Hokkaido Mathematical Journal Vol. 47 (2018) p. 33–67

Large-time behavior of solutions to a tumor invasion model of Chaplain–Anderson type with quasi-variational structure

Akio Ito

(Received March 25, 2015; Revised September 3, 2015)

Abstract. We treat 2D and 3D tumor invasion models with quasi-variational structures, which are composed of two PDEs, one ODE and certain constraint conditions. Although the original model was proposed by M. R. A. Chaplain and A. R. A. Anderson in 2003, the difference between their original model and ours is that the constraint conditions for the distributions of tumor cells and the extracellular matrix are imposed in our model, which give a quasi-variational structure. For 2D and 3D tumor invasion models with quasi-variational structures, we show the existence of global-in-time solutions and consider their large-time behaviors. Especially, for the large-time behaviors, we show that there exists at least one global-in-time solution such that it converges to a constant steady state in an appropriate function space as time goes to ∞.

Key words: large-time behavior, tumor invasion, quasi-variational structure.

1. Introduction

In this paper, we consider the following tumor invasion model with constraint conditions denoted by (P)={(1.1)–(1.7)}, of which the original model was proposed in [3]:

$$n_t = \nabla\cdot(d_1\nabla n - \lambda(f)n\nabla f) + \mu_p n(1-n-f) - \mu_d n \quad \text{in } Q, \tag{1.1}$$

$$f_t = -amf \quad \text{in } Q, \tag{1.2}$$

$$m_t = d_2\Delta m + bn - cm \quad \text{in } Q, \tag{1.3}$$

$$n \geq 0,\ f \geq 0,\ n+f \leq \alpha \quad \text{in } Q, \tag{1.4}$$

$$(d_1\nabla n - \lambda(f)n\nabla f)\cdot\nu = 0 \quad \text{on } \Sigma, \tag{1.5}$$

$$\nabla m\cdot\nu = 0 \quad \text{on } \Sigma, \tag{1.6}$$

$$n(0) = n_0,\ f(0) = f_0,\ m(0) = m_0 \quad \text{in } \Omega, \tag{1.7}$$

where Ω is a bounded domain in $\mathbf{R}^N$, $N = 2, 3$, with a smooth boundary

---

2010 Mathematics Subject Classification : 35B40, 35Q92, 35A01.

$\partial\Omega$ and $Q = \Omega \times (0, \infty)$, $\Sigma = \partial\Omega \times (0, \infty)$; ν is an outer unit normal vector on $\partial\Omega$; $a > 0$, $b > 0$, $c > 0$, $d_1 > 0$, $d_2 > 0$ and $\alpha \geq 1$ are constants; λ is a non-negative smooth function on $\mathbf{R}$; μ_p and μ_d are non-negative continuous functions on $\Omega \times [0, \infty)$; n_0, f_0 and m_0 are prescribed initial data.

The unknown functions n, f and m describe the distributions of tumor cells, extracellular matrix and enzyme degrading extracellular matrix, respectively. Of course we know that a lot of mathematical models for tumor invasion phenomena are proposed and analyzed mathematically, for example, [1], [2], [3], [4], [5], [6], [13], [14], [15], [16], [17], [18], [19], [20], [21], [22], [23], [24], but we do not say anything here and trust them to Introduction in [7], [13].

Next, we explain a quasi-variational structure of (P) following [7], [8], [9], [10], [11]. Such structure comes from the constraint conditions (1.4), which is not imposed in the original model proposed in [3], and makes it difficult to analyze (P) mathematically. In order to make the quasi-variational structure of (P) clear, for each $T > 0$ we prepare two operators $\Lambda_1(T)$ and $\Lambda_2(T)$ by the following ways. The operator $\Lambda_1(T)$ assigns each function $v \in W^{1,2}(0, T; L^2(\Omega)) \cap L^\infty(0, T; H^1(\Omega))$ to a unique solution $m = \Lambda_1(T)v \in W^{1,2}(0, T; L^2\Omega)) \cap L^\infty(0, T; H^1(\Omega)) \cap L^2(0, T; H^2(\Omega))$ to (S1), which really comes from $\{(1.3), (1.6), (1.7)\}$ of (P):

$$\text{(S1)} \begin{cases} m_t = d_2 \Delta m + bv - cm & \text{in } Q_T = \Omega \times (0, T), \\ \nabla m \cdot \nu = 0 & \text{on } \Sigma_T = \partial\Omega \times (0, T), \\ m(0) = m_0 & \text{in } \Omega, \end{cases}$$

whenever $m_0 \in H^1(\Omega)$. By using $m = \Lambda_1(T)v$, we define the operator $\Lambda_2(T)$ by

$$[\Lambda_2(T)v](x, t) = f_0(x) \exp\left(-a \int_0^t m(x, s) ds\right) \text{ for all } (x, t) \in \bar{Q}_T = \bar{\Omega} \times [0, T].$$

Then, we easily see that $f = \Lambda_2(T)v$ also is a unique solution to (S2), which comes from $\{(1.2), (1.7)\}$ of (P):

$$\text{(S2)} \begin{cases} f_t = -amf = -a[\Lambda_1(T)v]f & \text{in } Q_T, \\ f(0) = f_0 & \text{in } \Omega. \end{cases}$$

By using the operators $\Lambda_1(T)$ and $\Lambda_2(T)$, (P) can be formally rewritten into (S):

$$
\text{(S)}\begin{cases}
n_t = \nabla\cdot(d_1\nabla n - \lambda(f)n\nabla f) + \mu_p n(1-n-f) - \mu_d n & \text{in } Q_T,\\
0 \le n \le \alpha - f & \text{in } Q_T,\\
(d_1\nabla n - \lambda(f)n\nabla f)\cdot\nu = 0 & \text{on } \Sigma_T,\\
n(0) = n_0 & \text{in } \Omega,\\
f = \Lambda_2(T)n, \quad m = \Lambda_1(T)n.
\end{cases}
$$

From the formal expression (S) we see that the constraint condition $0 \le n \le \alpha - f$ for n depends upon n itself because of the relation $f = \Lambda_2(T)n$. We call this property of (P) "*a quasi-variational structure*", which was exactly used in [7]. More precisely, for each $T > 0$ and $v \in W^{1,2}(0,T;L^2(\Omega)) \cap L^\infty(0,T;H^1(\Omega))$ we consider a family $\{\varphi^t(v;\cdot); t \in [0,T]\}$ of time-dependent proper l.s.c. convex functions $\varphi^t(v;\cdot)$ on $L^2(\Omega)$, which is defined by

$$
\varphi^t(v;z) = \begin{cases}
\frac{d_1}{2}\int_\Omega |\nabla z|^2 - \int_\Omega \lambda([\Lambda_2(T)v](t))z\nabla[\Lambda_2(T)v](t) & \text{if } z \in D(v;t),\\
\infty & \text{if } L^2(\Omega)\setminus D(v,t),
\end{cases}
$$

where the effective domain $D(v;t)$ of $\varphi^t(v;\cdot)$ is given by

$$
D(v;t) = \{z \in H^1(\Omega); 0 \le z \le \alpha - [\Lambda_2(T)v](t) \text{ a.e. in } \Omega\}.
$$

Then, (S) is equivalent to the evolution inclusion (E) in $L^2(\Omega)$ associated with the time-dependent subdifferentials of a family $\{\varphi^t(v;\cdot); t \in [0,T]\}$:

$$
\text{(E)}\begin{cases}
n'(t) + \partial\varphi^t(n;n(t)) \ni \mu_p n(1-n-f) - \mu_d n & \text{in } L^2(\Omega), \text{ a.a. } t \in (0,T),\\
n(0) = n_0 & \text{in } L^2(\Omega),\\
f = \Lambda_2(T)n, \quad m = \Lambda_1(T)n,
\end{cases}
$$

where "$\prime$" implies the derivative with respect to the variable t and $\partial\varphi^t(n;\cdot)$ is the subdifferential operator of $\varphi^t(n;\cdot)$ on $L^2(\Omega)$. Now we can directly apply the theory of a quasi-variational inequality to (E), which was established in [12]. Actually, by using the general theory in [12], we have already seen that for each fixed $T > 0$ (E) has at least one solution $n \in W^{1,2}(0,T;L^2(\Omega)) \cap$

$L^\infty(0,T;H^1(\Omega))$. Since the solutions to (E) on $[0,T]$ is possibly not unique in general, we cannot show whether n_1 coincides with n_2 on $[0,T_1]$ or not whenever $T_1 \leq T_2$ and n_i, $i=1,2$, are solutions to (E) on $[0,T_i]$. Hence, until now we cannot consider the large-time behaviors of global-in-time solutions to (E), hence, (P).

Recently, in [7] we succeeded in considering the large-time behaviors of global-in-time solutions to (P) for the case that the space dimension N is equal to 1. As far as we know, this is the first result about the large-time behaviors of global-in-time solutions to the system which has a quasi-variational structure. Hence, the main purpose of this paper is to extend the results obtained in [7] to the 2D and 3D tumor invasion models of Chaplain–Anderson type with quasi-variational structures.

In the rest of this section, we clearly state our results in this paper. First of all, we impose the following assumptions for the prescribed data in (P).

(A1) $\lambda : \mathbf{R} \longrightarrow \mathbf{R}$ is a non-negative and globally Lipschitz continuous function. We denote by L its Lipschitz constant and put $\lambda_0 = \lambda(0)$.

(A2) $\mu_p : \Omega \times [0,\infty) \longrightarrow \mathbf{R}$ is a non-negative and continuous function. Moreover, there exist constants $\mu_1 > 0$ and $\mu_2 > 0$ such that

$$\mu_1 \leq \mu_p(x,t) \leq \mu_2 \quad \text{for all } (x,t) \in \Omega \times [0,\infty).$$

(A3) $\mu_d : \Omega \times [0,\infty) \longrightarrow \mathbf{R}$ is a non-negative and continuous function. Moreover, there exists a constant $\mu_3 > 0$ such that

$$0 \leq \mu_d(x,t) \leq \mu_3 \quad \text{for all } (x,t) \in \Omega \times [0,\infty).$$

(A4) $n_0 \in H^1(\Omega)$ and the following constraint condition is satisfied:

$$0 \leq n_0 \leq \alpha \quad \text{a.e. in } \Omega.$$

(A5) $f_0 \in W^{1,\infty}(\Omega)$ and the following constraint condition is satisfied:

$$0 \leq f_0 \leq \alpha - n_0 \quad \text{a.e. in } \Omega,$$

where n_0 is the same initial datum that has already been given in (A4).

(A6) $m_0 \in W^{1,\infty}(\Omega)$ and $m_0 \geq 0$ a.e. in Ω.

The first result stated in Theorem 1.1 guarantees the existence of global-in-time solutions to (P), which enable us to consider their large-time behaviors.

Theorem 1.1 *Assume that* (A1)–(A6) *are satisfied. Then,* (P) *has at least one global-in-time solution* (n, f, m) *satisfying the following properties for any* $T \in (0, \infty)$:

(1) $n \in W^{1,2}(0,T; L^2(\Omega)) \cap L^\infty(0,T; H^1(\Omega))$ *and* (1.1) *with* (1.5) *is satisfied in the sense of the following quasi-variational inequality in* $L^2(0,T; L^2(\Omega))$:

$$\begin{aligned} &\iint_{Q_T} n_t(n-\eta) + d_1 \iint_{Q_T} \nabla n \cdot \nabla(n-\eta) - \iint_{Q_T} \lambda(f) n \nabla f \cdot \nabla(n-\eta) \\ &\quad \leq \iint_{Q_T} \mu_p n(1-n-f)(n-\eta) - \iint_{Q_T} \mu_d n(n-\eta) \qquad (1.8) \\ &\qquad \textit{for any } \eta \in L^2(0,T; H^1(\Omega)) \textit{ with } 0 \leq \eta \leq \alpha - f \textit{ a.e. in } Q_T. \end{aligned}$$

(2) f *is given by the following expression*:

$$f(x,t) = f_0(x) \exp\left(- a \int_0^t m(x,s) ds \right) \quad \textit{for all } (x,t) \in \bar{Q}_T. \qquad (1.9)$$

(3) m *is given by the following variation-of-constants formula for all* $t \geq 0$:

$$m(t) = e^{t(d_2\Delta - c)} m_0 + b \int_0^t e^{(t-s)(d_2\Delta - c)} n(s) ds \quad \textit{in } L^\infty(\Omega). \qquad (1.10)$$

where $\{e^{td_2\Delta}; t \geq 0\}$ *is the homogeneous Neumann heat semigroup which is clearly defined at the end of this section.*

(4) *The following constraint conditions are satisfied*:

$$n \geq 0, \quad 0 \leq n + f \leq \alpha \quad \textit{a.e. in } Q_T.$$

(5) $(n(0), f(0), m(0)) = (n_0, f_0, m_0)$ *in* $H^1(\Omega) \times W^{1,\infty}(\Omega) \times W^{1,\infty}(\Omega)$.

For the large-time behaviors of global-in-time solutions to (P), we have Theorem 1.2 as the main result of this paper. You note that we cannot consider the large-time behaviors of all global-in-time solutions to (P). Roughly speaking, we can construct at least one global-in-times solutions to (P), which converges to a constant steady state as time goes to ∞, by considering appropriate approximate systems of (P).

Theorem 1.2 *Assume that* (A7)–(A10) *are satisfied as well as* (A1)–(A6):
(A7) $\mu_d \equiv 0$ *on* Q.
(A8) $0 \le n_0 \le 1 - f_0$ *in* Ω.
(A9) *There exists a constant* $n_* > 0$ *such that* $n_0 \ge n_*$ *a.e. in* Ω.
(A10) *There exists a constant* $m_* > 0$ *such that* $m_0 \ge m_*$ *a.e. in* Ω.
Then, there exists at least one global-in-time solution (n, f, m) *such that*

$$(n(t), f(t), m(t)) \longrightarrow (1, 0, b/c) \quad in \quad L^2(\Omega) \times (L^\infty(\Omega) \cap H^1(\Omega)) \times L^2(\Omega)$$

as $t \to \infty$.

As we consider the large-time behavior of global-in-time solutions to (P), it is important and essential to derive the global-in-time boundedness of n (cf. Lemma 2.6). For this, we mainly use two tools. One is the following Sobolev's embedding (1.11):

$$\|\varphi\|_{L^p(\Omega)} \le C_1(p)\|\varphi\|_{H^1(\Omega)} \quad \text{for all } \varphi \in H^1(\Omega), \tag{1.11}$$

instead of $H^1(\Omega) \subset C^0(\bar{\Omega})$ if $N = 1$, which is used in [7]. Moreover, although in [9] we showed the existence of global-in-time solutions to (P) in which the homogeneous Dirichlet boundary condition $n = 0$ on $\partial\Omega \times (0, \infty)$ is imposed, we could not derive any results about its large-time behavior. Actually, the theory of quasi-variational inequalities, which was established in [12] and used in [9], cannot be applied in order to consider a large-time behaviors of global-in-time solutions to (P).

The other is the $L^p - L^q$ estimate for the homogeneous Neumann heat semigroup, which was obtained in [25, Lemma 1.3]. For each $d > 0$ and $p \in [1, \infty]$ we define the homogeneous Neumann heat semigroup $\{e^{td\Delta}; t \ge 0\}$ on $L^p(\Omega)$ by the following way: for each $\varphi \in L^p(\Omega)$ the function $\psi(t) = e^{td\Delta}\varphi$ from $[0, \infty)$ into $L^p(\Omega)$ is a unique solution to (H):

$$
\text{(H)} \begin{cases} \psi_t = d\Delta\psi & \text{in } Q, \\ \nabla\psi \cdot \nu = 0 & \text{on } \Sigma, \\ \psi(0) = \varphi & \text{in } \Omega. \end{cases}
$$

Then, we have already obtained the following lemma.

Lemma 1.1 *The homogeneous Neumann heat semigroup $\{e^{td\Delta}; t \geq 0\}$ satisfies the following estimates* (1)–(3).

(1) *Let $1 \leq p \leq q \leq \infty$. Then, there exists a constant $C_2(d,p,q) > 0$ such that*

$$
\|e^{td\Delta}\varphi\|_{L^q(\Omega)} \leq C_2(d,p,q)\big(1 + t^{-(N/2)(1/p-1/q)}\big)\|\varphi\|_{L^p(\Omega)} \quad \textit{for any } \varphi \in L^p(\Omega) \textit{ and any } t > 0.
$$

(2) *Let $1 \leq p \leq q \leq \infty$. Then, there exists a constant $C_3(d,p,q) > 0$ such that*

$$
\|\nabla e^{td\Delta}\varphi\|_{L^q(\Omega)} \leq C_3(d,p,q)\big(1 + t^{-1/2-(N/2)(1/p-1/q)}\big)\|\varphi\|_{L^p(\Omega)} \quad \textit{for any } \varphi \in L^p(\Omega) \textit{ and for } t > 0.
$$

(3) *Let $2 \leq p \leq \infty$. Then, there exists a constant $C_4(d,p) > 0$ such that*

$$
\|e^{td\Delta}\varphi\|_{W^{1,p}(\Omega)} \leq C_4(d,p)\|\varphi\|_{W^{1,p}(\Omega)} \quad \textit{for any } \varphi \in W^{1,p}(\Omega) \textit{ and } t > 0.
$$

These tools play important roles to derive the uniform boundedness of global-in-time solutions to suitable approximate systems to (P), which enables us to construct a global-in-time solution to (P) by using the limit procedure argument in Section 2.

2. Existence of global-in-time solutions

We devote this section to show Theorem 1.1 by using a similar argument, which was originally and essentially given in [13] and slightly modified in [7, Sections 2 and 3]. Actually, the argument in [13] is modified in [7] for applying it to one-dimensional tumor invasion model of Chaplain–Anderson type with a quasi-variational structure, which is clearly stated in Introduction. Throughout this section, for each $\varepsilon \in (0,1)$ and $f \in \mathbf{R}$ we define an increasing and globally Lipschitz continuous function $\beta_\varepsilon(f;\cdot)$, whose Lipschitz constant is equal to $1/\varepsilon$, by

$$\beta_\varepsilon(f;r)=\begin{cases}\dfrac{r-\max\{0,\alpha-f\}}{\varepsilon} & \text{if } r\in(\max\{0,\alpha-f\},\infty),\\ 0, & \text{if } r\in[0,\max\{0,\alpha-f\}],\\ \dfrac{r}{\varepsilon}, & \text{if } r\in(-\infty,0),\end{cases}$$

and consider $(\mathrm{P})_\varepsilon$ as the approximate system of (P):

$$(\mathrm{P})_\varepsilon\begin{cases}n^\varepsilon_t=\nabla\cdot(d_1\nabla n^\varepsilon-\lambda(f^\varepsilon)n^\varepsilon\nabla f^\varepsilon)+\tilde g_\varepsilon(n,f) & \text{in } Q,\\ f^\varepsilon_t=-am^\varepsilon f^\varepsilon & \text{in } Q,\\ m^\varepsilon_t=d_2\Delta m^\varepsilon+bn^\varepsilon-cm^\varepsilon & \text{in } Q,\\ (d_1\nabla n^\varepsilon-\lambda(f^\varepsilon)n^\varepsilon\nabla f^\varepsilon)\cdot\nu=0 & \text{on } \Sigma,\\ \nabla m^\varepsilon\cdot\nu=0 & \text{on } \Sigma,\\ n^\varepsilon(0)=n_0,\ f^\varepsilon(0)=f_0,\ m^\varepsilon(0)=m_0 & \text{in } \Omega,\end{cases}$$

where $\tilde g_\varepsilon(n,f)=-\beta_\varepsilon(f;n)+\mu_p n(1-n-f)-\mu_d n$.

Moreover, we consider a change of variables, which was used in [7], [13]:

$$w=nz,\quad z=\exp\left(-\frac{1}{d_1}\int_0^f\lambda(r)dr\right). \tag{2.1}$$

Then, $(\mathrm{P})_\varepsilon$ is rewritten into $(\mathrm{Q})_\varepsilon$:

$$(\mathrm{Q})_\varepsilon\begin{cases}w^\varepsilon_t=d_1\Delta w^\varepsilon+\lambda(f^\varepsilon)\nabla w^\varepsilon\cdot\nabla f^\varepsilon+g_\varepsilon(w^\varepsilon,f^\varepsilon,m^\varepsilon) & \text{in } Q,\\ f^\varepsilon_t=-am^\varepsilon f^\varepsilon & \text{in } Q,\\ m^\varepsilon_t=d_2\Delta m^\varepsilon+bw^\varepsilon z^\varepsilon-cm^\varepsilon & \text{in } Q,\\ \nabla w^\varepsilon\cdot\nu=0 & \text{on } \Sigma,\\ \nabla m^\varepsilon\cdot\nu=0 & \text{on } \Sigma,\\ w^\varepsilon(0)=w_0,\ f^\varepsilon(0)=f_0,\ m^\varepsilon(0)=m_0 & \text{in } \Omega,\end{cases}$$

where w^ε and z^ε are given by (2.1), in which (w,n,z,f) is replaced by $(w^\varepsilon,n^\varepsilon,z^\varepsilon,f^\varepsilon)$, and

$$g_\varepsilon(w,f,m) = -z\beta_\varepsilon(f;wz^{-1}) + \mu_p w(1-wz^{-1}-f) - \mu_d w + \frac{a\lambda(f)wmf}{d_1}.$$

We note that $(\mathrm{Q})_\varepsilon$ is equivalent to $(\mathrm{P})_\varepsilon$ whenever w_0 is given by

$$w_0 = n_0 \exp\Big(-\frac{1}{d_1}\int_0^{f_0}\lambda(r)dr\Big). \tag{2.2}$$

In order to show Theorem 1.1, first of all we show the existence and uniqueness of non-negative global-in-time solutions to $(\mathrm{Q})_\varepsilon$, which is clearly stated in Proposition 2.1 and directly implies those of non-negative global-in-time solutions to $(\mathrm{P})_\varepsilon$.

Proposition 2.1 *Assume that* (A1)–(A6) *are satisfied and* w_0 *is given by* (2.2). *Then, for each* $\varepsilon \in (0,1)$ $(Q)_\varepsilon$ *has one and only one non-negative global-in-time solution* $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ *satisfying the following properties*:

(1) w^ε *is given by the variation-of-constants formula for all* $t \geq 0$:

$$w^\varepsilon(t) = e^{td_1\Delta}w_0 + \int_0^t e^{(t-s)d_1\Delta}\bar{g}_\varepsilon(w^\varepsilon(s), f^\varepsilon(s), m^\varepsilon(s))ds \quad in\ L^\infty(\Omega). \tag{2.3}$$

where $\bar{g}_\varepsilon(w,f,m) = \lambda(f)\nabla w\cdot\nabla f + g_\varepsilon(w,f,m)$.

(2) f^ε *is given by* (1.9), *in which* (f,m) *is replaced by* $(f^\varepsilon, m^\varepsilon)$.

(3) m^ε *is given by the variation-of-constants formula for all* $t \geq 0$:

$$m^\varepsilon(t) = e^{t(d_2\Delta - c)}m_0 + b\int_0^t e^{(t-s)(d_2\Delta-c)}w^\varepsilon(s)(z^\varepsilon)^{-1}(s)ds \quad in\ L^\infty(\Omega). \tag{2.4}$$

Remark 2.1 Let $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative global-in-time solution to $(\mathrm{Q})_\varepsilon$ and denote by $-\Delta_N : L^2(\Omega) \longrightarrow L^2(\Omega)$ the single-valued maximal monotone operator associated with the homogeneous Neumann boundary condition whose domain $D(\Delta_N)$ is given by

$$D(\Delta_N) = \{\varphi \in H^2(\Omega); \nabla\varphi\cdot\nu = 0 \quad \text{a.e. on } \Gamma\}.$$

Then, we see that w^ε and m^ε are unique solutions to (E1) and (E2), respectively:

$$
\text{(E1)}\begin{cases}(w^\varepsilon)'(t) - d_1\Delta_N w^\varepsilon(t) = \bar{g}_\varepsilon(w^\varepsilon(t), f^\varepsilon(t), m^\varepsilon(t)) & \text{in } L^2(\Omega), \text{ a.a. } t > 0,\\ w^\varepsilon(0) = w_0 & \text{in } L^2(\Omega),\end{cases}
$$

$$
\text{(E2)}\begin{cases}(m^\varepsilon)'(t) - d_2\Delta_N m^\varepsilon(t) + cm^\varepsilon(t) = bw^\varepsilon(t)(z^\varepsilon)^{-1}(t) & \\ & \text{in } L^2(\Omega), \text{ a.a. } t > 0,\\ m^\varepsilon(0) = m_0 & \text{in } L^2(\Omega).\end{cases}
$$

These expressions as the evolution equations in (E1) and (E2) are used when we have the uniform boundedness of the approximate solutions $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ to $(\mathrm{Q})_\varepsilon$.

As a direct consequence of Proposition 2.1, we derive the existence and uniqueness results of non-negative global-in-time solutions $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ to $(\mathrm{P})_\varepsilon$.

Proposition 2.2 *Assume that* (A1)–(A6) *are satisfied. Then, for each* $\varepsilon \in (0,1)$ $(P)_\varepsilon$ *has one and only one non-negative global-in-time solution* $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ *satisfying the following properties*: *for each* $T > 0$

(1) $n^\varepsilon \in W^{1,2}(0,T;L^2(\Omega)) \cap C^0([0,T];H^1(\Omega))$ *with* $n^\varepsilon(0) = n_0$ *in* $H^1(\Omega)$. *Moreover, the first equation and the forth condition in* $(P)_\varepsilon$ *are satisfied in the following sense*:

$$
\int_\Omega n_t^\varepsilon(t)\zeta + \int_\Omega \{d_1\nabla n^\varepsilon(t) - \lambda(f^\varepsilon(t))n^\varepsilon(t)\nabla f^\varepsilon(t)\}\cdot\nabla\zeta + \int_\Omega \beta_\varepsilon(f^\varepsilon(t); n^\varepsilon(t))\zeta
$$
$$
= \int_\Omega \{\mu_p(t)n^\varepsilon(t)(1 - n^\varepsilon(t) - f^\varepsilon(t)) - \mu_d(t)n^\varepsilon(t)\}\zeta
$$
$$
\text{for any } \zeta \in H^1(\Omega) \text{ and a.a. } t \in (0,T). \tag{2.5}
$$

(2) f^ε *is the same function that is given in* (2) *of Proposition* 2.1.

(3) m^ε *is given by* (2.4), *in which* $w^\varepsilon(z^\varepsilon)^{-1}$ *is replaced by* n^ε.

First of all, we mainly devote ourselves to show Proposition 2.1 by using the methods similar to those in [6], [7]. For each $\tau \in (0,1)$ we prepare a Banach space X^τ defined by

$$
X^\tau = C^0([0,\tau]; L^\infty(\Omega)\cap H^1(\Omega)) \times C^0([0,\tau]; W^{1,\infty}(\Omega)) \times C^0([0,\tau]; W^{1,\infty}(\Omega)),
$$

whose norm $\|(w,f,m)\|_{X^\tau}$ is given by

$$\max_{0\le t\le\tau}\big(\|w(t)\|_{L^\infty(\Omega)}+\|w(t)\|_{H^1(\Omega)}+\|f(t)\|_{W^{1,\infty}(\Omega)}+\|m(t)\|_{W^{1,\infty}(\Omega)}\big).$$

Furthermore, for each $\varepsilon\in(0,1)$ we define a mapping Φ^ε on X^τ by the following way: for each $(w,f,m)\in X^\tau$

$$(\Phi^\varepsilon(w,f,m))(t)=\begin{pmatrix}(\Phi_1^\varepsilon(w,f,m))(t)\\(\Phi_2^\varepsilon(w,f,m))(t)\\(\Phi_3^\varepsilon(w,f,m))(t)\end{pmatrix}^T$$

$$=\begin{pmatrix}e^{td_1\Delta}w_0+\displaystyle\int_0^t e^{(t-s)d_1\Delta}\bar g_\varepsilon(w(s),f(s),m(s))ds\\ f_0-a\displaystyle\int_0^t m(s)f(s)ds\\ e^{t(d_2\Delta-c)}m_0+b\displaystyle\int_0^t e^{(t-s)(d_2\Delta-c)}w(s)z^{-1}(s)ds\end{pmatrix}^T\qquad\text{for all } t\in[0,\tau].$$

For any $\rho>0$ we consider a ball $B^\tau(\rho)=\{(w,f,m)\in X^\tau;\|(w,f,m)\|_{X^\tau}\le\rho\}$ in Lemma 2.1 in order to apply Banach's fixed point theorem. In the following argument, we assume that (A1)–(A6) are satisfied unless otherwise mentioned.

Lemma 2.1 *There exists a constant $\rho_1>0$ such that for each $\varepsilon\in(0,1)$ there exists $\tau_\varepsilon\in(0,1)$ such that the following properties are satisfied*:

(1) $\Phi^\varepsilon(B^{\tau_\varepsilon}(\rho_1))\subset B^{\tau_\varepsilon}(\rho_1)$.

(2) Φ^ε *is a contraction mapping on* $B^{\tau_\varepsilon}(\rho_1)$.

Proof. By using the similar argument in [7, Section 2] and (1.11) with $p=4$, we see that there exist constants $C_i>0$ $(i=5,7,9)$, $C_6(\varepsilon,\rho)>0$ and $C_i(\rho)>0$ $(i=8,10)$ such that the following estimates are satisfied for all $(w,f,m)\in B^\tau(\rho)$:

$$\max_{0\le t\le\tau}\|(\Phi_1^\varepsilon(w,m,f))(t)\|_{H^1(\Omega)}\le C_5+C_6(\varepsilon,\rho)(\tau+2\tau^{1/2}),\tag{2.6}$$

$$\max_{0\le t\le\tau}\|(\Phi_2^\varepsilon(w,m,f))(t)\|_{W^{1,\infty}(\Omega)}\le C_7+C_8(\rho)\tau,\tag{2.7}$$

$$\max_{0\le t\le\tau}\|(\Phi_3^\varepsilon(w,m,f))(t)\|_{W^{1,\infty}(\Omega)}\le C_9+C_{10}(\rho)(\tau+2\tau^{1/2}). \tag{2.8}$$

Moreover, for the mapping Φ_1^ε we see from Lemma 1.1 and the maximal principle that there exists a constant $C_{11}(\varepsilon,\rho)>0$ such that

$$\begin{aligned}
&\|(\Phi_1^\varepsilon(w,f,m))(t)\|_{L^\infty(\Omega)}\\
&\quad\le\|e^{td_1\Delta}w_0\|_{L^\infty(\Omega)}+\int_0^t\|e^{(t-s)d_1\Delta}\bar g_\varepsilon(w(s),f(s),m(s))\|_{L^\infty(\Omega)}ds\\
&\quad\le\|w_0\|_{L^\infty(\Omega)}+C_2(d_1,2,\infty)\int_0^t(1+(t-s)^{-N/4})\\
&\qquad\qquad\cdot\|\bar g_\varepsilon(w(s),f(s),m(s))\|_{L^2(\Omega)}ds\\
&\quad\le\alpha+C_2(d_1,2,\infty)\max_{0\le t\le\tau}\|\bar g_\varepsilon(w(s),f(s),m(s))\|_{L^2(\Omega)}\int_0^\tau(1+\sigma^{-N/4})d\sigma,
\end{aligned}$$

hence,

$$\max_{0\le t\le\tau}\|(\Phi_1^\varepsilon(w,f,m))(t)\|_{L^\infty(\Omega)}\le\alpha+C_{11}(\varepsilon,\rho)\left(\tau+\frac{4\tau^{(4-N)/4}}{4-N}\right). \tag{2.9}$$

We choose $\rho_1>0$ and $\tau_{1,\varepsilon}\in(0,1)$ satisfying $\rho_1>C_5+C_7+C_9+\alpha=R_1$ and

$$\{C_6(\varepsilon,\rho_1)+C_8(\rho_1)+C_{10}(\rho_1)+C_{11}(\varepsilon,\rho_1)\}\left(\tau_{1,\varepsilon}+2\tau_{1,\varepsilon}^{1/2}+\frac{4\tau_{1,\varepsilon}^{(4-N)/4}}{4-N}\right)\le\rho_1-R_1.$$

Then, we see from (2.6)–(2.9) that for any $\tau\in(0,\tau_{1,\varepsilon}]$

$$\|\Phi^\varepsilon(w,m,f)\|_{X^\tau}\le\rho_1\quad\text{for any }(w,f,m)\in B^\tau(\rho_1), \tag{2.10}$$

which implies $\Phi^\varepsilon(B^\tau(\rho_1))\subset B^\tau(\rho_1)$ whenever $\tau\in(0,\tau_{1,\varepsilon}]$,

Next, let $\tau\in(0,\tau_{1,\varepsilon}]$. Then, we see that there exists constants $C_{12}(\varepsilon)>0$ and $C_i>0$ $(i=13,14)$ such that the following estimates are satisfied for any $(w_k,f_k,m_k)\in B^\tau(\rho_1)$, $k=1,2$, where $\rho_1>0$ is the same constant obtained in the above argument:

$$\begin{aligned}
&\max_{0\le t\le\tau}\|(\Phi_1^\varepsilon(w_1,m_1,f_1))(t)-(\Phi_1^\varepsilon(w_2,f_2,m_2))(t)\|_{H^1(\Omega)}\\
&\qquad\le C_{12}(\varepsilon)(\tau+2\tau^{1/2})\|(w_1,f_1,m_1)-(w_2,f_2,m_2)\|_{X^\tau},
\end{aligned}\tag{2.11}$$

$$\max_{0\le t\le \tau} \|(\Phi_2^\varepsilon(w_1,m_1,f_1))(t) - (\Phi_2^\varepsilon(w_2,f_2,m_2))(t)\|_{W^{1,\infty}(\Omega)}$$
$$\le C_{13}\tau\|(w_1,f_1,m_1)-(w_2,f_2,m_2)\|_{X^\tau}, \tag{2.12}$$
$$\max_{0\le t\le \tau} \|(\Phi_3^\varepsilon(w_1,m_1,f_1))(t) - (\Phi_3^\varepsilon(w_2,f_2,m_2))(t)\|_{W^{1,\infty}(\Omega)}$$
$$\le C_{14}(\tau+2\tau^{1/2})\|(w_1,f_1,m_1)-(w_2,f_2,m_2)\|_{X^\tau}. \tag{2.13}$$

Moreover, by using Lemma 1.1 and repeating the same method to derive (2.9), we see that there exists a constant $C_{15}(\varepsilon)>0$ such that

$$\max_{0\le t\le \tau} \|(\Phi_1^\varepsilon(w_1,m_1,f_1))(t) - (\Phi_1^\varepsilon(w_2,f_2,m_2))(t)\|_{L^{\infty}(\Omega)}$$
$$\le C_{15}(\varepsilon)\left(\tau+\frac{4\tau^{(4-N)/4}}{4-N}\right)\|(w_1,f_1,m_1)-(w_2,f_2,m_2)\|_{X^\tau}. \tag{2.14}$$

At last, we choose $\tau_\varepsilon\in(0,\tau_{1,\varepsilon}]$ satisfying

$$\{C_{12}(\varepsilon)+C_{13}+C_{14}+C_{15}(\varepsilon)\}\left(\tau_\varepsilon+2\tau_\varepsilon^{1/2}+\frac{4\tau_\varepsilon^{(4-N)/4}}{4-N}\right)<1.$$

Then, we see from (2.11)–(2.14) that

$$\|\Phi^\varepsilon(w_1,f_1,m_1)-\Phi^\varepsilon(w_2,f_2,m_2)\|_{X^{\tau_\varepsilon}} < \|(w_1,f_1,m_1)-(w_2,f_2,m_2)\|_{X^{\tau_\varepsilon}}$$
$$\text{for any } (w_k,f_k,m_k)\in B^{\tau_\varepsilon}(\rho_1),\ k=1,2,$$

which implies that Φ^ε is contraction on $B^{\tau_\varepsilon}(\rho_1)$. □

As a direct consequence of applying Banach's fixed point theorem to Φ^ε, we have the existence of local-in-time solutions to $(\mathrm{Q})_\varepsilon$, which is stated in Lemma 2.2.

Lemma 2.2 *For each $\varepsilon\in(0,1)$ there exists $T_\varepsilon\in(0,\infty]$ $(Q)_\varepsilon$ has at least one solution $(w^\varepsilon,f^\varepsilon,m^\varepsilon)$ on $[0,T_\varepsilon)$. Moreover, if $T_\varepsilon<\infty$, then we have*

$$\lim_{t\nearrow T_\varepsilon}\left(\|w^\varepsilon(t)\|_{L^\infty(\Omega)}+\|w^\varepsilon(t)\|_{H^1(\Omega)}+\|f^\varepsilon(t)\|_{W^{1,\infty}(\Omega)}+\|m^\varepsilon(t)\|_{W^{1,\infty}(\Omega)}\right)=\infty.$$

From Lemma 2.2 we have Lemma 2.3, which gives the existence and uniqueness of non-negative local-in-time solutions to $(\mathrm{P})_\varepsilon$. Since its proof is the same to that of [7, Theorem 2.1], we omit the detail one in this paper and trust it to [7].

Lemma 2.3 *For each $\varepsilon \in (0,1)$ $(P)_\varepsilon$ has one and only one non-negative solution $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ on $[0, T_\varepsilon)$, where T_ε is the same number that is obtained in Lemma 2.2.*

Proof. Let $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a solution to $(\mathrm{Q})_\varepsilon$ on $[0, T_\varepsilon)$. Defining n^ε by

$$n^\varepsilon = w^\varepsilon \exp\left(\frac{1}{d_1}\int_0^{f^\varepsilon} \lambda(r)dr\right) \quad \text{in } Q_{T_\varepsilon}, \tag{2.15}$$

we can show that $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ is a unique non-negative solution to $(\mathrm{P})_\varepsilon$ on $[0, T_\varepsilon)$. □

Remark 2.2 Since from Lemma 2.3 a local-in-time solution $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ to $(\mathrm{Q})_\varepsilon$ always gives a unique non-negative local-in-time solution $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ to $(\mathrm{P})_\varepsilon$, we see that local-in-time solutions to $(\mathrm{Q})_\varepsilon$ must be uniquely determined and non-negative.

Now, we prepare the boundedness of local-in-time solutions to $(\mathrm{Q})_\varepsilon$ and $(\mathrm{P})_\varepsilon$. At first, we give the boundedness of $(n^\varepsilon, f^\varepsilon)$ in $L^\infty(0, T_\varepsilon; L^1(\Omega)) \times L^\infty(0, T_\varepsilon; L^\infty(\Omega))$, whose proofs are similar to those of [7, Section 3]. So, we omit them in this paper.

Lemma 2.4 *For each $\varepsilon \in (0,1)$ let $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative local-in-time solution to $(P)_\varepsilon$. Then, the following boundedness are satisfied:*

(1) $\|n^\varepsilon\|_{L^\infty(0,T_\varepsilon;L^1(\Omega))} \le |\Omega| \max\left\{\alpha, \dfrac{\mu_2}{\mu_1}\right\}$.

(2) $\|f^\varepsilon\|_{L^\infty(0,T_\varepsilon;L^\infty(\Omega))} \le \alpha$.

(3) $\|z^\varepsilon\|_{L^\infty(0,T_\varepsilon;L^\infty(\Omega))} \le 1$, $\|(z^\varepsilon)^{-1}\|_{L^\infty(0,T_\varepsilon;L^\infty(\Omega))} \le \exp\left(\dfrac{1}{d_1}\displaystyle\int_0^\alpha \lambda(r)dr\right)$.

(4) $(z^\varepsilon)^{-1}(t) \ge 1$ *a.e. in Ω for all $t \in [0, T_\varepsilon)$.*

(5) $z^\varepsilon(t) \ge \exp\left(-\dfrac{1}{d_1}\displaystyle\int_0^\alpha \lambda(r)dr\right)$ *a.e. in Ω for all $t \in [0, T_\varepsilon)$,*

where z^ε is given by (2.1), in which (f, z) is replaced by $(f^\varepsilon, z^\varepsilon)$.

Next, we give the boundedness of m^ε in $L^\infty(0, T_\varepsilon; L^q(\Omega))$ for some $q \ge 1$.

Lemma 2.5 *For each $\varepsilon \in (0,1)$ let $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative local-in-time solution to $(P)_\varepsilon$ and q be any number satisfying*

$$q \in \begin{cases} [1,\infty) & \text{if } N = 2, \\ [1,3) & \text{if } N = 3. \end{cases} \tag{2.16}$$

Then, there exists a constant $C_{16}(q) > 0$ such that

$$\|m^\varepsilon\|_{L^\infty(0,T_\varepsilon;L^q(\Omega))} \le C_{16}(q). \tag{2.17}$$

Proof. By using (2.4), Lemma 1.1 and the maximal principle, we have

$$\begin{aligned}
&\|m^\varepsilon(t)\|_{L^q(\Omega)} \\
&\quad \le \|e^{t(d_2\Delta - c)}m_0\|_{L^q(\Omega)} + b\int_0^t \|e^{(t-s)(d_2\Delta-c)}n^\varepsilon(s)\|_{L^q(\Omega)}ds \\
&\quad \le |\Omega|^{\frac{1}{q}}\|m_0\|_{L^\infty(\Omega)} \\
&\qquad + b\bar{C}_2(q)\int_0^t e^{-c(t-s)}(1+(t-s)^{-(N/2)(1-1/q)})\|n^\varepsilon(s)\|_{L^1(\Omega)}ds \\
&\quad \le |\Omega|^{1/q}\|m_0\|_{L^\infty(\Omega)} \\
&\qquad + \frac{b\bar{C}_2(q)\|n^\varepsilon\|_{L^\infty(0,T_\varepsilon;L^1(\Omega))}}{c}\int_0^{T_\varepsilon} e^{-\sigma}\left\{1+\left(\frac{\sigma}{c}\right)^{-(N/2)(1-1/q)}\right\}d\sigma,
\end{aligned}$$

where $\bar{C}_2(q) = C_2(d_2, 2, q)$. Since we have

$$\Gamma_N = \Gamma\left(1 + \frac{N}{2q} - \frac{N}{2}\right) = \int_0^\infty e^{-\sigma}\sigma^{-(N/2)(1-1/q)}d\sigma < \infty,$$

when q satisfies (2.16), by using (1) of Lemma 2.4 and taking

$$C_{16}(q) = |\Omega|^{1/q}\|m_0\|_{L^\infty(\Omega)} + \frac{b\bar{C}_2(q)|\Omega|}{c}(1 + c^{(N/2)(1-1/q)}\Gamma_N)\max\left\{\alpha, \frac{\mu_2}{\mu_1}\right\},$$

we see that (2.17) holds. $\square$

Next, we give the boundedness of w^ε in $L^\infty(0,T_\varepsilon;L^\infty(\Omega))$. The proof of Lemma 2.6 is essentially same as that of [7, Lemma 3.3], whose original one was given in [13]. But we cannot use Sobolev's embedding $H^1(D) \subseteq C(\bar{D})$ for a bounded domain $D \subset \mathbf{R}$, which plays an important role in [7]. So, it must be modified in the proof of Lemma 2.6.

Lemma 2.6 *For each $\varepsilon \in (0,1)$ let $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative local-in-time solution to $(P)_\varepsilon$. Then, there exists a constant $C_{17} > 0$ such that*

$$\|w^\varepsilon\|_{L^\infty(0,T_\varepsilon;L^\infty(\Omega))} \leq C_{17}. \tag{2.18}$$

Proof. Throughout this proof, for simplicity we skip the index ε of functions w^ε and z^ε. Let p be any number in $[2,\infty)$. We multiply the first equation in $(\mathrm{Q})_\varepsilon$ by $pw^{p-1}z^{-1}$ and integrate its result over Ω. Then, we see that there exists a constant $C_{18} > 0$ such that

$$\begin{aligned}\frac{d}{dt}\int_\Omega (z^{-1}w^p)(t) \leq -\frac{4d_1(p-1)}{p}\int_\Omega |\nabla w^{p/2}(t)|^2 \\ + C_{18}p\int_\Omega w^p(t) + C_{18}(p-1)\int_\Omega (w^p m)(t) \\ \text{a.a. } t \in (0,T_\varepsilon).\end{aligned} \tag{2.19}$$

By using (1.11) with $p = 6$, we have

$$\begin{aligned}\int_\Omega (w^p m)(t) &\leq \|w^{p/2}(t)\|_{L^1(\Omega)}^{8/25}\|w^{p/2}(t)\|_{L^6(\Omega)}^{42/25}\|m(t)\|_{L^{5/2}(\Omega)} \\ &\leq C_1(6)^{42/25}\|w^{p/2}(t)\|_{L^1(\Omega)}^{8/25}\|w^{p/2}(t)\|_{H^1(\Omega)}^{42/25}\|m(t)\|_{L^{5/2}(\Omega)},\end{aligned}$$

hence, by using Young's inequality and Lemma 2.5 with $q = 5/2$, we see that there exists a constant $C_{19} > 0$ such that for any $\delta > 0$

$$\int_\Omega (w^p m)(t) \leq \frac{\delta d_1}{C_{18}(p-1)}\|w^{p/2}(t)\|_{H^1(\Omega)}^2 + C_{19}\left(\frac{p-1}{\delta}\right)^{21/4}\|w^{p/2}(t)\|_{L^1(\Omega)}^2. \tag{2.20}$$

Moreover, by using (1.11) with $p = 3$ again, we have

$$\int_\Omega w^p(t) \leq \|w^{p/2}(t)\|_{L^1(\Omega)}^{1/2}\|w^{p/2}(t)\|_{L^3(\Omega)}^{3/2}$$

$$
\begin{aligned}
&\le C_1(3)^{3/2}\|w^{p/2}(t)\|_{L^1(\Omega)}^{1/2}\|w^{p/2}(t)\|_{H^1(\Omega)}^{3/2} \\
&\le \delta\|w(t)\|_{H^1(\Omega)}^2 + \frac{C_1(3)^6}{4}\left(\frac{3}{4\delta}\right)^3\|w^{p/2}(t)\|_{L^1(\Omega)}^2,
\end{aligned}
$$

hence,

$$
\int_\Omega w^p(t) \le \frac{\delta}{1-\delta}\int_\Omega |\nabla w^{p/2}(t)|^2 + \frac{C_1(3)^6}{4(1-\delta)}\left(\frac{3}{4\delta}\right)^3\|w^{p/2}(t)\|_{L^1(\Omega)}^2. \quad (2.21)
$$

By substituting (2.20), (2.21) into (2.19) and using (3), (4) in Lemma 2.4, we have

$$
\begin{aligned}
&\frac{d}{dt}\int_\Omega (z^{-1}w^p)(t) + \delta d_1 \exp\left(-\frac{1}{d_1}\int_0^\alpha \lambda(r)dr\right)\int_\Omega (z^{-1}w^p)(t) \\
&\quad\le \left\{\frac{C_1(3)^6(C_{18}p + 2\delta d_1)}{4(1-\delta)}\left(\frac{3}{4\delta}\right)^3 + \frac{C_{18}C_{19}(p-1)^{25/4}}{\delta^{21/4}}\right\}\|w^{p/2}(t)\|_{L^1(\Omega)}^2 \\
&\qquad + d_1\left\{\delta + \frac{\delta}{1-\delta}\left(\frac{C_{18}p}{d_1} + 2\delta\right) - \frac{4(p-1)}{p}\right\}\int_\Omega |\nabla w^{p/2}(t)|^2. \quad (2.22)
\end{aligned}
$$

Here, we choose constants $C_{20} > 1$ and $C_{21} > d_1$ satisfying

$$
\delta_p = \frac{1}{C_{20}(p+1)}, \quad \delta_p + \frac{\delta_p}{1-\delta_p}\left(\frac{C_{18}p}{d_1} + 2\delta_p\right) \ge \frac{4(p-1)}{p},
$$

$$
\frac{C_1(3)^6(C_{18}p + 2\delta_p d_1)}{4(1-\delta_p)}\left(\frac{3}{4\delta_p}\right)^3 + \frac{C_{18}C_{19}(p-1)^{25/4}}{\delta_p^{21/4}} \le C_{21}(p+1)^{12}.
$$

Then, we see that the following inequality is satisfied:

$$
\begin{aligned}
&\frac{d}{dt}\int_\Omega (z^{-1}w^p)(t) + \delta_p d_1 \exp\left(-\frac{1}{d_1}\int_0^\alpha \lambda(r)dr\right)\int_\Omega (z^{-1}w^p)(t) \\
&\quad\le C_{21}(p+1)^{12}\|w^{p/2}(t)\|_{L^1(\Omega)}^2 \quad \text{a.a. } t \in (0, T_\varepsilon). \quad (2.23)
\end{aligned}
$$

By applying Gronwall's lemma to (2.23) and using (3), (4) in Lemma 2.4, we have

$$\max_{0\le t<T_\varepsilon}\|w(t)\|_{L^p(\Omega)} \le \left\{\frac{2C_{20}C_{21}(p+1)^{13}}{d_1}\exp\left(\frac{1}{d_1}\int_0^\alpha \lambda(r)dr\right)\right\}^{1/p} \times \max\left\{|\Omega|^{1/p}\alpha, \max_{0\le t<T_\varepsilon}\|w(t)\|_{L^{p/2}(\Omega)}\right\}.$$

By using the same argument in [13, Proposition 4.2], we see that this lemma holds. □

By using Lemma 2.6 and the argument in [7], we have the boundedness of $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ in $L^\infty(0,T_\varepsilon;H^1(\Omega)) \times L^\infty(0,T_\varepsilon;W^{1,\infty}(\Omega)) \times L^\infty(0,T_\varepsilon;W^{1,\infty}(\Omega))$. We omit their proofs in this paper and trust them to [7], [13].

Lemma 2.7 *For each $\varepsilon \in (0,1)$ let $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative local-in-time solution to $(Q)_\varepsilon$. Then, the following boundedness are satisfied*:

(1) *There exists a constant $C_{22} > 0$ such that*

$$\|m^\varepsilon\|_{L^\infty(0,T_\varepsilon;W^{1,\infty}(\Omega))} \le C_{22}, \tag{2.24}$$

$$\|\nabla f^\varepsilon(t)\|_{L^\infty(0,T_\varepsilon;(L^\infty(\Omega))^N)} \le C_{22}(t+1) \quad \text{for all } t\in[0,T_\varepsilon). \tag{2.25}$$

(2) *There exists a constant $C_{23}(\varepsilon) > 0$ such that*

$$\|w^\varepsilon\|_{L^\infty(0,T_\varepsilon;H^1(\Omega))} \le C_{23}(\varepsilon). \tag{2.26}$$

Now, we complete the proof of Proposition 2.1

Proof of Proposition 2.1. We assume $T_\varepsilon < \infty$. Then, we see from Lemmas 2.4, 2.6 and 2.7 that there exists a constant $C_{24}(\varepsilon, T_\varepsilon) > 0$ such that

$$\begin{aligned}&\|w^\varepsilon(t)\|_{L^\infty(\Omega)} + \|w^\varepsilon(t)\|_{H^1(\Omega)} + \|f^\varepsilon(t)\|_{W^{1,\infty}(\Omega)} + \|m^\varepsilon(t)\|_{W^{1,\infty}(\Omega)}\\ &\quad \le C_{24}(\varepsilon, T_\varepsilon), \qquad \text{for all } t\in[0,T_\varepsilon),\end{aligned}$$

which contradicts the condition for T_ε in Lemma 2.2. Hence $T_\varepsilon = \infty$ must holds. □

In the rest of this section, we construct a global-in-time solution to (P) by using the limit procedure for the sequence $\{(n^\varepsilon, f^\varepsilon, m^\varepsilon); \varepsilon\in(0,1)\}$ of non-negative global-in-time solutions to $(\mathrm{P})_\varepsilon$. For this, we note that we have already obtained some boundedness of $\{(n^\varepsilon, f^\varepsilon, m^\varepsilon); \varepsilon \in (0,1)\}$, which is clearly stated in the next lemma again.

Lemma 2.8 *For each $\varepsilon \in (0,1)$ let $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative global-in-time solution to $(P)_\varepsilon$. Then, there exist constants $C_{25} > 0$, which is independent of $\varepsilon \in (0,1)$, such that*

$$\sup_{\varepsilon\in(0,1)} \|n^\varepsilon\|_{L^\infty(0,\infty;L^\infty(\Omega))} + \sup_{\varepsilon\in(0,1)} \|m^\varepsilon\|_{L^\infty(0,\infty;W^{1,\infty}(\Omega))} \leq C_{25},$$

$$\sup_{\varepsilon\in(0,1)} \|\nabla f^\varepsilon\|_{L^\infty(0,T;(L^\infty(\Omega))^N)} \leq C_{25}(T+1) \quad \textit{for all } T > 0$$

as well as

$$\sup_{\varepsilon\in(0,1)} \|f^\varepsilon\|_{L^\infty(0,\infty;L^\infty(\Omega))} \leq \alpha,$$

$$\sup_{\varepsilon\in(0,1)} \|(z^\varepsilon)^{-1}\|_{L^\infty(0,\infty;L^\infty(\Omega))} \leq \exp\left(\frac{1}{d_1}\int_0^\alpha \lambda(r)dr\right),$$

$$\inf_{\varepsilon\in(0,1)} z^\varepsilon(t) \geq \exp\left(-\frac{1}{d_1}\int_0^\alpha \lambda(r)dr\right) \quad \textit{a.e. in } \Omega \quad \textit{for a.a. } t \geq 0.$$

Next, we give the boundedness of n^ε in $W^{1,2}(0,T;L^2(\Omega)) \cap L^\infty(0,T;H^1(\Omega))$ because the boundedness of w^ε in $L^\infty(0,\infty;H^1(\Omega))$, which is obtained in (2) of Lemma 2.7, depends upon ε.

Lemma 2.9 *For each $\varepsilon \in (0,1)$ let $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative global-in-time solution to $(P)_\varepsilon$. Then, for each $T > 0$ there exists a constant $C_{26}(T) > 0$, which is independent of $\varepsilon \in (0,1)$, such that*

$$\sup_{\varepsilon\in(0,1)} \left\{\|n_t^\varepsilon\|_{L^2(0,T;L^2(\Omega))} + \|n^\varepsilon\|_{L^\infty(0,T;H^1(\Omega))} + \int_\Omega \hat{\beta}_\varepsilon(f^\varepsilon(t); n^\varepsilon(t))\right\} \leq C_{26}(T),$$

where $\hat{\beta}_\varepsilon$ is a non-negative primitive function of β_ε satisfying $\hat{\beta}_\varepsilon(0) = 0$.

Proof. We define w^ε by (2.1), in which (w, n, f, z) is replaced by $(w^\varepsilon, n^\varepsilon, f^\varepsilon, z^\varepsilon)$. Then, we see from Remark 2.2 that $(w^\varepsilon, f^\varepsilon, m^\varepsilon)$ is a non-negative global-in-time solution to $(\mathrm{Q})_\varepsilon$. In the following argument, for simplicity we skip the index ε. By using Remark 2.1, we take the inner product between the evolution equation in (E1) and $w_t(t)$. Then, we have

$$\begin{aligned}
&\|w_t(t)\|^2_{L^2(\Omega)} + \frac{d_1}{2}\frac{d}{dt}\int_\Omega |\nabla w(t)|^2 + \int_\Omega (w_t z)(t)\beta_\varepsilon(f(t);(wz^{-1})(t)) \\
&\quad \leq \int_\Omega \lambda(f(t))|w_t(t)||\nabla w(t)||\nabla f(t)| + \int_\Omega |\ell_\varepsilon(w(t),f(t),m(t))||w_t(t)| \\
&\quad = I_1(t) + I_2(t) \qquad \text{a.a. } t>0, \qquad (2.27)
\end{aligned}$$

where

$$\ell_\varepsilon(w,f,m) = \mu_p w(1-wz^{-1}-f) - \mu_d w + \frac{a\lambda(f)wmf}{d_1}.$$

By using Lemma 2.8, we see that the following estimates for $I_1(t)$ and $I_2(t)$ are satisfied for a.a. $t \in (0,T)$:

$$\begin{aligned}
I_1(t) &\leq (L\|f(t)\|_{L^\infty(\Omega)} + \lambda_0)\|\nabla f(t)\|_{(L^\infty(\Omega))^N}\|w_t(t)\|_{L^2(\Omega)}\left(\int_\Omega |\nabla w(t)|^2\right)^{1/2} \\
&\leq \frac{1}{4}\|w_t(t)\|^2_{L^2(\Omega)} + (\alpha L+\lambda_0)^2 C_{25}^2 (T+1)^2\int_\Omega |\nabla w(t)|^2
\end{aligned}$$

and

$$\begin{aligned}
I_2(t) &\leq \frac{1}{4}\|w_t(t)\|^2_{L^2(\Omega)} + \int_\Omega |\ell_\varepsilon(w(t),f(t),m(t))|^2 \\
&\leq \frac{1}{4}\|w_t(t)\|^2_{L^2(\Omega)} + 5C_{25}^2|\Omega|\left\{\mu_3^2 + \frac{a^2\alpha^2(\alpha L+\lambda_0)^2 C_{25}^2}{d_1^2}\right\} \\
&\quad + 5\mu_2^2 C_{25}^2|\Omega|\left\{1+\alpha^2 + C_{25}^2\exp\left(\frac{2}{d_1}\int_0^\alpha \lambda(r)dr\right)\right\}.
\end{aligned}$$

Moreover, from [7, Lemma 4.2] we have

$$\frac{d}{dt}\int_\Omega z^2(t)\hat{\beta}_\varepsilon(f(t);(wz^{-1})(t)) \leq \int_\Omega (w_t z)(t)\beta_\varepsilon(f(t);(wz^{-1})(t)). \qquad (2.28)$$

By substituting the estimates for $I_i(t)$, $i=1,2$, and (2.28) into (2.27), we easily see that there exist constants $C_{27}>0$ and $C_{28}>0$ such that

$$\|w_t(t)\|^2_{L^2(\Omega)} + \frac{d}{dt}\Big(d_1 \int_\Omega |\nabla w(t)|^2 + 2\int_\Omega z^2(t)\hat{\beta}_\varepsilon(f(t);(wz^{-1})(t))\Big)$$
$$\le d_1 C_{27}(T+1)^2 \int_\Omega |\nabla w(t)|^2 + C_{28} \quad \text{a.a. } t \in (0,T). \tag{2.29}$$

By applying Gronwall's lemma to (2.29) and using $\hat{\beta}_\varepsilon(f_0; n_0) = 0$ (cf. (A5)), we have

$$\|w_t\|^2_{L^2(0,t;L^2(\Omega))} + d_1 \int_\Omega |\nabla w(t)|^2 + 2\int_\Omega z^2(t)\hat{\beta}_\varepsilon(f(t);(wz^{-1})(t))$$
$$\le e^{C_{27}T(T+1)^2}\Big(d_1 \int_\Omega |\nabla w_0|^2 + \frac{C_{28}}{C_{27}}\Big) \quad \text{for all } t \in [0,T]. \tag{2.30}$$

Since we have

$$\nabla w_0 = \exp\Big(-\frac{1}{d_1}\int_0^{f_0} \lambda(r)dr\Big)\nabla n_0 - w_0\lambda(f_0)\nabla f_0,$$
$$n_t = z^{-1}\{w_t - a\lambda(f)wmf\}, \quad \nabla n = z^{-1}\Big\{\nabla w + \frac{\lambda(f)w}{d_1}\nabla f\Big\},$$

we see from (2.30) and Lemma 2.8 that this lemma holds. □

Moreover, we have the boundedness of m^ε in $W^{1,2}(0,T;L^2(\Omega)) \cap L^2(0,T;H^2(\Omega))$ in the next lemma.

Lemma 2.10 *For each $\varepsilon \in (0,1)$ let $(n^\varepsilon, f^\varepsilon, m^\varepsilon)$ be a non-negative global-in-time solution to $(P)_\varepsilon$. Then, there exists a constant $C_{29} > 0$, which is independent of $\varepsilon \in (0,1)$, such that*

$$\sup_{\varepsilon\in(0,1)} \big(\|m^\varepsilon_t\|^2_{L^2(0,T;L^2(\Omega))} + \|\Delta m^\varepsilon\|^2_{L^2(0,T;L^2(\Omega))}\big) \le C_{29}(T+1) \quad \textit{for all } T > 0.$$

Proof. By using Remark 2.1, we take the inner products between the evolution equation in (E2) and $m^\varepsilon_t(t)$ in $L^2(\Omega)$, and use Lemma 2.8. Throughout this argument, we skip the index ε of m^ε. Then, we have

$$\|m_t(t)\|^2_{L^2(\Omega)} + \frac{d}{dt}\Big(d_2 \int_\Omega |\nabla m(t)|^2 + c\|m(t)\|^2_{L^2(\Omega)}\Big) \le \frac{bC_{25}^2|\Omega|}{c} \quad \text{a.a. } t > 0,$$

which implies that the following boundedness is satisfied for all $T > 0$:

$$\sup_{\varepsilon \in (0,1)} \|m_t\|^2_{L^2(0,T;L^2(\Omega))} \le \frac{bC_{25}^2|\Omega|T}{c} + \max\{c, d_2\}\|m_0\|^2_{H^1(\Omega)}. \tag{2.31}$$

By going back to the evolution equation in (E2), we have

$$\|\Delta m(t)\|_{L^2(\Omega)} \le \|m_t(t)\|_{L^2(\Omega)} + (b+c)C_{25}|\Omega|^{1/2} \quad \text{a.a. } t > 0. \tag{2.32}$$

Hence, we see from (2.31) and (2.32) that this lemma holds. □

Now, we are in a position to give the proof of Theorem 1.1.

Proof of Theorem 1.1. We see from the uniform boundedness of $\{(n^\varepsilon, m^\varepsilon);\ \varepsilon \in (0,1)\}$ that for each $i \in \mathbf{N}$ there exist a sequence $\{\varepsilon_{i,k}\} \subset (0,1)$ and a pair (n_i, m_i) such that $\varepsilon_{i,k} \longrightarrow 0$ as $k \to \infty$ and the following convergences are satisfied as $k \to \infty$:

$$n^{\varepsilon_{i,k}} \longrightarrow n_i \quad \begin{cases} \text{in } C^0([0,i]; L^2(\Omega)), \\ \text{weakly in } W^{1,2}(0,i; L^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,i; H^1(\Omega)), \\ \text{a.e. in } Q_i, \end{cases} \tag{2.33}$$

$$m^{\varepsilon_{i,k}} \longrightarrow m_i \quad \begin{cases} \text{in } C^0([0,i]; C^0(\bar\Omega)) \cap L^2(0,i; H^1(\Omega)), \\ \text{weakly in } W^{1,2}(0,i; L^2(\Omega)) \cap L^2(0,i; H^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,i; W^{1,\infty}(\Omega)). \end{cases} \tag{2.34}$$

In order to derive (2.34) we use the following Gagliardo–Nirenberg's inequality: there exists a constant $C_{30} > 0$ such that

$$\|\varphi\|_{C^0(\bar\Omega)} \le C_{30}\|\varphi\|^{\theta_N}_{W^{1,N+1}(\Omega)}\|\varphi\|^{1-\theta_N}_{L^2(\Omega)},$$
$$\theta_N = \frac{N(N+1)}{N^2+N+2} \quad \text{for all } \varphi \in W^{1,\infty}(\Omega).$$

Now, we consider $\{(n^{\varepsilon_{i,k}}, m^{\varepsilon_{i,k}}); k \in \mathbf{N}\}$, which is derived in the above argument, and use Lemmas 2.8–2.10. Then, there exist a subsequence $\{\varepsilon^{i+1,k}\} \subset \{\varepsilon^{i,k}\}$ and a pair (n_{i+1}, m_{i+1}) such that the following convergences are satisfied as $k \to \infty$:

$$n^{\varepsilon_{i+1,k}} \longrightarrow n_{i+1} \quad \begin{cases} \text{in } C^0([0,i+1];L^2(\Omega)), \\ \text{weakly in } W^{1,2}(0,i+1;L^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,i+1;H^1(\Omega)), \\ \text{a.e. in } Q_{i+1}, \end{cases}$$

$$m^{\varepsilon_{i+1,k}} \longrightarrow m_{i+1} \quad \begin{cases} \text{in } C^0([0,i+1];C^0(\bar{\Omega})) \cap L^2(0,i+1;H^1(\Omega)), \\ \text{weakly in } W^{1,2}(0,i+1;L^2(\Omega)) \cap L^2(0,i+1;H^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,i+1;W^{1,\infty}(\Omega)). \end{cases}$$

We repeat the above operation inductively and put $\varepsilon_i = \varepsilon_{i,i}$ for all $i \in \mathbf{N}$. Moreover, we define a pair (n,m) by the following way: for each $T > 0$

$$(n(t),m(t)) = (n_{[T]+1}(t), m_{[T]+1}(t)) \quad \text{for all } t \in [0,T]. \tag{2.35}$$

Then, we easily see from the construction method of (n,m) that $\varepsilon_i \longrightarrow 0$ as $i \to \infty$ as well as for any $T > 0$ the following convergences are also satisfied as $i \to \infty$:

$$n^{\varepsilon_i} \longrightarrow n \quad \begin{cases} \text{in } C^0([0,T];L^2(\Omega)), \\ \text{weakly in } W^{1,2}(0,T;L^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,T;H^1(\Omega)), \\ \text{a.e. in } Q_T, \end{cases} \tag{2.36}$$

$$m^{\varepsilon_i} \longrightarrow m \quad \begin{cases} \text{in } C^0([0,T];C^0(\bar{\Omega})) \cap L^2(0,T;H^1(\Omega)), \\ \text{weakly in } W^{1,2}(0,T;L^2(\Omega)) \cap L^2(0,T;H^2(\Omega)), \\ *\text{-weakly in } L^\infty(0,T;W^{1,\infty}(\Omega)). \end{cases} \tag{2.37}$$

Next, we define a function f by (1.9), where m in (1.9) is the same function defined by (2.35). By using Lemma 2.8 and the following inequalities:

$$\begin{aligned} &|(f^\varepsilon - f)(x,t)| \\ &\quad \le f_0(x)\left| \exp\left(-a\int_0^t m^\varepsilon(x,s)ds \right) - \exp\left(-a\int_0^t m(x,s)ds \right) \right| \end{aligned}$$

$$\leq a\alpha \exp\left(a\int_0^t (m^\varepsilon + m)(x,s)ds\right)\int_0^t |(m^\varepsilon - m)(x,s)|ds,$$

and

$$\begin{aligned}
&|\nabla(f^\varepsilon - f)(x,t)| \\
&\quad \leq |\nabla f_0(x)|\left|\exp\left(-a\int_0^t m^\varepsilon(x,s)ds\right) - \exp\left(-a\int_0^t m(x,s)ds\right)\right| \\
&\qquad + a|(f^\varepsilon - f)(x,t)|\int_0^t |\nabla m^\varepsilon(x,s)|ds + a\alpha\int_0^t |\nabla(m^\varepsilon - m)(x,s)|ds,
\end{aligned}$$

we have

$$\|f^\varepsilon(t) - f(t)\|_{C^0(\bar\Omega)} \leq a\alpha T e^{2aC_{25}T}\|m^\varepsilon - m\|_{C^0([0,T];C^0(\bar\Omega))}$$

and

$$\begin{aligned}
&\|\nabla(f^\varepsilon - f)(t)\|^2_{(L^2(\Omega))^N} \\
&\quad \leq 3a^2\alpha^2\int_\Omega\left(\int_0^t |\nabla(m^\varepsilon - m)(s)|ds\right)^2 \\
&\qquad + 3a^2\|(f^\varepsilon - f)(t)\|^2_{C^0(\bar\Omega)}\int_\Omega\left(\int_0^t |\nabla m(s)|ds\right)^2 \\
&\qquad + 3a^2|\Omega|\|f_0\|^2_{W^{1,\infty}(\Omega)}e^{4aC_{25}T}\left(\int_0^t \|(m^\varepsilon - m)(s)\|_{C^0(\bar\Omega)}ds\right)^2 \\
&\quad \leq 3a^2T\big(\alpha^2 + |\Omega|C_{25}^2T + |\Omega|\|f_0\|^2_{W^{1,\infty}(\Omega)}Te^{4\alpha C_{25}T}\big) \\
&\qquad \times \big(\|m^\varepsilon - m\|^2_{L^2(0,T;H^1(\Omega))} + \|f^\varepsilon - f\|^2_{C^0([0,T];C^0(\bar\Omega))} \\
&\qquad\qquad + \|m^\varepsilon - m\|^2_{C^0([0,T];C^0(\bar\Omega))}\big),
\end{aligned}$$

hence,

$$f^{\varepsilon_i} \longrightarrow f \quad \text{in } C^0([0,T];C^0(\bar\Omega)) \cap L^\infty(0,T;H^1(\Omega)) \quad \text{as} \quad i \to \infty. \tag{2.38}$$

Then, we immediately see from Lemma 2.8 that the triplet (n,f,m) is non-negative on Q and satisfies the following boundedness, which are used in the rest of this proof:

$$\|n\|_{L^\infty(0,\infty;L^\infty(\Omega))} + \|m\|_{L^\infty(0,\infty;W^{1,\infty}(\Omega))} \le C_{25}, \tag{2.39}$$

$$\|f\|_{L^\infty(0,\infty;L^\infty(\Omega))} \le \alpha, \tag{2.40}$$

Since we see from (A1), Lemma 2.8 and (2.39) that there exists a constant $C_{31} > 0$ such that the following inequality is satisfied for a.a. $t \in (0,T)$:

$$\begin{aligned}
&\|\lambda(f^\varepsilon(t))n^\varepsilon(t)\nabla f^\varepsilon(t) - \lambda(f(t))n(t)\nabla f(t)\|^2_{(L^2(\Omega))^N} \\
&\quad\le 3L^2 \int_\Omega |n^\varepsilon(t)|^2 |\nabla f^\varepsilon(t)|^2 |(f^\varepsilon - f)(t)|^2 \\
&\qquad + 3\int_\Omega (L|f(t)| + \lambda_0)^2 |\nabla f^\varepsilon(t)|^2 |(n^\varepsilon - n)(t)|^2 \\
&\qquad + 3\int_\Omega (L|f(t)| + \lambda_0)^2 |n(t)|^2 |\nabla(f^\varepsilon - f)(t)|^2 \\
&\quad\le C_{31}\big(\|(n^\varepsilon - n)(t)\|^2_{L^2(\Omega)} + \|(f^\varepsilon - f)(t)\|^2_{C^0(\bar\Omega)} + \|(f^\varepsilon - f)(t)\|^2_{H^1(\Omega)}\big),
\end{aligned}$$

we derive that the following convergences are satisfied as $i \to \infty$:

$$\lambda(f^{\varepsilon_i})n^{\varepsilon_i}\nabla f^{\varepsilon_i} \longrightarrow \lambda(f)n\nabla f \quad \text{in } L^\infty(0,T;(L^2(\Omega))^N) \tag{2.41}$$

as well as

$$\mu_p n^{\varepsilon_i}(1 - n^{\varepsilon_i} - f^{\varepsilon_i}) \longrightarrow \mu_p n(1-n-f) \quad \text{in } L^\infty(0,T;L^2(\Omega)), \tag{2.42}$$

$$\mu_d n^{\varepsilon_i} \longrightarrow \mu_d n \quad \text{in } L^\infty(0,T;L^2(\Omega)). \tag{2.43}$$

Now, we are in a position to show (1.8). Let η be any function in $L^2(0,T;H^1(\Omega))$ satisfying $0 \le \eta \le \alpha - f$ a.e. in Q_T. By using the same argument in [7, Lemma 4.5], we can choose a sequence $\{\eta_i; i \in \mathbf{N}\} \subset L^2(0,T;H^1(\Omega))$ so that the following properties are satisfied:

$$0 \le \eta_i \le \alpha - f^{\varepsilon_i} \quad \text{a.e. in } Q_T \quad \text{for all } i \in \mathbf{N}, \tag{2.44}$$

$$\eta_i \longrightarrow \eta \quad \text{in } L^2(0,T;H^1(\Omega)) \quad \text{as } i \to \infty. \tag{2.45}$$

We substitute $\zeta = n^{\varepsilon_i}(t) - \eta_i(t)$ in (2.5), integrate its result on $(0,T)$ and use the monotonicity of $\beta_{\varepsilon_i}(f^{\varepsilon_i};\cdot)$ with $\beta_{\varepsilon_i}(f^{\varepsilon_i};\eta_i)=0$ a.e. in Q_T (cf. (2.44)):

$$\iint_{Q_T}\beta_{\varepsilon_i}(f^{\varepsilon_i};n^{\varepsilon_i})(n^{\varepsilon_i}-\eta_i)\geq 0\quad\text{for all } i\in\mathbf{N}.$$

Then, we have the following inequalities are satisfied for all $i\in\mathbf{N}$:

$$\begin{aligned}\iint_{Q_T} n_t^{\varepsilon_i}(n^{\varepsilon_i}-\eta_i)&+\iint_{Q_T}\{d_1\nabla n^{\varepsilon_i}-\lambda(f^{\varepsilon_i})n^{\varepsilon_i}\nabla f^{\varepsilon_i}\}\cdot\nabla(n^{\varepsilon_i}-\eta_i)\\ &\leq\iint_{Q_T}\mu_p n^{\varepsilon_i}(1-n^{\varepsilon_i}-f^{\varepsilon_i})(n^{\varepsilon_i}-\eta_i)-\iint_{Q_T}\mu_d n^{\varepsilon_i}(n^{\varepsilon_i}-\eta_i).\end{aligned}\tag{2.46}$$

By taking the limit $i\to\infty$ in (2.46) and using all convergences in (2.36)–(2.38), (2.41)–(2.43) and (2.45), we see that (1.8) holds.

Finally, we show $0\leq n\leq\alpha-f$ a.e. in Q_T in (4) of Theorem 1.1. For each $(x,t)\in Q_T$ satisfying $f(x,t)\leq\alpha$ (cf. (2.40)) we denote by $\hat\beta(f(x,t);\cdot)$ the indicator function on the compact interval $[0,\alpha-f(x,t)]$. By using the similar argument in [7, Proposition 4.2], we have

$$\hat\beta(f(x,t);n(x,t))\leq\liminf_{i\to\infty}\hat\beta_{\varepsilon_i}(f^{\varepsilon_i}(x,t);n^{\varepsilon_i}(x,t))\quad\text{a.a. }(x,t)\in Q_T.\tag{2.47}$$

By using Lemma 2.9 and applying Fatou's lemma with (2.47), we have

$$\iint_{Q_T}\hat\beta(f;n)\leq\liminf_{i\to\infty}\iint_{Q_T}\hat\beta_{\varepsilon_i}(f^{\varepsilon_i};n^{\varepsilon_i})\leq TC_{25}(T),\ \text{so,}\ \iint_{Q_T}\hat\beta(f;n)=0,$$

which implies that the constraint condition $0\leq n\leq\alpha-f$ a.e. in Q_T is satisfied. □

3. Large-time behavior of global-in-time solutions

We devote this section to show Theorem 1.2 by using the argument similar to that in [7, Section 4]. Throughout this section, we assume that (A1)–(A10) are satisfied and let (n,f,m) the same triplet that is a global-in-time solution to (P) obtained by the limit procedure in the proof of Theorem 1.1.

At first, we show Lemma 3.1, which gives the uniform positivity of n and enables us to consider the large-time behavior of global-in-time solutions

(n, f, m) to (P).

Lemma 3.1 *There exists a constant $C_{32} > 0$ such that $n \geq C_{32}$ a.e. in Q.*

Proof. Let $\{(n^{\varepsilon_i}, f^{\varepsilon_i}, m^{\varepsilon_i}); i \in \mathbf{N}\}$ be the same sequence that is obtained in the proof of Theorem 1.1. We consider a sequence $\{(w_i, f_i, m_i) = (n^{\varepsilon_i} z^{\varepsilon_i}, f^{\varepsilon_i}, m^{\varepsilon_i}); i \in \mathbf{N}\}$ of non-negative global-in-time solutions to $(\mathrm{Q})_\varepsilon$, where z^{ε_i} is given by (2.1) in which (z, f) are replaced by $(z^{\varepsilon_i}, f^{\varepsilon_i})$, and take $C_{32} > 0$ by

$$C_{32} = n_* \exp\Big(- \frac{1}{d_1} \int_0^1 \lambda(r) dr \Big),$$

where n_* is the constant in (A9). By putting $(w_i - C_{32})_- = -\min\{0, w_i - C_{32}\}$, we multiply the first equation in $(\mathrm{Q})_{\varepsilon_i}$ by $z_i^{-1}(t)(w_i(t) - C_{32})_-$, and integrate its result over Ω. Since we see from the second equation and the boundary condition for w_i in $(\mathrm{Q})_{\varepsilon_i}$ that the following equalities are satisfied:

$$\begin{aligned}
&\int_\Omega (w_i)_t(t) z_i^{-1}(t)(w_i(t) - C_{32})_- \\
&\quad = -\frac{1}{2}\frac{d}{dt} \int_\Omega z_i^{-1}(t) |(w_i(t) - C_{32})_-|^2 \\
&\qquad - \frac{a}{2d_1} \int_\Omega z_i^{-1}(t) \lambda(f_i(t)) m_i(t) f_i(t) |(w_i(t) - C_{32})_-|^2
\end{aligned}$$

and

$$\begin{aligned}
&d_1 \int_\Omega z_i^{-1}(w_i - C_{32})_- \Delta w_i \\
&\quad = -d_1 \int_\Omega (w_i - C_{32})_- \nabla z_i^{-1} \cdot \nabla w_i - d_1 \int_\Omega z_i^{-1} \nabla (w_i - C_{32})_-) \cdot \nabla w_i \\
&\quad = -d_1 \int_\Omega z_i^{-1} \lambda(f_i)(w_i - C_{32})_- \nabla w_i \cdot \nabla f_i + d_1 \int_\Omega z_i^{-1} |\nabla (w_i - C_{32})_-)|^2,
\end{aligned}$$

by using the non-negativity of (w_i, f_i, m_i) we see that the following inequality is satisfied for a.a. $t > 0$:

$$
\begin{aligned}
&\frac{1}{2}\frac{d}{dt}\int_\Omega z_i^{-1}(t)|(w_i(t)-C_{32})_-|^2 \\
&\quad\le \int_\Omega \beta_{\varepsilon_i}(f_i(t);(w_iz_i^{-1})(t))(w_i(t)-C_{32})_- \\
&\qquad -\int_\Omega \mu_p(t)(z_i^{-1}w_i)(t)\{1-(w_iz_i^{-1})(t)-f_i(t)\}(w_i(t)-C_{32})_-. \quad (3.1)
\end{aligned}
$$

For each $t>0$ we put $\Omega_i(t)=\{x\in\Omega\,;\,w_(x,t)<C_{32}\}$. Since $f_i(x,t)$ is decreasing with respect to $t\in[0,\infty)$ for any fixed $x\in\Omega$, we see from (A8) that

$$
\exp\Big(-\frac{1}{d_1}\int_0^{f_i(x,t)}\lambda(r)dr\Big)\ge\exp\Big(-\frac{1}{d_1}\int_0^1\lambda(r)dr\Big),
$$

hence,

$$
C_{32}z_i^{-1}(x,t)\le n_*\le 1-f_0(x)\le 1-f_i(x,t)\quad\text{a.a. }(x,t)\in Q. \quad (3.2)
$$

We see from (3.2) that the following estimate is satisfied:

$$
1-(w_iz_i^{-1})(x,t)-f_i(x,t)<0\quad\text{a.a. }(x,t)\in E=\bigcup_{t>0}\Omega_i(t)\times\{t\}, \quad (3.3)
$$

which implies

$$
\int_\Omega(\mu_pz_i^{-1}w_i)(t)\{1-(w_iz_i^{-1})(t)-f_i(t)\}(w_i(t)-C_{32})_-\ge 0\quad\text{a.a. }t>0. \quad (3.4)
$$

Moreover, since $\beta_{\varepsilon_i}(f_i(x,t);\cdot)$ is an increasing function on $\mathbf{R}$ for any fixed $(x,t)\in Q$, we see from $\beta_{\varepsilon_i}(f_i(x,t);C_{32}z_i^{-1}(x,t))=0$ and (3.2) that the following estimate is satisfied:

$$
\begin{aligned}
&\beta_{\varepsilon_i}(f(x,t);(w_iz_i^{-1})(x,t))(w_i(x,t)-C_{32})_- \\
&\quad=-z_i(x,t)\beta_{\varepsilon_i}(f_i(x,t);(w_iz_i^{-1})(x,t))\{(w_iz_i^{-1})(x,t)-C_{32}z_i^{-1}(x,t)\} \\
&\quad\le 0\quad\text{a.a. }(x,t)\in E. \quad (3.5)
\end{aligned}
$$

Finally, we derive from (3.1), (3.4) and (3.5) that the following inequality is satisfied:

$$\frac{d}{dt}\int_\Omega z_i^{-1}(t)|(w_i(t)-C_{32})_-|^2 \le 0 \quad \text{a.a. } t>0, \tag{3.6}$$

By using (3.6) and

$$w_0 = n_0 \exp\left(-\frac{1}{d_1}\int_0^{f_0}\lambda(r)dr\right) \ge C_{32},$$

we have $w_i \ge C_{32}$, hence, $n^{\varepsilon_i} \ge C_{32}$ a.e. in Q. Hence, by taking the limit $i \to \infty$ and using (2.36), for any $T>0$ we have $n \ge C_{32}$ a.e. in Q_T. Since $T>0$ is arbitrary, we see that this lemma holds. □

Next, we give the positivity as well as the upper boundedness of m. Since we can show this lemma by using the same argument that is given in [7, Lemma 5.2], we omit its proof in this paper.

Lemma 3.2 *m satisfies the following estimates*:
(1) $m_* \le m \le \max\left\{\|m_0\|_{L^\infty(\Omega)}, \dfrac{b\alpha}{c}\right\}$ *a.e. in Q, where m_* is the constant in* (A10).
(2) *There exists a constant $C_{33}>0$ such that*

$$\iint_{Q_T} |\nabla m|^2 \le C_{33}(T+1) \quad \textit{for all } T>0.$$

In the rest of this section, we show Theorem 1.2. First of all, we give the large-time behavior of f in Lemma 3.3. Since its proof is also the same to [7, Lemma 5.3], we omit it in this paper. Actually, by using Lemma 3.2 and (1.9), we can easily show this lemma.

Lemma 3.3 *f satisfies the following estimates*:
(1) $\|f(t)\|_{L^\infty(\Omega)} \le e^{-\alpha m_* t} \le 1$ *for all $t>0$.*
(2) *There exists a constant $C_{34}>0$ and $C_{35}>0$ such that*

$$\|\nabla f(t)\|_{(L^2(\Omega))^N} \le C_{34}(t+1)e^{-\alpha m_* t} \le C_{35} \quad \textit{for all } t>0.$$

Finally, we give the large-time behaviors of n and m in Lemmas 3.4 and 3.5, respectively. Although their proofs are similar to those of [7, Lemmas 5.4 and 5.5], we give the detail ones in this paper. Actually, the proofs in

[7] are not so clear and complete that some readers cannot follow our ideas.

Lemma 3.4 *n satisfies the following estimates*:

(1) *There exists a constant $C_{36} > 0$ such that*

$$\int_0^\infty \|n(t) + f(t) - 1\|^2_{L^2(\Omega)} dt \le C_{36}.$$

(2) *There exists a constant $C_{37} > 0$ such that*

$$\sup_{t\ge 1} \left\{ \sup_{h\in(0,1]} \frac{\|n(t) + f(t) - 1\|^2_{L^2(\Omega)} - \|n(t-h) + f(t-h) - 1\|^2_{L^2(\Omega)}}{h} \right\} \le C_{37}.$$

Proof. Since we can show (1) by using the argument similar to that of [7, Lemma 5.3], we omit it and only give the proof of (2) in this paper. For simplicity, throughout this section we put $\psi_1(t) = \|n(t) + f(t) - 1\|^2_{L^2(\Omega)}$.

For any $T \ge 1$ and $h \in (0, 1]$ we define η_h by

$$\eta_h(t) = \begin{cases} n(t) & \text{if } t \in [0, T-h), \\ 1 - f(t) & \text{if } t \in [T-h, T], \end{cases}$$

which is in $L^2(0, T; H^1(\Omega))$ and satisfies $0 \le \eta_h \le \alpha - f$ a.e. in Q_T. By substituting $\eta = \eta_h$ in (1.8) and using (1.2), we have

$$\begin{aligned} &\frac{\psi_1(T) - \psi_1(T-h)}{2} + \frac{d_1}{2}\int_{T-h}^T \|\nabla n(t)\|^2_{(L^2(\Omega))^N} dt \\ &\le \frac{d_1}{2}\int_{T-h}^T \|\nabla f(t)\|^2_{(L^2(\Omega))^N} dt + \int_{T-h}^T \left(\int_\Omega f_t(t)(n(t) + f(t) - 1)\right) dt \\ &\quad + \int_{T-h}^T \left(\int_\Omega \lambda(f(t)) n(t) \nabla f(t) \cdot \nabla(n(t) + f(t))\right) dt. \end{aligned}$$

By using Lemmas 3.2 and 3.3, (1.2) and the non-negativity of (n, f, m), we have

$$\psi_1(T) - \psi(T-h) \le C_{37} h \quad \text{for any } T \ge 1 \text{ and any } h \in (0, 1],$$

where $C_{37} > 0$ is given by

$$C_{37} = 2\left[a|\Omega| \max\left\{\|m_0\|_{L^\infty(\Omega)}, \frac{b\alpha}{c}\right\} + C_{35}^2\left\{\frac{d_1}{2} + \alpha(L+\lambda_0) + \frac{\alpha^2(L+\lambda_0)^2}{2d_1}\right\}\right].$$

Hence, we see that (2) holds. □

Lemma 3.5 *n satisfies the following estimates*:

(1) *There exists a constant $C_{38} > 0$ such that*

$$\int_0^\infty \left\|m(t) - \frac{b}{c}\right\|_{L^2(\Omega)}^2 dt \leq C_{38}.$$

(2) *There exists a constant $C_{39} > 0$ such that*

$$\left|\frac{d}{dt}\left\|m(t) - \frac{b}{c}\right\|_{L^2(\Omega)}^2\right| \leq C_{39} \quad a.a.\ t > 0.$$

Proof. Since we can also show (1) by using the argument similar to that of [7, Lemma 5.4], we omit it and only give the proof of (2) in this paper. We note that m is a unique solution to the evolution equation

$$m'(t) - d_1\Delta_N m(t) + cm(t) = bn(t) \quad \text{in } L^2(\Omega), \text{ a.a. } t > 0 \tag{3.7}$$

with $m(0) = m_0$ in $L^2(\Omega)$. (cf. (E2))

In the following argument, for simplicity we put $\psi_2(t) = \|m(t) - b/c\|_{L^2(\Omega)}^2$. Then, we take the inner product between (3.7) and $m(t) - b/c$ to have

$$\frac{1}{2}\frac{d}{dt}\psi_2(t) + d_2\int_\Omega |\nabla m(t)|^2 + c\psi_2(t) = b\int_\Omega \left(m(t) - \frac{b}{c}\right)(n(t) - 1) \quad \text{a.a. } t > 0.$$

By using (2.39) and the estimate

$$\left|b\int_\Omega \left(m(t) - \frac{b}{c}\right)(n(t) - 1)\right| \leq \frac{c\psi_2(t)}{2} + \frac{b^2(\alpha+1)^2|\Omega|}{2c},$$

we have

$$\left|\frac{d}{dt}\psi_2(t)\right| \le 2d_2 \int_\Omega |\nabla m(t)|^2 + 3c\psi_2(t) + \frac{b^2(\alpha+1)^2|\Omega|}{c}$$
$$\le C_{25}^2|\Omega| \max\{2d_1, 3c\} + \frac{b^2\{3+(\alpha+1)^2\}|\Omega|}{c},$$

which implies that (2) holds. □

Now, we are in a position to show Theorem 1.2

Proof of Theorem 1.2. We easily see from Lemma 3.3 that

$$f(t) \longrightarrow 0 \quad \text{in } L^\infty(\Omega) \cap H^1(\Omega) \quad \text{as } t \to \infty. \tag{3.8}$$

Next, we assume $\lim_{t\to\infty} \psi_1(t) \neq 0$. Then, we can take a sequence $\{t_n; n \in \mathbf{N}\}$ and $\ell_1 > 0$ such that $\lim_{n\to\infty} \psi_1(t) = \ell_1$ and $t_{n+1} \ge t_n + 1$ for all $n \in \mathbf{N}$. By taking

$$h_1 = \min\left\{1, \frac{\ell_1}{2(C_{37}+1)}\right\},$$

and using Lemma 3.4, where C_{37} is the same constant that is obtained in (2) of Lemma 3.4, we see that there exists $n_1 \in \mathbf{N}$ such that

$$\ell_1 - \psi_1(t) \le |\psi_1(t_n) - \ell_1| + \psi_1(t_n) - \psi_1(t) \le \frac{\ell_1}{2(C_{37}+1)} + C_{37}(t_n - t) \le \frac{\ell_1}{2},$$

that is,

$$\psi_1(t) \ge \frac{\ell_1}{2} \quad \text{for any } n \ge n_1 \text{ and any } t \in [t_n - h_1, t_n). \tag{3.9}$$

We see from (3.9) that

$$\int_0^\infty \psi_1(t)dt \ge \sum_{n=n_1}^\infty \int_{t_{n-1}}^{t_n} \psi_1(t)dt \ge \sum_{n=n_1}^\infty \int_{t_n-h_1}^{t_n} \psi_1(t)dt \ge \sum_{n=n_1}^\infty \frac{\ell_1 h_1}{2} = \infty,$$

which contradicts (1) of Lemma 3.4. Hence, we have $n(t) + f(t) \longrightarrow 1$ in $L^2(\Omega)$, so, by using (3.8) $n(t) \longrightarrow 1$ in $L^2(\Omega)$ as $t \to \infty$.

Finally, we assume $\lim_{t\to\infty} \psi_2(t) \neq 0$. Then, we take a sequence $\{s_n\,;\, n \in \mathbf{N}\}$ and $\ell_2 > 0$ such that $\lim_{n\to\infty} \psi_1(s_n) = \ell_2$ and $s_{n+1} \ge s_n + s_0$

for all $n \in \mathbf{N}$, where $s_0 = \ell_2/2(C_{39}+1)$ and C_{39} is the same constant that is obtained in (2) of Lemma 3.5. Then, we see that there exists $n_2 \in \mathbf{N}$ such that

$$\ell_2 - \psi_1(s) \leq |\psi_1(s_n) - \ell_2| + \int_s^{s_n} |\psi_2'(\tau)| d\tau \leq \frac{\ell_2}{2(C_{39}+1)} + C_{39}(s_n - s) \leq \frac{\ell_2}{2},$$

that is,

$$\psi_2(t) \geq \frac{\ell_2}{2} \quad \text{for any } n \geq n_2 \text{ and any } s \in [s_n - s_0, s_n]. \tag{3.10}$$

We see from (3.10) that

$$\begin{aligned} \int_0^\infty \psi_2(t)dt &\geq \sum_{n=n_1}^{\infty} \int_{s_n - s_0}^{s_n} \psi_2(t)dt \geq \sum_{n=n_1}^{\infty} \int_{s_n - s_0}^{s_n} \frac{\ell_2}{2} dt \\ &\geq \sum_{n=n_1}^{\infty} \frac{\ell_2^2}{4(C_{38}+1)} = \infty, \end{aligned}$$

which contradicts (1) of Lemma 3.5, hence, $m(t) \longrightarrow b/c$ in $L^2(\Omega)$ as $t \to \infty$.
□

References

[1] Anderson A. R. A., Chaplain M. A. J., Newman E. L., Steele R. J. C. and Thompson A. M., *Mathematical modelling of tumor invasion and metastasis*. J. Theor. Med. **2** (2000), 129–154.

[2] Bellomo N., Li N. K. and Maini P. K., *On the foundations of cancer modelling: Selected topics, speculations, and perspectives*. Math. Models Methods Appl. Sci. **18** (2008), 593–646.

[3] Chaplain M. A. J. and Anderson A. R. A., Mathematical modelling of tissue invasion, in Cancer Modelling and Simulation, Chapman&Hall/CRC Mathematical Biology and Medicine Series, L. Preziosi, eds., Chapman&Hall/CRC, Boca Raton, 2003, pp. 269–297.

[4] Chaplain M. A. J. and Lolas G., *Mathematical modelling of cancer cell invasion of tissue: The role of the urokinase plasminogen activation system*. Math. Models Methods Appl. Sci. **15** (2005), 1685–1734.

[5] Friedman A. and Lolas G., *Analysis of a mathematical model of tumor lymphangiogenesis*. Math. Models Methods Appl. Sci. **15** (2005), 95–107.

[6] Fujie K., Ito A. and Yokota T., *Local existence and uniqueness of classical solutions to modified tumor invasion models of Chaplain–Anderson type*. Adv. Math. Sci. Appl. **24** (2014), 67–84.

[7] Ito A., *Asymptotic behaviors of solutions to one-dimensional tumor invasion model with quasi-variational structure*. J. Math. Sci. Univ. Tokyo **22** (2015), 569–612.

[8] Kano R., *The existence of solutions for tumor invasion models with time and space dependent diffusion*. Discrete Contin. Dyn. Syst. Ser. S. **7** (2014), 63–74.

[9] Kano R. and Ito A., The existence of time global solutions for tumor invasion models with constraints, Dynamical Systems, Differential Equations and Applications, 8th AIMS Conference, Discrete Contin. Dyn. Syst., Suppl., Vol. II, (2011), pp. 774–783.

[10] Kano R. and Ito A., *Tumor invasion model with a random motility of tumor cells depending upon extracellular matrix*. Adv. Math. Sci. Appl. **23** (2013), 397–411.

[11] Kano R., Ito A., Yamamoto K. and Nakayama H., Quasi-variational inequality approach to tumor invasion models with constraints, in Current advances in nonlinear analysis and related topics, GAKUTO Internat. Ser. Math. Sci. Appl., **32**, T. Aiki, N. Kenmochi, M. Niezgódka and M.Ôtani, eds., Gakkōtosho, Tokyo, 2010, pp. 365–388.

[12] Kano R., Kenmochi N. and Murase Y., Nonlinear evolution equations generated by subdifferentials with nonlocal constraints, in Nonlocal and abstract parabolic equations and their applications, Banach Center Publication, **86**, P. B. Mucha, C, M. Niezgódka and P. Rybka, eds., Polish Academy of Sciences, Institute of Mathematics, Warsaw, 2009, pp. 175-194.

[13] Liţcanu G. and Morales-Rodrigo C., *Asymptotic behavior of global solutions to a model of cell invasion*. Math. Models Methods Appl. Sci. **20** (2010), 1721–1758.

[14] Marciniak-Czochra A. and Ptashnyk M., *Boundedness of solutions of a haptotaxis model*. Math. Models Methods Appl. Sci. **20** (2010), 449–476.

[15] Morales-Rodrigo C., *Local existence and uniqueness of regular solutions in a model of tissue invasion by solid tumours*. Math. Comput. Model. **47** (2008), 604–613.

[16] Szymańska Z., Morales-Rodrigo C., Lachowicz M. and Chaplain M., *Mathematical modelling of cancer invasion of tissue: The role and effect of nonlocal interactions*. Math. Models Methods Appl. Sci. **19** (2009), 257–281.

[17] Szymańska Z., Urbański J. and Marciniak-Czochra A., *Mathematical modelling of the influence of heat shock proteins on cancer invasion of tissue*.

J. Math. Biol. **58** (2009), 819–844.

[18] Tao Y., *Global existence of classical solutions to a combined chemotaxis-haptotaxis model with logistic source*. J. Math. Anal. Appl., **354** (2009), 60–69.

[19] Tao Y., *Global existence for a haptotaxis model of cancer invasion with tissue remodeling*. Nonlinear Analysis: Real World Applications **12** (2011), 418–435.

[20] Tao Y. and Wang M., *Global solution for a chemotactic-haptotactic model of cancer invasion*. Nonlinearity. **21** (2008), 2221–2238.

[21] Tao Y. and Wang M., *A combined chemotaxis-haptotaxis system: The role of logistic source*. SIAM J. Math. Anal. **41** (2009), 1533–1558.

[22] Tao Y. and Winkler M., *A chemotaxis-haptotaxis model: The roles of non-linear diffusion and logistic source*. SIAM J. Math. Anal. **43** (2011), 685–704.

[23] Tao Y. and Zhu G., *Global solution to a model of tumor invasion*. Appl. Math. Sci. **1** (2007), 2385–2398.

[24] Walker C. and Webb G. F., *Global existence of classical solutions for a haptotaxis model*. SIAM. J. Math. Anal. **38** (2007), 1694–1713.

[25] Winkler M., *Aggregation vs. global diffusive behavior in the higher-dimensional Keller-Segel model*. J. Diff. Eqns. **248** (2010), 2889–2905.

Akio Ito
11678-1 Node, Sōsashi, Chiba, 289-3181, Japan
E-mail: ito.akio.2015@gmail.com