# GLOBAL WELL-POSEDNESS OF A HAPTOTAXIS MODEL WITH SPATIAL AND AGE STRUCTURE 

CHRISTOPH WALKER


#### Abstract

A system of non-linear partial differential equations modeling tumor invasion into surrounding healthy tissue is analyzed. The model incorporates haptotaxis, i.e., the directed migratory response of tumor cells to the extracellular environment, as well as spatial and age structure of the tumor cells. Global existence and uniqueness of nonnegative solutions is shown.


## 1. Introduction

Cancer is marked by several stages of development, each of which is progressively more aggressive than the last. In this paper we study the well-posedness of a mathematical model describing a certain stage of tumor growth: the early vascularized stage when the tumor begins to invade the surrounding healthy tissue. We thus assume that the tumor has just been vascularized, i.e. a blood supply has been established (angiogenesis). The tumor is supposed to be contained in a region of tissue $\Omega$. The proliferating and quiescent tumor cells are distinguished by position $x \in \Omega$ and age $a \geq 0$. Age for proliferating tumor cells corresponds to position in the cell cycle, and if a cell divides, then both daughter cells have age 0 . Age for quiescent cells corresponds to a rested position in the cell cycle (the age of a quiescent cell is fixed at the age it had when it transitioned from proliferation to quiescence, and if a quiescent cell transitions back to proliferating, then aging resumes). Proliferating cells of any age produce a matrix degradation enzyme which diffuses in the tumor environment and degrades the extracellular matrix locally. As well as making space into which tumor cells can move by simple diffusion, this produces oxygen (and other nutrients) essential for tumor growth and survival. We also assume that the degradation of the extracellular matrix results in a gradient of cell-adhesion molecules. Therefore, while the extracellular matrix may constitute of a barrier to normal cell movement, it also provides a substrate to which cells may adhere and upon which they may move. This directed migration up a gradient of bound (i.e. non-diffusible) cell-adhesion molecules is called haptotaxis.

The model considered herein has been proposed in [4] and focuses on five key components involved in tumor invasion, namely the densities of proliferating and quiescent tumor cells (denoted by $p=p(t, a, x)$ and $q=q(t, a, x)$, respectively), the matrix-degradative enzyme concentration (denoted by $m=m(t, x)$ ), the density of the bound extracellular macromolecules (denoted by $f=f(t, x)$ ), and the oxygen concentration (denoted by $w=w(t, x)$ ). We assume that the tumor cells, enzyme, and oxygen remain within the domain of tissue.

[^0]The equations modeling the above described processes read as follows:

$$
\begin{align*}
\partial_{t} f= & -\underbrace{k(x) m f}_{\text {degradation }},  \tag{1}\\
\partial_{t} m= & \underbrace{\alpha \Delta_{x} m}_{\text {dif fusion }}+\underbrace{d(x) P}_{\text {production }}-\underbrace{h(x) m}_{\text {decay }},  \tag{2}\\
\partial_{t} w= & \underbrace{\beta \Delta_{x} w}_{\text {diffusion }}+\underbrace{\Gamma(x, f)}_{\text {production }}-\underbrace{\Lambda(x, Q, P) w}_{\text {uptake }}-\underbrace{e(x) w}_{\text {decay }},  \tag{3}\\
\partial_{t} q= & \underbrace{\gamma \Delta_{x} q}_{\text {cell motility }}+\underbrace{\sigma(a, x, w, Q, P) p}_{\text {enter from proliferation }} \\
& -\underbrace{\epsilon(a, x, w, Q, P) q}_{\text {exit to proliferation }}-\underbrace{\tau(a, x, w, Q, P) q}_{\text {cell death }},  \tag{4}\\
\partial_{t} p= & \underbrace{\delta \Delta_{x} p}_{\text {cell motility }}-\underbrace{\partial_{a} p}_{\text {cell aging }}-\underbrace{\nabla_{x} \cdot\left(p \chi(f) \nabla_{x} f\right)}_{\text {haptotaxis }}+\underbrace{\epsilon(a, x, w, Q, P) q}_{\text {enter from quiescence }} \\
& -\underbrace{\sigma(a, x, w, Q, P) p}_{\text {exit to quiescence }}-\underbrace{\theta(a, x, w, Q, P) p}_{\text {cell death }}-\underbrace{b(a) p}_{\text {cell division }}, \tag{5}
\end{align*}
$$

for $(t, x) \in(0, \infty) \times \Omega$ and $a>0$ supplemented with no flux boundary conditions with respect to $x$,

$$
\begin{equation*}
\partial_{\nu} m=\partial_{\nu} w=\partial_{\nu} q=\partial_{\nu} p-p \chi(f) \partial_{\nu} f=0 \quad \text { on } \partial \Omega \tag{6}
\end{equation*}
$$

and

$$
\begin{equation*}
p(t, 0, x)=2 \int_{0}^{\infty} b(a) p(t, a, x) \mathrm{d} a, \quad(t, x) \in(0, \infty) \times \Omega \tag{7}
\end{equation*}
$$

with respect to $a$. The equations are subject to the initial conditions

$$
f(0, \cdot)=f^{0}, \quad m(0, \cdot)=m^{0}, \quad w(0, \cdot)=w^{0}, \quad q(0, \cdot, \cdot)=q^{0}, \quad p(0, \cdot, \cdot)=p^{0} . \quad\left(E_{8}\right)
$$

In $\left(E_{2}\right)-\left(E_{5}\right)$ we used the notation

$$
\begin{equation*}
Q(t, x):=\int_{0}^{\infty} q(t, a, x) \mathrm{d} a, \quad P(t, x):=\int_{0}^{\infty} p(t, a, x) \mathrm{d} a \tag{1}
\end{equation*}
$$

for the total population densities of quiescent and proliferating tumor cells, respectively.
The proliferation-quiescence transition rates $\sigma$, quiescence-proliferation rates $\epsilon$, proliferating cell death rates $\theta$, and quiescent cell death rates $\tau$ depend on the supply of oxygen $w(t, x)$ and the total population densities $P(t, x)$ and $Q(t, x)$ of proliferating and quiescent tumor cells. In equation $\left(E_{5}\right), b(a)$ is the rate at which a mother cell of age $a$ divides per unit time. All daughter cells have age zero as reflected by equation $\left(E_{7}\right)$.

The model presented above is a simplified version of the model presented in [27]. The latter in turn is derived from the hybrid discrete-continuous tumor invasion model of Anderson [4]. We refer to [4, 27] where the derivation of the models and the involved biological processes are described in more detail and numerical results are given (see also [5]).

Equations $\left(E_{1}\right)-\left(E_{8}\right)$ without age structure and without quiescent cells have been mathematically treated in [25]. For the so obtained equations global existence and uniqueness of non-negative classical solutions is shown. Our aim here is to demonstrate how one can incorporate age structure still obtaining global well-posedness. The inclusion of a cell life cycle is both biologically desirable and mathematically non-trivial.

Age-dependent population models with diffusion have been treated in many papers before, and different approaches have been used, see for instance $[8,9,16,17,18,22,23,26]$ and the references therein. But none of these papers includes haptotaxis. To the best of the author's knowledge, the only research on a haptotaxis model including age and spatial structure is [10]. The model considered there differs from the model above in that diffusion is added to equation $\left(E_{1}\right)$, which gives an additional smoothing for $f$.

We shall point out that the equations $\left(E_{1}\right)-\left(E_{8}\right)$ without age structure are mathematically related to chemotaxis equations

$$
\begin{aligned}
\partial_{t} m & =\alpha \Delta_{x} m+n(m, p) \\
\partial_{t} p & =\delta \Delta_{x} p-\nabla_{x} \cdot\left(p \chi(p, m) \nabla_{x} m\right)
\end{aligned}
$$

on the one hand and angiogenesis equations

$$
\begin{align*}
& \partial_{t} f=H(p, f)  \tag{2}\\
& \partial_{t} p=\delta \Delta_{x} p-\nabla_{x} \cdot\left(p \chi(f) \nabla_{x} f\right) \tag{3}
\end{align*}
$$

on the other, where often

$$
\begin{equation*}
H(f, p)=-p f^{r}, \quad r>0 \tag{4}
\end{equation*}
$$

For chemotaxis equations it is known that blow up of solutions may occur in finite time if $n>1$, e.g. [15]. The angiogenesis equations differ from our model in particular in that the coupling in our case of the $f$-equation $\left(E_{1}\right)$ and the $p$-equation $\left(E_{5}\right)$ (without age structure) is via the intermediate $m$-equation $\left(E_{2}\right)$, which imparts the smoothing property of the heat semigroup to $f$ needed to prove global existence. In this context we refer to $[6,7,11,12,20$, 21] and the references therein for results concerning (2), (3) and variants thereof. Seemingly, global existence of solutions to (2)-(4) is known merely in space dimension one [11, 20, 21], of weak solutions with finite energy [6] or with small initial value $p^{0}[7]$ or $f^{0}[12]$, respectively.

In this paper we show that the coupling of $f, m$, and $p$ in $\left(E_{1}\right)-\left(E_{8}\right)$ allows us to derive global existence and uniqueness of a 'smooth' solution for any space dimension $n \leq 3$ and without smallness assumptions on the initial data.

Throughout we assume that $\Omega$ is a bounded and smooth domain in $\mathbb{R}^{n}, n \leq 3$ and that the diffusion coefficients $\alpha, \beta, \gamma$, and $\delta$ are positive constants. Concerning the data in $\left(E_{1}\right)-\left(E_{8}\right)$ we assume in the sequel that there exists some number $s>0$ such that

$$
\left.\begin{array}{lr}
k \in W_{\infty}^{2}(\Omega), & \partial_{\nu} k=0 \text { on } \partial \Omega \\
d, h \in C^{s}(\bar{\Omega}), & e \in L_{\infty}(\Omega), \tag{5}
\end{array}\right\}
$$

and that all functions are non-negative. We also assume that the haptotactic sensitivity $\chi$ satisfies

$$
\begin{equation*}
\chi \in C^{1}\left(\mathbb{R}^{+}\right), \quad \chi \geq 0, \quad \chi, \chi^{\prime} \text { are uniformly Lipschitz continuous on bounded sets } \tag{6}
\end{equation*}
$$

Furthermore, regarding the functions

$$
\Gamma \in C(\bar{\Omega} \times \mathbb{R}, \mathbb{R}), \quad \Lambda \in C(\bar{\Omega} \times \mathbb{R} \times \mathbb{R}, \mathbb{R}), \quad \sigma, \epsilon, \tau, \theta \in C\left(\mathbb{R}^{+} \times \bar{\Omega} \times \mathbb{R} \times \mathbb{R} \times \mathbb{R}, \mathbb{R}\right)
$$

we suppose that they are all non-negative and that, for some $c_{0}>0$,

$$
\begin{align*}
|\Gamma(x, \xi)-\Gamma(x, \bar{\xi})| & \leq c_{0}|\xi-\bar{\xi}|  \tag{7}\\
|\Lambda(x, \xi, \eta)-\Lambda(x, \bar{\xi}, \bar{\eta})| & \leq c_{0}(|\xi-\bar{\xi}|+|\eta-\bar{\eta}|) \tag{8}
\end{align*}
$$

and

$$
\begin{equation*}
|\phi(a, x, \mu, \xi, \eta)-\phi(a, x, \bar{\mu}, \bar{\xi}, \bar{\eta})| \leq c_{0}(|\mu-\bar{\mu}|+|\xi-\bar{\xi}|+|\eta-\bar{\eta}|) \tag{9}
\end{equation*}
$$

for $a>0, x \in \Omega, \mu, \bar{\mu}, \xi, \bar{\xi}, \eta, \bar{\eta} \in \mathbb{R}$, and every $\phi \in\{\sigma, \epsilon, \tau, \theta\}$. Moreover, in order to prove global existence we will also require the existence of a function $\kappa: \mathbb{R}^{+} \rightarrow \mathbb{R}^{+}$, which is bounded on bounded sets, such that, for $\phi \in\{\sigma, \epsilon, \tau, \theta\}$,

$$
\begin{equation*}
|\Lambda(x, \xi, \eta)|+|\phi(a, x, \mu, \xi, \eta)| \leq \kappa(\mu), \quad a>0, \quad x \in \Omega, \quad \mu, \xi, \eta \in \mathbb{R} \tag{10}
\end{equation*}
$$

Finally, we assume that

$$
\begin{equation*}
b \in C\left(\mathbb{R}^{+}\right), \quad b \geq 0, \quad\|b\|_{\infty}<\infty \tag{11}
\end{equation*}
$$

Note that the boundary condition on $p$ in $\left(E_{6}\right)$ reduces to a Neumann boundary condition $\partial_{\nu} p=0$ in case that $\partial_{\nu} f=0$. The latter is obtained by assuming $\partial_{\nu} k=0$ in (5) and $\partial_{\nu} f^{0}=0$ as it follows from equation $\left(E_{1}\right)$. This assumption decouples $p$ and $f$ on the boundary.

We shall prove that assumptions (5)-(11) ensure the global well-posedness of $\left(E_{1}\right)-\left(E_{8}\right)$. More precisely, we will introduce a strongly continuous semigroup $\{\mathbb{S}(t) ; t \geq 0\}$ generated by $-\partial_{a}+\delta \Delta_{x}$ subject to the boundary conditions $\left(E_{6}\right),\left(E_{7}\right)$ (cf. section 2, in particular Proposition 2.2) allowing us to consider mild solutions to equation $\left(E_{5}\right)$. Our approach uses semigroup theory with characteristics and is similar to e.g. [16, 26, 27].

A simplified and somewhat informal version of our main result Theorem 3.1 is stated in the following

Theorem 1.1. Suppose (5)-(11) and let $\varrho>n$. Given any non-negative initial value

$$
\left(f^{0}, m^{0}, w^{0}, q^{0}, p^{0}\right) \in X:=W_{\varrho}^{2}(\Omega) \times W_{\varrho}^{1}(\Omega) \times L_{\varrho}(\Omega) \times L_{1}\left(\mathbb{R}^{+}, L_{\varrho}(\Omega)\right) \times L_{1}\left(\mathbb{R}^{+}, L_{\varrho}(\Omega)\right)
$$

with $\partial_{\nu} f^{0}=0$, there exists a unique global non-negative solution $(f, m, w, q, p) \in C\left(\mathbb{R}^{+}, X\right)$ to $\left(E_{1}\right)-\left(E_{8}\right)$ such that $f, m, w$ are classical solutions to $\left(E_{1}\right),\left(E_{2}\right),\left(E_{3}\right)$ and $q$ and $p$ are mild solutions to $\left(E_{4}\right)$ and $\left(E_{5}\right)$. Moreover, the solution depends continuously on the initial value.

As mentioned above, this theorem is a special case of a more general statement given in Theorem 3.1. In section 2 we collect some auxiliary results needed for the proof of Theorem 1.1 and Theorem 3.1. In particular, in subsection 2.1 we introduce the age-diffusion semigroup and derive properties being important to handle the haptotaxis term. Subsection 2.2 is devoted to some further auxiliary results used for positivity of solutions. In section 3 we first state precisely our global existence and uniqueness result. The proof will then be performed in several steps in subsections 3.1-3.3.

## 2. Preliminaries

We abbreviate the Lebesgue spaces and the Sobolev-Slobodeckii spaces by $L_{\varrho}:=L_{\varrho}(\Omega)$ and $W_{\varrho}^{\vartheta}:=W_{\varrho}^{\vartheta}(\Omega)$, respectively, for $1 \leq \varrho \leq \infty$ and $\vartheta \geq 0$. Moreover, we denote by $W_{\varrho, \mathcal{B}}^{\vartheta}:=W_{\varrho, \mathcal{B}}^{\vartheta}(\Omega)$ the Sobolev-Slobodeckii spaces including Neumann boundary conditions, that is,

Notice that

$$
W_{\varrho, \mathcal{B}}^{\vartheta}:= \begin{cases}\left\{u \in W_{\varrho}^{\vartheta} ; \partial_{\nu} u=0\right\}, & \vartheta>1+1 / \varrho \\ W_{\varrho}^{\vartheta}, & 0 \leq \vartheta<1+1 / \varrho\end{cases}
$$

$$
\left(L_{\varrho}, W_{\varrho, \mathcal{B}}^{2}\right)_{\vartheta, \varrho} \doteq W_{\varrho, \mathcal{B}}^{2 \vartheta}, \quad 2 \vartheta \in(0,2) \backslash\{1,1+1 / \varrho\}
$$

where $(\cdot, \cdot)_{\vartheta, \varrho}$ denotes the real interpolation functor and $\doteq$ means '(algebraically) equal with equivalent norms'. We also introduce the spaces

$$
\mathbb{L}_{\varrho}:=L_{1}\left(\mathbb{R}^{+}, L_{\varrho}\right) \quad \text { and } \quad \mathbb{W}_{\varrho, \mathcal{B}}^{\vartheta}:=L_{1}\left(\mathbb{R}^{+}, W_{\varrho, \mathcal{B}}^{\vartheta}\right)
$$

and we denote by $\mathbb{L}_{\varrho}^{+}$the positive cone in $\mathbb{L}_{\varrho}$. Given two Banach spaces $E$ and $F$ we write $\mathcal{L}(E, F)$ for the set of all bounded linear operators from $E$ into $F$, and we put $\mathcal{L}(E):=\mathcal{L}(E, E)$.
2.1. The Age-Diffusion Semigroup. Throughout this subsection, we fix $1<\varrho<\infty$ and we assume that

$$
\begin{equation*}
f \in C^{1}(\bar{\Omega}) \quad \text { with } \quad \partial_{\nu} f=0 \text { on } \partial \Omega \tag{12}
\end{equation*}
$$

We use the notation

$$
A_{f} \varphi:=-\alpha \Delta_{x} \varphi+\chi(f) \nabla_{x} f \cdot \nabla_{x} \varphi, \quad \varphi \in W_{\varrho, \mathcal{B}}^{2}
$$

so that $A_{0}=-\alpha \Delta_{x}$, and we recall that $-A_{f}$ generates a positive, strongly continuous analytic semigroup $\mathcal{U}_{f}:=\left\{U_{f}(t) ; t \geq 0\right\}$ on $L_{\varrho}[1,24]$. Due to $\partial_{\nu} f=0$, it is a semigroup of contractions by [1, Thm.11.1]. Moreover, there are constants $M:=M\left(\|f\|_{C^{1}(\bar{\Omega})}\right)$ and $\omega:=\omega\left(\|f\|_{C^{1}(\bar{\Omega})}\right)$ such that

$$
\begin{equation*}
\left\|U_{f}(t)\right\|_{\mathcal{L}\left(L_{e}, L_{\xi}\right)} \leq M e^{\omega t} t^{-(1 / \varrho-1 / \xi) n / 2}, \quad t>0 \tag{13}
\end{equation*}
$$

for $1<\varrho \leq \xi \leq \infty$, and also

$$
\begin{equation*}
\left\|U_{f}(t)\right\|_{\mathcal{L}\left(W_{e, \mathcal{B}}, W_{e, \mathcal{B}}^{2 \mu}\right)} \leq M e^{\omega t} t^{\eta-\mu}, \quad t>0 \tag{14}
\end{equation*}
$$

which is true provided that $0 \leq 2 \eta \leq 2 \mu \leq 2$ with $2 \eta, 2 \mu \neq 1+1 / \varrho$.
In order to introduce the age-diffusion semigroup, we study the solution $B_{\phi}$ to the linear Volterra equation

$$
\begin{equation*}
B_{\phi}(t)=2 \int_{0}^{t} b(a) U_{f}(a) B_{\phi}(t-a) \mathrm{d} a+2 U_{f}(t) \int_{0}^{\infty} b(a+t) \phi(a) \mathrm{d} a, \quad t \geq 0 \tag{15}
\end{equation*}
$$

where $\phi \in \mathbb{L}_{\varrho}$ is given. We put

$$
\begin{aligned}
& \mathbb{D}_{f}:=\left\{\phi \in \mathbb{L}_{\varrho} ;\right.
\end{aligned} \text { for a.a. } x \in \Omega, \phi(\cdot, x) \in C\left(R^{+}\right) \text {is differentiable a.e. on }(0, \infty) \text { ) } \quad \begin{aligned}
& \text { with } \phi(0, x)=2 \int_{0}^{\infty} b(a) \phi(a, x) \mathrm{d} a, \\
& \left.\phi(a, \cdot) \in W_{\varrho, \mathcal{B}}^{2} \text { for } a>0 \text { and } \partial_{a} \phi, A_{f} \varphi \in \mathbb{L}_{\varrho}\right\} .
\end{aligned}
$$

Lemma 2.1. Given any $\vartheta \in[0,2] \backslash\{1+1 / \varrho\}$ and $\phi \in \mathbb{W}_{\varrho, \mathcal{B}}^{\vartheta}$, there exists a unique solution $B_{\phi} \in C\left(\mathbb{R}^{+}, W_{\varrho, \mathcal{B}}^{\vartheta}\right)$ to the Volterra equation (15). If $\phi \in \mathbb{L}_{\varrho}^{+}$, then $B_{\phi}(t) \geq 0$ for $t \geq 0$. Moreover, if $\phi \in \mathbb{D}_{f}$, then $B_{\phi} \in C^{1}\left(\mathbb{R}^{+}, \mathbb{L}_{\varrho}\right)$ with $\partial_{t} B_{\phi}=B_{\Phi}$, where $\Phi:=-\partial_{a} \phi-A_{f} \phi$, and $A_{f} B_{\phi}=B_{A_{f} \phi}$. Finally, there are $\bar{M}:=\bar{M}\left(\|f\|_{C^{1}(\bar{\Omega})}\right)$ and $\bar{\omega}:=\bar{\omega}\left(\|f\|_{C^{1}(\bar{\Omega})}\right)$ such that

$$
\begin{equation*}
\left\|B_{\phi}(t)\right\|_{W_{\varrho, \mathcal{B}}^{\vartheta}} \leq \bar{M} e^{\bar{\omega} t}\|\phi\|_{\mathbb{W}_{\varrho, \mathcal{B}}^{\vartheta}}, \quad t \geq 0 \tag{16}
\end{equation*}
$$

In particular, there holds

$$
\begin{equation*}
\left\|B_{\phi}(t)\right\|_{L_{\varrho}} \leq 2\|b\|_{\infty} e^{2\|b\|_{\infty} t}\|\phi\|_{\mathbb{L}_{e}}, \quad t \geq 0 \tag{17}
\end{equation*}
$$

Proof. Using the fact that $\mathcal{U}_{f}$ is a strongly continuous semigroup on $W_{\varrho, \mathcal{B}}^{\vartheta}$ (of contractions if $\vartheta=0$ ), the unique solvability of (15) is obtained by standard arguments. Together with Gronwall's inequality, this also implies (16), (17). Clearly, $\phi \in \mathbb{L}_{\varrho}^{+}$implies $B_{\phi}(t) \geq 0$ for $t \geq 0$. Next, if $\phi \in \mathbb{D}_{f}$, then the second term on the right hand side of (15) is continuously differentiable with respect to $t \geq 0$ and values in $W_{\varrho, \mathcal{B}}^{\vartheta}$, whence $B_{\phi} \in C^{1}\left(\mathbb{R}^{+}, W_{\varrho, \mathcal{B}}^{\vartheta}\right)$. Since $\phi(0, \cdot)=B_{\phi}(0)$, there holds

$$
\partial_{t} B_{\phi}(t)=2 \int_{0}^{t} b(a) U_{f}(a) \partial_{t} B_{\phi}(t-a) \mathrm{d} a+2 U_{f}(t) \int_{0}^{\infty} b(a+t) \Phi(a) \mathrm{d} a
$$

and thus $\partial_{t} B_{\phi}=B_{\Phi}$ by uniqueness of solutions to (15). Also note that $A_{f} \phi \in \mathbb{L}_{\varrho}$ implies $\phi \in \mathbb{W}_{\varrho, \mathcal{B}}^{2}$. Therefore,

$$
A_{f} B_{\phi}(t)=2 \int_{0}^{t} b(a) U_{f}(a) A_{f} B_{\phi}(t-a) \mathrm{d} a+2 U_{f}(t) \int_{0}^{\infty} b(a+t) A_{f} \phi(a) \mathrm{d} a
$$

and so $A_{f} B_{\phi}=B_{A_{f} \phi}$ again by uniqueness.

We are now in a position to introduce the age-diffusion semigroup $\mathcal{S}_{f}:=\left\{\mathbb{S}_{f}(t) ; t \geq 0\right\}$ as follows: given $\phi \in \mathbb{L}_{\varrho}$ we put

$$
\left[\mathbb{S}_{f}(t) \phi\right](a):= \begin{cases}U_{f}(t) \phi(a-t), & 0 \leq t<a \\ U_{f}(a) B_{\phi}(t-a), & 0 \leq a \leq t\end{cases}
$$

with $\mathbb{S}(t):=\mathbb{S}_{0}(t)$, that is, for $f \equiv 0$. Observe then that

$$
\begin{equation*}
B_{\phi}(t)=2 \int_{0}^{\infty} b(a)\left[\mathbb{S}_{f}(t) \phi\right](a) \mathrm{d} a, \quad t \geq 0 \tag{18}
\end{equation*}
$$

The next proposition collects some important facts about the semigroup $\mathcal{S}_{f}$ and characterizes its generator.

Proposition 2.2. $\mathcal{S}_{f}$ is a strongly continuous positive semigroup on $\mathbb{L}_{\varrho}$ such that

$$
\begin{equation*}
\left\|\mathbb{S}_{f}(t)\right\|_{\mathcal{L}\left(\mathbb{L}_{\varrho}\right)} \leq e^{2\|b\|_{\infty} t}, \quad t \geq 0 \tag{19}
\end{equation*}
$$

and

$$
\begin{equation*}
\left\|\mathbb{S}_{f}(t)\right\|_{\mathcal{L}\left(\mathbb{L}_{e}, \mathbb{L}_{\xi}\right)} \leq c(T) t^{-(1 / \varrho-1 / \xi) n / 2}, \quad 0<t \leq T \tag{20}
\end{equation*}
$$

for $1<\varrho \leq \xi \leq \infty$ with $(1 / \varrho-1 / \xi) n<2$, and

$$
\begin{equation*}
\left\|\mathbb{S}_{f}(t)\right\|_{\mathcal{L}\left(\mathbb{W}_{e, \mathcal{B}}^{2 \eta}, \mathbb{W}_{e, \mathcal{B}}^{2 \mu}\right)} \leq c(T) t^{\eta-\mu}, \quad 0<t \leq T \tag{21}
\end{equation*}
$$

for $0 \leq 2 \eta \leq 2 \mu \leq 2$ with $2 \eta, 2 \mu \neq 1+1 / \varrho$, and $\mu-\eta<1$, where $c(T):=c\left(T,\|f\|_{C^{1}(\bar{\Omega})}\right)$.
If $-\mathbb{A}_{f}$ denotes the generator of $\mathcal{S}_{f}$ and if its domain $D\left(\mathbb{A}_{f}\right)$ is equipped with the graph norm, then $D\left(\mathbb{A}_{f}\right) \doteq D\left(\mathbb{A}_{0}\right)$,

$$
\begin{equation*}
D\left(\mathbb{A}_{0}\right) \hookrightarrow \mathbb{W}_{\varrho, \mathcal{B}}^{\mu}, \quad \mu \in[0,2) \backslash\{1+1 / \varrho\} \tag{22}
\end{equation*}
$$

and

$$
\begin{equation*}
D\left(\mathbb{A}_{0}\right) \subset W_{1}^{\mu}\left(\mathbb{R}^{+}, L_{\varrho}\right), \quad 0 \leq \mu<1 \tag{23}
\end{equation*}
$$

Moreover, $\mathbb{D}_{f}$ is a core for $\mathbb{A}_{f}$ and

$$
\begin{equation*}
\mathbb{A}_{f} \phi=\left(\partial_{a}+A_{f}\right) \phi, \quad \phi \in D\left(\mathbb{A}_{0}\right) \tag{24}
\end{equation*}
$$

Proof. (i) It follows from [27, Thm.4] that $\mathcal{S}_{f}$ is a strongly continuous semigroup on $\mathbb{L}_{\varrho}$ and that (19) holds since $\mathcal{U}_{f}$ consists of contractions. Lemma 2.1 implies that $\mathcal{S}_{f}$ is a positive semigroup.
(ii) Next, let $\phi \in \mathbb{W}_{\varrho, \mathcal{B}}^{2 \eta}$ and $0 \leq 2 \eta \leq 2 \mu \leq 2$ with $2 \eta, 2 \mu \neq 1+1 / \varrho$. Then, from (14) and (16),

$$
\begin{align*}
\left\|\mathbb{S}_{f}(t) \phi\right\|_{\mathbb{W}_{\varrho, \mathcal{B}}^{2 \mu}} \leq & \|b\|_{\infty} \int_{0}^{t}\left\|U_{f}(a)\right\|_{\mathcal{L}\left(W_{\varrho, \mathcal{B}}^{2}, W_{\varrho, \mathcal{B}}^{2 \mu}\right)}\left\|B_{\phi}(t-a)\right\|_{W_{\varrho, \mathcal{B}}^{2 \eta}} \mathrm{~d} a \\
& +\|b\|_{\infty}\left\|U_{f}(t)\right\|_{\mathcal{L}\left(W_{\varrho, \mathcal{B}}^{2 \eta}, W_{\varrho}^{2 \mu}\right)} \int_{t}\|\phi(a-t)\|_{W_{\varrho, \mathcal{B}}^{2 \eta}} \mathrm{~d} a  \tag{25}\\
\leq & \tilde{M} e^{\tilde{\omega} t}\left(t^{1+\eta-\mu}+t^{\eta-\mu}\right)\|\phi\|_{\mathbb{W}_{e, \mathcal{B}}^{2 \eta}}^{\infty}
\end{align*}
$$

for $t>0$, provided that $0 \leq \mu-\eta<1$. This proves (21), and (20) is obtained analogously using (13) and (17).
(iii) Let $-\mathbb{A}_{f}$ denote the generator of $\mathcal{S}_{f}$. Then

$$
\left(\lambda+\mathbb{A}_{f}\right)^{-1} \phi=\int_{0}^{\infty} e^{-\lambda t} \mathbb{S}_{f}(t) \phi \mathrm{d} t \in D\left(\mathbb{A}_{f}\right), \quad \phi \in \mathbb{L}_{\varrho}
$$

for $\lambda>0$ sufficiently large. Therefore, using (25) with $\eta=0$ and making $\lambda$ larger if necessary, we deduce $\left(\lambda+\mathbb{A}_{f}\right)^{-1} \in \mathcal{L}\left(\mathbb{L}_{\varrho}, \mathbb{W}_{\varrho, \mathcal{B}}^{2 \mu}\right)$ and hence

$$
\begin{equation*}
D\left(\mathbb{A}_{f}\right) \hookrightarrow \mathbb{W}_{\varrho, \mathcal{B}}^{2 \mu}, \quad 2 \mu \in[0,2) \backslash\{1+1 / \varrho\} \tag{26}
\end{equation*}
$$

(iv) Suppose $0<\mu<\vartheta<1$ and let $\phi \in D\left(\mathbb{A}_{f}\right)$. We recall that

$$
\left[\mathbb{S}_{f}(t) \phi\right](a)=U_{f}(t) \phi(a-t), \quad a>t
$$

Thus

$$
\begin{aligned}
\|\phi\|_{W_{1}^{\mu}\left(\mathbb{R}^{+}, L_{\varrho}\right)}= & 2 \int_{0}^{\infty} t^{-1-\mu} \int_{t}^{\infty}\|\phi(a-t)-\phi(a)\|_{L_{\varrho}} \mathrm{d} a \mathrm{~d} t \\
\leq & 2 \int_{0}^{1} t^{-1-\mu} \int_{t}^{\infty}\left\|\phi(a-t)-e^{-t} U_{f}(t) \phi(a-t)\right\|_{L_{\varrho}} \mathrm{d} a \mathrm{~d} t \\
& +2 \int_{0}^{1} t^{-\mu} \frac{1-e^{-t}}{t} \int_{t}^{\infty}\left\|U_{f}(t) \phi(a-t)\right\|_{L_{\varrho}} \mathrm{d} a \mathrm{~d} t \\
& +2 \int_{0}^{1} t^{-\mu} \frac{1}{t} \int_{t}^{\infty}\left\|\left[\mathbb{S}_{f}(t) \phi\right](a)-\phi(a)\right\|_{L_{\varrho}} \mathrm{d} a \mathrm{~d} t \\
& +2 \int_{1}^{\infty} t^{-1-\mu} \int_{t}^{\infty}\|\phi(a-t)-\phi(a)\|_{L_{\varrho}} \mathrm{d} a \mathrm{~d} t
\end{aligned}
$$

Since $\mu>0$ and $\phi \in \mathbb{L}_{\varrho}$, the last term is finite. The second last term is finite because of $\mu<1$ and $\phi \in D\left(\mathbb{A}_{f}\right)$. The third last term is clearly finite. Observing that $\left\{e^{-t} U_{f}(t) ; t \geq 0\right\}$ is an analytic semigroup of negative type, we may apply e.g. [19, II.Thm.6.13] to derive

$$
\left\|\phi(a-t)-e^{-t} U_{f}(t) \phi(a-t)\right\|_{L_{e}} \leq c t^{\vartheta}\|\phi(a-t)\|_{W_{e, \mathcal{B}}^{2, \vartheta}}, \quad a>t>0
$$

what is well-defined according to (26). Hence also the first term of the inequality above is finite and we conclude (23).
(v) Next we show that $\mathbb{D}_{f}$ is a core for $\mathbb{A}_{f}$. First, we obtain from [13, Ex.1.1.(a), Thm.1.2] that the set

$$
\mathcal{N}:=\left\{\varphi \in W_{1}^{1}\left(\mathbb{R}^{+}\right) ; \varphi(0)=2 \int_{0}^{\infty} b(a) \varphi(a) \mathrm{d} a\right\}
$$

is dense in $L_{1}\left(\mathbb{R}^{+}\right)$. Therefore, the tensor product $\mathcal{N} \otimes W_{\varrho, \mathcal{B}}^{2}$ is dense in $\mathbb{L}_{\varrho}$ and obviously a subset of $\mathbb{D}_{f}$. Thus $\mathbb{D}_{f}$ is dense in $\mathbb{L}_{\varrho}$.

Given $\phi \in \mathbb{D}_{f}$ we set $\Phi:=-\partial_{a} \phi-A_{f} \phi \in \mathbb{L}_{\varrho}$. Then, due to $\partial_{t} B_{\phi}=B_{\Phi}$ and $A_{f} B_{\phi}=B_{A_{f} \phi}$ by Lemma 2.1, we derive $\partial_{a} \mathbb{S}_{f}(t) \phi \in \mathbb{L}_{\varrho}$ and $A_{f} \mathbb{S}_{f}(t) \phi \in \mathbb{L}_{\varrho}$. Moreover, one easily checks that $\mathbb{S}_{f}(t) \phi \in \mathbb{D}_{f}$ for $t>0$. Therefore, $\mathbb{D}_{f}$ is invariant under $\mathbb{S}_{f}(t)$. We then use again $\partial_{t} B_{\phi}=B_{\Phi}$ together with

$$
\partial_{s}\left(U_{f}(s) \phi(a-s)\right)=U_{f}(s) \Phi(a-s), \quad a>s
$$

for the second equality of the next computation to obtain, for $t>0$ and a.a. $a>0$, that

$$
\begin{array}{rlrl}
\left(\int_{0}^{t} \mathbb{S}_{f}(s) \Phi \mathrm{d} s\right)(a) & = \begin{cases}\int_{0}^{t} U_{f}(s) \Phi(a-s) \mathrm{d} s, & a \geq t \\
\int_{0}^{a} U_{f}(s) \Phi(a-s) \mathrm{d} s+\int_{a}^{t} U_{f}(a) B_{\Phi}(s-a) \mathrm{d} s, & a<t\end{cases} \\
& = \begin{cases}U_{f}(t) \phi(a-t)-\phi(a), \\
U_{f}(a) \phi(0)-\phi(a)+U_{f}(a) B_{\phi}(t-a)-U_{f}(a) B_{\phi}(0), & a \geq t\end{cases} \\
& =\left[\mathbb{S}_{f}(t) \phi-\phi\right](a), &
\end{array}
$$

the last equality stemming from (18). Thus we conclude

$$
\begin{equation*}
\mathbb{A}_{f} \phi=\left(\partial_{a}+A_{f}\right) \phi, \quad \phi \in \mathbb{D}_{f} \subset D\left(\mathbb{A}_{f}\right) \tag{27}
\end{equation*}
$$

Gathering now the facts that $\mathbb{D}_{f}$ is a subset of $D\left(\mathbb{A}_{f}\right)$, dense in $\mathbb{L}_{\varrho}$, and invariant under $\mathbb{S}_{f}(t)$, it is indeed a core for $\mathbb{A}_{f}$.
(vi) Finally, since $\mathbb{D}_{f}$ is dense in $D\left(\mathbb{A}_{f}\right)$ (equipped with the graph norm), we readily infer from (27) that $D\left(\mathbb{A}_{f}\right)$ is independent of $f$, that is, $D\left(\mathbb{A}_{f}\right)=D\left(\mathbb{A}_{0}\right)$, and that (24) holds.
2.2. Further Auxiliary Results. The next two results will be needed to prove positivity of the solutions.

Lemma 2.3. $D\left(\mathbb{A}_{0}\right) \cap \mathbb{L}_{\varrho}^{+}$is dense in $\mathbb{L}_{\varrho}^{+}$.
Proof. Since $-\mathbb{A}_{0}$ is the generator of the strongly continuous positive semigroup $\mathcal{S}_{0}$ on $\mathbb{L}_{\varrho}$ according to Proposition 2.2, we may choose $\omega$ sufficiently large to obtain from [2, II.Sect.6.4] that $\omega+\mathbb{A}_{0}$ is resolvent positive with spectrum entirely in the complex left half-plane, that is, $\omega+\mathbb{A}_{0}$ is a positive operator in the sense of [2]. The assertion follows then from $D\left(\mathbb{A}_{0}\right)=D\left(\omega+\mathbb{A}_{0}\right)$ and [2, V.Prop.2.7.2].

We recall that $W_{\varrho}^{2} \hookrightarrow C^{1}(\bar{\Omega})$ for $\varrho>n$.
Lemma 2.4. Let $\varrho>n$ and $f \in C^{1}\left([0, T], W_{\varrho, \mathcal{B}}^{2}\right)$ with $T>0$. Let $M_{i j} \in C^{1}\left([0, T], \mathcal{L}\left(\mathbb{L}_{\varrho}\right)\right)$ with $M_{12}(t), M_{21}(t) \geq 0$ for $t \in[0, T]$. Define

$$
\mathcal{A}(t):=\left[\begin{array}{cc}
\mathbb{A}_{f(t)} & 0 \\
0 & -\gamma \Delta_{x}
\end{array}\right], \quad \mathcal{M}(t):=\left[\begin{array}{ll}
M_{11}(t) & M_{12}(t) \\
M_{21}(t) & M_{22}(t)
\end{array}\right]
$$

for $t \in[0, T]$. Then, given any $u^{0} \in\left(D\left(\mathbb{A}_{0}\right) \cap \mathbb{L}_{\varrho}^{+}\right) \times\left(\mathbb{W}_{\varrho, \mathcal{B}}^{2} \cap \mathbb{L}_{\varrho}^{+}\right)$, there exists a unique classical solution

$$
u \in C^{1}\left([0, T], \mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}\right) \cap C\left([0, T], D\left(\mathbb{A}_{0}\right) \times \mathbb{W}_{\varrho, \mathcal{B}}^{2}\right)
$$

with $u(t) \in \mathbb{L}_{\varrho}^{+} \times \mathbb{L}_{\varrho}^{+}, t \in[0, T]$, to the evolution equation

$$
\begin{equation*}
\dot{u}+(\mathcal{A}(t)-\mathcal{M}(t)) u=0, \quad u(0)=u^{0} \tag{28}
\end{equation*}
$$

Proof. Set $\mathbb{F}_{0}:=\mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}, \mathbb{F}_{1}:=D\left(\mathbb{A}_{0}\right) \times \mathbb{W}_{\varrho, \mathcal{B}}^{2}$ and denote by $\mathbb{F}_{0}^{+}:=\mathbb{L}_{\varrho}^{+} \times \mathbb{L}_{\varrho}^{+}$the positive cone in $\mathbb{F}_{0}$. Clearly, $\gamma \Delta_{x}$ (naturally defined on $\mathbb{W}_{\varrho, \mathcal{B}}^{2}$ ) generates an analytic semigroup of contractions on $\mathbb{L}_{\varrho}$. Hence, it follows from Proposition 2.2 that $-\mathcal{A}(t)$ is for every $t \in[0, T]$ the generator of a strongly continuous semigroup $\left\{e^{-s \mathcal{A}(t)} ; s \geq 0\right\}$ on $\mathbb{F}_{0}$ satisfying

$$
\left\|e^{-s \mathcal{A}(t)}\right\|_{\mathcal{L}\left(\mathbb{F}_{0}\right)} \leq e^{2\|b\|_{\infty} s}, \quad s \geq 0
$$

In particular, $(-\mathcal{A}(t))_{t \in[0, T]}$ is stable in the sense of [19, §5.2]. Moreover, the domain of $\mathcal{A}(t)$ equals $\mathbb{F}_{1}$ for every $t \in[0, T]$ and $(t \mapsto \mathcal{A}(t) \phi) \in C^{1}\left([0, T], \mathbb{F}_{0}\right)$ for $\phi \in \mathbb{F}_{1}$. According to $[19, \S 5.2]$ this warrants the existence of a unique evolution system $U_{\mathcal{A}}(t, s), 0 \leq s \leq t \leq T$, on $\mathbb{F}_{0}$. By construction of this evolution system (cf. [19, p.136f]) it is obviously positive since the semigroups corresponding to $\gamma \Delta_{x}$ and $-\mathbb{A}_{f(t)}$ are all positive. Owing to $\mathcal{M} \in C^{1}\left([0, T], \mathcal{L}\left(\mathbb{F}_{0}\right)\right)$ and $[19,5 . T h m .2 .3]$, the same arguments show that there is an evolution system corresponding to $(-\mathcal{A}(t)+\mathcal{M}(t))_{t \in[0, T]}$. Consequently, (28) possesses a unique classical solution $u \in C^{1}\left([0, T], \mathbb{F}_{0}\right) \cap C\left([0, T], \mathbb{F}_{1}\right)$ since $u^{0} \in \mathbb{F}_{1}$. Letting

$$
\omega:=\max _{t \in[0, T]}\left(\left\|M_{11}(t)\right\|_{\mathcal{L}\left(\mathbb{L}_{e}\right)}+\left\|M_{22}(t)\right\|_{\mathcal{L}\left(\mathbb{L}_{e}\right)}\right)
$$

and defining

$$
\mathcal{A}_{\omega}(t):=\omega \mathbf{1}_{\mathbb{F}_{0}}+\mathcal{A}(t), \quad G_{\omega}(t):=\omega \mathbf{1}_{\mathbb{F}_{0}}+\mathcal{M}(t)
$$

we have $G_{\omega}(t) \phi \in \mathbb{F}_{0}^{+}$and $U_{\mathcal{A}_{\omega}}(t, s) \phi \in \mathbb{F}_{0}^{+}$for $\phi \in \mathbb{F}_{0}^{+}$. Recalling that $u^{0} \in \mathbb{F}_{1}^{+}$, Banach's fixed point theorem guarantees that the sequence $\left(u_{j}\right)_{j \in \mathbb{N}} \subset \mathbb{F}_{0}^{+}$, defined by
$u_{0}:=u^{0}, \quad u_{j+1}(t):=U_{\mathcal{A}_{\omega}}(t, 0) u^{0}+\int_{0}^{t} U_{\mathcal{A}_{\omega}}(t, s) G_{\omega}(s) u_{j}(s) \mathrm{d} s, \quad t \in[0, T], \quad j \in \mathbb{N}$,
converges towards $u$ in $C\left([0, \tilde{T}], \mathbb{F}_{0}\right)$ for $\tilde{T}>0$ sufficiently small. This proves $u(t) \in \mathbb{F}_{0}^{+}$for $t \in[0, \tilde{T}]$ since $\mathbb{F}_{0}^{+}$is closed in $\mathbb{F}_{0}$. The assertion now readily follows.

In order to state the next results, we need some notation. Let $E$ be a Banach space. For an interval $J \subset \mathbb{R}^{+}$containing 0 we put $\dot{J}:=J \backslash\{0\}$. Given $\mu \in \mathbb{R}$, we denote by $B C_{\mu}(\dot{J}, E)$ the Banach space of all functions $u: \dot{J} \rightarrow E$ such that $\left(t \mapsto t^{\mu} u(t)\right)$ is bounded and continuous from $\dot{J}$ into $E$, equipped with the norm

$$
u \mapsto\|u\|_{C_{\mu}(j, E)}:=\sup _{t \in \dot{J}} t^{\mu}\|u(t)\|_{E}
$$

We write $C_{\mu}(\dot{J}, E)$ for the closed linear subspace thereof consisting of all $u$ satisfying $t^{\mu} u(t) \rightarrow 0$ in $E$ as $t \rightarrow 0^{+}$. Note that $C_{\nu}((0, T], E) \hookrightarrow C_{\mu}((0, T], E)$ for $\nu \leq \mu$ and $T>0$.

If $\{U(t) ; t \geq 0\}$ is a strongly continuous semigroup on $E$, we set $U_{\xi}(t):=U(\xi t)$ for $t \geq 0$ and $\xi>0$. Furthermore, for any measurable function $u: \dot{J} \rightarrow E$ we put

$$
U \star u(t):=\int_{0}^{t} U(t-s) u(s) \mathrm{d} s, \quad t \in \dot{J}
$$

whenever these integrals exist.

We now take $f \equiv 0$ in the previous considerations and denote by $\{U(t) ; t \geq 0\}$ the analytic semigroup on $L_{\varrho}$ generated by $\Delta_{x}$ subject to Neumann boundary conditions. By $\{\mathbb{V}(t) ; t \geq 0\}$ we denote the analytic semigroup on $\mathbb{L}_{\varrho}$ generated by $\gamma \Delta_{x}$. Finally, we put $\mathbb{S}(t):=\mathbb{S}_{0}(t)$, i.e. $\{\mathbb{S}(t) ; t \geq 0\}$ is the semigroup on $\mathbb{L}_{\varrho}$ with generator $-\partial_{a}+\delta \Delta_{x}$ (cf. Proposition 2.2).

Lemma 2.5. Let $1<\varrho<\infty, 2 \mu \in(0,2) \backslash\{1+1 / \varrho\}$ and $T, \xi>0$. Then
(i) $U_{\xi} \varphi:=\left[t \mapsto U_{\xi}(t) \varphi\right] \in C_{\mu}\left((0, T], W_{\varrho, \mathcal{B}}^{2 \mu}\right)$ for $\varphi \in L_{\varrho}$,
(ii) $U_{\xi} \varphi \in C_{1-\mu}\left((0, T], W_{\varrho, \mathcal{B}}^{2}\right)$ for $\varphi \in W_{\varrho, \mathcal{B}}^{2 \mu}$,
(iii) $\mathbb{V} \phi, \mathbb{S} \phi \in C_{\mu}\left((0, T], \mathbb{W}_{\varrho, \mathcal{B}}^{2 \mu}\right)$ for $\phi \in \mathbb{L}_{\varrho}$.

Proof. Parts (i), (ii) and the first part of (iii) are shown analogously to [3, Prop.6] (see also $\left[25\right.$, Lem.2.3]). As for the second part of (iii) one shows that $\mathbb{S} \phi \in B C_{\mu}\left((0, T], \mathbb{W}_{\varrho, \mathcal{B}}^{2 \mu}\right)$ for $\phi \in \mathbb{L}_{\varrho}$ using Lemma 2.1 and Proposition 2.2. The density of $\mathbb{W}_{\varrho, \mathcal{B}}^{2 \mu}$ in $\mathbb{L}_{\varrho}$ and again Proposition 2.2 entail

$$
\lim _{t \rightarrow 0^{+}} t^{\mu}\|\mathbb{S}(t) \phi\|_{\mathbb{W}_{\varrho, \mathcal{B}}^{2 \mu}}^{2 \mu}=0
$$

as in [3, Prop.6].

## 3. The Main Result

To state our main result we recall the definition of a mild solution. Let $-A$ be the generator of a strongly continuous semigroup $\left\{e^{-t A} ; t \geq 0\right\}$ on a Banach space $E$. Given $u^{0} \in E$, we mean by a (global) mild E-solution to the Cauchy problem

$$
\dot{u}+A u=F(t, u), \quad u(0)=u^{0}
$$

a function $u \in C\left(\mathbb{R}^{+}, E\right)$ such that $F(\cdot, u) \in L_{1, l o c}\left(\mathbb{R}^{+}, E\right)$ and

$$
u(t)=e^{-t A} u^{0}+\int_{0}^{t} e^{-(t-s) A} F(s, u(s)) \mathrm{d} s, \quad t \geq 0
$$

The main result concerning the global well-posedness of $\left(E_{1}\right)-\left(E_{8}\right)$ reads as follows:
Theorem 3.1. Let assumptions (5)-(11) be satisfied, and let $(1 \vee n / 2)<\varrho<\infty$ and $2 \varepsilon \in(0,2) \backslash\{1+1 / \varrho\}$. Given any non-negative initial value

$$
\left(f^{0}, m^{0}, w^{0}, q^{0}, p^{0}\right) \in Y:=W_{\varrho, \mathcal{B}}^{2} \times W_{\varrho, \mathcal{B}}^{2 \varepsilon} \times L_{\varrho} \times \mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}
$$

there exists a global non-negative solution $(f, m, w, q, p)$ to $\left(E_{1}\right)-\left(E_{8}\right)$ such that

$$
\begin{aligned}
& f \in C\left(\mathbb{R}^{+}, W_{\varrho, \mathcal{B}}^{2}\right) \cap C^{1}\left(\dot{\mathbb{R}}^{+}, W_{\varrho, \mathcal{B}}^{2}\right) \\
& m \in C\left(\mathbb{R}^{+}, W_{\varrho, \mathcal{B}}^{2 \varepsilon}\right) \cap C\left(\dot{\mathbb{R}}^{+}, W_{\varrho, \mathcal{B}}^{2}\right) \cap C^{1}\left(\dot{\mathbb{R}}^{+}, L_{\varrho}\right), \\
& w \in C\left(\mathbb{R}^{+}, L_{\varrho}\right) \cap C\left(\dot{\mathbb{R}}^{+}, W_{\varrho, \mathcal{B}}^{2}\right) \cap C^{1}\left(\dot{\mathbb{R}}^{+}, L_{\varrho}\right), \\
& q, p \in C\left(\mathbb{R}^{+}, \mathbb{L}_{\varrho}\right) \cap C\left(\dot{R}^{+}, \mathbb{W}_{\varrho, \mathcal{B}}^{\xi}\right), \quad \xi \in(0,2) \backslash\{1+1 / \varrho\},
\end{aligned}
$$

where $q$ and $p$ are mild solutions to $\left(E_{4}\right)$ and $\left(E_{5}\right)$, respectively. This solution satisfies

$$
\begin{equation*}
t^{\lambda}\|m(t)\|_{W_{e}^{2}} \rightarrow 0 \quad \text { and } \quad t^{\eta}\left(\|p(t)\|_{\mathbb{W}_{e}^{2 \eta}}+\|q(t)\|_{\mathbb{W}_{e}^{2 \eta}}\right) \rightarrow 0 \quad \text { as } \quad t \rightarrow 0^{+} \tag{29}
\end{equation*}
$$

for all $(\eta, \lambda)$ such that

$$
\begin{equation*}
n / \varrho<2 \eta<2, \quad 2 \eta \geq 1, \quad(1-\varepsilon) \vee \eta \leq \lambda<1 \tag{30}
\end{equation*}
$$

and it is the only solution satisfying (29) for some $(\eta, \lambda)$ as in (30). Moreover, $P$ and $Q$ belong to $C^{1}\left(\dot{\mathbb{R}}^{+}, L_{\varrho}\right) \cap C\left(\dot{\mathbb{R}}^{+}, W_{\varrho, \mathcal{B}}^{2}\right)$. Finally, the solution depends continuously in $Y$ on the initial value.

Provided $\epsilon, \sigma$, and $\tau$ possess more regularity with respect to $x, w, Q$, and $P$, the mild solution $q$ to $\left(E_{4}\right)$ is actually a classical solution.

We shall point out that the restriction on the integrability index $\varrho$ and also the regularity assumptions on the initial values seem to be fairly weak (except for the first equation $\left(E_{1}\right)$ which lacks a smoothing effect due to diffusion).

Moreover, the uniqueness (and existence) result in Theorem 3.1 is more general than in Theorem 1.1 in the sense that any (mild) solution in $C\left(\mathbb{R}^{+}, X\right)$ satisfies (29) for some $(\eta, \lambda)$ as in (30).

The proof of Theorem 3.1 will be divided into several steps.
3.1. Proof of Thm. 3.1: Local Existence and Uniqueness. We first rewrite equations $\left(E_{1}\right)-\left(E_{8}\right)$ in a more convenient form. In the following, we will suppress the variables $a$ and $x$ if no confusion seems to arise and we thus simply write $\phi(w, Q, P)$ instead of $\phi(a, x, w, Q, P)$ for $\phi \in\{\sigma, \tau, \epsilon, \theta\}$. Similarly we do this for $\Gamma$ and $\Lambda$. For $u:=(f, m, w, q, p)$ we use (1) and put

$$
\begin{aligned}
& R_{1}(u):=d P-h m \\
& R_{2}(u):=\Gamma(f)-\Lambda(Q, P) w-e w \\
& R_{3}(u):=\sigma(w, Q, P) p-\epsilon(w, Q, P) q-\tau(w, Q, P) q \\
& R_{4}(u):=-\nabla_{x} \cdot\left(p \chi(f) \nabla_{x} f\right)-b p+\tau(w, Q, P) q-\sigma(w, Q, P) p-\theta(w, Q, P) p .
\end{aligned}
$$

Local existence and uniqueness is based on the following proposition whose proof is adapted from [25, Prop.3.1].

Proposition 3.2. Let $1<\varrho<\infty$ and $n / \varrho<2 \eta \leq 2 \xi \leq 2 \mu<2$ with $2 \eta \geq 1$. Given $r \geq 1$ there exists $T:=T(r)>0$ such that, for any

$$
u^{0}:=\left(f^{0}, m^{0}, w^{0}, q^{0}, p^{0}\right) \in E_{1-\mu}:=W_{\varrho, \mathcal{B}}^{2} \times W_{\varrho, \mathcal{B}}^{2(1-\mu)} \times L_{\varrho} \times \mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}
$$

with $\left\|u^{0}\right\|_{E_{1-\mu}} \leq r$, the problem

$$
\left.\begin{array}{rlrl}
f(t) & =\exp \left(-k \int_{0}^{t} m(s) \mathrm{d} s\right) f^{0}, & & t \in I  \tag{M}\\
m(t) & =U_{\alpha}(t) m^{0}+U_{\alpha} \star R_{1}(u)(t), & & t \in I \\
w(t) & =U_{\beta}(t) w^{0}+U_{\beta} \star R_{2}(u)(t), & & t \in I \\
q(t) & =\mathbb{V}(t) q^{0}+\mathbb{V} \star R_{3}(u)(t), & & t \in I \\
p(t) & =\mathbb{S}(t) p^{0}+\mathbb{S} \star R_{4}(u)(t), & & t \in I,
\end{array}\right\}
$$

has a unique solution

$$
u:=(f, m, w, q, p) \in \mathcal{V}_{T}:=\mathcal{V}_{T}(\mu, \xi, \eta):=W_{T} \times X_{T} \times Y_{T} \times Z_{T} \times Z_{T}
$$

where $I:=[0, T]$ and

$$
\begin{aligned}
W_{T} & :=C\left(I, W_{\varrho, \mathcal{B}}^{2}\right),
\end{aligned} \quad X_{T}:=C_{\mu}\left(\dot{I}, W_{\varrho, \mathcal{B}}^{2}\right) \cap C\left(I, W_{\varrho, \mathcal{B}}^{2(1-\mu)}\right), ~ 子\left(I, L_{\varrho}\right), \quad Z_{T}:=C_{\xi}\left(\dot{I}, \mathbb{W}_{\varrho, \mathcal{B}}^{2 \eta}\right) \cap C\left(I, \mathbb{L}_{\varrho}\right) .
$$

Moreover, the solution depends continuously on the initial value in the sense that, if $\bar{u} \in \mathcal{V}_{T}$ denotes the solution corresponding to $\bar{u}^{0} \in E_{1-\mu}$ with $\left\|\bar{u}^{0}\right\|_{E_{1-\mu}} \leq r$, then $\bar{u} \rightarrow u$ in $\mathcal{V}_{T}$ as $\bar{u}^{0} \rightarrow u^{0}$ in $E_{1-\mu}$.

Proof. In the following we take $T \in(0,1)$. First we claim that whenever $0 \leq \vartheta-\nu<1$, $\zeta<1$, and $R \in C_{b}^{1-}\left(\mathcal{V}_{T}, C_{\zeta}\left(\dot{I}, W_{\varrho, \mathcal{B}}^{2 \nu}\right)\right)$ there holds

$$
\begin{equation*}
U \star R \in C_{b}^{1-}\left(\mathcal{V}_{T}, C_{\vartheta+\zeta-\nu-1}\left(\dot{I}, W_{\varrho, \mathcal{B}}^{2 \vartheta}\right)\right), \tag{31}
\end{equation*}
$$

where $C_{b}^{1-}$ means 'uniformly Lipschitz continuous on bounded sets'. In addition, analogous statements also hold for $\mathbb{V}$ and $\mathbb{S}$, where the spaces $W_{\varrho, \mathcal{B}}^{2 \nu}$ are replaced by $\mathbb{W}_{\varrho, \mathcal{B}}^{2 \nu}$. To prove (31) observe that, if

$$
\|R(v)(t)-R(\bar{v})(t)\|_{W_{e, \mathcal{B}}^{2 \nu}} \leq c(r) t^{-\zeta}\|v-\bar{v}\|_{\mathcal{V}_{T}}, \quad t \in(0, T], \quad\|v\|_{\mathcal{V}_{T}},\|\bar{v}\|_{\mathcal{V}_{T}} \leq r
$$

then, by (14),

$$
\begin{aligned}
\|U \star(R(v)-R(\bar{v}))(t)\|_{W_{\varrho, \mathcal{B}}^{2 \vartheta \vartheta}} & \leq c \int_{0}^{t}(t-s)^{\nu-\vartheta}\|R(v)(s)-R(\bar{v})(s)\|_{W_{\varrho, \mathcal{B}}^{2 \nu}} \mathrm{~d} s \\
& \leq c(r) \mathrm{B}(1+\nu-\vartheta, 1-\zeta) t^{1+\nu-\vartheta-\zeta}\|v-\bar{v}\|_{\mathcal{V}_{T}}
\end{aligned}
$$

with $\operatorname{B}$ denoting the beta function, whence (31). Similarly one shows this for $\mathbb{V}$ and $\mathbb{S}$, in the latter case using Proposition 2.2. Notice then that $p \in C_{\xi}\left((0, T], \mathbb{W}_{\varrho, \mathcal{B}}^{2 \eta}\right)$ implies $P \in C_{\xi}\left((0, T], W_{\varrho, \mathcal{B}}^{2 \eta}\right)$ and that $W_{\varrho, \mathcal{B}}^{2 \eta} \hookrightarrow L_{\infty}$. Therefore, analogously to (15) in [25] (see also [25, Lem.2.1]) we obtain for $2 \zeta>0$ sufficiently small that

$$
R_{1} \in C_{b}^{1-}\left(\mathcal{V}_{T}, C_{\mu}\left((0, T], W_{\varrho, \mathcal{B}}^{2 \zeta}\right)\right)
$$

Furthermore, (7), (9) imply

$$
R_{2} \in C_{b}^{1-}\left(\mathcal{V}_{T}, C_{\xi}\left((0, T], L_{\varrho}\right)\right), \quad R_{3}, R_{4} \in C_{b}^{1-}\left(\mathcal{V}_{T}, C_{\xi}\left((0, T], \mathbb{L}_{\varrho}\right)\right)
$$

Hence, defining $\vartheta:=\zeta \wedge(1-\xi)>0, \mathcal{R}:=\left(R_{1}, R_{2}, R_{3}, R_{4}\right)^{t}$, and the diagonal matrix

$$
\mathcal{U}:=\operatorname{diag}\left[U_{\alpha}, U_{\beta}, \mathbb{V}, \mathbb{S}\right]
$$

we derive from (31) that

$$
\begin{equation*}
\|\mathcal{U} \star(\mathcal{R}(u)-\mathcal{R}(\bar{u}))\|_{X_{T} \times Y_{T} \times Z_{T} \times Z_{T}} \leq c(r) T^{\vartheta}\|u-\bar{u}\|_{\mathcal{V}_{T}}, \quad\|u\|_{\mathcal{V}_{T}},\|\bar{u}\|_{\mathcal{V}_{T}} \leq r \tag{32}
\end{equation*}
$$

We also put

$$
F_{1}(u)(t):=\exp \left(-k \int_{0}^{t} m(s) \mathrm{d} s\right) f^{0}
$$

and notice that

$$
\left\|F_{1}(u)-F_{1}(\bar{u})\right\|_{W_{T}} \leq c(r) T^{1-\mu}\|u-\bar{u}\|_{\mathcal{V}_{T}}
$$

for $\|u\|_{\mathcal{V}_{T}},\|\bar{u}\| \mathcal{V}_{T} \leq r$ and $\left\|f^{0}\right\|_{W_{e, \mathcal{B}}^{2}} \leq r$ as it follows from [25, Lem.2.2]. Finally, setting

$$
\tilde{u}^{0}:=\left(m^{0}, w^{0}, q^{0}, p^{0}\right) \in W_{\varrho, \mathcal{B}}^{2(1-\mu)} \times L_{\varrho} \times \mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}
$$

and

$$
F(u)(t):=\left(F_{1}(u)(t), \mathcal{U}(t) \tilde{u}^{0}+\mathcal{U} \star \mathcal{R}(u)(t)\right)
$$

problem $(M)$ can be rewritten as a fixed point equation of the form $F(u)=u \in \mathcal{V}_{T}$. In order to solve this fixed point equation, we observe that $V^{0}:=\left(f^{0}, \mathcal{U} \tilde{u}^{0}\right) \in \mathcal{V}_{T}$ by Lemma 2.5 and hence

$$
\begin{aligned}
\|F(u)-F(\bar{u})\|_{\mathcal{V}_{T}} & \leq c(r) T^{\vartheta}\|u-\bar{u}\|_{\mathcal{V}_{T}} \\
\left\|F(u)-V^{0}\right\|_{\mathcal{V}_{T}} & \leq c(r) T^{\vartheta}
\end{aligned}
$$

provided $T \in(0,1),\|u\|_{\mathcal{V}_{T}},\|\bar{u}\|_{\mathcal{V}_{T}} \leq r$, and $\left\|f^{0}\right\|_{W_{e, \mathcal{B}}} \leq r$. Existence of a unique fixed point and the continuous dependence on the initial value is then obtained as in [25, Prop.3.1].

We now turn to the proof of the existence and uniqueness statement of Theorem 3.1. Thus choose an initial value

$$
\left(f^{0}, m^{0}, w^{0}, q^{0}, p^{0}\right) \in W_{\varrho, \mathcal{B}}^{2} \times W_{\varrho, \mathcal{B}}^{2 \varepsilon} \times L_{\varrho} \times \mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}
$$

with parameters as stated in Theorem 3.1. Fixing $(\eta, \lambda)$ as in (30) and putting $(\xi, \mu):=(\eta, \lambda)$, Proposition 3.2 yields a mild solution

$$
(f, m, w, q, p) \in \mathcal{V}_{T}(\lambda, \eta, \eta)
$$

to $\left(E_{1}\right)-\left(E_{8}\right)$ on an interval $[0, T]$ that depends continuously on the initial value. Given another pair $(\bar{\eta}, \bar{\lambda})$ obeying (30), we set

$$
\eta_{*}:=\eta \wedge \bar{\eta}, \quad \xi_{*}:=\eta \vee \bar{\eta}, \quad \mu_{*}:=\lambda \vee \bar{\lambda}
$$

and obtain $n / \varrho<2 \eta_{*} \leq 2 \xi_{*} \leq 2 \mu_{*}<2,2 \eta_{*} \geq 1$, and

$$
\mathcal{V}_{T}(\lambda, \eta, \eta) \cup \mathcal{V}_{T}(\bar{\lambda}, \bar{\eta}, \bar{\eta}) \hookrightarrow \mathcal{V}_{T}\left(\mu_{*}, \xi_{*}, \eta_{*}\right)
$$

According to Proposition 3.2 this implies the uniqueness statement of Theorem 3.1. Moreover, we derive (29) and $q, p \in C\left((0, T], \mathbb{W}_{\varrho, \mathcal{B}}^{\xi}\right)$ for $\xi \in(0,2) \backslash\{1+1 / \varrho\}$. Finally, we may extend this solution to a maximal solution $(f, m, w, q, p)$ on some interval $J=\left[0, t^{+}\right)$, which would blow up in $W_{\varrho}^{2} \times W_{\varrho}^{2 \varepsilon} \times L_{\varrho} \times \mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}$ if $t^{+}<\infty$.

As for the regularity, one shows that $f \in C^{1}\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2}\right)$ and that $m$ is a classical solution and belongs to $C^{1}\left(\dot{J}, L_{\varrho}\right) \cap C\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2}\right)$ as in [25, Prop.3.1] (note that $P \in C_{\xi}\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2 \eta}\right)$ ). Next, from [2, II.Thm.5.3.1] it follows that there is $\nu>0$ such that

$$
\begin{equation*}
w \in C^{\nu}\left(\dot{J}, L_{\varrho}\right) \quad \text { and } \quad q \in C^{\nu}\left(\dot{J}, \mathbb{W}_{\varrho, \mathcal{B}}^{2 \eta}\right) \tag{33}
\end{equation*}
$$

Furthermore, owing to (18) and

$$
\begin{equation*}
p(t)=\mathbb{S}(t) p^{0}+\int_{0}^{t} \mathbb{S}(t-s) R_{4}(u(s)) \mathrm{d} s, \quad t \in J \tag{34}
\end{equation*}
$$

we deduce that

$$
2 \int_{0}^{\infty} b(a) p(t, a) \mathrm{d} a=B_{p^{0}}(t)+\int_{0}^{t} B_{R_{4}(u(s))}(t-s) \mathrm{d} s, \quad t \in J
$$

Therefore, integrating (34) with respect to $a$ we see that $P \in C\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2 \eta}\right) \cap C\left(J, L_{\varrho}\right)$ is a mild solution to

$$
\begin{aligned}
\partial_{t} P-\delta \Delta_{x} P= & -\nabla_{x} \cdot\left(P(t) \chi(f(t)) \nabla_{x} f(t)\right)-\int_{0}^{\infty}(\theta+\sigma)(w(t), Q(t), P(t)) p(t, a) \mathrm{d} a \\
& +\int_{0}^{\infty} b(a) p(t, a) \mathrm{d} a+\int_{0}^{\infty} \tau(w(t), Q(t), P(t)) q(t, a) \mathrm{d} a \\
= & z(t)
\end{aligned}
$$

so that $P \in C^{\nu}\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2 \eta}\right)$ by [2, II.Thm.5.3.1]. On the one hand, (9) together with (33) yield $z \in C^{\nu}\left(\dot{J}, L_{\varrho}\right)$, and invoking [2, II.Thm.1.2.2] we conclude that $P \in C^{1}\left(\dot{J}, L_{\varrho}\right) \cap C\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2}\right)$ is a classical solution to

$$
\begin{equation*}
\partial_{t} P-\delta \Delta_{x} P=z(t), \quad P(0)=P^{0}, \quad \partial_{\nu} P=0 \tag{35}
\end{equation*}
$$

Analogously we conclude $Q \in C^{1}\left(\dot{J}, L_{\varrho}\right) \cap C\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2}\right)$. On the other hand, it follows from (7), (8), and (33) that $R_{2} \in C^{\nu}\left(\dot{J}, L_{\varrho}\right)$, and therefore $w \in C^{1}\left(\dot{J}, L_{\varrho}\right) \cap C\left(\dot{J}, W_{\varrho, \mathcal{B}}^{2}\right)$ is a classical solution again by [2, II.Thm.1.2.2].
3.2. Proof of Thm. 3.1: Positivity. (i) Suppose first that $\varrho>n$ and let

$$
m^{0}, w^{0} \in W_{\varrho, \mathcal{B}}^{2} \cap L_{\varrho}^{+}, \quad q^{0} \in \mathbb{W}_{\varrho, \mathcal{B}}^{2} \cap \mathbb{L}_{\varrho}^{+}, \quad p^{0} \in D\left(\mathbb{A}_{0}\right) \cap \mathbb{L}_{\varrho}^{+} \hookrightarrow \mathbb{W}_{\varrho, \mathcal{B}}^{\vartheta}, \vartheta<2
$$

Then we clearly have $P \in C\left(J, W_{\varrho, \mathcal{B}}^{\vartheta}\right)$, whence $m \in C\left(J, W_{\varrho, \mathcal{B}}^{2}\right)$ by $\left(E_{2}\right)$, [25, Lem.2.1(iii)], and assumption (5). Moreover, there holds $f \in C^{1}\left(J, W_{\varrho, \mathcal{B}}^{2}\right)$ by $\left(E_{1}\right)$. In addition, we obtain $q \in C\left(J, \mathbb{W}_{\varrho, \mathcal{B}}^{\vartheta}\right)$ and $w \in C\left(J, W_{\varrho, \mathcal{B}}^{\vartheta}\right)$. We set

$$
\phi(t):=\phi(w(t), Q(t), P(t)) \quad \text { for } \quad \phi \in\{\epsilon, \tau, \sigma, \theta\}
$$

and approximate $\epsilon, \tau, \sigma, \theta \in C\left(J, L_{\infty}^{+}\left(\mathbb{R}^{+} \times \Omega\right)\right)$ by $\epsilon_{k}, \tau_{k}, \sigma_{k}, \theta_{k} \in C^{1}\left(J, L_{\infty}^{+}\left(\mathbb{R}^{+} \times \Omega\right)\right)$. Moreover, due to [1] we may choose $f_{k} \in C^{1}\left(J, C_{\mathcal{B}}^{2}(\bar{\Omega})\right)$ with $f_{k} \rightarrow f$ in $C\left(J, W_{\varrho, \mathcal{B}}^{2}\right)$. Defining then

$$
\mathcal{M}_{k}(t):=\left[\begin{array}{cc}
-\nabla_{x} \cdot\left(\chi(f(t)) \nabla_{x} f_{k}(t)\right)-\theta_{k}(t)-\sigma_{k}(t)-b & \tau_{k}(t) \\
\sigma_{k}(t) & -\epsilon_{k}(t)-\tau_{k}(t)
\end{array}\right]
$$

we have $\mathcal{M}_{k} \in C^{1}\left(J, \mathcal{L}\left(\mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}\right)\right)$. Given any $T \in \dot{J}$, we may then apply Lemma 2.4 to obtain a unique classical solution $u_{k}=\left(p_{k}, q_{k}\right) \geq 0$ on $[0, T]$ to

$$
\dot{u}_{k}+\mathcal{A}(t) u_{k}=\mathcal{M}_{k}(t) u_{k}, \quad u_{k}(0)=\left(p^{0}, q^{0}\right)
$$

where

$$
\mathcal{A}(t)=\left[\begin{array}{cc}
\mathbb{A}_{f(t)} & 0 \\
0 & -\gamma \Delta_{x}
\end{array}\right]
$$

From (21) it readily follows that

$$
\left(p_{k}, q_{k}\right) \rightarrow(p, q) \quad \text { in } \quad C\left([0, T], \mathbb{W}_{\varrho, \mathcal{B}}^{\vartheta} \times \mathbb{W}_{\varrho, \mathcal{B}}^{\vartheta}\right) .
$$

Thus $q(t), p(t) \geq 0$ for $t \in[0, T]$ while $f(t), m(t), w(t) \geq 0$ are obvious.
(ii) Positivity in the general case now follows from Lemma 2.3 and the continuous dependence of the solution on the initial values as stated in Proposition 3.2.
3.3. Proof of Thm. 3.1: Global Existence. We first observe that the no flux boundary conditions, (35) and its analogue for $Q$ imply

$$
\begin{aligned}
\frac{\mathrm{d}}{\mathrm{~d} t} \int_{\Omega}(P+Q) \mathrm{d} x & =\int_{\Omega} \int_{0}^{\infty} b p \mathrm{~d} a \mathrm{~d} x-\int_{\Omega} \int_{0}^{\infty}\{\theta(w, Q, P) p+\tau(w, Q, P) q\} \mathrm{d} a \mathrm{~d} x \\
& \leq\|b\|_{\infty} \int_{\Omega} P \mathrm{~d} x
\end{aligned}
$$

hence, for $T>0$,

$$
\begin{equation*}
\|Q(t)\|_{L_{1}}+\|P(t)\|_{L_{1}} \leq c(T), \quad t \in J \cap[0, T] \tag{36}
\end{equation*}
$$

Global existence will then be an immediate consequence of the next lemma. In the following, we put $J_{T}:=J \cap[0, T]$ for $T>0$.
Lemma 3.3. Suppose that $\|P(t)\|_{L_{\rho}} \leq c(T)$ for $t \in J_{T}$ with $\rho \in[1, \varrho)$ and suppose there exists $\xi \in(\rho, 2 \rho \wedge \varrho]$ such that $\xi\left(\frac{n}{\rho}-2\right)<2\left(\rho-1+\frac{2 \rho}{n}\right)$. Then $\|P(t)\|_{L_{\xi}} \leq c(T)$ for $t \in J_{T}$.
Proof. The proof follows closely the lines of [25, Prop.5.1] and we thus just give a brief sketch. Note that (35) is of the same form as the $p$-equation considered in [25]. Hence, introducing

$$
\phi(z):=e^{\frac{1}{\delta} \int_{0}^{z} \chi(s) \mathrm{d} s}
$$

and using $\left(E_{1}\right),\left(E_{5}\right)$ and the fact that $f$ is bounded on $J \times \Omega$, we have for $t \in \dot{J}$

$$
\begin{align*}
\frac{\mathrm{d}}{\mathrm{~d} t} \int_{\Omega} \phi(f)\left(\frac{P}{\phi(f)}\right)^{\xi} \mathrm{d} x \leq & -c_{0} \int_{\Omega} \phi(f)\left|\nabla_{x}\left(\frac{P}{\phi(f)}\right)^{\xi / 2}\right| \mathrm{d} x \\
& +c_{1} \int_{\Omega} m\left(\frac{P}{\phi(f)}\right)^{\xi} \mathrm{d} x  \tag{37}\\
& +\xi \int_{\Omega}\left(\frac{P}{\phi(f)}\right)^{\xi-1} \int_{0}^{\infty} \tau(w, Q, P) q \mathrm{~d} a \mathrm{~d} x \\
& +\xi\|b\|_{\infty} \int_{\Omega}\left(\frac{P}{\phi(f)}\right)^{\xi} \mathrm{d} x
\end{align*}
$$

In order to handle the third term we note that

$$
\begin{equation*}
\|w(t)\|_{\infty} \leq c(T), \quad t \in J_{T} \cap[\zeta, \infty)=: J_{T, \zeta} \tag{38}
\end{equation*}
$$

for $\zeta \in(0, T)$ by $\left(E_{3}\right)$ and $f \in L_{\infty}(J \times \Omega)$. Therefore

$$
\left\|\int_{0}^{\infty} \sigma(w(t), Q(t), P(t)) p(t) \mathrm{d} a\right\|_{L_{\rho}} \leq c(T), \quad t \in J_{T, \zeta}
$$

owing to (10) and $P \in L_{\infty}\left(J_{T}, L_{\rho}\right)$. We use (13) when applying this estimate to the inequality

$$
\partial_{t} Q-\gamma \Delta_{x} Q \leq \int_{0}^{\infty} \sigma(w(t), Q(t), P(t)) p(t) \mathrm{d} a
$$

which holds by $\left(E_{4}\right)$ and the positivity of $p$ and $q$. We hence derive that

$$
\begin{equation*}
\|Q(t)\|_{L_{r^{\prime}}} \leq c(T), \quad t \in J_{T, \zeta} \tag{39}
\end{equation*}
$$

where $r^{\prime}$ is the dual exponent of $r>1$ with

$$
\frac{n \xi}{n \xi+2 \rho}<\frac{1}{r}<1+\frac{2}{n}-\frac{1}{\rho}
$$

Also, there holds

$$
\|m(t)\|_{L_{r^{\prime}}} \leq c(T), \quad t \in J_{T, \zeta}
$$

by $\left(E_{2}\right)$ and (13). Using this last estimate, Young's inequality, and the Gagliardo-Nirenberg inequality in [14] we deduce

$$
\begin{aligned}
\int_{\Omega} m\left(\frac{P}{\phi(f)}\right)^{\xi} \mathrm{d} x & \leq c(\delta)\|m(t)\|_{L_{r^{\prime}}}^{r^{\prime}}+\delta \int_{\Omega}\left(\frac{P}{\phi(f)}\right)^{\xi r} \mathrm{~d} x \\
& \leq c(T, \delta)+\delta c_{0}\left\|\frac{P}{\phi(f)}\right\|_{L_{\rho}}^{\xi(r-1)}\left\|\left(\frac{P}{\phi(f)}\right)^{\xi / 2}\right\|_{W_{2}^{1}}^{2} \\
& \leq c(T, \delta)\left(1+\left\|\frac{P}{\phi(f)}\right\|_{L_{\xi}}^{\xi}\right)+c(T) \delta \int_{\Omega}\left|\nabla\left(\frac{P}{\phi(f)}\right)^{\xi / 2}\right|^{2} \mathrm{~d} x
\end{aligned}
$$

Similar arguments and (39) yield an analogous estimate for the third term in (37). We may choose then $\delta>0$ sufficiently small so that from (37)

$$
\frac{\mathrm{d}}{\mathrm{~d} t} \int_{\Omega} \phi(f)\left(\frac{P}{\phi(f)}\right)^{\xi} \mathrm{d} x \leq c(T)+c(T) \int_{\Omega} \phi(f)\left(\frac{P}{\phi(f)}\right)^{\xi} \mathrm{d} x
$$

whence $\|P(t)\|_{L_{\xi}} \leq c(T)$ for $t \in J_{T}$.
To finish off the proof of Theorem 3.1, we recall that it is sufficient to show that the solution $(f, m, w, q, p)$ does not blow up in finite time in the space $W_{\varrho}^{2} \times W_{\varrho}^{2 \varepsilon} \times L_{\varrho} \times \mathbb{L}_{\varrho} \times \mathbb{L}_{\varrho}$ according to subsection 3.1. Starting with (36), a repeated application of Lemma 3.3 shows that $\|P(t)\|_{L_{e}} \leq c(T), t \in J_{T}$, for any $T>0$ since $n \leq 3$. Using maximal regularity for the $m$-equation $\left(E_{2}\right)$ we may argue then as in section 5 of [25] to conclude that this estimate ensures

$$
\|m(t)\|_{W_{e, \mathcal{B}}^{2 \varepsilon}}+\|w(t)\|_{L_{\varrho}}+\|f(t)\|_{W_{e, \mathcal{B}}^{2}} \leq c(T), \quad t \in J_{T} .
$$

In particular, the estimate on $f$ yields

$$
\left\|\nabla_{x} \cdot\left(p \chi(f(t)) \nabla_{x} f(t)\right)\right\|_{\mathbb{L}_{e}} \leq c(T)\|p\|_{\mathbb{W}_{e}, \mathcal{B}}^{2 \eta}, \quad t \in J_{T}
$$

for $n / \varrho<2 \eta<2$ and $2 \eta \geq 1$ (see [25, Lem.2.1]). Therefore, setting for $v=(p, q)$

$$
F(t, v):=\left[\begin{array}{cc}
-\sigma(t)-\theta(t)-b & \tau(t) \\
\sigma(t) & -\epsilon(t)-\tau(t)
\end{array}\right]\binom{p}{q}+\binom{-\nabla_{x} \cdot\left(p \chi(f(t)) \nabla_{x} f(t)\right)}{0}
$$

and using (10) and (38), we obtain

$$
\|F(t, v)\|_{\mathbb{L}_{e} \times \mathbb{L}_{e}} \leq c(T)\|v\|_{\mathbb{W}_{e, \mathcal{B}}^{2 \eta} \times \mathbb{L}_{e}}, \quad t \in J_{T}
$$

Since $v=(p, q)$ is a mild solution to

$$
\dot{v}+\mathcal{A} v=F(t, v), \quad v(0)=\left(p^{0}, q^{0}\right)
$$

where

$$
\mathcal{A}:=\left[\begin{array}{cc}
\mathbb{A}_{0} & 0 \\
0 & -\gamma \Delta_{x}
\end{array}\right]
$$

we deduce with the aid of the estimate

$$
\left\|e^{-t \mathcal{A}}\right\|_{\mathcal{L}\left(\mathbb{L}_{e} \times \mathbb{L}_{e}, \mathbb{W}_{e, \mathcal{B}}^{2 \eta} \times \mathbb{L}_{e}\right)} \leq c(T) t^{-\eta}, \quad t \in \dot{J}_{T}
$$

(cf. (21)), that $\|v(t)\|_{\mathbb{W}_{e, \mathcal{B}}^{2 \eta} \times \mathbb{L}_{e}} \leq c(T)$ for $t \in J_{T} \cap[\zeta, \infty)$ with $\zeta>0$. Hence, the solution $(f, m, w, q, p)$ does not blow up in finite time which proves that it exists globally. The proof
of Theorem 3.1 is thus complete.

## Acknowledgment

I would like to thank Glenn Webb for introducing me to the subject and for many enlightening discussions.

## References

[1] H. Amann. Dual semigroups and second order linear elliptic boundary value problems. Israel J. Math. 45 (1983), 225-254.
[2] H. Amann. Linear and quasilinear parabolic problems, volume I: Abstract linear theory. Birkhäuser, Basel, Boston, Berlin 1995.
[3] H. Amann, Ch. Walker. Local and global strong solutions to continuous coagulation-fragmentation equations with diffusion. J. Diff. Eq. 218 (2004), 1-28.
[4] A.R.A. Anderson. A hybrid mathematical model of solid tumour invasion: The importance of cell adhesion. Math. Med. Biol. IMA Journal 22 (2005), 163-186.
[5] B. Ayati, A.R.A. Anderson, G.F. Webb. Computational methods and results for structured multiscale models of tumor invasion. SIAM Multiscale Modeling and Simulation 5 (2006), 1-20.
[6] L. Corrias, B. Perthame, H. Zaag. A chemotaxis model motivated by angiogenesis. C. R. Acad. Sci. Paris, Ser. I 336 (2003), 114-146.
[7] L. Corrias, B. Perthame, H. Zaag. Global solutions of some chemotaxis and angiogenesis systems in high space dimensions. Milan J. Math. 72 (2004), 159-186.
[8] C. Cusulin, M. Iannelli, G. Marinoschi. Age-structured diffusion in multi-layer environment. Nonlin. Anal. Real World Appl. 6 (2005), no. 6, 207-223.
[9] G. DiBlasio, L. Lamberti. An initial-boundary value problem for age-dependent population diffusion. SIAM J. Appl. Math. 35 (1978), no. 3, 593-615.
[10] J. Dyson, E. Sánchez, R.Villella-Bressan, G. Webb. An age and spatially structured model of tumor invasion with haptotaxis. Discr. Cont. Dyn. Sys. B 8 (2007), no. 1, 45-60.
[11] M. A. Fontelos, A. Friedman, B. Hu. Mathematical analysis of a model for the initiation of angiogenesis. SIAM J. Math. Anal. 33 (2002), 1330-1355.
[12] A. Friedman, J. I. Tello. Stability of solutions of chemotaxis equations in reinforced random walks. J. Math. Anal. Appl. 272 (2002), 138-163.
[13] G. Greiner. Perturbing the boundary conditions of a generator. Houston J. Math. 13 (1987), no. 2, 213-229.
[14] D. Henry. Geometric theory of semilinear parabolic equations. Lecture Notes in Mathematics 840, Springer, Berlin, Heidelberg, New York 1981.
[15] D. Horstmann. From 1970 until present: The Keller-Segel model in chemotaxis and its consequences I. Jahresbericht Deutscher Math. Verein 105 (2003), no.3, 103-165.
[16] K. Kunisch, W. Schappacher, G.F. Webb. Nonlinear age-dependent population dynamics with diffusion. Inter. J. Comput. Math. Appl. 11 (1985), 155-173.
[17] M. Langlais. A nonlinear problem in age-dependent population diffusion. SIAM J. Math. Anal. 16 (1985), no. 3, 510-529.
[18] G. Nickel, A. Rhandi. On the essential spectral radius of semigroups generated by perturbations of Hille-Yosida operators. Tübinger Berichte zur Funktionalanalysis 4 (1995), 207-220.
[19] A. Pazy. Semigroups of linear operators and applications to partial differential equations. Springer Verlag, Berlin, New York, Heidelberg 1983.
[20] M. Rascle. On a system of non-linear strongly coupled partial differential equations arising in biology. Conf. on Ordinary and Partial Differential Equations, Lecture Notes in Math. 846, Everitt and Sleeman (eds.) Springer-Verlag, New York 1980, 290-298.
[21] M. Rascle., C. Ziti. Finite time blow-up in some models of chemotaxis. J. Math. Biol. 33 (1995), 388-414.
[22] A. Rhandi. Positivity and stability for a population equation with diffusion on $L^{1}$. Positivity 2 (1998), 101-113.
[23] A. Rhandi, R. Schnaubelt. Asyptotic behaviour of a non-autonomous population equation with diffusion in $L^{1}$. Disc. Cont. Dyn. Syst. 5 (1999), 663-683.
[24] F. Rothe. Global solutions of reaction-diffusion systems. Lecture Notes in Mathematics 1072, Springer, Berlin, Heidelberg, New York, Tokio 1984.
[25] Ch. Walker, G.F. Webb. Global existence of classical solutions for a haptotaxis model. To appear in: SIAM J. Math. Anal.
[26] G.F. Webb. Diffusive age-dependent population models and an application to genetics. Math. Biosci. 61 (1982), 1-16.
[27] G.F. Webb. Population models structured by age, size, and spatial position. To appear.

Vanderbilt University, Department of Mathematics, 1326 Stevenson Center, Nashville, TN 37240, USA, christoph.walker@vanderbilt.edu


[^0]:    Key words and phrases. Tumor growth, haptotaxis, age structure, diffusion, global existence, uniqueness Mathematics Subject Classifications (2000): 35K55, 92C17, 92D25.

