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Global Existence And Uniqueness Of A Parabolic Haptotaxis Model*

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Abstract

We study parabolic ODE systems modeling tumour invasion proposed by Anderson and Chaplain [3]. According to Yagi's arguments [12], we reduce them to corresponding evolution equations and show the existence of time global solutions.

1 Introduction

In this paper, we shall deal with the following parabolic system modeling haptotaxis

$$\begin{cases} \partial_t u = D\triangle u - \rho\nabla.(u\nabla w), & \\ \partial_t v = \delta\triangle v - \mu v + \alpha u, & t > 0,\ x \in \Omega, \\ \partial_t w = -\gamma w v, & \\ \begin{cases} \partial_n u = 0, \quad \partial_n v = 0, \quad \partial_n w_0 = 0 & \text{in } \partial\Omega, \\ u(0,.) = u_0,\ v(0,.) = v_0,\ w(0,.) = w_0 & \text{on } \Omega. \end{cases} \end{cases} \tag{1}$$

Here $\Omega \subset \mathbb{R}^d$ $(d = 2, 3)$ is a bounded domain with C^3 boundary $\partial\Omega$ and the initial data u_0, v_0, w_0 are assumed to be nonnegative and ∂_n denotes the derivative with respect to the outer normal of $\partial\Omega$. This system is a mathematical model describing the motion of some species due to haptotaxis, the function $u(t, x)$ corresponds to the cell density of the species at place $x \in \Omega$ and time $t \in [0, +\infty[$, and $v(t, x)$ to the concentration of the chemical substance that is produced by the individuals while $w = w(t, x)$ is the concentration of the extracellular matrix (ECM). The coefficients $D, \rho, \gamma, \delta, \alpha, \mu$ are given positive constants.

We first devote ourselves to the Cauchy problem for a semilinear evolution equation of the form (4) in a Banach space X. We present existence and uniqueness results in a way so that [12, Theorem 4.1] may be applied. Next, we use [12, Corollary 4.1] to show that the a priori estimate for local solutions of (4) with respect to the $A^{\frac{\beta}{2}}U(t)$

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norm ensures extension of local solutions without limit in order to construct the global solutions.

2 Local Existence of a Solution

Let Ω be a bounded domain in $\mathbb{R}^d$. For $1 \leq p \leq \infty$, $L^p(\Omega)$ is the usual Lebesgue space endowed with the norm $\|.\|_{L^p(\Omega)}$. Next for $s > 0$, $H^s(\Omega)$ is the usual fractional Sobolev space. We assume Ω has a C^3 class boundary $\partial\Omega$, and for $\frac{3}{2} < s \leq 3$

$$H_N^s(\Omega) = \{u \in H^s(\Omega) : \ \partial_n u = 0 \text{ on } \partial\Omega \},$$

and for $s < \frac{3}{2}$, we set $H_N^s(\Omega) = H^s(\Omega)$, with the norm $\|.\|_{H^s(\Omega)}$. We denote for $\frac{d}{2} < \beta < 2$ $(d = 2, 3)$,

$$\mathcal{K} = \left\{U_0 = (u_0, v_0, w_0)^t : \ 0 \leq u_0 \in H_N^\beta(\Omega), \ 0 \leq v_0 \in H_N^{1+\beta}(\Omega), \ 0 \leq w_0 \in H_N^2(\Omega)\right\}.$$

The aim of this section is to prove the following Theorem:

THEOREM 2.1. Let β be a fixed exponent satisfying $d/2 < \beta < 2$ $(d = 2, 3)$. For any $U_0 = (u_0, v_0, w_0) \in \mathcal{K}$, (1) possesses a unique local solution in the function space

$$\begin{aligned} u &\in C(]0, T_{U_0}]; H_N^2(\Omega)) \cap C([0, T_{U_0}]; H_N^\beta(\Omega)) \cap C^1(]0, T_{U_0}]; L^2(\Omega)), \\ v &\in C(]0, T_{U_0}]; H_N^3(\Omega)) \cap C([0, T_{U_0}]; H_N^{1+\beta}(\Omega)) \cap C^1(]0, T_{U_0}]; H^1(\Omega)), \\ w &\in C([0, T_{U_0}]; H_N^2(\Omega)) \cap C^1(]0, T_{U_0}]; H_N^2(\Omega)), \end{aligned} \tag{2}$$

where $T_{U_0} > 0$ depends only on the norm $\|u_0\|_{H^\beta(\Omega)} + \|v_0\|_{H^{\beta+1}(\Omega)} + \|w_0\|_{H^2(\Omega)}$. In addition, for all $t \in [0, T_{U_0}]$, the solution satisfies the estimates

$$\|u(t)\|_{H^\beta(\Omega)} + \|v(t)\|_{H^{\beta+1}(\Omega)} + \|w(t)\|_{H^2(\Omega)} \leq C_{U_0}, \tag{3}$$

with some constant $C_{U_0} > 0$ depending on the norm $\|u_0\|_{H^\beta(\Omega)} + \|v_0\|_{H^{\beta+1}(\Omega)} + \|w_0\|_{H^2(\Omega)}$.

2.1 Proof of THEOREM 2.1

We formulate problem (1) as the Cauchy problem for an abstract semilinear equation

$$\begin{cases} \frac{dU}{dt} + AU = F(U), \\ U(0) = U_0, \end{cases} \tag{4}$$

in the Banach space

$$X = \left\{U = (u, v, w)^t : \ u \in L^2(\Omega), \ v \in H^1(\Omega), \ w \in H_N^2(\Omega)\right\},$$

endowed with the norm $\|(u, v, w)^t\| = \|u\|_{L^2(\Omega)} + \|v\|_{H^1(\Omega)} + \|w\|_{H^2(\Omega)}$ and A is a linear operator acting in X given by

$$A = diag\{A_1, A_2, A_3\} = diag\{-D\triangle + 1, -\delta\triangle + \mu, \gamma\}.$$

A is a sectorial linear operator of X, the spectrum of which is contained in a sectorial domain $\sigma(A) \subset \sum_{\omega} = \{\lambda \in \mathbb{C}, |\arg \lambda| < \omega_A\}$ with some angle $0 < \omega_A < \frac{\pi}{2}$. We refer to [12, Theorem 2.4] which ensures that the resolvent satisfies for $\lambda \notin \sigma(A)$ the estimate

$$\left\|(\lambda - A)^{-1}\right\| \leq \left\|(\lambda - A_1)^{-1}\right\|_{\mathcal{L}(L^2(\Omega))} + \left\|(\lambda - A_2)^{-1}\right\|_{\mathcal{L}(H^1(\Omega))} + \frac{1}{|\lambda - \gamma|}$$
$$\leq \frac{1 + \max\left\{D, \frac{1}{D}, \frac{\delta}{\mu}, \frac{\mu}{\delta}\right\}}{|\lambda|}.$$

In $L_2(\Omega)$, under the Neumann boundary conditions on $\partial\Omega$, we have $\mathcal{D}(A_1) = H_N^2(\Omega)$ and according to [12, Theorem 16.7], we further have

$$\mathcal{D}(A_1^{\theta}) = \begin{cases} H^{2\theta}(\Omega), & 0 \leq \theta < \frac{3}{4}, \\ H_N^{2\theta}(\Omega), & \frac{3}{4} < \theta \leq 1, \end{cases} \tag{5}$$

with norm equivalence

$$c_\Omega^{-1} \|u\|_{H^{2\theta}(\Omega)} \leq \left\|A_1^{\theta} u\right\|_{L^2(\Omega)} \leq c_\Omega \|u\|_{H^{2\theta}(\Omega)}, \quad u \in \mathcal{D}(A_1^{\theta}). \tag{6}$$

In $H^1(\Omega)$, under the Neumann boundary conditions on $\partial\Omega$, it is known [12, Theorem 2.9] that $\mathcal{D}(A_2) = \left\{v \in H_N^2(\Omega) : \ \triangle v \in H^1(\Omega)\right\}$. Note that the fact that Ω has a C^3 class boundary $\partial\Omega$ ensures the shift property $\triangle v \in H^1(\Omega)$ with $\frac{\partial v}{\partial n} = 0$, implies that $\mathcal{D}(A_2) = H_N^3(\Omega)$; and according to [12, Theorem 16.1], we have $\mathcal{D}(A_2^{\theta}) = \left[H^1(\Omega), H_N^3(\Omega)\right]_{\theta}$, $0 \leq \theta \leq 1$. According to [12, Theorem 1.35],

$$\mathcal{D}(A_2^{\theta}) = \begin{cases} H^{2\theta+1}(\Omega), & 0 \leq \theta < \frac{1}{4}, \\ H_N^{2\theta+1}(\Omega), & \frac{1}{4} < \theta \leq 1, \end{cases} \tag{7}$$

with norm equivalence

$$c_\Omega^{-1} \|u\|_{H^{2\theta+1}(\Omega)} \leq \left\|A_2^{\theta} u\right\|_{H^1(\Omega)} \leq c_\Omega \|u\|_{H^{2\theta+1}(\Omega)}, \quad u \in \mathcal{D}(A_2^{\theta}), \tag{8}$$

where $c_\Omega > 0$ is determined by Ω. In $H_N^2(\Omega)$, the operator $A_3 = \gamma$ is a positive definite self-adjoint operator. By [12, Theorem 16.1] and [12, Theorem135], we have $\left[H_N^2(\Omega), H_N^2(\Omega)\right]_{\theta} = H_N^2(\Omega)$, therefore

$$\mathcal{D}(A_3^{\theta}) = H_N^2(\Omega) \ \ 0 \leq \theta \leq 1. \tag{9}$$

Consequently

$$\mathcal{D}(A) = \left\{(u, v; w)^t : u \in H_N^2(\Omega), v \in H_N^3(\Omega), w \in H_N^2(\Omega)\right\}. \tag{10}$$

Moreover it is clear that $A^{\theta} = diag\left\{A_1^{\theta}, A_2^{\theta}, A_3^{\theta}\right\}$. According to [12, Theorem 16.1], we have $\mathcal{D}(A^{\theta}) = [X, \mathcal{D}(A)]_{\theta}$. Then

$$\begin{aligned} \mathcal{D}(A^{\theta}) &= \left\{U = (u, v, w)^t \ ; \ u \in H^{2\theta}(\Omega), \ v \in H^{2\theta+1}(\Omega), \ w \in H_N^2(\Omega)\right\}, \ 0 < \theta < \frac{1}{4}, \\ \mathcal{D}(A^{\theta}) &= \left\{U = (u, v, w)^t \ ; \ u \in H^{2\theta}(\Omega), \ v \in H_N^{2\theta+1}(\Omega), \ w \in H_N^2(\Omega)\right\}, \ \frac{1}{4} < \theta < \frac{3}{4}, \\ \mathcal{D}(A^{\theta}) &= \left\{U = (u, v, w)^t \ ; \ u \in H_N^{2\theta}(\Omega), \ v \in H_N^{2\theta+1}(\Omega), \ w \in H_N^2(\Omega)\right\}, \ \frac{3}{4} < \theta \leq 1. \end{aligned} \tag{11}$$

The nonlinear operator F from $D(A^{\eta})$ $(\beta \leq \eta < 2)$ into X is defined by

$$F(U) = \left(-\rho\nabla.\left(u\nabla w\right) + u,\ \alpha u,\ -\gamma(v-1)w\right)^{t}.$$

Let $U, V \in D(A^{\eta})$ $(\beta \leq \eta < 2)$. Since $U = (u_1, v_1, w_1)^t$, $V = (u_2, v_2, w_2)^t$, we have

$$\begin{aligned} \|F(U) - F(V)\| \leq\ & \rho\left\|\nabla.\left(u_1\nabla w_1 - u_2\nabla w_2\right)\right\|_{L^2(\Omega)} + \alpha\left\|u_1 - u_2\right\|_{H^1(\Omega)} \\ & +\gamma\left\|(v_1-1)w_1 - (v_2-1)w_2\right\|_{H^2(\Omega)} + \left\|u_1 - u_2\right\|_{L^2(\Omega)}. \end{aligned} \tag{12}$$

Since

$$\left\|\nabla.\left[u\nabla w\right]\right\|_{L^2(\Omega)} \leq \left\|\nabla u\right\|_{L^4(\Omega)}\left\|\nabla w\right\|_{L^4(\Omega)} + \left\|u\right\|_{L^{\infty}(\Omega)}\left\|\triangle w\right\|_{L^2(\Omega)},$$

in the sequel, we need the following embeddings $H_N^{\beta}(\Omega) \rightarrow L^{\infty}(\Omega)$ and $H^1(\Omega) \rightarrow L^4(\Omega)$, $\frac{d}{2} < \beta < 2$ $(d = 2, 3)$, to see that

$$\left\|\nabla.\left[u\nabla w\right]\right\|_{L^2(\Omega)} \leq c_{\Omega}\left\|u\right\|_{H^{\beta}(\Omega)}\left\|w\right\|_{H^2(\Omega)},\ u \in H^{\beta}(\Omega), w \in H_N^2(\Omega). \tag{13}$$

Moreover

$$\begin{aligned} & \left\|\nabla.\left(u_1\nabla w_1 - u_2\nabla w_2\right)\right\|_{L^2(\Omega)} \\ \leq\ & c_{\Omega}\left\|w_1\right\|_{H^2(\Omega)}\left\|u_1 - u_2\right\|_{H^{\beta}(\Omega)} + c_{\Omega}\left\|w_1 - w_2\right\|_{H^2(\Omega)}\left\|u_2\right\|_{H^{\beta}(\Omega)}. \end{aligned} \tag{14}$$

$H^2(\Omega)$ is a Banach algebra, therefore

$$\begin{aligned} & \left\|(v_1-1)w_1 - (v_2-1)w_2\right\|_{H^2(\Omega)} \\ \leq\ & c_{\Omega}\left\|w_1 - w_2\right\|_{H^2(\Omega)}\left(\left\|v_1\right\|_{H^2(\Omega)} + 1\right) + c_{\Omega}\left\|v_1 - v_2\right\|_{H^2(\Omega)}\left\|w_2\right\|_{H^2(\Omega)}. \end{aligned} \tag{15}$$

Let η be such that $\beta < \eta \leq 2$. Since $H_N^{\eta}(\Omega) \hookrightarrow H^1(\Omega) \hookrightarrow L^2(\Omega)$, we have

$$\left\|u_1 - u_2\right\|_{L^2(\Omega)} + \alpha\left\|u_1 - u_2\right\|_{H^1(\Omega)} \leq c_{\Omega}(\alpha + 1)\left\|u_1 - u_2\right\|_{H^{\eta}(\Omega)}. \tag{16}$$

We substitute (14), (15), (16) in (12) for $\beta \leq \eta < 2$. Then

$$\begin{aligned} & \|F(U) - F(V)\| \\ \leq\ & c_{\Omega}\left(\left\|u_2\right\|_{H^{\beta}(\Omega)} + \left\|v_1\right\|_{H^{\beta+1}(\Omega)} + 1\right) \times \Big[\left\|u_1 - u_2\right\|_{H^{\eta}(\Omega)} + \left\|w_1 - w_2\right\|_{H^2(\Omega)} \\ & + \left(\left\|w_1\right\|_{H^2(\Omega)} + \left\|w_2\right\|_{H^2(\Omega)}\right)\left(\left\|u_1 - u_2\right\|_{H^{\beta}(\Omega)} + \left\|v_1 - v_2\right\|_{H^{\beta+1}(\Omega)}\right)\Big]. \end{aligned}$$

Therefore, in view of (11), (6), (8) and (9), we deduce that

$$\begin{aligned} \|F(U) - F(V)\| \leq\ & c_{\Omega}\left(\left\|A^{\frac{\beta}{2}}U\right\| + \left\|A^{\frac{\beta}{2}}V\right\| + 1\right)\Big[\left\|A^{\frac{\eta}{2}}(U - V)\right\| \\ & + \left(\left\|A^{\frac{\eta}{2}}U\right\| + \left\|A^{\frac{\eta}{2}}V\right\|\right)\left\|A^{\frac{\beta}{2}}(U - V)\right\|\Big],\ U, V \in D(A^{\eta}). \end{aligned}$$

Theorem 4.1 in [12] then provides the existence of local solutions. Indeed, for any $U_0 \in \mathcal{K}$, (4) possesses a unique local solution U in the function space:

$$U \in C((0, T_{U_0}]; \mathcal{D}(A)) \cap C([0, T_{U_0}]; \mathcal{D}(A^{\frac{\beta}{2}})) \cap C^1((0, T_{U_0}]; X).$$

Furthermore, the solution satisfies the estimates $\|A^{\frac{\beta}{2}}U\| \leq C_{U_0}$. Here, $C_{U_0}, T_{U_0} > 0$ are determined by the norm $\left\|U_0\right\|_{\mathcal{D}(A^{\frac{\beta}{2}})}$ only. The proof of Theorem 2.1 is completed.

3 Nonnegativity of Local Solutions

We shall show that the local solution constructed above is nonnegative for $U_0 \in \mathcal{K}$. In the following we assume that $\Omega \subset \mathbb{R}^d (d = 2, 3)$ is a bounded domain with C^3 boundary. We denote by G the C^1 function defined by

$$G(s) = \begin{cases} \frac{1}{2}s^2, & s < 0, \\ 0, & s \geq 0. \end{cases}$$

PROPOSITION 3.1. Under the assumptions of THEOREM 2.1, we have

$$u(t, x) \geq 0, \ x \in \Omega, \ t \geq 0. \tag{17}$$

PROOF. We set $\psi(t) = \int_\Omega G(u(t, x))dx$. We have $\psi'(t) = \int\limits_\Omega G'(u)u_t dx$. Then

$$\psi'(t) = D \int\limits_\Omega G'(u) \triangle u dx - \rho \int\limits_\Omega G'(u) \nabla. (u \nabla w)\, dx.$$

Observing that $G'(u) = u$ if $u < 0$ and $G'(u) = 0$ if $u \geq 0$ and $G'(u) \in H^1(\Omega)$ for $u \in H^1(\Omega)$. Assuming $\frac{\partial w_0}{\partial n} = 0$ on $\partial\Omega$, we obtain $\frac{\partial w}{\partial n} = 0$ on $\partial\Omega$ and hence by Hölder's inequality, we have

$$\psi'(t) \leq -D \|\nabla(G'(u))\|^2_{L^2(\Omega)} + \frac{\rho}{2} \|G'(u)\|^2_{L^4(\Omega)} \|\triangle w\|_{L^2(\Omega)}. \tag{18}$$

We use the interpolation inequality for $d = 2, 3$ to obtain

$$\|G'(u)\|^2_{L^4(\Omega)} \leq c_\Omega \|G'(u)\|^{\frac{d}{2}}_{H^1(\Omega)} \|G'(u)\|^{\frac{4-d}{2}}_{L^2(\Omega)}.$$

Then (3) shows that $\|\triangle w\|_{L^2(\Omega)} \leq C_{U_0}$, for $0 \leq t \leq T_{U_0}$. Therefore,

$$\rho \|\triangle w\|_{L^2(\Omega)} \|G'(u)\|^2_{L^4(\Omega)} \leq \frac{D}{2} \|\nabla(G'(u))\|^2_{L^2(\Omega)} + C_{U_0} \|G'(u)\|^2_{L^2(\Omega)}. \tag{19}$$

Thus, in view of (19) and (18), $\psi'(t) \leq c_{T,U_0} \psi(t)$. By Gronwall's inequality $\psi(t) \leq \psi(0) \exp(t c_{T,U_0})$. Thus $\psi(0) = \int_\Omega G(u_0(t, x))dx = 0$ so that $\psi(t) = 0$. Hence $u \geq 0$.

PROPOSITION 3.2. Under the assumptions of Theorem 2.1, we have

$$v(t, x) \geq 0, \ x \in \Omega, \ t \geq 0. \tag{20}$$

PROOF. We set $\psi(t) = \int\limits_\Omega G(v)dx$. Using the third equation of system (1), we have

$$\psi'(t) = -\delta \int\limits_\Omega |\nabla G'(v)|^2 \, dx + \alpha \int\limits_\Omega u G'(v) - \mu \int\limits_\Omega v G'(v) dx,$$

since $vG'(v) \geq 0$, $G'(v) \leq 0$, and $u \geq 0$ we have $\psi'(t) \leq 0$, then $\psi(t) \leq \psi(0)$. Since $\psi(0) = \int_\Omega G(v_0(t, x))dx = 0$, we have $\psi(t) = 0$. Consequently $v \geq 0$.

4 Global Solutions

In the following we assume that $\Omega \subset \mathbb{R}^d (d = 2, 3)$ is a bounded domain with C^3 boundary. As [12, Corollary 4.1] shows, the a priori estimates for local solutions of (4) with respect to the $A^{\frac{\beta}{2}}U(t)$ norm ensure extension of local solutions without limit. We may thus construct the global solutions.

For later use we state the following auxiliary results:

LEMMA 4.1. Under the assumptions of Theorem 2.1, for $0 \le t \le T_U$,

$$\|u(t)\|_{L^1(\Omega)} = \|u_0\|_{L^1(\Omega)}. \tag{21}$$

PROOF. Thanks to the homogeneous boundary conditions $\triangledown u.\vec{n} = 0$ and $\triangledown w_0.\vec{n} = 0$ on $\partial\Omega$, we may directly integrate (1) over Ω; consequently $\int_\Omega \partial_t u dx = 0$, as $u \ge 0$, from (17) we have $\frac{d}{dt}\|u\|_{L^1(\Omega)} = 0$, and mass conservation (21) is satisfied.

Next, we may easily prove the following lemma.

LEMMA 4.2. Suppose that $(u_0, v_0, w_0) \in \mathcal{K}$. Then for $0 \le t \le T_U$,

$$w(t, x) = w_0(x)e^{-\int_0^t \gamma v(\tau,x)d\tau}. \tag{22}$$

Moreover, we have

$$\|w(t)\|_{L^\infty(\Omega)} \le \|w_0\|_{L^\infty(\Omega)}. \tag{23}$$

PROPOSITION 4.3. Let Ω be a bounded smooth open domain of $\mathbb{R}^d$ $(d = 2, 3)$. Let $u \in H^1(\Omega)$. Then there exists a constant $c_{\Omega,\epsilon} > 0$ (depending on Ω, ϵ) such that

$$\|u\|^2_{L^4(\Omega)} \le \epsilon \|\triangledown u\|^2_{L^2(\Omega)} + c_{\Omega,\epsilon} \|u\|^2_{L^1(\Omega)}. \tag{24}$$

PROOF. With the help of the Cauchy inequality for the Gagliardo-Nirenberg inequality $\|u\|^2_{L^2(\Omega)} \le c_\Omega \|u\|^{\frac{3d}{2+d}}_{H^1(\Omega)} \|u\|^{\frac{4-d}{2+d}}_{L^1(\Omega)}$, $(d = 2, 3)$, we get that

$$\|u\|^2_{L^2(\Omega)} \le \frac{\epsilon}{4}\|\triangledown u\|^2_{L^2(\Omega)} + \frac{1}{2}\|u\|^2_{L^2(\Omega)} + (\tfrac{c_\Omega^2}{2} + \tfrac{c_\Omega^2}{\epsilon})\|u\|^2_{L^1(\Omega)}. \tag{25}$$

We simplify (25) so as to find

$$\|u\|^2_{L^2(\Omega)} \le \frac{\epsilon}{2}\|\triangledown u\|^2_{L^2(\Omega)} + (\frac{2c_\Omega^2}{\epsilon} + \frac{c_\Omega^2}{2})\|u\|^2_{L^1(\Omega)}. \tag{26}$$

We take again the Gagliardo-Nirenberg's inequality $\|u\|^2_{L^4(\Omega)} \le c_\Omega \|u\|^{\frac{d}{2}}_{H^1(\Omega)}.\|u\|^{\frac{4-d}{2}}_{L^2(\Omega)}$, with the Cauchy's inequality, then $\|u\|^2_{L^4(\Omega)} \le \frac{\epsilon}{2}\|\triangledown u\|_{L^2(\Omega)} + (1 + \frac{c_\Omega^2}{2\varepsilon})\|u\|^2_{L^2(\Omega)}$. By combining with (26), (24) is proved.

LEMMA 4.4. Suppose that $U_0 = (u_0, v_0, w_0) \in \mathcal{K}$. Then there exists a constant $c_\Omega > 0$ (depending on Ω) so that for $0 \le t \le T_U$,

$$\|v\|_{L^2(\Omega)} \le c_\Omega(\|v_0\|_{L^2(\Omega)} + \|u_0\|_{L^1(\Omega)}). \tag{27}$$

PROOF. The second equation of (1) is written as the abstract equation

$$v\,(t) = e^{-tA_2}v_0 + \alpha\int_0^t e^{-(t-s)A_2}u\;ds,\;\; 0 \le t \le T_U, \tag{28}$$

in $L^2(\Omega)$. Therefore,

$$\begin{aligned}\|v\|_{L^2(\Omega)} &\le \left\|e^{-tA_2}\right\|_{\mathcal{L}(L^2(\Omega))}\|v_0\|_{L^2(\Omega)}\\ &+ \alpha\int_0^t \left\|e^{-\frac{(t-s)}{2}A_2}\right\|_{\mathcal{L}(L^2(\Omega),L^1(\Omega))}\left\|e^{-\frac{(t-s)}{2}A_2}\right\|_{\mathcal{L}(L^1(\Omega))}\|u\|_{L^1(\Omega)}\,ds.\end{aligned}$$

From the estimate in [12, Eq. (2.128)] and [12, Theorem 2.28], and the formula $\mu^{-z}\Gamma\,(z) = \int\limits_0^{+\infty} s^{z-1}e^{-\mu s}ds\;\left(Re(z) \in \mathbb{R}_+^*\right)$, we have, for $0 \le t \le T_U$,

$$\|v\|_{L^2(\Omega)} \le c_\Omega\,\|v_0\|_{L^2(\Omega)} + \alpha c_\Omega \mu^{-\frac{4-d}{4}}\Gamma\left(\tfrac{4-d}{4}\right)\|u_0\|_{L^1(\Omega)}.$$

The proof is completed.

We shall prove the following result.

PROPOSITION 4.5. Suppose that $U_0 = (u_0, v_0, w_0) \in \mathcal{K}$. Then

$$\left\|A^{\frac{\beta}{2}}U\right\| \le p(t + \|A^{\frac{\beta}{2}}U_0\|),\; 0 \le t \le T_U, \tag{29}$$

with some continuous increasing function $p\,(.)$.

PROOF. We first derive the desired X bound. We employ a change of variable of the form $u \to \frac{u}{\varphi}$ where $\varphi\,(w) = e^{\frac{\rho}{D}w}$. This leads to the equation (1) in the form

$$\varphi(\frac{u}{\varphi})_t = D\nabla.\left(\varphi\nabla(\frac{u}{\varphi})\right) - u(\frac{\varphi_t}{\varphi}). \tag{30}$$

Moreover, φ satisfies $\varphi_t = \varphi'(w)w_t = -\frac{\gamma\rho}{D}\varphi wv$. By multiplying the equation (30) by $\frac{2u}{\varphi}$ and integrating over Ω, we obtain

$$\frac{d}{dt}\int_\Omega \varphi(\frac{u}{\varphi})^2dx + D\int_\Omega \varphi\left|\nabla(\frac{u}{\varphi})\right|^2dx = \tfrac{\gamma\rho}{D}\int_\Omega(\frac{u}{\varphi})^2\varphi wv dx. \tag{31}$$

Applying Hölder's inequality to (31),

$$\frac{d}{dt}\int\limits_{\Omega}\varphi(\frac{u}{\varphi})^2dx+D\int\limits_{\Omega}\varphi\left|\nabla(\frac{u}{\varphi})\right|^2dx\leq\tfrac{\gamma\rho}{D}\|\varphi w\|_{L^\infty(\Omega)}\|\frac{u}{\varphi}\|^2_{L^4(\Omega)}\|v\|_{L^2(\Omega)},$$

in view of (23), we may then conclude that $\|\varphi w\|_{L^\infty(\Omega)}\leq\|w_0\|_{L^\infty(\Omega)}e^{\frac{\rho}{D}\|w_0\|_{L^\infty(\Omega)}}$. Hence, this, together with (27) and (24), yield that

$$\begin{aligned}&\frac{d}{dt}\int\limits_{\Omega}\varphi(\frac{u}{\varphi})^2dx+D\int\limits_{\Omega}\varphi\left|\nabla(\frac{u}{\varphi})\right|^2dx\\ \leq\ &(\|v_0\|_{L^2(\Omega)}+\|u_0\|_{L^2(\Omega)})\|w_0\|_{L^\infty(\Omega)}e^{\frac{\rho}{D}\|w_0\|_{L^\infty(\Omega)}}\|\frac{u}{\varphi}\|^2_{L^4(\Omega)}\\ \leq\ &\tfrac{D}{2}\|\nabla(\frac{u}{\varphi})\|^2_{L^2(\Omega)}+\|\frac{u}{\varphi}\|^2_{L^1(\Omega)}c_{\|w_0\|_{H^2(\Omega)},\|u_0\|_{L^1(\Omega)},\|v_0\|_{L^2(\Omega)}}.\end{aligned}\tag{32}$$

Since $(\frac{u}{\varphi})^2\varphi=u^2e^{-\frac{\rho}{D}w}\geq u^2e^{-\frac{\rho}{D}\|w_0\|_{L^\infty(\Omega)}}$, by solving the differential inequality (32), we obtain

$$\sup_{0\leq t\leq T_U}\|u\|_{L^2(\Omega)}(t)\leq tc(\|w_0\|_{L^\infty(\Omega)},\|u_0\|_{L^2(\Omega)},\|v_0\|_{L^2(\Omega)}).\tag{33}$$

It remains to prove the estimate in the space X for the two solution components v,w of (1). Multiplying the third equation of (1) by A_2v and integrating over Ω, and taking into account (8), we see that

$$\begin{aligned}\int_0^t\|v\|^2_{H^2(\Omega)}&\leq c_\Omega\|v_0\|^2_{H^1(\Omega)}+c_\Omega\int_0^t\|u\|^2_{L^2(\Omega)}ds\\&\leq c_\Omega\|v_0\|^2_{H^1(\Omega)}+c_\Omega t\sup_{t\geq0}\|u\|^2_{L^2(\Omega)}.\end{aligned}\tag{34}$$

Next, we know that for $\Omega\subset\mathbb{R}^d$ $(d=2,3)$, so

$$\|w_0e^{-\int_0^t\gamma v}\|^2_{H^2(\Omega)}\leq c_\Omega\|w_0\|^2_{H^2(\Omega)}\|e^{-\int_0^t\gamma v}\|^2_{H^2(\Omega)}.$$

Using the same arguments as in [12, inequality (13.34)], we see that

$$\|w\|^2_{H^2(\Omega)}\leq c_\Omega\|w_0\|^2_{H^2(\Omega)}\left(1+\int_0^t\|v\|_{H^2(\Omega)}\right)^2\|e^{-\int_0^t\gamma v}\|^2_{L^\infty(\Omega)}.$$

Recalling (23), (34) and (33), we see that

$$\|w\|_{H^2(\Omega)}\leq\left(1+t^2\right)c(\|v_0\|_{H^1(\Omega)},\|w_0\|_{H^2(\Omega)},\|u_0\|_{L^1(\Omega)},\Omega).\tag{35}$$

The next step is devoted to showing the estimate in the space $\mathcal{D}(A^{\frac{\beta}{2}})$. Using (13), [12, Eq. (2.128)] and [12, Theorem 2.28] with some exponent $\frac{d}{2}<\beta'<\beta$ and a constant

$c_\Omega > 0$,

$$\begin{aligned}\left\|A_1^{\frac{\beta}{2}}u\right\|_{L^2(\Omega)} &\leq \left\|e^{-tA_1}\right\|_{\mathcal{L}(L^2(\Omega))}\left\|A_1^{\frac{\beta}{2}}u_0\right\|_{L^2(\Omega)} \\ &\quad+\int\limits_0^t \left\|A_1^{\frac{\beta}{2}}e^{-\frac{1}{2}(t-s)A_1}\right\|_{\mathcal{L}(L^2(\Omega))}\left\|e^{-\frac{1}{2}(t-s)A_1}\right\|_{\mathcal{L}(L^2(\Omega))}\left\|\nabla.\left(u\nabla w\right)\right\|_{L^2(\Omega)}ds \\ &\leq c_\Omega\left\|u_0\right\|_{H^\beta(\Omega)}+\int\limits_0^t c_\Omega\left(t-s\right)^{-\frac{\beta}{2}}e^{-\frac{1}{2}(t-s)}\left\|u\right\|_{H^{\beta'}(\Omega)}\left\|w\right\|_{H^2(\Omega)}ds. \qquad (36)\end{aligned}$$

By the same arguments as in [12, inequality (2.119)], (6), (33) and (35), we see that, for all $\varepsilon > 0$,

$$\begin{aligned}\left\|w\right\|_{H^2(\Omega)}\left\|u\right\|_{H^{\beta'}(\Omega)} &\leq c_\Omega\left(1+t^2\right)\left\|A_1^{\frac{\beta'}{2}}u\right\|_{L^2(\Omega)} \\ &\leq c_\Omega\left(1+t^2\right)\left\|u\right\|_{L^2(\Omega)}^{1-\frac{\beta'}{\beta}}.\left\|A_1^{\frac{\beta}{2}}u\right\|_{L^2(\Omega)}^{\frac{\beta'}{\beta}} \\ &\leq c_{\Omega,\varepsilon}\left(1+t\right)^{\frac{3\beta}{\beta-\beta'}}+\varepsilon\left\|A_1^{\frac{\beta}{2}}u\right\|_{L^2(\Omega)}. \qquad (37)\end{aligned}$$

Therefore, summing up (28), (37) and (36), we have for $0 \leq t \leq T_U$,

$$\begin{aligned}\sup_{0\leq t'\leq t}\left\|A_1^{\frac{\beta}{2}}u\right\|_{L^2(\Omega)} &\leq c_\Omega\left\|u_0\right\|_{H^\beta(\Omega)}+c_{\Omega,\varepsilon}\left(1+t\right)^{\frac{3\beta}{\beta-\beta'}}\int\limits_0^{+\infty}\left(t-s\right)^{-\frac{\beta}{2}}e^{-\frac{1}{2}(t-s)}ds \\ &\quad+\frac{\varepsilon c_\Omega\int\limits_0^{+\infty}(t-s)^{-\frac{\beta}{2}}e^{-\frac{1}{2}(t-s)}ds}{2}\sup_{0\leq t'\leq t}\left\|A_1^{\frac{\beta}{2}}u\right\|_{L^2(\Omega)}.\end{aligned}$$

Let $(\frac{\beta}{2})^{1-\frac{\beta}{2}}\Gamma\left(1-\frac{\beta}{2}\right) = \int\limits_0^{+\infty} s^{-\frac{\beta}{2}}e^{-\frac{\beta s}{2}}ds$ and $\varepsilon^{-1} = c_\Omega(\frac{\beta}{2})^{1-\frac{\beta}{2}}\Gamma\left(1-\frac{\beta}{2}\right)$. From (6) and (35), it follows that

$$\sup_{0\leq t\leq T_U}\left\|u\right\|_{H^\beta(\Omega)} \leq \left(1+t\right)^{\frac{3\beta}{\beta-\beta'}}c(\left\|v_0\right\|_{H^{1+\beta}(\Omega)},\left\|w_0\right\|_{H^2(\Omega)},\left\|u_0\right\|_{H^\beta(\Omega)},\Omega). \qquad (38)$$

In a similar manner, thanks to (28) and (38), we have for all $0 \le t \le T$,

$$
\begin{aligned}
\|v\|_{H^{1+\beta}(\Omega)} &\le \|v_0\|_{H^{1+\beta}(\Omega)} \\
&\quad + \alpha c_{\Omega,\omega} \int_0^t \left\| A_2^{\frac{1}{2}} e^{-\frac{\varrho}{2}(t-s)A_2} \right\|_{\mathcal{L}(L^2(\Omega))} \left\| e^{-\frac{\varrho}{2}(t-s)A_1} \right\|_{\mathcal{L}(L^2(\Omega))} \|u\|_{H^\beta(\Omega)} \, ds \\
&\le \|v_0\|_{H^{1+\beta}(\Omega)} + \sup_{t\ge 0} \|u\|_{H^\beta(\Omega)} \, \alpha c_{\Omega,\omega} \int_0^t (t-s)^{-\frac{1}{2}} e^{-\frac{\varrho}{2}(t-s)} ds \\
&\le (1+t)^{\frac{3\beta}{\beta-\beta'}} c(\|v_0\|_{H^{1+\beta}(\Omega)}, \|v_0\|_{H^2(\Omega)}, \|u_0\|_{L^1(\Omega)}, \Omega). \qquad (39)
\end{aligned}
$$

Finally we use (35), (38) and (39), for $0 \le t \le T_U$, there exists a continuous increasing function $p(\cdot)$ such that

$$
\|u\|_{H^\beta(\Omega)} + \|v\|_{H^{1+\beta}(\Omega)} + \|w\|_{H^2(\Omega)} \le p(t + \|u_0\|_{H^\beta(\Omega)} + \|v_0\|_{H^{1+\beta}(\Omega)} + \|w_0\|_{H^2(\Omega)}).
$$

We will take the same steps and expressions of the proof of global existence in [12] to prove the following result.

THEOREM 4.6. For any $U_0 = (u_0, v_0, w_0) \in \mathcal{K}$, there exists a unique global solution of (1) in the function space:

$$
\begin{aligned}
u &\in C(]0,+\infty[\,; H_N^2(\Omega)) \cap C([0,+\infty[\,; H_N^\beta(\Omega)) \cap C^1\,]0,+\infty[\,; L^2(\Omega)), \\
v &\in C(]0,+\infty[\,; H_N^3(\Omega)) \cap C([0,+\infty[\,; H_N^{1+\beta}(\Omega)) \cap C^1(]0,+\infty[\,; H^1(\Omega)), \\
w &\in C([0,+\infty[\,; H_N^2(\Omega)) \cap C^1(]0,+\infty[\,; H_N^2(\Omega)).
\end{aligned}
$$

PROOF**.** Utilizing the a priori estimate (29), we shall construct a global solution to (1). For $U_0 \in \mathcal{K}$, we know that there exists a local solution at least on an interval $[0, T_{U_0}]$. Let $0 < t_1 < T_{U_0}$. Then, $U_1 = U(t_1) \in \mathcal{K}$. We next consider problem (1) with the initial value U_1 on an interval $[t_1, T]$, where the end time $T > 0$ is any finite time. The estimate (29) ensures for any local solution V, $\left\| A^{\frac{\beta}{2}} V(t) \right\| \le p(\|A^{\frac{\beta}{2}} U_1\| + T)$, $t_1 \le t \le T_V$. Then, the local solution V can always be extended over an interval $[t_1, T_V + \tau]$ as local solution, $\tau > 0$ being dependent only on $p(\|A^{\frac{\beta}{2}} U_1\|_X + T)$ and hence being independent of the extreme time T_V (cf. [12. Corollary 4.1]). This means that our Cauchy problem possesses a global solution on the interval $[t_1, T]$.

This argument is meaningful for any finite time $T > 0$. So, we conclude the global existence of solution. For any initial value $U_0 \in \mathcal{K}$, there exists a unique global solution to (1) with $U(t) \in \mathcal{K}, 0 \le t < \infty$, in the function space

$$
U \in C(]0,+\infty[; \mathcal{D}(A)) \cap C([0,+\infty[; \mathcal{D}(A^{\frac{\beta}{2}})) \cap C^1((]0,+\infty[; X).
$$

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