GLOBAL EXISTENCE AND ASYMPTOTIC BEHAVIOUR OF SOLUTIONS FOR NONLINEAR EVOLUTION EQUATIONS RELATED TO A TUMOUR INVASION MODEL

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ABSTRACT. We study the global existence in time and asymptotic behaviour of solutions of nonlinear evolution equations with strong dissipation and proliferation terms arising in mathematical models of biology and medicine including tumour invasion models.

1. Introduction and notations. In this paper we study the following initial Neumann-boundary value problem of nonlinear evolution equations arising from chemotaxis type of models with logistic term:

\[
\begin{aligned}
\frac{d^2 u}{dt^2} &= D \Delta u_t + \nabla \cdot (\chi(u_t, e^{-u})e^{-u} \nabla u) + \mu (1 - u_t)u_t \quad \text{in } \Omega \times (0, T) \quad (1.1) \\
\frac{\partial u}{\partial \nu} &= 0 \quad \text{on } \partial \Omega \times (0, T) \quad (1.2) \\
\begin{cases}
    u(x, 0) = u_0(x), & u_t(x, 0) = u_1(x) \quad \text{in } \Omega
\end{cases} \quad (1.3)
\end{aligned}
\]

where the function \( \chi(\cdot, \cdot) \) will be specified later in the assumption (A), \( D, \mu \) are positive constants, \( \Omega \) is a bounded domain in \( \mathbb{R}^n \) with smooth boundary \( \partial \Omega \) and \( \nu \) is the outer unit normal vector on \( \partial \Omega \).

Our purpose is to establish the existence theorem of time global solutions to (N) and apply the result to a mathematical model from biology and medicine. The aim of this paper is in the same line as in [18]. Some of the results in this paper have been announced and some sketches or outlines of their proofs have been stated in [18]. In this paper, we improve and extend them, give the full proof, self-containedness and a broader class of applications than the one presented in [18]. The equation (1.1) is a generalisation of nonlinear evolution equations related to a tumour invasion model (CL) (see section 4) so that we study (N) in advance.

For our convenience we first consider a special case of (N) for \( \mu = 0 \), which is written as

\[
\begin{aligned}
\frac{d^2 u}{dt^2} &= D \Delta u_t + \nabla \cdot (\chi(u_t, e^{-u})e^{-u} \nabla u), \quad (1.4) \\
\frac{\partial u}{\partial \nu} &= 0, \\
\begin{cases}
    u(x, 0) = u_0(x), & u_t(x, 0) = u_1(x).
\end{cases}
\end{aligned}
\]

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We deal with $(N)'$ in section 2. Next, by developing the results for $(N)'$, we get the desired result for $(N)$ in the section 3. In the final section, applying the arguments in sections 2 and 3 we investigate the properties of the solution to a mathematical model arising from tumour invasion. On the other hand, initial–Dirichlet boundary value problems for this type and $3$ we investigate the properties of the solution to a mathematical model arising from biology and biomedicine (see [1], [2], [17]).

In order to discuss the existence of the solution and its asymptotic behaviour of $(N)'$ we seek the solution in the form of 

$$ u(x,t) = a + bt + v(x,t) $$

for positive parameters $a$ and $b$. Then $(N)'$ is rewritten as

$$ \begin{align*}
    \{ P[v] &= v_{tt} - D \Delta v_t - \nabla \cdot (\chi_{a,b}(v)e^{-a-bt-v\nabla v}) = 0, \\
    \frac{\partial v}{\partial \nu} &= 0, \\
    v(x,0) &= v_0(x), v_t(x,0) = v_1(x),
\end{align*} $$

(1.5)

where we denote $\chi(v_t+b, e^{-a-bt-r})$ by $\chi_{a,b}(v)$. Levine and Sleeman [14] obtained explicit solutions of the form: $u = \gamma t + (\gamma > 0)$ of a simplified equation of (1.5) for $n = 1$ (cf. [10], [16]). In this line, the papers [10]-[13] showed the existence of the solution in the same form as above of a special case of $(N)'$ for any spatial dimension, which arises from mathematical biology and biomedicine (see [1], [2], [17]).

Let us denote an upper semicircle $B_{r+} = B_r \cap (R \times R_+)$ where $B_r$ is a circle of radius $r$ at $0$ in $R^2$. We assume that for a constant $r > 0$ and $(s_1, s_2) \in B_{r+}$ there exists a positive constant $c_r$ such that for any integer $m \geq \lfloor n/2 \rfloor + 3$ it holds

$$ (A) : \chi(s_1 + b, s_2) \in C^m(R \times R_+), $$

$$ \chi(s_1 + b, s_2) \leq c_r (b + 1). $$

**Remark 1.** In the previous paper [9] additionally we need the assumption that $\chi(s_1 + b, s_2)$ is positive and the parameter $b$ should be taken sufficiently large to obtain the global existence theorem in time of $(N)'$. In this paper it is shown that without such additional conditions we can obtain the same results as in [9].

**Example.** The assumption $(A)$ covers the case where $\chi(\xi_1, \xi_2) = \xi_1^{p_1} \xi_2^{p_2}$, $p_1$ is an integer and $p_2$ is a positive constant.

Now let us introduce the function spaces $H^l(\Omega)$ and $W^l(\Omega)$. First, $H^l(\Omega)$ denotes the usual Sobolev space $W^{l,2}(\Omega)$ of order $l$ on $\Omega$. For functions $h(x,t)$ and $k(x,t)$ defined in $\Omega \times [0, \infty)$, putting

$$ (h, k)(t) = \int_{\Omega} h(x,t)k(x,t)dx, \quad \|h\|^2 = (h, h)(t), $$

then we define the norm of $H^l(\Omega)$ by

$$ \|h\|^2_l(t) = \sum_{|\beta| \leq l} ||\partial_x^\beta h(\cdot, t)||^2, $$

where $\partial_x = (\partial_{x_1}, \ldots, \partial_{x_n})$ and $\beta$ is a multi-index for $\beta = (\beta_1, \ldots, \beta_n)$. Especially in the case of $\Omega = R^n$ we denote the norm of $H^l(R^n)$ by $\|h\|_{l, R^n}(t)$.

The eigenvalues of $-\Delta$ with the homogeneous Neumann boundary conditions are denoted by $\{\lambda_i | i = 0, 1, 2, \cdots \}$, which are arranged as $0 = \lambda_0 < \lambda_1 \leq \cdots \rightarrow +\infty$ and $\varphi_i = \varphi_i(x)$ indicates the $L^2$ normalized eigenfunction corresponding to $\lambda_i$. Then we put for $h(x), k(x) \in H^l(\Omega)$, if $l = 2j$, for a non-negative integer $j$,

$$ (h, k)_l = (h, k) + (\Delta^j h, \Delta^j k), \quad \|h\|^2_l = (h, h)_l $$

and if $l = 2j + 1$

$$ (h, k)_l = (h, k) + (\nabla \cdot \Delta^j h, \nabla \cdot \Delta^j k), \quad \|h\|^2_l = (h, h)_l. $$
We set \( W^l(\Omega) \) as a closure of \( \{\varphi_1, \varphi_2, \cdots, \varphi_n, \cdots\} \) in the function space \( H^l(\Omega) \). Taking \( \lambda_1 > 0 \) into account, it is noticed that we have \( \int_{\Omega} h(x) dx = 0 \) for \( h(x) \in W^l(\Omega) \), which enables us to use Poincare’s inequality. We know the equivalence of norms \( | \cdot |_t, \| \cdot \|_t \), which will be used frequently.

2. The case \( \mu = 0 \). When we derive the energy estimates, we assume the regularity condition \( v \in \bigcap_{i=0}^{2} C^i([0, \infty); W^{m+1-i}(\Omega)) \) and \( v_t \in L^2([0, \infty); W^m(\Omega)) \) and the boundedness condition \( (v_t, e^{-t-v}) \in B_{r+} \) for \( l = a + bt \). We first prepare some results required to derive energy estimates of \( (R)^{\prime} \).

2.1. Preparation. The following Lemma 2.1 has been obtained in \([10]\).

**Lemma 2.1.** If \( u = u(x, t) \) satisfies the above regularity condition, then it holds that for \( m \geq M \geq \lfloor n/2 \rfloor + 1 \)
\[
\|u\|_M^2(t) \leq 4t\|u\|_{L^2([0, \infty); H^l(\Omega))}^2 + 2\|u\|_M^2(0)
\]
for any \( t \in [0, \infty) \).

By using Lemma 2.1 we obtain the following result (see \([10]\)).

**Lemma 2.2.** If \( u = u(x, t) \) satisfies the above regularity condition with \( m \geq M \geq \lfloor n/2 \rfloor + 1 \), then it holds that for positive constants \( C_1 \) and \( C_2 \)
\[ i) \|e^{-u}\|_M(t) \leq C_1 \exp(C_1 \sqrt{t}) \]
\[ ii) \text{for any constant } 0 < b' < b \]
\[ e^{-a-bt-u} < \|e^{-a-bt-u}\|_M(t) \leq C_2 e^{-b't} \]
where \( C_2 \to 0 \) as \( a \to \infty \).

We can also get the following result by integration by parts.

**Lemma 2.3.** Assume that \( u = u(x, t) \) satisfies the above regularity condition with \( m > M \geq \lfloor n/2 \rfloor + 1 \). For \( 0 < b' < b \) and \( i = 1, 2, \cdots, n \), it holds that
\[
\|e^{-b't}u, x, i, \|_M^2(t) + \int_{0}^{t} e^{-2b's} \|u, x, i, \|_M^2(s) ds \leq C \left( \int_{0}^{t} e^{-2b's} \|u, x, i, \|_M^2(s) ds + \|u, x, i, \|_M^2(0) \right).
\]

**Proof.** For any \( \varepsilon > 0 \), we have
\[
\|e^{-b't}u, x, i, \|^2(t) + 2b' \int_{0}^{t} e^{-2b's} \|u, x, i, \|^2(s) ds
\]
using integration by parts for the second term
\[
\leq C \left( \frac{1}{\varepsilon} \int_{0}^{t} e^{-2b's} \|u, x, i, \|^2(s) ds + \varepsilon \int_{0}^{t} e^{-2b's} \|u, x, i, \|^2(s) ds + \|u, x, i, \|^2(0) \right).
\]
Taking \( \varepsilon \) sufficiently small, finally we have the desired result. \( \square \)

Now let us state basic results required for the estimate of the nonlinear term. The following results have been obtained by Dionne \([5]\) for \( x \in R^n \). It will be shown that the corresponding results restricted the domain \( R^n \) to \( \Omega \) in \([5]\) hold. Denote
\[
\|f\|_\infty^{(l)}(t) = \max_{|\alpha| + |\omega| \leq l, x \in Y} |\partial_x^\alpha \partial_\xi^\omega f(x, t; \xi)|
\]
where \( f(x, t; \xi) \) is defined in \( \Omega \times [0, T] \times Y \) and \( Y \) is an open set in \( R^{n+2} \) and \( \partial_\xi = \left( \frac{\partial}{\partial \xi_1}, \cdots, \frac{\partial}{\partial \xi_{n+2}} \right) \) and \( \omega \) is a multi-index for \( \omega = (\omega_1, \cdots, \omega_{n+2}) \). We define \( W_\infty^{(l)}(\Omega \times [0, T]; Y) \) to consist of functions \( f(x, t; \xi) \) satisfying \( \|f\|_\infty^{(l)}(t) < +\infty \).
Lemma 2.4. For $u \in C([0, T]; H^l(\Omega))$, there exists a function $\tilde{u} \in C([0, T]; H^l(R^n))$ and a constant $C > 0$ such that $\tilde{u} = u$ in $\Omega \times [0, T)$ and the support of $\tilde{u}$ lies in an arbitrary bounded open set in $R^n$ whose interior contains $\bar{\Omega}$ and that it holds
\[
\|\tilde{u}\|_{l, R^n}(t) \leq C\|u\|_l(t).
\] (2.1)

Proof. Applying Proposition 3.4 and Theorem 3.13 in Mizohata [15] to $u$, we can extend $u$ to $\tilde{u} \in C(R^n \times [0, T))$ and (2.1) holds.

Proposition 1. Assuming that $|\alpha| \leq l, |\beta| \leq M, l \leq M, n/2 < l + M - |\alpha| - |\beta|$, for $q$ and $r \in C([0, T]; H^H(\Omega))$, there exists a constant $C > 0$ such that it holds that
\[
\|\partial^\alpha q \partial^\beta r\|_H(t) \leq C\|q\|_H(t)\|r\|_H(t),
\] (2.2)
\[
\|qr\|_H(t) \leq C\|q\|_H(t)\|r\|_H(t).
\] (2.3)

Proof. Applying Dionne [5, Theorem 6.3] we have
\[
\|\partial^\alpha q \partial^\beta r\|_H(t) \leq C\|\tilde{q}\|_{l, R^n}(t)\|\tilde{r}\|_{l, R^n}(t)
\]
and by using Lemma 2.4 we arrive at (2.2). In the same manner we have (2.3).

Denote $Du = (u_t, \nabla u)$ for simplicity. By applying Proposition 1 we obtain the following result in the same way as in [5].

Proposition 2. Assume that $q(x, t; \xi) \in W^{(M)}(\Omega \times [0, T); Y)$ and that $u \in C([0, T); H^l(\Omega))$ for $l \leq M$ and $n/2 < M - 1$ and $(u, Du) \in Y$ for $t \in [0, T)$. Then, there exists a constant $C > 0$ such that it holds
\[
\|q(x, t; u, Du)\|_H(t) \leq C\|q\|_{H'}(t) \times (1 + \|u\|_{M-1}(t) + \|u_t\|_{M}(t))^l.
\]

By using Propositions 1, 2 and Dionne [5; Theorem 6.4] we obtain the following result.

Proposition 3. Suppose that $V$ and $z \in C([0, T); H^{M+1}(\Omega))$ satisfying $(V, DV)_n$, $(V + \tau z, D(V + \tau z)) \in Y$ for $\tau \in [0, 1]$ and $t \in [0, T)$. For $l \leq M$ and $n/2 \leq M - 1$ it holds that for $q(x, t; \xi) \in W^{(M)}(\Omega \times [0, T); Y)$ and a constant $C > 0$
\[
\|\{q(x, t; V + z, D(V + z)) - q(x, t; V, DV)\}\|_{l-1} \leq C(\|z\|_M(t) + \|z_t\|_{M-1}(t)),
\]
where $C$ depends on $\|q\|_{H'}(t) \times (1 + (\|z\|_{M+1}(t) + \|V\|_{M+1}(t) + \|z_t\|_M(t) + \|V_t\|_M(t)))^{l-1}$

2.2. A priori estimates.

Lemma 2.5 (Basic estimate of $(R')$). We have a basic energy estimate of $(R')$ under the regularity and boundedness conditions on $v = v(x, t)$,
\[
\|v_t\|^2(t) + \int_0^t D\|\nabla v_s\|^2ds \leq CE_v[v](0),
\]
for sufficiently large $a$ where $E_v[v] = \|v_t\|^2 + e^{-2a}\|\nabla v\|^2$.

Proof. In order to obtain a basic estimate of $(R')$ we consider
\[
(P[v], v_t) = 2(\partial^2_t v - D\Delta v_t - \nabla \cdot (\chi_{a,b}(v)e^{-a-bt-v}\nabla v), v_t)
\]
by the integration by parts
\[
= \frac{\partial}{\partial t}\|v_t\|^2 + 2D\|\nabla v_t\|^2 + 2(\chi_{a,b}(v)e^{-a-bt-v}\nabla v, \nabla v_t) = 0.
\] (2.4)

Since we have for any $\varepsilon > 0$ by using Proposition 2 and Lemma 2.2,
\[
\int_0^t (\chi_{a,b}(v)e^{-a-bt-v}\nabla v, \nabla v_s)ds \leq C(\varepsilon^{-1}) \int_0^t (e^{-2a-2b\varepsilon}\nabla v, \nabla v)ds + \varepsilon \int_0^t \|\nabla v_s\|^2ds,
\]
by integrating the equality (2.4) over (0, t) and using the above estimate we get
\[ \|v_t\|^2(t) + \int_0^t 2D\|\nabla v_s\|^2(s) \, ds \leq C(E[v](0) + \varepsilon^{-1} \int_0^t (e^{-2(a+b)t}\nabla v, \nabla v) \, ds +\varepsilon \int_0^t \|\nabla v_s\|^2 \, ds). \] (2.5)

Since the last term of the right hand side of (2.5) is negligible for sufficiently small \( \varepsilon \), we have by using Lemma 2.3 for the second term of the right hand side of (2.5)
\[ \|v_t\|^2(t) + \int_0^t 2D\|\nabla v_s\|^2(s) \, ds \leq CE[v](0) + C\varepsilon^{-a} \int_0^t \|\nabla v_s\|^2 \, ds. \] (2.6)

Taking \( a \) sufficiently large the last term of (2.6) can be negligible. Hence we have a basic energy estimate of \((R)'\).

**Lemma 2.6** (Higher order estimates for \((R)'\)). Under the regularity and boundedness conditions on \( v = v(x,t) \) with \( m > M \geq \lceil n/2 \rceil + 1 \), we have the result of higher order energy estimate \((R)'\) for sufficiently large \( a\):
\[ \sum_{j=1}^{M+1} \{\|\nabla^{j-1} v_t\|^2(t) + \int_0^t D\|\nabla^j v_s\|^2(s) \, ds\} \leq CE_{a,M}[v](0), \] (2.7)

where we denote for any non-negative integer \( k \), \( E_{a,k}[v](t) = E_a[\nabla^k v] \).

**Proof.** Suppose that the estimate (2.7) holds for \( M = k - 1 \). Considering \( \nabla^k v \) instead of \( v \) in (2.4), in the same way as in Lemma 2.5 we can obtain (2.7) for \( M = k \). In order to show it, it is enough to prove that the following estimate holds for \( l = a + bt \) and a parameter \( \kappa > 0 \)
\[ (\nabla^k(\chi_{a,b} v) e^{-l-v} \nabla v) - \chi_{a,b} v e^{-l-v} \nabla^{k+1} v, \nabla^k v) \]
by using Proposition 2 and the above assumption
\[ \leq C(\kappa^{-1} \sum_{j=1}^k (e^{-a-bt} \nabla^j v, \nabla^j v) + \kappa|v|_2^2 + E_{a,k-1}[v](0)) \] (2.8)

where the first and second terms in (2.8) are negligible for sufficiently large \( a \) and small \( \kappa > 0 \) respectively. In fact, by using Lemma 2.3 and taking \( a \) sufficiently large, we see that the first term of (2.8) is negligible. Hence we obtain (2.7).

**Remark 2.** The estimate (2.7) implies that for any fixed \( r \) by taking \( E_{a,M}[v](0) \) sufficiently small we have \( (v_t, e^{-l-v}) \in B_{r+} \). As will be seen, considering an iteration scheme of the problem, (2.7) also guarantees global existence in time of the solution satisfying the condition \((A)\) and the regularity of the solution.

Now we state our result of \((N)'\).

**Theorem 2.7** (Existence and asymptotic behavior of the solution to \((N)'\)). Assume that \((A)\) holds and \((v_0(x), v_1(x)) \in W^{m+1}(\Omega) \times W^m(\Omega)\) for \( v_0(x) = u_0(x) - a \) and \( v_1(x) = u_1(x) - b \). For sufficiently large \( a \) and large enough \( r \), there exists a solution \( u(x,t) = a + bt + v(x,t) \in \bigcup_{i=0}^1 C^i([0,\infty); H^{m-i}(\Omega)) \) to \((N)'\) such that for \( \overline{u}_1 = |\Omega|^{-1} \int_\Omega u_1(x) \, dx \)
\[ \lim_{t \to \infty} ||u_t(x,t) - \overline{u}_1||_{m-1} = 0. \] (2.9)
Proof. The proof will be shown in the same manner as in [9]-[13]. We take an iteration scheme and derive the energy estimate of it.

\[
(R'_{i+1}) \left\{ \begin{array}{l}
P_i [v_{i+1}] = \partial_t^2 v_{i+1} - \partial_t \Delta v_{i+1} - \nabla \cdot (e^{-a-bt} \chi_{a,b}(v_i)e^{-v_i} \nabla v_{i+1}) = 0, \\
\frac{\partial}{\partial \nu} v_{i+1}(x,0) = h_0(x), \quad v_{i+1}(x,0) = h_1(x)
\end{array} \right.
\]

where \( v_i = \sum_{j=1}^{\infty} f_{ij}(t) \varphi_j(x), h_0(x) = \sum_{j=1}^{\infty} h_j \varphi_j(x), h_1(x) = \sum_{j=1}^{\infty} h_j \varphi_j(x) \). Taking account of Remark 2 the energy estimate, we find that (2.7) guarantees the estimate with a uniform upper bound of each problem \((R'_{i+1})\) for \( i = 1, 2, \cdots \).

We determine \( f_{ij}(t) \) by Galerkin method and by applying (2.7) to the following system of ordinary equations with initial data, for \( j = 1, 2, \cdots \) we obtain the global smooth solution in time.

\[
\left\{ \begin{array}{l}
(P_i [v_{i+1}], \varphi_j) = 0, \\
f_{i+1}(0) = h_{i+1}, \quad f_{i+1}(0) = h'_{i+1}
\end{array} \right.
\]

Also the energy estimate enables us to get the solution of \((R')\) by considering \( P_i [v_{i+1}] - P_{i-1}[v_i] \) and the standard argument of convergence for \( v_{i+1} - v_i \) we actually, we consider the following problem.

\[
(R'_{(i+1)-(i)}) \left\{ \begin{array}{l}
P_i [v_{i+1}] - P_{i-1}[v_i] = \partial_t^2 w_{i+1} - \partial_t \Delta w_{i+1} - \nabla \cdot (e^{-a-bt} \chi_{a,b}(v_i)e^{-v_i} \nabla w_i) \\
- \nabla \cdot (e^{-t} \chi_{a,b}(v_i)e^{-v_i} - \chi_{a,b}(v_i) e^{-v_i}) \nabla v_i = 0,
\end{array} \right.
\]

\[ w_{i+1}(0, x) = w_{i+1}(0, x) = 0. \]

In order to obtain the estimate of \((R'_{(i+1)-(i)})\) we only deal with the last term of \( P_i - P_{i-1} \) as follows: for \( \theta > 0 \) and \( m \geq M \geq [n/2] + 2 \)

\[ 2 \int_0^t \nabla \cdot \nabla^{M-1} (e^{-a-bt} \chi_{i_{\infty}} e^{-v_i} - e^{-v_i} \chi_{i_{\infty}} e^{-v_i}) \nabla v_i, \nabla^{M-1} w_{i_{\infty}} d s \]

by using Proposition 3

\[ \leq \frac{C_a}{\theta} \left( \int_0^t e^{-2bs} \sum_{j=0}^{1} \| \partial_j^2 w_{i_{\infty}} \|_{M-1}^2 d s + \theta \int_0^t \| \nabla w_{i_{\infty}} \|_{M-1}^2 d s \right). \quad (2.10) \]

Then by the same method as derived the energy estimate of \((R')\), we have for sufficiently large \( a \) by taking account of (2.10) and Lemma 2.3

\[ \| w_{it} \|_{M-1}^2 (t) + D \int_0^t \| \nabla w_{i_{\infty}} \|_{M-1}^2 d s \leq C_a \| w_{i-1t} \|_{M-1}^2, \quad (2.11) \]

where \( C_a \) depends on \( \sup \| \partial_t v_i \|_{M}^2, \sup \| \partial_t v_{i-1} \|_{M}^2 \) and \( e^{-a}, C_a \to 0 \) as \( a \to \infty \). Here we took \( \theta \) sufficiently small to neglect the last term of (2.10). Hence taking \( a \) sufficiently large we see \( C_a < 1 \). By the standard argument we see that the solutions \( \{ v_i \} \) converges strongly such that for \( m \geq [n/2] + 3 \)

\[ \lim_{i \to \infty} v_i = v \quad \text{in} \quad \bigcap_{i=0}^{1} C^i ([0, \infty); H^{m-i}(\Omega)). \quad (2.12) \]

The proof of (2.9) is shown in the same way as in Theorem 2 of [10].

Remark 3. We can apply Theorem 2.7 to mathematical models of tumour angiogenesis by Anderson and Chaplain [1], [2] and Othmer-Stevens model [17], which is a continuum model of the theory of reinforced random walks by Davis [4] (see [9]-[13]).
3. **The case** $\mu \neq 0$. In this section we consider the case of $\mu \neq 0$ in (1.1) developing the way used in the previous section. Put $u(x,t) = a + t + v(x,t)$, then (N) is rewritten as

\[
\begin{aligned}
Q[v] &= v_{tt} - D\Delta v_t - \nabla \cdot \left( \chi(1 + v_t, e^{-a-t-v}) e^{-a-t-v} \nabla v \right) - \mu v_t (-1 - v_t) = 0, \\
\frac{\partial}{\partial \nu} v|_{\partial \Omega} &= 0, \\
v(x,0) &= v_0(x), \quad v_t(x,0) = v_1(x).
\end{aligned}
\]  

(3.1)

In order to derive the estimate of (R), in the same way as used in section 2, it is enough to deal with the inner product from the proliferation term

\[
2\mu(v_t(v_t + 1), v_t)
\]

supposed that $|v_t| \ll 1$,

\[
\geq 2\mu((- \sup_t |v_t| + 1)v_t, v_t) \geq C\|v_t\|^2.
\]

Therefore we have for sufficiently large $a$

\[
\|v_t\|^2 + \int_0^t \|v_{s}\|^2 ds + \int_0^t \|v_{s}\|^2 ds \leq CE_a[v](0).
\]

(3.4)

For the smooth solution of our problem $v(x,t)$ satisfying $|v_t| \ll 1$ and regularity and boundedness conditions we have in the same way as derived (2.7) for $m > M \geq \lfloor n/2 \rfloor + 3$ and sufficiently large $a$

\[
\|v_t\|^2_M + \int_0^t \|v_{s}\|^2_M ds \leq CE_{a,M}[v](0).
\]

(3.5)

**Lemma 3.1.** Under the same conditions as in Lemma 2.6 for $v = v(x,t)$ and $|v_t| \ll 1$, for sufficiently large $a$ we have the energy estimate (3.5) of (R).

**Remark 4.** When we take $E_{a,m}[v](0)$ sufficiently small, e.g., $a$ is large enough and $\|v_t\|_m(0)$ is small enough, the assumption $|v_t| \ll 1$ in the proof is verified by (3.5).

**Theorem 3.2.** Assume that (A) holds and $(v_0(x), v_1(x)) \in W^{m+1}(\Omega) \times W^m(\Omega)$ for $v_0(x) = u_0(x) - a, v_1(x) = u_1(x) - 1$. For sufficiently large $a$ and small $r$, there is a solution $u(x,t) = a + t + v(x,t) \in \bigcap_{t=0}^1 C^r([0,\infty); H^{m-i}(\Omega))$ to (N) such that

\[
\lim_{t \to \infty} \|u_t(x,t) - 1\|_{m-1} = 0.
\]

**Proof.** We consider the following iteration scheme of (R)

\[
\begin{aligned}
(Q_{i}[v_{i+1}]) &= P_i[v_{i+1}] - \mu v_{i+1,t}(-1 - v_{i,t}) = 0, \\
\frac{\partial}{\partial \nu} v_{i+1}|_{\partial \Omega} &= 0, \\
v_{i+1}(x,0) &= h_0(x), \quad v_{i+1,t}(x,0) = h_1(x).
\end{aligned}
\]

(R)_{i+1}

The time global smooth solution of (R)_{(i+1)} is obtained successively in the same way as in the proof of Theorem 2.7. Since it is enough to derive the estimate of (R)_{(i+1)-(i)} for

\[
Q_i[v_{i+1}] - Q_i[v_i] = P_i[v_{i+1}] - P_i[v_i] + \mu (v_{i+1,t}(1 + v_{i,t}) - v_{i,t}(1 + v_{i-1,t})),
\]

we only deal with the inner product from the proliferation term

\[
-(v_{i+1,t}(1 + v_{it}) - v_{it}(1 + v_{i-1,t}), w_{it}) = -(1 + v_{it})w_{it} + v_{it}w_{it-1,t}, w_{it}
\]

dominated by

\[
\leq -(1 - \sup_t |v_{it}|)\|w_{it}\|^2 + C(\|w_{i-1,t}\|^2 + \|w_{it}\|^2)
\]

(3.6)
where \( C \) depends on \( \|v_{it}\|_M \). Since we may assume that \( \|v_{it}\|_M \) is small enough for \( M \geq n/2 + 2 \), neglecting the last term of the right hand side of the above inequality, we have finally

\[
\|w_{it}\|_{M-1}^2 + \int_0^t \|\nabla w_{is}\|_{M-1}^2 ds + \int_0^t \|w_{is}\|_{M-1}^2 ds \leq C \|v_{i-1t}\|_{M-1}^2,
\]

where \( C \) depends on \( \sup_t \|v_{it}\|_M^2 \), \( \sup_t \|v_{i-1t}\|_M^2 \) and \( e^{-\alpha} \). Taking \( a \) sufficiently large and initial data sufficiently small we obtain the desired result. \( \square \)

**Remark 5.** In [10]-[13] our solution is in the form of \( u(x,t) = bt + v(x,t) \) for sufficiently large \( b > 0 \), but in [9] we can get the solution in more general form \( u(x,t) = a + bt + v(x,t) \) for sufficiently large \( a, b > 0 \). Since in section 2 we obtain the existence theorem for sufficiently large \( a \) and any \( b > 0 \), it enables us to deal with (1.1) for \( \mu \neq 0 \) in the section 3.

4. **Application to a tumour invasion model.** The following is a mathematical model of tumour invasion by the Chaplain-Lolas [3].

\[
(CL) \begin{cases}
\frac{\partial n}{\partial t} = d_n \Delta n - \gamma \nabla \cdot (n \nabla f) + \mu_1 n (1 - n - f) & \text{in } \Omega \times (0, \infty) \\
\frac{\partial f}{\partial t} = -\eta m f + \mu_2 f (1 - n - f) & \text{in } \Omega \times (0, \infty) \\
\frac{\partial m}{\partial t} = d_m \nabla^2 m + \alpha n - \beta m \\
\frac{\partial v}{\partial \nu} = \frac{\partial f}{\partial \nu} = \frac{\partial m}{\partial \nu} = 0 & \text{on } \partial \Omega \times (0, \infty) \\
n(x,0) = n_0(x) > 0, f(x,0) = f_0(x) > 0, m(x,0) = m_0(x) > 0 
\end{cases}
\]

where \( n := n(x,t) \) is the density of tumour cells, \( m := m(x,t) \) is the degradation enzymes concentration and \( f := f(x,t) \) is the extra cellular matrix density and \( d_n, \gamma, \mu_1, \eta, \mu_2, d_m, \alpha \) and \( \beta \) are positive constants. It follows from (4.2) that

\[
\frac{\partial}{\partial t} (\log f) = -\eta m + \mu_2 (1 - n - f).
\]

Integrating the both sides of (4.4) over \( (0, t) \) we have

\[
f(x,t) = f_0(x) \cdot e^{-\eta \int_0^t m ds + \mu_2 \int_0^t (1 - n - f) ds}.
\]

Since our aim is to seek solutions \( \{n, f, m\} \) of \( (CL) \), we may substitute \( \int_0^t m ds \) and \( \int_0^t m ds \) by \( a_n + t + u \) and \( a_m + b_m + v \) respectively for new unknown functions \( u, v \) and the parameters \( a_n, a_m, b_m > 0 \). Setting \( a_m \eta + a_n \mu_2 = a \) and \( b_m \eta = b \) it is reduced to

\[
f(x,t) = f_0(x) \cdot e^{a - bt -\eta v - \mu_2 (u + f)}
\]

where \( \tilde{f} = f_0 + f ds \). Then substituting \( f(x,t) \) by the right hand side of (4.5), (4.1) and (4.3) are reduced to the following two equations respectively

\[
\frac{\partial^2}{\partial t^2} u = d_n \Delta u_t - \gamma \nabla \cdot ((1 + u_t) \nabla (f_0(x) \cdot e^{a - bt -\eta v - \mu_2 (u + f)})) \\
+ \mu_1 (u_t + 1) - u_t - f_0(x) \cdot e^{a - bt -\eta v - \mu_2 (u + f)}
\]

(4.6)

\[
\frac{\partial^2}{\partial t^2} v = d_m \Delta v_t + \alpha u_t - \beta v_t + \alpha - \beta \beta.
\]

(4.7)

They are essentially regarded as the same type of equation as (1.1). Here the initial data are written as \( u_t(0) = n_0 - 1, v_t(0) = m_0 - b_m \). Setting \( \Theta = a + bt + \eta v + \mu_2 (u + f) \), (4.6) is rewritten as

\[
u_{tt} = d_n \Delta u_t + \gamma \nabla \cdot \{(f_0(x) \nabla \Theta - \nabla f_0(x))(1 + u_t) e^{-\Theta}) - \mu_1 (1 + u_t)(u_t + f_0(x)) e^{-\Theta})
\]

\[\]

\[\]

\[\]
Lemma 4.1. Assume that $u, v$ and $\tilde{f}$ satisfy the regularity condition stated in section 2.

i) Suppose $|f| \ll b$, then there exist a positive constant $b' < b$ such that we have

$$e^{-a - bt - ny - \mu_2 u - \mu_2 \tilde{f}} \leq Ce^{-a - b't}.$$ 

ii) The following estimate for $f$ is obtained for $m > M \geq [n/2] + 1$,

$$\|\nabla f(x, t)\|_M^2 + \int_0^t \|\nabla f(x, s)\|_M^2 \, ds \leq C_a(1 + \|\nabla v_i\|_M^2 + \|\nabla u_i\|_M^2 + \|f\|_M^2) + Ce^{-2a(\|\nabla u_i\|_M^2(0) + \|v\|^2_M(0))}$$

where $C_a \to 0$ as $a \to 0$.

Proof. i) By Lemmas 2.1 and 2.2 we have for a positive constant $\tilde{b} < b$

$$e^{-a - bt - ny - \mu_2 u - \mu_2 \tilde{f}} \leq Ce^{-a - b't}.$$ 

Assuming $|f| \leq \frac{\tilde{b}}{2}b$ and putting $b' = \frac{\tilde{b}}{2}$, we get our desired inequality.

ii) Since it holds that

$$\nabla f(x, t) = (\nabla f_0(x) - \eta f_0(x)\nabla v - \mu_2 f_0(x)\nabla u - \mu_2 f_0(x)\nabla \tilde{f})e^{-a - bt - ny - \mu_2 u - \mu_2 \tilde{f}}$$

by Proposition 2 and the above result we have for a positive constant $b' < b$

$$\int_0^t \|\nabla f(x, s)\|_M^2 \, ds \leq \int_0^t C(1 + \|\nabla v\|_M^2 + \|\nabla u\|_M^2 + \|\nabla \tilde{f}\|_M^2)e^{-2a - 2b's} \, ds$$

by using Lemma 2.3

$$\leq \int_0^t C(1 + \|\nabla v_i\|_M^2 + \|\nabla u_i\|_M^2 + \|\nabla \tilde{f}\|_M^2)e^{-2a - 2b's} \, ds + Ce^{-2a(\|\nabla u_i\|_M^2(0) + \|v\|^2_M(0))}.$$ 

Notice that for sufficiently large $a$ the assumption: $|f| \ll b$ is recursively satisfied due to (4.5) and Lemma 4.1 ii). In the same manner as derived (2.7) and (3.5) the estimates of (4.6) and (4.7) are obtained as follows respectively.

Lemma 4.2. Assume that $u, v$ and $\tilde{f}$ satisfy the regularity condition stated in section 2.

For $m > M \geq [n/2] + 1$ we have the following estimates.

i) The energy estimate of (4.6) holds as follows for $\|u_i\| \ll 1$ and sufficiently large $a$

$$\|u_i\|_M^2 + d_n \int_0^t \|u_s\|_{M+1}^2 \, ds + \mu_1 \int_0^t \|u_s\|_M^2 \, ds \leq CE_{a,M}[u](0) + C_a$$

(4.8)

where $C_a \to 0$ as $a \to 0$.

ii) When $b = \frac{\alpha}{\beta}$, the energy estimate of (4.7) is obtained

$$\|u_i\|_M^2 + d_m \int_0^t \|u_s\|_{M+1}^2 \, ds \leq CE_{a,M}[v](0) + \int_0^t \|u_s\|_M^2 \, ds.$$ 

(4.9)

Proof. Since (4.6) and (4.7) are essentially regarded as the same type of equation as (1.1), we apply the estimate obtained in section 2 and use the argument of section 3.

i) We consider the inner product from the proliferation term

$$-\mu_1((u_t + 1)(u_t + f_0(x)e^{-\Theta}), u_t) = -\mu_1((u_t + 1 + f_0(x)e^{-\Theta})u_t, u_t) - \mu_1(f_0(x)e^{-\Theta}, u_t)$$

dominated by

$$\leq -\mu_1((u_t + (1 - \varepsilon) + f_0(x)e^{-\Theta})u_t, u_t) + (\mu_1/\varepsilon)\|f_0(x)e^{-\Theta}\|^2$$

where $\varepsilon > 0$ is a sufficiently small constant. As $a \to \infty$, considering Lemma 4.1 i), it is seen that

$$\|f_0(x)e^{-\Theta}\|^2 \to 0.$$ 

If $\|u_t\| \ll 1$ holds, in the same way as derived Lemma 3.1 we have the desired estimate.
ii) When \( b = \frac{\alpha}{3} \), it seems to be easy to derive the estimate of (4.7) by the usual way deriving the energy estimate.

Combining these estimates we obtain the desired estimate of \( u, v \) and \( f \).

**Lemma 4.3** (Energy estimate of (4.5)-(4.7)). Assume that \( u, v \) and \( \tilde{f} \) satisfy the assumptions assumed in Lemmas 4.1 and 4.2. We obtain the energy inequality of the reduced problem (4.5)-(4.7) for \( m > M \geq [n/2] + 1 \) and sufficiently large \( a \)

\[
\|u_i\|_M^2 + d_n \int_0^t \|u_s\|_{M+1}^2 ds + \|v_i\|_M^2 + d_m \int_0^t \|v_s\|_{M+1}^2 ds \\
+ \|f\|_M^2 + \int_0^t \|f\|_{M+1}^2 ds \leq C(E_{a,M}[u](0) + E_{a,M}[v](0) + E_{a,M}[f](0)) + C_a
\]

(4.10) where \( C_a \to 0 \) as \( a \to \infty \).

**Proof.** Multiplying the both sides of (4.8) by an appropriately large positive constant and combining it with (4.9) we have

\[
\|u_i\|_M^2 + d_n \int_0^t \|u_s\|_{M+1}^2 ds + \|v_i\|_M^2 + d_m \int_0^t \|v_s\|_{M+1}^2 ds \leq C(E_{a,M}[u](0) + E_{a,M}[v](0)) + C_a
\]

where the last term of the right hand side of (4.9) is negligible. Taking account of Lemma 4.1 ii) we arrive at (4.10).

**Remark 6.** (4.10) implies that \( H^M(\Omega), L^2((0,T); H^M(\Omega)) \)-norms of \( u, v \) and \( f \) are small enough respectively, if the energies of initial data of \( u_t, v_t, f \) are sufficiently small and \( a \) is sufficiently large. In this case (4.10) verifies \( |u_t| \ll 1 \) and assures the existence theorem of (4.5)-(4.7),

Applying the same argument as used for Theorem 3.2 to \( CL \), we have existence and asymptotic behaviour of the solutions to \( CL \).

**Theorem 4.4.** For smooth initial data \( \{n_0(x), f_0(x), m_0(x)\} \) assume that \( H^m(\Omega) \)-norms of \( u_t(x,0) = n_0(x) - 1, v_t(x,0) = m_0(x) - b_m \) and \( f_0(x) \), are sufficiently small. For sufficiently large \( a \) there exist classical solutions of \( CL \): \( \{n(x,t), f(x,t), m(x,t)\} \) such that they belong to \( C([0,\infty); H^{m-1}(\Omega)) \) and satisfy the following asymptotic behaviour

\[
\lim_{t \to \infty} n(x,t) = 1, \quad \lim_{t \to \infty} m(x,t) = \overline{m_0}, \quad \lim_{t \to \infty} f(x,t) = 0.
\]

**Proof.** Let us consider the iteration scheme of (4.5)-(4.7) for \( i = 0, 1, 2, \cdots \)

\[
(CL)_{(i)} \begin{cases}
\partial^2_t u_{i+1} = d_n \Delta u_{i+1} - \gamma \nabla \cdot u_{i+1} \nabla (f_0(x)e^{-\Theta_i}) + \mu_1(u_t + 1)(-u_{i+1}f_0(x)e^{-\Theta_i}) + \mu_2(u_t + 1)(-u_{i+1}f_0(x)e^{-\Theta_i}) \\
\partial^2_t v_{i+1} = d_n \Delta v_{i+1} + \alpha u_{i+1} - \beta v_{i+1}, \quad f_{i+1} = e^{-\Theta_i},
\end{cases}
\]

where \( \Theta_i = a + bt + \eta v_i + \mu_2 u_i + \mu_2 f_i \) and \( \tilde{f}_i = \int_0^t f ds \). The time global solutions of \( CL_{(i)} \) exist by the same way as in the proof of Theorem 2.7. In order to obtain the estimate for \( (CL)_{(i)} \) for \( U_i = u_{i+1} - u_i \) we rewrite the proliferation term by

\[
-\mu_1(u_t + 1)(f_{i+1} - f_0(x)e^{-\Theta_i}) + \mu_1(u_t + 1)(f_{i+1} - f_0(x)e^{-\Theta_i}) - \mu_1(u_t + 1)(f_{i+1} - f_0(x)e^{-\Theta_i})U_{i-1} := \zeta_{(i)}.
\]

Then the estimate of the proliferation term is derived in the same way as derived (3.6) and by Proposition 3

\[
\langle \zeta_{(i)}, U_{i+1} \rangle \leq -\mu_1 \sup_t |u_{i+1}| + 1 \|U_{i+1}\|^2 + C(\|U_{i-1}\|^2 + \|U_{i+1}\|^2).
\]
In section 3 for a more general form of the solution of the first term of \((C^L)_{i-1}\) we obtain the estimate of sufficiently large \(a\)
\[
\|U_{it}\|_{m-1} + \int_0^t \|U_{is}\|_{m}^2 ds \leq C_{a,u,v,f}\|U_{i-1t}\|_{m-1}^2
\]
and further considering Lemmas 4.1-4.3
\[
\|U_{it}\|_{m-1} + \|V_{it}\|_{m-1} + \|F_i\|_{m-1} \leq C_{a,u,v,f}\|U_{i-1t}\|_{m-1}^2 + \|V_{i-1t}\|_{m-1}^2 + \|F_{i-1}\|_{m-1}^2
\]
where \(U_i = u_{i+1} - u_i, F_i = f_{i+1} - f_i\). We can take \(C_{a,u,v,f} < 1\) due to Remark 6, so each sequence of \(\{U_i\}, \{V_i\}\) and \(\{F_i\}\) converges strongly such that
\[
\lim_{i \to \infty} u_i = u, \lim_{i \to \infty} v_i = v, \lim_{i \to \infty} f_i = f
\]
in \(C([0, \infty); H^{m-1}(\Omega))\). Considering into \(\lim_{t \to \infty} u_t(x, t) = 0, \lim_{t \to \infty} v_t(x, t) = 0, \lim_{t \to \infty} f(x, t) = 0\), we obtain the desired asymptotic behaviour of \(\{u(x, t), m(x, t), f(x, t)\}\).

Concluding remark. In section 3 for a more general form of the solution \(u(x, t) = L_a(t) + v(x, t)\) instead of \(u(x, t) = a + t + v(x, t)\) we can deal with \((N)\) for \(\mu \neq 0\) where \(L_a(t) = \int_0^t l(\tau) d\tau + a\) and \(l(t)\) satisfies the logistic equation. In the same way we can discuss the mathematical model in section 4. This result will be published somewhere soon.

REFERENCES

[1] A. R. A. Anderson and M. A. J. Chaplain, A mathematical model for capillary network formation in the absence of endothelial cell proliferation, Appl. Math. Lett., 11 (1998), 109-114.
[2] A. R. A. Anderson and M. A. J. Chaplain, Continuous and discrete mathematical models of tumour-induced angiogenesis, Bull. Math. Biol., 60 (1998), 857-899.
[3] M. A. J. Chaplain and G. Lolas, Mathematical modeling of cancer invasion of tissue: Dynamic heterogeneity, Networks and Heterogeneous Media, 1 (2006), 399-439.
[4] B. Davis, Reinforced random walks, Probability Theory and Related Fields, 84 (1990), 203-229.
[5] P. Dionne, Sur les problemes de Cauchy hyperboliques bien poses, J. Anal. Math., 10 (1962), 1-90.
[6] Y. Ebihara, On some nonlinear evolution equations with the strong dissipation, J. Differential Equations, 30 (1978), 149-164.
[7] Y. Ebihara, On some nonlinear evolution equations with the strong dissipation, II, J. Differential Equations, 34 (1979), 339-352.
[8] Y. Ebihara, On some nonlinear evolution equations with strong dissipation, III, J. Differential Equations, 45 (1982), 332-355.
[9] A. Kubo, Nonlinear evolution equations associated with mathematical models, Discrete and Continuous Dynamical Systems supplement 2011, (2011), 881-890.
[10] A. Kubo and T. Suzuki, Asymptotic behavior of the solution to a parabolic ODE system modeling tumour growth, Differential and Integral Equations, 17 (2004), 721-736.
[11] A. Kubo, T. Suzuki and H. Hoshino, Asymptotic behavior of the solution to a parabolic ODE system, Mathematical Sciences and Applications, 22 (2005), 121-135.
[12] A. Kubo and T. Suzuki, Mathematical models of tumour angiogenesis, Journal of Computational and Applied Mathematics, 204 (2007), 48-55.
[13] A. Kubo, N. Saito, T. Suzuki and H. Hoshino, Mathematical models of tumour angiogenesis and simulations, Theory of Bio-Mathematics and Its Applications, in RIMS Kokyuroku, 1499 (2006), 135-146.
[14] H. A. Levine and B. D. Sleeman, A system of reaction and diffusion equations arising in the theory of reinforced random walks, SIAM J. Appl. Math., 57 (1997), 683-730.
[15] S. Mizohata, The Theory of Partial Differential Equations, Cambridge Univ. Press. London, (1973).
[16] B. D. Sleeman and H. A. Levine, Partial differential equations of chemotaxis and angiogenesis, Math. Mech. Appl. Sci., 24 (2001), 405-426.
[17] H. G. Othmer and A. Stevens, Aggregation, blowup, and collapse: The ABCs of taxis in reinforced random walks, SIAM J. Appl. Math., 57 (1997), 1044-1081.
[18] A. Kubo and H. Hoshino, Nonlinear evolution equations with strong dissipation and proliferation, Current Trends in Analysis and Applications, 233-241, Birkhauser, Springer, 2015.
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