

Parabolic Problems with Nonlinear Boundary Conditions in Cell Tissues ¹

A. N. de Carvalho

Abstract: In this paper we consider reaction diffusion problems with nonlinear boundary conditions in two dimensional domains for which the diffusion is large except in a neighborhood of a one dimensional set where it becomes small. We regard the domain as a cell tissue. The cell tissue is divided into several subdomains (called cells) by piecewise smooth curves. The boundary of a domain is called cell wall. Inside each cell the diffusion is large except in a neighborhood of the cell wall. We prove, under certain assumptions, that the asymptotic dynamics of these reaction diffusion problems can be described through a system of ordinary differential equations which can be exhibited explicitly. In this system each coordinate represents the average concentration inside the corresponding cell.

Key words: Parabolic Equations, Nonlinear Boundary Conditions, Cell Tissues, Invariant Manifolds, Attractors, Reduction to Finite Dimensions

1 Introduction

Let $\Omega \subset \mathbb{R}^2$, be an open, bounded and smooth domain. We regard Ω as a cell tissue and $\Gamma := \partial\Omega$ as tissue wall. Consider a reaction occurring inside the cell tissue and involving N different substances. Assuming that there is a nonlinear flux of concentration through Γ ; that is, the flux of concentration through the tissue wall is a nonlinear function of the concentration and taking into account the diffusion, we arrive at the following model

$$\begin{aligned} u_t &= \text{Div}(\mathbf{a}_\nu \nabla u) + f(u), \quad \text{in } \Omega, \\ \frac{\partial u}{\partial \bar{n}_\nu} &= g(u), \quad \text{in } \Gamma, \end{aligned} \tag{1.1}$$

where

$$\frac{\partial u}{\partial \bar{n}_\nu} = \mathbf{a}_\nu \nabla u \cdot \bar{\mathbf{n}},$$

is the covariant normal derivative and $\bar{\mathbf{n}}$ is the outward normal at the boundary, $u \in \mathbb{R}^N$ is the concentration vector (each coordinate represents the concentration of a substance), \mathbf{a}_ν is the diffusion coefficient. We assume throughout and without loss of generality that $|\Omega| = 1$.

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To simplify the presentation let us consider the simplest nontrivial situation. Let Ω represent a single cell which is divided into two compartments; the citoplasm Ω_1 and the nucleus Ω_0 . Suppose that Ω_0 is a smooth open subregion of Ω with boundary Γ_0 and such that $\overline{\Omega_0} \subset \Omega$. Assume that Γ_0 is a smooth closed simple curve in Ω , which encloses Ω_0 . Thus $\Omega \setminus \Gamma_0 = \Omega_1 \cup \Omega_0$.

So far the model does not take into account the fact that the nucleus and the citoplasm are separated by a permeable membrane. This will be dealt with in the following way, assume that the substances diffuse quickly throughout the nucleus or citoplasm but the diffusion through the membrane Γ_0 is slow. Mathematically speaking this means that \mathbf{a}_ν is large inside Ω_0 and Ω_1 but gets small at Γ_0 . We assume that $\mathbf{a}_\nu : \overline{\Omega} \rightarrow \mathbb{R}$ is a continuously differentiable function satisfying

$$\begin{aligned} \mathbf{a}_\nu(x) &\geq \frac{\epsilon}{\nu}, \quad \text{for } x \in \Omega_0^{l\nu\eta(\nu)} \cup \Omega_1^{l\nu\eta(\nu)} \\ \mathbf{a}_\nu(x) &\leq a\rho(\nu)\nu, \quad \text{for } x \in \Omega \setminus \overline{\Omega_0^{l\nu\eta(\nu)} \cup \Omega_1^{l\nu\eta(\nu)}} \\ \mathbf{a}_\nu(x) &\geq a\nu, \quad \text{for } x \in \Omega. \end{aligned} \quad (1.2)$$

where $\rho : \mathbb{R}^+ \rightarrow \mathbb{R}^+$ and $\eta : \mathbb{R}^+ \rightarrow \mathbb{R}^+$ are continuous strictly increasing functions satisfying $\rho(0) = \eta(0) = 1$ and $\Omega_i^r = \{x \in \Omega_i : \text{dist}(x, \Gamma_0) > r\}$.

With these assumptions in mind we intuitively guess that the concentrations should approach spatially constant functions in Ω_0 and Ω_1 and therefore, we should be able to approximate the problem (1.1) by a system of two coupled ordinary differential equations describing the average concentrations in the nucleus and in the citoplasm. If that is the case, it would be very interesting to determine this *limiting system* explicitly. This problem has been addressed in [3] for the case $g = 0$.

To establish which is the *limiting system* for the problem (1.1) we need to better understand the following eigenvalue problem

$$\begin{aligned} \text{Div}(\mathbf{a}_\nu \nabla \phi^\nu) &= -\lambda^\nu \phi^\nu, \quad \text{in } \Omega \\ \frac{\partial \phi^\nu}{\partial \overline{n}_\nu} &= 0, \quad \text{in } \Gamma. \end{aligned} \quad (1.3)$$

Let $\lambda_1^\nu < \lambda_2^\nu \leq \lambda_3^\nu, \dots$ be the sequence of eigenvalues, solutions of the problem (1.3), counting multiplicity and $\phi_1^\nu, \phi_2^\nu, \phi_3^\nu, \dots$ be a corresponding sequence of orthonormalized eigenfunctions. Then, the following result holds (see [3]).

Lemma 1.1 *Under the assumption (1.2) we have that*

$$\begin{aligned} \lambda_1^\nu &\equiv 0, \quad \phi_1^\nu \equiv 1 \\ \lambda_2^\nu &\rightarrow \frac{a}{2l} \frac{1}{|\Omega_0| |\Omega_1|} |\Gamma_0| \\ \phi_2^\nu &\xrightarrow{s-L^2(\Omega)} \sum_{i=0}^1 k_i \chi_{\Omega_i} \end{aligned} \quad (1.4)$$

as $\nu \rightarrow 0$, where $k_0 = \left(\frac{|\Omega_1|}{|\Omega_0|}\right)^{\frac{1}{2}}$ and $k_1 = -\left(\frac{|\Omega_0|}{|\Omega_1|}\right)^{\frac{1}{2}}$. Furthermore, $\lambda_3^\nu \rightarrow \infty$ as $\nu \rightarrow 0$.

Next we proceed to guess which is the *limiting system*. For simplicity of notation we assume that $N = 1$, the proofs go through unchanged in the case $N > 1$. Let u be a solution of (1.1) and consider the following decomposition

$$u = u_1\phi_1^\nu + u_2\phi_2^\nu + w$$

where $u_1 = \int_\Omega u\phi_1^\nu$, $u_2 = \int_\Omega u\phi_2^\nu$ and $w = u - u_1\phi_1^\nu - u_2\phi_2^\nu$. This decomposition induces a decomposition in the equation (1.1) in the following way

$$\begin{aligned} \dot{u}_1 &= \int_\Omega f(u_1\phi_1^\nu + u_2\phi_2^\nu + w)\phi_1^\nu + \int_\Gamma \gamma(g(u_1\phi_1^\nu + u_2\phi_2^\nu + w))\gamma(\phi_1^\nu)d\Gamma \\ \dot{u}_2 &= -\lambda_2^\nu u_2 + \int_\Omega f(u_1\phi_1^\nu + u_2\phi_2^\nu + w)\phi_2^\nu \\ &+ \int_\Gamma \gamma(g(u_1\phi_1^\nu + u_2\phi_2^\nu + w))\gamma(\phi_2^\nu)d\Gamma \\ w_t &= \text{Div}(\mathbf{a}_\nu \nabla w) + f(u_1\phi_1^\nu + u_2\phi_2^\nu + w) - \left(\int_\Omega f(u)\phi_1^\nu\right)\phi_1^\nu \\ &- \left(\int_\Omega f(u)\phi_2^\nu\right)\phi_2^\nu - \left(\int_\Gamma \gamma(g(u))\gamma(\phi_1^\nu)d\Gamma\right)\phi_1^\nu \\ &- \left(\int_\Gamma \gamma(g(u))\gamma(\phi_2^\nu)d\Gamma\right)\phi_2^\nu \\ \frac{\partial w}{\partial \bar{n}_\nu} &= g(u). \end{aligned} \quad (1.5)$$

Since the third eigenvalue λ_3^ν is blowing up to infinity, we guess that w will play no role in the asymptotic behavior and we have

$$\begin{aligned} \dot{u}_1 &\sim \int_\Omega f(u_1\phi_1^\nu + u_2\phi_2^\nu)\phi_1^\nu + \int_\Gamma \gamma(g(u_1\phi_1^\nu + u_2\phi_2^\nu + w))\gamma(\phi_1^\nu)d\Gamma \\ \dot{u}_2 &\sim -\lambda_2^\nu u_2 + \int_\Omega f(u_1\phi_1^\nu + u_2\phi_2^\nu)\phi_2^\nu + \int_\Gamma \gamma(g(u_1\phi_1^\nu + u_2\phi_2^\nu + w))\gamma(\phi_2^\nu)d\Gamma, \end{aligned} \quad (1.6)$$

using the convergence of eigenvalues and eigenfunctions we obtain that the limiting system should be

$$\begin{aligned} \dot{u}_1 &= |\Omega_0| f(u_1 + k_0 u_2) + |\Omega_1| f(u_1 + k_1 u_2) + |\Gamma|g(u_1 + k_1 u_2) \\ \dot{u}_2 &= -\frac{\alpha}{2l} \frac{1}{|\Omega_0||\Omega_1|} |\Gamma_0| u_2 + |\Omega_0| f(u_1 + k_0 u_2) k_0 + k_1 |\Omega_1| f(u_1 + k_1 u_2) \\ &+ |\Gamma|k_1 g(u_1 + k_1 u_2) \end{aligned} \quad (1.7)$$

The variables u_1 and u_2 may not be the best choice of variables to study this problem. A better choice would probably be a variable that reflected the average over Ω_0 and Ω_1 . To relate u_1 and u_2 with these average we consider

$$v_1 = |\Omega_0|^{-1} \int_{\Omega_0} u(x)dx, \quad \text{and} \quad v_2 = |\Omega_1|^{-1} \int_{\Omega_1} u(x)dx$$

thus,

$$u_1 = (|\Omega_0|v_1 + |\Omega_1|v_2) \quad (1.8)$$

$$u_2 = (|\Omega_0||\Omega_1|)^{\frac{1}{2}}(v_1 - v_2)$$

and

$$v_1 = (u_1 + k_0 u_2) \quad (1.9)$$

$$v_2 = (u_1 + k_1 u_2).$$

With this change of coordinates the system (1.7) becomes

$$\begin{aligned} \dot{v}_1 &= -\frac{a}{2l} \frac{1}{|\Omega_0||\Omega_1|} \frac{|\Gamma_0|}{|\Omega_0|} (v_1 - v_2) + f(v_1) \\ \dot{v}_2 &= \frac{a}{2l} \frac{1}{|\Omega_1||\Omega_0|} \frac{|\Gamma_0|}{|\Omega_1|} (v_1 - v_2) + f(v_2) + \frac{|\Gamma|}{|\Omega_1|} g(v_2). \end{aligned} \quad (1.10)$$

Note that the concentrations in Ω_0 and in Ω_1 depend on the reaction occurring inside Ω_0 or Ω_1 respectively plus the flow through the nucleus membrane which is proportional to the difference between the concentrations in the nucleus and cytoplasm. Also note that the coupling is proportional to the length of the permeable membrane. Models of this type appear in synthesis of mRNA in the nucleus and the consequent production of the inhibiting protein in the cytoplasm, in this case the model should also consider a delay in the production of the inhibiting protein. The model presented here is just a simple model used to introduce the results, much more general models with several cells (or compartments) and taking into account delays can be considered. For applications of these results see [6, 7, 8].

More generally, results similar to Lemma 1.1 hold for tissues with any number of cells. That is, consider an open, bounded and smooth domain $\Omega \subset \mathbb{R}^n$, which we will regard as a cell tissue. Assume that there is a positive integer ℓ and smooth subregions Ω_i , $1 \leq i \leq \ell$, of Ω , such that

- i) $\Omega_i \cap \Omega_j = \emptyset$, $i \neq j$,
- ii) $\Omega \subset \cup_{i=1}^{\ell} \bar{\Omega}_i$
- iii) If $\Gamma_i = \partial\Omega_i \setminus \Gamma$ and $\Gamma_{ij} := \Gamma_i \cap \Gamma_j$. Assume that Γ_{ij} is a piecewise smooth curve in Ω .

The regions Ω_i are called cells and its boundary Γ_i will be referred to as cell walls or membranes. We assume that the inner walls; that is, $\Gamma_i \setminus \Gamma$ are permeable membranes whereas the flux through the outer wall, Γ , is a nonlinear function of the concentration; that is, the outer wall is an active membrane. The no flux condition, at the boundary Γ , assumed in (1.1) reflects the fact that the outer wall is a barrier. The fact that the inner walls, Γ_{ij} , are permeable membranes is

reflected through the assumption that the diffusion coefficient becomes small in a neighborhood of Γ_{ij} .

Let a, e, l , be positive constants and $\Omega_i^r := \{x \in \Omega_i : \text{dist}(x, \Gamma_i) > r\}$. Assume that the diffusion coefficient $\mathbf{a}_\nu : \bar{\Omega} \rightarrow \mathbb{R}$ is a continuously differentiable function satisfying the following conditions

$$\begin{aligned} \mathbf{a}_\nu(x) &\geq \frac{\varepsilon}{\nu}, \quad \forall x \in \Omega_i^{l\nu\eta(\nu)} \quad 1 \leq i \leq \ell \\ \mathbf{a}_\nu(x) &\leq a\rho(\nu)\nu, \quad \forall x \in \Omega \setminus \cup_{i=1}^{\ell} \Omega_i^{l\nu} \\ \mathbf{a}_\nu(x) &\geq a\nu, \quad \forall x \in \Omega \end{aligned} \quad (1.11)$$

where $\rho : \mathbb{R}^+ \rightarrow \mathbb{R}^+$ and $\eta : \mathbb{R}^+ \rightarrow \mathbb{R}^+$ are continuous strictly increasing functions satisfying $\rho(0) = 1$ and $\eta(0) = 1$.

These conditions mean that for a reaction occurring inside cells of a tissue and taking into account the spatial diffusion, the diffusion is large inside the cells whereas it becomes small at the membranes. Hence, we expect that concentrations will rapidly homogenize inside the cells and any changes in the concentration will occur at the membranes.

Intuitively we guess that the equations (1.1) inside a cell will be much like an ordinary differential equation where the unknowns are the average concentrations inside the cells. Any coupling with equations describing the average concentrations of adjacent cells would be made through the membrane. Thus, the problem (1.1) would be described by a system of ℓ ordinary differential equations. Our first intent is to determine how this limiting ordinary differential equations should look like.

Consider the eigenvalue problem

$$\begin{aligned} \text{Div}(\mathbf{a}_\nu \nabla \phi) &= -\lambda^\nu \phi, \quad \text{in } \Omega, \\ \frac{\partial \phi}{\partial \mathbf{n}} &= g(u). \end{aligned} \quad (1.12)$$

and assume that $(\lambda_n^\nu, \phi_n^\nu)$ is a sequence of eigensolutions of the problem (1.12) with the eigenvalues ordered so that they are increasing and counting multiplicity.

With these assumptions the following result to hold.

Lemma 1.2 *Let $(\lambda_n^\nu, \phi_n^\nu)$, $n \geq 1$ be a sequence of solutions of (1.12) such that the eigenvalues λ_n^ν are ordered increasingly, counting multiplicity, and the eigenfunctions ϕ_n^ν are normalized. Then, there are $\xi_i \geq 0$, $k_i^j \in \mathbb{R}$, $1 \leq i, j \leq \ell$, such that $\xi_1 = 0$, $k_1^j = 1$, $1 \leq j \leq \ell$ and*

$$\lim_{\nu \rightarrow 0} \lambda_i^\nu = \xi_i, \quad 1 \leq i \leq \ell$$

$$\phi_\nu^i \xrightarrow{s-L^2(\Omega)} \sum_{j=1}^{\ell} k_i^j \chi_{\Omega_j} := \chi_i, \quad 1 \leq i \leq \ell$$

where $\sum_{j=1}^{\ell} k_i^j k_m^j |\Omega_j| = \delta_{im}$, $1 \leq i, m \leq \ell$. Furthermore, $\lambda_{\ell+1}^\nu \rightarrow \infty$ as $\nu \rightarrow 0$.

Let $v = (v_1, \dots, v_\ell) \in \mathbb{R}^\ell$, $\Phi_\nu = (\phi_1^\nu, \dots, \phi_\ell^\nu)$ and $\Phi_\nu \cdot v = \sum_{j=1}^{\ell} \phi_j^\nu v_j$.

If $u(t, x)$ is a solution of (1.1) in $H^1(\Omega)$, it can be written as

$$u(t, x) = \Phi_\nu(x) \cdot v(t) + w(t, x)$$

where $v(t) \in \mathbb{R}^\ell$, $v_j = \int_{\Omega} u \phi_j$.

Using the above decomposition the equation (1.1) can be rewritten as

$$\begin{aligned} \frac{dv}{dt} &= -\text{diag}(\lambda_1, \dots, \lambda_\ell) v + \int_{\Omega} f(\Phi_\nu \cdot v + w(t, y)) \text{diag}(\phi_1, \dots, \phi_\ell) dy \\ &\quad + \int_{\Gamma} \gamma(g(\Phi_\nu \cdot v + w)) \gamma(\text{diag}(\phi_1, \dots, \phi_\ell)) d\Gamma, \\ w_t &= \text{Div}(\mathbf{a}_\nu \nabla w) + f(\Phi_\nu \cdot v + w(t)) - \Phi_\nu \cdot \int_{\Omega} \Phi_\nu f(\Phi_\nu \cdot v + w(t, y)) dy, \\ &\quad - \Phi_\nu \cdot \int_{\Gamma} \gamma(\Phi_\nu) \gamma(g(\Phi_\nu \cdot v + w)) d\Gamma \end{aligned} \quad (1.13)$$

$$\frac{\partial w}{\partial \nu} = g(u).$$

From Lemma 1.2 one expects that the component w does not play much role in the asymptotic behavior of (1.1). Therefore,

$$\dot{v}_j \sim -\lambda_j^\nu v_j + \int_{\Omega} f \left(\sum_{i=1}^{\ell} v_i \phi_i(y) \right) \phi_j(y) dy + \int_{\Gamma} \gamma \left(g \left(\sum_{i=1}^{\ell} v_i \phi_i \right) \right) \gamma(\phi_j) d\Gamma,$$

$1 \leq j \leq \ell$.

From the assumptions on the eigenfunctions ϕ_j^ν , one expects that

$$\begin{aligned} \dot{v}_j &\sim -\lambda_j^\nu v_j + \sum_{q=1}^{\ell} \int_{\Omega_q} f \left(\sum_{i=1}^{\ell} v_i \phi_i(y) \right) \phi_j(y) dy \\ &\quad + \sum_{q=1}^{\ell} \int_{\Gamma_q} \gamma \left(g \left(\sum_{i=1}^{\ell} v_i \phi_i \right) \right) \gamma(\phi_j) d\Gamma \\ &\sim -\xi_j v_j + \sum_{q=1}^{\ell} \int_{\Omega_q} f \left(\sum_{i=1}^{\ell} k_i^q v_i \right) k_j^q dy + \sum_{q=1}^{\ell} \int_{\Gamma_q} g \left(\sum_{i=1}^{\ell} k_i^q v_i k_j^q \right) d\Gamma \\ &\sim -\xi_j v_j + \sum_{q=1}^{\ell} |\Omega_q| f \left(\sum_{i=1}^{\ell} k_i^q v_i \right) k_j^q + \sum_{q=1}^{\ell} |\Gamma_q| g \left(\sum_{i=1}^{\ell} k_i^q v_i k_j^q \right), \quad 1 \leq j \leq \ell. \end{aligned}$$

where $\Gamma_q = \Gamma \cap \partial\Omega_q$ and $|\Gamma_q| = 0$ if Ω_q does not intersect Γ . Therefore, the following *limiting* ordinary differential equation is associated with (1.1)

$$\dot{v}_j = -\xi_j v_j + f_j(v_1, \dots, v_\ell) + g_j(v_1, \dots, v_\ell), \quad 1 \leq j \leq \ell, \quad (1.14)$$

where

$$f_j(v) = \sum_{q=1}^{\ell} |\Omega_q| f \left(\sum_{i=1}^{\ell} k_i^q v_i \right) k_j^q, \quad \text{and} \quad g_j(v) = \sum_{q=1}^{\ell} |\Gamma_q| g \left(\sum_{i=1}^{\ell} k_i^q v_i k_j^q \right),$$

$1 \leq j \leq \ell$.

Let us rewrite this system in a better way. Let $K = (k_1, \dots, k_\ell)$, $k_i = (k_i^1, \dots, k_i^\ell)^\top$, $1 \leq i \leq \ell$ and $M = \text{diag}(|\Omega_1|, \dots, |\Omega_\ell|)$; then, from the orthogonality of the normalized eigenfunctions ϕ_i it follows that

$$\begin{aligned} \left| \int_{\Omega} \phi_j \phi_i dx - \sum_{p=1}^{\ell} \int_{\Omega_p} k_j^p k_i^p dx \right| &= \left| \int_{\Omega} [\phi_j [\phi_i - \mathcal{X}_i] + [\phi_j - \mathcal{X}_j] \mathcal{X}_i] dx \right| \\ &\leq \|\phi_i - \mathcal{X}_i\|_{L^2(\Omega)} + \|\phi_j - \mathcal{X}_j\|_{L^2(\Omega)} \end{aligned}$$

therefore,

$$\delta_{ij} = \int_{\Omega} \phi_j(x) \phi_i(x) dx \rightarrow \sum_{p=1}^{\ell} |\Omega_p| k_j^p k_i^p$$

and $\sum_{p=1}^{\ell} |\Omega_p| k_j^p k_i^p = \delta_{ij}$. With this information we have $K^\top M K = M K K^\top = I$, and

$$\sum_{j=1}^{\ell} |\Omega_j| \sum_{p=1}^{\ell} k_p^j k_p^i = 1.$$

If $w = K v$ and $\Xi = \text{diag}(\xi_1, \dots, \xi_\ell)$, we can rewrite (1.14) as

$$\dot{w} = -K \Xi K^\top M w + F(w) + G(w) \quad (1.15)$$

where $F(w) = (f(w_1), \dots, f(w_\ell))^\top$ and $g(w) = \left(\frac{|\Gamma_1|}{|\Omega_1|} g(w_1), \dots, \frac{|\Gamma_\ell|}{|\Omega_\ell|} g(w_\ell) \right)^\top$.

The aim of this paper is to show that the dynamics of (1.1) can be described by (1.15).

Now that we have intuitively obtained the results that we would like to prove we are in condition to state the main theorem of this paper.

Consider the following decomposition of $H^1(\Omega)$ ($\|\phi\|_{H^1(\Omega)}^2 = \int_{\Omega} \mathbf{a}_\nu |\nabla \phi|^2 dx + \lambda \int_{\Omega} \phi^2 dx$)

$$H^1(\Omega) = W \oplus W_{\nu, \frac{1}{2}}^\perp$$

where

$$W = \text{span}[\phi_1, \dots, \phi_\ell], \quad W_{\nu, \frac{1}{2}}^\perp = \{\phi \in H^1(\Omega) : \langle \phi, \Phi_\nu \cdot v \rangle = 0, v \in \mathbb{R}^\ell\},$$

$$\langle \phi, \psi \rangle = \int_\Omega \phi(x)\psi(x)dx.$$

Let

$$P_j : \mathbb{R}^\ell \oplus W_{\nu, \frac{1}{2}}^\perp \rightarrow \mathbb{R}, \quad 1 \leq j \leq \ell$$

$$P_j(v, \psi) = \int_\Omega f \left(\sum_{i=1}^\ell v_i \phi_i(y) + \psi(y) \right) \phi_j(y) dy - f_j(v) \quad (1.1\epsilon)$$

$$+ \int_\Gamma \gamma(g(\Phi_\nu(y) \cdot v + \psi(y))\gamma(\text{diag}(\phi_1(y), \dots, \phi_\ell(y))dy - g_j(v),$$

Lemma 1.3 *Assume that f is smooth. Then, for $\|(v, w)\|_{H^1(\Omega)} \leq r$ there exist $L_{P_j}(r, \nu)$, $M_{P_j}(r, \nu)$ such that*

$$\|P_j(v, w)\|_{\mathbb{R}} \leq L_{P_j} \|w\|_{H^1(\Omega)} + M_{P_j}(r, \nu)$$

and

$$\|\nabla_v P_j(v, w)\|_{\mathbb{R}^\ell} \leq L_{P_j} \|w\|_{H^1(\Omega)} + M_{P_j}(r, \nu)$$

where $L_{P_j}(r, \nu)$, $M_{P_j}(r, \nu) \rightarrow 0$ as $\nu \rightarrow \infty$.

Theorem 1.1 *There is an exponentially attracting invariant manifold S_ν which is the graph of a function $\sigma_\nu : \mathbb{R}^\ell \rightarrow H^1(\Omega)$ such that the attractor \mathcal{A}_ν is contained in S_ν . The flow in S_ν is given by $(v(t), w(t)) = (v(t), \sigma_\nu(v(t)))$, where $v(t)$ is the solution of*

$$\dot{v} = -\text{diag}(\lambda_1, \dots, \lambda_\ell)v + \begin{pmatrix} f_1(v) + g_1(v) \\ \vdots \\ f_\ell(v) + g_\ell(v) \end{pmatrix} + P_\nu(v, \sigma_\nu(v)), \quad (1.17)$$

where $P_\nu(v, w) = (P_1(v, w), \dots, P_\ell(v, w))^\top$. If f is smooth and the flow defined by (1.14) is structurally stable, for ν small enough, the flow defined by (1.17) is structurally stable and they are topologically equivalent; in addition, the family of attractors $\{\mathcal{A}_\nu, \nu \geq 0\}$ is continuous at zero.

The proof of this result follows from the invariant manifold theory (see, [5] or [2]) and from Lemma 1.2.

2 Proof of the Results.

We start with the local existence (Theorem 2.3) of solutions and then proceed to existence of global attractors (Theorem 2.4) for the problem (1.1). The proof of Theorem 1.1 will then follow as in [3].

2.1 Local Existence.

Assume A is an unbounded, selfadjoint positive operator in a Hilbert space X . In particular, A is a sectorial operator in X and we can define the fractional powers A^α of A , and the fractional power spaces $X^\alpha := D(A^\alpha)$, endowed with the graph norm, $\alpha \in \mathbb{R}$, where $X^{-\alpha} = (X^\alpha)'$, for $\alpha > 0$. Even more, A is sectorial in X^α with domain $X^{\alpha+1}$, for any α , see [5, 9].

Theorem 2.1 *With the above notations, assume $h : X^\alpha \rightarrow X^\beta$ is locally Lipschitz and bounded on bounded sets, where $0 \leq \alpha - \beta < 1$. Then, the abstract parabolic problem*

$$\frac{du}{dt} + Au = h(u) \tag{2.18}$$

$$u(0) = u_0 \in X^\alpha$$

has a unique locally defined solution, given by the Variation of Constants Formula

$$u(t, u_0) = e^{-At}u_0 + \int_0^t e^{-A(t-s)}h(u(s)) ds.$$

where e^{-At} denotes the analytic semigroup generated by A . Moreover, u verifies,

$$u \in C([0, T], X^\alpha) \cap C(0, T, X^{\beta+1}), \quad u_t \in C(0, T, X^\gamma)$$

for every $\gamma < \beta + 1$ and the equation is verified in X^β . Even more, either the solution is defined for all $t \geq 0$ or it blows up, in X^α norm, in finite time. \square

For (1.1), let $X = L^2(\Omega)$ and $A_\nu : D(A_\nu) \subset X \rightarrow X$ be the operator defined by

$$D(A_\nu) = \{u \in H^2(\Omega) : \frac{\partial u}{\partial n_\nu} = 0, \text{ in } \Gamma\} \tag{2.19}$$

$$A_\nu u = -\text{Div}(a_\nu \nabla u) + \lambda u, \quad u \in D(A_\nu).$$

Then, we have the following well known result

Proposition 2.1 *The operator A_ν defined above is positive, selfadjoint and has compact resolvent in $X = L^2(\Omega)$. In particular*

$$X_\nu^1 = D(A_\nu), \quad X_\nu^{1/2} = H^1(\Omega), \quad X_\nu^0 = L^2(\Omega), \quad X_\nu^{-1/2} = H^{-1}(\Omega)$$

where we have set $H^{-1}(\Omega) \stackrel{def}{=} (H^1(\Omega))'$.

The operator A_ν , as an operator between $H^1(\Omega)$ and $H^{-1}(\Omega)$, coincides with the operator L_ν defined by the continuous coercive bilinear form in $H^1(\Omega)$ defined by

$$\langle L_\nu(u), v \rangle_{-1,1} = a_\nu(u, v) = \int_\Omega a_\nu \nabla u \nabla v + \lambda \int_\Omega uv$$

for every $u, v \in H^1(\Omega)$. \square

Note that the norm in $X_\nu^{1/2} = H^1(\Omega)$ is given by

$$\|u\|_\nu^2 = \int_\Omega a_\nu(x) |\nabla u|^2 + \lambda \int_\Omega |u|^2$$

which, for fixed ν , is equivalent to the usual norm in $H^1(\Omega)$.

As shown in [4], for solving problems with nonhomogeneous boundary conditions, it is natural to consider a special class of elements $h \in H^{-1}(\Omega)$ defined as

$$\langle h, \phi \rangle_{-1,1} = \langle f, \phi \rangle_\Omega + \langle g, \gamma(\phi) \rangle_\Gamma$$

for every $\phi \in H^1(\Omega)$, where $f \in L^2(\Omega)$ and $g \in H^{-1/2}(\Gamma)$. So, for short, $h \stackrel{def}{=} f_\Omega + g_\Gamma$. In particular, for nonlinear problems we consider nonlinear mappings

$$h(u) := f_\Omega(u) + g_\Gamma(u)$$

where at least, $f_\Omega : X_\nu^\alpha \rightarrow L^2(\Omega)$ and $g_\Gamma : X_\nu^\alpha \rightarrow H^{-1/2}(\Gamma)$, for some $\alpha \geq 0$. Depending on extra regularity properties of g_Γ , to be made precise below, we will get

$$h : X_\nu^\alpha \rightarrow X_\nu^\beta$$

for suitable chosen $\alpha > 0$ and $\beta \leq 0$.

Now, we will show some natural apriori requirements on the exponents α and β . Recall that for the abstract result we need $0 \leq \alpha - \beta < 1$.

On the one hand, since we want to give account of nonhomogeneous terms on the boundary, i.e. we consider the case $g \neq 0$, that implies necessarily $\beta < 0$. Otherwise, we can always take $\beta = 0$. Since, from the results in [4], we are interested in reading the equation in $H^{-1}(\Omega)$, then we need $0 > \beta \geq -1/2$.

On the other hand, if we want to have initial data at least in $H^1(\Omega)$, we then require $\alpha \geq 1/2$. Finally, as shown below, for obtaining energy estimates on the solution, we are interested in having enough regularity to have $u_t \in H^1(\Omega)$, for $t > 0$, and that implies $\beta + 1 > 1/2$ and then $\beta > -1/2$.

Also note that, in the case of nonzero terms on the boundary, there is another natural upper bound for α . In fact, $\alpha < 3/4$, since for $\alpha \geq 3/4$ the space X_ν^α incorporates the boundary condition $\frac{\partial u}{\partial \bar{n}_\nu} = 0$. Therefore, $\beta + 1 < 3/4$, i.e. $\beta < -1/4$.

Summarizing, if $g \neq 0$, then

$$3/4 > \alpha \geq 1/2, \quad -1/4 > \beta > -1/2, \quad \text{and} \quad 0 \leq \alpha - \beta < 1$$

while if $g = 0$, we have the standard case $\beta = 0, \alpha < 1$.

Then we have

Theorem 2.2 *Assume $f_\Omega, g_\Gamma, \alpha$ and β are as above and*

$$h : X_\nu^\alpha \rightarrow X_\nu^\beta$$

is locally Lipschitz and bounded on bounded sets. Then, for every $u_0 \in X_\nu^\alpha$, there exists a unique, locally defined solution of

$$u_t + L_\nu(u) = h(u) \quad (2.20)$$

such that it verifies

$$u \in C([0, T], X_\nu^\alpha) \cap C(0, T, X_\nu^{\beta+1}) \quad u_t \in C(0, T, X_\nu^\gamma)$$

for every $\gamma < \beta + 1$ and

$$\int_\Omega u_t \phi + \int_\Omega a_\nu(x) \nabla u \nabla \phi + \lambda \int_\Omega u \phi = \int_\Omega f(u) \phi + \langle g(u), \gamma(\phi) \rangle_\Gamma \quad (2.21)$$

for every $\phi \in H^1(\Omega)$. In particular, it holds

$$\begin{aligned} u_t &= \text{Div}(a_\nu(x) \nabla u) - \lambda u + f(u) \quad \text{on } \Omega \\ \frac{\partial u}{\partial n_\nu} &= g(u), \quad \text{on } \Gamma \end{aligned} \quad (2.22)$$

and either the solution is defined for all $t > 0$ or it blows up, in X_ν^α norm, in finite time.

In particular, assume

$$f_\Omega : X_\nu^\alpha \rightarrow L^2(\Omega)$$

$$g_\Gamma : X_\nu^\alpha \rightarrow L^2(\Gamma) \text{ or even } H^{-r}(\Gamma)$$

with $0 \leq r < 1/2$, are locally Lipschitz nonlinear functions, for $\alpha \geq 1/2$. Then, there exists β such that $-1/4 > \beta > -1/2$ verifying all the above.

Assume now that $f, g : \mathbb{R} \rightarrow \mathbb{R}$ are C^1 and C^2 functions, respectively, satisfying the following growth condition

$$\lim_{|s| \rightarrow \infty} \frac{|f'(s)|}{e^{\eta|s|^2}} = 0, \quad \forall \eta > 0, \quad (2.23)$$

and

$$\lim_{|s| \rightarrow \infty} \frac{|g''(s)|}{e^{\eta|s|^2}} = 0, \forall \eta > 0. \quad (2.24)$$

The conditions (2.23) and (2.24), for $N = 2$, are called subcritical growth condition for the functions f' and g'' , respectively. Note that we need these conditions to hold for arbitrarily small η . Also note that always (2.24) implies (2.23).

We denote by f_Ω and g_Ω the composition Nemitsky operators defined by f and g , for functions defined on Ω , while we denote by f_Γ and g_Γ the Nemitsky operators defined for f and g for functions defined on Γ . Observe that if the trace of u and $g_\Omega(u)$ are defined then

$$\gamma(g_\Omega(u)) = g_\Gamma(\gamma(u))$$

We will show below that, under the growth assumptions (2.23) and (2.24), the maps f_Ω and g_Γ are such that $h = f_\Omega + g_\Gamma$, verifies the assumptions of Theorem 2.2 above.

For this, recall the Sobolev embeddings

$$H^1(\Omega) \subset L^p(\Omega), p \geq 1, \quad (2.25)$$

and, from the trace theorem, the trace operator

$$\gamma : W^{1,q}(\Omega) \rightarrow L^p(\Gamma)$$

is bounded for $q \leq p \leq \frac{q}{2-q}$, if $q < 2$, [1].

We also make use of the following result due to N. S. Trudinger, [10].

Lemma 2.1 *There exist two positive constants σ and K such that if $\|u\|_{H^1(\Omega)} \leq 1$ then,*

$$\|e^{\sigma|u(\cdot)|^2}\|_{L^2(\Omega)} \leq K. \quad (2.26)$$

Furthermore, the constant σ is bounded above by 2π . \square

With this result we obtain the following.

Lemma 2.2 *Assume f verifies (2.23), then the mapping*

$$f_\Omega : H^1(\Omega) \rightarrow L^p(\Omega)$$

for any $1 \leq p < \infty$, is well defined and Lipschitz continuous on bounded subsets of $H^1(\Omega)$.

Assume now g verifies (2.24). As noted above, then g also verifies (2.23) and then g_Ω verifies Lemma 2.2. However, the function g_Ω has better properties. As observed above, if the trace of $g_\Omega(u)$ is defined, we have

$$\gamma(g_\Omega(u)) = g_\Gamma(\gamma(u))$$

Now, we have

Lemma 2.3 *If g verifies (2.24), the map*

$$g_\Omega : H^1(\Omega) \rightarrow W^{1,q}(\Omega)$$

is Lipschitz continuous on bounded subsets of $H^1(\Omega)$ for any $1 \leq q < 2$.

Then, we have

Lemma 2.4 *If g verifies (2.24) and $\rho < 1$; then, $g_\Gamma : H^1(\Omega) \rightarrow L^2(\Gamma)$ is Lipschitz continuous on bounded sets.*

Theorem 2.3 *Assuming the growth conditions (2.23) and (2.24), Theorem 2.2 applies with $\alpha = 1/2$. Therefore, (1.1) defines a local semigroup in $H^1(\Omega)$.*

In the following subsection we will also consider the Nemitsky operators induced by the primitives $F(u) = \int_0^u f(s)ds$ and $G(u) = \int_0^u g(s)ds$. Note that $G(u)$ satisfies the same growth condition as $g(u)$ in the case $N = 2$ and therefore the trace of $G_\Omega(u)$ is well defined and since $G_\Omega(u) \in W^{1,q}(\Omega)$, $1 \leq q < 2$ we have that $\gamma(G_\Omega(u)) \in L^p(\Gamma)$, $1 \leq p \leq \frac{2}{2-q}$, in particular it is in $L^1(\Gamma)$.

Using the growth conditions (2.23) and (2.24) we also obtain that $\lim_{|u| \rightarrow \infty} \frac{F(s)}{e^{\eta s^2}} = 0, \forall \eta > 0$ and $\lim_{|u| \rightarrow \infty} \frac{G(s)}{e^{\eta s^2}} = 0, \forall \eta > 0$.

2.2 Existence of Global Attractors

Next we consider the existence of attractors for the problem (1.1) for nonlinearities f and g satisfying the growth assumptions (2.23), (2.24) and either one of the following dissipativeness conditions

$$\begin{cases} \limsup_{|u| \rightarrow \infty} \frac{f(u) - \lambda u}{u} < 0 \\ \limsup_{|u| \rightarrow \infty} \frac{g(u)}{u} \leq 0 \end{cases} \tag{2.27}$$

or

$$\begin{cases} \limsup_{|u| \rightarrow \infty} \frac{f(u) - \lambda u}{u} \leq 0, \\ \limsup_{|u| \rightarrow \infty} \frac{g(u)}{u} < 0. \end{cases} \tag{2.28}$$

The existence of global attractors for the problems (1.1) when $g \neq 0$ and f, g satisfy the hypotheses above has been established in [4].

Consider the energy functional $V_\epsilon : H^1(\Omega) \rightarrow \mathbb{R}$ defined by

$$V_\epsilon(\phi) = \frac{1}{2} \int_\Omega a_\nu |\nabla \phi|^2 + \frac{\lambda}{2} \int_\Omega \phi^2 - \int_\Omega F(\phi) - \int_\Gamma G(\gamma(\phi)) \tag{2.29}$$

where $F(u) = \int_0^u f(s)ds$ and $G(u) = \int_0^u g(s)ds$.

The following result is proved in [4].

Theorem 2.4 *Assume $N \leq 3$, $\nu > 0$ and (2.23), (2.24) and either (2.27) or (2.28) are satisfied. Then*

i) V_ν is a Lyapunov function for (1.1).

ii) All solutions of (1.1) are globally defined.

iii) The problem (1.1) has a global attractor \mathcal{A}_ν in $H^1(\Omega)$. Furthermore (1.1) is a gradient system and therefore, $\mathcal{A}_\nu = W^s(E_\nu)$, where E_ν is the set of equilibria of (1.1) and $W^u(E_\nu)$ denotes the unstable manifold of the set E_ν . Moreover there is a constant \mathcal{M} independent of ν such that

$$|u(x)| \leq \mathcal{M}, \quad \forall x \in \bar{\Omega}, \quad \forall \nu > 0.$$

This result is essential to the proof Theorem 1.1 for it allow us to cut f outside $[-\mathcal{M}, \mathcal{M}]$ in order that the map becomes globally bounded and globally Lipschitz without affecting the attractor.

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Alexandre Nolasco de Carvalho

Departamento de Matemática do ICMSC-USP

13560-970 São Carlos SP

andcarva@icmsc.sc.usp.br

Brasil