Mathematical analysis and stability of a chemotaxis model with logistic term

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Summary

In this paper we study a nonlinear system of differential equations arising in chemotaxis. The system consists of a PDE that describes the evolution of a population and an ODE which models the concentration of a chemical substance. We study the number of steady states under suitable assumptions, the existence of one global solution to the evolution problem in terms of weak solutions and the stability of the steady states.

 $\underline{KEY\ WORDS}$: chemotaxis; stability of stationary solutions; parabolic equations; reinforced random walks

1 Introduction

Chemotaxis is the ability of microorganisms to respond to chemical signals by moving along the gradient of the chemical substance, either toward the higher concentration (positive taxis) or away from it (negative taxis).

Over the last few decades a rich variety of mathematical models for studying chemotaxis has appeared. One of the first was presented by Keller and Segel [7], [8]. It describes the density distribution of a type of bacteria "Dyctyostelium discoideum" (denoted by p) and a chemical concentration, w, in a coupled system of partial differential equations

$$\frac{\partial p}{\partial t} = \Delta p - \operatorname{div} (p\chi(w)\nabla w),$$
$$0 = \Delta w + (p-1).$$

After this study, there has been great interest in the analysis of similar models (see [2] - [6] and reference there).

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In the last fifteen years another model, called *reinforced random walks*, has been developed to understand the mechanism of chemotaxis (see [12], [9] and reference there). Chemotaxis also appears in many other phenomena, such us for instance in the formation of capillary blood by endothelial cells. Recently, Anderson and Chaplain [1] and Levine, Sleeman and Nilsen-Hamilton [10] have introduced several models for angiogenesis. These authors study the growth of tumors based on the analysis of the relevant biochemical processes and the methodology of reinforced random walks.

Friedman and Tello [4] study the models proposed in Levine and Sleeman [9] and Othmer and Stevens [12] under suitable conditions in chemotactic coefficient and production terms.

Fontelos, Friedman and Hu [3] study the model proposed in Levine, Sleeman and Nilsen-Hamilton [10]. This system of equations does not have a logistic growth term and nonconstant steady states appear (see [3]). Fontelos *et al* [3] prove the existence of global solutions in the space $C_{x,t}^{2+\beta,1+\frac{1}{\beta}}$ and analyze the asymptotic behavior of the solutions and their stability. They consider that the production of the chemical substance depends on p and x. Therefore the production term is nondecreasing in w (essential assumption in the proof of the results of this paper).

In this paper we consider the system

$$\frac{\partial p}{\partial t} = \operatorname{div}(d\nabla p - p\chi(w)\nabla w) + rp(N-p) \quad x \in \Omega \ t > 0,$$
(1)

$$\frac{\partial w}{\partial t} = h(p, w) \quad x \in \Omega \ t > 0, \tag{2}$$

where d is the diffusion constant, $\chi(w)$ is the chemotactic sensitivity and r, N are positive constants. h(p, w) represents the production of the chemical substance by the living organisms. Depending on the process, $\chi(w)$ and h(p, w) can take different forms. The boundary conditions for p are

$$\frac{\partial p}{\partial n} - p\chi(w)\frac{\partial w}{\partial n} = 0 \quad x \in \partial\Omega \ t > 0, \tag{3}$$

where $\frac{\partial p}{\partial n}$ is the outward normal derivative and initial conditions are

$$p(x,0) = p_0(x), \quad w(x,0) = w_0(x) \quad x \in \Omega.$$
 (4)

As in Reference [11] we consider the logistic growth term rp(N-p) in the equation which models the density of the population.

Myerscough, Maini and Painter [11] performed a numerical study of the steady states in case that w satisfies an elliptic equation of the type

$$-\Delta w = h(p, w) \qquad x \in \Omega.$$

They focus on the role of boundary conditions and find spatially non-constant solutions for different boundary conditions and some nonlinear functions h.

We assume throughout the paper that the positive constants $\bar{q}, \bar{p}, \bar{w}$ exist and satisfy

$$\bar{q} > \max_{x \in \Omega} \{ p_0(x), N \}, \qquad \bar{w} > \max_{x \in \Omega} \{ w_0(x) \}, \qquad \bar{p} = \bar{q} exp\{ \int_0^w \chi(w) dw \}$$
(5)

$$h(\bar{p}, \bar{w}) = 0$$
 $h(0, 0) = 0.$ (6)

 χ and h satisfy

$$\chi, h \text{ belong to } C^2, \text{ for } 0 \le p \le \bar{p}, \qquad 0 \le w \le \bar{w},$$
(7)

$$\frac{\partial h}{\partial p} > 0 \quad \text{if} \quad 0 \le p \le \bar{p}, \qquad 0 \le w \le \bar{w}, \tag{8}$$

$$p\chi \frac{\partial h}{\partial p} + \frac{\partial h}{\partial w} < 0 \quad \text{if} \quad 0 \le p \le \bar{p}, \qquad 0 \le w \le \bar{w}, \tag{9}$$

$$\chi(w) > 0, \qquad \text{for } 0 \le w \le \bar{w}. \tag{10}$$

 $\Omega \subset \mathbb{R}^n \ (n \leq 3)$ is an open and bounded domain with $\partial \Omega \in C^{2+\beta}$. (11)

Assumption (10) means that the organisms move toward the higher concentration of the chemical substance.

We also assume that the initial data satisfy

$$0 \le p_0(x) \in H^1(\Omega) \cap L^{\infty}(\Omega) \qquad 0 \le w_0(x) \in H^2(\Omega) \quad \text{and}$$

$$\frac{\partial p_0}{\partial n} = \frac{\partial w_0}{\partial n} = 0 \quad \text{on } \partial\Omega.$$
(12)

Assumptions (7)-(10) are satisfied, for instance,

$$h(p,w) = \mu p - w \qquad \chi = constant, \tag{13}$$

$$h(p,w) = \mu p - \frac{w}{\alpha + w} \qquad \chi = \frac{\beta + w}{\alpha + w}$$
(14)

$$h(p,w) = \mu p \frac{w}{\alpha + w} - \nu w \qquad \chi = \frac{\gamma}{\beta + w}$$
(15)

for a range of parameters and some initial data. Several researchers in this area are particularly interested in the case (15) where $\chi(w)$ appears in the literature in the form $ln(\phi(w))'$ for $\phi(w) = (\beta + w)^{\gamma}$. In case (15) assumptions (5)-(9) hold and Theorems 1.1-1.3 can be applied if \bar{p} satisfies $N < \bar{p} < \frac{\nu\beta\alpha}{\gamma\bar{w}}$ where \bar{p} and \bar{w} are defined by (5), (6).

Solutions to (1)-(4) which are biologically meaningful must satisfy

$$0 \le p(x,t) < \infty, \ 0 \le w(x,t) < \infty.$$
(16)

Set $\Omega_T = \Omega \times (0, T)$ $(0 < T < \infty)$. We will assume throughout the paper that d = 1. The main results of this work are the following theorems:

Theorem 1.1 Under the assumptions (7)-(11), the steady states (p_*, w_*) of (1)-(4) satisfying (16) are constant and given by

 $(0,0) \quad or \quad (N,\Psi(N)) \tag{17}$

where $\Psi(N)$ is the unique solution to $h(N, \Psi(N)) = 0$.

Theorem 1.2 Under the assumptions (7)-(11), there exists a unique global solution (p, w) to (1)-(4) satisfying

$$p \in L^2(0,T:H^2(\Omega)) \cap L^\infty(\Omega_T) \quad w \in L^\infty(0,T:H^2(\Omega)) \cap L^\infty(\Omega_T)$$

for any $T < \infty$.

Theorem 1.3 If the initial values (p_0, w_0) satisfy

$$\sup_{x\in\Omega} |p_0(x) - N| + \sup_{x\in\Omega} |w_0(x) - \Psi(N)| \le \epsilon,$$
(18)

where ϵ is small enough and (7)-(11) hold. Then, the solution (p, w) to (1)-(4) has the asymptotic behavior

$$p \to N, \quad w \to \Psi(N) \quad when \ t \to \infty \quad in \ L^s(\Omega)$$

for any $s \leq \infty$ if n = 1, $s < \infty$ if n = 2 and s < 6 if n = 3.

Assumptions (8) and (9) define the behavior of the solution. Following Levine and Sleeman [9] the equation (1)-(4) can be considered in the "Hodograph plane": applying the *implicit function theorem* to equation (2) and as a result of (8) and (9) we obtain

$$p = \psi(w_t, w)$$
 $\frac{\partial \psi}{\partial w_t} = \left(\frac{\partial h}{\partial p}\right)^{-1}$ $\frac{\partial \psi}{\partial w} = -\frac{\partial h}{\partial w} \left(\frac{\partial h}{\partial p}\right)^{-1}$

If $\Omega = (0, L) \subset \mathbb{R}$, substituting it in (1) it results

$$\psi_{w_t}w_{tt} + \psi_w w_t - (\psi_{w_t}w_{xxt} + \psi_w w_{xx} + 2\psi_{ww_t}w_{xw}) +$$

$$\chi \psi w_{xx} + \chi \psi_{w_t} w_{xt} w_x + (\chi \psi_w + \chi' \psi) (w_x)^2 = r \psi (N - \psi).$$

Consider now the second order operator

$$\mathcal{L}(w) := w_{tt}\psi_{w_t} + (-\psi_w + \chi\psi)w_{xx} + 2bw_{xt}$$

where $b = \frac{1}{2}(-2\psi_{ww_t}w_x + \chi\psi_{w_t}w_x)$. Then equations (1), (2) become

$$\mathcal{L}(w) = k(w, w_x, w_t, w_{xxt}, \psi, \psi_w, \psi_{w_t}, \psi_{ww_t}).$$

$$(19)$$

Since the discriminant

$$b^{2} - \psi_{w_{t}}(-\psi_{w} + \chi\psi) = b^{2} - \left[\frac{\partial h}{\partial p}\right]^{-1} \left(\frac{\partial h}{\partial w}\left(\frac{\partial h}{\partial p}\right)^{-1} + \chi\psi\right) = b^{2} - \left[\frac{\partial h}{\partial p}\right]^{-2} \left(\frac{\partial h}{\partial w} + \chi\psi\frac{\partial h}{\partial p}\right)$$

is strictly positive (by (9)) \mathcal{L} is clearly an hyperbolic operator. Assumption (9) implies that h is strictly increasing in w. If (9) is substituted by $p\chi \frac{\partial h}{\partial p} + \frac{\partial h}{\partial w} > 0$, there are no control on the type of the differential operator \mathcal{L} , and it could be parabolic, elliptic or hyperbolic. Then the arguments used to prove Lemma 3.2 can not be applied and blow-up could occur (as in case r = 0 for some values of the parameters, see [9] for details).

2 On the steady states

2.1 Proof of Theorem 1.1

Let us consider the solutions to the stationary problem

$$\operatorname{div}(\nabla p - p\chi(w)\nabla w) + rp(N - p) = 0 \quad x \in \Omega,$$
(20)

$$h(p,w) = 0 \quad x \in \Omega. \tag{21}$$

Since $h_p > 0$, $h_w < 0$ (by (8) and (9)), we can apply the implicit function theorem to solve the equation (20) in the form $p = \Psi(w)$ and obtain

$$\Psi'(w) = -\frac{h_w}{h_p} > 0 \quad \text{and} \quad \Psi(0) = 0.$$
(22)

Let (p_*, w_*) be a stationary solution, then $h(p_*, w_*) = 0$ and $p_* = \Psi(w_*)$. Substituting this in (1) we get

$$-\operatorname{div}\{\frac{1}{h_p}(h_w + p_*\chi(w_*)h_p)\nabla w_*\} + r\Psi(w_*)(N - \Psi(w_*)) = 0 \quad \text{in } \Omega$$
(23)

with boundary conditions

$$\Psi'(w_*)\frac{\partial w_*}{\partial n} - p_*\chi(w_*)\frac{\partial w_*}{\partial n} = \frac{-1}{h_p}(h_w + p_*\chi(w_*)h_p)\frac{\partial w_*}{\partial n} = 0,$$

i.e.

$$\frac{\partial w_*}{\partial n} = 0 \quad x \in \partial\Omega. \tag{24}$$

Lemma 2.1 Any solution w_* to (23), (24) satisfying (16) belongs to $C^1(\Omega)$.

Proof: Let us consider the function Φ defined by

$$\Phi(w_*) = \int_0^{w_*} \frac{1}{h_p(\Psi(s), s)} (h_w(\Psi(s), s) + \Psi(s)\chi(s)h_p(\Psi(s), s)) ds$$

By (7), (8) and (9) we know that $\Phi \in C^1$ and $\Phi' < 0$. Substituting this into (23) we get (assuming (16))

$$-\Delta\Phi(w_*)\in L^\infty(\Omega),$$

and then $\Phi(w_*) \in W^{2,\infty}(\Omega) \subset C^1(\Omega)$. By regularity of Φ we get the desired result. Extra regularity can be obtained if χ and h have additional regularity.

Let us consider the *positive part* function defined by

$$(s)_{+} = \begin{cases} s & \text{if } s > 0\\ 0 & \text{otherwise.} \end{cases}$$

Taking $(N - \Psi(w_*))_+$ as test function in (23), we obtain

$$\int_{\Omega} \frac{1}{h_p} (h_w + p_* \chi(w_*) h_p) \frac{1}{-\Psi'} [\nabla (N - \Psi(w_*))_+]^2 d\sigma + \int_{\Omega} r \Psi(w_*) (N - \Psi(w_*))_+^2 d\sigma = 0.$$

By (22), (8) and (9) we get

$$\int_{\Omega} r\Psi(w_*)(N-\Psi(w_*))_+^2 d\sigma = 0,$$

hence, by (22) and (16), w_* satisfies

$$\Psi(w_*) = 0 \qquad \text{or} \quad \Psi(w_*) \ge N. \tag{25}$$

Integrating (23), (24) we get

$$\int_{\Omega} \Psi(w_*)(N - \Psi(w_*))d\sigma = 0.$$

By Lemma 2.1, continuity of Ψ and (25), we deduce the desired result.

2.2 On infinitely many steady states (a simple example)

If assumption (9) is not satisfied then infinitely many solutions to (20), (21) can occur.

Let us consider a simple case where χ is a positive constant and $h(p, w) = \mu p - w$ for $\frac{\mu\chi N}{2} = 1$. Then $w = \mu p$, and p satisfies

$$\begin{cases} -\operatorname{div}\{\nabla p - \chi \mu p \nabla p\} = rp(N-p) & x \in \Omega\\ \frac{\partial p}{\partial n} = 0 & x \in \partial \Omega \end{cases}$$

Let us define $u = p - \frac{1}{N}p^2$ which satisfies the well known problem

$$\begin{cases} -\Delta u = rNu & x \in \Omega, \\ \frac{\partial u}{\partial n} = 0 & x \in \partial\Omega. \end{cases}$$

Let $rN = \lambda_m$ $(m \in \mathbb{N})$ be an eigenvalue of the Laplacian operator $-\Delta$ with zero flux on the boundary and u_m be the eigenfunction associated to λ_m . Then

$$p = N\left(\frac{1}{2} + \frac{1}{2}\left(1 - 4\frac{u_m}{CN}\right)^{\frac{1}{2}}\right)$$
(26)

is a solution to the problem for any $C \ge C^* := \frac{4}{N} \max_{x \in \Omega} \{|u_m|\}$. Notice that p > 0.

3 Existence of solution (proof of Theorem 1.2)

We introduce the function

$$f(w) = exp[\int_0^w \chi(s)ds]$$
(27)

and the unknown q defined by

$$p = f(w)q. (28)$$

In terms of q and w the system (1)-(3) becomes

$$\mathcal{L}q \equiv \frac{\partial q}{\partial t} - \Delta q - \chi(w)\nabla w \cdot \nabla q =$$

$$-q\chi(w)h(qf(w), w) + rq(N - qf(w)) \quad x \in \Omega \quad t > 0,$$
(29)

$$\frac{\partial w}{\partial t} = h(qf(w), w) \quad x \in \Omega \quad t > 0$$
(30)

and

$$\frac{\partial q}{\partial n} = 0 \quad x \in \partial \Omega \quad t > 0.$$
(31)

The initial conditions (4) become

$$q(x,0) = q_0(x) = \frac{p_0(x)}{f(w_0(x))} \quad w(0,x) = w_0(x).$$
(32)

Notice that

$$f(w) \cdot \mathcal{L}q = f(w)\frac{\partial q}{\partial t} - \operatorname{div}\{f(w)\nabla q\}.$$

Denote the right hand side of (29) by g(q, w).

Definition 3.1 $q \in L^2(0, T : H^2(\Omega)) \cap H^1(0, T : L^2(\Omega))$ and $w \in L^{\infty}(0, T : L^2(\Omega))$ is a weak solution to (29)-(32) if

$$\int \int_{\Omega_T} f(w) q_t \eta d\sigma dt + \int \int_{\Omega_T} f(w) \nabla q \nabla \eta d\sigma dt = \int \int_{\Omega_T} f(w) g(q, w) \eta d\sigma dt$$
(33)

for any $\eta \in L^2(0, T : H^1(\Omega))$ and

$$w_t = h(qf(w), w)$$
 a.e. $0 < t < T \ x \in \Omega$

In order to establish the existence of a global solution, we consider the sequence q_i defined as the unique solution to (29), (31) where $w = w_i$ and w_i satisfies

$$\frac{\partial w_i}{\partial t} = h(q_{i-1}f(w_i), w_i) \quad x \in \Omega \quad 0 < t < T, \qquad w(x, 0) = w_0(x).$$

Let us denote q_i by q and w_i by w, then

Lemma 3.1 $q \ge 0$ and $0 \le w \le \overline{w}$.

Proof: By the maximum principle we get $q \ge 0$. Since $\frac{\partial h}{\partial q} = f(w) \frac{\partial h}{\partial p} > 0$, we have $h(0, w) \le w_t \le h(\bar{q}, w)$. By (7) and (6) we conclude the result. \Box

Lemma 3.2

$$q(x,t) \le \bar{q}.\tag{34}$$

Proof: Let us take $f(w)(q - \bar{q})_+$ as test function in (29), then

$$\frac{1}{2} \int_{\Omega} f(w)(q-\bar{q})_{+}^{2} d\sigma dt + \frac{1}{2} \int \int_{\Omega_{T}} f'(w) w_{t}(q-\bar{q})_{+}^{2} d\sigma dt +$$

 $\int \int_{\Omega_T} f(w) (\nabla (q - \bar{q})_+)^2 d\sigma dt = \int \int_{\Omega_T} f(w) g(q, w) (q - \bar{q})_+^2 d\sigma dt + \int_{\Omega} f(w_0) (q_0 - \bar{q})_+^2 d\sigma dt.$ Since $g(q, w)(q - \bar{q})_+ \leq 0$ provided that $0 \leq w \leq \bar{w}$ we get

$$\int_{\Omega} f(w)(q-\bar{q})_{+}^{2} d\sigma dt \leq C \int \int_{\Omega_{T}} (q-\bar{q})_{+}^{2} d\sigma dt$$

By Gronwall's Lemma we prove the lemma.

Provided that $0 \le q < \overline{q}$ and $0 \le w < \overline{w}$, we show the following *a priori* estimates:

Lemma 3.3

$$\int_{\Omega} q^2 d\sigma + \int \int_{\Omega_T} |\nabla q|^2 d\sigma dt + \int_{\Omega} |\nabla w|^2 d\sigma \le C_0(T+1).$$

Proof: From (2) we have

$$\nabla w_t = f(w)h_p \nabla q + (h_p f(w)q\chi(w) + h_w) \nabla w.$$
(35)

Taking the scalar product with ∇w , integrating over Ω_T and using (8), (9) we find that

$$\int_{\Omega} |\nabla w|^2 d\sigma \le C_1 \int \int_{\Omega_T} |\nabla q|^2 d\sigma dt + \int_{\Omega} |\nabla w_0|^2 d\sigma.$$
(36)

Taking f(w)q as test function in (29) and integrating by parts, it follows

$$\frac{d}{dt}\frac{1}{2}\int_{\Omega}q^{2}f(w)d\sigma + \int_{\Omega}f(w)|\nabla q|^{2}d\sigma = -\frac{1}{2}\int_{\Omega}q^{2}f(w)\chi(w)h(qf(w),w)d\sigma + \int_{\Omega}q^{2}f(w)(N-qf(w))d\sigma \leq C_{2}$$

and then

$$\frac{1}{2}\int_{\Omega}q^2f(w)d\sigma + \int\int_{\Omega_T}f(w)|\nabla q|^2d\sigma dt \le C_2T + \frac{1}{2}\int_{\Omega}q_0^2f(w_0)d\sigma.$$

Since $w \ge 0$, by (27) and (10) we get

$$\int_{\Omega} q^2 d\sigma + \int \int_{\Omega_T} |\nabla q|^2 d\sigma dt \le C_2(T+1).$$
(37)

Substituting (37) into (36) we prove the lemma.

Lemma 3.4

$$\int \int_{\Omega_T} q_t^2 d\sigma dt + \int_{\Omega} |\nabla q|^2 d\sigma \le C_3(T+1)$$

Proof: Let us take $f(w)q_t$ as test function in (29), we obtain

$$\int_{\Omega} f(w)|q_t|^2 d\sigma - \int_{\Omega} (\operatorname{div} f(w)\nabla q) q_t d\sigma = \int_{\Omega} f(w)g(q,w)q_t d\sigma.$$
(38)

Since

$$-\int_{\Omega} (\operatorname{div} f(w) \nabla q) q_t d\sigma = \frac{1}{2} \int_{\Omega} f(w) \frac{\partial}{\partial t} |\nabla q|^2 d\sigma = \frac{\partial}{\partial t} \frac{1}{2} \int_{\Omega} f(w) |\nabla q|^2 d\sigma - \frac{1}{2} \int_{\Omega} f(w) \chi(w) w_t |\nabla q|^2 d\sigma = \frac{\partial}{\partial t} \frac{1}{2} \int_{\Omega} f(w) |\nabla q|^2 d\sigma - \frac{1}{2} \int_{\Omega} f(w) \chi(w) h(qf(w), w) |\nabla q|^2 d\sigma$$

and

$$\int_{\Omega} f(w)g(q,w)q_t d\sigma \leq \frac{1}{2} \int_{\Omega} f(w)|q_t|^2 d\sigma + \frac{1}{2} \int_{\Omega} f(w)g^2(q,w)d\sigma$$

then, substituting it into (38) we find

$$\int_{\Omega} f(w) |q_t|^2 d\sigma + \frac{\partial}{\partial t} \frac{1}{2} \int_{\Omega} f(w) |\nabla q|^2 d\sigma - \frac{1}{2} \int_{\Omega} f(w) \chi(w) h(qf(w), w) |\nabla q|^2 d\sigma \le C.$$

Integrate with respect to time to get

$$\int \int_{\Omega_T} f(w) |q_t|^2 d\sigma + \int_{\Omega} f(w) |\nabla q|^2 d\sigma \leq C_5 [\int \int_{\Omega_T} |\nabla q|^2 d\sigma dt + \int_{\Omega} f(w_0) |\nabla q_0|^2 d\sigma + T].$$

By selection of f and Lemma 3.3 we obtain the desired result. \Box

By selection of f and Lemma 3.3 we obtain the desired result.

Lemma 3.5 q belongs to $L^2(0, T : H^2(\Omega))$.

Proof: By the previous lemma we know that $\frac{1}{f(w)} \operatorname{div} \{f(w) \nabla q\}$ belongs to $L^2(\Omega_T)$ i.e.

$$\int \int_{\Omega_T} \frac{1}{f^2(w)} (\operatorname{div}\{f(w)\nabla q\})^2 d\sigma dt = \int \int_{\Omega_T} (\frac{1}{f^2(w)} (\nabla f(w) \cdot \nabla q)^2 + (\Delta q)^2) d\sigma dt + \int \int_{\Omega_T} \frac{2}{f(w)} (\Delta q) (\nabla f(w) \cdot \nabla q) d\sigma dt \le C_3 (T+1).$$
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$$\int \int_{\Omega_T} \frac{1}{f(w)} (\Delta q) (\nabla f(w) \cdot \nabla q) d\sigma dt \le \frac{C_3}{2} (T+1).$$
(39)

Let us take $-\Delta q$ as test function in (29) then:

$$\int \int_{\Omega_T} (-\Delta q) q_t d\sigma dt + \int \int_{\Omega_T} (\Delta q)^2 d\sigma dt + \int \int_{\Omega_T} \frac{1}{f(w)} (\Delta q) (\nabla f(w) \cdot \nabla q) d\sigma dt = \int \int_{\Omega_T} g(q, w) (-\Delta q) d\sigma dt \le \frac{T|\Omega|}{2} (\max\{g(q, w)\})^2 + \frac{1}{2} \int \int_{\Omega_T} (\Delta q)^2 d\sigma dt.$$

Then, integrating by parts on the left hand side of the equation and as a result of (39)we conclude

$$\frac{1}{2} \int_{\Omega} |\nabla q|^2 d\sigma \Big|_0^T + \frac{1}{2} \int \int_{\Omega_T} (\Delta q)^2 d\sigma dt \le C_4 (T+1)$$

emma.

which proves the lemma.

Lemma 3.6 $\int_{\Omega} |\nabla w|^4 d\sigma \leq C_5(T+1).$

Proof: As a consequence of Lemma 3.5 and (29) we obtain that $\nabla q \cdot \nabla w$ belongs to $L^2(\Omega_T)$ (using (10) and (7)). Multiplying by $|\nabla w|^2 \nabla w$ in (35) and integrating over Ω_T we conclude the claim of the lemma.

Lemma 3.7 $w \in L^{\infty}(0, T : H^{2}(\Omega)).$

Proof: By (30) we know that

$$\Delta w_t = h_q \Delta q + h_{qq} |\nabla q|^2 + 2h_{qw} \nabla q \cdot \nabla w h_{ww} |\nabla w|^2 + h_w \Delta w \tag{40}$$

Multiplying by Δw in (40) and applying Hölder inequality, one gets in view of (9)

$$\frac{\partial}{\partial t}\frac{1}{2}|\Delta w|^2 \le \frac{h_q^2}{|h_w|}|\Delta q|^2 + \frac{h_{qq}^2}{|h_w|}|\nabla q|^4 + 4\frac{h_{qw}^2}{|h_w|}|\nabla q|^2|\nabla w|^2 + \frac{h_{ww}^2}{|h_w|}|\nabla w|^4.$$

Integrating over Ω_T we conclude the lemma.

Proof of Theorem 1.2

Let us consider the sequence $\{p_i = q_i f(w_i)\}_{i=1,\infty}$. From Lemma 3.1, 3.2 and 3.4

 p_i are uniformly bounded in $H^1(0, T : L^2(\Omega)) \cap L^\infty(\Omega_T)$ (41)

and by Lemma 3.5 and 3.6

$$p_i$$
 are uniformly bounded in $L^2(0, T : H^2(\Omega))$. (42)

Let us consider

$$\tilde{p} = p_i - p_j,$$
 $\tilde{p}_{-1} = p_{i-1} - p_{j-1},$ $\gamma(w) = \int_0^w \chi(s) ds$ and $\tilde{\gamma} = \gamma(w_i) - \gamma(w_j).$

Then $(\tilde{p}, \tilde{\gamma})$ satisfy

$$\frac{\partial \tilde{p}}{\partial t} - \Delta \tilde{p} + \operatorname{div}\{\tilde{p}\nabla\gamma(w_i)\} + \operatorname{div}\{p_j\nabla\tilde{\gamma}\} = \tilde{p}(1 - (p_i + p_j)) \quad \text{in } \Omega_T$$
(43)

$$\frac{\partial \tilde{\gamma}}{\partial t} = \chi(w_i)h(p_{i-1}, w_i) - \chi(w_j)h(p_{j-1}, w_j) \quad \text{in } \Omega_T.$$
(44)

Take $f(w_i)\tilde{p}$ as test function in (43), then

$$\begin{split} \frac{1}{2} \int_{\Omega} f(w_i) \tilde{p}^2 d\sigma \Big|_T &- \frac{1}{2} \int \int_{\Omega_T} f'(w_i) \frac{\partial w_i}{\partial t} \tilde{p}^2 d\sigma dt + \int \int_{\Omega_T} f(w_i) |\nabla \tilde{p}|^2 d\sigma dt + \\ &\int \int_{\Omega_T} \tilde{p} \nabla \tilde{p} \nabla f(w_i) d\sigma dt - \int \int_{\Omega_T} \tilde{p}^2 \nabla \gamma(w_i) \nabla f(w_i) d\sigma dt \\ &- \int \int_{\Omega_T} f(w_i) \tilde{p} \nabla \gamma(w_i) \nabla \tilde{p} d\sigma dt - \int \int_{\Omega_T} f(w_i) p_j \nabla \tilde{\gamma} \nabla \tilde{p} d\sigma dt \\ &- \int \int_{\Omega_T} p_j \tilde{p} \nabla \tilde{\gamma} \nabla f(w_i) d\sigma dt = \int \int_{\Omega_T} \tilde{p} f(w_i) (\hat{g}(p_i, w_i) - g(p_i, w_i)) d\sigma dt. \end{split}$$

Since $\left|\frac{\partial}{\partial t}w_i\right| \leq C$, $1 \leq f(w_i) \leq C$ and $\nabla f(w_i) = f(w_i)\nabla\gamma(w_i)$, we obtain

$$\frac{1}{2} \int_{\Omega} \tilde{p}^2 d\sigma \Big|_T + \int \int_{\Omega_T} |\nabla \tilde{p}|^2 d\sigma dt \leq$$

$$\bar{p} \int \int_{\Omega_T} |\nabla \tilde{\gamma}| |\nabla \tilde{p}| d\sigma dt + \int \int_{\Omega_T} |\tilde{p}| |\nabla \tilde{\gamma}| |\nabla \gamma(w_i)| d\sigma dt + k_0 \int \int_{\Omega_T} \tilde{p}^2 + \tilde{\gamma}^2 d\sigma dt.$$

$$\tag{45}$$

Let us consider the integral

$$\bar{p} \int \int_{\Omega_T} |\nabla \tilde{\gamma}| |\nabla \tilde{p}| d\sigma \le \bar{p}^2 \|\nabla \tilde{\gamma}\|_{L^2(\Omega_T)}^2 + \frac{1}{4} \|\nabla \tilde{p}\|_{L^2(\Omega_T)}^2$$

and

$$\int \int_{\Omega_T} |\tilde{p}| |\nabla \gamma(w_i)| |\nabla \tilde{\gamma}| d\sigma dt \le \|\tilde{p}\|_{L^2(0,T:L^4(\Omega))} \|\nabla \gamma(w_i)\|_{L^\infty(0,T:L^4(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le C_{1,1} \|\tilde{p}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le C_{1,1} \|\tilde{p}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le C_{1,1} \|\tilde{p}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le C_{1,1} \|\tilde{p}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le C_{1,1} \|\tilde{p}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le C_{1,1} \|\tilde{p}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le C_{1,1} \|\tilde{p}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(\Omega)} \|\nabla \tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \|\nabla \tilde{\gamma}\|_{L^2(\Omega)} \|\nabla \tilde{\gamma}\|_{L^2(\Omega)}$$

$$k_1 \|\tilde{p}\|_{L^2(0,T:H^1(\Omega))} \|\nabla\tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))} \le \frac{1}{4} \|\tilde{p}\|_{L^2(0,T:H^1(\Omega))}^2 + k_1^2 \|\nabla\tilde{\gamma}\|_{L^2(0,T:L^2(\Omega))}^2$$

Substituting it in (45) we get

$$\frac{1}{2} \int_{\Omega} \tilde{p}^2 d\sigma \Big|_T + \frac{1}{2} \int \int_{\Omega_T} |\nabla \tilde{p}|^2 d\sigma dt \le k_2 (\int \int_{\Omega_T} \tilde{p}^2 + \tilde{\gamma}^2 d\sigma dt + \int \int_{\Omega_T} |\nabla \tilde{\gamma}|^2 d\sigma dt).$$
(46)

Notice that, as below, if $t \leq T$ we obtain

$$\frac{1}{2} \int_{\Omega} \tilde{p}^2 d\sigma \Big|_t \le k_2 (\int_0^T \int_{\Omega} \tilde{p}^2 + \tilde{\gamma}^2 d\sigma dt + \int_0^T \int_{\Omega} |\nabla \tilde{\gamma}|^2 d\sigma dt)$$

and integrating again in time we get

$$\frac{1}{2} \int \int_{\Omega_T} \tilde{p}^2 d\sigma dt \le Tk_2 (\int \int_{\Omega_T} \tilde{p}^2 + \tilde{\gamma}^2 d\sigma dt + \int \int_{\Omega_T} |\nabla \tilde{\gamma}|^2 d\sigma dt).$$

Taking $T < \frac{1}{4k_2}$ it results

$$\int \int_{\Omega_T} \tilde{p}^2 d\sigma dt \le 4T k_2 (\int \int_{\Omega_T} \tilde{\gamma}^2 d\sigma dt + \int \int_{\Omega_T} |\nabla \tilde{\gamma}|^2 d\sigma dt).$$
(47)

Then, by (46) and (47) \tilde{p} satisfies

$$\int \int_{\Omega_T} \tilde{p}^2 d\sigma dt + \int \int_{\Omega_T} |\nabla \tilde{p}|^2 d\sigma dt \le (4Tk_2 + 2k_2(1 + 4Tk_2)) \int \int_{\Omega_T} (\tilde{\gamma}^2 + |\nabla \tilde{\gamma}|^2) d\sigma dt.$$
(48)

On the other hand, $\tilde{\gamma}$ satisfies:

$$\frac{\partial}{\partial t}\tilde{\gamma} = h_p|_{\hat{p},\hat{w}}\,\tilde{p}_{-1} + h_\gamma|_{\hat{p},\hat{w}}\,\tilde{\gamma}$$

where $p_i \leq \hat{p} \leq p_j$ or $p_i \geq \hat{p} \geq p_j$ and $w_i \leq \hat{w} \leq w_j$ or $w_i \geq \hat{w} \geq w_j$ and $h_{\gamma} = \frac{h_w}{\gamma'} < 0$.

Multiply by $\tilde{\gamma}$, integrate and apply Hölder inequality to get

$$\int_{\Omega} \tilde{\gamma}^2 d\sigma|_t \le k_3 \int \int_{\Omega_T} \tilde{p}_{-1}^2 d\sigma dt + \frac{1}{2} \int \int_{\Omega_T} h_{\gamma} \tilde{\gamma}^2 d\sigma dt$$

i.e.

$$\int \int_{\Omega_T} \tilde{\gamma}^2 d\sigma dt \le k_3 T \int \int_{\Omega_T} \tilde{p}_{-1}^2 d\sigma dt + \frac{T}{2} \int \int_{\Omega_T} h_\gamma \tilde{\gamma}^2 d\sigma dt.$$
(49)

Since $\nabla \tilde{\gamma}$ satisfies

$$\frac{\partial}{\partial t} \nabla \tilde{\gamma} = h_p |_{\hat{p}, \hat{\gamma}} \nabla \tilde{p}_{-1} + h_{pp} |_{\hat{p}, \hat{\gamma}} \tilde{p}_{-1} \nabla \hat{p} + h_{p\gamma} |_{\hat{p}, \hat{\gamma}} \left(\tilde{p}_{-1} \nabla \hat{\gamma} + \tilde{\gamma} \nabla \hat{p} \right) + h_{\gamma} |_{\hat{p}, \hat{\gamma}} \nabla \tilde{\gamma} + h_{\gamma\gamma} |_{\hat{p}, \hat{\gamma}} \tilde{\gamma} \nabla \hat{\gamma}$$

$$(50)$$

taking $\nabla \tilde{\gamma}$ as test function and by Hölder inequality we get

$$\int_{\Omega} |\nabla \tilde{\gamma}|^2 d\sigma dt|_t \le k_4 (\|\tilde{p}_{-1}\|_{L^2(0,T:H^1(\Omega))}^2 + \|\tilde{\gamma}\|_{L^2(0,T:H^1(\Omega))}^2)$$

and

$$\int \int_{\Omega_T} |\nabla \tilde{\gamma}|^2 d\sigma dt \le Tk_4(\|\tilde{p}_{-1}\|_{L^2(0,T;H^1(\Omega))}^2 + \|\tilde{\gamma}\|_{L^2(0,T;H^1(\Omega))}^2).$$
(51)

Adding (49) to (51) we get

$$\|\tilde{\gamma}\|_{L^{2}(0,T:H^{1}(\Omega))}^{2} \leq Tk_{5}(\|\tilde{p}_{-1}\|_{L^{2}(0,T:H^{1}(\Omega))}^{2} + \|\tilde{\gamma}\|_{L^{2}(0,T:H^{1}(\Omega))}^{2}).$$

Taking $T \leq \frac{1}{2k_5}$ it results

$$\int \int_{\Omega_T} \tilde{\gamma}^2 d\sigma dt + \int \int_{\Omega_T} |\nabla \tilde{\gamma}|^2 d\sigma dt \le 2T k_5 \|\tilde{p}_{-1}\|_{L^2(0,T:H^1(\Omega))}^2.$$
(52)

Substitute (52) into (48)

$$\int \int_{\Omega_T} \tilde{p}^2 d\sigma dt + \int \int_{\Omega_T} |\nabla \tilde{p}|^2 d\sigma dt \le (4Tk_2 + 2k_2(1 + 4Tk_2))2Tk_5 \|\tilde{p}_{-1}\|_{L^2(0,T:H^1(\Omega))}^2.$$

Choose T small enough, then

$$\|\tilde{p}\|_{L^{2}(0,T:H^{1}(\Omega))} \leq \frac{1}{2} \|\tilde{p}_{-1}\|_{L^{2}(0,T:H^{1}(\Omega))}.$$
(53)

Then p_i is a Cauchy sequence satisfying $p_i \to p$ in $L^2(0, T : H^1(\Omega))$. By (52) we get the same result for w_i and $\gamma(w_i)$. Since $\{p_i, \gamma(w_i)\}_{i=1}^{\infty}$ are uniformly bounded in

$$[L^{2}(0,T:H^{2}(\Omega)) \cap H^{1}(0,T:L^{2}(\Omega)) \cap L^{\infty}(\Omega_{T})]^{2},$$

there exists a subsequence $(p_{ij}, \gamma(w_{ij}))$ such that $(p_{ij}, \gamma(w_{ij})) \to (p, \gamma(w))$ in $[L^2(0, T : W^{1,s}(\Omega))]^2$ for any $s \leq \infty$ if $n = 1, s < \infty$ if n = 2 and $s < \frac{2n}{n-2}$ if n = 3 and weakly in $[H^1(0, T : L^2(\Omega))]^2$. By (50) and a priori estimates, we obtain that $\gamma(w_{ij}) \to \gamma(w)$ in $L^r(0, T : H^1(\Omega))$ for arbitrary $r < \infty$.

Taking limits in the weak formulation

$$\int \int_{\Omega_T} \frac{\partial}{\partial t} p_{ij} \eta d\sigma dt + \int \int_{\Omega_T} \nabla p_{ij} \cdot \nabla \eta d\sigma dt =$$
$$\int \int_{\Omega_T} p_{ij} \nabla \gamma(w_{ij}) \cdot \nabla \eta d\sigma dt + \int \int_{\Omega_T} \hat{g}(p_{ij}, w_{ij}) \eta d\sigma dt$$
$$\frac{\partial}{\partial t} w_{ij} = h(p_{ij}, w_{ij})$$

we get the existence of weak solutions for small T. Repeating the process, starting now from T, we conclude the existence of solutions for arbitrary T > 0 by lemmata 3.1-3.7.

Remark 3.1 Uniqueness of solutions is a consequence of (53).

4 On stability (proof of Theorem 1.3)

Taking p - N as test function in (1) we get

$$\frac{1}{2} \int_{\Omega} (p-N)^2 d\sigma |_0^T + \int \int_{\Omega_T} |\nabla p|^2 d\sigma dt =$$
$$\int \int_{\Omega_T} p\chi(w) \nabla p \cdot \nabla w d\sigma dt + r \int \int_{\Omega_T} p(p-N)^2 d\sigma dt$$

Since $\nabla w_t = h_p \nabla p + h_w \nabla w$, taking scalar product with $\gamma \nabla w$ (for a positive constant γ) and integrating over Ω_T (as in [4]) we find that

$$\frac{\gamma}{2} \int_{\Omega} |\nabla w|^2 d\sigma|_0^T = \gamma \int \int_{\Omega_T} h_w |\nabla w|^2 d\sigma dt + \gamma \int \int_{\Omega_T} h_p \nabla p \cdot \nabla w d\sigma dt.$$

Adding both expressions one concludes

$$\frac{1}{2} \int_{\Omega} (p-N)^2 d\sigma \Big|_T + \int \int_{\Omega_T} |\nabla p^2 d\sigma dt + \frac{\gamma}{2} \int_{\Omega} |\nabla w|^2 d\sigma \Big|_T$$
$$-\gamma \int \int_{\Omega_T} h_w |\nabla w|^2 d\sigma dt = r \int \int_{\Omega_T} p(p-N)^2 d\sigma dt + \int \int_{\Omega_T} (p\chi(w) + \gamma h_p) \nabla p \cdot \nabla w d\sigma dt + O(1).$$

By Schwarz's inequality, the last integral is bounded by

$$(1-\delta) \int \int_{\Omega_T} |\nabla p|^2 d\sigma dt + \frac{1}{4(1-\delta)} \int \int_{\Omega_T} (p\chi(w) + \gamma h_p)^2 |\nabla w|^2 d\sigma dt$$

for any $1 > \delta > 0$ and $\gamma > 0$.

Consider the quadratic equation in γ :

$$(\gamma h_p + p\chi(w))^2 + 4\gamma h_w = 0$$

and denote its two roots by

$$\gamma_{1,2}(p,w) = \frac{2}{h_p^2} \{ (-2h_w - h_p p\chi(w)) \pm [(2h_w + h_p p\chi(w))^2 - (p\chi(w))^2 h_p^2]^{\frac{1}{2}} \}.$$

By assumption (9) there exists $\gamma > 0$ such that

$$(\gamma h_p + p\chi(w))^2 < 4\gamma h_w.$$

Therefore

$$\begin{split} \int_{\Omega} (p-N)^2 d\sigma \Big|_T + r \int \int_{\Omega_T} p(p-N)^2 d\sigma dt + \int_{\Omega} |\nabla w|^2 d\sigma \Big|_T + \\ \delta \int \int_{\Omega_T} |\nabla p|^2 d\sigma dt + \epsilon \int \int_{\Omega_T} |\nabla w|^2 d\sigma dt \leq O(1) \end{split}$$

which implies

$$\int \int_{\Omega_{\infty}} |\nabla p|^2 d\sigma dt + \int \int_{\Omega_{\infty}} |\nabla w|^2 d\sigma dt \le C.$$

Integrating the equation we get

$$\frac{\partial}{\partial t} \int_{\Omega} p d\sigma = r \left(N \int_{\Omega} p d\sigma - \int_{\Omega} p^2 d\sigma \right)$$

which implies that p = 0 is unstable, and we deduce that

 $p \longrightarrow N$ and $w \longrightarrow \Psi(N)$ in $L^{s}(\Omega)$

where $s = \infty$ if n = 1, $s < \infty$ if n = 2 and s < 6 if n = 3.

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References

- [1] ANDERSON ARA, CHAPLAIN MAJ. Continuous and discrete mathematical models of tumor-induced angiogenesis, *Bull. Math. Biology* 1998; **60**: 857-899.
- [2] CORRIAS L, PERTHAME B, ZAAG H. A chemotaxis model motivated by angiogenesis. R. Math. Acad. Sci. Paris 2003; 336: 141-146.
- [3] FONTELOS MA, FRIEDMAN A, HU B. Mathematical analysis of a model for the initiation of angiogenesis. *SIAM Math. Anal.* 2002; **33**: 1330-1355.
- [4] FRIEDMAN A, TELLO JI. Stability of solutions of chemotaxis equations in reinforced random walks. J. Math. Anal. Appl. 2002; 272: 138-163.

- [5] HERRERO MA, VELÁZQUEZ JJL. A blow-up mechanism for a chemotaxis model. Ann. Scuola. Norm. Sup. Pisa. Cl. Sci. 1997; 24 (4): 633-683.
- [6] JÄGER W, LUCKHAUS S. On explosions of solutions to a system of partial differential equations modeling chemotaxis. *Trans. Amer. Math. Soc.* 1992; **329**: 819-824.
- [7] KELLER EF, SEGEL LA. Initiation of slime mold aggregation viewed as an instability. J. Theoret. Biol. 1970; 26: 399-415.
- [8] KELLER EF, SEGEL LA. A model for chemotaxis. J. Theoret. Biol. 1971; 30: 225-234.
- [9] LEVINE HA, SLEEMAN BP. A system of reaction diffusion equations arising in the theory of reinforced random walks. *SIAM J. Appl. Math.* 1997; **57**: 683-730.
- [10] LEVINE HA, SLEEMAN BP, NILSEN-HAMILTON N. A mathematical modeling for the roles of pericytes and macrophages in the initiation of angiogenesis I. The role of protease inhibitors in preventing angiogenesis. *Mathematical Biosciences*. 2000; 168: 75-115.
- [11] MYERSCOUGH MR, MAINI PK, PAINTER J. Pattern formation in a generalized chemotactic model. Bull. Math. Biol. 1998; 60: 1-26.
- [12] OTHMER HG, STEVENS A. Aggregation, blowup, and collapse: The ABC's of taxis in reinforced random walks. *SIAM J. Appl. Math.* 1997 **57**: 1044-1081.