the following estimates:*

$$\int_\Omega m_\varepsilon(x,t)\ \mathrm{d}x \leq B := \max\left\{ \sup_{\varepsilon\in(0,1)} \int_\Omega m_{0\varepsilon}, \frac{\lambda A\,|\Omega|}{\gamma} \right\}, \qquad t \in (0, T_\varepsilon),$$

$$\varepsilon \int_t^{t+1} \int_\Omega m_\varepsilon^\theta(x,s)\ \mathrm{d}x\ \mathrm{d}s \leq B + \lambda A\,|\Omega|, \qquad t \in (0, T_\varepsilon - 1).$$

Proof. Using Lemma 2.3, the positivity of m_ε, the divergence theorem as well as the Neumann conditions on $m_\varepsilon, q_\varepsilon$ and v_ε, an integration of the first equation of (2.1) yields

$$\frac{\mathrm{d}}{\mathrm{d}t} \int_\Omega m_\varepsilon \leq \lambda A\,|\Omega| - \gamma \int_\Omega m_\varepsilon - \varepsilon \int_\Omega m_\varepsilon^\theta$$

for $t \in (0, T_\varepsilon)$. Then, the first estimate follows by a comparison principle for ODEs (see Lemma A.2). The second estimate is an easy consequence after a time integration and dropping the second term on the right hand side. □

Now, we can prove the global in time existence of solutions of (2.1).

Lemma 2.5. *For each $\varepsilon \in (0,1)$ the solution to* (2.1) *exists globally in time and we have $T_\varepsilon = \infty$.*

Proof. We fix $\varepsilon \in (0,1)$ and $T > 0$ and set $\widehat{T_\varepsilon} := \min\{T, T_\varepsilon\}$. As $m_\varepsilon \in \mathrm{L}^\theta\left(\Omega \times (0, \widehat{T_\varepsilon})\right)$ by the previous lemma, we obtain that $f_\varepsilon := -\alpha m_\varepsilon v_\varepsilon - \beta q_\varepsilon v_\varepsilon + \mu_v v_\varepsilon(1 - v_\varepsilon) - r_v(t) v_\varepsilon$ is bounded in $\mathrm{L}^\theta\left(\Omega \times (0, \widehat{T_\varepsilon})\right)$. Our choice of $\theta > n$ implies $\mathrm{W}^{2,\theta}(\Omega) \hookrightarrow \mathrm{W}^{1,\infty}(\Omega)$ as a continuous embedding (see e.g. [Bré11, Corollary 9.14]). Combining this with results on maximal Sobolev regularity [HP97, 3.1 Theorem and 3.2 Example] applied to the third equation in (2.1) and $\theta > 2$, we deduce the existence of $C_9(\varepsilon, T) > 0$ such that

$$
\begin{aligned}
\int_0^{\widehat{T_\varepsilon}} \|\nabla v_\varepsilon(\cdot,t)\|^2_{\mathrm{L}^\infty(\Omega)} \, \mathrm{d}t &\le \int_0^{\widehat{T_\varepsilon}} \|v_\varepsilon(\cdot,t)\|^2_{\mathrm{W}^{1,\infty}(\Omega)} \, \mathrm{d}t \le \int_0^{\widehat{T_\varepsilon}} \|v_\varepsilon(\cdot,t)\|^\theta_{\mathrm{W}^{1,\infty}(\Omega)} + 1 \, \mathrm{d}t \\
&\le C(T) \left(1 + \int_0^{\widehat{T_\varepsilon}} \|v_\varepsilon(\cdot,t)\|^\theta_{\mathrm{W}^{2,\theta}(\Omega)} \, \mathrm{d}t\right) \\
&\le C_9(\varepsilon, T)
\end{aligned}
$$

holds. Here we used that $\|\cdot\|_{\mathrm{L}^\theta(\Omega)} + \|\Delta \cdot\|_{\mathrm{L}^\theta(\Omega)}$ is an equivalent norm on $\mathrm{W}^{2,\theta}(\Omega)$ due to [Sim90, Theorem 3.4] and a density argument.

With a similar argument, we may choose $C_9(\varepsilon, T)$ in such a way that also

$$
\int_0^{\widehat{T_\varepsilon}} \|\nabla q_\varepsilon(\cdot,t)\|^2_{\mathrm{L}^\infty(\Omega)} \, \mathrm{d}t \le C_9(\varepsilon, T)
$$

holds true. Next, we fix $A > 0$ and $L > 0$ as defined in Lemma 2.3, so by assumption on D (see (1.7)) there exists $C_2 > 0$ such that $D(m_\varepsilon, q_\varepsilon, v_\varepsilon) \ge C_2$ for $x \in \Omega$ and $t \in \left(0, \widehat{T_\varepsilon}\right)$. Hence, for fixed $p > 1$ we multiply the first equation in (2.1) by m_ε^{p-1} and obtain by dropping non-negative terms and using integration by parts, Young's inequality and Lemma 2.3

$$
\begin{aligned}
\frac{1}{p}\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega m_\varepsilon^p \le& \int_\Omega \nabla \cdot (D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\nabla m_\varepsilon) m_\varepsilon^{p-1} - \int_\Omega \nabla \cdot \left(\frac{v_\varepsilon}{1+v_\varepsilon} m_\varepsilon \nabla v_\varepsilon\right) m_\varepsilon^{p-1} \\
&+ \int_\Omega \nabla \cdot (g(q_\varepsilon) m_\varepsilon \nabla q_\varepsilon) m_\varepsilon^{p-1} + \int_\Omega \lambda q_\varepsilon m_\varepsilon^{p-1} \\
\le& -(p-1)C_2 \int_\Omega m_\varepsilon^{p-2} |\nabla m_\varepsilon|^2 + (p-1)\int_\Omega \frac{v_\varepsilon}{1+v_\varepsilon} m_\varepsilon^{p-1} \nabla v_\varepsilon \cdot \nabla m_\varepsilon \\
&- (p-1)\int_\Omega g(q_\varepsilon) m_\varepsilon^{p-1} \nabla q_\varepsilon \cdot \nabla m_\varepsilon + \int_\Omega \lambda q_\varepsilon (m_\varepsilon^p + 1) \\
\le& \frac{(p-1)}{C_2}\left(\|g\|^2_{\mathrm{C}^0([0,A])} \|\nabla q_\varepsilon(\cdot,t)\|^2_{\mathrm{L}^\infty} + L^2 \|\nabla v_\varepsilon(\cdot,t)\|^2_{\mathrm{L}^\infty}\right)\int_\Omega m_\varepsilon^p \\
&+ \lambda A \left(|\Omega| + \int_\Omega m_\varepsilon^p\right)
\end{aligned}
$$

for $t \in (0, \widehat{T_\varepsilon})$. Therefore, Lemma A.2 yields

$$
\int_\Omega m_\varepsilon^p(\cdot,t) \le C_{10}(\varepsilon, p, T) \tag{2.8}
$$

for all $t \in (0, \widehat{T_\varepsilon})$ and for some constant $C_{10}(\varepsilon, p, T) > 0$. Hence, as q_ε, v_ε and r_v are bounded, we deduce that $f_\varepsilon \in \mathrm{L}^\infty\left((0, \widehat{T_\varepsilon}), \mathrm{L}^p(\Omega)\right)$ for any $p > 1$ is satisfied. Similarly we obtain $h_\varepsilon := \mu_q q_\varepsilon(1 - (m_\varepsilon + q_\varepsilon) - \eta_1 v_\varepsilon) - \lambda q_\varepsilon + \gamma m_\varepsilon - r_q(t) q_\varepsilon \in \mathrm{L}^\infty\left((0, \widehat{T_\varepsilon}), \mathrm{L}^p(\Omega)\right)$ for any $p > 1$.

Using this in conjunction with properties of the Neumann heat semigroup [Win10, Lemma 1.3] and the variation of constants formula (see e.g. [DKM92, 2.5 Theorem]), we obtain

$$\begin{aligned}
\|\nabla v_\varepsilon(\cdot, t)\|_{\mathrm{L}^\infty(\Omega)} &\leq \left\|\nabla \mathrm{e}^{\varepsilon t \Delta} v_\varepsilon(\cdot, 0)\right\|_{\mathrm{L}^\infty(\Omega)} + \int_0^t \left\|\nabla \mathrm{e}^{\varepsilon(t-s)\Delta} f_\varepsilon\right\|_{\mathrm{L}^\infty(\Omega)} \mathrm{d}s \\
&\leq C(1 + (\varepsilon t^{-\frac{1}{2}})\mathrm{e}^{-\lambda_1 \varepsilon t} \|v_{0\varepsilon}\|_{\mathrm{L}^\infty(\Omega)} \\
&\quad + \int_0^t C(1 + (\varepsilon(t-s))^{-\frac{1}{2} - \frac{n}{2}\frac{1}{p}})\mathrm{e}^{-\lambda_1 \varepsilon(t-s)} \|f_\varepsilon(\cdot, s)\|_{\mathrm{L}^p(\Omega)} \mathrm{d}s
\end{aligned}$$

for all $t \in (0, \widehat{T_\varepsilon})$ and all $p \in (1, \infty)$. Here $\lambda_1 > 0$ denotes the first nonzero eigenvalue of the Neumann-Laplacian in Ω. Choosing $p \in (n, \infty)$ and using the boundedness of $\|f_\varepsilon(\cdot, s)\|_{\mathrm{L}^p(\Omega)}$ for $s \in (0, \widehat{T_\varepsilon})$ the integral converges.

Repeating the above arguments for q_ε instead of v_ε and h_ε in place of f_ε we deduce the existence of some $C_{11}(\varepsilon, T) > 0$ such that

$$\|\nabla q_\varepsilon(\cdot, t)\|_{\mathrm{L}^\infty(\Omega)} + \|\nabla v_\varepsilon(\cdot, t)\|_{\mathrm{L}^\infty(\Omega)} \leq C_{11}(\varepsilon, T) \quad t \in (0, \widehat{T_\varepsilon}),$$

holds.

Now, we may proceed as in [SSW14] to show that T_ε cannot be finite. Nevertheless, we slightly need to adapt the proof presented there due to the considered splitting of the cancer cells. In particular, we need to derive bounds not only for m_ε but also for q_ε in the Hölder space $\mathrm{C}^{\beta, \frac{\beta}{2}}\left(\overline{\Omega} \times [0, T_\varepsilon]\right)$ for some appropriate $\beta \in (0, 1)$. This is the reason why the extensibility criterion in Theorem 2.2 is formulated in terms of Hölder norms.

So, for the sake of contradiction assume $T_\varepsilon < \infty$. We first derive a bound for m_ε. We know that m_ε satisfies the following PDE in divergence form:

$$\partial_t m_\varepsilon = \nabla \cdot (a_\varepsilon(x, t, \nabla m_\varepsilon)) + b_\varepsilon(x, t), \quad (x, t) \in (\Omega \times (0, T_\varepsilon),$$

with

$$a_\varepsilon(x, t, r) := D(m_\varepsilon, q_\varepsilon, v_\varepsilon) r - \frac{v_\varepsilon}{1 + v_\varepsilon} m_\varepsilon \nabla v_\varepsilon + g(q_\varepsilon) m_\varepsilon \nabla q_\varepsilon, \; (x, t, r) \in \Omega \times (0, T_\varepsilon) \times \mathbb{R}^n),$$

and

$$b_\varepsilon(x,t) := \lambda q_\varepsilon - \gamma m_\varepsilon - r_m(t) m_\varepsilon - \varepsilon m_\varepsilon^\theta,\ (x,t) \in \Omega \times (0,T_\varepsilon).$$

Those coefficient functions satisfy (using Young's inequality)

$$\begin{aligned} a_\varepsilon(x,t,r)r &= D(m_\varepsilon, q_\varepsilon, v_\varepsilon) r^2 - \frac{v_\varepsilon}{1+v_\varepsilon} m_\varepsilon \nabla v_\varepsilon r + (g(q_\varepsilon) m_\varepsilon \nabla q_\varepsilon) r \\ &\geq C_2 r^2 - \frac{v_\varepsilon^2}{C_2(1+v_\varepsilon)^2} m_\varepsilon^2 \left|\nabla v_\varepsilon\right|^2 - \frac{C_2}{4} r^2 - \frac{1}{C_2} g(q_\varepsilon)^2 m_\varepsilon^2 \left|\nabla q_\varepsilon\right|^2 - \frac{C_2}{4} r^2 \\ &= \frac{C_2}{2} r^2 - \frac{v_\varepsilon^2}{C_2(1+v_\varepsilon)^2} m_\varepsilon^2 \left|\nabla v_\varepsilon\right|^2 - \frac{1}{C_2} g(q_\varepsilon)^2 m_\varepsilon^2 \left|\nabla q_\varepsilon\right|^2 \\ &=: \frac{C_2}{2} r^2 - \psi_0(x,t) \end{aligned}$$

with $\psi_0 \in \mathrm{L}^p(\Omega \times (0,T_\varepsilon))$ for all $p > 1$ as $m_\varepsilon \in \mathrm{L}^p(\Omega \times (0,T_\varepsilon))$ for all $p > 1$ and v_ε, $g(q_\varepsilon)$, $\left|\nabla v_\varepsilon\right|^2$ and $\left|\nabla q_\varepsilon\right|^2$ are bounded. Similarly, we have

$$\begin{aligned} \left|a_\varepsilon(x,t,r)\right| &\leq C_1 \left|r\right| + \frac{v_\varepsilon}{1+v_\varepsilon} m_\varepsilon \left|\nabla v_\varepsilon\right| + g(q_\varepsilon) m_\varepsilon \left|\nabla q_\varepsilon\right| \\ &\leq C_1 \left|r\right| + \frac{v_\varepsilon^2}{2(1+v_\varepsilon)^2} m_\varepsilon^2 + 2\left|\nabla v_\varepsilon\right|^2 + \frac{1}{2} g(q_\varepsilon)^2 m_\varepsilon^2 + 2\left|\nabla q_\varepsilon\right|^2 \\ &\leq C_1 \left|r\right| + \psi_1(x,t) \end{aligned}$$

with $\psi_1(x,t) \in \mathrm{L}^p(\Omega \times (0,T_\varepsilon))$ for all $p > 1$. Moreover, we have $b_\varepsilon(x,t) \in \mathrm{L}^p(\Omega \times (0,T_\varepsilon))$ for all $p > 1$ due to (2.8) and the boundedness of q_ε. Hence we could deduce from [PV93, Theorem 1.3 and Remark 1.4] the existence of some $\beta_1 \in (0,1)$ and $C_{12}(\varepsilon) > 0$ such that

$$\left\|m_\varepsilon\right\|_{\mathrm{C}^{\beta_1, \frac{\beta_1}{2}}\left(\overline{\Omega} \times [0,T_\varepsilon]\right)} \leq C_{12}(\varepsilon)$$

holds.

Next, we prove a similar estimate for q_ε. Consider the PDE

$$\partial_t q_\varepsilon = \nabla \cdot (a_\varepsilon(x,t,\nabla q_\varepsilon)) + b_\varepsilon(x,t), \quad (x,t) \in \Omega \times (0,T_\varepsilon),$$

with $a_\varepsilon(x,t,r) := \varepsilon r$ for $(x,t,r) \in \Omega \times (0,T_\varepsilon) \times \mathbb{R}^n$ and

$$b_\varepsilon(x,t) := \mu_q q_\varepsilon (1 - (m_\varepsilon + q_\varepsilon) - \eta_1 v_\varepsilon) - \lambda q_\varepsilon + \gamma m_\varepsilon - r_q(t) q_\varepsilon, \quad (x,t) \in \Omega \times (0,T_\varepsilon).$$

Clearly, we have

$$a_\varepsilon(x,t,r) r \geq \varepsilon \left|r\right|^2,$$

and

$$|a_\varepsilon(x,t,r)| \leq \varepsilon\,|r|\,,$$

and $b_\varepsilon \in \mathrm{L}^p(\Omega \times (0,T_\varepsilon))$ due to (2.8) and Lemma 2.3. So we could again apply [PV93, Theorem 1.3 and Remark 1.4] to find some $\beta_2 \in (0,1)$ as well as $C_{13}(\varepsilon) > 0$ with

$$\|q_\varepsilon\|_{\mathrm{C}^{\beta_2,\frac{\beta_2}{2}}\left(\overline{\Omega}\times[0,T_\varepsilon]\right)} \leq C_{13}(\varepsilon).$$

For $\beta \coloneqq \min\{\beta_1,\beta_2\}$ parabolic Schauder theory (Theorem A.4) and the above estimates would imply $v_\varepsilon \in \mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_\varepsilon]\right)$. As an immediate consequence of (Theorem A.4) we would then also obtain $m_\varepsilon, q_\varepsilon \in \mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T_\varepsilon]\right)$. In total, this is a contradiction to the extensibility criterion from Theorem 2.2. Hence, T_ε cannot be finite. □

2.2. An Entropy-type Functional

The aim of this section is to prove an important estimate (Proposition 2.13) coming from an entropy-type functional. This estimate will be an essential step towards the existence of a global weak solution of the original problem. To this end we follow the ideas presented in [SSU16]. In this section we need further assumptions on g which go beyond $g \in \mathrm{C}^2([0,\infty))$ and g being positive.

We first consider the case where g is constant and satisfies some smallness condition to be specified when it becomes important (Proposition 2.13). The following is the first of several preparatory lemmata and is essentially the same as Lemma 3.9 in [SSU16] where the additional term is due to the new term in the time evolution of m_ε. Note, that here we do not need any restrictions on g which go further the ones required in (1.7).

Lemma 2.6. *There exists $C_{14} > 0$ such that for any $\varepsilon \in (0,1)$ and all $t > 0$ we have*

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega m_\varepsilon \ln m_\varepsilon + \int_\Omega D(m_\varepsilon,q_\varepsilon,v_\varepsilon)\frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} + \frac{\varepsilon}{2}\int_\Omega m_\varepsilon^\theta \ln(m_\varepsilon+2)\\
&\leq \int_\Omega \frac{v_\varepsilon}{1+v_\varepsilon}\nabla m_\varepsilon\cdot\nabla v_\varepsilon - \int_\Omega g\nabla q_\varepsilon\cdot\nabla m_\varepsilon + C_{14}.
\end{aligned}$$

Proof. Using the positivity of m_ε, the boundedness of r_m (see (1.7)) as well as the divergence theorem (based on which several integrals vanish) we obtain

$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega m_\varepsilon \ln m_\varepsilon &= \int_\Omega (\ln m_\varepsilon \partial_t m_\varepsilon + \partial_t m_\varepsilon) \\
&= -\int_\Omega D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} + \int_\Omega \frac{v_\varepsilon}{1+v_\varepsilon}\nabla m_\varepsilon \cdot \nabla v_\varepsilon \\
&\quad - \int_\Omega g\nabla q_\varepsilon \cdot \nabla m_\varepsilon + \int_\Omega \lambda q_\varepsilon \ln m_\varepsilon - \int_\Omega \gamma m_\varepsilon \ln m_\varepsilon \\
&\quad - \int_\Omega r_m(t) m_\varepsilon \ln m_\varepsilon - \varepsilon \int_\Omega m_\varepsilon^\theta \ln m_\varepsilon + \int_\Omega \lambda q_\varepsilon - \int_\Omega \gamma m_\varepsilon \\
&\quad - \int_\Omega r_m(t) m_\varepsilon - \varepsilon \int_\Omega m_\varepsilon^\theta \\
&\le -\int_\Omega D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} + \int_\Omega \frac{v_\varepsilon}{1+v_\varepsilon}\nabla m_\varepsilon \cdot \nabla v_\varepsilon - \int_\Omega g\nabla q_\varepsilon \cdot \nabla m_\varepsilon \\
&\quad + \lambda AB + (\gamma + C_3)\frac{|\Omega|}{\mathrm{e}} - \frac{\varepsilon}{2}\int_\Omega m_\varepsilon^\theta \ln(m_\varepsilon + 2) + C + \lambda A\,|\Omega|
\end{aligned}
$$

for all $t > 0$, where in the last estimate we made use of

$$
\int_\Omega \lambda q_\varepsilon \ln m_\varepsilon \le \lambda \int_{\{m_\varepsilon \ge 1\}} q_\varepsilon \ln m_\varepsilon \le \lambda A \int_{\{m_\varepsilon \ge 1\}} m_\varepsilon \le \lambda AB,
$$

as well as $\xi \ln \xi \ge -\frac{1}{\mathrm{e}}$ for all $\xi > 0$ and that there exists $C > 0$ such that

$$
\xi^\theta \ln \xi \le -\frac{1}{2}\xi^\theta \ln(\xi + 2) + C
$$

holds for all $\xi > 0$ (Lemma 4.2 in [SSW14]). This completes the proof. □

Now, we want to cancel the two terms on the right-hand side. For the first term we may proceed as in [SSU16], we note that we obtain some simplified version as we assumed $\kappa_\varepsilon \equiv 1$.

Lemma 2.7. *For any $\varepsilon \in (0,1)$ we have*

$$
\begin{aligned}
\partial_t \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon} &\le 2\varepsilon \frac{1}{1+v_\varepsilon}\nabla v_\varepsilon \cdot \nabla \Delta v_\varepsilon - \varepsilon \frac{1}{(1+v_\varepsilon)^2}|\nabla v_\varepsilon|^2 \Delta v_\varepsilon \\
&\quad - 2\alpha \frac{v_\varepsilon}{1+v_\varepsilon}\nabla m_\varepsilon \cdot \nabla v_\varepsilon + \frac{\beta^2}{2\mu_v}|\nabla q_\varepsilon|^2 - 2\alpha m_\varepsilon \frac{|\nabla v_\varepsilon|^2}{(1+v_\varepsilon)^2} + 2\mu_v \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon}
\end{aligned}
$$

for all $x \in \Omega$ and $t > 0$.

Proof. This is essentially Lemma 3.10 in [SSU16]. □

In the above estimate the first two terms are not controllable yet so we examine them separately. As the previous lemma, this is similar to [SSU16] but again easier, as no derivatives of κ_ε appear.

Lemma 2.8. *For any $T > 0$ there exists $C_{15}(T) > 0$ such that for each $\varepsilon \in (0,1)$*

$$2\varepsilon \int_\Omega \frac{1}{1+v_\varepsilon} \nabla v_\varepsilon \cdot \nabla \Delta v_\varepsilon - \varepsilon \int_\Omega \frac{1}{(1+v_\varepsilon)^2} |\nabla v_\varepsilon|^2 \Delta v_\varepsilon \leq \varepsilon C_{15}(T) \int_\Omega \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon}$$

is satisfied for all $t \in (0,T)$.

Proof. This is an immediate consequence of Lemma 3.11 in [SSU16] (with $\kappa_\varepsilon \equiv 1$). □

Now, we need to deal with the second term on the right-hand side in Lemma 2.6 and choose g to be constant. For this purpose we mimic Lemma 2.7 above.

Lemma 2.9. *Let g be constant. For any $\varepsilon \in (0,1)$ and arbitrary $\delta \in (0,2)$ we have*

$$\begin{aligned} \partial_t \left(g |\nabla q_\varepsilon|^2 \right) \leq{}& 2\varepsilon g \nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + 2g\gamma \nabla q_\varepsilon \cdot \nabla m_\varepsilon + 3g\mu_q |\nabla q_\varepsilon|^2 \\ &+ g\mu_q \eta_1^2 A^2 (1+L) \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon} + \frac{1}{(2-\delta)} g\mu_q A^2 \frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} - \delta g \mu_q m_\varepsilon |\nabla q_\varepsilon|^2 \end{aligned}$$

for all $x \in \Omega$ and $t > 0$.

Proof. We use the second equation of (2.1), as well as the chain and product rule to obtain

$$\begin{aligned} \partial_t (g |\nabla q_\varepsilon|^2) &= 2g \nabla q_\varepsilon \cdot \nabla (\partial_t q_\varepsilon) \\ &= 2\varepsilon g \nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + 2g\mu_q |\nabla q_\varepsilon|^2 - 2g\mu_q m_\varepsilon |\nabla q_\varepsilon|^2 - 2g\mu_q q_\varepsilon \nabla q_\varepsilon \cdot \nabla m_\varepsilon \\ &\quad - 4g\mu_q q_\varepsilon |\nabla q_\varepsilon|^2 - 2g\mu_q \eta_1 q_\varepsilon \nabla v_\varepsilon \cdot \nabla q_\varepsilon - 2g\mu_q \eta_1 v_\varepsilon |\nabla q_\varepsilon|^2 \\ &\quad - 2g\lambda |\nabla q_\varepsilon|^2 + 2g\gamma \nabla q_\varepsilon \cdot \nabla m_\varepsilon - 2g r_q(t) |\nabla q_\varepsilon|^2 \\ &\leq 2\varepsilon g \nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + 2g\gamma \nabla q_\varepsilon \cdot \nabla m_\varepsilon + 2g\mu_q |\nabla q_\varepsilon|^2 - 2g\mu_q m_\varepsilon |\nabla q_\varepsilon|^2 \\ &\quad - 2g\mu_q q_\varepsilon \frac{\sqrt{m_\varepsilon}}{\sqrt{m_\varepsilon}} \nabla q_\varepsilon \cdot \nabla m_\varepsilon - 2g\mu_q \eta_1 q_\varepsilon \nabla q_\varepsilon \cdot \nabla v_\varepsilon \end{aligned}$$

for all $x \in \Omega$ and $t > 0$ after dropping most of the negative terms. Applying Young's inequality to the two last terms yields

$$\partial_t (g |\nabla q_\varepsilon|^2) \leq 2\varepsilon g \nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + 2g\gamma \nabla q_\varepsilon \cdot \nabla m_\varepsilon + 3g\mu_q |\nabla q_\varepsilon|^2$$

$$+\frac{1}{(2-\delta)} g\mu_q A^2 \frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} + g\mu_q \eta_1^2 A^2 |\nabla v_\varepsilon|^2 - \delta g\mu_q m_\varepsilon |\nabla q_\varepsilon|^2$$

for all $x \in \Omega$ and $t > 0$ which after expanding with $\frac{1+v_\varepsilon}{1+v_\varepsilon}$ and estimating the numerator proves the claim. □

The second term will cancel out with the respective term in Lemma 2.6. The reason for expanding the second last term will become clear later. The last term will be absorbed into the left-hand side later on. In order to achieve this, we need to require an appropriate smallness condition on g to be stated in Proposition 2.13.

Similar to Lemma 2.8 it remains to estimate the first term separately.

Lemma 2.10. *Let g be constant. For any $T > 0$ there exists $C_{16}(T) > 0$ such that for any $\varepsilon \in (0,1)$ we have*

$$2\varepsilon g \int_\Omega \nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon \le \varepsilon C_{16}(T) \int_\Omega g |\nabla q_\varepsilon|^2$$

for all $t \in (0,T)$.

Proof. Using that the Neumann condition on v_ε implies $\partial_\nu |\nabla q_\varepsilon|^2 \le C(\Omega) |\nabla q_\varepsilon|^2$ on $\partial\Omega$ with some $C(\Omega)$ depending only on the curvatures of Ω (see [MS14, Lemma 4.2]), we may integrate by parts and have

$$\begin{aligned}
2\varepsilon g \int_\Omega \nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon &= 2\varepsilon g \sum_{i,j=1}^n \int_\Omega \partial_j q_\varepsilon \partial_{iij} q_\varepsilon \\
&\le -2\varepsilon g \sum_{i,j=1}^n \int_\Omega (\partial_{ij} q_\varepsilon)^2 + \varepsilon C(\Omega) \int_{\partial\Omega} g |\nabla q_\varepsilon|^2 \,\mathrm{d}\sigma \\
&= -2\varepsilon g \int_\Omega \left| \mathrm{D}^2 q_\varepsilon \right|^2 + \varepsilon C(\Omega) \int_{\partial\Omega} g |\nabla q_\varepsilon|^2 \,\mathrm{d}\sigma.
\end{aligned}$$

The boundary term will be estimated similarly as in Lemma 3.11 of [SSU16]. We fix $r \in (0, \frac{1}{2})$, set $a \coloneqq r + \frac{1}{2}$ and use the compact embedding of $\mathrm{W}^{r+\frac{1}{2},2}(\Omega)$ into $\mathrm{L}^2(\partial\Omega)$ (see [HT08, Theorem 4.24 and Proposition 4.22]) and the fractional Gagliardo-Nirenberg inequality (see [ISY14, Lemma 2.5]). Then we obtain with Young's inequality that for any $\eta > 0$ there is $C_\eta > 0$ such that

$$\begin{aligned}
\varepsilon g \int_{\partial\Omega} |\nabla q_\varepsilon|^2 \,\mathrm{d}\sigma &\le \varepsilon g C \|\nabla q_\varepsilon\|^2_{\mathrm{W}^{r+\frac{1}{2},2}(\Omega)} \\
&\le \varepsilon g C \left(\|\nabla |\nabla q_\varepsilon|\|^{2a}_{\mathrm{L}^2(\Omega)} \|\nabla q_\varepsilon\|^{2(1-a)}_{\mathrm{L}^2(\Omega)} + \|\nabla q_\varepsilon\|^2_{\mathrm{L}^2(\Omega)} \right)
\end{aligned}$$

$$\leq g\eta\varepsilon \left\|\nabla \left|\nabla q_\varepsilon\right|\right\|_{L^2(\Omega)}^2 + \varepsilon C_\eta g \left\|\nabla q_\varepsilon\right\|_{L^2(\Omega)}^2$$
$$\leq \eta\varepsilon \int_\Omega g \left|D^2 q_\varepsilon\right|^2 + \varepsilon C_\eta g \left\|\nabla q_\varepsilon\right\|_{L^2(\Omega)}^2$$

holds true. Choosing $\eta = 2$ and combining this with the previous estimate proves the claim. Note that the constant C may change from the first to the second line. □

Having dealt with the case where $g(q_\varepsilon)$ is constant, we want to examine other possible choices of $g(q_\varepsilon)$. In the non-constant case derivatives of $g(q_\varepsilon)$ will come into play which will have an impact on Lemmas 2.9 and 2.10. Following the method presented in [SSU16] seems to suggest that the analogue of Lemma 2.9 requires less restrictions on $g(q_\varepsilon)$ than the one of Lemma 2.10. In the sequel we consider $g(q_\varepsilon) := \frac{c}{1+q_\varepsilon}$ where $c > 0$ is a constant to be restricted later.

Lemma 2.11. *For any $\varepsilon \in (0,1)$ and $\delta \in (0,2)$ we have*

$$\begin{aligned}\partial_t \frac{c\left|\nabla q_\varepsilon\right|^2}{1+q_\varepsilon} \leq &- \varepsilon \frac{c\left|\nabla q_\varepsilon\right|^2}{(1+q_\varepsilon)^2}\Delta q_\varepsilon + 2\varepsilon \frac{c}{1+q_\varepsilon}\nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + \frac{c}{2-\delta}\mu_q A^2 \frac{\left|\nabla m_\varepsilon\right|^2}{m_\varepsilon} \\ &- \delta \frac{c\mu_q m_\varepsilon}{(1+q_\varepsilon)^2}\left|\nabla q_\varepsilon\right|^2 + (1+L)\mu_q \eta_1^2 c A^2 \frac{\left|\nabla v_\varepsilon\right|^2}{1+v_\varepsilon} + 3\mu_q c \frac{\left|\nabla q_\varepsilon\right|^2}{(1+q_\varepsilon)^2} \\ &+ 2\gamma g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla m_\varepsilon\end{aligned}$$

for all $x \in \Omega$ and $t > 0$.

Proof. The proof is done similarly as the one of Lemma 3.10 in [SSU16]. Again by the second equation of (2.1) together with the chain and product rule we obtain

$$\begin{aligned}\partial_t \frac{c\left|\nabla q_\varepsilon\right|^2}{1+q_\varepsilon} &= - \frac{c}{(1+q_\varepsilon)^2}\partial_t q_\varepsilon \left|\nabla q_\varepsilon\right|^2 + 2\frac{c}{1+q_\varepsilon}\nabla q_\varepsilon \nabla(\partial_t q_\varepsilon) \\ &= - \frac{c\left|\nabla q_\varepsilon\right|^2}{(1+q_\varepsilon)^2}\varepsilon\Delta q_\varepsilon + 2\varepsilon\frac{c}{1+q_\varepsilon}\nabla q_\varepsilon \cdot \nabla\Delta q_\varepsilon - 2\mu_q q_\varepsilon \frac{c}{1+q_\varepsilon}\nabla q_\varepsilon \cdot \nabla m_\varepsilon \\ &\quad - 2\mu_q \eta_1 q_\varepsilon \frac{c}{1+q_\varepsilon}\nabla v_\varepsilon \cdot \nabla q_\varepsilon + 2\gamma g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla m_\varepsilon + \frac{c\left|\nabla q_\varepsilon\right|^2}{(1+q_\varepsilon)^2}\Big(- \mu_q q_\varepsilon \\ &\quad + \mu_q m_\varepsilon q_\varepsilon + \mu_q q_\varepsilon^2 + \mu_q q_\varepsilon \eta_1 v_\varepsilon + \lambda q_\varepsilon - \gamma m_\varepsilon + r_q(t) q_\varepsilon + 2\mu_q(1+q_\varepsilon) \\ &\quad - 2\mu_q m_\varepsilon(1+q_\varepsilon) - 4\mu_q q_\varepsilon(1+q_\varepsilon) - 2\mu_q \eta_1 v_\varepsilon(1+q_\varepsilon) - 2\lambda(1+q_\varepsilon) \\ &\quad - 2r_q(t)(1+q_\varepsilon)\Big)\end{aligned}$$

for all $x \in \Omega$ and $t > 0$. Next, we apply Young's inequality to the third and fourth term and drop most negative parts of the last term. This gives us

$$
\begin{aligned}
\partial_t \frac{c\,|\nabla q_\varepsilon|^2}{1+q_\varepsilon} \le& -\varepsilon \frac{c\,|\nabla q_\varepsilon|^2}{(1+q_\varepsilon)^2}\Delta q_\varepsilon + 2\varepsilon \frac{c}{1+q_\varepsilon}\nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + \frac{c}{2-\delta}\mu_q q_\varepsilon^2 \frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} \\
&+ (2-\delta)\frac{c\mu_q m_\varepsilon}{(1+q_\varepsilon)^2}|\nabla q_\varepsilon|^2 + \mu_q \eta_1^2 c q_\varepsilon^2 |\nabla v_\varepsilon|^2 + \mu_q c \frac{|\nabla q_\varepsilon|^2}{(1+q_\varepsilon)^2} \\
&+ \frac{c\,|\nabla q_\varepsilon|^2}{(1+q_\varepsilon)^2}(-2\mu_q m_\varepsilon + 2\mu_q) + 2\gamma g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla m_\varepsilon \\
\le& -\frac{c\,|\nabla q_\varepsilon|^2}{(1+q_\varepsilon)^2}\varepsilon \Delta q_\varepsilon + 2\varepsilon \frac{c}{1+q_\varepsilon}\nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + \frac{c}{2-\delta}\mu_q A^2 \frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} \\
&- \delta \frac{c\mu_q m_\varepsilon}{(1+q_\varepsilon)^2}|\nabla q_\varepsilon|^2 + (1+L)\mu_q \eta_1^2 c A^2 \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon} + 3\mu_q c \frac{|\nabla q_\varepsilon|^2}{(1+q_\varepsilon)^2} \\
&+ 2\gamma g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla m_\varepsilon
\end{aligned}
$$

for all $x \in \Omega$ and $t > 0$ which proves the claim. □

In contrast to Lemma 2.10 but very similarly to Lemma 2.8 we have more terms on the right hand side which we cannot control yet.

Lemma 2.12. *For any $T > 0$ there exists $C_{17}(T) > 0$ such that for each $\varepsilon \in (0,1)$*

$$
2\varepsilon \int_\Omega \frac{c}{1+q_\varepsilon}\nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon - \varepsilon \int_\Omega \frac{c}{(1+q_\varepsilon)^2}|\nabla q_\varepsilon|^2 \Delta q_\varepsilon \le \varepsilon C_{17}(T) \int_\Omega \frac{c\,|\nabla q_\varepsilon|^2}{1+q_\varepsilon}
$$

is satisfied for all $t \in (0,T)$.

Proof. Here, we will only show why our choice of $g(q_\varepsilon)$ is a good one and why, at least with this method, other choices which work in the previous lemma fail here. So, for general $g(q_\varepsilon)$ the to be estimated term is

$$
2\varepsilon \int_\Omega g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon + \varepsilon \int_\Omega g'(q_\varepsilon)|\nabla q_\varepsilon|^2 \Delta q_\varepsilon.
$$

Performing integration by parts on both terms separately, we obtain

$$
\begin{aligned}
\int_\Omega 2g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla \Delta q_\varepsilon =& \sum_{i,j=1}^n \int_\Omega 2g(q_\varepsilon)\partial_j q_\varepsilon \partial_{iij} q_\varepsilon \\
=& -\sum_{i,j=1}^n \int_\Omega 2g'(q_\varepsilon)\partial_i q_\varepsilon \partial_j q_\varepsilon \partial_{ij} q_\varepsilon - \sum_{i,j=1}^n \int_\Omega 2g(q_\varepsilon)\partial_{ij} q_\varepsilon \partial_{ij} q_\varepsilon
\end{aligned}
$$

$$
\begin{aligned}
&+ \int_{\partial\Omega} \sum_{i,j=1}^{n} 2g(q_\varepsilon)\partial_j q_\varepsilon \partial_{ij} q_\varepsilon \cdot \nu_i \\
&= - \sum_{i,j=1}^{n} \int_\Omega 2g'(q_\varepsilon)\partial_i q_\varepsilon \partial_j q_\varepsilon \partial_{ij} q_\varepsilon - \sum_{i,j=1}^{n} \int_\Omega 2g(q_\varepsilon)\partial_{ij} q_\varepsilon \partial_{ij} q_\varepsilon \\
&+ \int_{\partial\Omega} g(q_\varepsilon)\partial_\nu \left|\nabla q_\varepsilon\right|^2
\end{aligned}
$$

as well as

$$
\begin{aligned}
\int_\Omega g'(q_\varepsilon) \left|\nabla q_\varepsilon\right|^2 \Delta q_\varepsilon &= \int_\Omega \sum_{i,j=1}^{n} g'(q_\varepsilon)(\partial_j q_\varepsilon)^2 \partial_{ii} q_\varepsilon \\
&= - \sum_{i,j=1}^{n} \int_\Omega g''(q_\varepsilon)(\partial_j q_\varepsilon)^2(\partial_i q_\varepsilon)^2 - \sum_{i,j=1}^{n} \int_\Omega 2g'(q_\varepsilon)\partial_{ij} q_\varepsilon \partial_i q_\varepsilon \partial_j q_\varepsilon \\
&+ \sum_{i,j=1}^{n} \int_{\partial\Omega} g'(q_\varepsilon)(\partial_j q_\varepsilon)^2 \partial_i q_\varepsilon \nu_i
\end{aligned}
$$

where the boundary integral vanishes due to the Neumann boundary condition. Neglecting the boundary term and adding the remaining terms, we are left to estimate the following term

$$
- \sum_{i,j=1}^{n} \int_\Omega g''(q_\varepsilon)(\partial_j q_\varepsilon)^2(\partial_i q_\varepsilon)^2 - \sum_{i,j=1}^{n} 4 \int_\Omega g'(q_\varepsilon)\partial_{ij} q_\varepsilon \partial_i q_\varepsilon \partial_j q_\varepsilon - \sum_{i,j=1}^{n} \int_\Omega 2g(q_\varepsilon)(\partial_{ij} q_\varepsilon)^2.
$$

A possible way to deal with this term is to add an appropriate term to apply the binomial theorem. A suitable choice would be

$$
- \left(2g \left(\frac{g'}{g} \right)^2 - g'' \right) (\partial_i q_\varepsilon)^2 (\partial_j q_\varepsilon)^2.
$$

This term is positive if and only if g satisfies the differential inequality

$$
\left(2g \left(\frac{g'}{g} \right)^2 - g'' \right) \leq 0. \tag{2.9}
$$

The above is satisfied with equality by functions of the form $\frac{c}{1+q_\varepsilon}$ and so these are a possible choice for g. With that choice we are in the situation of Lemma 3.11 in [SSU16] and the proof is identical to the one presented there (after changing v_ε to q_ε and $\kappa_\varepsilon \equiv c$). □

Other functions which work in Lemma 2.11, as for example exponential functions of the form e^{Cx} with some for Lemma 2.11 suitable $C > 0$ fail to satisfy the differential inequality (2.9). Hence, the method presented here does not work for such choices and it is left open whether an analogue of Lemma 2.12 can be shown in that case.

Finally, we can put the previous results together to obtain the following estimate based on an entropy-type functional.

Proposition 2.13. *Let* $\delta \in (0,2)$ *and either* $0 < g \leq \frac{1}{2}\left(\frac{4\gamma C_2(1-\frac{\delta}{2})}{\mu_q A^2}\right)$ *be constant or* $g(q_\varepsilon) = \frac{c}{1+q_\varepsilon}$ *where* c *satisfies* $0 < c \leq \frac{1}{2}\left(\frac{4\gamma C_2(1-\frac{\delta}{2})}{\mu_q A^2}\right)$ *where* C_2 *denotes the lower bound for* D *(see* (1.7)*) and let* $T > 0$*. Then there exists* $C_{18}(T) > 0$ *such that for any* $\varepsilon \in (0,1)$ *the solution to* (2.1) *satisfies*

$$\sup_{t\in(0,T)}\left\{\int_\Omega m_\varepsilon \ln m_\varepsilon + \int_\Omega \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon} + \int_\Omega g(q_\varepsilon)\,|\nabla q_\varepsilon|^2\right\} + \int_0^T\int_\Omega D(m_\varepsilon,q_\varepsilon,v_\varepsilon)\frac{|\nabla m_\varepsilon|^2}{m_\varepsilon}$$
$$+ \int_0^T\int_\Omega m_\varepsilon\frac{|\nabla v_\varepsilon|^2}{(1+v_\varepsilon)^2} + \int_0^T\int_\Omega g(q_\varepsilon) m_\varepsilon\,|\nabla q_\varepsilon|^2 + \varepsilon\int_0^T\int_\Omega m_\varepsilon^\theta \ln(m_\varepsilon+2) \leq C_{18}(T).$$

Proof. We first prove the proposition for the case that $g(q_\varepsilon)$ is constant. The proof for the non-constant case is the same after changing Lemma 2.9 and 2.10 to Lemma 2.11 and 2.12.

The proof relies on finding an estimate for an energy-type functional. To this end we integrate the result of Lemma 2.7 over Ω and combine it with Lemma 2.8 to deduce the existence of $C_{19}(T) > 0$ such that

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon} + \int_\Omega 2\alpha m_\varepsilon\frac{|\nabla v_\varepsilon|^2}{(1+v_\varepsilon)^2} \leq -\int_\Omega 2\alpha\frac{v_\varepsilon}{1+v_\varepsilon}\nabla m_\varepsilon\cdot\nabla v_\varepsilon$$
$$+ C_{19}(T)\left(\int_\Omega |\nabla q_\varepsilon|^2 + \int_\Omega \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon}\right)$$

holds for all $t \in (0,T)$. Multiplying the last inequality with $\frac{1}{2\alpha}$ and adding it to Lemma 2.6, we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\left(\int_\Omega m_\varepsilon \ln m_\varepsilon + \int_\Omega \frac{1}{2\alpha}\frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon}\right) + \int_\Omega D(m_\varepsilon,q_\varepsilon,v_\varepsilon)\frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} + \int_\Omega m_\varepsilon\frac{|\nabla v_\varepsilon|^2}{(1+v_\varepsilon)^2}$$
$$+\frac{\varepsilon}{2}\int_\Omega m_\varepsilon^\theta\ln(m_\varepsilon+2) \leq -\int_\Omega g\nabla q_\varepsilon\cdot\nabla m_\varepsilon + \frac{C_{19}(T)}{2\alpha}\left(\int_\Omega |\nabla q_\varepsilon|^2 + \int_\Omega\frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon}\right) + C_{14} \tag{2.10}$$

for all $t \in (0,T)$. Next, we combine Lemma 2.10 with the integrated version of Lemma 2.9 and have

$$\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega g\,|\nabla q_\varepsilon|^2 + \delta\int_\Omega g\mu_q m_\varepsilon\,|\nabla q_\varepsilon|^2 \leq \int_\Omega 2\gamma g\nabla q_\varepsilon\cdot\nabla m_\varepsilon + \frac{1}{(2-\delta)}\int_\Omega g\mu_q A^2\frac{|\nabla m_\varepsilon|^2}{m_\varepsilon}$$

$$+ C_{20}(T)\left(\int_\Omega g\left|\nabla q_\varepsilon\right|^2 + \int_\Omega \frac{\left|\nabla v_\varepsilon\right|^2}{1+v_\varepsilon}\right)$$

for all $t \in (0,T)$ with some $C_{20}(T) > 0$. Now, we multiply the last equation with $\frac{1}{2\gamma}$ and add it to (2.10) to obtain (noting the smallness condition on g)

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t}\left(\int_\Omega m_\varepsilon \ln m_\varepsilon + \int_\Omega \frac{1}{2\alpha}\frac{\left|\nabla v_\varepsilon\right|^2}{1+v_\varepsilon} + \int_\Omega \frac{1}{2\gamma} g\left|\nabla q_\varepsilon\right|^2\right) + \int_\Omega \frac{1}{2} D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\frac{\left|\nabla m_\varepsilon\right|^2}{m_\varepsilon} \\
&\quad + \int_\Omega m_\varepsilon \frac{\left|\nabla v_\varepsilon\right|^2}{(1+v_\varepsilon)^2} + \int_\Omega \frac{\delta}{2\gamma}\mu_q g m_\varepsilon \left|\nabla q_\varepsilon\right|^2 + \frac{\varepsilon}{2}\int_\Omega m_\varepsilon^\theta \ln(m_\varepsilon + 2) \\
&\leq C_{21}(T)\left(\int_\Omega g\left|\nabla q_\varepsilon\right|^2 + \int_\Omega \frac{\left|\nabla v_\varepsilon\right|^2}{1+v_\varepsilon}\right) + C_{14} \qquad (2.11)
\end{aligned}$$

for all $t \in (0,T)$ and some $C_{21}(T) > 0$ where C_{14} was specified in Lemma 2.6. We define for $t \geq 0$ the non-negative functions

$$\mathcal{E}_\varepsilon(t) := \int_\Omega m_\varepsilon \ln m_\varepsilon + \int_\Omega \frac{1}{2\alpha}\frac{\left|\nabla v_\varepsilon\right|^2}{1+v_\varepsilon} + \int_\Omega \frac{1}{2\gamma} g\left|\nabla q_\varepsilon\right|^2 + \frac{|\Omega|}{\mathrm{e}}$$

and

$$\begin{aligned}
\mathcal{D}_\varepsilon(t) := &\frac{1}{2}\int_\Omega D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\frac{\left|\nabla m_\varepsilon^2\right|}{m_\varepsilon} + \int_\Omega m_\varepsilon \frac{\left|\nabla v_\varepsilon\right|^2}{(1+v_\varepsilon)^2} \\
&+ \int_\Omega \frac{\delta g}{2\gamma}\mu_q m_\varepsilon \left|\nabla q_\varepsilon\right|^2 + \frac{\varepsilon}{2}\int_\Omega m_\varepsilon^\theta \ln(m_\varepsilon + 2).
\end{aligned}$$

We note that the last term in the definition of $\mathcal{E}_\varepsilon$ guarantees the positivity of this function. Moreover, it is necessary to deal with the constant on the right-hand side in the previous estimate. Now, we obtain from (2.11) that there exists $C_{22}(T) > 0$ such that

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathcal{E}_\varepsilon(t) + \mathcal{D}_\varepsilon(t) \leq C_{22}(T)\mathcal{E}_\varepsilon(t) \qquad (2.12)$$

holds for all $t \in (0,T)$.

Now, we derive a similar estimate for the non-constant case. We note that (2.10) still holds (of course after replacing g by $g(q_\varepsilon)$). Combining Lemma 2.12 with the integrated version of Lemma 2.11 and dividing by 2γ we obtain

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\int_\Omega \frac{g(q_\varepsilon)}{2\gamma}\left|\nabla q_\varepsilon\right|^2 + \int_\Omega \frac{\delta}{2\gamma}\frac{g(q_\varepsilon)}{1+q_\varepsilon} m_\varepsilon \left|\nabla q_\varepsilon\right|^2 &\leq \int_\Omega g(q_\varepsilon)\nabla q_\varepsilon \cdot \nabla m_\varepsilon + \int_\Omega \frac{c\mu_q A^2}{2\gamma(2-\delta)}\frac{\left|\nabla m_\varepsilon\right|^2}{m_\varepsilon} \\
&\quad + C_{23}(T)\left(\int_\Omega g(q_\varepsilon)\left|\nabla q_\varepsilon\right|^2 + \int_\Omega \frac{\left|\nabla v_\varepsilon\right|^2}{1+v_\varepsilon}\right)
\end{aligned}$$

for all $t \in (0,T)$ and $C_{23}(T) > 0$. Now, adding the above estimate to (2.10) we find $C_{24}(T) > 0$ satisfying

$$\begin{aligned}
&\frac{\mathrm{d}}{\mathrm{d}t}\left(\int_\Omega m_\varepsilon \ln m_\varepsilon + \int_\Omega \frac{1}{2\alpha}\frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon} + \int_\Omega \frac{1}{2\gamma} g(q_\varepsilon)\,|\nabla q_\varepsilon|^2\right) + \int_\Omega \frac{1}{2} D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} \\
&\quad + \int_\Omega m_\varepsilon \frac{|\nabla v_\varepsilon|^2}{(1+v_\varepsilon)^2} + \int_\Omega \frac{\delta}{2\gamma}\mu_q \frac{g(q_\varepsilon)}{1+q_\varepsilon} m_\varepsilon\,|\nabla q_\varepsilon|^2 + \frac{\varepsilon}{2}\int_\Omega m_\varepsilon^\theta \ln(m_\varepsilon + 2) \\
&\le C_{24}(T)\left(\int_\Omega g\,|\nabla q_\varepsilon|^2 + \int_\Omega \frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon}\right) + C_{14} \qquad (2.13)
\end{aligned}$$

which is very similar to (2.11) after replacing g by $g(q_\varepsilon)$. Due to the positivity of q_ε we may replace $(1+q_\varepsilon)$ by $(1+A)$ in the denominator of the second term in the second line of (2.13) to obtain the analogous estimate of (2.12) (once more after the obvious change from g to $g(q_\varepsilon)$ in the definition of $\mathcal{E}_\varepsilon$ and $\mathcal{D}_\varepsilon$).

Now, we may proceed as in the proof of Lemma 4.1 in [SSW14]. Noting the positivity of $\mathcal{D}_\varepsilon$ and integrating (2.12) we obtain

$$\mathcal{E}_\varepsilon(t) \le \mathcal{E}_\varepsilon(0)\mathrm{e}^{C_{22}(T)t}.$$

Using that $C_{25} := \sup_{\varepsilon\in(0,1)} \mathcal{E}_\varepsilon(0)$ is finite due to the choice of the approximating initial conditions, this implies

$$\mathcal{E}_\varepsilon(t) \le C_{25}\cdot \mathrm{e}^{C_{22}(T)T}.$$

for all $t \in (0,T)$. With another integration of (2.12) we deduce the existence of some $C_{26}(T) > 0$ such that

$$\sup_{t\in(0,T)} \mathcal{E}_\varepsilon(t) \le C_{26}(T) \quad \text{and} \quad \int_0^T \mathcal{D}_\varepsilon(t)\,\mathrm{d}t \le C_{26}(T)$$

holds. This completes the proof. □

Note that we can improve the bound on g by exchanging $\frac{1}{2}$ by $(1-\delta_1)$ for some $\delta_1 \in (0,1)$. The previous estimate will enable us to find a suitable sequence $(\varepsilon_j) \searrow 0$ such that the solution components converge to a weak solution of the original problem.

3. Global Weak Solution to the Original Problem

In this chapter we will construct a global weak solution of the original problem (1.2)-(1.4) in the sense of Definition 1.1 under the assumptions stated in Theorem 1.2. To this end we show compactness properties of the solutions of (2.1) based on the ideas of Section 3.3 of [SSU16]. A central tool in this chapter is the Aubin-Lions lemma (for details and several versions of this compactness result we refer the interested reader to [Tem77, Chapter III, Section 2]).

First we examine m_ε. The proof of the following lemma is based on Lemma 3.14 in [SSU16] and has to be adapted only slightly in view of the additional term in the first equation of (2.1).

Lemma 3.1. *Let $T > 0$ be arbitrary. Then there exists a constant $C_{27}(T) > 0$ such that for any $\varepsilon \in (0,1)$ the estimate*

$$\int_0^T \left\| \sqrt{1 + m_\varepsilon(\cdot,t)} \right\|_{\mathrm{W}^{1,2}(\Omega)}^2 \mathrm{d}t \leq C_{27}(T) \tag{3.1}$$

is satisfied. In addition, $(\sqrt{1+m_\varepsilon})_{\varepsilon\in(0,1)}$ is strongly precompact in $\mathrm{L}^2((0,T);\mathrm{L}^p(\Omega))$ for any $p \in (1,6)$ and $(m_\varepsilon)_{\varepsilon\in(0,1)}$ is strongly precompact in $\mathrm{L}^1((0,T);\mathrm{L}^2(\Omega))$.

Proof. We want to apply the Aubin-Lions lemma to the family $(\sqrt{1+m_\varepsilon})_{\varepsilon\in(0,1)}$. To this end we need to find ε-independent bounds for both the above family and the family of the respective time derivatives in suitable spaces. We start with the bound on $(\sqrt{1+m_\varepsilon})_{\varepsilon\in(0,1)}$. In view of the assumption on D (see (1.7)) as well as Lemma 2.4 and Proposition 2.13 we obtain (3.1) similarly as in [SSU16], noting that we chose $\kappa_\varepsilon \equiv 1$.

It remains to estimate the time derivatives. For this purpose let $k \in \mathbb{N}$ such that $k > \frac{n+2}{2}$.

We claim that

$$\int_0^T \left\|\partial_t \sqrt{1+m_\varepsilon(\cdot,t)}\right\|_{(\mathrm{W}_0^{k,2}(\Omega))^*} \mathrm{d}t \le C_{28}(T) \tag{3.2}$$

holds for some $C_{28}(T) > 0$. By Hölder's inequality it is clear that for each $\varepsilon \in (0,1)$ and $t \in (0,T)$ the function $\partial_t \sqrt{1+m_\varepsilon(\cdot,t)}$ induces a linear and continuous functional on $\mathrm{W}_0^{k,2}(\Omega)$. In order to prove the above estimate we fix $\Psi \in \mathrm{C}_0^\infty(\Omega)$ and integrate by parts to deduce from the first equation in (2.1)

$$\begin{aligned}
2\int_0^T\int_\Omega \partial_t\sqrt{1+m_\varepsilon}\Psi &= \int_0^T\int_\Omega \partial_t m_\varepsilon \frac{\Psi}{\sqrt{1+m_\varepsilon}}\\
&= \int_0^T\int_\Omega \nabla\cdot(D(m_\varepsilon,q_\varepsilon,v_\varepsilon)\nabla m_\varepsilon)\frac{\Psi}{\sqrt{1+m_\varepsilon}}\\
&\quad - \int_0^T\int_\Omega \nabla\cdot\left(\frac{v_\varepsilon}{1+v_\varepsilon}m_\varepsilon\nabla v_\varepsilon\right)\frac{\Psi}{\sqrt{1+m_\varepsilon}}\\
&\quad + \int_0^T\int_\Omega \nabla\cdot(g(q_\varepsilon)m_\varepsilon\nabla q_\varepsilon)\frac{\Psi}{\sqrt{1+m_\varepsilon}}\\
&\quad + \int_0^T\int_\Omega (\lambda q_\varepsilon - \gamma m_\varepsilon - r_m(t)m_\varepsilon - \varepsilon m_\varepsilon^\theta)\frac{\Psi}{\sqrt{1+m_\varepsilon}}\\
&= -\int_0^T\int_\Omega \frac{D(m_\varepsilon,q_\varepsilon,v_\varepsilon)}{(1+m_\varepsilon)^{\frac12}}\nabla m_\varepsilon\cdot\nabla\Psi + \frac12\int_0^T\int_\Omega \frac{D(m_\varepsilon,q_\varepsilon,v_\varepsilon)}{(1+m_\varepsilon)^{\frac32}}|\nabla m_\varepsilon|^2\Psi\\
&\quad + \int_0^T\int_\Omega \frac{v_\varepsilon}{(1+v_\varepsilon)(1+m_\varepsilon)^{\frac12}}m_\varepsilon\nabla v_\varepsilon\cdot\nabla\Psi\\
&\quad - \frac12\int_0^T\int_\Omega \frac{v_\varepsilon}{(1+v_\varepsilon)(1+m_\varepsilon)^{\frac32}}m_\varepsilon\Psi\nabla v_\varepsilon\cdot\nabla m_\varepsilon - \int_0^T\int_\Omega \frac{g(q_\varepsilon)m_\varepsilon}{(1+m_\varepsilon)^{\frac12}}\nabla q_\varepsilon\cdot\nabla\Psi\\
&\quad + \frac12\int_0^T\int_\Omega \frac{g(q_\varepsilon)m_\varepsilon}{(1+m_\varepsilon)^{\frac32}}\nabla q_\varepsilon\cdot\nabla m_\varepsilon\Psi\\
&\quad + \int_0^T\int_\Omega (\lambda q_\varepsilon - \gamma m_\varepsilon - r_m(t)m_\varepsilon - \varepsilon m_\varepsilon^\theta)\frac{\Psi}{\sqrt{1+m_\varepsilon}}.
\end{aligned}$$

All the terms without $g(q_\varepsilon)$ can be estimated as in the proof of Lemma 3.14 in [SSU16] (note again that here we have $\kappa_\varepsilon \equiv 1$). Hence, it remains to find a suitable estimate on the second and third last term. Using Cauchy-Schwarz, Young's inequality, norm equivalence in $\mathbb{R}^n$ as well as Lemma 2.4 and Proposition 2.13 we find

$$\begin{aligned}
-\int_0^T\int_\Omega \frac{g(q_\varepsilon)m_\varepsilon}{(1+m_\varepsilon)^{\frac12}}\nabla q_\varepsilon\cdot\nabla\Psi &\le \sqrt{n}\,\|\nabla\Psi\|_{\mathrm{L}^\infty(\Omega)}\int_0^T\int_\Omega \frac{g(q_\varepsilon)m_\varepsilon}{(1+m_\varepsilon)^{\frac12}}|\nabla q_\varepsilon|\\
&\le \frac{\sqrt{n}}{2}\|\nabla\Psi\|_{\mathrm{L}^\infty(\Omega)}\left(\int_0^T\int_\Omega \frac{g(q_\varepsilon)m_\varepsilon^2}{1+m_\varepsilon} + \int_0^T\int_\Omega g(q_\varepsilon)|\nabla q_\varepsilon|^2\right)\\
&\le T\,\|\nabla\Psi\|_{\mathrm{L}^\infty(\Omega)}\left(B\,\|g\|_{\mathrm{L}^\infty([0,A])} + C_{18}(T)\right)
\end{aligned}$$

with $C_{18}(T)$ from Proposition 2.13. The other term including $g(q_\varepsilon)$ can be estimated similarly to obtain

$$\begin{aligned}
&\int_0^T \int_\Omega \frac{g(q_\varepsilon) m_\varepsilon}{(1+m_\varepsilon)^{\frac{3}{2}}} \nabla q_\varepsilon \cdot \nabla m_\varepsilon \Psi \\
&\leq \|\Psi\|_{\mathrm{L}^\infty(\Omega)} \frac{1}{4} \left(\int_0^T \int_\Omega g(q_\varepsilon) |\nabla q_\varepsilon|^2 + \int_0^T \int_\Omega \frac{g(q_\varepsilon) m_\varepsilon^2}{(1+m_\varepsilon)^3} |\nabla m_\varepsilon|^2 \right) \\
&\leq \frac{\|\Psi\|_{\mathrm{L}^\infty(\Omega)}}{4} \left(\int_0^T \int_\Omega g(q_\varepsilon) |\nabla q_\varepsilon|^2 + \frac{\|g\|_{\mathrm{L}^\infty([0,A])}}{C_2} \int_0^T \int_\Omega D(m_\varepsilon, q_\varepsilon, v_\varepsilon) \frac{|\nabla m_\varepsilon|^2}{m_\varepsilon} \right) \\
&\leq \|\Psi\|_{\mathrm{L}^\infty(\Omega)} C_{29}(T)
\end{aligned}$$

for some $C_{29}(T) > 0$. Combining the previous two estimates with the calculation in Lemma 3.14 in [SSU16] we deduce the existence of some $C_{30}(T) > 0$ such that

$$2 \int_0^T \int_\Omega \partial_t \sqrt{1+m_\varepsilon} \Psi \leq C_{30}(T) \|\Psi\|_{\mathrm{W}^{1,\infty}(\Omega)}$$

holds for all $\Psi \in \mathrm{C}_0^\infty(\Omega)$. It suffices to consider functions in $\mathrm{C}_0^\infty(\Omega)$ as that space is by definition dense in $W_0^{k,2}(\Omega)$. As $k > \frac{n+2}{2}$ implies that $W_0^{k,2}(\Omega)$ is continuously embedded into $\mathrm{W}^{1,\infty}(\Omega)$ we deduce in view of the previous estimate the existence of some $C_{31} > 0$ such that

$$\begin{aligned}
\int_0^T \left\| \partial_t \sqrt{1+m_\varepsilon(\cdot,t)} \right\|_{(\mathrm{W}_0^{k,2}(\Omega))^*} \mathrm{d}t &= \int_0^T \sup_{\Psi \in \mathrm{C}_0^\infty(\Omega), \|\Psi\|_{\mathrm{W}_0^{k,2}(\Omega)} \leq 1} \int_\Omega \partial_t \sqrt{1+m_\varepsilon(\cdot,t)} \Psi \, \mathrm{d}t \\
&\leq C_{31} C_{30}(T)
\end{aligned}$$

which proves (3.2). Now, let $p \in (1,6)$ be arbitrary. Since $n \leq 3$, we obtain from the Rellich-Kondrachov theorem (see [Bré11, Theorem 9.16]) that the embedding $\mathrm{W}^{1,2}(\Omega) \hookrightarrow \mathrm{L}^p(\Omega)$ is compact. Moreover, as $k > \frac{n+2}{2}$ implies that $\mathrm{W}_0^{k,2}(\Omega)$ is continuously embedded into $\mathrm{L}^q(\Omega)$ with dense image for all $q \in [1,\infty]$ (see [Bré11, Corollary 9.15]), we deduce the continuous embedding of $\mathrm{L}^p(\Omega)$ into the Hilbert space $(\mathrm{W}_0^{k,2}(\Omega))^*$.

Now, (3.1) and (3.2) imply that $(\sqrt{1+m_\varepsilon})_{\varepsilon \in (0,1)}$ is bounded in $\mathrm{L}^2((0,T); \mathrm{W}^{1,2}(\Omega))$ and $(\partial_t \sqrt{1+m_\varepsilon})_{\varepsilon \in (0,1)}$ is bounded in $\mathrm{L}^1((0,T); (W_0^{k,2}(\Omega))^*)$. Hence, the strong precompactness of $\left(\sqrt{1+m_\varepsilon}\right)_{\varepsilon \in (0,1)}$ in $\mathrm{L}^2((0,T); \mathrm{L}^p(\Omega))$ is an immediate consequence of the Aubin-Lions lemma (see e.g. [Tem77, Theorem 2.3 and Remark 2.1 in Chapter III]). For the precompactness of $(m_\varepsilon)_{\varepsilon \in (0,1)}$ in $\mathrm{L}^1((0,T); \mathrm{L}^2(\Omega))$ we consider the above for $p = 4$ and note

$$\int_0^T \int_\Omega \left\| \sqrt{1+m_\varepsilon} \right\|_{\mathrm{L}^4(\Omega)}^2 \mathrm{d}t = \int_0^T \left(\int_\Omega \sqrt{1+m_\varepsilon}^4 \right)^{\frac{1}{2}} \mathrm{d}t$$

$$= \int_0^T \left(\int_\Omega (1+m_\varepsilon)^2 \right)^{\frac{1}{2}} \mathrm{d}t = \|1+m_\varepsilon\|_{\mathrm{L}^1((0,T);\mathrm{L}^2(\Omega))}$$

This proves the claimed precompactness. □

In the next step we prove precompactness properties for the other solution components.

Lemma 3.2. *Let $T>0$ be arbitrary. Then there exists a constant $C_{32}(T)>0$ such that for any $\varepsilon \in (0,1)$ the estimate*

$$\sup_{t\in(0,T)} \left(\int_\Omega |\nabla q_\varepsilon(\cdot,t)|^2 + \int_\Omega |\nabla v_\varepsilon(\cdot,t)|^2 \right) \le C_{32}(T) \tag{3.3}$$

is fulfilled. Moreover, $(q_\varepsilon)_{\varepsilon\in(0,1)}$ and $(v_\varepsilon)_{\varepsilon\in(0,1)}$ are strongly precompact in $\mathrm{L}^2(\Omega \times (0,T))$.

Proof. The estimate claimed in (3.3) follows immediately from Proposition 2.13 using the strict positivity of $g(q_\varepsilon)$ together with $q_\varepsilon \in [0,A]$ and $|\nabla v_\varepsilon|^2 \le (1+L)\frac{|\nabla v_\varepsilon|^2}{1+v_\varepsilon}$ (see Lemma 2.3). Together with the estimates on q_ε and v_ε established in Lemma 2.3 this proves that $(q_\varepsilon)_{\varepsilon\in(0,1)}$ as well as $(v_\varepsilon)_{\varepsilon\in(0,1)}$ are bounded in $\mathrm{L}^2((0,T);\mathrm{W}^{1,2}(\Omega))$. The boundedness of the respective time derivatives in $\mathrm{L}^1((0,T);(\mathrm{W}_0^{k,2}(\Omega))^*)$ for $k > \frac{n+2}{2}$ can be proven analogously to the previous lemma. Applying once more the Aubin-Lions lemma (as in Lemma 3.1) yields the claimed strong precompactness. □

Before coming to the proof of our main result, we state useful tools, the first coming from [SSW14].

Lemma 3.3. *Let $d \ge 1$, $G \subset \mathbb{R}^d$ be measurable and be $(u_j)_{j\in\mathbb{N}} \subseteq \mathrm{L}^2(G)$ and $(w_j)_{j\in\mathbb{N}} \subseteq \mathrm{L}^\infty(G)$. Assume that $u_j \to u$ in $\mathrm{L}^2(G)$ and $w_j \to w$ a.e. in G as $j\to\infty$ for some $u \in \mathrm{L}^2(G)$ and $w \in \mathrm{L}^\infty(G)$ as well as $\sup_{j\in\mathbb{N}} \|w_j\|_{\mathrm{L}^\infty(G)} < \infty$. Then we have $u_j w_j \to uw$ in $\mathrm{L}^2(G)$ as $j \to \infty$.*

Proof. This is [SSW14, Lemma 5.10]. □

We further need the following elementary result on a combination of weak and strong convergence.

Lemma 3.4. *Let $(f_n)_{n\in\mathbb{N}}$ and $(g_n)_{n\in\mathbb{N}}$ be sequences in the space $\mathrm{L}^2(\Omega\times(0,T))$ and $f,g \in \mathrm{L}^2(\Omega\times(0,T))$. Assume that $f_n \to f$ strongly and $g_n \rightharpoonup g$ weakly in $\mathrm{L}^2(\Omega\times(0,T))$. Then we have $\langle f_n, g_n\rangle \to \langle f,g\rangle$ as $n\to\infty$.*

Proof. We have

$$\begin{aligned}|\langle f_n, g_n\rangle - \langle f, g\rangle| &\le |\langle f_n, g_n\rangle - \langle f, g_n\rangle| + |\langle f, g_n\rangle - \langle f, g\rangle| \\ &\le \|g_n\|_2 \|f_n - f\|_2 + |\langle f, g_n\rangle - \langle f, g\rangle|\end{aligned}$$

for all $n \in \mathbb{N}$. As weakly convergent sequences are bounded, the above calculation shows the claim. ☐

Proof of Theorem 1.2. First, by Lemmas 3.1 and 3.2 we deduce the existence of non-negative functions m, q and v satisfying the regularity properties stated in Definition 1.1 such that along a suitable subsequence $\varepsilon = \varepsilon_j \searrow 0$ as $j \to \infty$ we have for any $T > 0$:

$$\begin{aligned} l_\varepsilon &\to l && \text{strongly in } \mathrm{L}^2(\Omega \times (0,T)) \text{ and a.e. in } \Omega \times (0,T), \\ & && \text{for } l \in \{\sqrt{1+m}, q, v\}, \\ m_\varepsilon &\to m && \text{strongly in } \mathrm{L}^1((0,T); \mathrm{L}^2(\Omega)) \text{ and a.e. in } \Omega \times (0,T). \end{aligned} \tag{3.4}$$

For $\sqrt{1+m} \in \mathrm{L}^2((0,T); \mathrm{W}^{1,2}(\Omega))$ note that Lemma 3.1 implies that $(\sqrt{1+m_\varepsilon})_{\varepsilon\in(0,1)}$ has a subsequence that converges weakly in $\mathrm{L}^2((0,T); \mathrm{W}^{1,2}(\Omega))$ (as this space is reflexive). Moreover, we also obtain from Lemma 3.1 that this subsequence converges weakly to $\sqrt{1+m}$ in $\mathrm{L}^2(\Omega \times (0,T))$ (as strong convergence implies weak convergence). Due to $\mathrm{L}^2(\Omega) \hookrightarrow (\mathrm{W}^{1,2}(\Omega))^*$ and the uniqueness of weak limits, this implies $\sqrt{1+m} \in \mathrm{L}^2((0,T); W^{1,2}(\Omega))$. The stronger regularity properties as claimed in Theorem 1.2 are consequences of Lemma 2.3 and Lemma 2.4, respectively.

Furthermore, it follows that $(\nabla\sqrt{1+m_\varepsilon})_{\varepsilon_j}$ is bounded in $\mathrm{L}^2(\Omega\times(0,T))$ as $(\sqrt{1+m_\varepsilon})_{\varepsilon\in(0,1)}$ is bounded in $\mathrm{L}^2((0,T); \mathrm{W}^{1,2}(\Omega))$. Since $\mathrm{L}^2(\Omega \times (0,T))$ is reflexive, the sequence possesses a weakly convergent subsequence converging to $\nabla\sqrt{1+m}$. With a similar reasoning and passing to further subsequences we also obtain $\nabla v_\varepsilon \rightharpoonup \nabla v$ and $\nabla q_\varepsilon \rightharpoonup \nabla q$ in $\mathrm{L}^2(\Omega \times (0,T))$. Moreover, we need weak convergence of $(\sqrt{m_\varepsilon}\nabla v_\varepsilon)_{\varepsilon_j}$ and $(\sqrt{m_\varepsilon}\nabla q_\varepsilon)_{\varepsilon_j}$ in $\mathrm{L}^2(\Omega \times (0,T))$. After passing to further subsequences, this is a consequence of this space being reflexive as well as the boundedness of the above sequences in that space. For the boundedness note that

$$\int_0^T \int_\Omega m_\varepsilon |\nabla v_\varepsilon|^2 \le (1+L)^2 \int_0^T \int_\Omega m_\varepsilon \frac{|\nabla v_\varepsilon|^2}{(1+v_\varepsilon)^2} \le C_{33}(T)$$

holds true for all $\varepsilon \in (0,1)$ with some $C_{33}(T) > 0$ due to Proposition 2.13. The boundedness of $(\sqrt{m_\varepsilon}\nabla q_\varepsilon)_{\varepsilon_j}$ in $\mathrm{L}^2(\Omega \times (0,T))$ can be shown in a similar way. For fixed

$T > 0$ and $\varphi \in \mathrm{C}_0^\infty\left(\overline{\Omega} \times [0,T)\right)$ we obtain using integration by parts from the first equation in (2.1) that

$$\begin{aligned}
&-\int_0^T \int_\Omega m_\varepsilon \partial_t \varphi - \int_\Omega m_{0\varepsilon}\varphi(\cdot,0) \\
&= -2\int_0^T \int_\Omega D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\sqrt{1+m_\varepsilon}\nabla\sqrt{1+m_\varepsilon}\cdot\nabla\varphi \\
&\quad + \int_0^T \int_\Omega \frac{v_\varepsilon}{1+v_\varepsilon}\sqrt{m_\varepsilon}\sqrt{m_\varepsilon}\nabla v_\varepsilon \cdot \nabla\varphi \\
&\quad - \int_0^T \int_\Omega g(q_\varepsilon)\sqrt{m_\varepsilon}\sqrt{m_\varepsilon}\nabla q_\varepsilon \cdot \nabla\varphi \\
&\quad + \int_0^T \int_\Omega (\lambda q_\varepsilon - \gamma m_\varepsilon - r_m(t) m_\varepsilon)\varphi - \varepsilon\int_0^T\int_\Omega m_\varepsilon^\theta \varphi
\end{aligned} \tag{3.5}$$

for all $\varepsilon \in (0,1)$. Using Lemma 3.3 we deduce from the almost everywhere convergence in (3.4) and (1.7) that $D(m_\varepsilon, q_\varepsilon, v_\varepsilon)\sqrt{1+m_\varepsilon} \to D(m,q,v)\sqrt{1+m}$ strongly in $\mathrm{L}^2(\Omega \times (0,T))$. Since $0 \le \frac{v_\varepsilon}{1+v_\varepsilon} \le L$ and $0 \le g(q_\varepsilon) \le c$, we obtain similarly $\frac{v_\varepsilon}{1+v_\varepsilon}\sqrt{m_\varepsilon} \to \frac{v}{1+v}\sqrt{m}$ as well as $g(q_\varepsilon)\sqrt{m_\varepsilon} \to g(q)\sqrt{m}$ strongly in $\mathrm{L}^2(\Omega \times (0,T))$.

Applying Lemma 3.4 then yields that the first three terms on the right hand side converge to the corresponding terms of (1.8). The fourth term and the terms on the left hand side converge to corresponding terms in (1.8) due to (3.4) and the choice of the initial values for the regularized problems in (2.5). The last term can be dealt with as in [SSU16]. For the sake of completeness we nevertheless present the proof. For given $\eta > 0$ we choose $S > 0$ large enough such that $\frac{C_{18}(T)}{\ln(S+2)} \le \frac{\eta}{2}$ with $C_{18}(T)$ from Proposition 2.13. Using Proposition 2.13 we obtain

$$\begin{aligned}
\varepsilon\int_0^T\int_\Omega m_\varepsilon^\theta &= \varepsilon\int_0^T\int_\Omega \chi_{\{m_\varepsilon \le S\}} m_\varepsilon^\theta + \varepsilon\int_0^T\int_\Omega \chi_{\{m_\varepsilon > S\}} m_\varepsilon^\theta \\
&\le \varepsilon T\left|\Omega\right| S^\theta + \frac{\varepsilon}{\ln(S+2)}\int_0^T\int_\Omega m_\varepsilon^\theta \ln(m_\varepsilon+2) \le \frac{\eta}{2} + \frac{\eta}{2}
\end{aligned}$$

for $\varepsilon \in (0,\varepsilon_0)$ where ε_0 satisfies $\varepsilon_0 T\left|\Omega\right| S^\theta \le \frac{\eta}{2}$. As we can estimate φ by $\|\varphi\|_{\mathrm{L}^\infty(\Omega)}$, this shows convergence for the last term.

The equations for q_ε and v_ε can be verified analogously. $\square$

Conclusion and Outlook

In this thesis we considered an extended version of the model presented in [SSU16]. We introduced a term modeling chemorepulsion in the equation for the migrating cancer cells and examined for which choices we can adapt the method presented in [SSU16] and [SSW14] to show the existence of a global weak solution. We identified two possible cases, namely, if the coefficient function g in (1.2) is either constant or of the form $\frac{c}{1+q}$ and in both cases is sufficiently small.

There are several ways for further investigation. One would be to consider the full model of [SSU16] this is to say not to neglect the integrins bound to ECM fibers and not to assume the contractivity function of the cancers cells to be constant. Moreover, it is a natural question to ask whether other choices of g are possible and to which extent this can be done with the method used here. It seems that Lemma 2.12 is the point where most of the work would need to be done if one wants to consider such generalizations. Furthermore, it remains open whether solutions are bounded or unique.

Additionally, potential research might consider how chemorepulsion can be included in other tumor invasion models. For instance one could examine how it behaves in the context of degenerate diffusion as for example studied in [ZSH18].

A. Appendix

First, we show a result on Hölder spaces.

Lemma A.1. *Let $\Omega \subseteq \mathbb{R}^n$ be a bounded domain and $T > 0$. For $u \in \mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$ which is strictly positive also $\frac{1}{u} \in \mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$ holds true.*

Proof. We only prove the finiteness of Hölder seminorm in x, the one in t is dealt with similarly. We have for $x \neq x'$

$$\frac{1}{|x-x'|^\beta}\left|\frac{1}{u(x,t)} - \frac{1}{u(x',t)}\right| = \frac{1}{|x-x'|^\beta}\frac{|u(x',t)-u(x,t)|}{|u((x,t)u(x',t)|} \leq \frac{1}{\vartheta_1^2}\frac{|u(x',t)-u(x,t)|}{|x-x'|^\beta} < \infty$$

by assumption where $\vartheta_1 > 0$ is a lower bound for u in $\overline{\Omega} \times [0,T]$. This shows the claim. □

Next, we show a comparison principle for ODEs based on Gronwall's inequality.

Lemma A.2. *Let $T > 0$ and f, $g\colon [0,T] \to \mathbb{R}$ be two continuously differentiable functions satisfying $f'(t) \leq C + a(t)f(t)$, $g'(t) \geq C + a(t)g(t)$ for some continuous function $a\colon [0,T] \to \mathbb{R}$ as well as $f(0) \leq g(0)$. Then $f \leq g$ holds on $[0,T]$.*

Proof. Define $h \coloneqq f - g$ and assume that there exists $t_1 > 0$ such that $h(t_1) > 0$. By continuity of h we deduce the existence of some $t_2 \in [0,t_1)$ with $h(t_2) = 0$ and $h(t) > 0$ in $(t_2,t_1]$. Hence, for $t \in [t_2,t_1]$ we obtain

$$h'(t) \leq a(t)(f(t) - g(t)) = a(t)h(t)$$

which by a special case of Gronwall's inequality implies $h(t_1) \leq h(t_2)\mathrm{e}^{\int_{t_2}^{t_1} a(s)\ \mathrm{d}s} = 0$ which is a contradiction to the choice of t_1. □

Next, we introduce a comparison principle for the semilinear heat equation with Neumann boundary condition.

Theorem A.3. *Let $\Omega \subseteq \mathbb{R}^n$ be a bounded domain with smooth boundary and $T > 0$. Let $f \colon \Omega \times [0,T] \times \mathbb{R}$ be continuous in the first two arguments and continuously differentiable in the last one. Moreover, let $u, v \in \mathrm{C}^0\left(\overline{\Omega} \times [0,T]\right) \cap \mathrm{C}^{2,1}\left(\overline{\Omega} \times (0,T]\right)$ satisfy*

$$\begin{aligned}(u_t - \Delta u)(x,t) &\leq f(x,t,u) \text{ in } \Omega \times (0,T],\\ (v_t - \Delta v)(x,t) &\geq f(x,t,v) \text{ in } \Omega \times (0,T],\\ u(x,0) &\leq v(x,0) \text{ on } \Omega,\\ \partial_\nu u &\leq \partial_\nu v \text{ on } \partial\Omega \times [0,T].\end{aligned}$$

If $u(\cdot,0) \not\equiv v(\cdot,t)$ then $u < v$ holds in $\overline{\Omega} \times [0,T]$.

Proof. This is a special case of Proposition 52.7 in [QS19]. □

Next, we state two existence results for (quasi)linear parabolic equations from [LSU68].

Theorem A.4. *Let $\beta \in (0,1)$ and $\Omega \subseteq \mathbb{R}^n$ be a smoothly bounded domain, $\mathcal{L}$ be a linear uniformly parabolic differential operator, i.e.,*

$$\mathcal{L}u = u_t - \sum_{i,j=1}^{n} a_{ij}(x,t)\partial_{ij}u + \sum_{i=1}^{n} a_i(x,t)\partial_i u + a(x,t)u$$

with $\mu_1 |\xi|^2 \leq \sum_{i,j=1}^n a_{ij}\xi_i\xi_j \leq \mu_2 |\xi|^2$ for some μ_1, $\mu_2 > 0$ and all $\xi \in \mathbb{R}^n$. We consider the PDE

$$\begin{cases}\mathcal{L}w = f & \text{in } \Omega \times (0,T),\\ \partial_\nu w = 0 & \text{on } \partial\Omega \times (0,T),\\ w(\cdot,0) = \phi(\cdot) & \text{in } \overline{\Omega}.\end{cases} \tag{A.1}$$

We further assume that the coefficients of $\mathcal{L}$ are in $\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$. Then for all $f \in \mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$, $\phi \in \mathrm{C}^{2+\beta}(\overline{\Omega})$ satisfying the compatibility condition $\partial_\nu \phi = 0$ on $\partial\Omega \times \{0\}$ the system (A.1) *has a unique solution $w \in \mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$ and there is a constant $\vartheta_2 > 0$ depending on the norms of the coefficients of $\mathcal{L}$ in $\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega} \times [0,T]\right)$ such that*

$$\|w\|_{\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} \leq \vartheta_2 \left(\|f\|_{\mathrm{C}^{\beta,\frac{\beta}{2}}\left(\overline{\Omega}\times[0,T]\right)} + \|\phi\|_{\mathrm{C}^{2+\beta}\left(\overline{\Omega}\right)} \right).$$

Proof. This is Theorem IV.5.3 in [LSU68]. □

The following is an existence result for a quasilinear PDE, but already adapted for our intended use.

Theorem A.5. *Let $\beta \in (0,1)$ and $\Omega \subseteq \mathbb{R}^n$ be a bounded domain with smooth boundary. Consider the PDE*

$$\begin{cases} u_t = a(x,t,u)\Delta u + b(x,t,u,u_x) & \text{in } \Omega \times (0,T) \\ a(x,t,u)\partial_\nu u = 0 & \text{on } \partial\Omega \times (0,T) \\ u(\cdot,0) = u_0(\cdot) & \text{in } \overline{\Omega}. \end{cases} \tag{A.2}$$

Assume that the coefficients satisfy the following conditions.

(i) There exists some $C > 0$ such that for any solution $u \in \mathrm{C}^{2,1}(\overline{\Omega} \times [0,T])$ of (A.2) $\|u\|_{\mathrm{C}^0(\overline{\Omega}\times[0,T])} \leq C$ is satisfied or we have estimates on the coefficients of the PDE:

$$0 \leq a(x,t,u) \leq \mu_1 \text{ in } \overline{\Omega} \times (0,T] \tag{A.3}$$

$$-ub(x,t,u,p) \leq c_0p^2 + c_1u^2 + c_2 \text{ in } \overline{\Omega} \times (0,T] \tag{A.4}$$

$$\nu_1 \leq a(x,t,u) \text{ on } \partial\Omega \times (0,T) \tag{A.5}$$

where $\mu_1, \nu_1 > 0$ and $c_0, c_1, c_2 \geq 0$ are constants.

(ii) For $(x,t) \in \overline{\Omega} \times [0,T]$, $|u| \leq M$ where M is an upper bound for u and for arbitrary p the functions $a(x,t,u)$ and $b(x,t,u,p)$ are continuous in their arguments, possess the derivatives entering into the following conditions and satisfy those

$$\nu \leq a(x,t,u) \leq \mu, \quad \nu > 0, \tag{A.6}$$

$$\left|\frac{\partial a(x,t,u)}{\partial u}\right|, \left|\frac{\partial a(x,t,u)}{\partial x}\right| \leq \mu, \tag{A.7}$$

$$|b(x,t,u,p)| \leq \mu(1+p^2), \tag{A.8}$$

$$|\partial_p b|\,(1+|p|) + |\partial_u b| + |\partial_t b| \leq \mu(1+p^2), \tag{A.9}$$

$$|\partial_{uu} a|\,, |\partial_{ut} a|\,, |\partial_{ux} a|\,, |\partial_{xt} a| \leq \mu. \tag{A.10}$$

(iii) For $(x,t) \in \overline{\Omega} \times [0,T]$, $|u| \leq M$ and $|p| \leq M_1$ where M_1 is an upper bound for p, the functions $\partial_x a(x,t,u)$ and $b(x,t,u,p)$ are Hölder continuous in the variables x with exponent β.

Then (A.2) has a unique solution $u(x,t)$ in the class $\mathrm{C}^{2+\beta,1+\frac{\beta}{2}}(\overline{\Omega} \times [0,T])$.

Proof. This is a special case, in particular for $\tau = 1$, of Theorem V.7.4 in [LSU68]. □

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