数理解析研究所講究録
第 1994 巻 2016 年 121-127

Global asymptotic stability in a chemotaxis-growth model for tumor invasion

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1. Introduction

In recent decades, mathematical analysis of *taxis* mechanisms has been received considerable interest. Keller and Segel firstly introduced the system

$$\begin{cases} u_t = \Delta u - \nabla \cdot (u \nabla z), \\ z_t = \Delta z - z + u, \end{cases} \tag{1.1}$$

describing a biological phenomenon *chemotaxis* which means the oriented movement of cells as a response to a chemical substance ([**10**]). From their study, a large variety of mathematical analysis has been devoted, especially global existence and blow-up of solutions in variants of (1.1) are well studied (see [**1, 7, 8**]). In particular, it is known that a blow-up phenomenon may occur in (1.1) when the spacial dimension $n \geq 2$ ([**6, 23**]). Some mathematical models describing tumor invasion phenomenon also have been proposed as a *taxis* model ([**2**]) and analytical results about global existence and boundedness of solutions are established ([**13**], [**14**], [**15**], [**18**], [**19**], [**21**]). On the other hand, asymptotic behavior of solutions is precisely analysed only in certain special cases ([**3**], [**9**]).

In this paper we consider global asymptotic stability of the following *taxis* model:

$$\begin{cases} u_t = \Delta u - \nabla \cdot (u \nabla v) + f(u), \\ v_t = \Delta v + wz, \\ w_t = -wz, \\ z_t = \Delta z - z + u, \end{cases} \tag{1.2}$$

which describes tumor invasion phenomenon in accounting for the role of an active extracellular matrix, ECM*, which is produced by a biological reaction between an extracellular matrix, ECM, and a matrix-degrading enzyme, MDE ([**4**]).

From a mathematical point of view, since one can collect three diffusion steps in the system (1.2), a strongly stabilizing effect is expected. As compared with Keller–Segel system (1.1), the destabilizing effect of the cross-diffusive term is overbalanced by the diffusion terms in (1.2). Actually, in [**5**] it has been shown that in the lower dimensional case $n \leq 3$ the system (1.2) with $f \equiv 0$ possesses a unique global and bounded solution (u, v, w, z). Moreover, it has been established that if $u_0 \not\equiv 0$ then the solution approaches a certain spatially homogeneous steady state in the sense that as $t \to \infty$,

$$u(x,t) \to \overline{u_0}, \qquad v(x,t) \to \overline{v_0} + \overline{w_0}, \qquad w(x,t) \to 0 \qquad \text{and} \qquad z(x,t) \to \overline{u_0},$$

uniformly with respect to $x \in \Omega$, where $\overline{u_0} := \frac{1}{|\Omega|}\int_\Omega u_0$, $\overline{v_0} := \frac{1}{|\Omega|}\int_\Omega v_0$ and $\overline{w_0} := \frac{1}{|\Omega|}\int_\Omega w_0$.

Dampening effect of logistic source. We recall some results which describes a dampening effect of the logistic source $f(u) = ru - \mu u^\alpha$ ($r > 0$, $\mu > 0$, $\alpha > 1$) in (1.1). When the dimension n is lower ($n \leq 2$) and $\alpha = 2$, global existence and boundedness of (1.1) is established in [**16, 17**]. As to the higher dimensional case ($n \geq 3$) and $\alpha = 2$, global existence and boundedness of a smooth solution is established when $\mu > 0$ is sufficiently large in [**20, 22**]. Global existence of certain weak solutions is derived for arbitrary small $\mu > 0$ in [**12**] (see [**20**] for a simplified model) and moreover some eventual smoothness of the weak solution has been established in [**12**]. At all, global existence and boundedness of a classical solution in higher space dimensions for arbitrary small $\mu > 0$ has been left as a challenging open problem. In [**24**], asymptotic stability of constant equilibria is also established, that is, if $r = 1$ and $\mu > 0$ is sufficiently large then

$$u(x,t) \to \frac{1}{\mu} \qquad \text{and} \qquad z(x,t) \to \frac{1}{\mu},$$

as $t \to \infty$.

Main results. We consider the initial-boundary value problem

$$\text{(1.3)} \qquad \begin{cases} u_t = \Delta u - \nabla \cdot (u \nabla v) + f(u), & x \in \Omega,\ t > 0, \\ v_t = \Delta v + wz, & x \in \Omega,\ t > 0, \\ w_t = -wz, & x \in \Omega,\ t > 0, \\ z_t = \Delta z - z + u, & x \in \Omega,\ t > 0, \\ \frac{\partial u}{\partial \nu} = \frac{\partial v}{\partial \nu} = \frac{\partial z}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0, \\ u(x,0) = u_0(x), \quad v(x,0) = v_0(x), & \\ w(x,0) = w_0(x), \quad z(x,0) = z_0(x), & x \in \Omega, \end{cases}$$

in a bounded domain $\Omega \subset \mathbb{R}^n$ ($n \leq 3$) with smooth boundary. As to the initial data we assume that

$$\text{(1.4)} \quad 0 \leq u_0 \in C^0(\bar{\Omega}), \quad 0 \leq v_0 \in W^{1,\infty}(\Omega), \quad 0 \leq w_0 \in C^2(\bar{\Omega}) \quad \text{and} \quad 0 \leq z_0 \in C^0(\bar{\Omega}),$$

and moreover we suppose that $f(u)$ is the logistic source such as

$$\text{(1.5)} \qquad f(u) = ru - \mu u^\alpha \quad \text{with} \quad r > 0, \quad \mu > 0, \quad \alpha > 1.$$

The main results read as follows.

Theorem 1.1. *Assume that u_0, v_0, w_0 and z_0 comply with* (1.4) *and that f satisfies* (1.5). *Then there exists a uniquely determined quadruple (u, v, w, z) of nonnegative functions which solve* (1.3) *classically in $\Omega \times (0, \infty)$. Moreover the solution is bounded in the sense that there exists some constant $M > 0$ such that*

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} + \|v(\cdot,t)\|_{W^{1,\infty}(\Omega)} + \|w(\cdot,t)\|_{L^\infty(\Omega)} + \|z(\cdot,t)\|_{L^\infty(\Omega)} \leq M \qquad \textit{for all } t \geq 0.$$

Remark 1.1. As to the Keller–Segel system (1.1) with the logistic source in higher dimensions ($n \geq 3$), global existence has been left as an open problem when $\mu > 0$ is arbitrary small ([**22**]). However, using signal production mechanism (see the discussion in [**5**]) we can establish global existence for arbitrary $\mu > 0$ in $n = 3$.

Remark 1.2. Our method rests on the overbalanced structure of the problem (1.3) without using dampening effect of logistic source. It is an open question to establish global existence and boundedness of solutions to (1.3) in higher spacial dimensions $n \geq 4$.

To determine asymptotic behavior, the method in [**5**] can not directly be applied more realistic case (1.3) with the logistic source (for more details, see Section 3). As a way out of this situation, we make a comparison with a suitable ODE and then this idea enables us to apply the fashion in [**5**].

Theorem 1.2. *Assume that u_0, v_0, w_0 and z_0 comply with* (1.4)*, and that $u_0 \not\equiv 0$. Moreover, f is supposed to satisfy* (1.5)*. Then the solution (u, v, w, z) satisfies*

$$\left\| u(\cdot, t) - \left(\frac{r}{\mu}\right)^{\frac{1}{\alpha-1}} \right\|_{L^\infty(\Omega)} \to 0, \qquad \|v(\cdot, t) - (\overline{v_0} + \overline{w_0})\|_{L^\infty(\Omega)} \to 0,$$

$$\|w(\cdot, t)\|_{L^\infty(\Omega)} \to 0, \qquad \left\| z(\cdot, t) - \left(\frac{r}{\mu}\right)^{\frac{1}{\alpha-1}} \right\|_{L^\infty(\Omega)} \to 0$$

as $t \to \infty$, where the constants $\overline{v_0}$ and $\overline{w_0}$ are given by

$$\overline{v_0} := \frac{1}{|\Omega|} \int_\Omega v_0 \qquad \text{and} \qquad \overline{w_0} := \frac{1}{|\Omega|} \int_\Omega w_0.$$

Plan of paper. After preparing some regularity arguments in Section 2, we will establish Theorem 1.2 in Section 3. Using ODE comparison method, the asymptotic stability of solutions to (1.3) is precisely determined.

2. Preliminaries

Noting that $f(u) = ru - \mu u^\alpha \leq C$ with some constant $C > 0$, the following local existence statement can be proved by modifying the proof of [**4**, Theorem 3.1].

Lemma 2.1. *Assume that u_0, v_0, w_0 and z_0 satisfy* (1.4) *and f fulfils* (1.5)*. Then there exist $T_{\max} \in (0, \infty]$ and a unique classical solution (u, v, w, z) of* (1.3) *in $\Omega \times (0, T_{\max})$ which is such that*

$$\begin{aligned}
&0 \leq u \in C^0(\bar\Omega \times [0, T_{\max})) \cap C^{2,1}(\bar\Omega \times (0, T_{\max})),\\
&0 \leq v \in C^0(\bar\Omega \times [0, T_{\max})) \cap C^{2,1}(\bar\Omega \times (0, T_{\max})) \cap L^\infty_{\mathrm{loc}}([0, \infty); W^{1,\infty}(\Omega)),\\
&0 \leq w \in C^0(\bar\Omega \times [0, T_{\max})) \cap C^{0,1}(\bar\Omega \times (0, T_{\max})) \qquad \text{and}\\
&0 \leq z \in C^0(\bar\Omega \times [0, T_{\max})) \cap C^{2,1}(\bar\Omega \times (0, T_{\max})),
\end{aligned}$$

and such that

$$\text{(2.1)} \quad \text{if } T_{\max} < \infty \text{ then } \lim_{t \nearrow T_{\max}} \left(\|u(\cdot, t)\|_{L^\infty(\Omega)} + \|v(\cdot, t)\|_{W^{1,\infty}(\Omega)} + \|z(\cdot, t)\|_{L^\infty(\Omega)} \right) = \infty.$$

Although in the system (1.3) the total mass $\int_\Omega u$ is not preserved due to the logistic source, we can immediately derive an upper bound for the total mass $\int_\Omega u$. As a preparation, let us introduce the following statement.

Lemma 2.2. *There exists some constant $m > 0$ such that*

$$\int_\Omega u(x,t)dx \le m \qquad \text{for all } t \in (0, T_{\max}).$$

Proof. We integrate the first equation in (1.3) and use the Hölder inequality to see that

$$\frac{d}{dt}\int_\Omega u = r\int_\Omega u - \mu\int_\Omega u^\alpha \le r\int_\Omega u - \frac{\mu}{|\Omega|^{\alpha-1}}\left(\int_\Omega u\right)^\alpha \qquad \text{for all } t \in (0, T_{\max}).$$

Therefore, by invoking a straightforward ODE comparison argument we complete the proof. □

Furthermore, as a preparation to establish asymptotic stability of solutions, we state the following boundedness result.

Proposition 2.3. *Suppose that* (1.4) *and* (1.5) *hold. the solution* (u, v, w, z) *of* (1.3) *is global and bounded in the sense that there exist* $\theta \in (0,1)$ *and* $C > 0$ *such that*

$$\|u(\cdot,t)\|_{L^\infty(\Omega)} + \|v(\cdot,t)\|_{W^{1,\infty}(\Omega)} + \|w(\cdot,t)\|_{L^\infty(\Omega)} + \|z(\cdot,t)\|_{L^\infty(\Omega)} \le C \qquad \text{for all } t > 0$$

as well as

$$\|u\|_{C^{2+\theta,1+\frac{\theta}{2}}(\bar\Omega\times[t,t+1])} + \|v\|_{C^{2+\theta,1+\frac{\theta}{2}}(\bar\Omega\times[t,t+1])} + \|z\|_{C^{2+\theta,1+\frac{\theta}{2}}(\bar\Omega\times[t,t+1])} \le C \qquad \text{for all } t \ge 1.$$

Proof. Thanks to Lemma 2.2 we can proceed similar way as in [**5**, Section 3]. In light of the extensibility statement in Lemma 2.1, the local solution actually exists globally in time and standard parabolic regularity arguments ([**11**]) guarantee some further boundedness properties. □

Proof of Theorem 1.1. Combining Lemma 2.1 and Proposition 2.3 finishes the proof. □

3. Asymptotic stability

Before proving Theorem 1.2, we review the sketch of the proof of asymptotic behavior in the case that (1.3) without any logistic source in [**5**, Section 4]. From the Arzelà–Ascoli theorem boundedness of solutions firstly asserts a convergence of v. Next, we rewritten the first equation of (1.3) as

$$u(\cdot,t) - \overline{u_0} = e^{t\Delta}(u_0 - \overline{u_0}) - \int_0^t e^{(t-s)\Delta}\nabla\cdot u\nabla v \tag{3.1}$$

and then semigroup property and the convergence result of v make sure that the limit of the right hand side of (3.1) as $t \to \infty$ must be zero. Accordingly we deduce the stabilization property of u such as $\|u(\cdot,t) - \overline{u_0}\|_{L^\infty(\Omega)} \to 0$ as $t \to \infty$. Finally semigroup techniques and convergence results of v and u ensure the convergence property of z and then determine the convergence of w.

In this paper we consider the case that (1.3) with the logistic source $ru - \mu u^\alpha$ and so this term disturbs estimating (3.1). To overcome this difficulty we employ the comparison principle.

Proof of Theorem 1.2. Since Proposition 2.3 claims that $(v(\cdot,t))_{t\geq 1}$ is bounded in $C^{2+\theta}(\bar{\Omega})$ and hence relatively compact in $C^2(\bar{\Omega})$ by the Arzelà–Ascoli theorem, we apply [**5**, Lemma 4.3] to have

$$\|v(\cdot,t)-L\|_{W^{2,\infty}(\Omega)}\to 0 \qquad \text{as } t\to\infty$$

with some constant $L\geq 0$. In particular we see

$$\|\Delta v(\cdot,t)\|_{L^\infty(\Omega)}\to 0 \qquad \text{as } t\to\infty,$$

so for all $\varepsilon>0$ we can choose some $t_0>0$ fulfilling

$$\|\Delta v(\cdot,t)\|_{L^\infty(\Omega)}\leq\varepsilon \qquad \text{for all } t\geq t_0.$$

Thus, the first equation of (1.3) is estimated as

$$u_t\leq \Delta u-\nabla v\cdot\nabla u+(r+\varepsilon)u-\mu u^\alpha.$$

Noting that $\bar{y}(t)$ is a solution of the following problem:

$$\begin{cases} \bar{y}'(t)=(r+\varepsilon)\bar{y}-\mu\bar{y}^\alpha,\ t>t_0,\\ \bar{y}(t_0)=\|u(\cdot,t_0)\|_{L^\infty(\Omega)},\end{cases}$$

the comparison principle gives immediately the estimate

$$u(x,t)\leq\bar{y}(t) \qquad \text{for all } x\in\Omega,\ t>t_0.$$

Therefore it follows that

$$\limsup_{t\to\infty}\sup_{x\in\Omega}u(x,t)\leq\limsup_{t\to\infty}\bar{y}(t)=\lim_{t\to\infty}\bar{y}(t)=\left(\frac{r+\varepsilon}{\mu}\right)^{\frac{1}{\alpha-1}}.$$

Since $\varepsilon>0$ is arbitrary, we conclude that

$$\limsup_{t\to\infty}\sup_{x\in\Omega}u(x,t)\leq\left(\frac{r}{\mu}\right)^{\frac{1}{\alpha-1}}. \tag{3.2}$$

Proceeding similarly, we also have

$$u_t\geq \Delta u-\nabla v\cdot\nabla u+(r-\varepsilon)u-\mu u^\alpha$$

and

$$\liminf_{t\to\infty}\inf_{x\in\Omega}u(x,t)\geq\left(\frac{r}{\mu}\right)^{\frac{1}{\alpha-1}}. \tag{3.3}$$

Collecting (3.2) and (3.3) yields that

$$\left\|u-\left(\frac{r}{\mu}\right)^{\frac{1}{\alpha-1}}\right\|_{L^\infty(\Omega)}\to 0 \qquad \text{as } t\to\infty. \tag{3.4}$$

In the rest of proof, using (3.4) instead of [**5**, Lemma 4.4] we can proceed in the same way as in [**5**, Section 4]. The proof is completed. □

Remark 3.1. We underline that the proof of Theorem 1.2 remains valid for any spacial dimensions if the solution enjoys some boundedness property as Proposition 2.3.

Acknowledgment. The author is supported by JSPS Research Fellowships for Young Scientists (No. 15J01986).

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