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Cahn–Hilliard Models for Glial Cells

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Abstract
Our aim in this paper is to study a Cahn–Hilliard model with a symport term. This equation is proposed to model some energy mechanisms (e.g., lactate) in glial cells. The main difficulty is to prove the existence of a biologically relevant solution. This is achieved by considering a modified equation and taking a logarithmic nonlinear term. A second difficulty is to prove additional regularity on the solutions which is essential to prove a strict separation from the pure states 0 and 1 in one and two space dimensions. We also consider a second model, based on the Cahn–Hilliard–Oono equation.

Keywords Cahn–Hilliard equation · Cahn–Hilliard–Oono equation · Symport term · Logarithmic nonlinear term · Existence · Regularity · Strict separation

Mathematics Subject Classification 35K55 · 35B45 · 35Q92

1 Introduction

We are interested in this paper in the analysis of PDEs models for energy mechanisms in the brain.

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ODEs of the form

$$x' + \frac{kx}{k' + x} = J(x, t), \; k, \; k' > 0, \; J \geq 0,$$

are often relevant in such situations. We can mention, e.g., lactate or oxygen exchanges in glial cells (see [2,9,32]). Such ODEs were also proposed in [18] to model brain metabolites concentrations in the circadian rhythm. Here, $\frac{kx}{k'+x}$ is known as symport term and accounts for exchanges, e.g., from a cell to its environment (see [19]).

Now, in all these mechanisms, one should also account for spatial diffusion, having in mind different zones in the brain or in cells. In particular, we studied in [24] (see also [17]) a reaction–diffusion equation of the form

$$\frac{\partial u}{\partial t} - \Delta u + \frac{ku}{k' + u} = J(x, t)$$

(we can more generally consider a source term of the form $J = J(u, x, t)$). Such an equation also appears in models in [8,15,23].

In this paper, we consider instead a Cahn–Hilliard type fourth-order equation, namely,

$$\frac{\partial u}{\partial t} + \Delta^2 u - \Delta f(u) + \frac{ku}{k' + u} = J(x, t).$$

The original Cahn–Hilliard equation,

$$\frac{\partial u}{\partial t} + \Delta^2 u - \Delta f(u) = 0,$$

was initially proposed to model phase separation processes in binary alloys (see [4,5]). Since then, this equation, or some of its variants, were successfully applied to many other applications than just phase separation in alloys. We can mention, for instance, dealloying (this can be observed in corrosion processes; see [11]), population dynamics (see [7]), tumor growth (see [1,12,13,20,26]), bacterial films (see [21]), thin films (see [31]), chemistry (see [36]), image processing (see [3,6,10]) and even astronomy, with the rings of Saturn (see [35]), and ecology (for instance, the clustering of mussels can be perfectly well described by the Cahn–Hilliard equation; see [22]). We refer the interested reader to [25,29] for reviews on the Cahn–Hilliard equation and some of its variants, as well as their mathematical analysis.

In view of the energy metabolism in the brain and in glial cells, one interest in considering a Cahn–Hilliard type model is that, in addition to spatial diffusion, we can also account for the phase separation process (having again in mind different zones in the brain or in cells in which, typically, the concentration of a metabolite may be high or very low) and clustering effects.

Compared to the reaction–diffusion model, one essential difficulty is to prove that the order parameter u remains nonnegative; recall indeed that u generally corresponds to a concentration (of a metabolite) and should belong to [0, 1]. This is due to the fact that we no longer have the maximum principle/comparison principle. Also note that the symport term $\frac{ku}{k'+u}$ can become singular when u is negative.

The original Cahn–Hilliard equation usually is associated with a regular (typically, cubic) nonlinear term. However, as we will see below, the order parameter can indeed become negative in that case, preventing us from proving a global in time existence result. To overcome this, we instead consider a logarithmic nonlinear term f. Actually, as far as the original Cahn–Hilliard equation is concerned, a logarithmic nonlinear term is the one which is thermodynamically relevant; it is thus natural to also consider such a nonlinear term for our model. In addition, we consider a modified problem to avoid the symport term to become singular. A second major difficulty is to prove a strict separation property of the order parameter from the singular points of f. This necessitates further regularity on the time derivative of u which is in general not known for variants of the Cahn–Hilliard equation of the form

$$\frac{\partial u}{\partial t} + \Delta^2 u - \Delta f(u) + h(x, u) = 0.$$

Surprisingly, this is already challenging for the simple linear term $h(x, s) = \alpha s$, $\alpha > 0$, when considering logarithmic nonlinear terms f (see [14]); in that case, one has the Cahn–Hilliard–Oono equation, proposed in [30] to account for nonlocal effects in phase separation processes. In our case, we are able to prove such a regularity under conditions on the parameters.

This paper is organized as follows. We first define the mathematical setting for our problem. We then prove the existence of a local in time biologically relevant solution which is global under (unfortunately rather restrictive) conditions on the parameters. We next prove further regularity on the solutions, allowing us to prove the strict separation in one and two space dimensions. We finally consider a second model, based on the Cahn–Hilliard–Oono equation, and obtain similar results, this time under more realistic conditions on the parameters.

2 Setting of the Problem

We assume in what follows that J is a constant. We will however discuss the extension of some of our results to more general functions $J = J(x, t)$.

We consider the following initial and boundary value problem, in a bounded and regular domain Ω of $\mathbb{R}^n$, $n = 1, 2$ or 3, with boundary Γ:

$$\frac{\partial u}{\partial t} + \Delta^2 u - \Delta f(u) + \frac{ku}{k'+u} = J,\ k,\ k' > 0, \tag{2.1}$$

$$\frac{\partial u}{\partial \nu} = \frac{\partial \Delta u}{\partial \nu} = 0 \text{ on } \Gamma, \tag{2.2}$$

$$u|_{t=0} = u_0. \tag{2.3}$$

Remark 2.1 As mentioned in the introduction, u corresponds to a concentration. It is thus important to ensure that this quantity takes values between 0 and 1. Furthermore, as mentioned in the introduction, one usually takes regular (typically, cubic) nonlinear terms with Cahn–Hilliard type models. Unfortunately, such nonlinear terms do not ensure biologically relevant solutions. Let us indeed take $J = 0$, $f(s) = (s - \frac{1}{2})^3 - (s - \frac{1}{2})$ and consider the one-dimentional equation

$$u_t + u_{xxxx} - (f(u))_{xx} + \frac{ku}{k' + u} = 0,$$

with obvious notation. Let us now take u_0 smooth enough satisfying the Neumann boundary conditions and such that $u_0 \in [0, 1]$ and $u_0(x) = (x - \frac{1}{2})^4$ in a neighborhood of $\frac{1}{2}$. Thus, we easily see that $u_0(\frac{1}{2}) = u_0'(\frac{1}{2}) = u_0''(\frac{1}{2}) = 0$, so that $(f(u))_{xx}(\frac{1}{2}, 0) = 0$, and $u_0^{(iv)}(\frac{1}{2}) = 24$. It thus follows that $u_t(\frac{1}{2}, 0) = -24$ and

$$u(\frac{1}{2}, t) = -24t + o(t),$$

for t close to 0. This yields that u can indeed become negative, which is problematic here, as the equation may become singular if u approaches $-k'$.

In view of the above remark, we take f logarithmic, namely,

$$f(s) = -c_0(s - \frac{1}{2}) + \theta \ln \frac{s}{1 - s}, \ c_0, \ \theta > 0, \ s \in (0, 1).$$

Remark 2.2 In the case of the original Cahn–Hilliard equation, one further takes $\theta < \frac{c_0}{4}$ to ensure that f is the derivative of a double-well potential F and that phase separation can occur.

We can note that f is of class C^∞ and satisfies

$$f' \geq -c_0. \tag{2.4}$$

Furthermore, the following holds, for $s, m \in (0, 1)$:

$$f(s)(s - m) \geq c_m(|f(s)| + F(s)) - c_m', \ c_m > 0, \ c_m' \geq 0, \tag{2.5}$$

where $F(s) = \int_{\frac{1}{2}}^{s} F(\xi)\, d\xi$ and c_m and c_m' depend continuously on m. We refer the reader to, e.g., [25] for the proof. Note that, there, the order parameter u takes values in $(-1, 1)$; we can come back to $(0, 1)$ by a proper rescaling.

In order to prove the existence of solutions, we consider the following modified problem:

$$\frac{\partial u}{\partial t} + \Delta^2 u - \Delta f(u) + g(u) = J, \tag{2.6}$$

$$\frac{\partial u}{\partial \nu} = \frac{\partial \Delta u}{\partial \nu} = 0 \text{ on } \Gamma, \tag{2.7}$$

$$u|_{t=0} = u_0, \tag{2.8}$$

where $g(s) = \frac{ks}{k'+|s|}$. Note that g is of class $\mathcal{C}^1$, with $g'(s) = \frac{kk'}{(k'+|s|)^2}$, so that g is (strictly) monotone increasing and maps $\mathbb{R}$ onto $[-k, k]$. Here, the only difficulty occurs at $s = 0$ and note that

$$\frac{g(s) - g(0)}{s} = \frac{k}{k' + |s|} \to \frac{k}{k'} \text{ as } s \to 0.$$

Furthermore, if $s > 0$, then

$$g'(s) = \frac{kk'}{(k' + s)^2} = \frac{kk'}{(k' + |s|)^2} \to \frac{k}{k'} \text{ as } s \to 0^+,$$

while, if $s < 0$,

$$g'(s) = \frac{kk'}{(k' - s)^2} = \frac{kk'}{(k' + |s|)^2} \to \frac{k}{k'} \text{ as } s \to 0^-.$$

Notation

We denote by $((\cdot, \cdot))$ the usual L^2-scalar product, with associated norm $\|\cdot\|$. We also set $\|\cdot\|_{-1} = \|(-\Delta)^{-\frac{1}{2}} \cdot\|$, where $(-\Delta)^{-1}$ denotes the inverse of the minus Laplace operator associated with Neumann boundary conditions and acting on functions with null spatial average. More generally, we denote by $\|\cdot\|_X$ the norm on the Banach space X.

We set $\langle\cdot\rangle = \frac{1}{\mathrm{Vol}(\Omega)} \int_\Omega \cdot\, dx$, being understood that, if $v \in H^{-1}(\Omega) = H^1(\Omega)'$, then $\langle v\rangle = \frac{1}{\mathrm{Vol}(\Omega)} \langle v, 1\rangle_{H^{-1}(\Omega), H^1(\Omega)}$. We also set, whenever this makes sense, $\overline{v} = v - \langle v\rangle$.

We note that

$$v \mapsto (\|\overline{v}\|_{-1}^2 + \langle v\rangle^2)^{\frac{1}{2}}, \ v \mapsto (\|\overline{v}\|^2 + \langle v\rangle^2)^{\frac{1}{2}},$$
$$v \mapsto (\|\nabla v\|^2 + \langle v\rangle^2)^{\frac{1}{2}} \text{ and } v \mapsto (\|\Delta v\|^2 + \langle v\rangle^2)^{\frac{1}{2}}$$

are norms on $H^{-1}(\Omega)$, $L^2(\Omega)$, $H^1(\Omega)$ and $H^2(\Omega)$, respectively, which are equivalent to the usual norms on these spaces; furthermore, $\|\cdot\|_{-1}$ is a norm on $\{v \in H^{-1}(\Omega),\ \langle v\rangle = 0\}$ which is equivalent to the usual H^{-1}-norm.

Throughout this paper, the same letters c and c' denote (generally positive) constants which may vary from line to line, or even in a same line.

3 Existence of Solutions

We first prove a local in time existence result.

Theorem 3.1 *We assume that u_0 is given such that $u_0 \in H^1(\Omega)$, $0 < \langle u_0\rangle < 1$ and $0 < u_0(x) < 1$, a.e. $x \in \Omega$. Then, there exists $T_0 = T_0(u_0) > 0$ and a weak solution u to (2.1)–(2.3) on $[0, T_0]$ such that $u \in \mathcal{C}([0, T_0]; H^1(\Omega)_w) \cap L^\infty(0, T_0; H^1(\Omega)) \cap$*

$L^2(0, T_0; H^2(\Omega))$ and $\frac{\partial u}{\partial t} \in L^2(0, T_0; H^{-1}(\Omega))$, where w *denotes the weak topology. Furthermore,* $0 < u(x, t) < 1$, *a.e.* $(x, t) \in \Omega \times (0, T_0)$.

Proof We actually prove the existence of a local in time solution to the auxiliary problem (2.6)–(2.8) satisfying the regularity and weak separation property stated in the theorem. Then, since $u > 0$ almost everywhere, it immediately follows that it is solution to the original problem.

The idea, to prove existence, is to approximate the singular nonlinear term f by regularized ones defined on the whole real line and then pass to the limit in the approximated problems. For instance, one can consider the following $\mathcal{C}^1$-functions defined on the real line and having a linear growth at infinity, $N \in \mathbb{N}$:

$$f_N(s) = \begin{cases} f(1-\frac{1}{N}) + f'(1-\frac{1}{N})(s-1+\frac{1}{N}), \ s > 1-\frac{1}{N}, \\ f(s), \ s \in [\frac{1}{N}, 1-\frac{1}{N}], \\ f(\frac{1}{N}) + f'(\frac{1}{N})(s-\frac{1}{N}), \ s < \frac{1}{N}, \end{cases}$$

and replace f by f_N in the equations. As this procedure is now standard for the Cahn–Hilliard equation, we will not detail it here and will instead work directly on the original equation (2.6) and refer the interested reader to [25]. Note that the approximated functions satisfy (2.4), as well as a property similar to (2.5), with constants which are independent of the approximation parameter N, at least when N is large enough (see [25]). Therefore, the constants which appear below are independent of the approximation parameter when considering approximated solutions. Also note that, as the approximated functions go to infinity as s goes to infinity, the solutions to the approximated problems may also exit [0, 1] and may, in particular, become negative, as mentioned above. This explains why one only has a local in time existence result when considering this scheme. We finally mention that the crucial step is to prove that $f(u)$ belongs to $L^2(\Omega \times (0, T_0))$, for some $T_0 > 0$ (this allows to pass to the limit in the nonlinear term in the approximated problems).

That said, we rewrite (2.6) in the following equivalent weaker form:

$$(-\Delta)^{-1}\frac{\partial \overline{u}}{\partial t} - \Delta \overline{u} + \overline{f(u)} + (-\Delta)^{-1}\overline{g(u)} = 0, \tag{3.1}$$

$$\frac{d\langle u \rangle}{dt} + \langle g(u) \rangle = J, \tag{3.2}$$

$$\frac{\partial \overline{u}}{\partial \nu} = 0 \text{ on } \Gamma, \tag{3.3}$$

$$\overline{u}|_{t=0} = \overline{u}_0, \ \langle u \rangle|_{t=0} = \langle u_0 \rangle. \tag{3.4}$$

Note that (3.2) is obtained by formally integrating (2.6) over Ω and integrating by parts.

The a priori estimates derived below will be formal. Note that, on the approximated problems level, they can easily be justified by a standard Galerkin scheme.

First, note that

$$-k \leq \langle g(u) \rangle \leq k$$

(note indeed that g is bounded, so that so is $\langle g(u)\rangle$), so that

$$\langle u_0\rangle + (J-k)t \leq \langle u(t)\rangle \leq \langle u_0\rangle + (J+k)t,$$

as long as it exists. Assume that

$$2\delta \leq \langle u_0\rangle \leq 1-2\delta,\ \ \delta \in (0, \frac{1}{2}).$$

It then follows from the above that there exists $T_0 = T_0(\delta, u_0) > 0$ such that

$$\delta \leq u(t) \leq 1-\delta,\ \ t \in [0, T_0]. \tag{3.5}$$

Let us emphasize that, when working with the approximated problems, T_0 can be chosen independent of the approximation parameter, which is essential to pass to the limit. Indeed, the equation for the spatial average of the approximated solutions (i.e., the equivalent of (3.2)) would be the same, so that the constants in the corresponding estimates would also be the same.

We assume from now on that $t \in [0, T_0]$.

Let us multiply (3.1) by $\overline{u}$ and integrate over Ω and by parts. This gives

$$\frac{1}{2}\frac{d}{dt}\|\overline{u}\|_{-1}^2 + \|\nabla u\|^2 + ((\overline{f(u)}, \overline{u})) + (((-\Delta)^{-1}\overline{g(u)}, \overline{u})) = 0. \tag{3.6}$$

Note that it follows from (2.5) and (3.5) that

$$((\overline{f(u)}, \overline{u})) = ((f(u), \overline{u})) \geq c(\|f(u)\|_{L^1(\Omega)} + \int_\Omega F(u)\,dx) - c',\ \ c>0, \tag{3.7}$$

where the above constants depend on δ. Furthermore, we have

$$|(((-\Delta)^{-1}\overline{g(u)}, \overline{u}))| \leq c\|\overline{g(u)}\|\|\overline{u}\| \leq c\|\nabla u\|. \tag{3.8}$$

We deduce from (3.6)–(3.8) that

$$\frac{d}{dt}\|\overline{u}\|_{-1}^2 + c(\|\nabla u\|^2 + \|f(u)\|_{L^1(\Omega)} + \int_\Omega F(u)\,dx) \leq c',\ \ c>0. \tag{3.9}$$

Let us next multiply (3.1) by $\frac{\partial \overline{u}}{\partial t}$ to obtain

$$\frac{1}{2}\frac{d}{dt}\|\nabla u\|^2 + \|\frac{\partial \overline{u}}{\partial t}\|_{-1}^2 + ((\overline{f(u)}, \frac{\partial \overline{u}}{\partial t})) + (((-\Delta)^{-1}\overline{g(u)}, \frac{\partial \overline{u}}{\partial t})) = 0. \tag{3.10}$$

Note that

$$((\overline{f(u)}, \frac{\partial \overline{u}}{\partial t})) = ((f(u), \frac{\partial \overline{u}}{\partial t})) = \frac{d}{dt}\int_\Omega F(u)\,dx - ((f(u), \frac{d\langle u\rangle}{dt})) \tag{3.11}$$
$$= \frac{d}{dt}\int_\Omega F(u)\,dx + \mathrm{Vol}(\Omega)(\langle g(u)\rangle - J)\langle f(u)\rangle$$
$$\geq \frac{d}{dt}\int_\Omega F(u)\,dx - c\|f(u)\|_{L^1(\Omega)},$$

recalling that g is bounded. Furthermore,

$$|(((-\Delta)^{-1}\overline{g(u)}, \frac{\partial \overline{u}}{\partial t}))| = ((\overline{g(u)}, (-\Delta)^{-1}\frac{\partial \overline{u}}{\partial t}))| \leq c\|\overline{g(u)}\|\|\frac{\partial \overline{u}}{\partial t}\|_{-1} \leq c\|\frac{\partial \overline{u}}{\partial t}\|_{-1}. \tag{3.12}$$

It thus follows from (3.10)–(3.12) that

$$\frac{d}{dt}(\|\nabla u\|^2 + 2\int_\Omega F(u)\,dx) + \|\frac{\partial \overline{u}}{\partial t}\|_{-1}^2 \leq c\|f(u)\|_{L^1(\Omega)} + c'. \tag{3.13}$$

Let us now add (3.9) and (3.13), multiplied by $\delta_1 > 0$ small enough, to find a differential inequality of the form

$$\frac{dE_1}{dt} + c(E_1 + \|f(u)\|_{L^1(\Omega)} + \|\frac{\partial \overline{u}}{\partial t}\|_{-1}^2) \leq c',\ c > 0, \tag{3.14}$$

where

$$E_1 = \|\overline{u}\|_{-1}^2 + \delta_1(\|\nabla u\|^2 + 2\int_\Omega F(u)\,dx)$$

satisfies

$$E_1 \geq c\|\nabla u\|^2 - c',\ c > 0.$$

Multiplying (3.1) by $-\Delta\overline{u}$, we find, employing (2.4),

$$\frac{1}{2}\frac{d}{dt}\|\overline{u}\|^2 + \|\Delta u\|^2 \leq c_0\|\nabla u\|^2 - ((g(u), \overline{u})), \tag{3.15}$$

which yields, noting that

$$|((g(u), \overline{u}))| \leq c\|\overline{u}\|^2 + c',$$

the differential inequality

$$\frac{d}{dt}\|\overline{u}\|^2 + \|\Delta u\|^2 \leq c\|\overline{u}\|^2 + c'. \tag{3.16}$$

Here, we have also used the fact that

$$\|\nabla u\|^2 \le \frac{1}{2}\|\Delta u\|^2 + c\|\overline{u}\|^2,$$

which follows from standard elliptic regularity results and a proper interpolation inequality.

Next, we deduce from (3.2) and (3.5) that

$$\frac{d}{dt}\langle u\rangle^2 + \langle u\rangle^2 \le c. \tag{3.17}$$

Furthermore, it follows from (3.16) that

$$\frac{d}{dt}\|\overline{u}\|^2 + c\|\overline{u}\|^2_{H^2(\Omega)} \le c'(\|\overline{u}\|^2 + \langle u\rangle^2) + c'',\ c > 0. \tag{3.18}$$

Summing finally (3.14), (3.17) and (3.18), multiplied by $\delta_2 > 0$ small enough, we have a differential inequality of the form

$$\frac{dE_2}{dt} + c(E_2 + \|\overline{u}\|^2_{H^2(\Omega)} + \|\frac{\partial u}{\partial t}\|^2_{H^{-1}(\Omega)} + \|f(u)\|_{L^1(\Omega)}) \le c',\ c > 0, \tag{3.19}$$

where

$$E_2 = E_1 + \langle u\rangle^2 + \delta_2\|\overline{u}\|^2$$

satisfies

$$E_2 \ge c\|u\|^2_{H^1(\Omega)} - c',\ c > 0.$$

Note indeed that it follows from (3.2) and the boundedness of g that $\frac{d\langle u\rangle}{dt}$ is bounded.

Having this, we note that (3.1) yields

$$\overline{f(u)} = \Delta u - (-\Delta)^{-1}\frac{\partial \overline{u}}{\partial t} - (-\Delta)^{-1}\overline{g(u)},$$

so that

$$\|\overline{f(u)}\| \le c(\|\Delta u\| + \|\frac{\partial \overline{u}}{\partial t}\|_{-1} + 1) \tag{3.20}$$

and

$$\|\overline{f(u)}\|^2_{L^2(0,T_0;L^2(\Omega))} \le cE_2(0). \tag{3.21}$$

Next, taking $s = u$ and $m = \langle u \rangle$ in (2.5), it follows from (3.5) that

$$|\langle f(u)\rangle| \le c((f(u), \overline{u})) + c' = c((\overline{f(u)}, u)) + c' \\ \le c\|\overline{f(u)}\|\|u\| + c',$$

where the above constants depend on δ. Therefore,

$$\|f(u)\|^2_{L^2(0,T_0;L^2(\Omega))} \le c(\|\overline{f(u)}\|^2_{L^2(0,T_0;L^2(\Omega))} + \int_0^{T_0} \langle f(u)\rangle^2\, dt) \\ \le cE_2(0) + c'E_2(0)\|u\|^2_{L^\infty(0,T_0;L^2(\Omega))} + c'' \\ \le cE_2^2(0) + c'$$

and

$$\|f(u)\|_{L^2(0,T_0;L^2(\Omega))} \le c(E_2(0) + 1). \tag{3.22}$$

As mentioned above, (3.22) is the crucial estimate to pass to the limit in the nonlinear term and prove the existence of a local in time solution. The rest of the proof is standard and we omit the details. □

Remark 3.2 The separation property from the singular points 0 and 1 given in the above theorem says that there will be no zone where the metabolite under study is totally absent; there will always be at least some trace of it.

Remark 3.3 For a regular, in particular, cubic, nonlinear term f, we can similarly prove the existence, and also the uniqueness, of the local in time solution. Note however that, as already mentioned, the solution may become negative (or strictly larger than one), in which case, the equation may become singular. Consequently, we are not able to prove a global in time existence result in that case.

Theorem 3.1 can be extended to more general functions $J = J(x, t)$ as follows.

Theorem 3.4 *We assume that the assumptions of Theorem 3.1 hold and that $J \in L^\infty(\Omega \times (0, T))$, $T > 0$. Then, the assertions of Theorem 3.1 still hold.*

Proof Note that the weaker formulation of the problem now reads

$$(-\Delta)^{-1}\frac{\partial \overline{u}}{\partial t} - \Delta\overline{u} + \overline{f(u)} + (-\Delta)^{-1}\overline{g(u)} = (-\Delta)^{-1}\overline{J}, \tag{3.23}$$

$$\frac{d\langle u\rangle}{dt} + \langle g(u)\rangle = \langle J\rangle, \tag{3.24}$$

$$\frac{\partial \overline{u}}{\partial \nu} = 0 \text{ on } \Gamma, \tag{3.25}$$

$$\overline{u}|_{t=0} = \overline{u}_0,\ \langle u\rangle|_{t=0} = \langle u_0\rangle. \tag{3.26}$$

We can then repeat the estimates made above, with minor changes. In particular, when estimating the spatial average of u, we obtain

$$\langle u_0\rangle - (\|J\|_{L^\infty(\Omega\times(0,T))} + k)t \le \langle u(t)\rangle \le \langle u_0\rangle + (\|J\|_{L^\infty(\Omega\times(0,T))} + k)t.$$

Also note that, e.g., when multiplying (3.23) by $\frac{\partial \overline{u}}{\partial t}$, we have to estimate the term $(((-\Delta)^{-1}\overline{J}, \frac{\partial \overline{u}}{\partial t}))$. To do so, we write

$$\begin{aligned}(((-\Delta)^{-1}\overline{J}, \frac{\partial \overline{u}}{\partial t})) &= (((-\Delta)^{-\frac{1}{2}}\overline{J}, (-\Delta)^{-\frac{1}{2}}\frac{\partial \overline{u}}{\partial t}))\\ &\le c\|J\|\|\frac{\partial \overline{u}}{\partial t}\|_{-1} \le \varepsilon\|\frac{\partial \overline{u}}{\partial t}\|_{-1}^2 + c_\varepsilon,\ \ \forall \varepsilon > 0.\end{aligned}$$

□

We then have the following.

Theorem 3.5 *Let us assume that* $0 \le J\frac{k'+1}{k} \le 1$ *and let* u *be a local in time weak solution as in Theorem* 3.1. *Then, it is global in time, i.e., defined on* $[0, T]$, $\forall T > 0$.

Proof Let u be a local in time weak solution on $[0, T]$, $T > 0$ given, and $T^\star$ be its maximal time of existence. Let us assume that $T^\star < T$. Then, necessarily, u belongs to $[0, 1]$ for $t \in [0, T^\star)$. In particular, this yields

$$\frac{ku}{k'+1} \le g(u) \le \frac{ku}{k'}$$

and

$$J - \frac{k}{k'}\langle u\rangle \le J - \langle g(u)\rangle \le J - \frac{k}{k'+1}\langle u\rangle.$$

Therefore, noting that J is nonnegative and recalling that $J\frac{k'+1}{k} \le 1$,

$$\begin{aligned}\langle u_0\rangle e^{-\frac{k}{k'}t} \le \langle u(t)\rangle &\le \langle u_0\rangle e^{-\frac{k}{k'+1}t} + J\frac{k'+1}{k}(1 - e^{-\frac{k}{k'+1}t}) \\ &\le \langle u_0\rangle e^{-\frac{k}{k'+1}t} + 1 - e^{-\frac{k}{k'+1}t},\ \ t \in [0, T^\star).\end{aligned} \tag{3.27}$$

Finally, it follows from (3.27) that there exists $\delta \in (0, 1)$ (which can be taken independent of $T^\star$) such that

$$\delta < \langle u(t)\rangle < 1 - \delta,\ \ \forall t \in [0, T^\star).$$

Note indeed that, setting

$$\varphi(t) = \langle u_0\rangle e^{-\frac{k}{k'+1}t} + 1 - e^{-\frac{k}{k'+1}t},$$

then

$$\varphi'(t) = \frac{k}{k'+1}(1 - \langle u_0 \rangle)e^{-\frac{k}{k'+1}t} \geq 0.$$

Therefore, φ is monotone increasing and takes values in $[\varphi(0), \varphi(T)] = [\langle u_0 \rangle, (\langle u_0 \rangle - 1)e^{-\frac{k}{k'+1}T} + 1] \subset (0, 1)$. The lower bound is straightforward. This yields that, necessarily, the solution is global in time, since, otherwise, owing to continuity, it can be extended (recall that $T^\star < T$). □

Remark 3.6 (i) Note that the above argument does not work for the approximated problems (and regular nonlinear terms f).

(ii) In the case of lactate exchanges in glial cells, possible biologically relevant values are (see, e.g., [16] and the references therein)

$$k = 0.01\text{mM.s}^{-1},\ k' = 3.5\text{mM},$$
$$J = 5.7.10^{-3}\text{mM.s}^{-1},$$

so that the condition $J\frac{k'+1}{k} \leq 1$ is a restrictive one. It is however satisfied if one considers a sufficiently small external flux J. Note nevertheless that our equation should be regarded as only a very simplified model in this situation. More concrete models should account for different energy mechanisms (e.g., glucose and glutamate/glutamine) or for the tumor growth in case of cancerous cells. Such more elaborate models will be studied elsewhere.

(iii) Note that, since g is monotone increasing,

$$\frac{d\langle u \rangle}{dt} \in [J - \frac{k}{k'+1}, J].$$

Therefore, if $J = 0$, then $\langle u \rangle$ is monotone decreasing and, since it belongs to $[0, 1]$, it converges to some limit. A similar situation arises when $J - \frac{k}{k'+1} \geq 0$, in which case $\langle u \rangle$ is monotone increasing. Also note that it follows from (3.27) that, when $J = 0$, then $\langle u \rangle$ converges to 0 as time goes to $+\infty$, as expected.

We aslo have the following result, for nonconstant functions $J = J(x, t)$.

Theorem 3.7 *We assume that the assumptions of Theorem 3.4 hold and that* $J \in [0, J^\star]$*, where* $J^\star\frac{k'+1}{k} \leq 1$*. Then, a solution as in Theorem 3.4 is global in time, i.e., defined on* $[0, T]$.

Proof The proof is similar to that of Theorem 3.5, noting that we now have

$$-\frac{k}{k'}\langle u \rangle \leq J - \langle g(u) \rangle \leq J^\star - \frac{k}{k'+1}\langle u \rangle,$$

so that

$$\langle u_0\rangle e^{-\frac{k}{k'}t} \le \langle u(t)\rangle \le \langle u_0\rangle e^{-\frac{k}{k'+1}t} + J^\star \frac{k'+1}{k}(1-e^{-\frac{k}{k'+1}t})$$
$$\le \langle u_0\rangle e^{-\frac{k}{k'+1}t} + 1 - e^{-\frac{k}{k'+1}t}.$$

□

Remark 3.8 In the study of brain metabolites concentrations in the circadian rhythm, one considers in [18] functions J of the form

$$J = a\sin^2(bt+c),\ a,\ b,\ c > 0.$$

The condition in Theorem 3.7 on the parameters is again restrictive when compared to the numerical values taken in [18].

Remark 3.9 In the case of a logarithmic nonlinear term f, uniqueness is an open problem (see however the next section below for a partial uniqueness result).

4 Regularity of Solutions

We assume in this section that J is a constant.

We have the following.

Theorem 4.1 *We assume that the assumptions of Theorem 3.5 hold and that* $0 < J\frac{k'+1}{k} < 1$. *Then, any weak solution u to* (2.1)–(2.3) *satisfies*

$$\frac{\partial u}{\partial t} \in L^\infty(r,T;H^{-1}(\Omega)) \cap L^2(r,T;H^1(\Omega)),$$

$\forall r < T$, $r > 0$ *and* $T > 0$ *given.*

Proof The estimates below are again formal, but they can also be justified within a Galerkin scheme for the approximated problems and Theorem 3.5.

Rewrite the equations in the equivalent form

$$\frac{\partial u}{\partial t} + g(u) - J = \Delta\mu, \tag{4.1}$$
$$\mu = -\Delta u + f(u), \tag{4.2}$$
$$\frac{\partial u}{\partial \nu} = \frac{\partial \mu}{\partial \nu} = 0 \text{ on } \Gamma. \tag{4.3}$$

First, note that it follows from (4.2) that

$$\langle \mu\rangle = \langle f(u)\rangle,$$

so that, owing to the regularity obtained in the previous section, $\mu \in L^2(0, T; H^1(\Omega))$, since

$$\overline{\mu} = -(-\Delta)^{-1}\frac{\partial \overline{u}}{\partial t} - (-\Delta)^{-1}\overline{g(u)}. \tag{4.4}$$

Next, let us multiply (4.1) by $\frac{\partial \mu}{\partial t}$ to have

$$((\frac{\partial u}{\partial t}, \frac{\partial \mu}{\partial t})) = -\frac{1}{2}\frac{d}{dt}\|\nabla \mu\|^2 - ((g(u) - J, \frac{\partial \mu}{\partial t})). \tag{4.5}$$

Let us then differentiate (4.2) with respect to time to obtain

$$\frac{\partial \mu}{\partial t} = -\Delta \frac{\partial u}{\partial t} + f'(u)\frac{\partial u}{\partial t}. \tag{4.6}$$

Multiply (4.6) by $\frac{\partial u}{\partial t}$ to find

$$((\frac{\partial u}{\partial t}, \frac{\partial \mu}{\partial t})) = \|\nabla \frac{\partial u}{\partial t}\|^2 + ((f'(u)\frac{\partial u}{\partial t}, \frac{\partial u}{\partial t})) \geq \|\nabla \frac{\partial u}{\partial t}\|^2 - c_0\|\frac{\partial u}{\partial t}\|^2, \tag{4.7}$$

owing to (2.4). Combine (4.5) and (4.7) to have

$$\begin{aligned} \frac{1}{2}\frac{d}{dt}\|\nabla \mu\|^2 + \|\nabla \frac{\partial u}{\partial t}\|^2 + ((g(u) - J, \frac{\partial \mu}{\partial t})) &\leq c_0\|\frac{\partial u}{\partial t}\|^2 \\ &\leq \frac{1}{2}\|\nabla \frac{\partial u}{\partial t}\|^2 + c(\|\frac{\partial \overline{u}}{\partial t}\|_{-1}^2 + \langle \frac{\partial u}{\partial t}\rangle^2), \end{aligned} \tag{4.8}$$

owing to a proper interpolation inequality. Now, note that

$$((g(u) - J, \frac{\partial \mu}{\partial t})) = \frac{d}{dt}((g(u) - J, \mu)) - ((g'(u)\frac{\partial u}{\partial t}, \mu)). \tag{4.9}$$

Let us then combine (4.8) and (4.9) to obtain

$$\begin{aligned} \frac{d}{dt}(\|\nabla \mu\|^2 + ((g(u) - J, \mu))) + \|\nabla \frac{\partial u}{\partial t}\|^2 &\leq c\|\frac{\partial u}{\partial t}\|_{H^{-1}(\Omega)}^2 + c'\|\frac{\partial u}{\partial t}\|\|\mu\| \\ &\leq \frac{1}{2}\|\nabla \frac{\partial u}{\partial t}\|^2 + c(\|\frac{\partial u}{\partial t}\|_{H^{-1}(\Omega)}^2 + \|\mu\|^2), \end{aligned}$$

noting that g' is bounded, so that

$$\frac{d}{dt}(\|\nabla \mu\|^2 + ((g(u) - J, \mu))) + \frac{1}{2}\|\nabla \frac{\partial u}{\partial t}\|^2 \leq c(\|\frac{\partial u}{\partial t}\|_{H^{-1}(\Omega)}^2 + \|\mu\|^2). \tag{4.10}$$

Set finally

$$\Lambda = \|\nabla \mu\|^2 + ((g(u) - J, \mu)).$$

Note that, since $g' \geq 0$,

$$((g(u) - J, \mu)) = ((g(u) - J, -\Delta u + f(u))) = ((g'(u)\nabla u, \nabla u)) + ((g(u) - J, f(u)) \\ \geq ((g(u) - J, f(u))).$$

Also note that

$$g(u) - J = \frac{k - J}{k' + u}(u - \frac{Jk'}{k - J}),$$

so that it follows from (2.5) (indeed, $0 < J\frac{k'+1}{k} < 1$ implies that $k > J$ and $0 < \frac{Jk'}{k-J} < 1$) that

$$((g(u) - J, f(u))) \geq c \int_{\Omega} F(u)\, dx - c',\ c > 0.$$

Therefore,

$$\Lambda \geq \|\nabla\mu\|^2 - c,\ c \geq 0,$$

and an application of the uniform Gronwall's lemma yields that

$$\overline{\mu} \in L^{\infty}(r, T_0; H^1(\Omega)),$$

$r > 0$ given, owing also to (3.19) and (4.4) which allow to see that the assumptions of this lemma indeed hold.

The result finally follows from (4.4), recalling that $\frac{d\langle u\rangle}{dt}$ is uniformly bounded and extending the solution. □

The regularity obtained in Theorem 4.1 is the key regularity for proving a strict separation of the order parameter u (and not just its spatial average) from the pure states 0 and 1 (see [25]). More precisely, we have the following.

Theorem 4.2 *We assume that $n = 1$ or 2 and that the assumptions of Theorems 3.5 and 4.1 hold. Then, there exists $\delta \in (0, 1)$ depending on the $H^1(\Omega)$-norm of u_0 such that*

$$\delta \leq u(x, t) \leq 1 - \delta,\ \text{for almost all } (x, t),\ x \in \Omega,\ t \geq r,$$

$r > 0$ *given.*

The proof of this theorem is very similar to those given in [25], Chapter 4 (see also [14,27]), and we omit the details.

Remark 4.3 (i) This result says that, as soon as time is positive, the nonlinear term becomes regular (and also bounded). Note that this then allows to prove additional regularity on u and, in particular, that the solution is strong as soon as time is positive.

(ii) The strict separation is not known in three space dimensions, already for the original Cahn–Hilliard equation, unless we make some growth assumptions on the singular nonlinear term f which are not satisfied by the relevant logarithmic ones (see [27]).

Remark 4.4 From a biological point of view, the strict separation property says that, in the phase separation process, there is always some amount (and not just some trace) of the metabolite in, say, all regions of the cell.

A consequence of the above results is the following.

Corollary 4.5 *We assume that $n = 1$ or 2 and that $u_0 \in H^3(\Omega)$, with $\frac{\partial u_0}{\partial \nu} = 0$ on Γ and $\delta \leq u_0(x) \leq 1 - \delta$, a.e. $x \in \Omega$, $\delta \in (0, 1)$. Then, a solution as given in Theorem 4.1 is unique.*

Proof We first note that the regularity on u_0 implies that $\frac{\partial u}{\partial t}(0) \in H^{-1}(\Omega)$ and, thus, $\mu(0) \in H^1(\Omega)$, allowing us to take $r = 0$ in the above results.

Next, having the strict separation property, we can essentially proceed as for the original Cahn–Hilliard equation with a regular nonlinear term to prove uniqueness, as well as the continuous dependence with respect to the initial data (say, with respect to the $H^{-1}(\Omega)$-norm). Let us just mention that the difference, when compared to the original Cahn–Hilliard equation, is that we have to handle a term of the form

$$((f(u_1) - f(u_2), \langle u_1 - u_2 \rangle)),$$

where u_1 and u_2 are two solutions which satisfy the strict separation property (in the case of the original Cahn–Hilliard equation, this term does not appear, due to the conservation of the spatial average of the order parameter; see [25], also for several other variants of the Cahn–Hilliard equation). Without the strict separation property, we would not know how to estimate this term, whereas, here, noting that the nonlinear term f is globally Lipschitz continuous when considering two solutions which are strictly separated from the pure states, we can write

$$|f(u_1) - f(u_2)| \leq c|u_1 - u_2|.$$

□

Remark 4.6 (i) Having the strict separation property and uniqueness, we can study the asymptotic behavior of the associated dynamical system. In particular, we can prove the existence of finite dimensional attractors, meaning, roughly speaking, that the limit dynamics can be described by a finite number of degrees of freedom. We refer the interested reader to, e.g., [25,28,34] for discussions on this.

(ii) Another interesting problem is the convergence of single trajectories to steady states. Note that, already for the original Cahn–Hilliard equation, such a question is not a trivial one, since one may have a continuum of steady states (see [33]). Here, due to the additional symport term, the problem is particularly challenging and we cannot proceed as in [33].

(iii) When $k > J$, one has a unique spatially homogeneous equilibrium given by

$$u_e = \frac{k'J}{k-J}.$$

In particular, when $J = 0$, $u_e = 0$ and we already saw that $\langle u(t)\rangle$ tends to 0 as t goes to $+\infty$. Proving a full stability result is however challenging and will be studied elsewhere.

5 A Second Model

We consider in this section the following initial and boundary value problem:

$$\frac{\partial u}{\partial t} + \Delta^2 u - \Delta f(u) + \alpha u + \frac{ku}{k'+u} = J,\ \alpha,\ k,\ k' > 0, \tag{5.1}$$

$$\frac{\partial u}{\partial \nu} = \frac{\partial \Delta u}{\partial \nu} = 0 \text{ on } \Gamma, \tag{5.2}$$

$$u|_{t=0} = u_0. \tag{5.3}$$

We again assume that J is a constant. When the symport term does not appear and $J = 0$, we recover the Cahn–Hilliard–Oono equation.

Considering again a modified problem, namely,

$$\frac{\partial u}{\partial t} + \Delta^2 u - \Delta f(u) + \alpha u + g(u) = J, \tag{5.4}$$

$$\frac{\partial u}{\partial \nu} = \frac{\partial \Delta u}{\partial \nu} = 0 \text{ on } \Gamma, \tag{5.5}$$

$$u|_{t=0} = u_0, \tag{5.6}$$

we can prove the following.

Theorem 5.1 *We assume that u_0 is given such that $u_0 \in H^1(\Omega)$, $0 < \langle u_0\rangle < 1$ and $0 < u_0(x) < 1$, a.e. $x \in \Omega$. Then, there exists $T_0 = T_0(u_0) > 0$ and a weak solution u to (5.1)–(5.3) on $[0, T_0]$ such that $u \in \mathcal{C}([0, T_0]; H^1(\Omega)_w) \cap L^\infty(0, T_0; H^1(\Omega)) \cap L^2(0, T_0; H^2(\Omega))$ and $\frac{\partial u}{\partial t} \in L^2(0, T_0; H^{-1}(\Omega))$. Furthermore, $0 < u(x,t) < 1$, a.e. $(x,t) \in \Omega \times (0, T_0)$.*

Proof We first note that the equation for the spatial average of the order parameter now reads

$$\frac{d\langle u\rangle}{dt} + \alpha\langle u\rangle = J - \langle g(u)\rangle,$$

which yields

$$\langle u_0\rangle e^{-\alpha t} + \frac{J-k}{\alpha}(1-e^{-\alpha t}) \le \langle u(t)\rangle \le \langle u_0\rangle e^{-\alpha t} + \frac{J+k}{\alpha}(1-e^{-\alpha t}), \tag{5.7}$$

allowing us to deduce the existence of $T_0 > 0$ such that, for $t \in [0, T_0]$,

$$\delta \leq \langle u(t) \rangle \leq 1 - \delta,\ \delta \in (0, \frac{1}{2}).$$

Here, we again assume that $2\delta \leq \langle u_0 \rangle \leq 1 - 2\delta$.

We then consider the weaker formulation

$$(-\Delta)^{-1}\frac{\partial \overline{u}}{\partial t} - \Delta\overline{u} + \overline{f(u)} + \alpha(-\Delta)^{-1}\overline{u} + (-\Delta)^{-1}\overline{g(u)} = 0, \tag{5.8}$$

$$\frac{\partial \overline{u}}{\partial \nu} = 0 \text{ on } \Gamma, \tag{5.9}$$

$$u|_{t=0} = u_0. \tag{5.10}$$

Let us multiply (5.8) by $\frac{\partial \overline{u}}{\partial t}$ to obtain, for $t \in [0, T_0]$,

$$\begin{aligned} &\frac{1}{2}\frac{d}{dt}\|\nabla u\|^2 + \|\frac{\partial \overline{u}}{\partial t}\|_{-1}^2 + ((\overline{f(u)}, \frac{\partial \overline{u}}{\partial t})) + \frac{\alpha}{2}\frac{d}{dt}\|\overline{u}\|_{-1}^2 \\ &\quad + (((-\Delta)^{-1}\overline{g(u)}, \frac{\partial \overline{u}}{\partial t})) = 0. \end{aligned} \tag{5.11}$$

Note that

$$\begin{aligned} ((\overline{f(u)}, \frac{\partial \overline{u}}{\partial t})) &= ((f(u), \frac{\partial \overline{u}}{\partial t})) = \frac{d}{dt}\int_\Omega F(u)\,dx - ((f(u), \frac{d\langle u \rangle}{dt})) \\ &= \frac{d}{dt}\int_\Omega F(u)\,dx + \mathrm{Vol}(\Omega)(\langle g(u) \rangle + \alpha\langle u \rangle - J)\langle f(u) \rangle \\ &\geq \frac{d}{dt}\int_\Omega F(u)\,dx - c\|f(u)\|_{L^1(\Omega)}, \end{aligned} \tag{5.12}$$

since $\langle u \rangle$ belongs to $[0, 1]$. It thus follows from (5.11)–(5.12) that, for $t \in [0, T_0]$,

$$\frac{d}{dt}(\|\nabla u\|^2 + \alpha\|\overline{u}\|_{-1}^2 + 2\int_\Omega F(u)\,dx) + \|\frac{\partial \overline{u}}{\partial t}\|_{-1}^2 \leq c\|f(u)\|_{L^1(\Omega)} + c'. \tag{5.13}$$

The rest of the proof is similar to that of Theorem 3.1 and we omit the details. □

Remark 5.2 (i) Note that if $J \geq k$ and $J + k \leq \alpha$, then it follows from (5.7) that $\delta \leq \langle u(t) \rangle \leq 1 - \delta$ for all times (in a finite time interval), so that the solution is actually global in time.

(ii) When $k = J = 0$, it follows from (5.7) that $\langle u \rangle \in (0, 1)$ for all times and we recover the global in time existence for the Cahn–Hilliard–Oono equation. This slightly simplifies the proof given in [25].

We then have the following theorem which improves the global existence result mentioned in the above remark.

Theorem 5.3 *Let us assume that* $0 \leq J \leq \alpha$ *and let* u *be a local in time weak solution as in Theorem 5.1. Then, it is global in time.*

Proof We proceed as in the proof of Theorem 3.5.

Let again u be a local in time weak solution on $[0, T]$, $T > 0$ given, and $T^\star$ be its maximal time of existence. Assume that $T^\star < T$. Noting once more that u belongs to $[0, 1]$ for $t \in [0, T^\star)$, it follows that

$$0 \leq g(u) \leq \frac{k}{k'+1},$$

so that, proceeding as above,

$$\langle u_0\rangle e^{-\alpha t} + \frac{1}{\alpha}(J - \frac{k}{k'+1})(1 - e^{-\alpha t}) \leq \langle u(t)\rangle \leq \langle u_0\rangle e^{-\alpha t} + \frac{J}{\alpha}(1 - e^{-\alpha t}),$$

which allows us to conclude when $J\frac{k'+1}{k} \geq 1$, i.e., $J \geq \frac{k}{k'+1}$. When $J\frac{k'+1}{k} \leq 1$, we can write

$$-(\frac{k}{k'} + \alpha)\langle u\rangle \leq J - \alpha\langle u\rangle - \langle g(u)\rangle \leq J - \frac{k}{k'+1}\langle u\rangle,$$

yielding

$$\langle u_0\rangle e^{-(\frac{k}{k'}+\alpha)t} \leq \langle u(t)\rangle \leq \langle u_0\rangle e^{-\frac{k}{k'+1}t} + J\frac{k'+1}{k}(1 - e^{-\frac{k}{k'+1}t}).$$

We can again conclude as in the proof of Theorem 3.5. □

Remark 5.4 Note that the value of J given in Remark 3.6, (ii), is compatible with the condition $J \leq \alpha$, for a rather small value of α. This is no longer the case for the values considered in [18], with a proper extension of the results when J is nonconstant, as in Sect. 3. In that case, indeed, α should be large, i.e., less but close to 1. It is interesting to note here that, as far as the original Cahn–Hilliard theory is concerned, the dynamics of the Cahn–Hilliard–Oono equation is close, in a proper sense, to that of the Cahn–Hilliard equation when α is small (see [25]).

We next have the following.

Theorem 5.5 *We assume that the assumptions of Theorem 5.3 hold and that* $k > \varepsilon J$, $0 < \frac{\varepsilon J k'}{k - \varepsilon J} < 1$ *and* $(1-\varepsilon)J < \alpha$, $\varepsilon \in (0, 1)$. *Then, any weak solution* u *to (5.1)–(5.3) satisfies*

$$\frac{\partial u}{\partial t} \in L^\infty(r, T; H^{-1}(\Omega)) \cap L^2(r, T; H^1(\Omega)),$$

$\forall r < T$, $r > 0$ *and* $T > 0$ *given.*

Proof We proceed as in the Proof of Theorem 4.1. The only difference here is that

$$\Lambda = \|\nabla\mu\|^2 + ((g(u) + \alpha u - J, \mu))$$

and we have to estimate

$$((g(u) + \alpha u - J, f(u)))$$

from below. Writing

$$g(u) + \alpha u - J = g(u) - \varepsilon J + \alpha(u - (1-\varepsilon)\frac{J}{\alpha}),$$

it follows that

$$((g(u) + \alpha u - J, f(u))) \geq c \int_\Omega F(u)\,dx - c',\ c > 0,$$

which finishes the proof.

We finally have the following.

Theorem 5.6 *We assume that* $n = 1$ *or* 2 *and that the assumptions of Theorems* 5.3 *and* 5.5 *hold. Then, there exists* $\delta \in (0, 1)$ *depending on the* $H^1(\Omega)$*-norm of* u_0 *such that*

$$\delta \leq u(x,t) \leq 1 - \delta,\ \text{for almost all } (x,t),\ x \in \Omega,\ t \geq r,$$

$r > 0$ *given.*

Remark 5.7 Let us assume that $J = 0$ and let us consider the spatially homogeneous equilibrium $u_e = 0$. Then, multiplying (5.1) by u, we obtain

$$\frac{1}{2}\frac{d}{dt}\|u\|^2 + \|\Delta u\|^2 + \alpha\|u\|^2 \leq c_0\|\nabla u\|^2 + \frac{k}{k'}\|u\|^2.$$

Let λ_1 be the first eigenvalue of the operator $-\Delta$ associated with Neumann boundary conditions and acting on functions with null spatial average. Writing (see, e.g., [25,34])

$$\|\Delta u\|^2 = \|(-\Delta)\overline{u}\|^2 \geq \lambda_1\|(-\Delta)^{\frac{1}{2}}\overline{u}\|^2 = \lambda_1\|\nabla u\|^2,$$

we find

$$\frac{1}{2}\frac{d}{dt}\|u\|^2 + (\lambda_1 - c_0)\|\nabla u\|^2 + (\alpha - \frac{k}{k'})\|u\|^2 \leq 0.$$

Therefore, if $c_0 \leq \lambda_1$ and $\frac{k}{k'} \leq \alpha$, then 0 is stable. Furthermore, if $\frac{k}{k'} < \alpha$, then we have a differential inequality of the form

$$\frac{d}{dt}\|u\|^2 + c\|u\|^2 \leq 0, \ c > 0,$$

and it follows from Gronwall's lemma that 0 is asymptotically stable. Note however that the condition $c_0 \leq \lambda_1$ is a restrictive one.

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