University of Alberta

Analysis of Some Biosensor Models with Surface Effects

by

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A thesis submitted to the Faculty of Graduate Studies and Research
in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in

Applied Mathematics

Department of Mathematical and Statistical Sciences

Fall 2009

Edmonton, Alberta

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Abstract

In this thesis, we study the mathematical modelling of some problems that involve surface effects. These include an optical biosensor, which uses optical principles qualitatively to convert chemical and biochemical concentrations into electrical signals. A typical sensor of this type was constructed in Badley et al., [6], and Jones et al., [18],but diffusion was considered in only one direction in [18] to simulate the reaction between the antigen and the antibody. For realistic applications, we propose the biosensor model in R^3. Our theoretical approach is explicitly presented since it is simple and directly applicable to the numerical part of the thesis. In particular, we present existence and uniqueness results based on Maximum Principle and weak solution arguments. These ideas are later applied to systems and to the numerical analysis of the approximate discretized problems. It should be noted that without one dimensional symmetry, the equations can not be decoupled in order to reduce the problem to a single equation. We also show the long time monotonic convergence to the steady state. Next, a finite volume method is applied to the equations, and we obtain existence and uniqueness for the approximate solution as well as the convergence of the the first order temporal norm and the L^2 spatial norm. We illustrate the results via some numerical simulations. Finally we consider a mathematically related system motivated by lagoon ecology. We show that under suitable conditions on the coefficients, the system has a periodic solution under harvesting conditions. The mathematical techniques now depend on estimates for periodic parabolic problems.

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Chapter 1

Introduction

1.1 System with Surface Effects

It is the purpose of this thesis to consider systems of nonlinear parabolic equations that model problems in which surface effects are important. These have received much less attention than problems where the effects take place inside domains rather than on their boundary. Usually the situation on the boundary is dealt with by assuming some form of "no flux" (i.e. Neumann) condition or "prescribed value" (i.e. Dirichlet) condition or of mixed type: Neumann on part of the boundary and Dirichlet on the other part. But these are not the case here.

Specifically we consider two problems that are physically diverse but mathematically related: The first involves a biosensor device that has been implemented as a "pregnancy" sensor. It involves coating part of the sensor boundary area with an antibody and then monitoring the reaction between this coating and a test fluid introduced in the sensor. A more detailed description is given below. The second problem involves, for example, the ecology of a shallow lagoon. It is well known that interaction with the bottom sediments is of actual importance. Since the lagoon depth is of the order of meters, while the sediment thickness is of the order of centimeters, we treat the sediments as if they were a surface, and examine the question of the existence of periodic solutions subject to harvesting of some of the biomass.

1.2 Thesis Outline

The thesis is structured as follows.

In Chapter 2 we discuss briefly the general mathematical background which is needed later in this thesis. We present chosen results from functional spaces, parabolic equations and their maximum principles, solvability of parabolic equation in Holder spaces, Leray-Schauder Degree and finite volume method, estimates for parabolic problems.

In Chapter 3 we address the analytic properties of a biosensor model, its solvability and uniqueness of solutions, steady state and long-time behavior as well as system results.

In Chapter 4, we apply the finite volume method to the biosensor model, obtaining L^2 norm stability and error estimates for the numerical scheme.

In Chapter 5, we consider a biological problem that is mathematically closely related in formulation to the biosensor model, i.e., a coupled system with boundary effects and harvesting. Existence of nonnegative periodic solutions is obtained.

Finally we present some topics for future work.

Chapter 2

Mathematical Background

In this chapter we recall and discuss briefly some results which will be used later in this thesis.

2.1 Function spaces

In this section we describe certain classes of function spaces, which turn out often to be the proper setting in which to apply the ideas of functional analysis to study parabolic problems. General detailed developments are found in classical books, e.g: [1], [19], [21].

Throughout the whole section Ω is a bounded domain in R^n, $n \geq 1$, $Q = \Omega \times (0,T)$.

An n-tuple $\alpha = (\alpha_1, \cdots, \alpha_n)$ of nonnegative integers α_j is called a multi-index with $|\alpha| = \sum_{j=1}^{n} \alpha_j$. We denote by D^α the differential operator of order $|\alpha|$

$$D^\alpha = (\frac{\partial}{\partial x_1})^{\alpha_1} \cdots (\frac{\partial}{\partial x_n})^{\alpha_n} \tag{2.1.1}$$

We also define the support of a function u defined on the domain Ω as

$$\mathbf{supp} u = \overline{\{x \in \Omega : u(x) \neq 0\}}. \tag{2.1.2}$$

Let $C^k(\Omega)$, $k \geq 0$ denote the set of all the function u that are continuous in Ω together with all their partial derivatives D^α of orders $|\alpha| \leq k$. We put $C^\infty(\Omega) = \bigcap_{k=0}^{\infty} C^k(\Omega)$. The subspaces $C_0^1(\Omega)$ and $C_0^\infty(\Omega)$ of $C^1(\Omega)$ and $C^\infty(\Omega)$ respectively consist of all the functions from these spaces which have compact support in Ω.

Let $C^k(\bar{\Omega})$, $k \geq 0$ be a subspace of functions $u \in C^k(\Omega)$ for which all derivatives $D^\alpha u$ are bounded on $\bar{\Omega}$ for $0 \leq |\alpha| \leq k$. These spaces are Banach spaces under the norm

$$\|u\|_{C^k} = \max_{0\leq|\alpha|\leq k} \sup_{x\in\Omega} |D^\alpha u|. \tag{2.1.3}$$

Now we define the space $C^{k,\gamma}(\bar{\Omega})$, $k \geq 0, 0 \leq \gamma \leq 1$ as the set of functions such that

$$u \in C^k(\bar{\Omega}), \sup_{x,y\in\bar{\Omega}} \frac{|D^\alpha u(x) - D^\alpha u(y)|}{|x-y|^\gamma} < \infty, 0 \leq |\alpha| \leq k. \tag{2.1.4}$$

$C^{k,\gamma}(\bar{\Omega})$ is a Banach space under the norm

$$\|u\|_{C^{k,\gamma}} = \|u\|_{C^k} + \max_{0\leq|\alpha|\leq k} \sup_{x,y\in\bar{\Omega}} \frac{|D^\alpha u(x) - D^\alpha u(y)|}{|x-y|^\gamma} < \infty, 0 \leq |\alpha| \leq k. \tag{2.1.5}$$

This condition generalizes to functions between any two metric spaces. The number α is called the exponent of the Hölder condition. If $\alpha = 1$, then the function satisfies a Lipschitz condition. If $\alpha = 0$, then the function is bounded.

It is easy to see that $C^{k,0}(\bar{\Omega}) = C^k(\bar{\Omega})$. Note that functions from $C^{0,1}$ are called Lipschitz continuous functions. The important property of these spaces is that for $0 \leq k \leq 1$ and $0 \leq \gamma < \nu \leq 1$ the space $C^{k,\nu}(\bar{\Omega})$ is compactly embedded into $C^{k,\gamma}(\bar{\Omega})$.

Our next definition is in accord with observation that in the heat equation two x-derivatives are equivalent to one t-derivative. This equivalence makes the definition of higher order holder semi-norms slightly more complicated than in the elliptic case. First, for $\beta \in (0, 2]$, we define

$$\langle f \rangle_{\beta;X_0} = \sup\{\frac{|f(x_0,t) - f(X_0)|}{|t-t_0|^{\beta/2}} : (x_0,t) \in Q \backslash X_0\}, \tag{2.1.6}$$

and $\langle f \rangle_{\beta;\Omega} = \sup_{X_0\in\Omega} \langle f \rangle_{\beta;X_0}$

Then for any $a > 0$, we write $a = k + \alpha$, where k is a nonnegative integer and $\alpha \in (0, 1]$, and we define

$\langle f \rangle_{a;Q} = \sum_{|\beta|+2j=k-1} \langle D_x^\beta D_t^i f \rangle_{a+1}$

$[f]_{a;Q} = \sum_{|\beta|+2j=k}[D_x^\beta D_t^i f]_a$

$|f|_{a;Q} = \sup_{|\beta|+2j\leq k}|D_x^\beta D_t^i f| + \langle f\rangle_{a;Q} + [f]_{a;Q}$

It is easy to verify that $|\cdot|_a$ defines a norm on $H_a(Q) = \{f : |f|_a < \infty\}$ which makes $H_a(Q)$ a Banach space. If $a < 1$, we set $H_a(Q) = C^{a,a/2}(Q)$.

Now we will give the definition and discuss properties of Sobolev Spaces.

Let $L^p(\Omega)$, $1 \leq p < \infty$, denote the set of all measurable functions which are p-integrable. This space is complete under the norm

$$\|u\|_{L^p} = (\int_\Omega |u|^p)^{1/p}. \tag{2.1.7}$$

Let also L^∞ denote the set of essentially bounded functions on Ω with the norm

$$\|u\|_{L^\infty} = ess\sup_{x\in\Omega}|u|. \tag{2.1.8}$$

We define the weak derivative for a locally integrable function u on Ω in the following way. For any multi-index α a locally integral function is called the α-th order derivative of u and is denoted as $D^\alpha u$ if

$$\int_\Omega \varphi v dx = (-1)^{|\alpha|}\int_\Omega (D^\alpha\varphi)u dx. \tag{2.1.9}$$

for all $\varphi \in C_0^\infty(\Omega)$.

Finally we say that a function u belongs to the Sobolev space $W^{k,p}(\Omega)$ with integer $k \geq 0$ if $D^\alpha u \in L^p(\Omega)$ for all $|\alpha| \leq k$. $W^{k,p}(\Omega)$ is a Banach space under the following norm

$$\|u\|_{W^{k,p}} = \sum_{|\alpha|\leq k}\|D^\alpha u\|_{L^p}. \tag{2.1.10}$$

We denote $W_0^{k,p}(\Omega)$ the closure of $C_0^\infty(\Omega)$ in $W^{k,p}(\Omega)$ and note that it is also a Banach space under this norm.

In studying parabolic equations, it is useful to have a notion of solution that allows for functions that are not smooth. In fact, our hypotheses will often be enough to guarantee that the solutions considered here are actually $C^{2,1}$, but it will be very convenient to use weak solutions in developing the existence theory. To motivate the notion of weak solution, we observe that if u solves a parabolic equation in a cylinder $Q = Q(X_0, R)$ and if $\zeta \in C^1(\bar{Q}) = 0$ if $|x - x_0| = R$, then an integration by parts gives

$$\int_Q (-u\zeta_t + a^{ij} D_j u D_i \zeta - f\zeta) dX = 0, \tag{2.1.11}$$

We shall use this as the basis of our definition of a weak solution because it makes sense as long as u has weak x derivatives. This weak solution of an initial problem is defined analogously [19], [21].

2.2 Parabolic theory: Maximum principles

In this section, we introduce an important tool in the theory of second order parabolic equations: the classical (strong) maximum principle, which asserts that the maximum of a solution to a homogenous linear parabolic equation in a domain must occur on the boundary of that domain. In fact, this maximum must occur on a special subset of the boundary, called the parabolic boundary.

We consider linear operators L defined by

$$Lu = a^{ij}(X) D_{ij} u + b^i(X) D_i u + c(X) u - u_t \tag{2.2.1}$$

in an $(n+1)$-dimensional domain Ω. We assume that L is weakly parabolic. In other words,

$$a^{ij} \xi_i \xi_j \geq 0 \tag{2.2.2}$$

for all $\xi \in R^n$ and all $X \in \Omega$.

For a domain $\Omega \subset R^{n+1}$, we define the parabolic boundary $P\Omega$ to be the set of all points $X_0 \in \partial\Omega$ such that for any $\varepsilon > 0$, the cylinder $Q(X_0, \varepsilon)$ contains points not in Ω. In the special case that $\Omega = D \times (0, T)$ for some $D \subset R^n$ and $T > 0$, $P\Omega$ is the union of the sets $B\Omega = D \times \{0\}$, $S\Omega = \partial D \times (0, T)$, and $C\Omega = \partial D \times \{0\}$.

The simplest maximum principle is the following.

Lemma 2.2.1 *If $u \in C^{2,1}(\bar{\Omega}\backslash P\Omega)\bigcap C^0(\bar{\Omega})$, if $Lu > 0$ in $\bar{\Omega}\backslash P\Omega$ and if $u < 0$ on $P\Omega$, then $u < 0$ in $\bar{\Omega}$.*

Analogous to our operator L is the boundary operator M defined by

$$Mu = \beta \cdot \partial u + \beta^0 u. \tag{2.2.3}$$

Lemma 2.2.2 *Suppose that there is a positive constant k such that*

$$c \leq k \tag{2.2.4}$$

in Ω

$$\beta^0 < 0 \tag{2.2.5}$$

on $P\Omega$

If $u \in C^{2,1}(\Omega)\bigcap C^0(\bar{\Omega})$, if $Lu \geq 0$ on Ω and if $Mu \geq 0$ on $P\Omega$, then $u \leq 0$ in Ω.

The maximum principle is used to prove uniqueness results for various boundary problems, L^∞ bounds for solutions and their derivatives, and various continuity estimates as well.

Crucial tools in the study of parabolic equations are the following comparison principle and uniqueness result.

Theorem 2.2.1 *Suppose $u \in C^{2,1}(\Omega)\bigcap C^0(\bar{\Omega})$ for some Ω with $t \geq 0$ in Ω, and suppose conditions (2.2.2), (2.2.4) and (2.2.5) hold. If $Lu \geq 0$ in Ω and if $Mu \geq \beta^0\phi$ on $P\Omega$ for some nonnegative constant ϕ, then $u(X) \leq e^{kt}\phi$ for all $X \in \Omega$.*

There are versions for weak solutions in $C^{\alpha,\alpha/2}$ (see [19], [21]).

2.3 Solvability of parabolic equation in Hölder spaces

Now, we recall the definition of a Hölder space. We also define the Morrey space $M^{p,\delta}$ to be the set of all function $u \in H_1$ with finite norm

$$\|u\|_{p,\delta} = \sup_{Y\in\Omega, r<diam\Omega}(r^{-\delta}\int_{\Omega[Y,r]}|u|^p dX)^{1/p}. \tag{2.3.1}$$

For $\alpha \in (0,1)$ and given domain Ω, we assume that a^{ij} and b are in H_α and that $c^j \in M^{1,1+n+\alpha}$ for $j = 0, ..., n$.

We also suppose that

$$a^{ij}\xi_i\xi_j \geq \lambda|\xi|^2 \tag{2.3.2}$$

for all $\xi \in R^n$ and all $X \in \Omega$, and

$$|a^{ij}| \leq \Lambda\lambda, \tag{2.3.3}$$

$$[a^{ij}]_\alpha + [b]_\alpha + \|c^j\|_{1,n+1+\alpha} \leq \Lambda_1. \tag{2.3.4}$$

for some nonnegative constant Λ_1. We then have the following existence, uniqueness, and regularity theorem. ([19], [21], [28]).

Theorem 2.3.1 *Suppose $P\Omega \in H_{1+\alpha}$ and that the coefficients of L, as defined in (2.2.1), satisfy condition (2.3.2)-(2.3.4). Then for any $\varphi \in H_{1+\alpha}$, $f \in H_\alpha$ and $g \in M^{1,n+1+\alpha}$, there is a unique H_1 weak solution of $Lu = D_i f^i + g$ in Ω, $u = \varphi$ on $P\Omega$. Moreover, $u \in H_{1+\alpha}$ and*

$$|u|_{1+\alpha} \leq C(n, \alpha, \lambda, \Lambda, \Lambda_1, \Omega)(|\varphi|_{1+\alpha} + |f|_\alpha + \|g\|_{1,n+1+\alpha}) \tag{2.3.5}$$

For oblique derivative problems, i.e., the boundary operator M defined by

$$Mu = \beta \cdot \partial u + \beta^0 u. \tag{2.3.6}$$

the same arguments apply and we infer the following result.

Theorem 2.3.2 *Suppose L and Ω are as in Theorem 2.3.1, and let β^0 and β^i be $H_\alpha(S\Omega)$ function with $\beta \cdot \gamma \geq \chi$ on $S\Omega$ and $|\beta|_\alpha + |\beta^0|_\alpha \leq B_1\chi$ for some positive constant B_1. Then for any $\varphi \in H_{1+\alpha}$, $\psi \in H_\alpha$, $f \in H_\alpha$ and $g \in M^{1,n+1+\alpha}$, there is a unique H_1 weak solution of $Lu = D_i f^i + g$ in Ω, $\beta \cdot Du + \beta^0 u = \psi$ on $S\Omega$, and $u = \varphi$ on $B\Omega$. Moreover, $u \in H_{1+\alpha}$ and*

$$|u|_{1+\alpha} \leq C(B_1, n, \alpha, \lambda, \Lambda, \Lambda_1, \Omega)(|\varphi|_{1+\alpha} + |\psi|_\alpha + |f|_\alpha + \|g\|_{1,n+1+\alpha}) \tag{2.3.7}$$

2.4 Leray-Schauder Degree

In this paragraph we will formulate the main properties of the Leray-Schauder Degree. For a detailed discussion see [11].

Let X be a real Banach space, $G \subset X$ an open bounded domain. F a compact operator from G to X, I an identity operator and $y \notin (I-F)(\partial G)$. On these triples $(I-F, G, y)$ an integer-valued function deg, which is called Leray-Schauder Degree, is defined and it satisfies the following properties:

(L1) $deg(I, G, y) = 1$ for $y \in \Omega$;

(L2) (addiditivity) $deg(I-F, G, y) = deg(I-F, G_1, y) + deg(I-F, G_2, y)$ whenever G_1 and G_2 are disjoint open subsets of $G = G_1 \cup G_2$and $y \notin (I-F)(\partial G \cup \partial G_1 \cup \partial G_2)$

(L3) (homotopy)$deg(I - H(t, \cdot), G, y(t))$ is independent of $t \in [0, a]$ whenever $H : [0, a] \times \bar{G} \rightarrow X$ is compact, y: $[0, a] \rightarrow X$ is continuous and $y(t) \notin (I - H(t, \cdot), (\partial G))$ on $[0, a]$;

(L4)$deg(I-F, G, y) \neq 0$ implies $(I-F)^{-1}(y) \neq \emptyset$, i.e. there exists x in G such that $(I-F)x = y$.

One of the important consequences of the Learay-Schauder Degree theory is the Schauder Fixed Point Theorem.

Theorem 2.4.1 *(The Schauder Fixed Point Theorem). Let G be a closed convex set in a Banach space X and let F be a continuous mapping of G into itself such that the image FG is precompact. Then F has a fixed point.*

The proof of this theorem can be found in [17].

2.5 Periodic parabolic problem

We consider next the existence of a periodic solution to a linear parabolic problem, see eg. [14], [15]. We also draw the reader's attention to the important book [33] of X. Zhao for a through discussion and analysis of dynamical systems arising in population biology.

The results of specific interest to us are:

Lemma 2.5.1 *Assume all coefficients are smooth, as well as $\partial\Omega$.*

(a) Let M be a positive constant. Then the equation

$$\begin{cases} \omega_t - \nabla(D\nabla\omega + \vec{b}\omega) + M\omega = f \geq 0, \quad \text{in } Q_T, \quad (2.5.1.1) \\ D\dfrac{\partial\omega}{\partial n} + \vec{b}\cdot\vec{n}\omega + k_1\omega c_0 = g \geq 0, \quad \text{on } Q'_T, \quad (2.5.1.2) \end{cases} \tag{2.5.1}$$

has a unique periodic solution.

(b) Let ω be a nonnegative sub-solution of

$$\begin{cases} \omega_t - \nabla(D\nabla\omega + \vec{b}u) + M\omega \leq 0, \quad \text{in } \Omega\times(0,T), \quad (2.5.2.1) \\ D\dfrac{\partial\omega}{\partial n} + \vec{b}\cdot\vec{n}\omega \leq g, \quad \text{on } \partial\Omega, \quad (2.5.2.2) \end{cases} \tag{2.5.2}$$

with $\omega(x,0) = \omega(x,T)$, $g \geq 0$ smooth bounded.
If $\int_{Q_T} \omega$ is bounded then so is ω in $L^\infty(\bar{Q}_T)$ for some $\alpha > 0$.

Proof. (a) For system (2.5.1) to have a unique solution it suffices that the periodic parabolic eigenvalue problem:

$$\begin{cases} u_t - \nabla(D\nabla v + \vec{b}v) + Mv = \lambda v, \quad \text{in } Q_T, \\ D\dfrac{\partial v}{\partial n} + \vec{b}\cdot\vec{n}v + k_1 v c_0 = 0, \quad \text{in } Q'_T, \\ v(x,0) = v(x,T), \quad x \text{ in } \Omega \end{cases} \tag{2.5.3}$$

have a positive principle eigenvalue λ, to which there corresponds a positive eigenvector v. Refer to [10]. It is convenient to note that λ equals the principle eigenvalue of the formal adjoint problem:

$$\begin{cases} (v_1)_t - \nabla(D\nabla v_1) + \vec{b}\nabla v_1 + Mv_1 = \lambda v_1, \quad \text{in } Q_T, \\ \dfrac{\partial v_1}{\partial n} = 0, \quad \text{in } Q'_T, \\ v_1(x,0) = v_1(x,T), \quad x \text{ in } \Omega \end{cases} \tag{2.5.4}$$

where in the coefficient functions we have replaced t by $T - t$. Refer to [3].

Since $v_1 > 0$ and $M > 0$ then $\lambda \leq 0$ would give an immediate contradiction by the strong Maximum principle whence $\lambda > 0$, and the proof follows.

(b) This is immediate by classical results ([21]).

2.6 Finite volume method

We next introduce a finite volume scheme, which is a technique commonly employed in practice, for approximating solutions [16], [9]. Generally, a simulation begins with the formulation of a mathematical model which usually is a partial differential system. An appropriate numerical method to solve the corresponding system is always needed to illustrate the theoretical analysis, to further its application in realistic situations, and to modify the modeling.

The finite volume method represents partial differential equations as algebraic equations. It's also called the box method. It is a numerical method similar to the finite difference method, with values calculated at discrete places on a meshed geometry, however, it occupies an intermediate position between the finite difference and finite element methods. It is generally understood that the "Finite volume" refers to a small volume surrounding each node point on a mesh, called a "cell". In the finite volume method, volume integrals over a cell for a partial differential equation that contain a divergence term are converted to surface integrals, using the divergence theorem. These terms are then evaluated as discrete fluxes at the surfaces of each finite volume. Because the flux entering a given volume is identical to that leaving the adjacent volume by construction, these methods are flux conservative. Another advantage of the finite volume method is that it is easily formulated for unstructured meshes. The method is used for example in many computational fluid dynamics packages.

The finite volume method has been extensively and successfully used to derive efficient simulation for partial differential equations and systems. Consequently, many mathematical papers have dealt with the analysis of the applications of the finite volume method to a variety of differential equations. As mentioned above, Finite Volume Methods are known to be well applicable to the numerical simulation of partial differential equations, with irregular geometry or unstructed mesh partition. Many papers have been written on their construction and application, as well as theoretical studies. Elliptic equations with general boundary conditions are studied in [16], [13]; while for parabolic equations, the L^2 and H^1 error estimate for the Dirichlet boundary problem and for the Robin boundary problem are considered respectively in [16] and [9].

For our situation, the finite volume method is preferable to other methods due to the fact that boundary conditions can be applied easily. This is true because the values of the conserved variables are located within the volume element, and not at nodes or surfaces. While the finite volume methods are especially useful on coarse nonuniform grids, or even in calculations where the mesh moves to track interfaces or shocks for hyperbolic equations, in our specific case there are some difficulties in deriving the stability properties and the convergence of this approach since the biosensor model is a highly coupled system with a nonlinear term in the boundary condition.

2.7 Basics of Finite volume method

For the reader's convenience we recall the basics of Finite Volume Methods. A finite volume mesh for Ω, denoted by $\mathcal{T}$, is given by: a family of "control volumes", which are open polygonal (if $d = 2$) or polyhedral (if $d = 3$) convex subsets of Ω (with positive measure), a family of subsets of $\bar{\Omega}$ contained in hyperplanes of R^d, denoted by ε (these are the edges (if $d = 2$) or sides (if $d = 3$) of the control volumes), with strictly positive $(d-1)$-dimensional measure and a family of fixed points (nodes) of $\bar{\Omega}$ denoted by P. We refer to [16] for detailed information on constructing restricted admissible meshes.

Define the mesh size by $h = size(\mathcal{T}) = \sup\{diam(K), K \in \mathcal{T}\}$, where $diam(K)$ is the diameter of $K \in \mathcal{T}$. For any $K \in \mathcal{T}$ and $\sigma \in \varepsilon$, $m(K)$ is the d-dimensional Lebesgue measure of K (i.e. area if $d = 2$, volume if $d = 3$), $m(\sigma)$ is the $(d-1)$-dimensional measure of σ, and $\eta_{K,\sigma}$ denotes the unit normal vector to σ outward from K. It is noted that U_K is the approximate value of u at a fixed node point of K(for instance, the barycenter of K).

For convenience, we note $K \in \{K \in \mathcal{T}_{int}\} \bigcup \{K \in \mathcal{T}_{ext}\}$, i.e. if $\bar{K} \bigcap \varepsilon_{ext} = \sigma_{ext} \neq \Phi$, then we say $K \in \mathcal{T}_{ext}$. Otherwise, $K \in \mathcal{T}_{int}$.

It should be noted that in choosing the nodes for $K \in \mathcal{T}_{ext}$, we always assume that $U_\sigma = U_K$ for $K \in \mathcal{T}_{ext}$, i.e. nodes are chosen on $\partial\Omega$, instead of possibly different U_σ, U_K as in [13]. Accordingly, we use the same nodes for U_σ, Γ_σ for external σ, but keep the notation for simplicity.

For any $(K, L) \in \mathcal{T}^2$ with $K \neq L$, either the $(d-1)$-dimensional Lebesgue measure of $\bar{K} \cap \bar{L}$ is 0 or $\bar{K} \cap \bar{L} = \bar{\sigma}$ for some $\sigma \in \varepsilon$, which will then be denoted by $K|L$.

Denote by $\varepsilon_{int} = \{\sigma \in \varepsilon; \sigma \not\subset \partial\Omega\}$, $\varepsilon_{ext} = \{\sigma \in \varepsilon; \sigma \subset \partial\Omega\}$. For $K \in \mathcal{T}$, let $V_{K,\sigma} = \{\alpha x_K + (1-\alpha)x, x \in \sigma, \alpha \in [0,1]\}$. For $\sigma \in \varepsilon_{int}$, let $V_\sigma = V_{K,\sigma} \cap V_{L,\sigma}$, where K and L are the control volumes such that $\sigma = K|L$. For $\sigma \in \varepsilon \cap \varepsilon_{ext}$, let $V_\sigma = V_{K,\sigma}$.

Denote by $d_{K|L}$ the Euclidean distance between x_K and x_L (which is positive) and by $d_{K,\sigma}$ the distance from x_K to σ. If $\sigma = K|L \in \varepsilon_{int}$, let $d_\sigma = d_{K|L} = d_{K,\sigma} + d_{L,\sigma}$; if $\sigma \in \varepsilon_K \cap \varepsilon_{ext}$, let $d_\sigma = d_{K,\sigma}$.

For any $\sigma \in \varepsilon$, the "transmissibility" through σ is defined by $\tau_\sigma = \frac{m(\sigma)}{d_\sigma}$ if $d_\sigma \neq 0$ and $\tau_\sigma = 0$ if $d_\sigma = 0$. In the results and proofs given below, $d_\sigma \neq 0$ for all $\sigma \in \varepsilon$ is assumed for simplicity.

For the reader's convenience, we illustrate some of the above terminology in Figure 1.

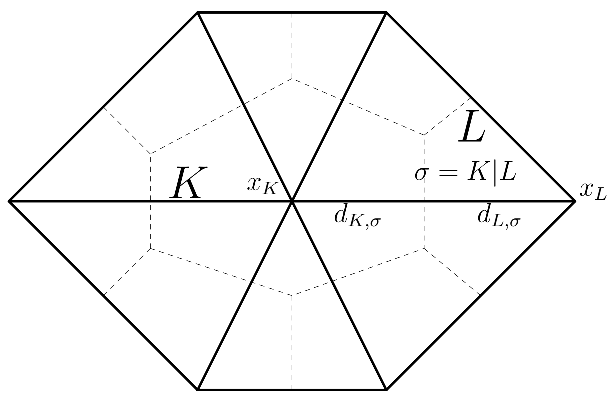

Figure 2.1: The mesh terminology associated with the internal cell K.

Chapter 3

Analytic Properties of a Biosensor Model in R^3

3.1 The optical biosensor Model

An optical biosensor is a device which uses optical principles qualitatively to convert chemical and biochemical concentrations into electrical signals.

The sensor may also itself incorporate biological molecules, such as antibodies, to provide a transducing element that gives the desired specificity. The sensor to be considered here is a disposable type of immunosensor, the fluorescence capillary fill device.

It consists of two pieces of plastic, separated by a narrow gap, as shown in schematic form in Fig. 3.1. The lower plate is coated with an immobilized layer of specific antibody and acts as an optical waveguide. One of the plates has a dissoluble reagent layer of antigen labelled with fluorescent dye.

When a sample is presented to one end of the capillary fill device it is drawn into the gap by capillary action and dissolves the reagent. If the device is set up for competition assay, the fluorescently labelled antigen in the reagent will compete with simple antigen for the limited number of antibody binding sites on the waveguide solid face. Since the reactions are reversible a steady state will be reached in which there are a certain proportion of labelled antigen/antibody complexes. If there were no antigen present in the sample all the labelled antigen would react with the specific antibody displaying, through the optical waveguide, a different signature.

Metering of the sample and the reagent then becomes unnecessary provided the capillary gap is precise and there is accurate loading of the antibody and reagent during the device manufacture. A typical medical product based on this antigen/antibody technology is a particular kind of pregnancy kit. A full description of the fluorescent capillary fill device can be found in Badley et al. [18]. Technologically, the primary interest is in the determination of the size of the device and the amount of specific antibody to be coated on the lower plate within a specified time. For this reason the labelled and unlabelled antigen will not be differentiated and will be considered to be one species X, which reacts with the labelled antibody Y, on the lower plate to produce a complex XY. Even the concentration of the complex (the substance resulting from the chemical reaction of the antibody and the antigen) might not be a smooth function of time. Refer to [22]. Thus an accurate representation for the chemical process is needed, which provides a useful check on the numerical results.

3.2 Mathematical modeling in R^1

The mathematical model of the reaction-diffusion process is developed for readers' convenience. The detailed description of the following modeling analysis can be found in Burgess et al. [7] and Mckee [18].

Let X be the antigen and Y denote the antibody.
The reaction is stated as

$$X + Y \rightleftharpoons XY,$$

where k_1 and k_{-1} are the forward and backward reaction rates due to the reversibility of the reaction in between the antigen and the antibody.

Let [X] denote the concentration of X (in moles/m^3), [Y] denote the concentration of Y (in moles/m^2) and [XY] denote the concentration of XY (in moles/m^2).

The following constants are listed:

a_0: initial X concentration ,

c_0: initial Y concentration at the reaction side wall,

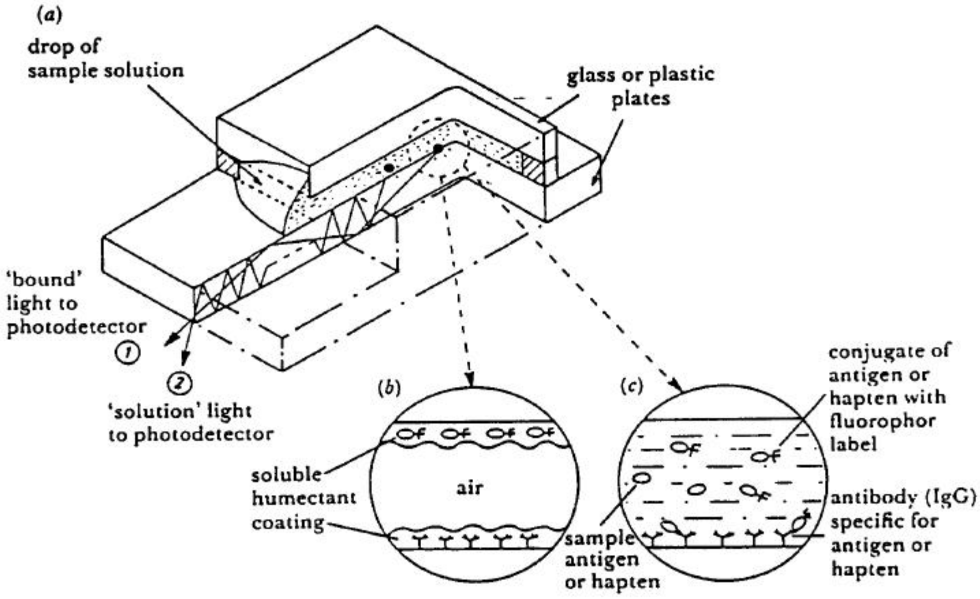

Fig. 1. Schematic diagram of the fluorescence capillary-fill device (FCFD) illustrating a competition immunoassay for a desired antigen or hapten. *(a)* Cutaway view of device showing construction and optical waveguiding principles. *(b)* Enlarged inset of gap in the empty device showing immobilized antibody layer on lower plate and dissoluble reagent layer on upper plate. *(c)* Enlarged inset of gap in the filled device showing competitive immunological binding of the desired antigen or hapten and its fluorescently labelled counterpart (the conjugate) to the limited number of antibody molecules. Sandwich-type immunoassays are also possible in this device.

Figure 3.1: The figure that describes a typical biosensor device from Jones et al.[12].

d: edge of vessel to surface,

D: diffusion coefficient of X.

To facilitate the discussion let us introduce the notation:

u(x, t) denotes concentration of X i.e. [X],

and $\gamma(t)$ is concentration of XY, i.e. [XY].

If edge effects are ignored, one can neglect any diffusion except that in the x-direction and [X] satisfies the diffusion equation

$$u_t - D\frac{\partial^2 u}{\partial x^2}(x,t) = 0.$$

Also $\frac{\partial u}{\partial x}(0,t) = 0$ at x=0.

Furthermore, $[X]_{t=0} = a_0$ since the concentration of the antigen is assumed uniform initially.

Thus we have to define the boundary condition $D\frac{\partial u}{\partial x}(x,t)$ at $x = d$ on the antibody surface.

However, the behavior of solutions in dynamic equilibrium yields

$$D\frac{\partial u}{\partial x}(d,t) = k_{-1}\gamma(t) - k_1 u(d,t)(c_0 - \gamma(t))$$

due to the fact that we have assumed that one molecule of X and one molecule of Y combine to give one molecule of the complex XY. Considering that the initial concentration of Y is c_0, we may obtain the amount of X used up in the reaction.

Consequently,

$$[Y](t) = c_0 - (a_0 d - \int_0^d u(x,t)dx).$$

Therefore,

$$\begin{aligned} & D\frac{\partial u}{\partial x}(d,t)c_0 - (a_0 d - \int_0^d u(x,t)dx) \\ = \quad & k_{-1}\gamma(t) - k_1 u(d,t)(c_0 - \gamma(t)). \end{aligned} \tag{3.2.1}$$

Moreover, the conservation of the total amount of species X, either in solution or in terms of the complex XY, gives

$$\int_0^d u(x,t)dx + \gamma(t) = a_0 d.$$

Then,

$$D\frac{\partial u}{\partial x}(d,t) = k_{-1}\gamma(t) - k_1 u(d,t)(c_0 - \gamma(t)).$$

To summarize, a consistent 1D model of the antibody-antigen reaction is given by:

$$u_t - D\frac{\partial^2 u}{\partial x^2}(x,t) = 0 \tag{3.2.2}$$

subject to

$$u(x,0) = a_0 \tag{3.2.3}$$

and the boundary conditions

$$\begin{aligned} &\frac{\partial u}{\partial x}(0,t) = 0, \\ &D\frac{\partial u}{\partial x}(d,t) = k_{-1}\gamma(t) - k_1 u(d,t)(c_0 - \gamma(t)), \end{aligned} \tag{3.2.4}$$

together with the conservation form

$$\int_0^d u(x,t)dx + \gamma(t) = a_0 d. \tag{3.2.5}$$

To continue with the numerical analysis for the derived biosensor model, an integro-differential equation reformulation is derived in Mckee[18], where, for convenience, the non-dimensional variables,

$$x' = \frac{x}{d}, t' = (\frac{D}{d^2})t,$$

and scaling the dependent variables

$$u'(x',t') = \frac{u(x,t)}{a_0}, \gamma'(t') = \frac{\gamma(t)}{c_0},$$

are also introduced.

Thus (3.2.2) may be rewritten as

$$u_t = \frac{\partial^2 u}{\partial x^2}(x,t) \tag{3.2.6}$$

together with

$$u(x,0) = 1 \tag{3.2.7}$$

and the boundary conditions

$$\begin{aligned} &\frac{\partial u}{\partial x}(0,t) = 0, \\ &D\frac{\partial u}{\partial x}(1,t) = \frac{Em}{1+L}(L\gamma(t) - u(1,t)(1-\gamma(t))), \end{aligned} \tag{3.2.8}$$

subject to

$$\int_0^1 u(x,t)dx + m\gamma(t) = 1. \tag{3.2.9}$$

Where the same notations are applied.

The constant $m = c_0/(a_0 d)$ is the molar ratio, $L = k_{-l}/k_1$ is the reaction time scale ratio, and $E = (k_1 + k_{-l})d^2/D$ is the diffusion reaction time scale ratio.

3.3 Some known approximation results in R^1

Differentiating (3.2.9) with respect to time we obtain

$$\int_0^1 \frac{\partial u(x,t)}{\partial t}dx + m\frac{d\gamma(t)}{dt} = 0, \tag{3.3.1}$$

and using (3.2.6) and (3.2.8) gives

$$\frac{\partial u(1,t)}{\partial x} = -m\frac{d\gamma(t)}{dt}. \tag{3.3.2}$$

Taking Laplace transforms of (3.2.6) with respect to t, after some manipulation involving the convolution theorem (see Burgess et al. [7]), we obtain

$$u(1,t) = 1 + \int_0^t k(t-s)\frac{\partial u(1,s)}{\partial x}ds, \tag{3.3.3}$$

where the integral kernel is given by

$$k(t) = \frac{1}{\sqrt{\pi t}}(1 + \sum_{n=0}^{\infty} e^{(-\frac{n^2}{t})}). \tag{3.3.4}$$

Thus, using (3.3.1), we obtain

$$u(1,t) = 1 + \int_0^t k(t-s)\frac{\partial \gamma(s)}{\partial x}ds. \tag{3.3.5}$$

Using (3.3.1) and (3.3.3) in equation (3.2.8) yields

$$\frac{d\gamma(t)}{dt}(t) = C - E\gamma(t) - \frac{Em}{1+L}(L\gamma(t) - (1-\gamma(t))) \int_0^t k(t-s)\frac{\partial\gamma(s)}{\partial x}ds, \quad (3.3.6)$$

where

$$C = \frac{E}{1+L}, \quad (3.3.7)$$

with initial condition $\gamma(0) = 0$.

Once γ is known, equation (3.3.5) may be used to obtain u on the boundary $x = 1$, and thus (3.2.6) may be solved using (3.2.7), (3.2.8) and the value of $u(1, t)$ to determine u in the interior $0 < x < t, t > 0$(see Burgess et al. [7]).

We conclude by briefly mentioning some of the other results obtained in [18].

1. An asymptotic solution of $\gamma(t)$ for small t, based on the integro-differential equation (3.3.6).

2. A perturbation solution of the analytic expansion of $\gamma(t) = \gamma(t, m)$ in powers of the molar ratio m.

3. For $u(x, t)$, an equivalent system of Volterra integral equations is obtained for the initial boundary value problem (3.2.6-3.2.9). Using this integral formulation, high order product integration schemes are derived.

In short, the paper [18] is mainly concerned with the derivation of the asymptotic result and perturbation solution through an integro-differential reformulation. The fully mathematical derivation can be found in [18] and [7].

But unfortunately, such kind of decoupling technique is not available for the biosensor model in R^3 due to fact the function of $\gamma(t)$ is defined in a surface other than at a single point as the case in R^1. This poses difficulties in obtaining the analytic and numerical properties for our model in R^3.

3.4 Degenerate systems modeling biosensors

Another reaction diffusion system with nonlinear boundary conditions modeling optical biosensors, named Fluorescence Capillary Fill Devices (FCFD), was investigated qualitatively in [22]. In its simplest form the device consists of two glass plates separated by a narrow gap. The device is shown in Fig 3.2.

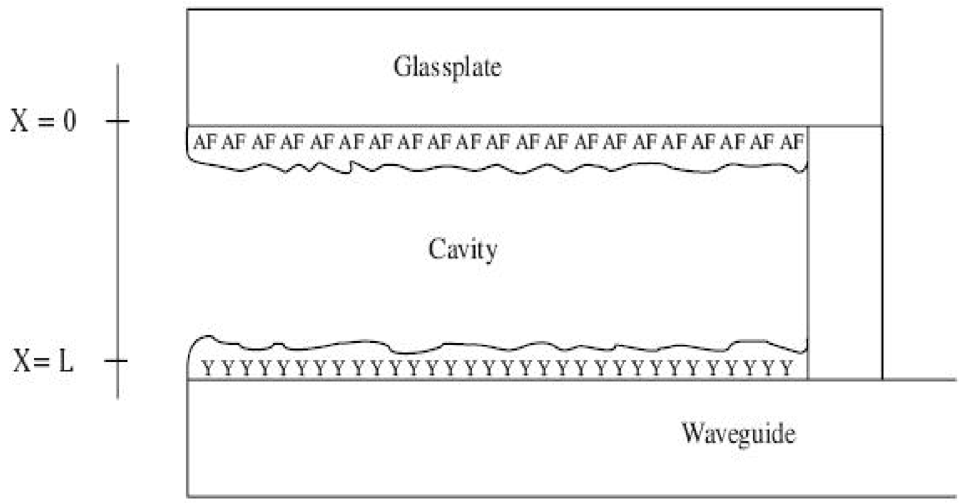

Figure 3.2: Fluorescence Capillary Fill Devices (FCFD) from Merino, et al. [22].

The upper glass plate is coated with a labeled antigen AF (here F stands for a fluorescent molecule).
The lower plate is coated with a special antibody Y .
The purpose of the device is to analyse whether a given test solution contains the unlabeled antigen A. To this end the test solution is presented at the open end of the device where it is drawn into the cavity by capillary forces. The labeled antigen AF is soluble and diffuses into the solution, whereas the antibody Y is insoluble and remains on the lower plate. At the lower plate the antibody and antigens react in the following way

$$A + Y \rightleftharpoons AY,$$

$$AF + Y \rightleftharpoons AFY,$$

Thus on the lower plate labeled and unlabeled antigen-antibody molecules are created and the labeled and unlabeled antigens compete for the available binding sites as is shown in Fig. 3.3.

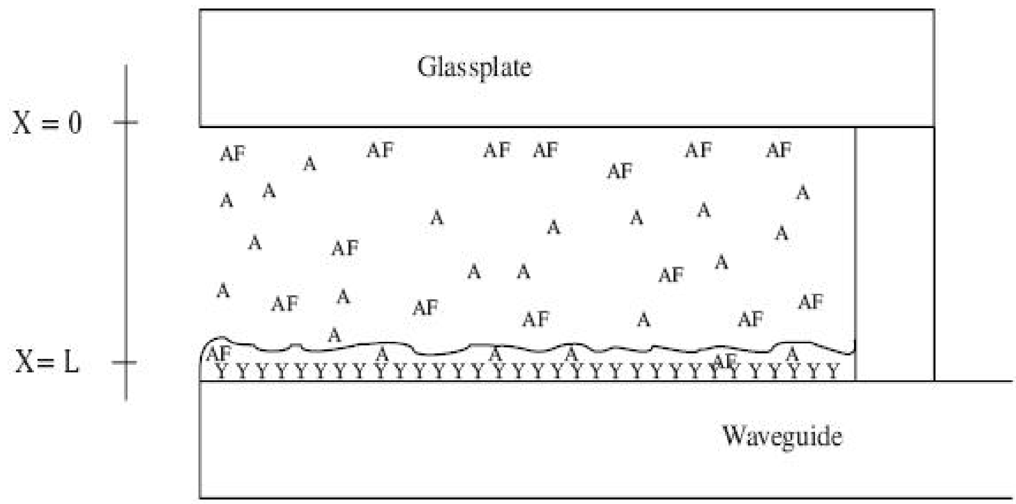

Figure 3.3: Antigen-antibody molecules are created for the Fluorescence Capillary Fill Devices (FCFD), figure from Merino, et al.

When this reaction-diffusion process has reached equilibrium a flash lamp is used to exite the fluorescent molecules F.
The lower glass plate then acts as a wave-guide leading the emitted light to an optoelectronic device that is able to analyse the arriving light impulse. The intensity of the pulse depends on the ratio of the concentrations of labeled and unlabeled complexes on the lower plate and thus permitting us to infer the presence or absence of the antigen A in the test sample.

In a preliminary step of our analysis we assume that the reaction occurs in a well-stirred isothermal reactor of constant volume. The wall-bound antigen $AF^{(b)}$ is treated as an independent species and we consider its dissolution as a further reaction

$$AF^{(b)} \leftrightarrow AF$$

The reactions is interpreted as a reaction network in the sense of e deficiency zero theory of chemical reaction networks with an important property : it is reversible and of deficiency index zero. The deficiency index can be determined easily from the structure of the reaction network.

The purpose of paper [22] is to place the evolution problem of biosensor reaction into the context of the existence and regularity theory as it is presented in the review article [4]. Since some degenerate aspects due to the fact that some species are only depended on the boundary of the domain, they found it is necessary to generalize the theory in some detail. The degenerate evolution problem has the following structure

$$\begin{cases} \partial_t u_1 + A u_1 = g_1(x; u_1) & in(0, L) \times (0, \infty); \\ \partial_t u_2 = g_2(x; \gamma_\partial u_1; u_2) & on\{0, 1\} \times (0, \infty); \\ B u_1 = g_3(x; \gamma_\partial u_1; u_2) & on\{0, 1\} \times (0, \infty); \\ u_1(x; 0) = u_1^0(x) & in(0, 1); \\ u_2(x; 0) = u_2^0(x) & on\{0, 1\}, \end{cases} \tag{3.4.1}$$

for the moment it is assumed

$$u_1 = (c_1; c_2), u_2 = (c_3; c_4; c_5; c_6), \Omega = (0; L), g_1 = 0$$

$\gamma_\partial u_1$ denotes the formal trace of u_1 on $\partial\Omega$. Note that in the above system the evolution of the two species u_1 and u_2 is only coupled through the values of u_1 and u_2 on the boundary of the domain.

The abstract setting of the theory presented by H. Amann[5] and [4] was then applied to prove the existence of a global continuous semiflow on a positive cone in a suitable Banach space. The general existence theory presented in [5] was then applied to a class of problems that contains the model in question as a special case. The determination of the qualitative behaviour of this semiflow is the main contribution in the paper, and the main tool of the analysis is an infinite dimensional version of the invariance principle of LaSalle ([16, Theorem 2.3]). The construction of a Liapunov function is based on analogies between the degenerate model and systems of nonlinear ODE's appearing in the theory of chemical reaction networks (CRNs). The Deficiency Zero Theorem in [9] establishes a relation between the graph structure of a chemical reaction network and the qualitative behaviour of the (positive) solutions of the nonlinear system of ODEs that is obtained by applying the mass action law of chemistry. No considerations were given regarding numerical approximation, nor of periodic solutions.

It is our interest to generalize the results of [6], [18] in R^3 for realistic applications, in a way suitable for numerical analysis. Specifically, let again X denote the antigen and Y denote the antibody, and recall that we have the reaction:

$$X + Y \rightleftharpoons XY,$$

with k_1 and k_{-1} denoting the forward and backward reaction rates.
The reaction-diffusion system for the biosensor model in R^3 [2] states:

$u = u(x,t) \in \Omega \times (0,T)$; $\gamma = \gamma(x,t) \in \partial\Omega \times (0,T)$ such that:

$$\begin{cases} u_t - D\Delta u = 0, & in\ \Omega \times (0,T), \quad (3.4.2.1) \\ D\dfrac{\partial u}{\partial n} = k_{-1}\gamma - k_1 u(c_0 - \gamma), & on\ \partial\Omega, \quad (3.4.2.2) \\ u \mid_{t=0} = a_0, & in\ \Omega, \quad (3.4.2.3) \\ \dfrac{d\gamma}{dt} = -k_{-1}\gamma + k_1 u(c_0 - \gamma), & on\ \partial\Omega \times (0,T), \quad (3.4.2.4) \\ \gamma \mid_{t=0} = 0, & on\ \partial\Omega. \quad (3.4.2.5) \end{cases} \tag{3.4.2}$$

The rest of this chapter is as follows. We first note that it is definitely true that only positive solutions are of interest when realistic applications are considered since our unknown function are densities and the modelling will not have physical significance if there arose solutions of negative sign. Consequently, we obtain first of all positivity results for the solutions by some comparison theorems with an auxiliary linear equation for v:

$$\begin{cases} v_t - D\Delta v = 0, & in\ \Omega \times (0,T) \\ D\dfrac{\partial v}{\partial n} + K_1 v = 0, & on\ \partial\Omega \\ v = a_0, & t = 0 \end{cases}$$

with $K_1 = k_1 \max(c_0)$.

Next, we construct another decoupled equation for ω in order to obtain an

L^∞ bound of u.

$$\begin{cases} \omega_t - D\Delta\omega = 0, & in\ \Omega \times (0,T) \\ D\dfrac{\partial\omega}{\partial n} = k_{-1}max(c_0), & on\ \partial\Omega \\ \omega = a_0. & at\ t = 0 \end{cases}$$

From the classic regularity theory for parabolic equations mentioned earlier, we know that $u(x,t)$ is Holder continuous for all time t, for a given Holder continuous initial data $u_0(x)$.

Next, the existence of (u,γ) follows from the Leray-Schauder Degree Theory.

Finally, the uniqueness of the solution pair for(u,γ) is derived by energy integral method.

We also investigate the solution behavior as t $\to \infty$ and begin by noting that the solution to the steady-state problem, obtained by letting,

$$u_t = 0,$$
$$\frac{d\gamma}{dt} = 0,$$

in equation (3.5.1.1) and (3.5.1.4) respectively, is given by (u_s,γ_s) where $\gamma_s = (k_1 u_s c_0)/(k_{-1}+k_1 u_s)$ and u_s is the positive constant root of the quadratic equation:

$$u_s|\Omega|(k_{-1} + k_1 u_s) + k_1 u_s \int_{\partial\Omega} c_0 = (k_{-1} + k_1 u_s) \int_{\Omega} a_0. \tag{3.4.3}$$

We next consider $\omega_1 = u_s - u$ and $e_1 = \gamma_s - \gamma$, and observe that ω_1, e_1 satisfy equations (3.6.2.1), (3.6.2.2) and (3.6.2.4), but that equation (3.6.2.3) and (3.6.2.5) are replaced by:

$$\omega_1 \mid_{t=0} = u_s - a_0, \tag{3.4.4}$$

and

$$e_1 \mid_{t=0} = \gamma_s, \tag{3.4.5}$$

respectively.

Exponential decay and upper bound for this new system are considered at the end of Chapter 3.

3.5 Model and Assumption

We recall the following.

Let Ω be a smooth bounded domain in R^3 and $\partial\Omega$ its boundary.

Let u denote the antigen concentration in Ω and c_0, γ denote respectively the initial antibody concentration and that of the combined antigen-antibody species on (part of) $\partial\Omega$.

It is convenient for our presentation to assume $c_0 \geq 0$ on $\partial\Omega$, rather than specifying the part of $\partial\Omega$ where $c_0 > 0$.

Our problem then is to find: $u = u(x,t) \in \Omega \times (0,T)$; $\gamma = \gamma(x,t) \in \partial\Omega \times (0,T)$ such that:

$$\begin{cases} u_t - D\Delta u = 0, & in\ \Omega \times (0,T), \quad (3.5.1.1) \\ D\dfrac{\partial u}{\partial n} = k_{-1}\gamma - k_1 u(c_0 - \gamma), & on\ \partial\Omega, \quad (3.5.1.2) \\ u\mid_{t=0} = a_0, & in\ \Omega, \quad (3.5.1.3) \\ \dfrac{d\gamma}{dt} = -k_{-1}\gamma + k_1 u(c_0 - \gamma), & on\ \partial\Omega \times (0,T), \quad (3.5.1.4) \\ \gamma\mid_{t=0} = 0, & on\ \partial\Omega. \quad (3.5.1.5) \end{cases} \tag{3.5.1}$$

Motivated by physical consideration, we assume that the (weak) solution pair u, γ is at least of class $C^{\alpha,\frac{\alpha}{2}}(\Omega \times (0,T))$ and $C^{1+\frac{\alpha}{2}}$ in t for fixed x, respectively, for some $\alpha > 0$.

The function $a_0 = a_0(x)$(respectively $c_0 = c_0(x)$) is assumed positive(respectively nonnegative, nontrivial) and smooth (respectively C^{α_0} for some $\alpha_0 > 0$) in $\bar{\Omega}$, while the other parameters (D, k_1, k_{-1}) are taken to be positive constants.

We note however that several of the results hold without any change under more general conditions. For example: $D\Delta u$ can be replaced by $\vec{\nabla} \cdot D\vec{\nabla} u$ where now D is a positive definite symmetric matrix.

In relating (3.5.1) to the system (3.2.5) discussed in [18], we note the following:

First, by formal integration of (3.5.1.1), (3.5.1.4) we obtain the conservation law:

$$(\int_\Omega u)_t + (\int_{\partial\Omega} \gamma)_t = 0,$$

i.e.

$$\int_\Omega u + \int_{\partial\Omega} \gamma = \int_\Omega a_0.$$

Under the geometric/ constancy condition of [18], we thus recover (3.2.5) as:

$$\gamma + \int_0^d u dx = a_0 d.$$

Secondly, equation (3.5.1.4) shows that wherever $c_0(x) = 0$ on $\partial\Omega$, we have $\gamma = 0$ for all t, as is physically expected and is implicitly the case in [18].

Our analysis thus deals with a situation where the initial antibody concentration need not be piecewise constant, and nonzero only on a flat part of the boundary.

Clearly, (3.5.1) cannot be reduced to a one dimensional problem in space where γ is also explicitly known in terms of u.

3.6 Existence and Uniqueness results

We begin by making the regularity assumption on $\partial\Omega$:

There exists a globally defined calculable vector field $\vec{b} = \vec{b}(x) \in C^1(\overline{\Omega})$ such that

$$\vec{b} \cdot \vec{n} = 1$$

on $\partial\Omega \bigcap supp[c_0]$.

Observe that the construction of $\vec{b}$ depends on the support of c_0 rather than on the entire $\partial\Omega$.

We then recall:

Lemma 3.6.1 . *Let $\epsilon > 0$ given. Then there exists $K(\epsilon)$ such that for any $\omega_1 \in C^1(\overline{\Omega})$ with $supp(\omega_1) \bigcap \partial\Omega \subset supp(c_0)$.*

We have:

$$\int_{\partial\Omega} \omega_1^2 \leq \epsilon \int_\Omega |\vec{\nabla} w_1|^2 + K(\epsilon) \int_\Omega \omega_1^2,$$

with $K(\epsilon) = \vec{\nabla}\cdot(\vec{b}) + \frac{1}{\epsilon}|\vec{b}|^2_{L^\infty}$.

Proof:

We merely note:

$$\begin{aligned}\int_{\partial\Omega}\omega_1^2 &= \int_{\partial\Omega}(\vec{b}\cdot\vec{n})\omega_1^2\\ &= \int_{\Omega}\vec{\nabla}\cdot(\vec{b})\omega_1^2 + \int_{\Omega}2(\vec{b}\cdot\nabla\vec{\omega}_1)\omega_1\\ &\leq \epsilon\int_{\Omega}|\vec{\nabla}\omega_1|^2 + \int_{\Omega}\omega_1^2\{\vec{\nabla}\cdot(\vec{b}) + \frac{|\vec{b}|^2_{L^\infty}}{\epsilon}\}.\end{aligned}$$

Let $Q_T = \Omega\times(0,T)$ and replace equations (3.5.1.2),(3.5.1.3) and (3.5.1.4) by multiplying the right hand side of each by the parameter λ,

$$0 \leq \lambda \leq 1.$$

We denote the resulting system by $(3.5.1)_\lambda$ and observe:

Lemma 3.6.2 *Let:* $u \in C^{\alpha,\alpha/2}(\overline{Q}_T)$*;* $\gamma \in C^1[0,T]$ *for each* $x\in\partial\Omega$*. Then for* $0 < \lambda \leq 1$*, we have* $u \geq 0$ *in* $\overline{Q}_T$*, and:* $0 < \gamma \leq c_0(x)$ *in (0,T] wherever* $c_0(x) > 0$*, while* $\gamma \equiv 0$ *wherever* $c_0(x) = 0$*.*

Proof:

Without loss of generality, put $\lambda = 1$ (the proof of the other cases is identical). Observe that $u > 0$ for t small and suppose $u = 0$ for the first time at some point (ρ, T_0) with $\rho \in \overline{\Omega}$ and $T_0 \leq T$.

We note that from equation (3.5.1.4),(3.5.1.5) we have $\gamma \geq 0$, nontrivial, up to $t = T_0$.

It follows that $u \geq v$ for $x \in \overline{\Omega}$ and $0 \leq t \leq T_0$ where v solves the linear problem:

$$\begin{cases} v_t - D\Delta v = 0, & in\ \Omega\times(0,T)\\ D\dfrac{\partial v}{\partial n} + K_1 v = 0, & on\ \partial\Omega\\ v = a_0, & t = 0\end{cases}$$

with $K_1 = k_1 \max(c_0)$.

But $v > 0$ at $t = T_0$ contradicting the assumption, and thus $u > 0$ in $\overline{Q}_T$.

Finally, note that at points x where $c_0 = 0$ we have $\gamma \equiv 0$ by integrating (3.5.1.4),(3.5.1.5).

While if $c_0(x) > 0$ then $\gamma > 0$ for $t > 0$.

By integrating (3.5.1.4),(3.5.1.5), we also know, while if $\gamma = c_0$ then

$$\frac{d\gamma}{dt} < 0$$

whence $\gamma \leq c_0$.

Lemma 3.6.3 *Let the condition of Lemma 3.6.2 hold.*

Then if (u, γ) *solve* $(3.5.1)_\lambda$*, we have* $| u |_{L_\infty(\overline{Q}_T)} \leq C$ *with* C *independent of* u, γ, λ.

Proof:

Observe that since $u \geq 0$ and $0 \leq \gamma \leq c_0$, then $u \leq \omega$ with ω solution of the linear problem:

$$\begin{cases} \omega_t - D\Delta\omega = 0, & in\ \Omega \times (0,T) \\ D\dfrac{\partial \omega}{\partial n} = k_{-1} max(c_0), & on\ \partial\Omega \\ \omega = a_0. & at\ t = 0 \end{cases}$$

If we apply [21, Theorem 6.44 or Theorem 6.46](see also [19], [27]), we then have:

Corollary 3.6.1 *There exists* $\beta > 0$ *(independent of* $\alpha, \lambda, u, \gamma$ *) such that* $u \in C^{\beta,\frac{\beta}{2}}(Q_T)$*. Consequently,* $\dfrac{d\gamma}{dt} \in C^{\beta,\frac{\beta}{2}}(\partial\Omega \times [0,T])$ *and* $\gamma \in C^{\beta,1+\frac{\beta}{2}}(\partial\Omega \times [0,T])$.

Theorem 3.6.1 *For any* $T < \infty$*, equations (3.5.1) have a unique solution* $u \in C^{\beta,\frac{\beta}{2}}(Q_T)$*,* $\gamma \in C^{\beta,1+\frac{\beta}{2}}(\partial\Omega \times [0,T])$ *for some* $\beta > 0$*. Here* $0 < u, 0 \leq \gamma \leq c_0$*. If* $c_0(x) > 0$ *then* $\gamma(x,t) > 0$ *for* $t > 0$*, if* $c_0(x) = 0$ *then* $\gamma(x,t) \equiv 0$.

Proof:

We may formulate equation (3.5.1) as:

$$u - Z(u) = 0,$$

with Z continuous and completely continuous from $C^{\beta,\frac{\beta}{2}}$ to itself in the usual way:

given a u calculate γ from equations (3.5.1.4), (3.5.1.5) and then $Z(u)$ from equation (3.5.1.1),(3.5.1.2),(3.5.1.3).

The properties of Z follow from Corollary 3.6.1, as does the fact that all solutions are uniformly bounded in $C^{\beta,\frac{\beta}{2}}$ for some $\beta > 0$.

The existence of (u, γ) follows from the Leray-Schauder Degree Theory. To see that the solution is unique, we observe:

Let (u_1, γ_1) and (u_2, γ_2) be two solutions, and set

$$\omega_1 = u_1 - u_2, \quad e_1 = \gamma_1 - \gamma_2. \tag{3.6.1}$$

We then have:

$$\begin{cases} (\omega_1)_t - D\Delta\omega_1 = 0, & in\ \Omega \times (0,T), \quad (3.6.2.1) \\ D\dfrac{\partial \omega_1}{\partial n} = k_{-1}e_1 - k_1\omega_1 c_0 + k_1(\omega_1\gamma_1 + u_2 e_1), & on\ \partial\Omega, \quad (3.6.2.2) \\ \omega_1 \mid_{t=0} = 0, & in\ \Omega, \quad (3.6.2.3) \\ \dfrac{de_1}{dt} = -k_{-1}e_1 + k_1\omega_1 c_0 - k_1(\omega_1\gamma_1 + u_2 e_1), & on\ \partial\Omega \times (0,T), \quad (3.6.2.4) \\ e_1 \mid_{t=0} = 0, & on\ \partial\Omega, \quad (3.6.2.5) \end{cases} \tag{3.6.2}$$

Hence:

$$(\frac{1}{2}\int_\Omega \omega_1^2)_t + D\int_\Omega |\nabla\omega_1|^2 + \int_{\partial\Omega} k_1\omega_1^2(c_0 - \gamma_1) = \int_{\partial\Omega}(k_{-1} + k_1 u_2)e_1\omega_1, \tag{3.6.3}$$

and:

$$(\frac{1}{2}\int_{\partial\Omega} e_1^2)_t + \int_{\partial\Omega}(k_{-1} + k_1 u_2)e_1^2 = \int_{\partial\Omega} k_1(c_0 - \gamma_1)e_1\omega_1. \tag{3.6.4}$$

We recall that γ_1, u_2 are bounded, nonnegative in Q_T, $\gamma_1 \leq c_0$. Whence adding (3.6.3),(3.6.4) yields:

$$(\frac{1}{2}\int_{\Omega}\omega_1^2 + \frac{1}{2}\int_{\partial\Omega}e_1^2)_t + D\int_{\Omega}|\nabla\omega_1|^2 \leq C(\int_{\partial\Omega}e_1^2 + \int_{\partial\Omega}\omega_1^2) \tag{3.6.5}$$

for some constant C.

We choose

$$\epsilon = \frac{D}{C}$$

in Lemma 3.6.1, and obtain from (3.6.5) for some constant E:

$$(\int_{\Omega}\omega_1^2 + \int_{\partial\Omega}e_1^2)_t - E(\int_{\Omega}\omega_1^2 + \int_{\partial\Omega}e_1^2) \leq 0. \tag{3.6.6}$$

Since as $t = 0$,

$$\int_{\Omega}\omega_1^2 + \int_{\partial\Omega}e_1^2 = 0,$$

the result follows.

3.7 Steady State and Long-Time Behavior

We now investigate the solution behavior as t $\rightarrow \infty$ and begin by noting that the solution to the steady-state problem, obtained by letting,

$$u_t = 0,$$

$$\frac{d\gamma}{dt} = 0,$$

in equation (3.5.1.1) and (3.5.1.4) respectively, is given by (u_s, γ_s) where

$$\gamma_s = (k_1 u_s c_0)/(k_{-1} + k_1 u_s)$$

and u_s is the positive constant root of the quadratic equation:

$$u_s|\Omega|(k_{-1} + k_1 u_s) + k_1 u_s \int_{\partial\Omega} c_0 = (k_{-1} + k_1 u_s)\int_{\Omega} a_0. \tag{3.7.1}$$

We next consider $\omega_1 = u_s - u$ and $e_1 = \gamma_s - \gamma$, and observe that ω_1, e_1 satisfy equations (3.6.2.1), (3.6.2.2) and (3.6.2.4), but that equation (3.6.2.3) and (3.6.2.5) are replaced by:

$$\omega_1 \mid_{t=0} = u_s - a_0, \tag{3.7.2}$$

and

$$e_1 \mid_{t=0} = \gamma_s, \tag{3.7.3}$$

respectively.

Consequently, equations (3.6.3)and (3.6.4) hold for the newly defined (ω_1, e_1) and we shall have the desired result under conditions on the problem which guarantee that the constant E of equation (3.6.6) is now negative.

To obtain such a result we need as preliminary considerations the following: Define the constant $K_1(p)$ by:

$$\|\omega - \overline{\omega}\|_{L^p(\Omega)} \leq K_1(p) \|\nabla \omega\|_{L^2(\Omega)},$$

for any $\omega \in H^{1,2}(\Omega)$, where $\bar{\omega} = \frac{1}{|\Omega|} \int_\Omega \omega.$

Observe that such $K_1(p)$: depends on Ω; n(which equals 3 in practical situations) but not on ω; exists for $p \leq \frac{2n}{n-2}$ and quite general Ω; may be easily explicitly estimated for $p < \frac{2n}{n-2}$ and Ω convex by the formula given e.g in [17].

From this, it is also easy to obtain an explicit estimate for domains that can be decomposed as the finite union of convex subdomains.

Lemma 3.7.1 *Let (u, γ) solve (3.5.1) and let $t \geq T_0 > 0$. Then:*

$$(\int_\Omega u^2)|_t \leq (\int_\Omega u^2) \mid_{T_0} e^{-\frac{(t-T_0)D}{2K_1^2(2)}} + (1 - e^{-\frac{(t-T_0)D}{2K_1^2(2)}})(A(\overline{a}_0^2) + |\gamma|^2_{L^\infty(t \geq T_0)} B)$$

with A, B computable constants, given below. (They depend on $K_1(2), \Omega, n$, but are independent of $u, \gamma, x, t, T_0, u_0, c_0$).

Proof:

By the usual energy estimates and since: $u_0 \geq 0; 0 \leq \gamma \leq c_0; \overline{u} \leq \overline{u}_0$;

we have:

$$(\frac{1}{2} \int_\Omega u^2)_t + D \int_\Omega |\vec{\nabla} u|^2 \leq k_{-1} \int_{\partial\Omega} \gamma u \leq k_{-1} |\gamma|_{L^\infty(t \geq T_0)} \int_\Omega \vec{\nabla} \cdot (\vec{b} u)$$
$$\leq k_{-1} |\gamma|_{L^\infty(t \geq T_0)} (\|\vec{\nabla} \cdot \vec{b}\|_{L^2} \|u\|_{L^2} + \|\vec{b}\|_{L^2} \|\vec{\nabla} u\|_{L^2})$$

Now

$$k_{-1}|\gamma|_{L^\infty}\|\vec{b}\|_{L^2}\|\vec{\nabla}u\|_{L^2} \leq \frac{D}{2}\|\nabla u\|_{L^2}^2 + \frac{1}{2D}k_{-1}^2|\gamma|_{L^\infty}^2\|\vec{b}\|_{L^2}^2$$

thus

$$(\frac{1}{2}\|u\|_{L^2}^2)_t + \frac{D}{2}\|\vec{\nabla}u\|_{L^2}^2 \leq k_{-1}|\gamma|_{L^\infty}(\|\vec{\nabla}\cdot\vec{b}\|_{L^2}\|u\|_{L^2}) + \frac{1}{2D}k_{-1}^2|\gamma|_{L^\infty}^2\|\vec{b}\|_{L^2}^2$$

or

$$(\frac{1}{2}\|u\|_{L^2}^2)_t + \frac{D}{2K_1^2(2)}\|u-\bar{u}\|_{L^2}^2 \leq k_{-1}|\gamma|_{L^\infty}(\|\vec{\nabla}\cdot\vec{b}\|_{L^2}\|u\|_{L^2}) + \frac{1}{2D}k_{-1}^2|\gamma|_{L^\infty}^2\|\vec{b}\|_{L^2}^2$$

Observing that:

$$\|u-\bar{u}\|_{L^2}^2 = \|u\|_{L^2}^2 - |\Omega|(\bar{u})^2$$

yields:

$$\begin{aligned}&(\frac{1}{2}\|u\|_{L^2}^2)_t + \frac{D}{2K_1^2(2)}\|u\|_{L^2}^2 \\ \leq\ & \frac{D|\Omega|}{2K_1^2(2)}(\bar{a}_0)^2 + \frac{1}{2D}k_{-1}^2|\gamma|_{L^\infty}^2\|\vec{b}\|_{L^2}^2 + k_{-1}|\gamma|_{L^\infty}\|\vec{\nabla}\cdot\vec{b}\|_{L^2}\|u\|_{L^2}D\end{aligned}$$

We conclude

$$\begin{aligned}(\frac{1}{2}\|u\|_{L^2}^2)_t + \frac{D}{4K_1^2(2)}\|u\|_{L^2}^2 \leq\ & \frac{D|\Omega|}{2K_1^2(2)}(\bar{a}_0)^2 + \frac{1}{2D}k_{-1}^2|\gamma|_{L^\infty}^2\|\vec{b}\|_{L^2}^2 \\ &+ \frac{k_{-1}^2|\gamma|_{L^\infty}^2\|\vec{\nabla}\cdot\vec{b}\|_{L^2}^2K_1^2(2)}{D}\end{aligned}$$

and the result follows with $A = \dfrac{|\Omega|}{2}$,

$$B = \frac{[\frac{1}{2D}k_{-1}^2\|\vec{b}\|_{L^2}^2] + k_{-1}^2[\|\vec{\nabla}\cdot\vec{b}\|_{L^2}^2K_1^2(2)/D]}{\frac{D}{4K_1^2(2)}}.$$

Theorem 3.7.1 *The solution u is globally bounded, and we have $\lim_{t\longrightarrow\infty} sup\|u(\cdot,t)\|_{L^\infty} \leq M$, where*

$$M = \frac{2\Lambda_1\bar{a}_0k_{-1}}{[(k_{-1}-k_1\Lambda_1\bar{a}_0-k_1|c_0|_{L^\infty}\Lambda_2)^2+4\Lambda_1\bar{a}_0k_1k_{-1}]^{\frac{1}{2}} - [k_1|c_0|_{L^\infty}\Lambda_2+k_1\Lambda_1\bar{a}_0-k_{-1}]}$$

with Λ_1, Λ_2 constants with calculable dependence on $K_1(p)$.

Proof:

Let $\varphi = \varphi(t)$ be a fixed function with $\varphi = 0$ if $t \leq 0$, $\varphi = 1$ if $t \geq 1$, $\varphi_t \geq 0$, and put for chosen T_0, h: $\omega(t) = \varphi(\frac{t-T_0}{h})$; $z = \omega u$.

We then have:

$$z_t - D\triangle z = \omega_t u$$

$$D\frac{\partial z}{\partial n} + k_1 z(c_0 - \gamma) = k_{-1}\gamma\omega$$

$$z|_{t=T_0} = 0.$$

We modify somewhat the procedure of [19] to estimate $|z|_{L^\infty}$ for $T_0 \leq t \leq T_1$ with $T_1 - T_0$ independent of u.

Note that we may use $z_k = (z-k)^+$ as a test function with $k \geq 1$, and obtain:

$$\begin{aligned} &(\frac{1}{2}\int_\Omega z_k^2)_t + D\int_\Omega |\vec{\nabla} z_k|^2 \\ \leq\ & p(t)\{\textstyle\int_\Omega (\vec{\nabla}\cdot\vec{b})z_k + \int_\Omega \vec{b}\cdot\vec{\nabla} z_k\} + \int_\Omega \omega_t u z_k \end{aligned} \quad . \tag{3.7.4}$$

with $p(t) = k_{-1}|\gamma|_{L^\infty(t>T_0)}\omega(t)$.

This is precisely the situation in [19, Page 184, eq 7.7] with(in the notation of [19])

$$f = \omega_t u + p(t)\vec{\nabla}\cdot\vec{b}$$

$$f_i = -p(t)b_i$$

$$\nu = D$$

We recall that $\Omega \in R^3$ and following [19], we choose $q = 2, r = \frac{1}{8}$ and thus $\chi_1 = \frac{1}{8}$(other choice are possible, but these are numerically simple).

Put $\mathcal{D} = ||f||_{q,r,Q[T_0\leq t\leq T_0+1]} + \frac{1}{2}||\sum f_i^2||^{\frac{1}{2}}_{q,r,Q[T_0\leq t\leq T_0+1]}$ and applying the process of [19] to the function

$$\frac{z}{\mathcal{D}}$$

we observe that there is a calculable $t_1 \leq 1$, constants Λ_1, Λ_2(both independent of T_0, u), such that (by Lemma 3.7.1)

$$\|u\|_{L^\infty(T_0+\frac{t_1}{2}\le t\le T_0+t_1)} \le \Lambda_1(\bar{a_0}) + \Lambda_2|\gamma|_{L^\infty(t\ge T_0)} \tag{3.7.5}$$

We observe that Λ_1, Λ_2 can be estimated if $K_1(p)$ can be estimated.

Since $\Lambda_1, \Lambda_2, t_1$ are independent of T_0, u, it follows that (3.7.5) holds for all t sufficiently large, i.e.

$$\|u\|_{L^\infty(t\ge T_0+1)} \le \Lambda_1[\bar{a_0}] + \Lambda_2|\gamma|_{L^\infty(t\ge T_0)} \tag{3.7.6}$$

Suppose that for $t \ge T^*$ we have $u(x,t) \le M$ for some constant M.

We recall that γ satisfies (3.5.1.4-3.5.1.5) and that $\gamma \le c_0$ for all t. We thus obtain that if $\gamma(x,T^*) > \dfrac{k_1uc_0}{k_{-1}+k_1u}$ then

$$\frac{d\gamma}{dt} < 0$$

for $t \ge T^*$ as long as this bound holds.

We conclude that if $u(x,t) \le M$ for $t \ge T^*$, then given any $\epsilon > 0$, there exists a finite time $T_1 \ge T^*$ such that

$\gamma(x,t) \le \epsilon + \dfrac{k_1Mc_0}{k_{-1}+k_1M}$ for $t \ge T_1$.

We can now iterate on equation (3.7.6) as follows.

Choose $M_0 = \Lambda_1\bar{a}_0 + |c_0|_{L^\infty}\Lambda_2$, and by induction (for any small $\epsilon > 0$):

$$M_i = \Lambda_1\bar{a}_0 + (\epsilon + \frac{k_1M_{i-1}|c_0|_{L^\infty}}{k_{-1}+k_1M_{i-1}})\Lambda_2. \tag{3.7.7}$$

Note that $|u(\cdot,t)|_{L^\infty(t\ge T_0)} \le M_0$, and that by the estimates on γ there exists an increasing sequence of times $\{T_i\}_{i=1}^\infty$ such that $|u(\cdot,t)|_{L^\infty(t\ge T_i)} \le M_i$. We note that (3.7.7) is a monotone decreasing sequence for the M_i .

Put $M = \lim_{i\to\infty}(M_i)$ and observe that by direct calculation,

$$M = \frac{2(\Lambda_1\bar{a_0} + \epsilon\Lambda_2)k_{-1}}{P1 - P2}.$$

Where:

$P1 = [(k_{-1} - k_1[\Lambda_1\bar{a_0} + \epsilon\Lambda_2] - k_1|c_0|_{L^\infty}\Lambda_2)^2 + 4(\Lambda_1\bar{a_0} + \epsilon\Lambda_2)k_1k_{-1}]^{\frac{1}{2}}$,

$P2 = [k_1|c_0|_{L^\infty}\Lambda_2 + k_1(\Lambda_1\bar{a_0} + \epsilon\Lambda_2) - k_{-1}]$.

Since after a finite number of time steps, $u \le M + \epsilon$ the result follows.

Remark 3.7.1 *If $K_1(p)$ can be calculated, then all other constants can be determined. In the case that Ω is convex, we can use for $p < \frac{2n}{n-2}$ (=6 in our case) Lemma 7.21 and Lemma 7.16 of [17, pages 152 and 156 respectively] to calculate*

$$\|\omega - \overline{\omega}\|_{L^p(\Omega)} \leq K_1(p)\|\nabla\omega\|_{L^2}$$

with $K_1(p)$ is in terms of Ω.

From this, we can also get the other needed estimate (eq. 31 of [19] on page 74) by Holder's Inequality, and note:

$$\|u - \bar{u}\|_{L^p} \leq \|u - \bar{u}\|^{\alpha}_{L^p}\|u - \bar{u}\|^{(1-\alpha)}_{L^2} \leq K_1(p)\|\nabla u\|^{\alpha}_{L^2}\|u - \bar{u}\|^{(1-\alpha)}_{L^2}$$

with $q < p$ and

$$\alpha = \frac{1 - \frac{2}{q}}{1 - \frac{2}{p}}.$$

Returning now to the system of equations (3.6.2) (with: $\gamma_1 = \gamma_s; u_1 = u_s; \gamma_2 = \gamma; u_2 = u$), we first establish a convergence result that does not require an estimate on $|u|_{L^\infty}$.

Specifically, note that now

$$\int_\Omega \omega_1 + \int_{\partial\Omega} e_1 = 0$$

and $e_1(x,t) = 0$ if $c_0(x) = 0$.

We add (3.6.3) and (3.6.4) to obtain once again:

$$\begin{aligned} &(\frac{1}{2}\int_\Omega \omega_1^2 + \frac{1}{2}\int_{\partial\Omega} e_1^2)_t + D\int_\Omega |\nabla\omega_1|^2 + \int_{\partial\Omega} k_1\omega_1^2(c_0 - \gamma) \\ &+ \int_{\partial\Omega}(k_{-1} + k_1 u_s)e_1^2 - \int_{\partial\Omega}[k_{-1} + k_1 u_s + k_1(c_0 - \gamma_1)]e_1\omega_1 \\ = \; & 0 \end{aligned} \quad (3.7.8)$$

We then have:

$$\begin{aligned} ||\nabla\omega_1||^2_{L^2} &\geq K_1^{-1}(2)[\|\omega_1 - \bar{\omega}_1\|^2_{L^2}] \\ &= K_1^{-1}(2)[\|\omega_1\|^2_{L^2} - \bar{\omega}^2|\Omega|] \end{aligned} \quad (3.7.9)$$

Since $\int_{\Omega} \omega_1 = -\int_{\partial\Omega} e_1$, we obtain:

$$|\int_{\Omega} \omega_1| \leq (\int_{\partial\Omega} e_1^2)^{\frac{1}{2}} [\mu(c_0)]^{\frac{1}{2}}$$

where

$\mu(c_0) = \mu[\{x | c_0(x) > 0\} \bigcap \partial\Omega]$.

Substituting into (3.7.9) yields

$$\int_{\Omega} |\nabla \omega_1|^2 + \frac{K_1^{-1}(2)[\mu(c_0)]}{|\Omega|} \int_{\partial\Omega} e_1^2 \geq K_1^{-1}(2) \int_{\Omega} \omega_1^2$$

From Lemma 3.6.1, we also recall:

$$\int_{\partial\Omega} \omega_1^2 \leq \int_{\Omega} |\nabla w_1|^2 + K(1) \int_{\Omega} \omega_1^2$$

Thus

$$K(1)K_1(2) \int_{\Omega} |\nabla \omega_1|^2 + \frac{K(1)[\mu(c_0)]}{|\Omega|} \int_{\partial\Omega} e_1^2 \geq K(1) \int_{\Omega} \omega_1^2$$

and consequently,

$$(1 + K(1)K_1(2)) \int_{\Omega} |\nabla \omega_1|^2 + \frac{K(1)[\mu(c_0)]}{|\Omega|} \int_{\partial\Omega} e_1^2 \geq \int_{\partial\Omega} \omega_1^2$$

whence:

$$D \int_{\Omega} |\vec{\nabla} \omega_1|^2 \geq \frac{D}{1 + K(1)K_1(2)} \int_{\partial\Omega} \omega_1^2 - \frac{D[\mu(c_0)]}{|\Omega|} \cdot \frac{K(1)}{1 + K(1)K_1(2)} \int_{\partial\Omega} e_1^2$$

Substituting in (3.7.8) gives:

$$\begin{aligned} &(\frac{1}{2} \int_{\Omega} \omega_1^2 + \frac{1}{2} \int_{\partial\Omega} e_1^2)_t + \int_{\partial\Omega} [\frac{D}{1 + K(1)K_1(2)} + k_1(c_0 - \gamma)]\omega_1^2 \\ &+ \int_{\partial\Omega} [k_{-1} + k_1 u_s - \frac{D[\mu(c_0)]}{|\Omega|} \cdot \frac{K(1)}{1 + K(1)K_1(2)}] e_1^2 \\ &- \int_{\partial\Omega} [k_{-1} + k_1 u_s + k_1(c_0 - \gamma_1)] e_1 \omega_1 \\ &\leq 0 \end{aligned}$$

From this estimate, we obtain:

Theorem 3.7.2 *Assume that for some constant* $\Pi > 0$ *we have*

$$[\frac{D}{1+K(1)K_1(2)} + k_1(c_0-\gamma)] \tag{3.7.10}$$

$$\times[k_{-1} + k_1 u_s - \frac{D[\mu(c_0)]}{|\Omega|} \cdot \frac{K(1)}{1+K(1)K_1(2)}]$$

$$- \quad \frac{1}{4}[k_{-1} + k_1 u_s + k_1(c_0-\gamma_1)]^2 \geq \Pi \tag{3.7.11}$$

then $\int_\Omega \omega_1^2 + \int_{\partial\Omega} e_1^2 \to 0$ *exponentially as* $t \to \infty$

We recall that u_s is known and that $0 \leq \gamma \leq c_0$. From Theorem 3.7.2 we thus obtain:

Corollary 3.7.1 *If*

$$[\frac{D}{1+K(1)K_1(2)}] \times [k_{-1} + k_1 u_s - \frac{D[\mu(c_0)]}{|\Omega|} \cdot \frac{K(1)}{1+K(1)K_1(2)}]$$
$$- \frac{1}{4}[(k_{-1} + k_1 u_s) + k_1 c_0]^2 \geq \Pi$$

then the result of Theorem 3.7.2 holds.

Observe that u_s is independent of D and the corollary will hold for situations where D is large but $D[\mu(c_0)]$ is small.

Remark 3.7.2 *If we interchange the definition of* (u, γ) *and* (u_s, γ_s) *in the definition of* ω_1, e_1 *then (3.7.8) holds but now "*γ*" is replaced by "*γ_s*" and "*u_s*" by "*u*".*

We know γ_s *explicitly, but now* u *must be estimated (as was done earlier). We obtain another result that now depends on the estimate* M *for* u *as follows:*

Define δ to be the least eigenvalue of the elliptic problem:

$$-\frac{D}{2}\triangle\omega = \delta\omega,$$

$$D\frac{\partial\omega}{\partial n} + k_1(c_0-\gamma_s)\omega = 0.$$

Whence (3.7.8) yields:

$$(\frac{1}{2}\int_{\Omega}\omega_1^2+\frac{1}{2}\int_{\partial\Omega}e_1^2)_t+\delta\|\omega_1\|_{L^2}^2+\frac{D}{2}\int_{\Omega}|\nabla\omega_1|^2 \tag{3.7.12}$$

$$-\frac{1}{2}\int_{\partial\Omega\bigcap supp(c_0)}(k_{-1}+k_1u)\omega_1^2$$

$$+\quad\frac{1}{2}\int_{\partial\Omega}[(k_{-1}+k_1u)-k_1(c_0-\gamma_s)]e_1^2\leq 0 \tag{3.7.13}$$

Since

$$\begin{aligned}\int_{\partial\Omega\bigcap supp(c_0)}(k_{-1}+k_1u)\omega_1^2 &\leq (k_{-1}+k_1M+\varepsilon)\int_{\partial\Omega\bigcap supp(c_0)}\omega_1^2\\ &= (k_{-1}+k_1M+\varepsilon)[\int_{\Omega}\nabla\cdot(\vec{b})\omega_1^2+2\vec{b}\cdot\omega_1\nabla\omega_1]\end{aligned}$$

Thus,

$$\begin{aligned}&2(k_{-1}+k_1M+\varepsilon)\int_{\Omega}\vec{b}\cdot\nabla\omega_1\omega_1 \\ \leq\quad &(k_{-1}+k_1M+\varepsilon)^2\frac{2}{D}|\vec{b}|_{L^\infty}^2\int_{\Omega}\omega_1^2+\frac{D}{2}\int_{\Omega}|\nabla\omega_1|^2\end{aligned} \tag{3.7.14}$$

whence if we assume:

$$\begin{cases}\delta>(k_{-1}+k_1M)\vec{\nabla}\cdot\vec{b}+\dfrac{2}{D}|\vec{b}|_{L^\infty}^2(k_{-1}+k_1M+\varepsilon)^2,\\ k_{-1}>k_1(c_0-\gamma_s),\end{cases} \tag{3.7.15}$$

we obtain:

Theorem 3.7.3 *If condition (3.7.15) hold, then* $\int_{\Omega}\omega_1^2+\int_{\partial\Omega}e_1^2\ \to\ 0$ *as* $t\to\infty$

3.8 System Results

We now consider the application of the previous ideas to situations where two (or more) antigens are present.

In this case, where without loss of generality we assume there are exactly two antigens, we obtain for $i = 1, 2$ the system:

$$\begin{cases} u_{it} - D\Delta u_i = 0, \\ D\dfrac{\partial u_i}{\partial n} = k_{-1,i}\gamma_i - k_{1,i}u_i(c_0 - \gamma_1 - \gamma_2), \\ u_i \mid_{t=0} = a_i > 0, \\ \dfrac{d\gamma_i}{dt} = -k_{-1,i}r_i + k_{1,i}u_i(c_0 - \gamma_1 - \gamma_2), \\ \gamma_i \mid_{t=0} = 0, \end{cases} \tag{3.8.1}$$

Here Ω, $k_{1,i}$, $k_{-1,i}$,a_i, c_0 satisfy the assumptions given earlier for the case of a single antigen. The earlier procedures apply with only small changes. Specifically, we note:

Theorem 3.8.1 *There exists a unique solution* $(u_1, u_2, \gamma_1, \gamma_2)$ *to system (3.8.1) with* $0 < u_1, u_2$; $0 \leq \gamma_1, \gamma_2$;$\gamma_1 + \gamma_2 \leq c_0$.

Proof: We need only replace the equation(s) of the model by

$$\begin{cases} \dfrac{d\gamma_1}{dt} = -k_{-1,1}\gamma_1 + k_{1,1}u_1[(c_0 - \gamma_2)^+ - \gamma_1], \\ \dfrac{d\gamma_2}{dt} = -k_{-1,2}\gamma_2 + k_{1,2}u_2[(c_0 - \gamma_1)^+ - \gamma_2], \end{cases}$$

The rest of the proof follows that given earlier.

For example, T_0 is now defined to be the time when one of u_1, u_2 is zero for the first time.

Note that we conclude

$$\gamma_1 \leq (c_0 - \gamma_2)^+, \quad \gamma_2 \leq (c_0 - \gamma_1)^+$$

and $0 \leq \gamma_1, \gamma_2$ where $\gamma_1 + \gamma_2 \leq c_0$.

It follows that we have found solutions of the original system. That there are no other solutions of this systems (satisfying the above conditions or not) follows as before by taking differences.

To estimate $\| u_1 \|_{L^\infty(t \geq T_0)}$ and $\| u_2 \|_{L^\infty(t \geq T_0)}$, we note that $\gamma_1 + \gamma_2 \leq c_0$ and $0 \leq \gamma_1, \gamma_2$ imply that the system essentially decouples.

Next, note that if $\| u_1 \|_{L^\infty(t\geq T_0)} \leq M_1$ and $\| u_1 \|_{L^\infty(t\geq T_0)} \leq M_2$, we have
$$\frac{d(\gamma_1+\gamma_2)}{dt} + \min_{i=1,2}[k_{1,i}](\gamma_1+\gamma_2) = \max_{i=1,2}(M_i k_{1,i})[c_0 - \gamma_1 - \gamma_2].$$
We proceed with the estimates of Lemma 3.7.1 and Theorem 3.7.1 for each u_i, the main difference now being the replacement of γ by $\gamma_1+\gamma_2$ in the earlier proof. The long time arguments of Theorem 3.7.2 follow.

Chapter 4

Numerical Analysis of a Biosensor Model in R^3

4.1 Introduction

Our main result in this chapter is the application and analysis of a finite element method used to obtain approximate solutions. Drawing in part on the analytical results given earlier, we establish the existence, stability and error estimates for the approximate solution, and derive L^2 spatial norm convergence properties.

4.2 L^2 Norm Stability

Let $k \in (0, T)$ be a constant time step, $N_k = max\{n \in \mathcal{N},\ nk < T\}$, i.e. we divide $[0, T]$ uniformly into $N_k + 1$ intervals. Set $t_n = nk$ for $n \in \{0, 1, \cdots, N_k + 1\}$, and let $\phi^n = \phi(t_n, x)$, $d_t\phi^n = \dfrac{\phi^{n+1} - \phi^n}{k}$.

To analyze the discretization scheme, it is assumed that the exact solution is at least of class $u \in L^\infty(0, T; H^2(\Omega))$, $\gamma \in L^\infty(0, T; H^1(\partial\Omega))$, with $u_t(\cdot, t), \gamma_t(\cdot, t)$ piecewise C^1 functions.

Integrating (3.5.1.1) on each cell of the mesh at time $t = t_{n+1}$ yields,

$$\int_K u_t^{n+1}(x)dx - D\int_{\partial K\setminus\sigma_{ext}} \nabla u^{n+1}(x)\cdot\eta_K(x)dS(x)$$
$$- \int_{\sigma_{ext}\bigcap\partial K} (k_{-1}\gamma^{n+1} - k_1 u^{n+1}(c_0-\gamma^{n+1}))dS(x) = 0 \qquad (4.2.1)$$

Accordingly, for (3.5.1.2),

$$D\int_\sigma \nabla u^{n+1}(x)\cdot\eta_{K,\sigma}(x)dS(x) = \int_\sigma (k_{-1}\gamma^{n+1} - k_1 u^{n+1}(c_0-\gamma^{n+1}))dS(x), \qquad (4.2.2)$$

$\forall\sigma\subset\partial\Omega$.

From (3.5.1.4), we obtain

$$\gamma_t^{n+1}(x) + (k_{-1}+k_1u^{n+1})\gamma^{n+1} = k_1u^{n+1}c_0. \qquad \forall\sigma\subset\partial\Omega. \qquad (4.2.3)$$

Next, we follow the finite volume scheme detailed in [16] to get the discrete form for (4.2.1)-(4.2.3) term by term and integrate (4.2.3) to obtain the approximation to γ^{n+1}.

We replace u_t^{n+1} in (4.2.1) by a backward Euler scheme.

More detailed discussions about the consistency and conservativity of the discrete scheme is available in [16].

We merely mention that the error estimates will be based on the consistent linear discretization of the normal flux of $-\nabla u\cdot n$ over the interface of only two control volumes K and L.

The discrete unknowns are denoted by $(U_K^{n+1})_{K\in\mathcal{T}}\cup(\Gamma_\sigma^{n+1})_{\sigma\in\varepsilon_{ext}}$, $n = 0,1,\cdots,N_k$, yielding the implicit discretization scheme,

$$m(K)d_tU_K^n + \sum_{\sigma\in\varepsilon_K} F_{K,\sigma}^{n+1} = 0, \qquad \forall K\in\mathcal{T}, \qquad (4.2.4)$$

$$F_{K,\sigma}^n = -m(K|L)D\frac{U_L^n-U_K^n}{d_{K,L}}, \qquad if\sigma = K|L, \qquad (4.2.5)$$

$$F_{K,\sigma}^{n+1} = -m(\sigma)(k_{-1}\Gamma_\sigma^{n+1} - k_1U_\sigma^{n+1}(c_\sigma-\Gamma_\sigma^{n+1})), \qquad if\sigma\in\varepsilon_K\cap\varepsilon_{ext}, \qquad (4.2.6)$$

$$c_\sigma = \frac{1}{m(\sigma)}\int_\sigma c_0(x)dS(x). \qquad (4.2.7)$$

Recalling $t_n - t_{n+1} = -k$, we obtain:

$$\frac{\Gamma_\sigma^{n+1} - \Gamma_\sigma^n e^{(k_{-1}+k_1 U_\sigma^{n+1})(-k)}}{\dfrac{1 - e^{-(k_{-1}+k_1 U_\sigma^{n+1})k}}{k_{-1} + k_1 U_\sigma^{n+1}}} = k_1 U_\sigma^{n+1} c_\sigma. \tag{4.2.8}$$

Corresponding to equation (4.2.3), this can be expressed as:

$$\frac{\Gamma_\sigma^{n+1} - \Gamma_\sigma^n}{\frac{1-e^{-(k_{-1}+k_1 U_\sigma^{n+1})k}}{k_{-1}+k_1 U_\sigma^{n+1}}} + (k_{-1} + k_1 U_\sigma^{n+1})\Gamma_\sigma^n \frac{1 - 2e^{-(k_{-1}+k_1 U_\sigma^{n+1})k}}{1 - e^{-(k_{-1}+k_1 U_\sigma^{n+1})k}} = k_1 U_\sigma^{n+1} c_\sigma. \tag{4.2.9}$$

For $n = 0, 1, \cdots, N_k + 1$, we define

$$U_K^0 = \frac{1}{m(K)} \int_K a_0(x)dx, U_\sigma^0 = \frac{1}{m(\sigma)} \int_\sigma a_0(x)dSx, \tag{4.2.10}$$

$$\Gamma_\sigma^0 = 0. \tag{4.2.11}$$

Iteration is required for the implicit nonlinear time-advancing calculation so as to obtain the solution pairs (Γ_σ^n, U_K^n).

In fact, We found the given iterative scheme more efficient from a practical point of view, with the exponential fitting given in (4.2.8) replacing the usual finite difference scheme for the time derivative.

However, theoretically this introduces no change to the accuracy of the scheme.

Actually, we have,

$$\frac{1}{\frac{1-e^{-(k_{-1}+k_1 U_\sigma^{n+1})k}}{k_{-1}+k_1 U_\sigma^{n+1}}} = \frac{1}{k} + l_1(k), \tag{4.2.12}$$

and,

$$\frac{1 - 2e^{-(k_{-1}+k_1 U_\sigma^{n+1})k}}{1 - e^{-(k_{-1}+k_1 U_\sigma^{n+1})k}} = 1 + l_2(k). \tag{4.2.13}$$

With, for k is small, $l_1(k)$ and $l_2(k)$ both $o(k)$, even though they are dependent on the numerical solution of (Γ_σ^n, U_K^n).

Furthermore, for $i = 1, 2$, since k is small, we observe that

$$-\frac{1}{2} < l_i(k) < \frac{1}{2}. \tag{4.2.14}$$

In this way, the scheme (4.2.8) may be represented as,

$$(\Gamma_\sigma^{n+1} - \Gamma_\sigma^n)(\frac{1}{k} + l_1(k)) + (k_{-1} + k_1 U_\sigma^{n+1})\Gamma_\sigma^n(1 + l_2(k)) = k_1 U_\sigma^{n+1} c_\sigma \quad (4.2.15)$$

Lemma 4.2.1 *For the above discretization form, recalling that* $(U_K^0)_{K\in\mathcal{T}} \geq 0$*, and* $\Gamma_\sigma^0 = 0$*, we have:*

(a) There exists a unique solution pair $(U_K^{n+1}, \Gamma_\sigma^{n+1})$

(b) $0 \leq \Gamma_\sigma^{n+1} \leq c_\sigma$*.*

Proof:

For convenience we write: $\vec{a} \geq \vec{b}$ for any two vector $\vec{a}, \vec{b}$ iff $\vec{a} - \vec{b}$ has nonnegative components, and $\vec{U}^{n+1}$ for $(U_K^{n+1})_{K\in\mathcal{T}}$, $\vec{\Gamma}^{n+1}$ for $(\Gamma_\sigma^{n+1})_{\sigma\in\epsilon_{ext}}$.

We then rewrite the scheme in a slightly modified form as:

$$\Gamma_\sigma^{n+1} = \Gamma_\sigma^n e^{-(k_{-1}+k_1U_\sigma^{n+1})k} + k_1(U_\sigma^{n+1})^+ c_\sigma[\frac{1 - e^{-(k_{-1}+k_1U_\sigma^{n+1})k}}{k_{-1} + k_1 U_\sigma^{n+1}}] \qquad (4.2.16)$$

and:

$$A\vec{U}^{n+1} + D_1\vec{U}^{n+1} = \vec{f} + \frac{\vec{U}^n}{k}m(k)$$

Here: D_1 is a diagonal matrix with entry zero if σ_K is internal, entry $k_1c_\sigma - \Gamma_\sigma^{n+1}$ if σ_K is external.

The entries of $\vec{f}$ are $k_{-1}\Gamma_\sigma^{n+1}$ if σ_K is external, 0 if σ_K is internal.

Finally, A is an M-matrix. M-matrices is a Z-matrix with eigenvalues whose real parts are positive, arising naturally in some discretizations of differential operators, particularly those with a minimum/maximum principle, such as the Laplacian, and as such are well-studied in scientific computing.

In particular, A^{-1} leaves invariant the cone of nonnegative functions.

Observe that if $\Gamma_\sigma^n \geq 0$, then $\Gamma_\sigma^{n+1} \geq 0$. It follows that if $\vec{U}_\sigma^n \geq 0$, then $\vec{U}_\sigma^{n+1} \geq 0$, whence $\vec{\Gamma}_\sigma^{n+1} \leq c_\sigma$. Thus $\vec{U}_\sigma^{n+1} \leq \vec{V}_\sigma$ where $\vec{V}$ solves

$$A\vec{V} = \frac{\vec{U}^n}{k}m(k)$$

We observe that $\vec{V}$ is independent of $\vec{U}^{n+1}$.

Introducing the homotopy parameter λ as for the continuous problem shows the existence of a nonnegative solution pair which thus solve the desired numerical equation.

The uniqueness is also obtained as was done for the continuous problem.

Definition 4.2.1 *(Discrete Norm)* *Let $\phi = \phi_{\mathcal{T}}$ be a function which is a constant on each control volume of $\mathcal{T}$ and on each edge on the boundary of $\partial\Omega$ with $\phi_{\mathcal{T}}(x) = \phi_K$ if $x \in K, K \in \mathcal{T}$ and $\phi_{\mathcal{T}}(x) = \phi_\sigma$ if $x \in \sigma, \sigma \in \varepsilon_{ext}$. The discrete L^2 norm, $L^2(\partial\Omega)$ norm and H^1 semi-norm are defined by:*

$$\|\phi_{\mathcal{T}}\| = \|\phi_{\mathcal{T}}\|_{L^2(\Omega)} = [\sum_{K\in\mathcal{T}} m(K)(\phi_K)^2]^{\frac{1}{2}}, \tag{4.2.17}$$

$$\|\phi_{\mathcal{T}}\|_{L^2(\partial\Omega)} = [\sum_{\sigma\in\varepsilon_{ext}} m(\sigma)(\phi_\sigma)^2]^{\frac{1}{2}}, \tag{4.2.18}$$

$$|\phi_{\mathcal{T}}|_{1,\mathcal{T}} = [\sum_{\sigma\in\varepsilon} \tau_\sigma(D_\sigma\phi)^2]^{\frac{1}{2}}, \tag{4.2.19}$$

where $D_\sigma\phi = |\phi_K - \phi_L|$ if $\sigma = K|L$.

We recall the following result from [9](also see [16]):

Lemma 4.2.2 *(Discrete Norm Inequality) Let $\Gamma \subset \partial\Omega$ such that its $(d-1)$-dimensional measure $m(\Gamma) \neq 0$ and $\mathcal{O} \subset \Omega$ such that its d-dimensional measure $m(\mathcal{O}) \neq 0$. Then there exists C, only depending on Ω, Γ and $\mathcal{O}$, such that for $\phi = \phi_{\mathcal{T}}$:*

$$\|\phi\|^2_{L^2(\Omega)} \leq C[|\phi|^2_{1,\mathcal{T}} + \|\phi\|^2_{L^2(\Gamma)}], \|\phi\|^2_{L^2(\partial\Omega)} \leq C[|\phi|^2_{1,\mathcal{T}} + \|\phi\|^2_{L^2(\mathcal{O})}]. \tag{4.2.20}$$

Let $e^n_{\mathcal{T}}(x) = e^n_K = u(x_K, t_n) - U^n_K$ for $x \in K, K \in \mathcal{T}$; $f^n_{\mathcal{T}}(x) = f^n_\sigma = \gamma(x_\sigma, t_n) - \Gamma^n_\sigma$ for $x \in \sigma, \sigma \in \varepsilon_{ext}$.

We then have our main results whose proof is given below.

Theorem 4.2.1 *(L^2 norm stability) For the finite volume scheme (4.2.4), (4.2.8) and (4.2.9), the inequality*

$$\|U^{N+1}_{\mathcal{T}}\|^2 + k\sum_{n=0}^{N} |U^{n+1}_{\mathcal{T}}|^2_{1,\mathcal{T}} + k^2\sum_{n=0}^{N} \|d_t U^n_{\mathcal{T}}\|^2 \tag{4.2.21}$$

$$+\|\Gamma^{N+1}_{\mathcal{T}}\|^2_{L^2(\partial\Omega)} + k^2\sum_{n=0}^{N} \|d_t\Gamma^n_{\mathcal{T}}\|^2_{L^2(\partial\Omega)}$$

$$\leq C(\|U^0_{\mathcal{T}}\|^2 + \|\Gamma^0_{\mathcal{T}}\|^2_{L^2(\partial\Omega)}), \tag{4.2.22}$$

holds.

Theorem 4.2.2 *(L^2 norm error estimates) For $\|e^0_{\mathcal{T}}\| = O(h+k)$, we have*

$$\begin{aligned} &\|e^{N+1}_{\mathcal{T}}\| + (k\sum_{n=0}^{N} |e^{n+1}_{\mathcal{T}}|^2_{1,\mathcal{T}})^{\frac{1}{2}} + [k\sum_{n=0}^{N} \|e^{n+1}_{\mathcal{T}}\|^2_{L^2(\partial\Omega)}]^{\frac{1}{2}} + k(\sum_{n=0}^{N} \|d_t e^n_{\mathcal{T}}\|^2)^{\frac{1}{2}} \\ &+\|f^{N+1}_{\mathcal{T}}\|^2_{L^2(\partial\Omega)} + k\sum_{n=0}^{N} \|d_t f^n_{\mathcal{T}}\|^2_{L^2(\partial\Omega)} \\ = \ & O(h+k), \end{aligned} \tag{4.2.23}$$

where $N = 0, 1, \cdots, N_k$.

Remark 4.2.1 *It is easy to choose an initial approximation that satisfies the condition $\|e^0_{\mathcal{T}}\| = O(h+k)$ in Theorem 4.2.2.*

A natural choice is
$U^0_K = \dfrac{1}{m(K)}\displaystyle\int_K u_0(x)dx$, $U^0_\sigma = \dfrac{1}{m(\sigma)}\displaystyle\int_\sigma u_0(x)dS(x)$.

Remark 4.2.2 *Theorem 4.2.1 and Theorem 4.2.2 show that scheme (4.2.4), (4.2.8) has a unique solution and first order convergence in both temporal norm and spatial L^2 norm to the original problem (3.5.1).*

4.3 Error Estimates

To derive the error estimates we define terms related to the error equations as follows.

Set

$$\begin{aligned} G^n_{K,\sigma} &= -\tau_\sigma D(e^n_L - e^n_K), \quad \forall K \in \mathcal{T}, \sigma = K|L \in \varepsilon_K, \\ m(\sigma)R^n_{K,\sigma} &= \tau_\sigma D[u(x_L, t_n) - u(x_K, t_n)] \\ &\quad - \int_\sigma D\nabla u(x, t_n)\cdot \eta_{K,\sigma} dS(x), \sigma = K|L \in \varepsilon_{int}, \\ m(\sigma)\rho^n_\sigma &= \int_\sigma [u(x, t_n) - u(x_\sigma, t_n)]dS(x), \\ m(\sigma)r^n_\sigma &= \int_\sigma [\gamma(x, t_n) - \gamma(x_\sigma, t_n)]dS(x), \\ S^{n+1}_K &= \frac{1}{m(K)}\int_K [u^{n+1}_t(x) - d_t u^n(x_K)]dx, \\ \bar{S}^{n+1}_\sigma &= \frac{1}{m(\sigma)}\int_\sigma [\gamma^{n+1}_t(x) - d_t\gamma^n(x_\sigma)]dS(x). \end{aligned} \tag{4.3.1}$$

In a similar way to [16], if $u \in L^\infty(0,T;H^2(\Omega))$, $u_t(\cdot,t), \gamma_t(\cdot,t)$ are piecewise C^1 functions, we have estimates of order $O(h+k)$ for the terms of (4.3.1). We refer to Lemma 2 and Lemma 3 in [16] for proof of similar estimates.

Next, we subtract (4.2.4) from (4.2.1), and either (4.2.8) or (4.2.15) from (4.2.2) after multiplication by $m(\sigma)$. We obtain:

$$\begin{aligned} & m(K)d_t e_K^n + \sum_{\sigma\in\varepsilon_K} G_{K,\sigma}^{n+1} \\ = & -\sum_{\sigma\in\varepsilon_K\bigcap\mathcal{T}_{int}} \{m(\sigma)R_{K,\sigma}^{n+1}\} - \sum_{\sigma\in\varepsilon_K} m(K)S_K^{n+1} \qquad (4.3.2) \\ & -\sum_{\sigma\in\varepsilon_K\bigcap\mathcal{T}_{ext}} \{\int_\sigma (k_{-1}\gamma^{n+1} - k_1 u^{n+1}(c_0-\gamma^{n+1}))dS(x) \\ & -m(\sigma)(k_{-1}\Gamma_\sigma^{n+1} - k_1 U_\sigma^{n+1}(c_\sigma - \Gamma_\sigma^{n+1}))\}, \qquad (4.3.3) \end{aligned}$$

for $K \in \mathcal{T}$.

While for $\sigma \in \varepsilon_K \cap \varepsilon_{ext}$, we have (by using explicitly (4.2.15) for convenience):

$$\begin{aligned} & m(\sigma)d_t f_\sigma^n \\ = & -m(\sigma)\bar{S}_\sigma^{n+1} + l_1(k)kd_t\Gamma_\sigma^n + l_2(k)\Gamma_\sigma^n(k_{-1}+k_1U_K^{n+1}) \\ & -\int_\sigma (k_{-1}\gamma^{n+1} - k_1u^{n+1}(c_0-\gamma^{n+1}))dS(x) \\ & +m(\sigma)(k_{-1}\Gamma_\sigma^n - k_1U_K^{n+1}(c_\sigma - \Gamma_\sigma^n)). \qquad (4.3.4) \end{aligned}$$

We now give:

Proof of Theorem 4.2.1.

Multiplying (6.5) by U_K^{n+1} and summing for all $\sigma \in \varepsilon_K$, multiplying (4.2.8)(or (4.2.15)) by $m(\sigma)\cdot\Gamma_\sigma^{n+1}$ for all $\sigma \in \varepsilon_K \cap \varepsilon_{ext}$, and summing for all $K \in \mathcal{T}$, yields

$$\begin{aligned}
\sum_{i=1}^{3} A_i^n =: & \sum_{K\in\mathcal{T}} m(K)(d_t U_K^n) U_K^{n+1} \\
& + \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K} F_{K,\sigma}^{n+1} U_K^{n+1} \\
& + \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} m(\sigma)(d_t\Gamma_\sigma^n)\Gamma_\sigma^{n+1}(1-kl_1(k)) \\
= & \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} m(\sigma)[k_{-1}\Gamma_\sigma - k_1 U_\sigma^{n+1}(c_\sigma - \Gamma_\sigma^{n+1})]U_\sigma^{n+1} \\
& + \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} m(\sigma)[-(k_{-1} + k_1 U_\sigma^{n+1})]\Gamma_\sigma^{n+1}\Gamma_\sigma^n(1-l_2(k)) \\
& + k_1 c_\sigma U_\sigma^{n+1}\Gamma_\sigma^{n+1} \\
= & \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} k_{-1}\Gamma_\sigma^{n+1} U_\sigma^{n+1} m(\sigma) \\
& - \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} k_1 (U_\sigma^{n+1})^2 (c_\sigma - \Gamma_\sigma^{n+1}) m(\sigma) \\
& + \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} m(\sigma)[-(k_{-1} + k_1 U_\sigma^{n+1})]\Gamma_\sigma^{n+1}\Gamma_\sigma^n(1-l_2(k)) \\
& + \sum_{K\in\mathcal{T}} \sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} k_1 c_\sigma U_\sigma^{n+1}\Gamma_\sigma^{n+1} \\
=: & \sum_{i=1}^{4} B_i^n,
\end{aligned}$$

We estimate the terms in the above equation term by term. From (4.2.17)-(4.2.19), one deduces

$$A_1^n = \frac{1}{2k}\|U_\mathcal{T}^{n+1}\|^2 - \frac{1}{2k}\|U_\mathcal{T}^n\|^2 + \frac{k}{2}\|d_t U_\mathcal{T}^n\|^2, \tag{4.3.5}$$

$$A_2^n = \sum_{\sigma\in\varepsilon_{int}} D\tau_\sigma (D_\sigma U^{n+1})^2 = D|U_\mathcal{T}^{n+1}|_{1,\mathcal{T}}^2, \tag{4.3.6}$$

Recalling (4.2.14), we obtain

$$A_3^n = (\frac{1}{2k}\|\Gamma_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 - \frac{1}{2k}\|\Gamma_\mathcal{T}^n\|_{L^2(\partial\Omega)}^2 + \frac{k}{2}\|d_t\Gamma_\mathcal{T}^n\|_{L^2(\partial\Omega)}^2)(1+kl_1(k)), \tag{4.3.7}$$

Noticing that $c_\sigma \geq \Gamma_\sigma^{n+1}$ from Lemma 4.2.1, we get

$$B_2 \leq 0, \tag{4.3.8}$$

$$B_1 + B_3 + B_4 \leq C\epsilon\|U_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 + (C + \frac{C}{\epsilon})\|\Gamma_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 + C\|\Gamma_\mathcal{T}^n\|_{L^2(\partial\Omega)}^2, \tag{4.3.9}$$

By the discrete inequality (4.2.20) for $\|U_{\mathcal{T}}^{n+1}\|_{L^2(\partial\Omega)}$

$$C\epsilon\|U_{\mathcal{T}}^{n+1}\|^2_{L^2(\partial\Omega)} \leq C\epsilon[|U_{\mathcal{T}}^{n+1}|^2_{1,\mathcal{T}} + \|U_{\mathcal{T}}^{n+1}\|^2]$$

Combining (4.3.5)-(4.3.9), yields

$$\begin{aligned}
&\tfrac{1}{2k}\|U_{\mathcal{T}}^{n+1}\|^2 - \tfrac{1}{2k}\|U_{\mathcal{T}}^{n}\|^2 + \tfrac{k}{2}\|d_t U_{\mathcal{T}}^{n}\|^2 \\
&+(1-kl_1(k))(\tfrac{1}{2k}\|\Gamma_{\mathcal{T}}^{n+1}\|^2_{L^2(\partial\Omega)} - \tfrac{1}{2k}\|\Gamma_{\mathcal{T}}^{n}\|^2_{L^2(\partial\Omega)} + \tfrac{k}{2}\|d_t\Gamma_{\mathcal{T}}^{n}\|^2_{L^2(\partial\Omega)}) \\
&+D|U_{\mathcal{T}}^{n+1}|^2_{1,\mathcal{T}} \\
\leq\ & C\epsilon|U_{\mathcal{T}}^{n+1}|^2_{1,\mathcal{T}} + C\epsilon\|U_{\mathcal{T}}^{n+1}\|^2 + (C+\tfrac{C}{\epsilon})\|\Gamma_{\mathcal{T}}^{n+1}\|^2_{L^2(\partial\Omega)} + C\|\Gamma_{\mathcal{T}}^{n}\|^2_{L^2(\partial\Omega)}
\end{aligned}$$

Collecting terms and multiplying this inequality by $2k$ and summing for $n = 0, 1, 2, \cdots, N$ leads to

$$\begin{aligned}
&\|U_{\mathcal{T}}^{N+1}\|^2 + 2(D-C\epsilon)k\sum_{n=0}^{N}|U_{\mathcal{T}}^{n+1}|^2_{1,\mathcal{T}} + k^2\sum_{n=0}^{N}\|d_t U_{\mathcal{T}}^{n}\|^2 \\
&+\|\Gamma_{\mathcal{T}}^{N+1}\|^2_{L^2(\partial\Omega)} + k^2\sum_{n=0}^{N}\|d_t\Gamma_{\mathcal{T}}^{n}\|^2_{L^2(\partial\Omega)} \\
\leq\ & C(\|U_{\mathcal{T}}^{0}\|^2 + \|\Gamma_{\mathcal{T}}^{0}\|^2_{L^2(\partial\Omega)}) + C\epsilon k\sum_{n=0}^{N}\|U_{\mathcal{T}}^{n+1}\|^2 \\
&+(Ck+\frac{Ck}{\epsilon})\sum_{n=0}^{N}\|\Gamma_{\mathcal{T}}^{n+1}\|^2_{L^2(\partial\Omega)}.
\end{aligned}$$

Applying Gronwall's inequality as in [26, pages 13-14], one gets

$$\begin{aligned}
&\|U_{\mathcal{T}}^{N+1}\|^2 + k\sum_{n=0}^{N}|U_{\mathcal{T}}^{n+1}|^2_{1,\mathcal{T}} + k^2\sum_{n=0}^{N}\|d_t U_{\mathcal{T}}^{n}\|^2 \\
&+\|\Gamma_{\mathcal{T}}^{N+1}\|^2_{L^2(\partial\Omega)} + k^2\sum_{n=0}^{N}\|d_t\Gamma_{\mathcal{T}}^{n}\|^2_{L^2(\partial\Omega)} \\
\leq\ & C(\|U_{\mathcal{T}}^{0}\|^2 + \|\Gamma_{\mathcal{T}}^{0}\|^2_{L^2(\partial\Omega)}).
\end{aligned}$$

Proof of Theorem 4.2.2.

We first rewrite the last term in (4.3.2) as follows:

$$\int_\sigma (k_{-1}\gamma^{n+1} - k_1 u^{n+1}(c_0 - \gamma^{n+1}))dS(x)$$
$$-m(\sigma)(k_{-1}\Gamma_\sigma^{n+1} - k_1 U_\sigma^{n+1}(c_\sigma^{n+1} - \Gamma_\sigma^{n+1}))$$
$$= k_{-1}[(\gamma(y_\sigma, t_{n+1}) - \Gamma_\sigma^{n+1})m(\sigma) + \int_\sigma [\gamma(x, t_{n+1}) - \gamma(x_\sigma, t_{n+1})]dS(x)]$$
$$+k_1 c_\sigma^{n+1}[(U_\sigma^{n+1} - u(y_\sigma, t_{n+1})]m(\sigma) - (\int_\sigma c_0[u(x, t_n) - u(x_\sigma, t_n))]$$
$$+k_1(\int_\sigma u^{n+1}[\gamma(x, t_{n+1}) - \gamma(x_\sigma, t_{n+1}) + (\gamma(x_\sigma, t_{n+1}) - \Gamma_\sigma^{n+1})]dS(x))$$
$$+k_1\Gamma_\sigma^{n+1}[\int_\sigma [u(x, t_{n+1}) - u(x_\sigma, t_{n+1})]dS(x) + (u(x_\sigma, t_{n+1}) - U_\sigma^{n+1})m(\sigma)]$$
$$= k_{-1} f_\sigma^{n+1} m(\sigma) + k_1 e_\sigma^{n+1}(\Gamma_\sigma^{n+1} - c_\sigma)m(\sigma) + k_1 f_\sigma^{n+1} u_\sigma^{n+1} m(\sigma) + E_1$$

Here

$$E_1$$
$$= \int_\sigma [\gamma(x, t_{n+1}) - \gamma(x_\sigma, t_{n+1})]dS(x) - \int_\sigma c_0[u(x, t_n) - u(x_\sigma, t_n)]dS(x)$$
$$+k_1 \int_\sigma u^{n+1}[\gamma(x, t_{n+1}) - \gamma(x_\sigma, t_{n+1})]dS(x)$$
$$+k_1\Gamma_\sigma^{n+1} \int_\sigma [u(x, t_{n+1}) - u(x_\sigma, t_{n+1})]dS(x)$$

Recalling the error estimates of (4.3.1), we have

$$E_1 = m(\sigma)O(h + k). \tag{4.3.10}$$

Next, we rewrite the last two terms in (4.3.4) as:

$$-\int_\sigma (k_{-1}\gamma^{n+1} - k_1 u^{n+1}(c_0 - \gamma^{n+1}))dS(x)$$
$$+m(\sigma)(k_{-1}\Gamma_\sigma^n - k_1 U_\sigma^{n+1}(c_\sigma^{n+1} - \Gamma_\sigma^n))$$

$$= -\int_\sigma (k_{-1} + k_1 u^{n+1})([\gamma(x, t_{n+1}) - \gamma(x_\sigma, t_{n+1})] + [\gamma(x_\sigma, t_{n+1}) - \gamma(x_\sigma, t_n)]$$

$$+[\gamma(y_\sigma, t_n) - \Gamma_\sigma^n])dS(x) - \int_\sigma k_1\Gamma_\sigma^n([u(x, t_{n+1}) - u(x_\sigma, t_{n+1})]$$

$$+[u(x_\sigma, t_{n+1}) - U_\sigma^{n+1}])dS(x) + \int_\sigma k_1 c_0([u(x, t_{n+1}) - u(x_\sigma, t_{n+1})]$$

$$+[u(x_\sigma, t_{n+1}) - U_\sigma^{n+1}])dS(x)$$

$$= -\int_\sigma (k_{-1} + k_1 u^{n+1}) f_\sigma^n dS(x) - \int_\sigma k_1\Gamma_\sigma^n e_\sigma^{n+1} dS(x) + \int_\sigma k_1 c_0 e_\sigma^{n+1} dS(x) + E_2$$

Rearranging the terms as was done earlier for E_1, we set

$$\begin{aligned}
&E_2 \\
=& -\int_\sigma (k_{-1}+k_1u^{n+1})([\gamma(x,t_{n+1})-\gamma(x_\sigma,t_{n+1})] \\
&+[\gamma(x_\sigma,t_{n+1})-\gamma(x_\sigma,t_n)])dS(x) \\
&-\int_\sigma k_1\Gamma_\sigma^n[u(x,t_{n+1})-u(x_\sigma,t_{n+1})]dS(x) \\
&+\int_\sigma k_1c_0[u(x,t_{n+1})-u(x_\sigma,t_{n+1})]dS(x)
\end{aligned}$$

Considering the properties in (4.3.1) again, we have

$$E_2 = m(\sigma)O(h+k). \tag{4.3.11}$$

Multiplying equation(4.3.2) by e_K^{n+1}, equation (4.3.4) by f_σ^{n+1}, and summing over all $K\in\mathcal{T}$, and $\sigma\in\varepsilon_K\cap\varepsilon_{ext}$ gives

$$\begin{aligned}
\sum_{i=1}^{4}C_i^n =:& \sum_{K\in\mathcal{T}} m(K)(d_te_K^n)e_K^{n+1} \\
&+\sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K} G_{K,\sigma}^{n+1}e_K^{n+1} \\
&+\sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} k_1m(\sigma)(c_\sigma-\Gamma_\sigma^{n+1})(e_\sigma^{n+1})^2 \\
&+\sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} m(\sigma)(d_tf_\sigma^n)f_\sigma^{n+1} \\
=& \sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} \{k_{-1}f_\sigma^{n+1}m(\sigma)+k_1f_\sigma^{n+1}u_\sigma^{n+1}m(\sigma)+E_1\}e_\sigma^{n+1} \\
&+\sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} \{-\int_\sigma (k_{-1}+k_1u^{n+1})f_\sigma^n dS(x)-\int_\sigma k_1\Gamma_\sigma^n e_\sigma^{n+1}dS(x) \\
&+\int_\sigma k_1c_0e_\sigma^{n+1}dS(x)+E_2\}f_\sigma^{n+1}-\sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K\cap\varepsilon_{int}} m(K)R_{K,\sigma}^{n+1}e_K^{n+1} \\
&-\sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} m(\sigma)\bar{S}_\sigma^{n+1}f_\sigma^{n+1}+\sum_{K\in\mathcal{T}} m(K)S_K^{n+1}e_K^{n+1} \\
&+\sum_{K\in\mathcal{T}}\sum_{\sigma\in\varepsilon_K\cap\varepsilon_{ext}} (l_1(k)kd_t\Gamma_\sigma^n+l_2(k)\Gamma_\sigma^n(k_{-1}+k_1U_\sigma^{n+1}))m(\sigma)f_\sigma^{n+1} \\
=:& \sum_{i=1}^{6}D_i^n
\end{aligned}$$

Now we estimate the above inequality term by term. From (4.2.17)-(4.2.19), we deduce

$$C_1^n = \frac{1}{2k}\|e_\mathcal{T}^{n+1}\|^2-\frac{1}{2k}\|e_\mathcal{T}^n\|^2+\frac{k}{2}\|d_te_\mathcal{T}^n\|^2, \tag{4.3.12}$$

$$C_2^n = \sum_{\sigma\in\varepsilon} D\tau_\sigma (D_\sigma e^{n+1})^2 = D|e_\mathcal{T}^{n+1}|_{1,\mathcal{T}}^2, \tag{4.3.13}$$

$$C_3^n \geq 0, \tag{4.3.14}$$

$$C_4^n = \frac{1}{2k}\|f_\mathcal{T}^{n+1}\|^2 - \frac{1}{2k}\|f_\mathcal{T}^n\|^2 + \frac{k}{2}\|d_t f_\mathcal{T}^n\|^2, \tag{4.3.15}$$

Recalling that $R_{K,\sigma}^{n+1} = -R_{L,\sigma}^{n+1}$ for $K \in \varepsilon_{int}, K \cap L = \sigma$, from (4.3.1), (4.3.10), (4.3.11) and Young's inequality we obtain:

$$D_1^n = \frac{C}{\epsilon}(h^2+k^2) + \frac{C}{\epsilon}\|f_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 + \epsilon\|e_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2, \tag{4.3.16}$$

with C a constant independent of h or k.

To justify this, in R^2, for example, we assume that the number of control volumes is of order $\frac{1}{h^2}$, the area of each control volume is of order h^2, while the number of edges on the boundary is of order $\frac{1}{h}$.

Thus the term of $C(h^2+k^2)$ above is obtained through the product of Total Number of Boundary Edges $\times$ Square of Local Error $\times$ Measure of Edge of Control Volume $= C\frac{1}{h} \times C(h^2+k^2) \times Ch = C(h^2+k^2)$.

In the same way:

$$D_2^n = C(1+\frac{1}{\epsilon})(h^2+k^2) + \frac{C}{\epsilon}\|f_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 + \epsilon\|e_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 + C\|f_\mathcal{T}^n\|_{L^2(\partial\Omega)}^2, \tag{4.3.17}$$

$$D_3^n = \frac{C}{\delta}(h^2+k^2) + \delta|e_\mathcal{T}^{n+1}|_{1,\mathcal{T}}^2, \tag{4.3.18}$$

Similarly,

$$D_4^n + D_5^n + D_6^n = \frac{C}{\delta}(h^2+k^2) + C\|e_\mathcal{T}^{n+1}\|^2 + \frac{C}{\epsilon}\|f_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2, \tag{4.3.19}$$

Thus,

$$\begin{aligned}\sum_{i=1}^4 C_i^n \quad &\leq \quad C(1+\frac{1}{\delta}+\frac{1}{\epsilon})(h^2+k^2) + \delta|e_\mathcal{T}^{n+1}|_{1,\mathcal{T}}^2 + \epsilon\|e_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 \\ &+C\|e_\mathcal{T}^{n+1}\|^2 + \frac{C}{\epsilon}\|f_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 + C\|f_\mathcal{T}^n\|_{L^2(\partial\Omega)}^2. \end{aligned} \tag{4.3.20}$$

By the discrete norm inequality (4.2.20):

$$\epsilon\|e_\mathcal{T}^{n+1}\|_{L^2(\partial\Omega)}^2 \leq C\epsilon(|e_\mathcal{T}^{n+1}|_{1,\mathcal{T}}^2 + \|e_\mathcal{T}^{n+1}\|^2),$$

Multiplying (4.3.20) by $2k$ and summing for $n = 0, 1, 2, \cdots, N$ leads to

$$
\begin{aligned}
& \|e_{\mathcal{T}}^{N+1}\|^2 + 2(D-\delta-C\epsilon)k\sum_{n=0}^{N}|e_{\mathcal{T}}^{n+1}|_{1,\mathcal{T}}^2 + k^2\sum_{n=0}^{N}\|d_t e_{\mathcal{T}}^n\|^2 + \|f_{\mathcal{T}}^{N+1}\|^2 \\
& + k^2\sum_{n=0}^{N}\|d_t f_{\mathcal{T}}^n\|_{L^2(\partial\Omega)}^2 \\
\leq \quad & C(\|e_{\mathcal{T}}^0\|^2 + \|f_{\mathcal{T}}^0\|_{L^2(\partial\Omega)}^2) + C(1+\frac{1}{\delta}+\frac{1}{\epsilon})(h^2+k^2) + Ck\sum_{n=0}^{N}\|e_{\mathcal{T}}^{n+1}\|^2 \\
& + \epsilon k\sum_{n=0}^{N}\|e_{\mathcal{T}}^{n+1}\|_{L^2(\partial\Omega)}^2 + Ck\sum_{n=0}^{N}\|f_{\mathcal{T}}^{n+1}\|_{L^2(\partial\Omega)}^2. \qquad (4.3.21)
\end{aligned}
$$

Again applying Gronwall's inequality as in [26, pages 13-14] to (4.3.21), with $\|e_{\mathcal{T}}^0\| = O(h+k)$, we observe that the left hand of the above relation can be bounded by $C(h^2+k^2)$, $N = 0, 1, \cdots, N_k$. Another use of Lemma 4.2.2 shows that the conclusion of Theorem 4.2.2 is valid, i.e.:

$$
\begin{aligned}
& \|e_{\mathcal{T}}^{N+1}\|^2 + 2(D-\delta-C\epsilon)k\sum_{n=0}^{N}|e_{\mathcal{T}}^{n+1}|_{1,\mathcal{T}}^2 + k^2\sum_{n=0}^{N}\|d_t e_{\mathcal{T}}^n\|^2 \\
& + \|f_{\mathcal{T}}^{N+1}\|^2 + k^2\sum_{n=0}^{N}\|d_t f_{\mathcal{T}}^n\|^2 \\
\leq \; & C(h^2+k^2).
\end{aligned}
$$

4.4 Numerical Simulation

We conclude by illustrating the above results by means of numerical simulations run on a PC.

We first simulated equations (3.5.1) with Ω given by the square domain: $\Omega = [0, 10] \times [0, 10]$. The coefficients were chosen to be:

$D = 1; k_1 = 5; k_{-1} = 0.5; a_0(x, y) \equiv 1;$

where c_0 was set to be: $c_0 = 1$ for $(x, y) \in [4, 6] \times \{0\}$, $c_0(x, y) = 0$ otherwise.

We implemented the numerical procedures described in Section 6 employing an unstructured grid generated using the software package TRIANGLE. At each time step the nonlinear equations were resolved by a simple iteration scheme, and the linear equations thus obtained were solved by a direct method. A typical result is shown in Figure 2 at the instant t=10 units. We observe that in this situation (and in other cases) it is possible to obtain an estimate of the actual accuracy of the simulation by comparing the simulated long-time result with the calculable steady-state value given by (3.7.1). The error was found to be of the order of 10^{-4}.

Next the situation for two antigens was considered, corresponding to equations (3.8.1) and again with $\Omega = [0, 10] \times [0, 10]$. In this case, for the first antigen the parameters were chosen to be :$D_1 = 1; k_{1,1} = 5; k_{-1,1} = 0.5; a_1(x, y) \equiv 1$; while for the second: $D_2 = 0.1; k_{1,2} = 5; k_{-1,2} = 0.5; a_2(x, y) \equiv 1$;

Finally c_0 was chosen to be $c_0(x, y) = 1$ for $(x, y) \in [4, 6] \times \{0\}; c_0(x, y) = 0$ otherwise. The simulation results are shown in Figure 3 and Figure 4 respectively at $t = 10$ units.

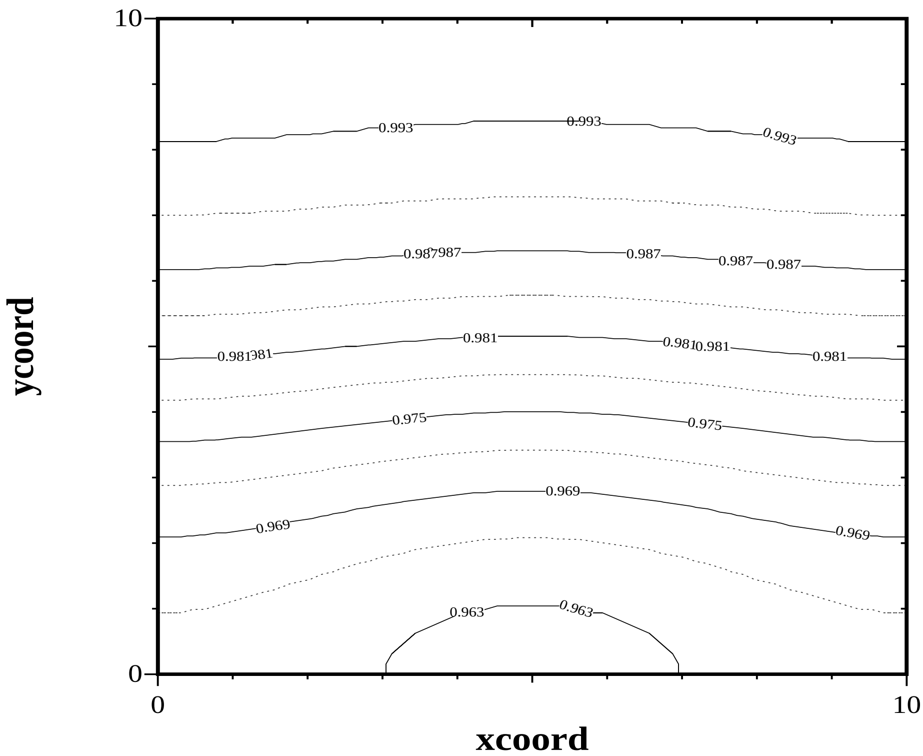

Figure 4.1: One Antigen concentration as $D = 1; k_1 = 5; k_{-1} = 0.5; a_0(x, y) \equiv 1; T = 10$.

In all these cases, the CPU time was measured in seconds.

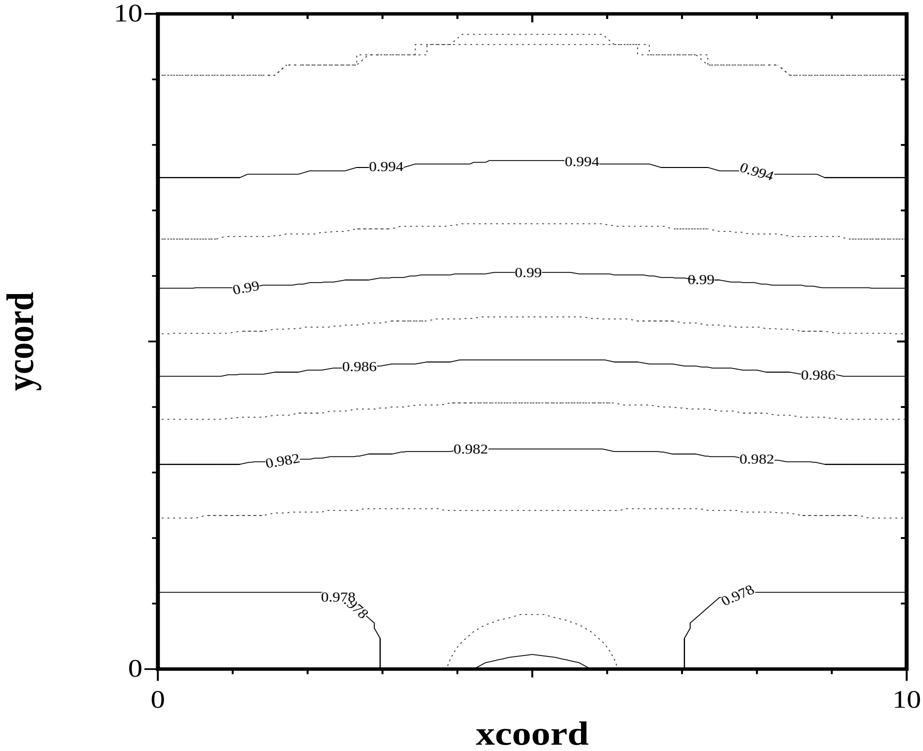

Figure 4.2: Antigen 1 concentration as $D_1 = 1; k_{1,1} = 5; k_{-1,1} = 0.5; a_1(x, y) \equiv 1; T = 10$.

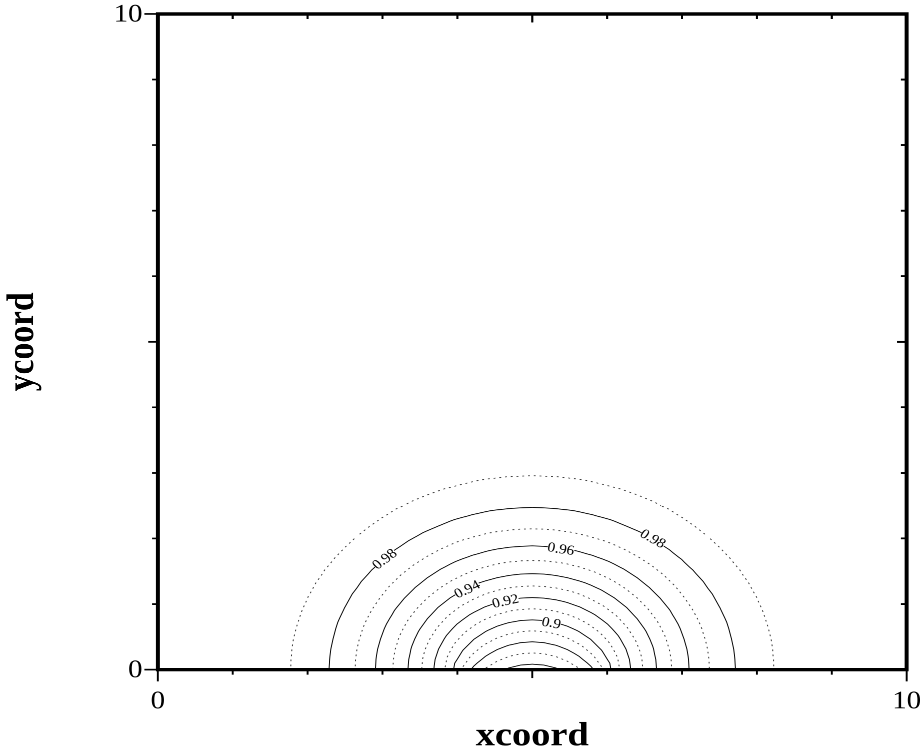

Figure 4.3: Antigen 2 concentration as $D_2 = 0.1; k_{1,2} = 5; k_{-1,2} = 0.5; a_2(x, y) \equiv 1; T = 10$.

Chapter 5

Periodic Solutions to Coupled Systems

5.1 Introduction

Let once again $Q_T = \Omega \times (0,T)$, and set $Q'_T = \partial\Omega \times (0,T)$ with Ω a smooth bounded domain in R^n. We now consider a biological problem that is mathematically closely related in formulation to what has been done in the earlier chapters. Specifically, we consider the system:

$$\begin{cases} u_t - \nabla(D\nabla u + \vec{b}u) = (A - Bu)u, & in\ Q_T, \quad (5.1.1.1) \\ D\dfrac{\partial u}{\partial n} + \vec{b} \cdot \vec{n}u = k_{-1}\gamma - k_1 u(c_0 - \gamma), & on\ Q'_T, \quad (5.1.1.2) \\ \dfrac{d\gamma}{dt} = -k_{-1}\gamma + k_1 u(c_0 - \gamma) - h\gamma, & on\ Q'_T, \quad (5.1.1.3) \end{cases} \tag{5.1.1}$$

The differences between this system and earlier work involve the function $\vec{b}$, the right hand side of equation (5.1.1.1) and the last term on the right hand side of equation (5.1.1.3). We maintain the earlier assumption on $D, c_0, k_{-1}, k_1, \Omega$ and ask that $\vec{b}, A, B, h$ denote smooth functions on $\bar{Q}_T$ with A, B, h nonnegative.

As mentioned earlier, system (5.1.1) can be viewed as a model for various biological problems. For example: that of a species (of density u) in a fluid which can be stored in a thin layer from which it is harvested. The stored density is denoted by γ. In this context, $c_0(x,t)$ denotes the carrying capacity of the layer and $h(x,t)$, the harvesting intensity. Observe that the right hand side of (5.1.1.1) is the classical Volterra model. The right hand side of (5.1.1.2) represent the rate at which the stored density is returned to the fluid, together with the rate at which the density is stored from the fluid. An identical comment applies to the right hand side of (5.1.1.3). Finally, we point out that $\vec{b}$ represents motion in the fluid, due either to natural currents or to mechanical stirring.

We assume that the harvesting intensity h is sufficiently high, i.e. that it satisfies:

$$\frac{\partial c_0}{\partial t} \leq k_{-1} c_0 + h c_0 \tag{5.1.2}$$

This will ensure that we shall find solutions u, γ with γ not exceeding the carrying capacity c_0.

We note that once again it will follow that $\gamma(x_0, t) \equiv 0$ if $c_0(x_0, t) \equiv 0$ for all t. Thus $\gamma \geq 0$ precisely in parts of the boundary where $c_0 > 0$. As a consequence, equation (5.1.1.2) reduces to the standard natural (no flow) boundary conditions at places where $c_0 \equiv 0$. From this observation we observe that model (5.1.1) describes situations where deposition occurs only on parts of $\partial\Omega$. This is typical, for example, of the situation in lagoons, where deposition occurs only relative to the bottom layers.

In conclusion we point out that our results can be extended to cover more general situations. Furthermore, considerations of the initial value problem for (5.1.1) are similar to those given earlier (for the case $A = B = h = \vec{b} = 0$). Consequently here we focus on the periodic problem: we ask that all functions be periodic with period T, and seek nonnegative weak solutions also of period T. We start with an analysis for A, B positive and then consider what happens if $A = B \equiv 0$.

5.2 Existence

We rewrite system (5.1.1) in the form

$$\begin{cases} u_t - \nabla(D\nabla u + \vec{b}u) = (A - Bu)u, & in\ Q_T, \quad (5.2.1.1) \\ D\dfrac{\partial u}{\partial n} + \vec{b}\cdot\vec{n}u + k_1 u c_0 = (k_{-1} + k_1 u)\gamma, & on\ Q'_T, \quad (5.2.1.2) \\ \dfrac{d\gamma}{dt} + k_{-1}\gamma + h\gamma = +k_1 u(c_0 - \gamma), & on\ Q'_T, \quad (5.2.1.3) \end{cases} \tag{5.2.1}$$

subject to the periodic conditions $u(x, 0) = u(x, T)$.

For later convenience, we add a term Mu to both sides of (5.2.1.1) and then multiply the right hand side of equations (5.2.1) by a constant λ, with $0 \le \lambda \le 1$ and M large positive constant as needed below. We denote the resulting system by $(5.2.1_\lambda)$.

We begin by assuming that A, B are positive, and first state some preliminary results.

Lemma 5.2.1 *let (u, λ) solve $(5.2.1_\lambda)$.*

(a) $0 \le \gamma(t) \le c_0(x, t)$.

(b) Let M be a positive constant, f, g smooth. Then the equation

$$\begin{cases} \omega_t - \nabla(D\nabla\omega + \vec{b}\omega) + M\omega = f \ge 0, & in\ Q_T, \quad (5.2.2.1) \\ D\dfrac{\partial\omega}{\partial n} + \vec{b}\cdot\vec{n}\omega + k_1\omega c_0 = g \ge 0, & on\ Q'_T, \quad (5.2.2.2) \end{cases} \tag{5.2.2}$$

has a unique periodic solution.

(c) Let ω be a nonnegative sub-solution of

$$\begin{cases} \omega_t - \nabla(D\nabla\omega + \vec{b}u) + M\omega \le 0, & in\ \Omega\times(0, T), \quad (5.2.3.1) \\ D\dfrac{\partial\omega}{\partial n} + \vec{b}\cdot\vec{n}\omega \le g, & on\ \partial\Omega, \quad (5.2.3.2) \end{cases} \tag{5.2.3}$$

with $\omega(x, 0) = \omega(x, T)$, $g \ge 0$ smooth bounded.
If $\int_{Q_T}\omega$ is bounded then so is ω in $L^\infty(\bar{Q}_T)$ for some $\alpha > 0$.

Proof. (a) Assume that for some $x_0 \in \partial\Omega$ and all $t \in [0, T]$, we have $\gamma(x_0, t) \ge c_0(x_0, t)$. Then $\dfrac{\partial\gamma(x_0, t)}{\partial t} \le 0$, contradicting periodicity

unless $\gamma(x,t)$ is a constant. In such a case $\gamma \equiv c_0$ by nonnegativity and equation (5.2.1.3). Whence we may assume there exists t_0 such that $\gamma(x_0,t_0) < c_0(x_0,t)$. Since for any (x,t) where $\alpha = c_0$ we must have $\frac{\partial \alpha}{\partial t} \leq \frac{\partial c_0}{\partial t}$ we conclude that $\alpha(x,t) \leq c_0(x,t)$ for all (x,t) in Q'_T.
Proofs of (b) and (c) were given in Lemma 2.5.1.

Theorem 5.2.1 *Let* $\bar{f}(x,t) = \frac{1}{T}\int_0^T f(x,t)dt$. *If*

$$\inf_{\varphi \in H^1}[\int_\Omega D|\nabla\varphi|^2 + \frac{\overline{(|\vec{b}|^2)}}{4D}\varphi^2 + \nabla\varphi|\overline{\vec{b}}|\varphi - \bar{A}\varphi^2 + \int_{\partial\Omega} k_1\overline{c_0}\varphi^2] < 0$$

Then (5.1.1) has a periodic solution pair (u,γ) *of class* $C^{\alpha,\alpha/2}(\bar{Q}_T)$, $C^{\alpha,1+\alpha/2}(\bar{Q}'_T)$, *respectively, with* $u > 0$ *in* $\bar{Q}_T$ *and* $\gamma > 0$ *in* $Q'_T \cap \{(x,t)|c_0(x,t_1) \not\equiv 0, \forall 0 \leq t_1 \leq T\}$.

Remark: We observe that the simplest choice in Theorem 1 is $\varphi \equiv 1$. *The existence condition then becomes:*

$$\int_{Q_T}\{\frac{|\vec{b}|^2}{4D}\} + \int_{Q'_T} k_1 c_0 < \int_{Q_T} A$$

Proof. Choose $0 \leq \varepsilon \leq 1$, we rewrite (5.1.1) in perturbed form

$$\begin{cases} u_t - \nabla(D\nabla u + \vec{b}u) + Mu = (A + M - Bu)u^+ + \varepsilon, & in\ Q_T, \quad (5.2.4.1) \\ D\frac{\partial u}{\partial n} + (\vec{b}\cdot\vec{n} + k_1c_0)u = (k_{-1} + k_1u^+)\gamma^+, & on\ Q'_T, \quad (5.2.4.2) \\ \frac{d\gamma}{dt} + (k_{-1} + h)\gamma = k_1u^+(c_0 - \gamma^+), & on\ Q'_T, \quad (5.2.4.3) \end{cases} \tag{5.2.4}$$

with M chosen sufficiently large. Put $L_1(v) = \{f,g\}$ iff:

$$\begin{cases} v_t - \nabla(D\nabla v + \vec{b}v) + Mv = f, & in\ Q_T, \quad (5.2.5.1) \\ D\frac{\partial v}{\partial n} + (\vec{b}\cdot\vec{n} + k_1c_0)v = g, & on\ Q'_T, \quad (5.2.5.2) \\ v(x,0) = v(x,T), & (5.2.5.3) \end{cases} \tag{5.2.5}$$

Note that L^{-1} exists if f,g are smooth enough, since $M > 0$. Similarly, set

$L_2(\delta) = z$ iff:

$$\begin{cases} \dfrac{d\delta}{dt} + (k_{-1} + h)\delta = z, \quad in\ Q'_T, & (5.2.6.1) \\ \delta(x,0) = \delta(x,T). & (5.2.6.2) \end{cases} \qquad (5.2.6)$$

Finally, we define: $L\begin{pmatrix} v \\ \omega \end{pmatrix} = \begin{pmatrix} L_1(v) \\ L_2(\omega) \end{pmatrix}$.

$R\begin{pmatrix} u_1 \\ \gamma_1 \end{pmatrix} = \begin{pmatrix} (A + M - Bu_1^+)u_1^+ + \varepsilon, (k_{-1} + k_1 u_1^+)\gamma^+ \\ k_1 u_1^+(c_0 - \gamma_1^+) \end{pmatrix}$.

Our problem thus becomes to find u, γ such that $\begin{pmatrix} u \\ \gamma \end{pmatrix} = L^{-1}R\begin{pmatrix} u \\ \gamma \end{pmatrix}$,. Observe then that if $\begin{pmatrix} u \\ \gamma \end{pmatrix} = \lambda L^{-1}R\begin{pmatrix} u^+ \\ \gamma^+ \end{pmatrix}$ with $0 \leq \lambda \leq 1$, $u \in C^{\alpha,\alpha/2}$, $\gamma \in C^{\alpha,1+\alpha/2}$ for some $\alpha > 0$, then u, γ are classical solutions and $u \geq 0$, $\gamma \geq 0$ by the maximum principle. Furthermore $u > 0$ in $\overline{Q_T}$ by the maximum principle. Since once again $0 \leq \gamma \leq c_0$ integration gives, for $\lambda > 0$,

$$\int_{Q'_T} k_1 c_0 u + \int_{Q_T} Mu = \int_{Q'_T} \lambda(k_{-1} + k_1 u)\gamma + \lambda \int_{Q_T} \{[A + M - Bu]u + \varepsilon\}$$

We conclude: $\int_{Q_T} Bu^2 \leq \int_{Q_T} Au + \varepsilon|Q_T|$, whence $B > 0$ implies u is bounded in $L^2(Q_T)$, independent of $\lambda > 0$. If however $\lambda = 0$ then $M > 0$ yields $u \equiv 0$.

We conclude that u is bounded in L^2 uniformly for $0 \leq \lambda \leq 1$, whence $u \geq 0$ satisfies

$$u_t - \nabla(D\nabla u + \vec{b}u) + Mu - \lambda(A + M)u \leq \varepsilon\lambda$$

$$D\frac{\partial u}{\partial n} + (\vec{b} \cdot n)u \leq \lambda_1 k_{-1} c_0$$

We conclude from Lemma 2.2(c) that u is uniformly bounded in L^∞, and thus u, γ are also bounded in $C^{\alpha,\alpha/2}(\bar{Q_T})$, $C^{\alpha,1+\alpha/2}(\bar{Q'_T})$ respectively, for some $\alpha > 0$ [19, 21]. Next, consider the map $u = T(v)$ from $C^{\alpha,\alpha/2}(\overline{Q_T})$ to itself given as follows: for a chosen v calculate δ by: $L_2(\delta) = k_1 z^+(c_0 - \delta)$. For this δ, we find u by

$$L_1(u) = \{(A + M - Bv^+)v^+ + \varepsilon, (k_{-1} + k_1 v^+)\delta\}.$$

The earlier arguments then yield by Degree Theory that T has a fixed point for a suitable value of $\alpha > 0$, whence we conclude the existence of a fixed point of $L^{-1}R$, i.e.: of a solution pair $(u_\varepsilon, \delta_\varepsilon)$ that are uniformly bounded in $C^{\alpha,\alpha/2}, C^{\alpha,1+\alpha/2}$ independently of ε. We now select $0 < \alpha' < \alpha$ and observe that $(u_\varepsilon, \delta_\varepsilon)$ will have a subsequence (also denoted by $(u_\varepsilon, \delta_\varepsilon)$) that converges in $C^{\alpha',\alpha'/2}, C^{\alpha',1+\alpha'/2}$ to a solution pair (u, δ). We only need to show that $u \not\equiv 0$, since then $\delta \not\equiv 0$. Assume to the contrary that $u_\varepsilon \to 0$(whence $\delta_\varepsilon \to 0$). Choose a function $\varphi \in H^1(\Omega)$. We then note that $u_\varepsilon > 0$ is a classical solution and, completing the square yields,

$$0 \leq \int_\Omega D u_\varepsilon^2 |\nabla(\frac{\varphi}{u_\varepsilon})|^2 - \vec{b}\varphi u_\varepsilon \nabla(\frac{\varphi}{u_\varepsilon}) + \frac{|\vec{b}|^2}{4D}\varphi^2 \tag{5.2.7}$$

We expand the right hand side and obtain:

$$\begin{aligned} 0 \leq & \int_\Omega D|\nabla\varphi|^2 - \vec{b}\varphi\nabla\varphi + \frac{|\vec{b}|^2}{4D}\varphi^2 - \int_\Omega [D\nabla(\frac{\varphi^2}{u_\varepsilon})\nabla u_\varepsilon - (\vec{b}\nabla u_\varepsilon)[\frac{\varphi^2}{u_\varepsilon}]] \\ & = I + J \end{aligned} \tag{5.2.8}$$

Now

$$\begin{aligned} J = & \int_{\partial\Omega} [(\vec{b}\cdot\vec{n}) + k_1 c_0]\varphi^2 - \int_{\partial\Omega} \frac{k_{-1} + k_1 u_\varepsilon}{u_\varepsilon}\gamma_\varepsilon \varphi^2 + \int_\Omega \varphi^2(-\nabla\vec{b}) \\ & - \int_\Omega \frac{\varphi^2}{u_\varepsilon}[(A - Bu_\varepsilon)u_\varepsilon + \varepsilon] + \int_\Omega \frac{\varphi^2}{u_\varepsilon}(u_\varepsilon)_t \end{aligned} \tag{5.2.9}$$

We integrate over t, use periodicity to conclude:

$$0 \leq \int_0^T \int_\Omega D|\nabla\varphi|^2 + \vec{b}\varphi\nabla\varphi + \frac{|\vec{b}|^2}{4D}\varphi^2 + \int_0^T \int_{\partial\Omega} k_1 c_0 \varphi^2 - \int_0^T \int_\Omega \varphi^2[A - Bu_\varepsilon]$$

Since $u_\varepsilon \to 0$ by assumption we obtain the desired contradiction.

We now pass to consideration of the periodic problem for the case $A = B = 0$. We observe that formal integration of (5.1.1) gives: $(\int_\Omega u + \int_{\partial\Omega} \gamma)_t - \int_{\partial\Omega} h\gamma = 0$, hence we conclude that solutions will exist only for $h \equiv 0$, i.e. no harvesting. Since $A = B = 0$, the earlier a-priori estimate fails, and we proceed as follows.

We begin by considering an approximate version of system (5.1.1), specifically, let $0 < \pi < 1$, $F > 0$ be chosen constants, and set:

$$\begin{cases} v_t - \nabla(D\nabla v + \vec{b}v) + (1-\pi)v = 0 & in\ Q_T, \quad (5.2.10.1) \\ D\dfrac{\partial v}{\partial n} + \vec{b}\cdot\vec{n}v + k_1 v c_0 = \pi(k_{-1} + k_1 v)\delta + \dfrac{F}{|Q'_T|}(1-\pi), & on\ Q'_T, \quad (5.2.10.2) \\ \dfrac{d\delta}{dt} + k_{-1}\delta = \pi k_1 v(c_0 - \delta), & on\ Q'_T, \quad (5.2.10.3) \end{cases} \tag{5.2.10}$$

subject to periodic conditions.

Theorem 5.2.2 *For each* (π, A) *with* $0 < \pi < 1$ *and* $A > 0$ *system (5.2.10) has a positive solution pair* (v, δ) *with* $v \in C^{\alpha,\alpha/2}(\bar{Q}_T)$*,* $\delta \in C^{\alpha,1+\alpha/2}(\bar{Q}'_T)$ *for some* $\alpha > 0$*. Furthermore* v *satisfies an estimate independent of* π*:*

$$\int_{Q_T} v + \int_{Q'_T} (k_1 v c_0 + k_{-1}\delta) = F \tag{5.2.11}$$

and $0 \leq \delta \leq c_0$*.*

Proof. It is convenient to embed system (5.2.10) into a family of systems given by

$$\begin{cases} \omega_t - \nabla(D\nabla\omega + \vec{b}\omega) + (1-\pi)\omega = 0 & in\ Q_T, \quad (5.2.12.1) \\ D\dfrac{\partial \omega}{\partial n} + \vec{b}\cdot\vec{n}\omega + k_1 \omega c_0 = \lambda[\pi(k_{-1} + k_1)\beta + \dfrac{F}{|Q'_T|}(1-\pi)], & on\ Q'_T, \quad (5.2.12.2) \\ \dfrac{d\beta}{dt} + k_{-1}\beta = \lambda[\pi k_1 \omega(c_0 - \beta)], & on\ Q'_T, \quad (5.2.12.3) \end{cases} \tag{5.2.12}$$

with periodic boundary conditions, and some λ, $0 \leq \lambda \leq 1$. We observe that if the nonnegative pair (ω, β) solve (5.2.12) then $\beta \leq c_0$, by the earlier proof. We thus observe that (5.2.12) yields

$$D\frac{\partial \omega}{\partial n} + \vec{b}\cdot\vec{n}\omega + k_1(c_0 - \lambda\pi\beta)\omega = \lambda[\pi k_{-1}\beta + \frac{F}{|Q'_T|}(1-\pi)], \tag{5.2.13}$$

We recall that $0 \leq \lambda \leq 1$ and $0 < \pi < 1$, whence for all ω satisfies $0 \leq \omega \leq z$ where z is the solution to the linear periodic parabolic problem.

$$\begin{cases} z_t - \nabla(D\nabla z + \vec{b}z) + (1-\pi)z = 0 & in\ Q_T, \quad (d) \\ D\dfrac{\partial z}{\partial n} + \vec{b}\cdot\vec{n}z + k_1 z c_0(1-\pi) = \pi k_{-1}c_0 + \dfrac{F}{|Q'_T|}(1-\pi), & on\ Q'_T, \quad (e) \\ z(x,0) = z(x,T), & in\ \Omega \end{cases} \tag{5.2.14}$$

It follows once again that ω is uniformly bounded in $L^\infty(Q_T)$ and thus in $C^{\alpha,\alpha/2}(\overline{Q_T})$, for some $\alpha > 0$, by classical results [19, 21] . The analogous result for γ is then immediate. To conclude the existence result, we simply apply a Degree Theory argument in the usual way. Finally, we integrate (5.2.10.1) and employ (5.2.10.2), (5.2.10.3) to conclude.

$$\begin{aligned} (\int_\Omega v + \int_{\partial\Omega} \delta)_t + \int_{\partial\Omega}(k_1 v c_0 + k_{-1}\delta) + \int_\Omega (1-\pi)v \\ = \pi \int_{\partial\Omega}(k_1 v c_0 + k_{-1}\delta) + \int_{\partial\Omega} \frac{F}{T|\Omega|}(1-\pi) \end{aligned} \tag{5.2.15}$$

Whence, by periodicity and integration, we obtain the desired estimate (5.2.11) in this case.

Theorem 5.2.3 *Let $A = B = 0$. System (5.1.1) has a nonnegative periodic solution pair.*

Proof. Let (v_π, δ_π) denote the solutions found for system (5.2.12). We observe that δ_π is uniformly bounded (by c_0) and $\|v_\pi\|_{L^1(Q_T)} \leq F$, whence (v_π, δ_π) are uniformly bounded in $C^{\alpha,\alpha/2}(\overline{Q_T})$, $C^{\alpha,1+\alpha/2}(\overline{Q'_T})$ respectively.

We select $0 < \alpha' < \alpha$ and a subsequence of (v_π, δ_π) that converges in $C^{\alpha',\alpha'/2}(\overline{Q_T})$, $C^{\alpha',1+\alpha'/2}(\overline{Q'_T})$ to (v, δ) a weak solution to system (5.1.1). We conclude by observing that (u, γ) cannot be identically zero. Indeed if $u \equiv 0$, then $\gamma \equiv 0$. But this contradicts estimates (5.2.11). Whence $u \not\equiv 0$ and thus $\gamma \not\equiv 0$ by (5.1.1.3).

Chapter 6

Future Work

We first note that the degenerate diffusion case remains open since all our results are based on the classical parabolic system with constant diffusivity or at least diffusivity positive bounded above and below. More generally, the diffusivity is considered in the context of a porous medium permeated by an interconnected network of pores (voids) filled with a fluid (liquid or gas). Porous media problems are a subject of interest and have emerged as a separate field of study [20],[23]-[32]. This directly leads to new challenges in mathematical analysis for our problem.

In the numerical system we presented, we used the finite volume scheme to obtain approximate solutions. We observe that possibly we could employ instead a monotone iteration scheme, since positivity and boundness hold for the solution pair. Some more efficient numerical scheme may then be derived based on upper-lower solution (order) method. This is presently under consideration.

Many of today's biosensor applications and other "surface effects" involve organisms which respond to toxic substances at a much lower level than are apparent to human senses. Thus, such devices can be used in environmental monitoring that includes trace gas detection and in water treatment facilities. In order to do this, more mathematically complicated systems must be used in order to model other effects such as the stirring of fluid (convection terms added to the system and boundary setting) and more complicated physical interactions. We are presently beginning the study of some of these problems.

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