A Mathematical Approach to Othmer-Stevens Model

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Abstract: - We study a parabolic ODE system modeling tumour growth proposed by Othmer and Stevens [5]. In use of the transformation of Levine and Sleeman [4], we reduce it to a hyperbolic equation with strong dissipation. Then, we show the existence of collapse in arbitrary space dimension by the method of energy.

Key-Words: - Tumour angiogenesis, Othmer-Stevens model, Parabolic ODE system, Collapse, Hyperbolic.

1 Introduction

In [5] H.G. Othmer and A. Stevens derived a parabolic-ODE system modeling chemotactic aggregation of myxobacteria, where unknown functions $P = P(x,t)$ and $W = W(x,t)$ stand for the density of the bacteria and that of control species, respectively. That is,

$$P_t = D\nabla \cdot [P\nabla(\log \frac{P}{\Phi(W)})] \tag{1}$$

$$W_t = WP \qquad in \quad \Omega \times (0,\infty) \tag{2}$$

with

$$P\nabla(\log \frac{P}{\Phi(W)}) \cdot \boldsymbol{\nu} = 0 \qquad \text{on } \partial\Omega \times (0,T) \tag{3}$$

and

$$P(x,0) = P_0(x) \geq 0,$$

$$W(x,0) = W_0(x) \geq 0 \qquad \text{in} \quad \Omega, \tag{4}$$

where Ω is a bounded domain in R^n with smooth boundary $\partial\Omega$, $D > 0$ is a constant,

$$\Phi(W) = (\frac{W+\alpha}{W+\beta})^a$$

stands for the sensitivity function with the prescribed constants $\alpha,\beta > 0, a$ and ν denotes the outer unit normal vector. In fact, [5] provides the reinforced random walk on lattice points as in Davis [1], takes the renormalized limit, and gets the above system.

This method of mathematical modeling has gained the understanding of tumour angiogenesis by the numerical computation, and actually, [4] classified the solution according to its behavior as $t \to +\infty$:

1.(aggregation) $\|P(\cdot,t)\|_{L^\infty} < C$ for all t

$$lim \inf_{t\to\infty} \|P(\cdot,t)\|_{L^\infty} > \|P(\cdot,0)\|_{L^\infty}.$$

2.(blowup) $\|P(\cdot,t)\|_{L^\infty}$ becomes unbounded in finite time.

3.(collapse)

$$lim \sup_{t\to\infty} \|P(\cdot,t)\|_{L^\infty} < \|P(\cdot,0)\|_{L^\infty}.$$

Mathematical analysis of this model was done by Levine and Sleeman [4], and provided some understanding of numerical findings. However, their simplification of the model does not seem to be efficient in some cases, and the purpose of the present paper is to provide a mathematical study for the original system.

In fact, taking $logW = \Psi$, we get $\Psi_t = P$ from the second equation of (1) and it holds that

$$\nabla(\log \frac{P}{\Phi(W)}) = \frac{\nabla P}{P} - \frac{\Phi_\nabla(W)e^\Psi \nabla\Psi}{\Phi(W)}$$

for $\Phi_\nabla(W) = a(\beta-\alpha)(\frac{W+\alpha}{W+\beta})^{a-1}(W+\beta)^{-2}$.
We have

$$\frac{\Phi_\nabla(W)}{\Phi(W)} = a\frac{(\beta-\alpha)}{(W+\alpha)(W+\beta)},$$

and hence it follows that

$$P\nabla(\log \frac{P}{\Phi(W)}) = \nabla P - \frac{a(\beta-\alpha)e^\Psi}{(e^\Psi+\alpha)(e^\Psi+\beta)}\Psi_t\nabla\Psi.$$

Thus, (1) is reduced to

$$\Psi_{tt} = D\Delta\Psi_t - \nabla(\frac{aD(\beta-\alpha)e^\Psi}{(e^\Psi+\alpha)(e^\Psi+\beta)}\Psi_t\nabla\Psi) \qquad (4)$$

At this stage, [4] replaced the coefficient

$$\frac{a(\beta-\alpha)e^\Psi}{(e^\Psi+\alpha)(e^\Psi+\beta)} = \frac{a(\beta-\alpha)W}{(W+\alpha)(W+\beta)}$$

by a positive constant, under the agreement that $\alpha \gg W \gg \beta$ or $\beta \gg W \gg \alpha$. However,there is a case that $W = e^\Psi$ is unbounded, where this simplification is not valid.

On the other hand, the second equation of (1) is also a simplication of the original in [5],

$$W_t = R(P, W) \qquad (5)$$

for

$$R(P, W) = \frac{\lambda PW}{k_1 + W} + \frac{\gamma_r P}{k_2 + P} - \mu W,$$

where $\lambda,\ \gamma_r,\ k_1,\ k_2$ and μ are non-negative constants, but we can justify this process in the range of $0 < \mu \ll 1$ and $0 \le \gamma_r \ll 1$. In fact, multiplying both sides by $e^{\mu t}$, we have for $\tilde{W} = e^{\mu t}W$ that

$$\tilde{W}_t = \frac{\lambda P\tilde{W}}{k_1 + e^{-\mu t}\tilde{W}} + \frac{\gamma_r e^{\mu t}P}{k_2 + P}$$

$$= \frac{\lambda P}{(k_1/\tilde{W}) + e^{-\mu t}} + \frac{\gamma_r P}{k_2 e^{-\mu t} + Pe^{-\mu t}}.$$

Neglecting $e^{-\mu t}$, $k_2e^{-\mu t}$ in the right-hand side, we get that

$$\tilde{W}_t = \frac{\lambda P\tilde{W}}{k_1} + \gamma_r e^{\mu t},$$

or equivalently,

$$W_t + \mu W = \frac{\lambda PW}{k_1} + \gamma_r.$$

This equation may be replaced by W_t =constant$\times PW$ in the case of $W \gg \gamma_r$ and $P \gg \mu$.
Therefore, taking (1), we shall study the asymptotic profile of the solution. Differently from [4], mathematical tool applied here is the theory of dissipative hyperbolic systems. We need several more notations and exact statements are given in the next section.

2 Problem Formulation

In use of the above transformation of taking $\Psi = \log W$, the boundary condition (2) is reduced to

$$\frac{\partial\Psi}{\partial\nu}|_{\partial\Omega} = 0. \qquad (6)$$

In fact, this condition implies $\frac{\partial P}{\partial\nu} = \frac{\partial W}{\partial\nu} = 0$ on $\partial\Omega$, and hence (2) follows. Therefore, we shall construct time global solutions to (4) with (6).

2.1 Reduction Process

For the moment, let us put $\Psi = \gamma f(x,t) + u(t,x)$ and introduce the equation concerning $u = u(x,t)$:

$$u_{tt} = D\Delta u_t$$
$$+\nabla\cdot\left[\frac{aD(\alpha-\beta)e^\Psi}{(e^\Psi+\alpha)(e^\Psi+\beta)}(\gamma f_t + u_t)\nabla(\gamma f + u)\right] \qquad (7)$$
$$= -\gamma(f_{tt} - D\Delta f_t) + \nabla\cdot[\gamma A(f,u)f_t\nabla u]$$
$$+[A(f,u)u_t\nabla u] + \nabla\cdot[A(f,u)\Psi_t\nabla\gamma f]$$

where $A(f,u) = \frac{aD(\alpha-\beta)e^{-\gamma f}e^{-u}}{(1+\alpha e^{-\gamma f}e^{-u})(1+\beta e^{-\gamma f}e^{-u})}$. Therefore, we see that (7) is hyperbolic if $\beta > \alpha$, and henceforth we are concentrated on this case. Namely,

$$\text{(A-0)} \quad a < 0 \quad \text{and } \beta - \alpha > 0$$

and $f = f(x,t)$ satisfies

$$f_{tt} - D\Delta f_t = 0 \qquad \text{with} \qquad \frac{\partial f}{\partial \nu}|_{\partial\Omega} = 0. \tag{8}$$

(6) is reduced to

$$\frac{\partial u}{\partial \nu}|_{\partial\Omega} = 0. \tag{9}$$

Now, we describe more details on the reduced equation. In term of

$$\begin{aligned} P_v[u] = u_{tt} - \nabla \cdot \left[\gamma A(f,v) f_t(x,t) e^{-\gamma f - v} \nabla u\right] \\ -\nabla \cdot \left[e^{-\gamma f - v} A(f,v) u_t \nabla v\right] \\ -D\Delta u_t \ - \nabla \cdot \gamma \left[A(f,v) e^{-\gamma f - v} u_t \nabla f\right], \end{aligned} \tag{10}$$

equation (7) is written as $P_v[u]$

$$= -\gamma(f_{tt} - D\Delta f_t) + \gamma^2 \nabla \cdot \left[A(f,v) e^{-\gamma f - v} f_t \nabla f\right].$$

Therefore, in this case the problem is reduced to

$$(TM)_f \begin{cases} P_u[u] = \ \gamma^2 \nabla \cdot \left[A(f,v) e^{-\gamma f - v} f_t \nabla f\right] \\ \qquad\qquad\qquad\qquad \text{in} \quad \Omega \times (0,\infty) \\ \frac{\partial u}{\partial \nu} = 0 \qquad\qquad\quad \text{on} \quad \partial\Omega \times (0,\infty) \\ u(x,0) = h_0(x), u_t(0,x) = h_1(x) \text{ in } \quad \Omega \\ \bar{u}_1 = \int_\Omega u_t dx = 0. \end{cases}$$

Here, we imposed $\bar{u}_1 = 0$, regarding that

$$\begin{aligned} \partial_t \int_\Omega u_t dx = \int_\Omega \nabla \cdot \left[\gamma A(f,u) f_t e^{-\gamma f} e^{-u} \nabla u\right] \\ +\nabla \cdot \left[e^{-\gamma f} e^{-u} A(f,u) u_t \nabla u\right] \\ +D\Delta u_t + \nabla \cdot \gamma \left[A(f,u) e^{-\gamma f} e^{-u} f_t \nabla f\right] dx \\ = \int_{\partial\Omega} \{\gamma A(f,u) e^{-\gamma f - u} \nabla u \cdot \nu \\ +e^{-\gamma f - u} A(t,u) u_t \nabla u \cdot \nu \\ +D\nabla u_t \cdot \nu + \gamma A(f,u) e^{-\gamma f - u} f_t \nabla f) \cdot \nu\} dS = 0. \end{aligned}$$

Hencefore, we put $\partial_t = \partial/\partial t$,

$$\partial_x^\alpha = \left(\frac{\partial}{\partial x_1}\right)^{\alpha_1} \cdots \left(\frac{\partial}{\partial x_n}\right)^{\alpha_n}$$

and $|\alpha| = \sum_{i=1}^n |\alpha_i|$, where $\alpha = (\alpha_1, \cdots, \alpha_n)$ denotes the multi-index. Then, for given non-negative integer m and small $\varepsilon > 0$ we take $f = f(x,t)$ satisfying
(A-I) $f|_{t=0} = 0$ and for $|\alpha| + 2i \leq 2m$

$$\|\partial_x^\alpha \partial_t^i f\|_{L^\infty(\Omega \times (0,\infty))} < \varepsilon,$$

besides (8). Such f can be given explicitely, and it holds also that

$$\lim_{t \to +\infty} \|f_t(\cdot,t)\|_{L^\infty(\Omega)} = d, \tag{11}$$

where $d = \frac{1}{|\Omega|} \int_\Omega f_t(x,0) dx > 0$.

Remark 1. Levine and Sleeman [4] replaced $\frac{a(\beta-\alpha)W}{(W+\alpha)(W+\beta)}$ by a positive constant, and dealt with $(TM)_f$ for $n = 1$ and $f(t,x) = t$. Our reduction is its generalization, and still works to their simplified system. Discrepancy of the simplification [4] occurs for the solution constructed in each reduction.

2.2 Known results

For the simplified equation proposed by Levin and Sleeman, many results have been known. Levin and Sleeman in [4] constructed the solution of the problem with exponential growth case when $n = 1$ and $a = 1, -1$. They showed the existence of collapse type solution in the case of $n = 1$ and $a = -1$ and blow up solution in the case of $n = 1$ and $a = 1$. For the linear growth case, in [8] Yan, Chen and Liu obtained the collapse solution for $n = 1, 2, ..., a = -1$. Also they proved the existence of a time global solution even if $n = 1$ and $a = 1$. Further they stated there exists a collapse solution in the case of $n = 1, 2, ...$ and $a = -1$ without any poof. The existence of aggregatinon type solution is unknown at this present. Recently K-S[3] dealt with the problem in case $a < 0, n = 1, 2, ...$ and $f(x,t) = t$.

2.3 Our aim

Our aim is to guarantee the existence of time global solution to the problem without Levine and Sleeman's simplification under weakened condition on f and prove that it collapses. Further we deal with the case where γ depends on x.

3 Problem Solution

Now, we introduce functional spaces used in this paper. First, $H^l(\Omega)$ and $H^l((0,\infty)\times\Omega)$ denote the usual Sobolev spaces $W^{l,2}(\Omega)$ and $W^{l,2}(\Omega\times(0,\infty))$ of order l on Ω and $(0,\infty)\times\Omega$, respectively. Next, for functions $h(t,x)$ and $k(t,x)$ defined in $\Omega\times[0,\infty)$, we put that

$$(h,k)(t)=\int_\Omega h(t,x)k(t,x)dx \text{ and}$$

$$\|h\|_l^2(t)=\sum_{|\beta|\le l}\|\partial^\beta h(\cdot,t)\|_{L^2(\Omega)}^2(t),$$

and sometimes we write $\|h\|(t)$ for $\|h\|_0(t)$.
Thus, inner product $p(\ ,\ )$ stands for the L^2

3.1 Main result

Theorem 1 *the initial value* $(h_0,h_1)\in V^{2l+1}(\Omega)\times V^{2l}(\Omega)$ *be given, and the conditions* $(A-0)$, $(A-I)$ *and* (11) *be satisfied with* $\varepsilon>0$ *sufficiently small. Then, we have a unique solution*

$$u=u(t,x)\in\bigcap_{i=0}^{l}C^i\left(0,\infty;H^{2l+1-i}(\Omega)\right)$$

to $(TM)_f$ *and it holds that*

$$\sup_{t\ge0}\ E_{2l}[u](t)\le C(\delta+1), \tag{12}$$

where $C>0$ *is a constant,* $\delta=\|h_0\|_{2l+1}^2+\|h_1\|_{2l}^2$,

$$E_{2l}[u]=\sum_{|\alpha|\le2l}\|\partial^\alpha u_t\|^2$$

$$+\sum_{|\alpha|\le2l}\|\sqrt{\gamma A(f,u)e^{-\gamma f-u}}f_t\partial^\alpha\nabla u\|^2$$

for $\nabla=(\partial/\partial x_1,\cdots,\partial/\partial x_n)$. *Furthermore, we have*

$$\lim_{t\to+\infty}\|u_t\|_{2l}(t)=0.$$

From the above theorem, we get the solution (P,W) to the original system (1)-(3) by $P(x,t)=\gamma f_t(x,t)+u_t(x,t)$ and $W(x,t)=e^{\gamma f(x,t)+u(x,t)}$.

$$\lim_{t\to+\infty}\|P(\cdot,t)-\gamma d\|_{L^\infty(\Omega)}=0 \tag{13}$$

for $d=\frac{1}{|\Omega|}\int_\Omega f_t(x,0)dx>0$. On the other hand, we have

$$P(x,0)=\gamma f_t(x,0)+h_1(x)$$

and it is possible to take $h_1=h_1(x)$ satisfying

$$\|P(\cdot,0)\|_{L^\infty}<\gamma d \text{ or } \|P(\cdot,0)\|_{L^\infty}>\gamma d.$$

Thus, we have the following.

Corollary 1 *If* $(A-0)$ *is satisfied, then there are aggregation and collapse in* $(1)-(3)$.*More precisely,* (13) *holds and consequently, it follows that*

$$\lim_{t\to+\infty}\inf_\Omega W(\cdot,t)=+\infty.$$

3.2 Related result

We can apply the above result to a slightly different type of solution. $\Psi(x,t)=\gamma(x)t+u(x,t)$, where $\gamma(x)>0$ is a smooth function satisfying $\frac{\partial\gamma}{\partial\nu}|_{\partial\Omega}=0$. In this case, we have from (7) that

$$u_{tt}=D\Delta u_t$$

$$+\nabla\cdot\left[\frac{aD(\alpha-\beta)e^\Psi}{(e^\Psi+\alpha)(e^\Psi+\beta)}(\gamma(x)+u_t)\nabla u\right].$$

Therefore, writing γ for $\gamma(x)$, we obtain

$$u_{tt}=D\Delta\gamma+D\Delta u_t$$

$$+\nabla\cdot[\gamma A(\gamma(x),u)\nabla u]+\nabla\cdot[A(\gamma(x),u)u_t\nabla u].$$

where $A(\gamma(x),u)=$

$$\frac{aD(\beta-\alpha)}{(1+\alpha e^{-\gamma(x)t}e^{-u})(1+\beta e^{-\gamma(x)t}e^{-u})}.$$

We take an integer $M\ge[n/2]+1$ and parameter $\varepsilon,\gamma_0>0$ satisfying

(A-II) $\gamma(x)\ge\gamma_0>0,\ \gamma(x)\in C^\infty(\bar\Omega)$ and

$$\sum_{0<|\alpha|\le M}|\partial_x^\alpha\gamma|<\varepsilon.$$

Then, letting

$$P_v[u] = u_{tt} - \nabla \cdot \left[\gamma A(\gamma(x), v) e^{-\gamma(x)t} e^{-v} \nabla u\right]$$

$$-\nabla \cdot \left[e^{-\gamma(x)t} e^{-u} A(\gamma(x), u) v_t \nabla u\right] - D\Delta u_t,$$

we can reduce the problem to

$$(TM)_\gamma \begin{cases} P_v[u] = D\Delta\gamma(x) & \text{in} \quad \Omega \times (0, \infty) \\ \frac{\partial u}{\partial \nu} = 0 & \text{on} \quad \partial\Omega \times (0, \infty) \\ u(x, 0) = h_0(x), u_t(0, x) = h_1(x) & \text{on} \quad \Omega \\ \bar{u}_1 = \int_\Omega u_t dx = 0. \end{cases}$$

Here, it is imposed that $\bar{u}_1 = 0$ in $(TM)_\gamma$ rom the same reason as in the case (1).

Theorem 2 *Let l be an integer in $2l \geq [n/2] + 1$, the initial value $(h_0, h_1) \in V^{2l+1}(\Omega) \times V^{2l}(\Omega)$ be given, and the conditions $(A-0)$ and $(A-II)$ be satisfied with $\varepsilon > 0$ and large $\gamma_0 > 0$. Then, if $\delta = \|h_0\|^2_{2l+1} + \|h_1\|^2_{2l}$ is small, we have a unique solution*

$$u = u(x,t) \in \bigcap_{i=0}^{l} C^i \left(0, \infty; H^{2l+1-i}(\Omega)\right)$$

to $(TM)_\gamma$ and it holds that

$$E_{2l}[u](t) \leq C(\delta + \varepsilon t) \qquad (t \geq 0),$$

where $C > 0$ is a constant.

3.3 Outline of proof

Now, we describe the method to prove those results briefly. In each reduction, we take the following iteration scheme and derive energy estimates.

$$\begin{cases} P_{u_i}[u_{i+1}] = \gamma^2 \nabla(A(f, u_i) e^{-\gamma f} e^{-u_i} f_t \nabla f), \\ \qquad\qquad \text{in} \quad \Omega \times (0, \infty) \\ \frac{\partial}{\partial \nu} u_{i+1}|_{\partial\Omega} = 0 \qquad \text{on} \quad \partial\Omega \times (0, \infty) \\ u_{i+1}(x, 0) = \sum_{j=1}^{i+1} h_j \varphi_j(x), \\ u_{i+1t}(x, 0) = \sum_{j=1}^{i+1} h'_j \varphi_j(x) \end{cases}$$

where $u_i = \sum_{j=1}^{i} f_{ij}(t)\varphi_j(x)$ for $i \geq j$, $h_0(x) = \sum_{j=1}^{\infty} h_j \varphi_j(x)$, $h_1(x) = \sum_{j=1}^{\infty} h'_j \varphi_j(x)$. We determin $f_{ij}(t)$ by the solution of the following system of ordinary equations with initial data. For $j = 1, \cdots, i+1$

$$\begin{cases} (P_i[u_{i+1}], \varphi_j) = \gamma^2(\nabla(A(f, u_i) e^{-\gamma f - u_i} f_t \nabla f), \varphi_j), \\ f_{i+1j}(0) = h_{i+1}, \quad f_{i+1jt}(0) = h'_{i+1}. \end{cases}$$

In the first case of $(TM)_f$, we have a crucial obsevation of the degeneracy of the coefficients of $P_u[u]$ as $t \to +\infty$. This means that the term involving derivatives with respect to x must be dealt with carefully. Actually, differently from Kawashima and Shibata [2], exponential decay property of the solution to this system is not expected.(See Remark 2 below.) The second observation comes from the growth property of the nonlinear term e^{-u}. Fortunately, the degeneracy of the coefficients of the equation cancels this growth, and we can derive the energy estimates. This enables us to get the solution by considering $P_i[u_{i+1}] - P_{i-1}[u_i]$ and standard argument for $u_{i+1} - u_i = w_i$. $(TM)_\gamma$ is more diffiecult because of the term $\Delta\gamma(x)$ in the right hand side of the equation. Actually, this is the critical case to derive the energy estimate by the method employed for $(TM)_f$. Applying the same method as derived the energy estimate of $(TM)_f$, we obtain only estimate of which the right hand side increases as t increases. Here, we need to make use of degeneracy of the coefficients much more carefully than the previous case. Consequently, this reduction does not work for the simplified system of [4].

Remark 2 In [2], Kawashima and Shibata studied a quasilinear dissipative hyperbolic system arising in the thoery of viscoelasticity, and showed exponential decay of the energy. In contract with that system, the strict hyperbolicity of $P_u[u]$ is violated as $t \to \infty$ and it will be difficult to derive such a fast decay in our systems. Our reductions have similar structures, and we shall describe about $(TM)_f$ in the most detail.

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