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Existence of solutions of a parabolic system modeling particles dynamics with aggregation effects.

Michèle GRILLOT¹, Philippe GRILLOT¹ and Simona MANCINI ¹

Abstract : In this paper, we are interested in a parabolic system resulting from a problem of cell adhesion in biology. The model describes a protein dynamics and is given by a system of degenerate reaction diffusion equations, only one equation contains a diffusion term. The unknown couple (u, v) represents the distribution law of the free and linked proteins. Under sufficient conditions, we prove the existence of solution (u, v) of this system.

Keys words : degenerate parabolic system, existence of solutions, semi-linear system.

1 Introduction

The study and modeling of the adhesion process between cells is an active and complex research subject both in biology and in mathematics, and has implications with the tumoral growth and the formation of neuronal connections in the embryo (see for example [3], [4], [5],[6], [7] and [8]). In this paper, we analytically study a mathematical model describing the formation of cadherin aggregates underlying the cells adhesion. We consider two cells, one of which has fixed cadherins and the second one lying on the first one and having freely moving cadherins. The adhesion takes place at the cells surfaces and is governed by the cis and trans links between the cadherins of the cells. In order to simplify the problem and inspiring us by experimental situations, we represent the problem by a flat surface on which are distributed the targets, i.e. the cadherins of the fixed cell to which the cadherins of the second cell may link. These targets are fixed, whereas the cadherins on the second cell diffuse on the surface. When a cadherin get fixed on a target, it stops to diffuse, and the probability of other cadherins to be fixed on close targets increases. Fixed cadherines may also broke their link and diffuse again.

¹ Mathématiques - Analyse, Probabilités, Modélisation - Orléans (MAPMO)

CNRS : UMR6628 Université d'Orléans - Bâtiment de mathématiques - Route de Chartres - B.P. 6759 - 45067 Orléans cedex 2 - France - (33)2 38 49 48 92 - fax : (33)2 38 41 72 05 - michele.grillot@univ-orleans.fr - philippe.grillot@univ-orleans.fr - simona.mancini@univ-orleans.fr

Finally, since our goal is the modeling of the formation of cadherin aggregates, we neglect the association of these aggregates with the actin cytoskeleton filaments, although this is one of the main phenomena leading to the migration of the cells.

We consider the cadherins as particles and we describe their spatio-temporal dynamics on the flat surface by a mathematical model at the mesoscopic scale. The unknown is the couple (u, v) representing the particle distributions of the diffusing particles, $u = u(x, t)$, and of the fixed ones, $v = v(x, t)$. Considering the above biological description, the studied model consists of a system of two partial differential equations, in particular of two reaction-diffusion equations. We note that since one of the the family of particles are fixed in space, the corresponding diffusion coefficient is null. Hence we are dealing with a degenerate system of reaction-diffusion equations. The reaction term is composed of two main terms : one is proportional to the probability of a fixed particle to broke his link with a target, the other term is proportional to the number of free targets (i.e. those targets which have no particle linked to) and to the probability of a free particle to link to a target. This last term is given by an affine function depending on the distribution of linked particles. In fact, has said in the biology description, there is an aggregation effect and the probability of a particle to get linked to a target is larger if close to the target there already is a linked particle.

Obviously, a large number of parabolic, degenerate systems or not, were already studied, we can cite [2] and as well as the references therein.

The main result in this paper is the existence of solutions to the degenerate reaction-diffusion system. We discuss also the existence of solutions to the stationary problem and to the homogeneous in space problem. Our results shows that the chosen reaction term is not appropriate to recover the biology results shown by experiments. In fact, as shown in experiments, on the cell surface there are regions without aggregates and the distribution function for the linked particles of our model tends, at equilibrium, to occupy the whole cell surface without leaving empty regions. Nevertheless, the origin of this kind of aggregate distributions on the surface is not well understood in biology : it is not clear if this is due to the actin cytoscheleton or to the presence of other molecules preventing the occupation of the whole surface by the cadherin aggregates. Other reaction terms will be studied in future works, in particular a local aggregation term considering a convolution of the distribution function u with a Van-der-Pool type potential function.

The paper is organized as follows. In section 2 we detail the kinetic model of the cadherins dynamics and the main result. Section 3 is devoted to the proofs.

2 Description of the model and main result

In the chosen modeling, the unknown is the law of distribution (u, v) of both the unlinked and fixed cadherins, treated here as particles. For instance, given a bounded domain $\Omega \subset \mathbb{R}^2$, $u = u(x, t)$ represents the probability to find an unlinked particle at time t in the position $x \in \Omega$, and $v = v(x, t)$ the probability to find a fixed particle at time t in the position $x \in \Omega$. We assume the targets density to be constant in time and space, and we denote it by ρ . Hence, it must be $0 < \rho \leq 1$. We note that there can't be more fixed particles than targets, and that the critical case $v = \rho$ holds only if a fixed particle never unlinks from the target. Thus we have, for all time $t \geq 0$:

$$0 \leq u \quad \text{and} \quad 0 \leq v < \rho. \quad (1)$$

We recall, that the unlinked particles diffuse and may link to the targets, whereas the fixed ones don't diffuse and may unlink of a target. Their distribution function u and v must then satisfy the following degenerate system of reaction-diffusion equations:

$$\begin{cases} \partial_t u - \sigma \Delta u = -Q(u, v) \\ \partial_t v = Q(u, v) \end{cases} \quad (2)$$

in $(0, +\infty) \times \Omega$, where $\sigma > 0$ is the diffusion coefficient of the order of the unit. The function Q is the reaction term which describes how particles pass from a unlinked state to a fixed state. As explained in section 1, the gain term of Q , the term governing the linking of particles to targets, is proportional to the density of free targets $\rho - v$, to the density of free particles u and is a non-decreasing function ψ of the density of locally fixed particles. The loss term of Q , the term governing the unlinking of particles from targets, is proportional to the density of fixed particles. This leads us to the following choice :

$$Q(u, v) = (\rho - v)\psi(v)u - \varepsilon v \quad (3)$$

where $0 < \varepsilon \ll 1$ is the constant rate of the link break. The function ψ describes the gregarious effect : the probability of a particle to be linked is larger when there already are fixed particles in its neighborhood. The form of ψ will be

$$\psi(v) = a_0 + a_1 v,$$

where a_0 is the probability of a particle to get fixed if no other particle is fixed in its neighborhood. We choose $a_0 > 0$ and ε of the same order, and $a_1 \gg a_0$.

Let us summarize here the conditions of the parameters which are used afterward :

$$\begin{cases} 0 < \rho, \sigma, a_0, a_1, \varepsilon < 1 \\ a_0 < \rho a_1. \end{cases} \quad (4)$$

We complete the model by the initial condition $(u_0, v_0) = (u(0, x), v(0, x))$ representing the initial distribution of both unlinked and fixed particles. We assume here that the corresponding initial density of particles is normalized:

$$\int_{\Omega} u_0 + v_0 \, dx = 1$$

and that there is no flux for the free particles on the border of the domain $\partial\Omega$:

$$\frac{\partial u}{\partial \nu}(t, x) = 0. \quad (5)$$

Hence we can easily deduce the particle density conservation in time of the system. Indeed, since $\partial_t(u + v) - \sigma\Delta u = 0$, applying the Green formula, we get:

$$\frac{d}{dt} \int_{\Omega} (u + v) dx - \sigma \int_{\partial\Omega} \frac{\partial u}{\partial \nu} d\sigma = 0,$$

and thanks to (5) we conclude that:

$$\int_{\Omega} u + v \, dx = 1 \quad (6)$$

for all times $t > 0$.

2.1 Stationary solutions

We begin by searching solutions to the stationary problem associated to (2)-(5), which simplifies to, for $x \in \Omega$:

$$\begin{cases} \Delta u = 0 \\ Q(u, v) = 0 \end{cases} \quad (7)$$

These solutions are interesting since they give the stable states of the problem, i.e. the equilibrium solutions to which the solution of (2) should converge in large times. We have the following:

Proposition 1 *The positive solutions (u, v) of problem (7) with boundary conditions (5) satisfy :*

$$\begin{cases} u = C \\ v = |\Omega|^{-1} - C = \frac{Ca_1\rho - Ca_0 - \varepsilon + \sqrt{(Ca_1\rho - Ca_0 - \varepsilon)^2 + 4C^2\rho a_0 a_1}}{2Ca_1}. \end{cases}$$

which implies that C is solution of a third degree equation.

Proof :

Multiplying the first equation by u , integrating on Ω and applying the Green formula, we obtain that u must be constant in Ω , $u(x) = C$ for all $x \in \Omega$. (6) implies $v = |\Omega|^{-1} - C$. Hence, from the second equation in (7), we obtain that v must be a (constant) solution of the following second order equation:

$$Ca_1v^2 - (C\rho a_1 - Ca_0 - \varepsilon)v - C\rho a_0 = 0.$$

If $u = C = 0$ (i.e. there are no unlinked particles), then the only solution $v = 0$ in Ω . If $u = C > 0$, then

$$v = \frac{Ca_1\rho - Ca_0 - \varepsilon \pm \sqrt{(Ca_1\rho - Ca_0 - \varepsilon)^2 + 4C^2\rho a_0 a_1}}{2Ca_1}.$$

The discriminant being strictly positive there exist two possible solutions for v . But, the minus sign choice in the expression for v , yields to a negative value for v , which is not admissible, see (1). Then the only possible solution is the one with the sign plus. ■

We seek now to non trivial stationary solutions satisfying the normalization condition (6), assuming also that the domain Ω is normalized : $|\Omega| = 1$. We have the following :

Proposition 2 *Let (u, v) be a non trivial stationary solution to (7), with boundary condition (5), and let $|\Omega| = 1$. If the parameters a_0, a_1, ε and ρ satisfy (4) then the unique admissible stationary solution satisfying the normalization condition (6) is given by $(1 - \hat{v}, \hat{v})$ with \hat{v} the solution of*

$$(\rho - v)(a_0 + a_1v)(1 - v) - \varepsilon v = 0, \quad (8)$$

such that $\hat{v} \in]0, \rho]$.

Proof :

Consider a solution (u, v) to the stationary problem and $|\Omega| = 1$, then since (u, v) is constant and must satisfy (6), it must be $u + v = 1$. Hence, replacing $v = 1 - u$ in the equation $Q(u, v) = 0$, we easily obtain that v must be a solution of (8).

Assuming that $\varepsilon = 0$, it is easily seen that equation (8) admits three solutions :

$$v_1 = \rho, \quad v_2 = -a_0/a_1, \quad v_3 = 1.$$

Recalling that all the parameters are positive, hypothesis (4), yields that $v_2 < 0$, and therefore it is not an admissible physical solution. Analogously, since from (1) $v_3 \leq \rho < 1$, then v_3 is not physically admissible. So the only admissible solution is $v_1 = \rho$.

If now ε continuously grows from 0 to ∞ , the three solutions to (8) will have the following behavior (see Figure 1) : solution v_1 continuously move from ρ to 0, v_2 goes from $-a_0/a_1$ to $-\infty$ and v_3 from 1 to ∞ . Hence, again the only physically admissible solution to (8) is v_1 , belonging to the interval $]0, \rho]$. ■

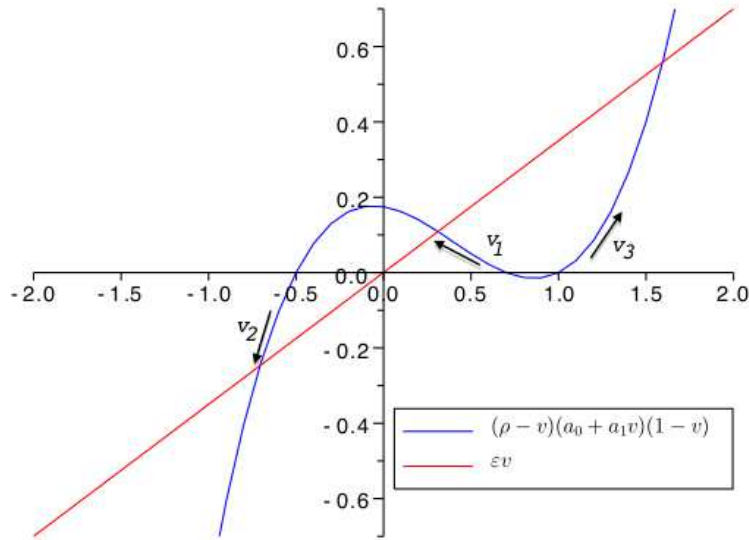


Figure 1: The third order polynome $(\rho - v)(a_0 + a_1v)(1 - v)$ and the straight line εv with $\rho = 0.7$, $a_0 = 0.25$, $a_1 = 0.5$ and $\varepsilon = 0.35$.

The evolution of the solution (u, v) towards the unique admissible steady state are also shown in Figure 2. The initial data being defined by :

$$u_0(x) = 1 - v_0(x), \quad v_0(x) = 0.4 + (0.2 \sin(3\pi x) \cos(3\pi y)).$$

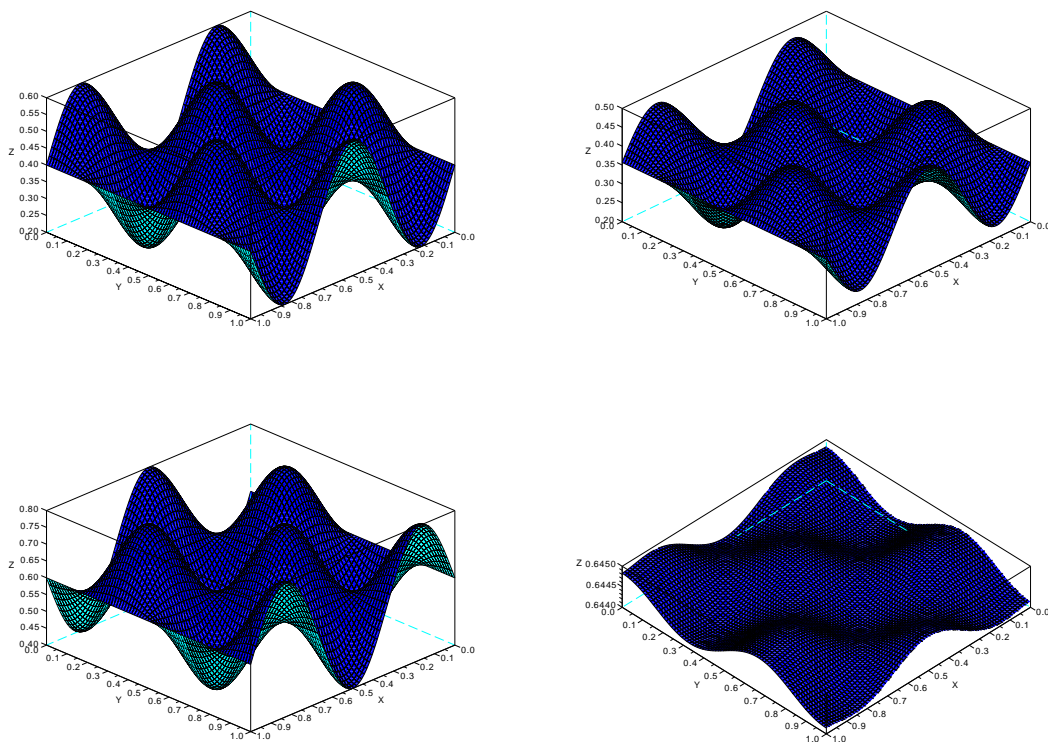


Figure 2: The initial data $v_0(x)$ (upper left) and $u_0(x)$ (bottom left) and the solutions $v(T, x)$ (upper right) and $u(T, x)$ (bottom right) computed with $\rho = 0.7$, $a_0 = 0.25$, $a_1 = 0.5$ and $\varepsilon = 0.35$, $\sigma = 1$ and $T = 1$.

Given the following parameters : $\rho = 0.7$, $a_0 = 0.25$, $a_1 = 0.5$ and $\varepsilon = 0.35$ the admissible solution v_1 to the third order equation (8) is:

$$v_1 = 0.3107435.$$

Computing the absolute error between v_1 and the mean value $v_m(t)$ of $v(t, x)$, defined by:

$$v_m(t) = \frac{\max(v(t, \cdot)) + \min(v(t, \cdot))}{2} \quad (9)$$

shows the time convergence of the maximum, minimum of $v(t, \cdot)$, and of the mean value $v_m(t)$ towards v_1 , see Figure 3. The computation has been stopped when the maximum between the absolute errors $|v_1 - \max(v)|$, $|v_1 - \min(v)|$ and $|v_1 - v_m|$ is smaller than 10^{-3} . A linear regression study of the three black curves shows that the convergences are exponential with a standard deviation of the order of 10^{-2} .

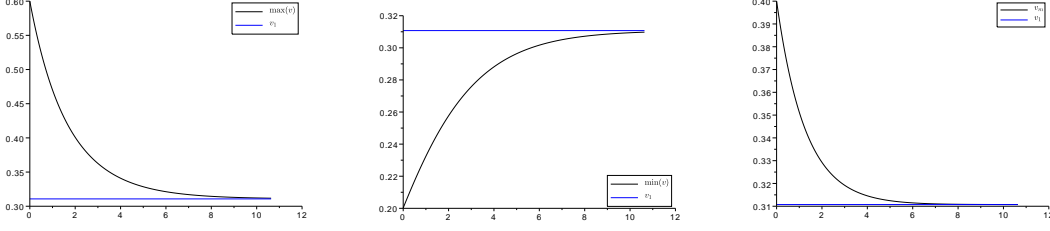


Figure 3: Convergence in time (black line) of the maximum (left), the minimum (middle) of $v(t, \cdot)$, and of mean value $v_m(t)$ defined by (9) (right) towards the value v_1 (blue line) for the parameters $\rho = 0.7$, $a_0 = 0.25$, $a_1 = 0.5$, $\varepsilon = 0.35$ and $\sigma = 1$.

2.2 Main theorem

Note that system (2) doesn't satisfy classical comparison principle and the unicity problem of the solutions stays open. Our main result is the following existence result :

Theorem 1 *Assume (4) and let $T > 0$. Consider two non-negative functions f and g in $C^0(\bar{\Omega})$ such that*

$$0 \leq f(x) \leq \lambda \quad \text{and} \quad 0 \leq \sup_{\bar{\Omega}} g(x) < \mu \quad (10)$$

for all $x \in \bar{\Omega}$ and where

$$\lambda = \frac{\varepsilon}{a_1 \rho - a_0} \quad \text{and} \quad \mu = \sqrt{\rho \frac{a_0}{a_1}}. \quad (11)$$

Then there exists two non-negative functions $u \in W^{1,p}((0, T) \times \Omega)$, $p > 1$ and $v \in L^\infty((0, T) \times \Omega)$, solutions of the following system

$$\left\{ \begin{array}{l} \partial_t u - \sigma \Delta u = -Q(u, v) \quad \text{in } (0, T) \times \Omega \\ \partial_t v = Q(u, v) \quad \text{in } (0, T) \times \Omega \\ \frac{\partial u}{\partial \nu} = 0 \quad \text{on } (0, T) \times \partial \Omega \\ u(0, \cdot) = f \quad \text{and} \quad v(0, \cdot) = g \quad \text{in } \Omega \end{array} \right. \quad (12)$$

where Q is defined by

$$Q(r, s) = (\rho - s)(a_0 + a_1 s)r - \varepsilon s. \quad (13)$$

The proof of the theorem is detailed in the next section. It is done proving that there exists two sequences of function $(u_n)_{n \geq 0}$ and $(v_n)_{n \geq 0}$ converging to two function u and v which are solutions to (12).

3 Proof of existence

In this part, we proof the theorem. Let $T > 0$ and assume (4), (10) and (11). We introduce two sequences $(u_n)_{n \geq 0}$ and $(v_n)_{n \geq 0}$ defined by

$$\begin{cases} u_0(t, x) = f(x) \\ v_0(t, x) = g(x) \end{cases} \quad (14)$$

for all $(t, x) \in [0, T] \times \bar{\Omega}$ and for all $n \geq 0$:

$$\begin{cases} \partial_t u_{n+1} - \sigma \Delta u_{n+1} = -Q(u_{n+1}, v_n) & \text{in } (0, T) \times \Omega \\ \partial_t v_{n+1} = Q(u_n, v_{n+1}) & \text{in } (0, T) \times \Omega \\ \frac{\partial u_{n+1}}{\partial \nu} = 0 & \text{on } (0, T) \times \partial \Omega \\ u_{n+1}(0, \cdot) = f \quad \text{and} \quad v_{n+1}(0, \cdot) = g & \text{in } \Omega \end{cases} \quad (15)$$

Note that those functions well exist and are continuous, the first equation is a linear heat equation with a continuous coefficient $(\rho - v_n)(a_0 + a_1 v_n)$ and the second equation is a Riccati equation in time.

We'll prove that $(u_n)_{n \geq 0}$ and $(v_n)_{n \geq 0}$ are two Cauchy sequences, thus converging to two function u and v , which are solution to (12). We first need some technical results.

Proposition 3 *Under the assumptions of the theorem both functions u_n and v_n defined by (14) and (15) satisfy*

$$0 \leq u_n(t, x) \leq \lambda \quad (16)$$

and

$$0 \leq v_n(t, x) \leq \mu \quad (17)$$

for all $(t, x) \in (0, T) \times \Omega$.

Proof :

We prove it by recurrence. For $n = 0$, this is (10).

Assume (16) and (17) for a fixed n . Then we have from (15) :

$$\partial_t(u_{n+1} - \lambda) - \sigma \Delta(u_{n+1} - \lambda) = Q(\lambda, v_n) - Q(u_{n+1}, v_n) - Q(\lambda, v_n) \quad (18)$$

in $(0, T) \times \Omega$. Multiplying (18) by $(u_{n+1} - \lambda)^+$ and integrating on Ω , we obtain for all $t \in (0, T)$:

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\Omega} ((u_{n+1} - \lambda)^+)^2 dx + \sigma \int_{\Omega} |\nabla(u_{n+1} - \lambda)^+|^2 dx = \\ & \int_{\Omega} \left[\int_{u_{n+1}}^{\lambda} \frac{\partial Q}{\partial r}(\alpha, v_n) d\alpha \right] (u_{n+1} - \lambda)^+ dx - \int_{\Omega} Q(\lambda, v_n)(u_{n+1} - \lambda)^+ dx. \end{aligned} \quad (19)$$

From (13) we have $\frac{\partial Q}{\partial r}(r, s) = (\rho - s)(a_0 + a_1 s)$. Moreover from (17), (11) and (4), we obtain $v_n \leq \mu \leq \rho$. Because of (4) and (17) we also have $a_0 + a_1 v_n \geq 0$. We deduce that $\frac{\partial Q}{\partial r}(\alpha, v_n) \geq 0$ and that the first term of the second member of (19) is non-positive. On the other hand, from (13) and (11) :

$$\begin{aligned} Q(\lambda, v_n) &= -a_1 \lambda v_n^2 + (a_1 \lambda \rho - a_0 \lambda - \varepsilon) v_n + \rho a_0 \lambda \\ &= \lambda a_1 \left(\frac{a_0}{a_1} \rho - v_n^2 \right) \\ &= \lambda a_1 (\mu^2 - v_n^2) \end{aligned} \quad (20)$$

which is non-negative because of (17). We deduce from (19) that :

$$\frac{1}{2} \frac{d}{dt} \int_{\Omega} ((u_{n+1} - \lambda)^+)^2 dx + \sigma \int_{\Omega} |\nabla(u_{n+1} - \lambda)^+|^2 dx \leq 0 \quad (21)$$

for all $t \in (0, T)$ and using (15) and (10), we derive $u_{n+1} \leq \lambda$ in $(0, T) \times \Omega$. In the same way, multiplying by $(-u_{n+1}^+)$ the equation on u_{n+1} in (15) and integrating on Ω , we obtain:

$$\begin{aligned} & \frac{1}{2} \frac{d}{dt} \int_{\Omega} ((-u_{n+1}^+)^2) dx + \sigma \int_{\Omega} |\nabla(-u_{n+1}^+)|^2 dx \\ &= \int_{\Omega} \left(- \int_{u_{n+1}}^0 \frac{\partial Q}{\partial r}(\alpha, v_n) d\alpha \right) (-u_{n+1}^+) dx + \int_{\Omega} Q(0, v_n)(-u_{n+1}^+) dx \end{aligned} \quad (22)$$

for all $t \in (0, T)$, and we obtain $u_{n+1} \geq 0$ in $(0, T) \times \Omega$ which ends the proof of (16) for $n + 1$.

Now we prove (17) for $n + 1$. We have from (15) :

$$\partial_t(v_{n+1} - \mu) = Q(u_n, v_{n+1}) - Q(u_n, \mu) + Q(u_n, \mu) \quad (23)$$

in $(0, T) \times \Omega$. Multiplying (23) by $(v_{n+1} - \mu)^+$ and integrating on Ω , we obtain for all $t \in (0, T)$:

$$\frac{1}{2} \frac{d}{dt} \int_{\Omega} ((v_{n+1} - \mu)^+)^2 dx \quad (24)$$

$$= \int_{\Omega} \left[\int_{\mu}^{v_{n+1}} \frac{\partial Q}{\partial s}(u_n, \alpha) d\alpha \right] (v_{n+1} - \mu)^+ dx + \int_{\Omega} Q(u_n, \mu)(v_{n+1} - \mu)^+ dx.$$

But definition (13) implies

$$\frac{\partial Q}{\partial s}(r, s) = -a_0 r - 2a_1 r s + a_1 \rho r - \varepsilon \leq -(a_0 - \rho a_1) r - \varepsilon. \quad (25)$$

From (4), we have $\frac{\partial Q}{\partial s}(r, s) \leq 0$ when $r \leq \frac{\varepsilon}{\rho a_1 - a_0}$ which is the case for u_n because of (11) and (16). Then the first term of the second member of (24) is non-positive. On the other hand we have from (13) :

$$Q(u_n, \mu) = (\rho - \mu)(a_0 + a_1 \mu) u_n - \varepsilon \mu \quad (26)$$

Because of (11), we have $\rho a_0 = a_1 \mu^2$ which implies $(\rho - \mu)(a_0 + a_1 \mu) = \mu(a_1 \rho - a_0)$ and then $\lambda = \frac{\varepsilon \mu}{(\rho - \mu)(a_0 + a_1 \mu)}$. Therefore we deduce from (16) and (26) that $Q(u_n, \mu) \leq 0$ in $(0, T) \times \Omega$. Thus (24) implies

$$\frac{d}{dt} \int_{\Omega} ((v_{n+1} - \mu)^+)^2 dx \leq 0 \quad (27)$$

for all $t \in (0, T)$ and using (15) and (10) we obtain $v_{n+1}(t, x) \leq \mu$ for all $(t, x) \in (0, T) \times \Omega$. In the same way multiplying the equation $-\partial_t v_{n+1} = -Q(u_n, v_{n+1}) + Q(u_n, 0) - Q(u_n, 0)$ by $(-v_{n+1})^+$, integrating on Ω and studying the sign lead us to the non-negativity of v_{n+1} which ends the proof of (17) for $n + 1$. \blacksquare

The goal is to prove that both sequences (u_n) and (v_n) are Cauchy sequences. We define for $n \in N^*$ and $t \in (0, T)$:

$$\begin{cases} U_n(t) = \int_{\Omega} (u_{n+1} - u_n)^2 dx \\ V_n(t) = \int_{\Omega} (v_{n+1} - v_n)^2 dx. \end{cases} \quad (28)$$

and we prove the following

Proposition 4 *Under the assumptions of the theorem, there exists a constant $k > 0$ such that for all $n \in N^*$ and $t \in (0, T)$:*

$$U'_n(t) \leq 3k U_n(t) + k V_{n-1}(t) \quad (29)$$

and

$$V'_n(t) \leq 3k V_n(t) + k V_{n-1}(t). \quad (30)$$

Note that (29) and (30) are completely analogous.

Proof :

The function $Q(r, s)$ defined by (13) is a Lipschitz function in $[0, \lambda] \times [0, \mu]$ where λ and μ are given by 11. Therefore there exists a constant $k = k(\lambda, \mu) > 0$ such that for all $((r, s), (r', s')) \in ([0, \lambda] \times [0, \mu])^2$:

$$|Q(r, s) - Q(r', s')| \leq k(|r - r'| + |s - s'|). \quad (31)$$

Both functions u_n and u_{n+1} satisfy (15). Then we have :

$$\partial_t(u_{n+1} - u_n) - \sigma \Delta(u_{n+1} - u_n) = -Q(u_{n+1}, v_n) + Q(u_n, v_{n-1}) \quad (32)$$

in $(0, T) \times \Omega$. Multiplying (32) by $(u_{n+1} - u_n)$ and integrating on Ω , we obtain for all $t \in (0, T)$:

$$\begin{aligned} \frac{1}{2} \frac{d}{dt} \int_{\Omega} (u_{n+1} - u_n)^2 dx + \sigma \int_{\Omega} |\nabla(u_{n+1} - u_n)|^2 dx \\ = \int_{\Omega} [Q(u_n, v_{n-1}) - Q(u_{n+1}, v_n)] [u_{n+1} - u_n] dx. \end{aligned} \quad (33)$$

Because of (31) and (28) we deduce from (33) :

$$\begin{aligned} \frac{1}{2} U'_n(t) &\leq k \int_{\Omega} (|u_{n+1} - u_n| + |v_n - v_{n-1}|) |u_{n+1} - u_n| dx \\ &\leq k \int_{\Omega} |u_{n+1} - u_n|^2 dx + \frac{k}{2} \int_{\Omega} (|v_n - v_{n-1}|^2 + |u_{n+1} - u_n|^2) dx \\ &\leq \frac{3k}{2} U_n(t) + \frac{k}{2} V_{n-1}(t) \end{aligned} \quad (34)$$

which implies (29). The proof of (30) is completely similar because the second term of the first member of (33) doesn't play any role. \blacksquare

The differential inequalities of proposition 4 allow us to obtain over-bounds inequalities of U_n and V_n :

Proposition 5 *Under the assumptions of the Theorem, we have for all $n \in N^*$ and $t \in (0, T)$:*

$$U_n(t) \leq kL(k e^{3kT})^n \frac{t^n}{n!} \quad (35)$$

and similarly :

$$V_n(t) \leq kL(k e^{3kT})^n \frac{t^n}{n!} \quad (36)$$

where k is the Lipschitz constant of Q in (31) and L is defined by :

$$L = 4[\max(\lambda, \mu)]^2 \text{mes}(\Omega) = 4[\max(\lambda, \mu)]^2 \int_{\Omega} dx. \quad (37)$$

Proof:

We prove it by recurrence. For $n = 1$, integrating (29) on $(0, T)$ for $t \in (0, T)$, we have :

$$U_1(t) - U_1(0) \leq 3k \int_0^t U_1(s) dx + k \int_0^t V_0(s) ds. \quad (38)$$

But $U_1(0) = \int_{\Omega} (u_2(0, x) - u_1(0, x))^2 dx = 0$ from (15). On the other hand Proposition 3 implies:

$$V_0(s) = \int_{\Omega} (v_1 - v_0)^2 dx \leq \int_{\Omega} (|v_1| + |v_0|)^2 dx \leq 4\mu^2 |\Omega|. \quad (39)$$

Thus for all $t \in (0, T)$:

$$U_1(t) \leq 4\mu^2 |\Omega| kt + 3k \int_0^t U_1(s) ds. \quad (40)$$

Gronwall lemma leads us to the following inequality : for all $t \in (0, T)$:

$$U_1(t) \leq 4\mu^2 |\Omega| kt + 3k \int_0^t 4\mu^2 |\Omega| k s e^{3k(t-s)} ds. \quad (41)$$

Integrating by parts we obtain for all $t \in (0, T)$:

$$U_1(t) \leq 4k\mu^2 |\Omega| \int_0^t e^{3k(t-s)} ds \leq \frac{4}{3}\mu^2 |\Omega| [e^{3kt} - 1] \quad (42)$$

and since $e^a - 1 \leq e^a$, we deduce for all $t \in (0, T)$:

$$U_1(t) \leq 4k\mu^2 |\Omega| e^{3kT} t \leq Lk^2 e^{3kT} \quad (43)$$

because we always can assume $k \geq 1$. In the same way we have for all $t \in (0, T)$:

$$V_1(t) \leq Lk\lambda^2 |\Omega| e^{3kT} t \leq Lk^2 e^{3kT} t. \quad (44)$$

Assume that we have for a fixed n :

$$\begin{cases} U_n(t) \leq Lk^{n+1} e^{3kTn} \frac{t^n}{n!} \\ V_n(t) \leq Lk^{n+1} e^{3kTn} \frac{t^n}{n!} \end{cases} \quad (45)$$

for all $t \in (0, T)$. Since (29) and (45) hold we have for all $t \in (0, T)$:

$$U'_{n+1}(t) \leq 3k U_{n+1}(t) + Lk^{n+2} e^{3kTn} \frac{t^n}{n!} \quad (46)$$

Therefore:

$$U_{n+1}(t) \leq 3k \int_0^t U_{n+1}(s) ds + Lk^{n+2} e^{3kTn} \frac{t^{n+1}}{(n+1)!} \quad (47)$$

Gronwall lemma implies for all $t \in (0, T)$:

$$U_{n+1}(t) \leq Lk^{n+2} e^{3kTn} \frac{t^{n+1}}{(n+1)!} + 3kLk^{n+2} e^{3kTn} \int_0^t \frac{s^{n+1}}{(n+1)!} e^{3k(t-s)} ds. \quad (48)$$

Integrating by parts we obtain for all $t \in (0, T)$:

$$U_{n+1}(t) \leq Lk^{n+2} e^{3kTn} \int_0^t \frac{s^n}{n!} e^{3k(t-s)} ds \quad (49)$$

and since $t - s \leq t \leq T$, we deduce for all $t \in (0, T)$:

$$U_{n+1}(t) \leq Lk^{n+2} e^{3kT(n+1)} \frac{t^{n+1}}{(n+1)!}. \quad (50)$$

In the same way we obtain (50) for V_{n+1} , which ends the proofs of proposition 5. ■

Proof of Theorem 1 :

Let $t \in (0, T)$. We have for all $(n, p) \in (N^*)^2$:

$$\begin{aligned} \|u_{n+p}(t, \cdot) - u_n(t, \cdot)\|_{L^2(\Omega)} &\leq \sum_{l=1}^p \|u_{n+l}(t, \cdot) - u_{n+l-1}(t, \cdot)\|_{L^2(\Omega)} \\ &\leq \sum_{l=1}^p (U_{n+l-1}(t))^{\frac{1}{2}}. \end{aligned} \quad (51)$$

Because of (35) we deduce

$$\|u_{n+p}(t, \cdot) - u_n(t, \cdot)\|_{L^2(\Omega)} \leq \sum_{l=1}^p kL \frac{(k^{\frac{1}{2}} e^{\frac{3}{2}kT} T^{\frac{1}{2}})^{n+l-1}}{((n+l-1)!)^{\frac{1}{2}}}. \quad (52)$$

Thus,

$$\|u_{n+p} - u_n\|_{L^2((0,T) \times \Omega)} \leq kL T^{\frac{1}{2}} \sum_{l=1}^p \frac{(k^{\frac{1}{2}} e^{\frac{3}{2}kT} T^{\frac{1}{2}})^{n+l-1}}{((n+l-1)!)^{\frac{1}{2}}} \quad (53)$$

This is the same for v_n and both sequences (u_n) and (v_n) are Cauchy sequences in $L^2((0, T) \times \Omega)$. Therefore there exists two functions u and v in $L^2((0, T) \times \Omega)$ such that:

$$\begin{cases} \|u_n - u\|_{L^2((0, T) \times \Omega)} \rightarrow 0 \\ \|v_n - v\|_{L^2((0, T) \times \Omega)} \rightarrow 0. \end{cases} \quad (54)$$

There also exists two subsequences, still denoted (u_n) and (v_n) , which respectively converge almost everywhere to u and v in $(0, T) \times \Omega$. Proposition 3 implies:

$$\begin{cases} 0 \leq u(t, x) \leq \lambda \\ 0 \leq v(t, x) \leq \mu \end{cases} \quad (55)$$

for almost all $(t, x) \in (0, T) \times \Omega$ and then both functions u and v are in $L^\infty((0, T) \times \Omega)$ and this is the same for $Q(u, v)$. Thus from classical parabolic equations arguments, see [1], we have that $u \in W^{1,p}((0, T) \times \Omega)$, $v \in L^\infty((0, T) \times \Omega)$ and they are solutions of (12). ■

Note that the above Theorem and proof no more hold if ρ is not a constant.

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