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Unique Solutions in a Chemotaxis-Convection Model with Sensitivity Functions for Tumor Angiogenesis

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Abstract

In this paper, we study a compressible chemotaxis-convection model with sensitivity functions for tumor angiogenesis system, arising as a simplified model for the initial phase of tumor-related angiogenesis. As essential characteristics, this system is the existence of a sequential coupling between two chemical attraction processes, that involve the production of a signal, as in classical Keller-Segel systems, and are linked to another repulsive mutual diffusion mechanism, driven by the frictional force. The existence and uniqueness of solution for this system is established by the classical energy method.

Keywords: chemotaxis; attraction-repulsion; tumor angiogenesis.

حلول وحيدة في نموذج الانجذاب الكيميائي والحمل الحراري مع دوال حساسية لتكوين الأوعية الدموية في الأورام

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الملخص

في هذه الورقة، ندرس نموذجًا انضغاطيًا للانجذاب الكيميائي والحمل الحراري مع دوال حساسية لنظام تكوين الأوعية الدموية الورمية، والذي يُعد نموذجًا مبسطًا للمرحلة الأولى من تكوين الأوعية الدموية المرتبط بالورم. ومن الخصائص الأساسية لهذا النظام وجود اقتران متسلسل بين عمليتي تجاذب كيميائي، تتضمنان إنتاج إشارة، كما هو الحال في أنظمة كيلر-سيجل الكلاسيكية، وترتبطان بآلية انتشار متبادل تنافري أخرى، مدفوعة بقوة الاحتكاك. وقد تم إثبات وجود حل وحيد لهذا النظام باستخدام طريقة الطاقة الكلاسيكية. **الكلمات المفتاحية:** الانجذاب الكيميائي؛ التجاذب والتنافر؛ تكوين الأوعية الدموية في الورم.

1.Introduction

The modeling and analysis of the Keller-Segel systems are extended to variations which describe not only biological phenomena [1-2] but also medical phenomena (e.g., Alzheimer's disease [3], the tumor invasion [4-5], the tumor angiogenesis [6-7]). Recently, as to the tuberculosis granuloma formation, Feng [8] developed mathematical models of the evolution of granuloma by the Keller-Segel system. In recent years, properties of cancer have been analyzed mathematically using partial differential equations. These equations have been studied extensively, and the role of targeted cell diffusion processes has been experimentally investigated in vitro [9]. Many researchers are involved in the analysis and in vivo for human health. The cancer is one of the most important areas of study in these themes. The growth of a solid tumor is dependent on an adequate supply of nutrients. A tumor can establish a blood supply

by inducing neighboring blood vessels to sprout and grow towards it, a process known as angiogenesis. The tumor cells may secrete a number of diffusible chemicals which stimulate endothelial cells to migrate, to rearrange themselves into capillary tubes or sprouts, and to proliferate. In the early stage of angiogenesis wherein the endothelial cells group together in the parent vessel to form the initial capillary-sprout buds. Orme and Chaplain [10] described the branching of capillary sprout during tumor angiogenesis according to chemotaxis.

In this paper, we study tumor angiogenesis models that describe the couple effects of chemotaxis and convection on capillary growth during tumor angiogenesis:

$$\begin{cases} \partial_t n = \Delta n - \nabla \cdot (\chi_1 n \nabla v) - \nabla \cdot (\chi_2 n \nabla w), & x \in \mathbb{R}^3, t > 0 \\ \partial_t v = \Delta v - \nabla \cdot (\xi v \nabla w) + \alpha n - \beta v, & x \in \mathbb{R}^3, t > 0 \\ \tau \partial_t w = \Delta w - \delta w + \gamma n, & x \in \mathbb{R}^3, t > 0. \end{cases} \quad (1.1)$$

With initial data

$$(n, v, w)|_{t=0} = (n_0(x), v_0(x), w_0(x)), \quad x \in \mathbb{R}^3, \quad (1.2)$$

Where $(n_0(x), v_0(x), w_0(x)) \rightarrow (0,0,0)$ as $|x| \rightarrow \infty$.

We begin with a brief description of the system (1.1), this model explains the hypotheses that the endothelial cells secrete both matrix and fibronectin, that the endothelial cells as well as the adhesive sites are carried with the extracellular matrix, and that the endothelial cells move chemotactically toward increasing fibronectin concentrations. Here, $n = n(t, x)$, $v = v(t, x)$, and $w = w(t, x)$ denote the density of endothelial cells, the concentration of a certain adhesive chemical, the distribution of the so-called extracellular matrix, respectively. Where $\chi_1, \chi_2, \xi, \alpha, \beta, \delta, \gamma$ are positive constants and $\tau = 1$. Chemotaxis term $-\chi \nabla \cdot (n \nabla v)$ indicates that cells move towards gradients of chemical concentration, the term $-\nabla \cdot (\chi_1 n \nabla w)$ represents chemotactic aggregation effect and causes difficulties in analyzing this system; for more details, (cf. also ([7], [10]) for more details about the background of (1.1). Li and Tao [11] showed global existence and boundedness in the one-dimensional setting. After that, Ren [12] derived small data global existence and stabilization in the two-

dimensional setting. Also, Tao and Winkler [13] established global existence and boundedness when $\tau = 0$. More related works can be found in ([14-19]).

For later use in this paper, we give some notations. Let $1 \leq P \leq \infty$, we denote L^p for the Lebesgue space on Ω , and the norms in the space $L^p(\mathbb{R}^3)$ are denoted by $\|\cdot\|_p$. For nonnegative integer K , we denote by H^K the Sobolev space of order K . Set $L^2 = H^0$, the norm of H^K is denoted by $\|\cdot\|_{H^K}$. We set $\partial^\alpha = \partial_{x_1}^{\alpha_1} \partial_{x_2}^{\alpha_2} \partial_{x_3}^{\alpha_3}$ for a multi-index $\alpha = [\alpha_1, \alpha_2, \alpha_3]$ and length of α is $|\alpha| = \alpha_1 + \alpha_2 + \alpha_3$. C and C_i , where $i = 1, 2$, denote some positive (generally small) constant, where both C and C_i may take different values in different places. Let us denote the space

$$X(0, T) = \left\{ \begin{array}{l} (n, v, w) \in C([0, T]; H^3(\mathbb{R}^3)) \cap C^1([0, T]; H^1(\mathbb{R}^3)), \\ (\nabla n, \nabla v, \nabla w) \in L^2([0, T]; H^3(\mathbb{R}^3)). \end{array} \right\}$$

The main goal of this paper is to establish the existence of unique local solutions in three dimensions for the above system (1.1). The main result of this paper is stated as follows:

Theorem 1.1. Let $W(t) = (n, v, w)$ be a smooth solution to the Cauchy problem of the chemotaxis system (1.1) with initial data $W_0 = (n_0, v_0, w_0)$. Suppose that there exists a positive constant ε_0 such that if

$$\|n_0, v_0, w_0\|_{H^3} \leq \varepsilon_0,$$

then the Cauchy problems (1.1)-(1.2) of the Keller-Segel system admits a unique local solution (n, v, w) with

$$(n, v, w) \in X(0, T).$$

The proof of Theorem (1.1) follows directly from the local existence of solutions and the uniqueness of solutions, which will be proved in the next section. The proof of the existence of local solutions by constructing a sequence of approximation functions based on iteration and some basic energy estimates.

2. Existence of local solutions

In this section, we show the proof of the existence of local solutions (n, v, w) by constructing a sequence of functions that converges to a function satisfying the Cauchy problem. We construct the sequence $(n^j, v^j, w^j)_{j \geq 0}$ by iteratively solving the Cauchy problem on the following

$$\begin{cases} \partial_t n^{j+1} - \Delta n^{j+1} = -\chi_1(n^j \cdot \nabla v^{j+1}) - \chi_2 \nabla \cdot (n^j \nabla w^{j+1}), \\ \partial_t v^{j+1} - \Delta v^{j+1} + \beta v^{j+1} = -\xi \nabla \cdot (v^j \nabla w^{j+1}) + \alpha n^j, \\ \partial_t w^{j+1} - \Delta w^{j+1} + \delta w^{j+1} = \gamma n^j, \quad x \in \mathbb{R}^3, \end{cases} \quad (2.1)$$

with initial data

$$(n^{j+1}, v^{j+1}, w^{j+1})|_{t=0} = (n_0, v_0, w_0), \quad x \in \mathbb{R}^3, \quad (2.2)$$

for $j \geq 0$, where $(n^0, v^0, w^0) \equiv (0, 0, 0)$ holds. For simplicity, In what follows, let us write $W_0 = (n_0, v_0, w_0)$ and $W^j = (n^j, v^j, w^j)_{j \geq 0}$. Now, we will need to prove the following result:

Theorem 3.1.

Suppose $\|W_0\|_N \leq \varepsilon_0$, for small constants $\varepsilon_0 > 0$, $T > 0$, $k > 0$. Then for each $j \geq 0$, $W^j \in C([0, T]; H^3)$ is well defined and

$$\sup_{0 \leq t \leq T_1} \|W^j(t)\|_{H^3} \leq K. \quad (2.3)$$

Moreover, $(W^j)_{j \geq 0}$ is a Cauchy sequence in Banach space $C([0, T]; H^3)$, the corresponding limit function denoted by W belongs to $C([0, T]; H^3)$ with

$$\sup_{0 \leq t \leq T} \|W(t)\|_{H^3} \leq K, \quad (2.4)$$

and $W = (n, v, w)$ is a solution to the Cauchy problem (1.1)-(1.2) over $[0, T]$. The Cauchy problem (1.1)-(1.2) admits at most one solution $W \in C([0, T]; H^3)$, which satisfies (2.4).

Proof

We use the induction to prove (2.3). The trivial case is $j = 0$ since by the assumption at the initial step. Suppose that (2.3) holds for some $j \geq 0$ where K is small enough. To prove (2.3) holds for $j + 1$, we need some energy estimates on $(n^{j+1}, v^{j+1}, w^{j+1})$.

Applying ∂^α to both sides of the first equation of (2.1), multiplying by $\partial^\alpha n^{j+1}$, and integrating over $\mathbb{R}^3$ with $|\alpha| \leq 3$, we obtain

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\mathbb{R}^3} |\partial^\alpha n^{j+1}|^2 dx - \int_{\mathbb{R}^3} \partial^\alpha \Delta n^{j+1} \partial^\alpha n^{j+1} dx \\ &= -\chi_1 \int_{\mathbb{R}^3} \partial^\alpha \nabla \cdot (n^j \cdot \nabla v^{j+1}) \partial^\alpha n^{j+1} dx - \\ & \quad \chi_2 \int_{\mathbb{R}^3} \partial^\alpha \nabla \cdot (n^j \nabla w^{j+1}) \partial^\alpha n^{j+1} dx. \end{aligned} \quad (2.5)$$

By using integration by parts, we get

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\mathbb{R}^3} |\partial^\alpha n^{j+1}|^2 dx + \int_{\mathbb{R}^3} |\partial^\alpha \nabla n^{j+1}|^2 dx \\ &= \chi_1 \int_{\mathbb{R}^3} \partial^\alpha (n^j \nabla v^{j+1}) \partial^\alpha \nabla n^{j+1} dx + \\ & \quad \chi_2 \int_{\mathbb{R}^3} \partial^\alpha (n^j \nabla w^{j+1}) \partial^\alpha \nabla n^{j+1} dx. \end{aligned} \quad (2.6)$$

Then

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\mathbb{R}^3} |\partial^\alpha n^{j+1}|^2 dx + \int_{\mathbb{R}^3} |\partial^\alpha \nabla n^{j+1}|^2 dx \\ & \leq C \|n^j\|_{H^3} \|\nabla v^{j+1}\|_{H^3} \|\nabla n^{j+1}\|_{H^3} \\ & \quad + C \|n^j\|_{H^3} \|\nabla w^{j+1}\|_{H^3} \|\nabla n^{j+1}\|_{H^3}. \end{aligned}$$

Then, after taking the summation over $|\alpha| \leq 3$ and using the Cauchy inequality, we have

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|n^{j+1}\|_{H^3}^2 + C_1 \|\nabla n^{j+1}\|_{H^3}^2 \\ & \leq C \|n^j\|_{H^3}^2 \|\nabla(n^{j+1}, v^{j+1}, w^{j+1})\|_{H^3}^2 + \\ & \quad C \|n^j\|_{H^3}^2. \end{aligned} \quad (2.7)$$

By the same way, for second equation of (2.1), we have

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\mathbb{R}^3} |\partial^\alpha v^{j+1}|^2 dx + \int_{\mathbb{R}^3} |\nabla \partial^\alpha v^{j+1}|^2 dx + \beta \int_{\mathbb{R}^3} |\partial^\alpha v^{j+1}|^2 dx = \\ & -\xi \int_{\mathbb{R}^3} \partial^\alpha \nabla \cdot (v^j \nabla w^{j+1}) \partial^\alpha v^{j+1} dx + \alpha \int_{\mathbb{R}^3} \partial^\alpha n^j \partial^\alpha v^{j+1} dx. \end{aligned} \quad (2.8)$$

Using integration by parts, the Cauchy inequality, and taking summation over $|\alpha| \leq 3$, we obtain

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|v^{j+1}\|_{H^3}^2 + C_1 \|\nabla v^{j+1}\|_{H^3}^2 + C_2 \|v^{j+1}\|_{H^3}^2 \\ & \leq C \|v^j\|_{H^3}^2 \|\nabla w^{j+1}\|_{H^3}^2 + C \|n^j\|_{H^3}^2. \end{aligned} \quad (2.9)$$

We have a similar way to estimate w^{j+1} as follows:

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\mathbb{R}^3} |\partial^\alpha w^{j+1}|^2 dx + \\ & \int_{\mathbb{R}^3} |\nabla \partial^\alpha w^{j+1}|^2 dx + \delta \int_{\mathbb{R}^3} |\partial^\alpha w^{j+1}|^2 dx = \\ & \gamma \int_{\mathbb{R}^3} \partial^\alpha n^j \partial^\alpha w^{j+1} dx. \end{aligned} \quad (2.10)$$

Using integration by parts and using the Cauchy inequality, we obtain

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|w^{j+1}\|_{H^3}^2 + \|\nabla w^{j+1}\|_{H^3}^2 + C_2 \|w^{j+1}\|_{H^3}^2 \\ & \leq C \|n^j\|_{H^3}^2. \end{aligned} \quad (2.11)$$

By taking the linear combination of inequalities (2.7), (2.9), and (2.11) leads to

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} [\|n^{j+1}\|_{H^3}^2 + \|v^{j+1}\|_{H^3}^2 + \|w^{j+1}\|_{H^3}^2] \\ & + C_2 \|\nabla(n^{j+1}, v^{j+1}, w^{j+1})\|_{H^3}^2 + C_2 \|v^{j+1}, w^{j+1}\|_{H^3}^2 \leq \\ & C \|n^j\|_{H^3}^2 + C \|(n^j, v^j)\|_{H^3}^2 \|\nabla(n^{j+1}, v^{j+1}, w^{j+1})\|_{H^3}^2. \end{aligned} \quad (2.12)$$

Thus, after integrating (2.12) over $[0, t]$ for all $t \in [0, T]$, we have

$$\begin{aligned} & \|W^{j+1}(t)\|_{H^3}^2 + C_1 \int_0^t \|\nabla W^{j+1}(s)\|_{H^3}^2 ds + C_2 \int_0^t \|(v^{j+1}, w^{j+1})\|_{H^3}^2 ds \\ & \leq C \|W_0\|_{H^3}^2 + C \int_0^t \|W^j(s)\|_{H^3}^2 ds + \\ & C \int_0^t \|W^j(s)\|_{H^3}^2 \|\nabla W^{j+1}(s)\|_{H^3}^2 ds. \end{aligned} \quad (2.13)$$

From the inductive assumption, the previous inequality can be re-estimated as

$$\begin{aligned} & \|W^{j+1}(t)\|_{H^3}^2 + C_1 \int_0^t \|\nabla W^{j+1}(s)\|_{H^3}^2 ds + C_2 \int_0^t \|(v^{j+1}, w^{j+1})\|_{H^3}^2 ds \\ & \leq C\varepsilon_1^2 + CM^2T + CM^2 \int_0^t \|\nabla W^{j+1}(s)\|_{H^3}^2 ds, \end{aligned} \quad (2.14)$$

for any $0 \leq t \leq T$. Now, we take the small constants $\varepsilon_0 > 0$, $K > 0$ and $T > 0$. Then, we obtain

$$\begin{aligned} & \|W^{j+1}(t)\|_{H^3}^2 + C_1 \|\nabla W^{j+1}(t)\|_{H^3}^2 \\ & \|(v^{j+1}, w^{j+1})\|_{H^3}^2 \leq K^2, \end{aligned} \quad (2.15)$$

for any $0 \leq t \leq T$. This implies that (2.3) holds for $j + 1$. Hence (2.3) is proved for all $j \geq 0$. Next, we define the equivalent energy functional

$$E(W^{j+1}(t)) := \|n^{j+1}\|_{H^3}^2 + \|v^{j+1}\|_{H^3}^2 + \|w^{j+1}\|_{H^3}^2.$$

Similar to prove (2.13), we have

$$\begin{aligned} & |E(W^{j+1}(t)) - E(W^{j+1}(s))| = \left| \int_s^t \frac{d}{d\tau} E(W^{j+1}(\tau)) d\tau \right| \\ & \leq C \int_s^t \|W^j(\tau)\|_{H^3}^2 d\tau + C \int_s^t (1 + \|W^j(\tau)\|_{H^3}^2) \|\nabla W^{j+1}(\tau)\|_{H^3}^2 d\tau + \\ & C \int_0^t \|(v^{j+1}, w^{j+1})\|_{H^3}^2 d\tau \\ & \leq CK^2(t-s) + C(1+K^2) \int_s^t \|\nabla W^{j+1}(\tau)\|_{H^3}^2 d\tau + \\ & C \int_s^t \|(v^{j+1}, w^{j+1})\|_{H^3}^2 d\tau, \end{aligned} \quad (2.16)$$

for any $0 \leq s \leq t \leq T$. Here, the time integral on the right-hand side from the above inequality is bounded by (2.15), and hence $E(W^{j+1}(t))$ is Continuous in t for each $j \geq 0$. By the same

argument, we can infer that $\|v^{j+1}\|_{H^3}^2$ and $\|w^{j+1}\|_{H^3}^2$ are continuous in t . From the continuity of $E(W^{j+1}(t))$, we can also infer the continuity of $\|n^{j+1}\|_{H^3}^2$. Therefore, $\|W^{j+1}(t)\|_{H^3}^2$ is continuous in time for any $j \geq 1$.

Now, we prove that the sequence $(W^j)_{j \geq 0}$ is a Cauchy sequence in the Banach space $C([0, T]; H^3)$, which converges to the solution $W = (n, v, w)$ of the Cauchy problem (1.1)-(1.2), and satisfies (2.4). For simplicity, we denote $\delta f^{j+1} = f^{j+1} - f^j$. Taking the difference of (2.1) for $j+1$ and j so that it gives:

$$\begin{cases} \partial_t \delta n^{j+1} - \Delta \delta n^{j+1} = -\chi_1 \nabla \cdot (n^j \nabla \delta v^{j+1}) - \chi_1 \nabla \cdot (\delta n^j \nabla v^j) \\ \quad - \chi_2 \nabla \cdot (n^j \nabla \delta w^{j+1}) - \chi_2 \nabla \cdot (\delta n^j \nabla w^j), \\ \partial_t \delta v^{j+1} - \Delta \delta v^{j+1} + \beta v^{j+1} = \\ \quad - \xi \nabla \cdot (v^j \nabla \delta w^{j+1}) - \xi \nabla \cdot (\delta v^j \nabla w^j) + \alpha \delta n^j, \\ \partial_t \delta w^{j+1} - \Delta \delta w^{j+1} + \delta \delta w^{j+1} = \gamma \delta n^j. \end{cases} \quad (2.17)$$

By using the same energy estimates as before, we have

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|\delta n^{j+1}\|_{H^3}^2 + \|\nabla \delta n^{j+1}\|_{H^3}^2 \\ & \leq C \|(\delta n^j, \delta v^j)\|_{H^3}^2 \|\nabla(v^j, w^j)\|_{H^3}^2 \\ & \quad + C \|n^j\|_{H^3}^2 \|(\delta v^{j+1}, \delta w^{j+1})\|_{H^3}^2 + \\ & \quad \|\nabla \delta v^{j+1}\|_{H^3}^2 + \delta \|\nabla \delta w^{j+1}\|_{H^3}^2, \quad (2.18) \\ & \frac{1}{2} \frac{d}{dt} \|\delta v^{j+1}\|_{H^3}^2 + \frac{1}{2} \|\nabla \delta v^{j+1}\|_{H^3}^2 + \beta \|\delta v^{j+1}\|_{H^3}^2 \\ & \leq C \|v^j\|_{H^3}^2 \|\nabla \delta w^{j+1}\|_{H^3}^2 + \\ & C \|\delta v^j\|_{H^3}^2 \|\nabla w^j\|_{H^3}^2 + \alpha \|\delta n^j\|_{H^3}^2, \quad (2.19) \end{aligned}$$

and

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|\delta w^{j+1}\|_{H^3}^2 + \delta \|\delta w^{j+1}\|_{H^3}^2 + \|\nabla \delta w^{j+1}\|_{H^3}^2 \\ & \leq \gamma \|\delta n^j\|_{H^3}^2. \quad (2.20) \end{aligned}$$

We combine the equations (2.18), (2.19), and (2.20) to get

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|\delta W^{j+1}\|_{H^3}^2 + C_1 \|\nabla \delta W^{j+1}\|_{H^3}^2 + \\ & C_2 \|(\delta v^{j+1}, \delta w^{j+1})\|_{H^3}^2 \\ & \leq C \|\delta W^j\|_{H^3}^2 + C \|\delta W^j\|_{H^3}^2 \|\nabla W^j\|_{H^3}^2 + \\ & C \|W^j\|_{H^3}^2 \|\nabla \delta W^{j+1}\|_{H^3}^2. \end{aligned} \quad (2.21)$$

By integrating over $[0, t]$ for any $0 \leq t \leq T$ from (2.21), we obtain

$$\begin{aligned} & \|\delta W^{j+1}\|_{H^3}^2 + C_1 \int_0^t \|\nabla \delta W^{j+1}\|_{H^3}^2 ds + C_2 \int_0^t \|(\delta v^{j+1}, \delta w^{j+1})\|_{H^3}^2 ds \\ & \leq C(1 + K^2) T \sup_{0 \leq t \leq T_1} \|\delta W^j\|_{H^3}^2 + CK^2 \int_0^t \|\nabla \delta W^{j+1}\|_{H^3}^2 ds, \end{aligned}$$

for any $0 \leq t \leq T$, which by smallness of K and T implies that there is a constant $\theta \in (0, 1)$ such that

$$\sup_{0 \leq t \leq T} \|\delta W^{j+1}\|_{H^3} \leq \theta \sup_{0 \leq t \leq T} \|\delta W^j\|_{H^3},$$

for any $j \geq 1$. It can be seen from the above inequality that $(W^j)_{j \geq 0}$ is a Cauchy sequence in the Banach space $C([0, T]; H^3)$. We have the limit function

$$W = W^0 + \lim_{i \rightarrow \infty} \sum_{j=0}^i (W^{j+1} - W^j),$$

exists in $C([0, T]; H^3(\mathbb{R}^3))$, and satisfies

$$\sup_{0 \leq t \leq T} \|W(t)\|_{H^3} \leq \sup_{0 \leq t \leq T} \lim_{j \rightarrow \infty} \inf \|W^j(t)\|_{H^3} \leq K. \quad (2.22)$$

Finally, we show that the Cauchy problem (1.1)-(1.2) admits at most one solution in $C([0, T]; H^3(\mathbb{R}^3))$. Suppose that there exist two solutions $W, \tilde{W}$ in $C([0, T]; H^3(\mathbb{R}^3))$ which satisfy (2.4). Let $\tilde{n} = n_1(x, t) - n_2(x, t)$, $\tilde{u} = u_1(x, t) - u_2(x, t)$, and $\tilde{c} = c_1(x, t) - c_2(x, t)$,
Solves

$$\begin{cases} \partial_t \tilde{n} - \Delta \tilde{n} = -\chi_1 \nabla \cdot (n_2 \nabla \tilde{v}) - \chi_1 \nabla \cdot (\tilde{n} \nabla v_1) \\ \quad - \chi_2 \nabla \cdot (n_2 \nabla \tilde{w}) - \chi_2 \nabla \cdot (\tilde{n} \nabla w_1), \\ \partial_t \tilde{v} - \Delta \tilde{v} + \beta \tilde{v} = -\xi \nabla \cdot (n_2 \nabla \tilde{v}) - \\ \quad \xi \nabla \cdot (\tilde{n} \nabla v_1) + \alpha \tilde{n}, \\ \partial_t \tilde{w} - \Delta \tilde{w} + \delta \tilde{w} = \gamma \tilde{n}. \end{cases} \quad (2.23)$$

Multiplying $\tilde{n}$ to both sides of the first equation of (2.23) and integrating over $\mathbb{R}^3$, we have

$$\begin{aligned} & \int_{\mathbb{R}^3} \tilde{n} \partial_t \tilde{n} dx - \int_{\mathbb{R}^3} \tilde{n} \Delta \tilde{n} dx \\ &= -\chi_1 \int_{\mathbb{R}^3} \tilde{n} \nabla \cdot (n_2 \nabla \tilde{v}) dx - \chi_1 \int_{\mathbb{R}^3} \tilde{n} \nabla \cdot (\tilde{n} \nabla v_1) dx \\ & \quad - \chi_2 \int_{\mathbb{R}^3} \tilde{n} \nabla \cdot (n_2 \nabla \tilde{w}) dx - \chi_2 \int_{\mathbb{R}^3} \tilde{n} \nabla \cdot (\tilde{n} \nabla w_1) dx. \end{aligned}$$

Then, after using integration by parts and the Cauchy inequality, we obtain

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|\tilde{n}\|_{L^2}^2 + \|\nabla \tilde{n}\|_{L^2}^2 \\ & \leq \chi_1 \|n_2\|_{L^\infty} \int_{\mathbb{R}^3} (|\nabla \tilde{n}|^2 + |\nabla \tilde{v}|^2) dx \\ & \quad + \chi_1 \|\nabla v_1\|_{L^\infty} \int_{\mathbb{R}^3} (|\tilde{n}|^2 + |\nabla \tilde{n}|^2) dx \\ & \quad + \chi_2 \|n_2\|_{L^\infty} \int_{\mathbb{R}^3} (|\nabla \tilde{n}|^2 + |\nabla \tilde{w}|^2) dx \\ & \quad + \chi_2 \|\nabla w_1\|_{L^\infty} \int_{\mathbb{R}^3} (|\tilde{n}|^2 + |\nabla \tilde{n}|^2) dx. \end{aligned}$$

Since L^∞ norms of n_i, v_i, w_i where $i = 1, 2$ are bounded, we have

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|\tilde{n}\|_{L^2}^2 + C \|\nabla \tilde{n}\|_{L^2}^2 \\ & \leq C (\|\tilde{n}\|_{L^2}^2 + \|\nabla \tilde{v}\|_{L^2}^2 + \|\nabla \tilde{w}\|_{L^2}^2). \end{aligned} \quad (2.24)$$

For the estimate of $\tilde{v}$, multiplying $\tilde{v}$ to both sides of the second equation of (2.23) and taking integrations in x , we obtain

$$\begin{aligned} & \int_{\mathbb{R}^3} \tilde{v} \partial_t \tilde{v} dx - \int_{\mathbb{R}^3} \tilde{v} \Delta \tilde{v} dx + \beta \int_{\mathbb{R}^3} |\tilde{v}|^2 dx = \\ & -\xi \int_{\mathbb{R}^3} \tilde{v} \nabla \cdot (v_2 \nabla \tilde{w}) dx - \xi \int_{\mathbb{R}^3} \tilde{v} \nabla \cdot (\tilde{v} \nabla w_1) dx + \\ & \alpha \int_{\mathbb{R}^3} \tilde{v} \tilde{n} dx. \end{aligned}$$

Then

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|\tilde{v}\|_{L^2}^2 + C \|\nabla \tilde{v}\|_{L^2}^2 + C \|\tilde{v}\|_{L^2}^2 \\ & \leq C(\|\tilde{v}\|_{L^2}^2 + \|\tilde{n}\|_{L^2}^2 + \|\nabla \tilde{w}\|_{L^2}^2). \end{aligned} \quad (2.25)$$

Similarly, as above, we estimate $\tilde{w}$ as follows:

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \|\tilde{w}\|_{L^2}^2 + \|\nabla \tilde{w}\|_{L^2}^2 + \delta \|\tilde{w}\|_{L^2}^2 \\ & \leq C(\|\tilde{n}\|_{L^2}^2 + \|\tilde{w}\|_{L^2}^2). \end{aligned} \quad (2.26)$$

Then, after taking the linear combination of above estimates, we obtain

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} (\|\tilde{n}\|_{L^2}^2 + \|\tilde{v}\|_{L^2}^2 + \|\tilde{w}\|_{L^2}^2) + \\ & C_1 (\|\tilde{v}\|_{L^2}^2 + \|\tilde{w}\|_{L^2}^2) \\ & + C_2 (\|\nabla \tilde{n}\|_{L^2}^2 + \|\nabla \tilde{v}\|_{L^2}^2 + \|\nabla \tilde{w}\|_{L^2}^2) \\ & \leq C(\|\tilde{n}\|_{L^2}^2 + \|\tilde{v}\|_{L^2}^2 + \|\tilde{w}\|_{L^2}^2). \end{aligned} \quad (2.27)$$

By applying Gronwall's inequality to the above equation, we have

$$\begin{aligned} & \sup_{0 \leq t \leq T} (\|\tilde{n}\|_{L^2}^2 + \|\tilde{v}\|_{L^2}^2 + \|\tilde{w}\|_{L^2}^2) \\ & \leq C e^{cT} (\|\tilde{n}(0)\|_{L^2}^2 + \|\tilde{v}(0)\|_{L^2}^2 + \|\tilde{w}(0)\|_{L^2}^2). \end{aligned}$$

Since the initial data of $(\tilde{n}, \tilde{v}, \tilde{w})$ are all zero for $T > 0$, that implies the uniqueness of the local solution.

Conclusion

In this paper, we prove the existence of local solutions for chemotaxis-convection model with sensitivity functions for tumor angiogenesis system in three dimensions. We show the existence of unique solutions by the energy method. We use integral by parts, Cauchy inequality, and

Gronwall's inequality to prove the local existence and uniqueness of solutions.

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