الجمهورية الجزائرية الديمقراطية الشعبية
People's Democratic Republic of Algeria
وزارة التعليــم العــالي والبحــث العلــمي
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جامعـــــة فرحات عباس، سطيف 1
كليـــة العلـــــــوم
قســـــم الرياضيـــــــات

Doctoral thesis

Field : Mathematics and Computer Science
Option : Mathematics

Specialty : Mathematics Applied to Biological and Medical Sciences

Theme :

MODELING AND MATHEMATICAL ANALYSIS OF SOME REACTION-DIFFUSION SYSTEMS DRIVEN FROM BIOLOGY AND MEDICINE

Presented by :

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Thesis defended on November 13th, 2021, in front of the jury composed of :

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November 2021

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بسم الله الرحمن الرحیم

If logic is the hygiene of the mathematician,
it is not logic that provides him with his food;
the daily bread on which he lives,
these are the great problems.

André Weil.

Dedication

To my dear parents,
To my sweet dear sister Oumaima Ghofrane,
To my brother Youcef Islam and his wonderful wife,
To all my family,
To my friends: Chaima, Asma, Salima, Wafa, Sabah, Naima, Nadjet, Basma,
To all my friends.

Acknowledgements

First of all, i thank God the Almighty for having given me the patience, the will and the energy to follow and carry out this humble work.

I would like to warmly thank my thesis director Pr. Salim Mesbahi for agreeing to report this thesis as well as for his constant availability during these years, his encouragement, his precious help, his advice, his commitment during the preparation of this thesis and his great scientic qualities which allowed me to lead this project. I appreciated their dedication to the students. I would like to express my thanks and appreciation for your great effort. You deserve all the words of thanks, thank you very much.

Besides my supervisor, I would like to thank the rest of my thesis committee: Pr. Abdelouahab Kadem, Pr. Noureddine Alaa, Pr. Nasserdine Kechkar, Pr. Abdellatif Boureghda, and Pr. Ahleme Bouakkaz, for reading my thesis and for taking out time to serve in my committee.

I also thank my teachers for their teaching me from primary school until now.

I would like to give a big thanks to my dear sister Omaima for her great and invaluable help. Without her this success would not have been achieved.

I also want to thank here my dear parents who stayed behind me in order to my success and my happiness, my brother Youcef, all my family and all my friends and friends, for everything they have given me and which has been invaluable.

In order not to forget anyone, my sincere thanks go to all those who helped me in the realization of this modest thesis.

Khaoula Imane Saffidine

Setif, September 17th, 2021

Doctoral thesis

in Mathematics Applied to Biological and Medical Sciences

Presented by : **Khaoula Imane SAFFIDINE**
Supervisor : **Professor Salim Mesbahi**

العنوان : النمذجة والتحليل الرياضي لبعض أنظمة تفاعل-انتشار المستمدة من علم الأحياء والطب.

ملخص : العمل الذي يشكل هذه الأطروحة هو مساهمة في النمذجة والتحليل الرياضي لأنظمة تفاعل-انتشار المستمدة من علم الأحياء والطب. نحن مهتمون بدراسة وجود حلول لبعض النماذج المكافئة والناقصة؛ باستخدام تقنيات تعتمد على التحليل الوظيفي وطريقة الحلول العلوية والسفلية. يتكون هذا العمل من ستة فصول مستقلة، مسبوقة بمقدمة عامة تسلط الضوء على فن الموضوع والمشكلات التي تم تناولها.

كلمات مفتاحية : أنظمة تفاعل-انتشار ، الأنظمة المكافئة المتدهورة ، الحلول العلوية والسفلية ، نمذجة ظواهر الانتشار.

Titre : MODÉLISATION ET ANALYSE MATHÉMATIQUE DE CERTAINS SYSTÈMES DE RÉACTION-DIFFUSION ISSUS DE LA BIOLOGIE ET DE LA MÉDECINE.

Résumé :

Le travail constituant cette thèse est une contribution à la modélisation et l'analyse mathématique de systèmes de réaction-diffusion issus de la biologie et de la médecine. Nous nous intéressons à l'étude de l'existence de solutions de certains modèles paraboliques et elliptiques ; utilisant des techniques basées sur l'analyse fonctionnelle et la méthode de sous et sur solutions. Ce travail est alors composé de six chapitres indépendants, précédés d'une introduction générale qui met en évidence l'art du sujet et les problèmes abordés.

Mots-clés : systèmes de réaction-diffusion, systèmes paraboliques dégénérés, sous et sur solutions, modélisation des phénomènes de diffusion.

Title : MODELING AND MATHEMATICAL ANALYSIS OF SOME REACTION-DIFFUSION SYSTEMS DRIVEN FROM BIOLOGY AND MEDICINE.

Abstract : The work constituting this thesis is a contribution to the modeling and mathematical analysis of reaction-diffusion systems driven from biology and medicine. We are interested in studying the existence of solutions of some parabolic and elliptical models; using techniques based on functional analysis and the method of upper and lower solutions. This work is then composed of six independent chapters, preceded by a general introduction which highlights the art of the subject and the problems addressed.

Keywords : reaction diffusion systems, degenerate parabolic systems, upper and lower solutions, modeling of diffusion phenomena.

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General Introduction

The applied mathematics is involved in research that utilizes and invents a variety of mathematical methods associated with asymptotic analysis, bifurcation theory, graph theory, numerical analysis, optimal control, ordinary and partial differential equations, probability and statistics, singular perturbations, stability theory, and stochastic processes. Much of the modern science is based on it. It is central to modern society, underpins scientific and industrial research, and is key to our economy. Mathematics is the engine of science and engineering. It also has an elegance and beauty that fascinates and inspires those who understand it.

Mathematics provides the theoretical framework for biosciences, for statistics and data analysis, for as well as computer science. New discoveries within mathematics affect not only science, but also our general understanding of the world, we live in. Problems in biological sciences, in physics, chemistry, engineering, biomechanics, fluid mechanics, geophysics, interfacial phenomena, molecular biology, neuroscience, solid mechanics, statistical mechanics, transport theory, and wave phenomena are using increasingly sophisticated mathematical techniques. For this strong reason, the bridge between the mathematical sciences and other disciplines is heavily traveled.

Biosciences are some of the most fascinating of all scientific disciplines and is an area of applied sciences we use to explore and try to explain the uncertain world in which we live. It is no surprise, then, that at the heart of a professional in this field is a fascination with, and a desire to understand, the ”how and why” of the material world around us.

Theoretical biology is an old subject, tracing back centuries. At times, theoretical developments have represented little more than mathematical exercises, making scant contact with reality. At the other extreme have been those works, such as the writings of Charles Darwin, or the models of Watson and Crick, in which theory and fact are intertwined, mutually nourishing one another in inseparable symbiosis. Indeed, one of the most exciting developments in biology within the last quarter-century has been the integration of mathematical and theoretical reasoning into all branches of biology, from the molecule to the ecosystem. It is such a unified theoretical biology, blending theory and empiricism seamlessly, that has inspired the development of this series.

The biochemical and biophysical parameters that determine the behavior of biological systems aren’t universal they differ vastly during the course of development and across organisms and yet there are qualitative features that biological systems share with each other. How do we describe these systems if not in terms of quantitative measurements of parameters and piecemeal construction of high-dimensional models for individual phenomena of interest? While advances in microscopy, genetic engineering, and single-cell sequencing provides an abundance of data, tailor-made models that "fit the data" are rarely transferable to other systems and fail to provide an explanation for the unity that we observe in the biological world. This is the challenge facing modern quantitative biology and the study of truly complex systems. This is what gives great importance to mathematical modeling (appeared in the half of twentieth century) using kind of differential equations needed for EDO/PDE/DDE or even stochastic and their qualitative study. especially reaction-diffusion equations.

The reaction-diffusion models that are partial differential equations which describe how population densities in space change over time. Since they describe the way that things change over time, it is natural to think of them as dynamical systems; were introduced in the 1930s by Ficher (1937) and Kolmogorov, Petrovsky and Piskounov (1938), for population genetics models. In 1952 Turing became interested in population dynamics and, from the reaction-diffusion equation, devised a biomathematics model of animal morphogenesis. In the 1990s, experiments in the chemistry of oscillating reactions will experimentally confirm the theoretical model. The theory of reaction-diffusion equations is based on three elephants: technology, ecology and public health.

It should be noted that diffusion and other transport processes can occur in various spaces. First of all, it is the usual physical space mostly used in chemical and physical applications. However, it can also be the spaces of different parameters which characterize biological populations. For example, intracellular concentrations p of some proteins. In this case the cell population can be characterized by the distribution $u(p,t)$ of cells as a function of the concentration p and of time t. The second property, which characterizes reaction-diffusion processes, is production. In the case of chemical reactions, it is production of chemical compounds or heat production. They are described by equations of chemical kinetics, often based on the mass action law, though other models also exist. Cell division and birth of biological individuals determine production in biological populations Their simplest description is based on the same assumption as for chemical reaction, that the rate of production is proportional to the population density. In more detailed models, time delay and various specific mechanisms are taken into account. In the case of biological cells, it can be cell cycle and various intracellular and extracellular regulatory mechanisms.

The recent development of reaction diffusion systems and properties of biosciences, nonlinear reaction and diffusion systems (RDSs) became equations governing many very important nonlinear models used to describe various processes in it which has lead to extensive study in it various aspects of nonlinear parabolic and elliptic partial differential equations.

However, as noted, the state space for a reaction-diffusion model will be a set of functions representing the possible spatial densities of a spatially distributed population, Thus, to formulate reaction-diffusion models as dynamical systems we need to define appropriate state spaces of functions and determine how the models act on them. In general we will not be able to solve reaction-diffusion models explicitly, but that is also the case with many nonlinear systems of ordinary differential equations. What we can do in many cases is determine when a model predicts persistence and when it predicts extinction, and perhaps describe some features of its dynamics, by using methods from the theory of dynamical systems.

The purpose of this thesis is to meet the current and future needs of the interaction between mathematics and various biosciences, especially the reaction-diffusion systems through the publication of significant monographs, textbooks, examples of models synthetic compendia in mathematical and computational biology. and encouraging the ways that mathematics may be applied in traditional areas such as biology, chemistry, or genetics, as well as pointing towards new and innovative areas of applications. And the importance objective is to encourage other scientific disciplines (mainly oriented to natural sciences) to engage in a dialog with mathematicians, outlining their problems to both access new methods and suggest innovative developments within mathematics it self.

The motivation of this Ph.D. thesis is to study some models using the reaction-diffusion systems applied in biology and medicine.

This thesis is part of a multidisciplinary theme, it is divided into 6 chapters, it is preceded by this general introduction which highlights the art of the subject and the problems addressed.

• In the first chapter, we give some results used in the theory of reaction-diffusion systems. We want to start with some basic functional analysis tools. Then we present the classic framework for elliptic and parabolic equations. Finally we summarize the necessary notations and analysis methods concerned of reaction-diffusion systems.

• In the second chapter, we present definitions on mathematical modeling, some concepts and examples, the link between mathematics, biology and medicine. We also devote a large part of this chapter to the mathematical modeling of diffusion phenomena by reaction-diffusion systems.

• In the third chapter, we present several models involving reaction diffusion systems in biology, medicine, ecology, biochemistry and engineering. The models were collected from published articles and specialist books. Most of them are similar to the models studied in the last three chapters of this thesis.

• The aim of fourth chapter is to prove the existence of positive maximal and minimal solutions for a class of degenerate elliptic reaction-diffusion systems, including the uniqueness of the positive solution. To answer these questions, we use a technique described by Pao based on the method of upper and lower solutions, its associated monotone interactions and various comparison principles. The work constituting this chapter is the subject of an article published in an international journal specialized in Mathematics (Nonlinear Dynamics and Systems Theory), in collaboration with S. Mesbahi.

• The objective of the fifth chapter is to study the existence and uniqueness of positive solutions for a class of quasi-linear degenerate parabolic reaction-diffusion problems defined in a bounded domain, which have many applications in various applied sciences. Its specificity lies in the introduction of degenerate diffusion. Our approach to our goal is mainly based on the upper and lower solution method. The result obtained is applied to the Lotka-Volterra model. Several partial results were obtained justifying two papers, one published in an international journal specialized in Mathematics (IEEE International

Conference on Recent Advances in Mathematics and Informatics) in collaboration with S. Mesbahi, and another paper submitted for publication in an international journal.

• In the sixth chapter, we are interested in the study of a quasilinear parabolic problem with an arbitrary growth nonlinearity in gradient and nonlinear boundary conditions. This model appears in the modeling of many diffusion phenomena in various sciences. Using techniques of functional analysis based on Schauder's fixed point theorem; we prove an existence result of weak periodic solutions. Several partial results were obtained with additional hypotheses justifying a paper accepted for publication in an international journal specialized in Mathematics (Journal of Applied Mathematics and Computational Mechanics) in collaboration with S. Mesbahi and N. Alaa.

• The thesis ends with a conclusion and some perspectives and a list of bibliographic references which adequately cover the subject studied.

CHAPTER 1

Definitions, notations and basic concepts

In this chapter, we give some results used in the theory of reaction-diffusion systems. We want to start with some basic functional analysis tools. Then we present the classic framework for elliptic and parabolic equations. Finally we summarize the necessary notations and analysis methods concerned of reaction-diffusion systems.

1.1 Basic tools

1.1.1 Integration results

In this paragraph, we mention some important results, but without proof. The reader may refer to Kavian [53] and Rudin [100]. In what follows, Ω is a bounded open set of $\mathbb{R}^N$ and we will use the Lebesgue measure, but these results remain true in a more general framework.

Lemma 1.1 (of Fatou)**.** *If (f_n) be a sequence of positive measurable functions on Ω. Then*

$$\int_\Omega \left(\lim_{n\to\infty} f_n\right) dx \leq \lim_{n\to\infty} \int_\Omega f_n dx$$

Theorem 1.1 (Lebesgue dominated convergence)**.** *Let (f_n) be a sequence of functions of $L^1(\Omega)$ converges almost everywhere to a measurable function f. It is assumed that there* *is* $g \in L^1(\Omega)$ *such as for all* $n \geq 1$, *we have* $|f_n(x)| \leq g(x)$ *almost everywhere on* Ω. *Then* $f \in L^1(\Omega)$, *and*

$$\lim_{n\to\infty}\left|\int_\Omega f_n - f\right| dx = 0, \quad \lim_{n\to\infty}\int_\Omega f_n dx = \int_\Omega f dx$$

Theorem 1.2 (Partial Reciprocal of the Dominated convergence)**.** *Let* $1 \leq p < \infty$, $f \in L^p(\Omega)$ *and* (f_n) *be a sequence of functions of* $L^p(\Omega)$ *such that* $\lim_{n\to\infty}\|f_n - f\|_p = 0$. *So there is a function* $g \in L^p(\Omega)$ *and a sub-suite* $\left(f_{n_k}\right)$ *such that*

$$|f_n| \leq g \quad and \quad f_n \to f \quad p.p.$$

Definition 1.1 (of equi-integrability)**.** We say that a sequence (f_n) of functions of $L^1(\Omega)$ is equi-integrable if: for all $\varepsilon > 0$, there exists $\delta > 0$ such that $\forall E \subset \Omega$ measurable with $\mathbf{meas}(E) < \delta$ we have

$$\int_\Omega |f_n| dx < \varepsilon$$

Theorem 1.3 (of Vitali)**.** *Let* (f_n) *be a sequence of functions of* $L^1(\Omega)$ *converging almost everywhere towards a measurable function* f. *Then* (f_n) *tends to* f *in* $L^1(\Omega)$, *if and only if, the sequence* (f_n) *is equi-integrable.*

Corollary 1.1. *If* (u_n) *is bounded in* $W^{1,p}(\Omega)$ *with* $p > 1$ *(and therefore converging in* $W^{1,p}(\Omega)$ *weak except for a subsequence) and if* (∇u_n) *converges almost everywhere, then* (u_n) *converge (at a sub-sequence near) in* $W^{1,q}(\Omega)$ *(strong)* $\forall q < p$.

Indeed, according to Vitali's theorem, it suffices to show that $(|\nabla u_n|^p)$ is equi-integrable or for E borelian

$$\int_E |\nabla u_n|^q \leq \left(\int_\Omega |\nabla u_n|^p\right)^{\frac{q}{p}} \left(\int_E 1\right)^{1-\frac{q}{p}} \leq C.\mathbf{mes}(E)^{1-\frac{q}{p}}$$

1.1.2 Basic definitions

Let X, Y be two normalized vector spaces.

Definition 1.2. The operator (A, D_A) is said to be closed, if its graph $G(A) = \{(x, Ax), x \in D_A\}$ is a closed part of $X \times Y$. In other words $G(x_n, Ax_n) \to (x, y)$ then $x \in D_A$ and $y = Ax$.

Definition 1.3. We say that an operator $A : X \to Y$ is bounded, if the image by A of all bounded of X is bounded of Y.

Definition 1.4. We say that an operator $A : X \to X'$ is semi-continuous, if for all (x, y, z) de X^3, the map $\mathbb{R} \to \mathbb{R}, \quad \lambda \mapsto \langle A(x + \lambda y), z\rangle$ is continuous.

Definition 1.5. We say that an operator $A : X \to X'$ is coercive, if

$$\lim_{\|x\| \to \infty} \frac{\langle A(x), x\rangle}{\|x\|} = +\infty$$

Definition 1.6. We say that an operator $A : X \to X'$ is monotonic if

$$\forall (x, y) \in X^2 \Rightarrow \langle A(x) - A(y), x - y\rangle \geq 0$$

Definition 1.7. We say that an operator $A : X \to X$ is maximal monotonic, if it is monotonic and if there is no monotonic operator A' such that $G(A)$ is strictly included in $G\left(A'\right)$. Another way of expressing the maximality of a monotonic operator$A$ is as follows

$$\forall (x, y) \in G(A),\ \left\langle y - y', x - x'\right\rangle \geq 0 \Rightarrow \left(x', y'\right) \in G(A)$$

Remark 1.1. *We say that A is monotonous if*

$$(Au, u) \geq 0,\ \forall u \in D(A)$$

So A is maximal monotonic, if moreover $R(I + A) = X$, *i.e.,*

$$\forall f \in X,\ \exists u \in D(A) \text{ such as } u + Au = f$$

1.1.3 Weak topology

Let E be a Banach space and let $f \in X'$. We denote by $\varphi_f : X \to \mathbb{R}$ the linear functional $\varphi_f(x) = \langle f, x\rangle$. As f runs through X' we obtain a collection $\left(\varphi_f\right)_{f \in X}$ of maps from X into $\mathbb{R}$. We now ignore the usual topology on X (associated to $\|\,\|$) and define a new topology on the set X as follows:

Definition 1.8. The weak topology $\sigma(X,X')$ on E is the coarsest topology associated to the collection $(\varphi_f)_{f\in X'}$

Note that every map φ_f is continuous for the usual topology and therefore the weak topology is weaker than the usual topology.

Proposition 1.1. *The weak topology $\sigma(X,X')$ is Hausdorff.*

So far, we have two topologies on X':

(a) The usual (strong) topology associated to the norm of X',

(b) the weak topology $\sigma(X',X'')$.

We are now going to define a third topology on X' called the weak * topology and denoted by $\sigma(X',X)$ (the $\star$ is here to remind us that this topology is defined only on dual spaces). For every $x\in X$ consider the linear functional $\varphi_x : X'\to\mathbb{R}$ defined by $f\mapsto\varphi_x(f)=\langle f,x\rangle$. As x runs through X we obtain a collection $(\varphi_x)_{x\in X}$ of maps from X' into $\mathbb{R}$.

Definition 1.9. The weak * topology, $\sigma(X',X)$, is the coarsest topology on X' associated to the collection $(\varphi_x)_{x\in X}$.

Since $X\subset X''$, it is clear that the topology $\sigma(X',X)$ is coarser than the topology $\sigma(X',X'')$; i.e., the topology $\sigma(X',X)$ has fewer open sets (resp. closed sets) than the topology $\sigma(X',X'')$, which in turn has fewer open sets (resp. closed sets) than the strong topology.

Proposition 1.2. *Let (f_n) be a sequence in X'. Then*

(i) *$f_n\overset{\star}{\rightharpoonup} f$ in $\sigma(X',X)\Leftrightarrow\langle f_n,x\rangle\to\langle f,x\rangle,\forall x\in E$.*

(ii) *If $f_n\to f$ strongly, then $f_n\to f$ in $\sigma(X',X'')$. If $f_n\to f$ in $\sigma(X',X'')$, then $f_n\overset{\star}{\rightharpoonup} f$ in $\sigma(X',X)$*

(iii) *If $f_n\overset{\star}{\rightharpoonup} f$ in $\sigma(X',X)$ then $(\|f_n\|)$ is bounded and $\|f\|\le\liminf\|f_n\|$.*

(iv) *If $f_n\overset{\star}{\rightharpoonup} f$ in $\sigma(X',X)$ and if $x_n\to x$ strongly in E, then $\langle f_n,x_n\rangle\to\langle f,x\rangle$.*

Theorem 1.4 (Weak compactness theorem of the closed unit ball of Hilbert spaces)**.** *If X is a Hilbert space, then any bounded sequence in X admits a weakly convergent subsequence.*

1.1.4 Functional spaces useful in the resolution of RDS

Let us now recall some definitions on Sobolev and Hölder spaces. We can find more specific details in Adams [2], Brezis [20], Kavian [53], Lions [65] and Pao [94].

1.1.4.1 Sobolev spaces

Let Ω is a bounded open of $\mathbb{R}^N$.

• We denote by $L^P(\Omega)$, $1 \leq p < \infty$, the space of functions (or more exactly classes of equivalence of functions, in the sense of equality almost everywhere) u measurable on Ω such that

$$\int_\Omega |u|^p \, dx < \infty$$

equipped with the norm

$$\|u\|^p_{L^P(\Omega)} = \int_\Omega |u|^p \, dx$$

• The spaces $L^p(\Omega)$ endowed with this norm are Banach spaces. In particular $L^2(\Omega)$ is a Hilbert space endowed with the scalar product

$$(u,v) = \int_\Omega u(x)v(x)dx$$

• We divide by $L^\infty(\Omega)$ the space of measurable and essentially bounded functions u on Ω, i.e.,

$$L^\infty(\Omega) = \{u \ : \Omega \longrightarrow \mathbb{R} \ \text{ measurable, } \exists c > 0, \ |u| \leq c \ \text{ a.e. on } \Omega\},$$

it is a complete vector space for the norm

$$\|u\|_{L^\infty(\Omega)} = \operatorname*{supess}_{x \in \Omega} |u(x)| = \inf\{c > 0 \ , \ |u| \leq c \ \text{ a.e. on } \ \Omega \ \}$$

• We define the spaces $L^p(0,T,X)$, $1 \leq p < \infty$, and $L^\infty(0,T,X)$ as follows:

$$L^p(0,T,X) = \left\{u : [0,T] \longrightarrow X \text{ measurable, } \int_0^T \|u\|^p_X \, dt < \infty\right\}$$

equipped with the norm

$$\|u\|^p_{L^p(0,T,X)} = \int_0^T \|u\|^p_X \, dt$$

$$L^{\infty}(0,T,X) = \{u : [0,T] \longrightarrow X \text{ measurable}, \sup_{t\in(0,T)} \text{ess} \|u\|_X < \infty\}$$

equipped with the norm

$$\|u\|_{L^{\infty}(0,T,X)} = \sup_{t\in(0,T)} \text{ess} \|u\|_X$$

Of course, we have

$$L^p(0,T,L^p(\Omega)) \equiv L^p((0,T)\times\Omega), \ 1 \le p \le \infty$$

• $C(\Omega)$ denotes the space of continuous functions with compact support in Ω, provided with the norm

$$\|u\|_{C(\Omega)} = \max_{x\in\Omega} |u(x)|$$

• $C^k(\Omega)$ (k positive integer), denote the space of functions k-times continuously differentiable on Ω, and we write

$$C^{\infty}(\Omega) = \bigcap_{k\ge 0} C^k(\Omega)$$

• $D(\Omega)$ is the space of functions C^{∞} with compact support.

• $H^1(\Omega)$ is the Sobolev space defined by

$$H^1(\Omega) = \{u \in L^2(\Omega) : \frac{\partial u}{\partial x_i} \in L^2(\Omega), \ 1 \le i \le n\}$$

equipped with the norm

$$\begin{aligned} \|u\|^2_{H^1(\Omega)} &= \int_{\Omega} |u|^2 \, dx + \int_{\Omega} \sum_{i=1}^{n} \left| \frac{\partial u}{\partial x_i} \right|^2 dx \\ &= \int_{\Omega} |u|^2 \, dx + \int_{\Omega} |\nabla u|^2 \, dx \end{aligned}$$

In general, for $m \in \mathbb{N}^*$ and $1 \le p < \infty$, the Sobolev spaces $H^m(\Omega)$ and $w^{m,p}(\Omega)$ are defined as follows

$$H^m(\Omega) = \left\{u \in L^2(\Omega) : D^{\alpha}u \in L^2(\Omega), \ \alpha \in \mathbb{N}^n, \ |\alpha| \le m\right\}$$

equipped with the norm

$$\|u\|^2_{H^m(\Omega)} = \sum_{|\alpha|\le m} \int_{\Omega} \left|D^{\alpha}u\right|^2 dx = \sum_{|\alpha|\le m} \left\|D^{\alpha}u\right\|^2_{L^2(\Omega)}$$

and

$$W^{m,p}(\Omega) = \left\{u \in L^p(\Omega) : D^{\alpha}u \in L^p(\Omega), \ |\alpha| \le m\right\}$$

equipped with the norm

$$\|u\|_{m,p}^{p} = \sum_{|\alpha|\le m} \left\|D^{\alpha}u\right\|_{L^{p}(\Omega)}^{p}$$

or

$$D^{\alpha} = \frac{\partial^{\alpha_1+\alpha_2+...+\alpha_n}}{\partial x_1^{\alpha_1}\partial x_2^{\alpha_2}...\partial x_n^{\alpha_n}},\ |\alpha| = \sum_{i=1}^{n}\alpha_i$$

is the derivative in the sense of distributions.

Of course, we have

$$w^{1,2}(\Omega) \equiv H^{1}(\Omega) \quad , \quad w^{m,2}(\Omega) \equiv H^{m}(\Omega)$$

1.1.4.2 Hölder spaces

Let $(0,T]\times\partial\Omega$. Denote by $C^{m}(\Omega)$ the set of all continuous functions whose partial derivatives up to the m-th order are continuous in Ω, and by $C^{l,m}(Q_T)$ the set of functions whose l-times derivatives in t and m-times derivatives in x are continuous in D_T. In particular, the set $C^{1,2}(Q_T)$ consists of all functions that are once continuously differentiable in t and twice continuously differentiable in x for all $(t,x)\in D_T$. Similar notations are used for $C^{m}(\bar{\Omega})$ and $C^{l,m}\left(\overline{Q}_T\right)$, where $\overline{\Omega},\overline{Q}_T$ are the respective closures of Ω and D_T. When $m=0$ we denote by $C(\Omega)$, $C\left(\overline{\Omega}\right)$, $C(Q_T)$, and $C\left(\overline{Q}_T\right)$ the set of continuous functions in Ω, $\overline{\Omega}$, D_T, and $\overline{Q}_T$, respectively. The norms in $C(\Omega)$ and $C(Q_T)$ are defined by

$$|u|_0^{\Omega} = \sup_{x\in\Omega}|u(x)|,\quad |u|_0^{Q_T} = \sup_{x\in Q_T}|u(t,x)|$$

(It is understood that all the norms are finite.). Similar norms with respect to $\overline{\Omega}$, $\overline{Q}_T$ are defined for $C(\overline{\Omega})$ and $C\left(\overline{Q}_T\right)$. When no confusion arises we omit the superscripts Ω, Q_T, etc.

A function $u\in C(\Omega)$ is said to be Hölder continuous of order $\alpha\in(0,1)$, if

$$H_{\alpha} \equiv \sup\left\{|u(x)-u(\xi)|/|x-\xi|^{\alpha};\ x,\xi\in\Omega \text{ and } x\neq\xi\right\} < \infty$$

The Hölder norm of u is defined by

$$|u|_{\alpha} \equiv |u|_0 + H_{\alpha}$$

and the set of all Hölder continuous functions in Ω with finite norm is denoted by $C^{\alpha}(\Omega)$. Let D_x^{m} be any partial derivative of order m with respect to the variables $x_1,\ldots,x_n$ and define

$$
\begin{aligned}
|u|_m &= |u|_0 + \sum |D_x u|_0 + \ldots + \sum \left|D_x^m u\right|_0 \\
|u|_{1+\alpha} &= |u|_0 + \sum |D_x u|_\alpha \\
|u|_{1+\alpha} &= |u|_0 + \sum |D_x u|_\alpha + \sum \left|D_x^m u\right|_\alpha
\end{aligned}
$$

where the sums are taken over all partial derivatives of the indicated order. The sets of all functions u for which $|u|_m < \infty, |u|_{1+\alpha} < \infty$, and $|u|_{2+\alpha} < \infty$ are denoted, respectively, by $C^m(\Omega)$, $C^{1+\alpha}(\Omega)$, and $C^{2+\alpha}(\Omega)$. It is well known that $C^m(\Omega)$, $C^{m+\alpha}(\Omega)$, $m = 0,1,2$, are all Banach spaces. Similar function spaces on $\partial\Omega$ are denoted by $C^{m+\alpha}(\partial\Omega)$ for $m = 0,1,2$. When the domain Ω is replaced by D_T we define the Hölder constant by

$$
H_\alpha \equiv \sup\left\{|u(t,x) - u(\tau,\xi)| / \left(|t-\tau| + |x-\xi|^2\right)^{\alpha/2};\ (t,x),(\tau,\xi) \in Q_T\right\}
$$

The Hölder norm of u is given by

$$
|u|_\alpha \equiv |u|_0 + H_\alpha \equiv \sup_{(t,x)\in Q_T} |u(t,x)| + H_\alpha
$$

The set of all Hölder-continuous functions in D_T with finite Hölder norm is denoted by $C^\alpha(Q_T)$. Similarly, the sets of functions in $C^\alpha(Q_T)$ with the finite norms

$$
\begin{aligned}
|u|_{1+\alpha} &= |u|_0 + \sum |D_x u|_\alpha + |u_t|_\alpha \\
|u|_{1+\alpha} &= |u|_0 + \sum |D_x u|_\alpha + \sum \left|D_x^m u\right|_\alpha + |u_t|_\alpha
\end{aligned}
$$

are denoted, respectively, by $C^{1+\alpha}(Q_T)$ and $C^{2+\alpha}(Q_T)$. The function spaces $C^{m+\alpha}(Q_T), m = 0,1,2$, are all Banach spaces.

1.1.4.3 Basic theorems about Sobolev spaces

Theorem 1.5 (of density)**.** *Let Ω be an open bounded with Lipschitzian border and $1 \le p \le +\infty$ then:*

► *if $p < +\infty$, the set $C^\infty(\bar{\Omega})$ of restrictions to Ω of functions $C_c^\infty(\mathbb{R}^N)$ is dense in $W^{1,p}(\Omega)$.*

► *it exists a continuous linear map $P : W^{1,p}(\Omega) \to W^{1,p}(\mathbb{R}^N)$ such that*

$$
\forall u \in W^{1,p}(\Omega),\ P(u) = u \quad \textit{p.p. in } \Omega
$$

Similar results are true with $W^{m,p}(\Omega)$, $m>1$, instead of $W^{1,p}(\Omega)$ but require more regularity on Ω (see [2]). We can also show that $C_c^{\infty}\left(\mathbb{R}^N\right)$ is dense in $W^{m,p}\left(\mathbb{R}^N\right)$ if $N\geq 1$, $m\in N$ and $1\leq p<+\infty$. But, this is false if we replace $\mathbb{R}^N$ by Ω, with Ω an open bounded and $m>0$. For example, if Ω is a bounded open, the space $C_c^{\infty}(\Omega)$ is not dense in $H^1(\Omega)$. Its adhesion is a strict subspace of $H^1(\Omega)$, which we denote by $H_0^1(\Omega)$.

Theorem 1.6 (of trace)**.** *Let Ω be a bounded open with a Lipschitzian border and $1\leq p<+\infty$. Then, there exists a unique map γ (continuous linear) defined from $W^{1,p}(\Omega)$ in $L^p(\partial\Omega)$ and such that*

$$\gamma u = u \;\; p.p. \text{ on } \partial\Omega \text{ if } u\in W^{1,p}(\Omega)\cap C\left(\bar{\Omega}\right)$$

The following theorems are a consequence of Kolmogorov's theorem (see [40], theorem 8.5).

Theorem 1.7 (of Rellich)**.** *Let Ω be a bounded open set of $\mathbb{R}^N$ $(N\geq 1)$ and $1\leq p<+\infty$. Any bounded part of $W_0^{1,p}(\Omega)$ is relatively compact in $L^p(\Omega)$. This amounts to saying that from any bounded sequence of $W_0^{1,p}(\Omega)$, we can extract a subsequence which converges in $L^p(\Omega)$. The previous theorem remains true with $W^{1,p}(\Omega)$ on condition of assuming the Lipschitz border.*

Theorem 1.8. *Let Ω a bounded open set of $\mathbb{R}^N$ $(N\geq 1)$, with Lipschitzian border, and $1\leq p<+\infty$. Any bounded part of $W^{1,p}(\Omega)$ is relatively compact in $L^p(\Omega)$. This amounts to saying that from any bounded sequence of $W^{1,p}(\Omega)$, we can extract a subsequence which converges in $L^p(\Omega)$.*

Proposition 1.3 (of separability)**.** *Let Ω be an open set of $\mathbb{R}^N$ $(N\geq 1)$, $m\in\mathbb{N}$ and $1\leq p<+\infty$; the space $W^{m,p}(\Omega)$ is separable space (i.e., a normed vector space which contains a dense countable part).*

Proposition 1.4 (of reflexivity)**.** *Let Ω be an open set of $\mathbb{R}^N$, $N\geq 1$, and $m\in N$. For all $p\in\,]1,+\infty[$, the space $W^{m,p}(\Omega)$ is a reflexive space.*

Theorem 1.9. *Let E be a separable Banach space and let (f_n) be a bounded sequence in E'. Then there exists a subsequence $\left(f_{n_k}\right)$ which converges for the weak topology $*$ of E'.*

This theorem is often used for $E = L^1(\Omega)$, which is well separable (but not reflexive), as $E' = L^\infty(\Omega)$, we can therefore extract from a bounded sequence in $L^\infty(\Omega)$, a subsequence which converges in $L^\infty(\Omega)$ weak $*$.

Theorem 1.10. *Let X be a reflexive Banach space and let (f_n) be a bounded sequence in X. Then there exists a subsequence $\left(f_{n_k}\right)$ which converges for the weak topology of E.*

1.2 Classic framework for elliptic and parabolic equations

Let be Ω a bounded open set of $\mathbb{R}^N$ with $N \geq 2$, we study elliptic and parabolic problems whose models are: for the linear elliptic

$$\begin{cases} -\Delta u = f & \text{in } \Omega \\ u = 0 & \text{on } \partial\Omega \end{cases}$$

and for the linear parabolic

$$\begin{cases} u_t - \Delta u = f & \text{in }]0,T[\times\Omega \\ u = 0 & \text{on }]0,T[\times\partial\Omega \\ u(0) = 0 & \text{on } \Omega \end{cases}$$

Model problems for nonlinear equations involve the p-Laplacian $\Delta_p(u) = \mathbf{div}\left(|\nabla u|^{p-2}\nabla u\right)$

$$\begin{cases} -\Delta_p u = f & \text{in } \Omega \\ u = 0 & \text{on } \partial\Omega \end{cases}$$

and

$$\begin{cases} u_t - \Delta_p u = f & \text{in }]0,T[\times\Omega \\ u = 0 & \text{on }]0,T[\times\partial\Omega \\ u(0) = u_0 & \text{on } \Omega \end{cases}$$

1.2.1 Linear elliptic and parabolic operators

Let the elliptic Dirichlet problem

$$\begin{cases} -\mathbf{div}(A\nabla u) = f & \text{in } \Omega \\ u = 0 & \text{on } \partial\Omega \end{cases}$$

where A is a matrix of size N. If we note a_{ij} the coefficients of A, the equation is written $-\partial_{x_i}\left(a_{ij}\partial_{x_j}u\right)=f$. We suppose that $a_{ij}\in L^\infty(\Omega)$ and satisfies the condition of ellipticity (or coercivity): there exists $\alpha>0$ such that

$$\forall(\xi_i)\in\mathbb{R}^N,\quad \sum_{i,j}\xi_i a_{ij}\xi_j\geq\alpha\sum_{i,j}\xi_i\xi_j$$

This problem then admits, for $f\in H^{-1}(\Omega)$, a unique variational solution, who belongs to $H_0^1(\Omega)$ and verified

$$\forall v\in H_0^1(\Omega),\quad \int_\Omega(A\nabla u)\nabla v=\langle f,v\rangle_{H^{-1},H_0^1}$$

The solution is obtained thanks to the theorem of Lax-Milgram [61].

Under the same assumptions on A (bounded and coercive matrix), the parabolic problem

$$\begin{cases} u_t-\mathbf{div}(A\nabla u)=f & \text{in }]0,T[\times\Omega\\ u=0 & \text{on }]0,T[\times\partial\Omega\\ u(0)=u_0 & \text{on } \Omega\end{cases}$$

admits, for $f\in L^2\left(0,T;H^{-1}(\Omega)\right)$ and $u_0\in L^2(\Omega)$, a unique variational solution u (see Lions-Magenes [66]) belong to $L^2\left(0,T;H_0^1(\Omega)\right)$ and verifies $u_t\in L^2\left(0,T;H^{-1}(\Omega)\right)$

$$\forall v\in L^2\left(0,T;H_0^1(\Omega)\right),\quad \int_0^T\langle u_t,v\rangle+\int_0^T\int_\Omega(A\nabla u)\nabla v=\int_0^T\langle f,v\rangle$$

and

$$u(0)=u_0\quad \text{in } L^2(\Omega)$$

which makes sense because $u\in L^2\left(0,T;H_0^1(\Omega)\right)$ and $u_t\in L^2\left(0,T;H^{-1}(\Omega)\right)$ implied $u\in C\left([0,T],L^2(\Omega)\right)$.

1.2.2 Nonlinear elliptic Leray-Lions operators

We first recall the definition of Carathéodory function.

Definition 1.10. Let N, p, $q\in\mathbb{N}^\star$ and Ω be an open set of $\mathbb{R}^N$. Let a be a mapping from $\Omega\times\mathbb{R}^p$ to $\mathbb{R}^q$. We say that a is a function of Carathéodory if $a(\cdot,s)$ is Borelian for all $s\in\mathbb{R}^p$ and $a(x,\cdot)$ is continuous for almost all $x\in\Omega$

For the elliptic problem

$$\begin{cases} -\mathbf{div}(a(x,u,\nabla u)) = f & \text{in}\Omega \\ u = 0 & \text{on } \partial\Omega \end{cases}$$

with $p > 1$ and f in $W^{-1,p'}(\Omega)$; $\left(p' = \frac{p}{p-1}\right)$, where Ω is a bounded open of $\mathbb{R}^N$ and a a Carathéodory function satisfying conditions, data below, coercivity, strict monotony and growth of the type of Leray-Lions, and defining an operator on $W_0^{1,p}(\Omega)$. The solution u, whose existence is given by [63], verified $u \in W_0^{1,p}(\Omega)$ and

$$\forall \varphi \in W_0^{1,p}(\Omega), \quad \int_\Omega a(x,u,\nabla u)\nabla\varphi = \langle f, \varphi\rangle$$

The solution is obtained by a Galerkin method, i.e., as a limit of solutions belonging to spaces of finite dimensions.

In fact $A(u) = -\mathbf{div}(a(x,u,\nabla u))$ defines a Leray-Lions operator, i.e., it satisfies the following general hypotheses:

- $u \longmapsto A(u)$ is an operator of V, Banach separable and reflexive, in V' its dual.
- $A(u)$ is a bounded operator, in the sense that it transforms the bounded ones of V into bounded ones of V'.
- $A(u)$ is continuous from any subspace of V of finite dimension in V' weak.
- A is coercive in the following sense

$$\lim_{|v|\to\infty} \frac{\langle A(v), v\rangle}{|v|} = +\infty$$

- A is monotonic, i.e., $\langle A(u) - A(v), u - v\rangle \geq 0$ for all u and $v \in V$.

These assumptions are sufficient to show that A is surjective [63], so $A(u) = f$ admits a solution for all $f \in V'$. They are verified, in particular, under the following hypotheses, with $V = W_0^{1,p}(\Omega)$ and $V' = W^{-1,p'}(\Omega)$. We assume that a satisfies the following assumptions (which make $A(u)$ a Leray-Lions operator): a is a Carathéodory function, i.e.,

- $a(x,s,\xi) : \mathbb{R}^N \times \mathbb{R} \times \mathbb{R}^N \to \mathbb{R}^N$ is measurable in $x \in \mathbb{R}^N$ for all $s \in \mathbb{R}$ and $\xi \in \mathbb{R}^N$ and continue in $\xi \in \mathbb{R}^N$ and $s \in \mathbb{R}$ for almost everything $x \in \mathbb{R}^N$. We will note $a(x,u,\nabla u) = a(x,u(x),\nabla u(x))$.

and a also verified the conditions of coercivity, strict monotony and growth: it exists p verify $1 < p \leq N$

- It exists $\alpha > 0$ such that for all s and ξ and almost all x we are

$$a(x,s,\xi)\xi \geq \alpha|\xi|^p$$

- For all s, ξ and η and almost all x we have

$$[a(x,s,\xi) - a(x,s,\eta)](\xi - \eta) > 0, \quad \text{for} \quad \xi \neq \eta$$

- It exists $b(x) \in L^{p'}(\Omega)\left(p' = \frac{p}{p-1}\right)$, and $\beta > 0$ such that for all s and ξ and almost all x we have

$$|a(x,s,\xi)| \leq \beta\left(b(x) + |s|^{p-1} + |\xi|^{p-1}\right)$$

These assumptions are classic for the study of nonlinear operators in divergent form.

1.2.3 Nonlinear parabolic operators

It is about solving the parabolic equation

$$\begin{cases} u_t - \mathbf{div}(a(x,u,\nabla u)) = f & \text{in }]0,T[\times\Omega \\ u = 0 & \text{on }]0,T[\times\partial\Omega \\ u(0) = u_0 & \text{on } \Omega \end{cases}$$

with $u_0 \in L^2(\Omega)$ and $f \in L^p\left(]0,T[;W^{-1,p'}(\Omega)\right)$ where a is a Carathéodory function satisfying the conditions of coercivity, of strict monotony and growth of the type of Leray-Lions, defining an operator on $L^p\left(]0,T[;W_0^{1,p}(\Omega)\right)$. The solution u, obtained by Lions [65] (here too thanks to a Galerkin method), verified

$$u \in L^p\left(]0,T[;W_0^{1,p}(\Omega)\right) \quad \text{and} \quad u_t \in L^{p'}\left(]0,T[;W^{-1,p'}(\Omega)\right)$$

$$\forall\varphi \in L^p\left(]0,T[;W_0^{1,p}(\Omega)\right), \int_0^T \langle u_t,\varphi\rangle + \int_0^T\int_\Omega a(t,x,u,\nabla u)\nabla\varphi = \int_0^T \langle f,\varphi\rangle$$
$$u(0) = u_0$$

Here too this last equality does have a meaning because $u \in C\left([0,T];L^2(\Omega)\right)$, which is a consequence of the regularity of u and u_t.

Let us give the hypotheses on a, which make $A(u) = -\mathbf{div}(a(t,x,u,\nabla u))$ a Leray-Lions operator:

- a is a function of Carathéodory, which means.
- $a(t,x,s,\xi):\mathbb{R}\times\mathbb{R}^N\times\mathbb{R}^N\to\mathbb{R}^N$ is measurable in $t\in\mathbb{R}$, $x\in\mathbb{R}^N$ for all $s\in\mathbb{R}$, $\xi\in\mathbb{R}^N$ and continue in $s\in\mathbb{R}$ and $\xi\in\mathbb{R}^N$, for almost all $t\in\mathbb{R}$ and $x\in\mathbb{R}^N$. We will note $a(t,x,u,\nabla u)=a(t,x,u(t,x),\nabla u(t,x))$ and a also verifies the conditions of coercivity, strict monotony and growth: it exists p verified $1<p\le N$.
- It exists $\alpha>0$ such that for all s and ξ and almost all t and x, we have

$$a(t,x,s,\xi)\xi\ge\alpha|\xi|^p$$

- For all s, ξ and η and almost all t and x, we have

$$[a(t,x,s,\xi)-a(t,x,s,\eta)](\xi-\eta)>0 \quad \text{for} \quad \xi\neq\eta$$

- It exists $b(t,x)\in L^{p'}(]0,T[\times\Omega)$, (where $p'=\frac{p}{p-1}$) and $\beta>0$ such that for all s and ξ and almost all t and x, we have

$$|a(t,x,s,\xi)|\le\beta\left(b(t,x)+|s|^{p-1}+|\xi|^{p-1}\right)$$

These assumptions are classic for the study of nonlinear operators in divergent form.

1.3 A degenerate elliptic and parabolic problems

In the last few decades, many researchers have been concerned with the study of degenerate elliptic or parabolic problems. We start with the following example

$$\begin{cases} -\mathbf{div}(a(x,u,\nabla u))=f & \text{in } \Omega \\ u=0 & \text{on} \partial\Omega \end{cases} \tag{1.1}$$

where Ω is an arbitrary domain in $\mathbb{R}^N$ $(N\ge1)$, and a is a nonnegative function that may have "essential" zeros at some points or even may be unbounded. The continuous function f satisfies $f(0)=0$ and $tf(t)$ behaves like $|t|^p$ as $|t|\to\infty$, with $2<p<2^*$, where 2^* denotes the critical Sobolev exponent. Notice that equations of this type come from the consideration of standing waves in anisotropic Schrödinger equations (see [24, 57, 109]). Equations like (1.1) are also introduced as models for several physical phenomena related to equilibrium of anisotropic media which possibly are somewhere "perfect" insulators or "perfect" conductors (see [27], p. 79). Problem (1.1) has also some interest in the framework of optimization and G-convergence (see, e.g., [38] and the references therein).

Classical results (see [10, 11]) ensure the existence and the multiplicity of positive or nodal solutions for problem (1.1), provided that the differential operator $Tu = \mathbf{div}(a(x)\nabla u)$ is uniformly elliptic. Several difficulties occur both in the degenerate case (if $\inf a = 0$) and in the singular case (if $\sup a = +\infty$). In these situations the classical methods fail to be applied directly so that the existence and the multiplicity results (which hold in the nondegenerate case) may become a delicate matter that is closely related to some phenomena due to the degenerate character of the differential equation. These problems have been intensively studied starting with the pioneering paper by Murthy and Stampacchia [84] (see also [25], as well as the monograph [110]).

A natural question that arises in concrete applications is to see what happens if these elliptic (degenerate or nondegenerate) problems are affected by a certain perturbation. It is worth pointing out here that the idea of using perturbation methods in the treatment of nonlinear boundary value problems was introduced by Struwe [111].

The problems which were studied in the fourth and fifth chapter (see [104]) based on the upper and lower solution method are good examples of this type of problems, and they have been the subject of two published scientific papers and two papers submitted for publication in renowned scientific journals specializing in mathematics and its applications. In the fourth and fifth chapter, we will find the results obtained, and we will also find the areas of their application.

1.4 Reaction-diffusion systems

In this section, we will rely mainly on the book of Mesbahi, but for a better understanding, we refer to the works of Alaa and Mesbahi et *al*. Alaa and Mesbahi et *al*. [4]-[5], [16], [50], [52], [70]-[74], [97], [102]-[104], Murray [78]-[81], Pao [91, 92, 94, 95], Volpert [116]

Reaction-diffusion systems have enjoyed a considerable amount of scientific interest. The reason for the large amount of work put into studying these equations is not only their practical relevance, but also interesting phenomena that can arise from such equations, such as multiple steady states and spatial patterns and oscillating solutions, just to mention a few. The study of these phenomena require a variety of different methods from many areas of mathematics for example bifurcation and stability theory, semigroup theory, singular perturbations, numerical analysis and many others.

From a qualitatively point of view, a reaction-diffusion system is a mathematical model describing how the concentration of one or more substances vary over time and space under the influence of two terms: Reaction term or source term, in which concentration is generated or degenerated by local interaction, diffusion term which causes the substances to spread out in space. A reaction-diffusion system (RDS) is therefore an equation heuristically like

Change in concentration = Diffusion of concentration + Source term

or algebraically reaction-diffusion systems are coupled systems of partial differential equations. The general form of these systems is

$$\frac{\partial u}{\partial t} = \mathbf{div}\ (D(t,x,u,\nabla u).\nabla u) + f(t,x,u,\nabla u)\quad,\ x\in\Omega,\ t\geq 0 \tag{1.2}$$

where $u = u(t,x) = (u_1,\dots,u_m) : \mathbb{R}^+ \times \Omega \to \mathbb{R}^m$ is a vector of variables. f is a linear or nonlinear vector function, which is called the reaction terms, it is a regular application (at least locally Lipschitzian). $D : \mathbb{R}^+ \times \Omega \times \mathbb{R}^m \times \mathbb{R}^{mN} \to \mathbb{R}^m$ is a regular function. When $D = (D_{ij})$ is a square matrix it is called the diffusion matrix, in this case $\mathbf{div}(D(t,x,u,\nabla u).\nabla u) = D\Delta u$ are the broadcast terms. D_{ij} characterize the diffusion of u_i in u_j. In this case we have what is called diffusion crossing between the densities u_i (cross diffusion).

It should be noted here that:

(i) Diffusion coefficients can represent molecular diffusions or a few random movements of individuals in a population.and they are not always positive. The positivity of these coefficients means that the flow of matter is from the more concentrated media to the less concentrated. It is possible that the organisms attract themselves towards their species and the movement is then in the direction of the concentration gradient, that is to say from the least concentrated to the most concentrated; and in this case, the diffusion coefficient is negative.

(ii) The reaction terms are the result of any interaction between the components of u; u can be a vector of chemical concentrations, and f is the effect of chemical reactions of these concentrations, or the components of u can be densities of plant or animal populations, and f represents the effect of relationships (of competition or symbiosis) between predators and prey. If the reaction term $f_i > 0$, there is a source or mass production for the i-th species. Otherwise $f_i < 0$, there is mass annihilation.

(iii) The diffusion coefficient D either constant if the region Ω is a homogeneous medium, and be regionalized (depends on the position x) if the region Ω is a heterogeneous medium.

The equation (1.2) is placed on an open domain $\Omega \subset \mathbb{R}^N$, with some appropriate boundary conditions and initial conditions. may be bounded or unbounded.

1.4.1 Emergence of the theory of reaction-diffusion equations

The theory of reaction-diffusion equations appeared in the first half of the XXth century under the influence of various applications, such as heat explosion, propagation of chemical and biological waves or pattern formation. It brought together the theories of heat conduction and mass diffusion, on the one hand, and equations of chemical and biological kinetics, on the other.

Mathematical models of heat explosion were introduced by Semenov and Frank-Kamenetskii in the 1930s. In order to describe temperature evolution in a closed vessel with a reacting gas, Semenov used an ordinary differential equation which took into account heat production due to a chemical reaction and heat loss through the boundaries of the vessel. It was assumed that the gas inside the vessel was well mixed and the temperature was uniformly distributed in space. Frank-Kamenetskii suggested a more complete model where the temperature distribution in space was taken into account:

$$\frac{\partial u}{\partial t} = \Delta u + e^u \tag{1.3}$$

This is a reaction-diffusion equation for the dimensionless temperature u. The first term in the right-hand side describes heat conduction and the second term heat production due to a chemical reaction. This equation is considered in a bounded domain Ω with the zero boundary condition, $u\,|_{\partial\Omega}= 0$. If there exists a stationary solution of this problem, then the temperature distribution can converge to it, and it remains bounded. If it does not exist, the temperature becomes unbounded. This situation corresponds to heat explosion. Obviously, temperature remains bounded in real physical situations. Its unbounded growth in the model is a mathematical approximation. Thus, the problem of heat explosion is related to the existence of solutions of elliptic equations.

The theory of combustion waves began in the end of the XIXth century with the works by Mikhelson. He determined the flame structure and suggested an approximate formula for the speed of propagation. In the late 1930s, reaction-diffusion waves were introduced and investigated by Kolmogorov–Petrovskii–Piskunov (KPP) and Fisher in relation with the problem of propagation of the dominant gene; Zeldovich and Frank-Kamenetskii studied them in the framework of combustion theory and Semenov for branching chain reactions. In this case, the reaction-diffusion equation

$$\frac{\partial u}{\partial t} = \frac{\partial^2 u}{\partial x^2} + F(u) \tag{1.4}$$

was considered on the whole axis, $-\infty < x < +\infty$. The variable u here can be the temperature, the concentration of some chemical substance or the density of some population. The form of the function $F(u)$ depends on the applications.

Travelling waves are solutions of the form $u(x,t) = w(x-ct)$, where c is a constant, the wave speed. Solutions of this type, which propagate with a constant speed and profile, describe not only flame propagation and propagation of dominant genes studied in the first works, but also many other applications, such as tumor growth, atherosclerosis development or propagation of nerve pulses. Though these are solutions of a particular form, they describe the asymptotic behavior of solutions of the Cauchy problem for wide classes of initial conditions. In other words, solutions of equation (1.4) can converge to a travelling wave solution as $t \to \infty$.

Another application, which had an important influence on the development of the theory of reaction-diffusion equations, was related to pattern formation. In 1952, Turing published a paper in which he studied a reaction-diffusion system of equations

$$\frac{\partial u}{\partial t} = d_u \frac{\partial^2 u}{\partial x^2} + F(u,v) \tag{1.5}$$

$$\frac{\partial v}{\partial t} = d_v \frac{\partial^2 v}{\partial x^2} + G(u,v) \tag{1.6}$$

If $F_0(u_0,v_0) = G_0(u_0,v_0) = 0$ for some u_0 and v_0, then this is a stationary point of the ordinary differential system of equations

$$\frac{\partial u}{\partial t} = F(u,v), \quad \frac{\partial v}{\partial t} = G(u,v)$$

Let us consider system (1.5), (1.6) in a bounded interval with the homogeneous Neumann boundary condition. Then (u_0,v_0) is also a stationary solution of system (1.5), (1.6). It appears that diffusion can destabilize the homogeneous-in-space solution which is stable without diffusion. This instability results in the emergence of inhomogeneous-in-space solutions, called Turing or dissipative structures. They play important role in mathematical biology, in particular for modelling morphogenesis.

1.4.2 Primary applications

The main fields of applications of reaction-diffusion equations are chemical physics, population dynamics and biomedical processes. Models in chemical physics were strongly developed in the XXth century under the influence of many technological applications, such as combustion engines and chemical reactors.

Population dynamics, though started at approximately the same time, had more gradual development. But it takes a more and more important part in the theory of reaction-diffusion equations, in particular, due to ecological modelling which has become one of the major issues of modern society. Models in chemical kinetics and in population dynamics have many features in common. However, the latter brings new and very important aspects related to the “struggle for life”: intraspecific competition, emergence of biological species, biological evolution.

Mathematical modelling in physiology is younger than the other two areas of application, and has developed slower because of the extreme complexity of physiological processes. However, during the last ten years we have observed a bursting development of biomedical modelling, especially for cancer. Modelling in physiology brings together chemical kinetics (intracellular and extracellular regulation) and cell population dynamics creating a new approach, multi-scale modelling in biology. We can expect an important development of this area of applications motivated by modelling of treatment of various diseases.

Thus, the theory of reaction-diffusion equations is based on three elephants: technology, ecology and public health. In Murray’s books, we find many diverse models in biology, ecology, medicine, and other natural sciences, modeled by reaction-diffusion systems.

1.4.3 Derivation of reaction-diffusion equations

One of the basic theories in the formulation of governing equations for physical problems is the principle of conservation. When the problem under consideration involves a reaction process accompanied by diffusion, this principle leads to a set of partial differential equations for the unknown quantities of the system. These quantities may be mass concentrations in chemical reaction processes, temperature in heat conduction, neutron flux in nuclear reactors, population density in population dynamics, and many others. In certain problems such as nonisothermal chemical reactions, a combination of these quantities is involved in the same set of equations. To give a description of the derivation of the governing equations let us first consider a single quantity $u(t,x)$, called the density function, at time t and position x in a diffusion medium Ω in $\mathbb{R}^n$. The principle of conservation states that "for any subdomain R of Ω with boundary surface S the rate of change of mass density is equal to the rate of flux across S plus the rate of generation within R." This statement is a balance relation in which the flux, denoted by the vector J, is the density flow per unit surface area per unit time. Let ν be the outward normal vector on S and q_o the rate of generation per unit volume per unit time in R. Assume that u, J, and q_o are continuous in x, J has a continuous partial derivatives with respect to the components of x, and u has a continuous derivative in t. Then the balance relation may be expressed as

$$\frac{d}{dt}\int_R a_o u\,dx = -\int_S J\cdot\nu\,ds + \int_R q_o\,dx \tag{1.7}$$

where a_o is a proportionality constant, which depends on the type of problem under consideration. For example, in chemical reaction processes, a_o is the Lewis number, and in heat-conduction problems it is the product of density and specific heat. The negative sign in the surface integral in (1.7) represents the density flow into the region R through the boundary surface S. Since by the divergence theorem

$$\int_S J\cdot\nu\,ds = \int_R \nabla\cdot J\,dx$$

Equation (1.7) is reduced to

$$\int_R (a_o u_t + \nabla\cdot J - q_o)\,dx = 0$$

The continuity assumption on u_t and $\nabla\cdot J$ and the arbitrariness of the subdomain R imply that

$$a_o u_t + \nabla\cdot J - q_o = 0 \quad \text{in } \Omega \tag{1.8}$$

This equation is often referred to as the equation of the principle of conservation. To relate the diffusion flux J to the density function u some physical principle is needed. This principle has different names in different contexts. It is called Fick's law in chemical reaction processes, Fourier law in heat conduction problems, and Darcy's law in porous-medium equations. In each case the law states that in the absence of convection, the flux is proportional to the negative gradient of density

$$J = -D^*\nabla u \tag{1.9}$$

where D^* is a strictly positive function in Ω. Substitution of this relation in (1.8) yields the equation

$$u_t = \nabla\cdot(D\nabla u) + q \tag{1.10}$$

where $D = \dfrac{D^*}{a_o}, q = \dfrac{q_o}{a_o}$. The function D is called the diffusion coefficient in chemical diffusion processes or the thermal diffusivity in heat conduction problems. The term $\nabla\cdot(D\nabla u)$ represents the rate of change due to diffusion, and q is the rate of change due to reaction. The reaction term q is the density per unit volume per unit time formed through the process of reaction or interaction. When q is a prescribed function Equation (1.10) is the standard linear diffusion equation or heat equation. In many reaction-diffusion-type problems, q depends on the density function u and possibly on (t,x) explicitly. Writing $q = f(t,x,u)$ in (1.10) leads to the reaction-diffusion equation

$$u_t - \nabla\cdot(D\nabla u) = f(t,x,u) \tag{1.11}$$

In the derivation of (1.10) it is assumed that there is just one density function in the problem. When the problem involves two or more density functions, say $u_1,\dots,u_N$, the same derivation leads to a coupled system of reaction-diffusion equations. Suppose the law of diffusion

$$J_i = -D_i^*\nabla u_i \quad i = 1,\dots,N$$

holds for each individual density function u_i but not for the other densities u_j for $j \neq i$. Then Equation (1.8) is reduced to

$$(u_i)_t = \nabla\cdot(D_i\nabla u_i) + q_i \quad i = 1,\dots,N \tag{1.12}$$

where $D_i = D_i^*/a_o$ is the diffusion coefficient of u_i. In general the reaction function q_i depends on u_i as well as on u_j for $j \neq i$. By writing $q_i = f_i(t,x,u,\dots,u_N)$, Equation (1.12) becomes a coupled system of reaction-diffusion equations

$$(u_i)_t - \nabla\cdot(D_i\nabla u_i) = f_i(t,x,u_1,\dots,u_N) \quad i = 1,\dots,N \tag{1.13}$$

Equations (1.11) and (1.13) are called time-dependent or nonstationary reaction-diffusion equations in the field of applied science. In the mathematical literature they are often referred to as semilinear parabolic equations and weakly coupled parabolic equations, respectively.

In the derivation of (1.11) and (1.13) it is assumed that the balance relation (1.8) holds without the effect of convection. When this effect is taken into consideration, the Fick or Fourier law requires that

$$J = -D^*\nabla u + \mu_o u \tag{1.14}$$

where μ_o is the flow velocity. Using the above relation in (1.2) leads to the reaction-diffusion-convection equation

$$u_t - \nabla\cdot(D\nabla u) + \mu^*\cdot\nabla u = f(t,x,u) \tag{1.15}$$

where $\mu^* = \dfrac{\mu_o}{a_o}$ is the velocity vector. A similar derivation for the N density functions u_i yields the coupled system

$$(u_i)_t - \nabla\cdot(D_i\nabla u_i) + \mu_i^*\cdot\nabla u_i = f_i(t,x,u_1,\dots,u_N) \quad i=1,\dots,N \tag{1.16}$$

when the reaction-diffusion process reaches a steady state, the density function $u \equiv u(x)$ is independent of t. This implies that $u_t = 0$, and therefore the governing equation for u without convection becomes

$$-\nabla\cdot(D\nabla u) = f(x,u) \tag{1.17}$$

The equation with the effect of convection is given by

$$-\nabla\cdot(D\nabla u) + \mu^*\cdot\nabla u = f(x,u) \tag{1.18}$$

In the case of N density functions the corresponding equations with and without the effect of convection become

$$-\nabla\cdot(D_i\nabla u_i) = f_i(x,u_1,\dots,u_N) \quad i=1,\dots,N \tag{1.19}$$

and

$$-\nabla\cdot(D_i\nabla u_i) + \mu_i^*\cdot\nabla u_i = f_i(x,u_1,\dots,u_N) \quad i=1,\dots,N \tag{1.20}$$

respectively. The equations (1.17)-(1.18) and (1.19)-(1.20) are called steady state or stationary reaction-diffusion equations in the applied sciences. In the mathematical literature they are referred to as semilinear elliptic equations and weakly coupled elliptic equations, respectively.

1.4.4 Derivation of some specific models

The reaction-diffusion equations derived in Section previous cover a number of physical and biological models in various fields of applied science. Here we give a brief description on some of these models whose density function is governed by (1.11).

1.4.4.1 Enzyme kinetics

Consider a simple irreversible monoenzyme reaction in a biochemical system. The reaction scheme for the free enzyme E and substrate concentration S is expressed by

$$E+S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \xrightarrow{k_2} E+P$$

where ES is the enzyme-substrate complex and P is the reaction product. The constants k_1, k_{-1} and k_2 represent the various rates of reaction. The above reaction scheme states that the reaction process from the substrate S to the product P takes place in two steps; the first represents a reversible binding to an enzyme, and the second dissociates the complex ES into the product with release of the enzyme. Suppose the reaction-diffusion takes place in an n-dimensional medium n ($n = 1,2$, or 3). Then the rate of change of the substrate concentration $S = S(t,x)$ at time t and position x is equal to the sum of the rates due to reaction and diffusion and is given by (1.10). The reaction term q is called the initial reaction rate and depends on both S and E. A similar reaction equation can be written for E. When the Michaelis-Menton hypothesis is applied the initial reaction rate is approximated by

$$q(t,x) = \frac{k_2 E_o S}{(k_M + S)}$$

where E_o is the total amount of enzyme and $k_M \equiv k_{-1}/k_1$ is the Michaelis constant (cf. [15]). In case the Briggs-Haldane approximation is used the same formula for q holds except that $k_M = (k_{-1}+k_2)/k_1$. In each case the substrate concentration is governed by (1.11) with $u = S$ and

$$f(u) = \frac{-\sigma u}{(1+au)}$$

where $\sigma = k_2 E_o k_M^{-1}$ and $a = k_M^{-1}$. If a competitive inhibitor, the so-called substrate inhibition, is present a different reaction rate leads to the reaction function

$$f(u) = \frac{-\sigma u}{\left(1+au+bu^2\right)}$$

where σ, a, and b are positive constants.

1.4.4.2 Population genetics

Consider a population of diploid individuals. If the gene occurs in two forms a and A, called alleles, then the population is divided into the three genotypes aa, aA, and AA, depending on the alleles each member carries. Let the population be distributed in a habitat Ω and let $u_i \equiv u_i(t,x), i = 1,2,3$, be the respective population densities of aa, aA, and AA. Assume that the population mates at random with a birth rate r^* and diffuses through the habitat with a diffusion constant D. Assume further that the death rates depend only on the genotypes with respect to the alleles a, A and are denoted respectively by $\tau_i, i = 1,2,3$. Under these conditions the population densities u_i satisfy a system of coupled equations of the form (1.13) with $N = 3$. It was shown in [14] that if the quantity $\tau_o = |\tau_1 - \tau_2| + |\tau_3 - \tau_2|$ is sufficiently small and r^* is very large then for initial data with small derivatives the relative density $u \equiv (u_3 + u_2/2)/(u_1 + u_2 + u_3)$ satisfies (1.11) with

$$f(u) = \sigma u(u-\theta)(1-u) \quad (0 < \theta < 1) \tag{1.21}$$

where σ, θ are positive constants, which depend on the relative death rate τ_i. Equation (1.11) with f given by (1.21) is often called Fisher's model and is an idealized model for the genetic process (see [14]). It turns out that this model also describes bistable transmission lines in electric circuit theory (see [86]).

In order to know how derived the model of reaction-diffusion in Thermal explosions, Chemical reactors and combustions, Nuclear reactor dynamics and heat conduction come back to [94].

1.4.5 Solve reaction-diffusion equations

There are no general solutions to reaction-diffusion systems. Because these systems model real-world phenomena, the important mathematical questions that concern them are:

(i) Existence and uniqueness of the solution.

(ii) Global nature of the solution.

(iii) Positivity of the solution.

(iv) Asymptotic behavior of the solution.

(v) Continued dependence on the original data solution.

1.5 Mathematical analysis of reaction-diffusion problems

For the mathematical analysis of RDS, see, for example, the works of Pao [91, 94], Alaa and Mesbahi et *al*. [4]-[5], [16], [50], [52], [70]-[74], [97], [102]-[104], Lions [65] where we find also many models studied by different techniques.

1.5.1 The upper and lower method

The method of upper and lower solutions and the construction of monotone sequences for proving the existence of maximal and minimal solutions of elliptic boundary-value problems were used as early as the 1920s by Müller [76] for ordinary differential equations and later by Nagumo [85] for both ordinary and partial differential equations. In the late 1950s Kalaba [51] constructed monotone sequences for elliptic equations, and in the early 1960s Ako [3] showed the existence of maximal and minimal solutions in the sector between upper and lower solutions for Dirichlet boundary-value problems. In the early 1970s, Amman [12] and Sattinger [106] formalized the properties of upper and lower solutions and obtained a more systematic approach for the construction of monotone sequences.

The method of upper and lower solutions and its associated monotone iteration are introduced for both the time-dependent and the steady-state reaction-diffusion equations. Based on the principle of conservation a derivation of the equations, including nonlinear boundary conditions, is given in the general framework of reaction-diffusion systems. This derivation formulates either a scalar equation or a coupled system of equations.

1.5.1.1 The Monotone method for time-dependent problems

To illustrate the method, consider the time-dependent problem

$$\begin{aligned} & u_t - \nabla^2 u = f(x,u) \;\; \Omega && \text{in } [0,T]\times\Omega \\ & \mathbf{B}u = h(x) && \text{on } [0,T]\times\partial\Omega \\ & u(0,x) = u_0(x) && \text{in } \Omega \end{aligned} \tag{1.22}$$

To establish an existence theorem for the time-dependent equation (1.22) we use the method of upper and lower solutions and its associated monotone iteration. Not only is this method useful in establishing an existence-comparison theorem for the present problem, but the same approach can be applied to systems of coupled equations and to equations with nonlinear boundary conditions. Moreover, the underlying monotone iterative scheme can be used for the computation of numerical solutions when these equations are replaced by suitable finite difference equations. In fact, the definition of upper and lower solutions and the techniques of monotone iterations can be carried over analogously to finite difference systems. The basic idea of this method is that by using an upper solution or a lower solution as the initial iteration in a suitable iterative process the resulting sequence of iterations is monotone and converges to a solution of the problem. We note that Monotone Method for Steady-State Problems is the same approach used for the time-dependent problem (1.22) it is possible to construct two monotone sequences using a similar iteration process.

Definition 1.11. A function $\tilde{u} \in C\left(\bar{D}_T\right) \cap C^{1,2}(D_T)$ is called an upper solution of (1.22) if it satisfies the inequalities

$$(1.23) \qquad \begin{aligned} &\tilde{u}_t - D\nabla^2\tilde{u} \geq f(x,\tilde{u}) && \text{in } D_T \\ &\mathbf{B}\tilde{u} \geq h(t,x) && \text{on } S_T \\ &\tilde{u}(0,x) \geq u_o(x) && \text{in } \Omega \end{aligned}$$

Similarly, $\hat{u} \in C\left(\bar{D}_T\right) \cap C^{1,2}(D_T)$ is called a lower solution if it satisfies all the reversed inequalities in (1.23).

The functions $\tilde{u}$, $\hat{u}$ are called ordered upper and lower solutions if $\tilde{u} \geq \hat{u}$ in $\bar{D}_T$. Note that in some literature upper and lower solutions are called super solution and sub solution or super function and sub function, respectively. For any ordered upper and lower solutions $\tilde{u}, \hat{u}$, we define the sector $\langle \hat{u}, \tilde{u} \rangle$ as the functional interval

$$\langle \hat{u}, \tilde{u} \rangle \equiv \left\{ u \in C\left(\bar{D}_T\right); \quad \hat{u} \leq u \leq \tilde{u} \right\}$$

1.5.1.2 Monotone Method for Steady-State Problems

The steady-state density function $u(x)$ is governed by the boundary-value problem

$$(1.24) \qquad \begin{aligned} -\nabla^2 u &= f(x,u) \ \text{ in } \Omega \\ \mathbf{B}u &= h(x) \ \text{ on } \partial\Omega \end{aligned}$$

Following the same approach used for the time-dependent problem (1.24) it is possible to construct two monotone sequences using a similar iteration process. Here the initial iteration is taken as either an upper solution or a lower solution of (1.24), defined as follows.

Definition 1.12. A function $\tilde{u} \in C(\bar{\Omega}) \cap C^2(\Omega)$ is called an upper solution of (1.24) if

$$-\nabla^2 \tilde{u} \geq f(x, \tilde{u}) \;\text{ in } \Omega$$
$$\mathbf{B}\tilde{u} \geq h(x) \;\text{ on } \partial\Omega \tag{1.25}$$

Similarly $\hat{u} \in C(\bar{\Omega}) \cap C^2(\Omega)$ is called a lower solution if it satisfies the reversed inequalities in (1.25).

1.5.1.3 The Method of Upper and Lower Solutions for Elliptic Boundary-Value Problems

When the time-dependent solution of the parabolic problem approaches a steady state as $t \to \infty$ the limit function is governed by the corresponding steady-state problem. This leads to the consideration of the elliptic boundary-value problem

$$-Lu = f(x,u) \;\text{ in } \Omega$$
$$Bu = h(x) \;\text{ on } \partial\Omega \tag{1.26}$$

where L and B are the operators given by (1.26). We assume that Ω is of class $C^{2+\alpha}$, f is Hölder continuous in (x,u), and h and the coefficients of L, B satisfy the same conditions given in Section 3.1 of [94] for the linear problem (1.26). To develop a similar monotone iterative scheme for problem (1.26) it is necessary to choose a suitable initial iteration. This function may be taken as either an upper solution or a lower solution defined as follows:

Definition 1.13. A function $\tilde{u} \in C^{\alpha}(\bar{\Omega}) \cap C^2(\Omega)$ is called an upper solution of (1.26) if

$$-\mathbf{L}\tilde{u} \geq f(x, \tilde{u}) \quad \text{in } \Omega$$
$$\mathbf{B}\tilde{u} \geq h(x) \quad \text{on } \partial\Omega \tag{1.27}$$

Similarly, $\hat{u} \in C^{\alpha}(\bar{\Omega}) \cap C^2(\Omega)$ is called a lower solution if it satisfies the reversed inequalities in (1.27).

1.5.2 Compact method

We work in this section with the following hypotheses:

$(H1)$ $N \geq 1, \Omega$ is a bounded open of $\mathbb{R}^N$.

$(H2)$ $a : \Omega \times \mathbb{R} \to \mathbb{R}$ is a Carathéodory function.

$(H3)$ there exists $\alpha > 0$ and $\beta > 0$ such that $\alpha \leq a(\cdot, s) \leq \beta$ a.e., and for all $s \in \mathbb{R}$,

$$f \in L^\infty(\Omega \times \mathbb{R})$$

Under hypotheses $H1 - H3$,we try to show the existence of u, solution of the following problem:

(1.28)
$$\begin{cases} u \in H_0^1(\Omega) \\ \int_\Omega a(x, u(x)) \nabla u(x) \cdot \nabla v(x) dx = \int_\Omega f(x, u(x)) v(x) dx, \text{ for everything } v \in H_0^1(\Omega) \end{cases}$$

Theorem 1.11. *Under the assumptions* $(H1) - (H3)$*, there exists* u *solution of* (1.28).

1.5.3 Monotonous method

For problem (1.28), in the case where f (the second member) depends on ∇u, we still know how to prove the existence of a solution with Schauder's theorem. The question is more difficult in the case where a depends on ∇u. We place ourselves under the following assumptions:

$$\begin{cases} \Omega \text{ open bounded by } \mathbb{R}^N \\ a \in C\left(\mathbb{R}^N, \mathbb{R}\right), \\ \exists \alpha, \beta \in \mathbb{R}_+^*; \alpha \leq a(\xi) \leq \beta, \forall \xi \in \mathbb{R}^N \\ f \in L^2(\Omega) \end{cases}$$

We try to show the existence of a solution to the following problem:

$$\begin{cases} u \in H_0^1(\Omega) \\ \int_\Omega a(\nabla u) \nabla u \cdot \nabla v \; dx = \int_\Omega f v \; dx, \forall v \in H_0^1(\Omega) \end{cases}$$

Can we apply Schauder's theorem? To apply it, it must be used in $H_0^1(\Omega)$ so that a $a(\nabla u)$ has a meaning. Let $\tilde{u} \in H_0^1(\Omega)$, by Lax-Milgram's lemma, there exists a unique $u \in H_0^1(\Omega)$ solution of

$$\begin{cases} u \in H_0^1(\Omega) \\ \int_\Omega a(\nabla \tilde{u}) \nabla u \cdot \nabla v \; dx = \int_\Omega f v \; dx, \forall v \in H_0^1(\Omega) \end{cases} \tag{1.29}$$

Let T solution of $H_0^1(\Omega)$ in $H_0^1(\Omega)$ defined by $T(\tilde{u}) = u$ solution of (1.29). The operator T is indeed from $H_0^1(\Omega)$ in $H_0^1(\Omega)$, and

(1) there exists $R > 0$ such that $\|u\|_{H_0^1(\Omega)} \le R$ for all $\tilde{u} \in H_0^1(\Omega)$,

(2) the map T is continuous from $H_0^1(\Omega)$ in $H_0^1(\Omega)$. Indeed, if $\tilde{u}_n \to \tilde{u}$ in $H_0^1(\Omega)$, we have $\nabla\tilde{u}_n \to \nabla\tilde{u}$ in $L^2(\Omega)^N$and it is not very difficult to show that $T(\tilde{u}_n) \to T(\tilde{u})$ in $H_0^1(\Omega)$.

But, the map T is (in general) not compact (from $H_0^1(\Omega)$ in $H_0^1(\Omega)$). If we were in finite dimension, points (1) and (2) would suffice to show the existence of a solution. The idea is therefore to consider problems approximated in finite dimension and to go to the limit by using the monotony of the operator (which is true under the assumptions given on a below).

Leray-Lions operator

We consider here a some what simplified case of Leray-Lions operators. We consider the following hypotheses:

(a) Ω open bounded by $\mathbb{R}^N, N \ge 1, 1 < p < +\infty$,

(b) $a : \mathbb{R}^N \to \mathbb{R}^N$ keep on going,

(c) (coercivity) $\exists \alpha > 0;\ a(\xi)\cdot\xi \ge \alpha|\xi|^p,\ \forall \xi \in \mathbb{R}^N$,

(d) (growth) $\exists C \in \mathbb{R};\ |a(\xi)| \le C\left(1 + |\xi|^{p-1}\right),\ \forall \xi \in \mathbb{R}^N$,

(e) (monotony) $\left(a(\xi) - a(\eta)\right)\cdot(\xi - \eta) \ge 0,\ \forall (\xi, \eta) \in \left(\mathbb{R}^N\right)^2$,

(f) $\sigma \in L^\infty(\Omega);\ \exists \sigma_0 > 0; \sigma \ge \sigma_0$ a.e.,

(g) $f \in L^{\frac{p}{p-1}}(\Omega)$

We also recall that if $f \in L^{p'}(\Omega)$, the map $v \mapsto \int_\Omega f(x)v(x)dx$ is continuous linear from $W_0^{1,p}(\Omega)$ in $\mathbb{R}$. It is therefore an element of the (topological) dual of $W_0^{1,p}(\Omega)$ (this dual is denoted $W^{-1,p'}(\Omega)$). By abuse of language, we again denote by f this element of f this element of $W^{-1,p'}(\Omega)$, that is to say that for $f \in L^{p'}(\Omega)$, on a

(1.30)
$$\langle f, v\rangle_{W^{-1,p'}(\Omega), W_0^{1,p}(\Omega)} = \int_\Omega f(x)v(x)dx \text{ for all } v \in W_0^{1,p}(\Omega)$$

The weak form of (1.30) that we consider is therefore

(1.31)
$$\begin{cases} u \in W_0^{1,p}(\Omega) \\ \int_\Omega \sigma a(\nabla u)\cdot\nabla v dx = \langle f, v\rangle_{W^{-1,p'}(\Omega), W_0^{1,p}(\Omega)}, \forall v \in W_0^{1,p}(\Omega) \end{cases}$$

Theorem 1.12 (of existence and uniqueness)**.** *Under the assumptions* $(a)-(g)$*, there exists* $u \in W_0^{1,p}(\Omega)$ *solution of* (1.31)*. If moreover a is strictly monotonic, i.e.,* $\left(a(\xi)-a(\eta)\right)\cdot\left(\xi-\eta\right)>0$ *for all* $\left(\xi,\eta\right)\in\left(\mathbb{R}^N\right)^2, \xi\neq\eta$*, then there exists a unique solution u of* (1.31)*.*

1.5.4 Compact and monotonous method

Proposition 1.5. *Let A be a monotonic maximal operator. Then*

i $D(A)$ *is dense in* H*,*

ii A *is closed,*

iii *For all* $\lambda, (I+\lambda A)$ *is bijective from* $D(A)$ *over* $H, (I+\lambda A)^{-1}$*is a bounded operator and* $\|(I+\lambda A)^{-1}\|\leq 1.$

Definition 1.14. We say that an operator $A : X \to X'$ is pseudo-monotonic if

i A is bounded,

ii when $u_j \to u$ in X weak and $\limsup\left(A\left(u_j\right), u_j-u\right)\leq 0$, then

$$\liminf\left(A\left(u_j\right), u_j-v\right)\geq (A(u), u-v), \forall v\in X$$

Theorem 1.13 (Monotonic maximal theorem)**.** *Let L be a linear closed, densely defined operator from the reflexive space V to* V^**, L maximal monotone and let A be a bounded hemicontinuous monotone mapping from V to* V^**, then* $L+A$ *is maximal monotone in* $V\times V^*$*, Moreover, if* $L+A$ *is coercive, then* $\mathbf{Rang}(L+A)=V^*$.

Theorem 1.14. *The existence of weak periodic solutions to systems will be based on the research of fixed points for the nonlinear mapping*

$$\Phi : V \to V$$

defined by

$$\Phi(w)=u$$

CHAPTER 2

MATHEMATICAL MODELING AND REACTION-DIFFUSION SYSTEMS IN BIOLOGY AND MEDICINE

In this chapter, we present definitions on mathematical modeling, some concepts and examples, the link between mathematics, biology and medicine. We also devote a large part of this chapter to the mathematical modeling of diffusion phenomena by reaction-diffusion systems.

2.1 Modeling and mathematical models

2.1.1 What is mathematical modelling ?

■ A mathematical model is a mathematical description of a real life situation. So, if a mathematical model can reflect or mimic the behavior of a real life situation, then we can get a better understanding of the system through proper analysis of the model using appropriate mathematical tools. Moreover, in the process of building the model, we discover various factors which govern the system, factors which are most important to the system and that reveal how different aspects of the system are related.

■ Models describe our beliefs about how the world functions. In mathematical modelling, we translate those beliefs into the language of mathematics. This has many advantages

• Mathematics is a very precise language. This helps us to formulate ideas and identify underlying assumptions.

• Mathematics is a concise language, with well-defined rules for manipulations.

• All the results that mathematicians have proved over hundreds of years are at our disposal.

• Computers can be used to perform numerical calculations.

■ There is a large element of compromise in mathematical modelling. The majority of interacting systems in the real world are far too complicated to model in their entirety. Hence the first level of compromise is to identify the most important parts of the system. These will be included in the model, the rest will be excluded. The second level of compromise concerns the amount of mathematical manipulation which is worthwhile. Although mathematics has the potential to prove general results, these results depend critically on the form of equations used. Small changes in the structure of equations may require enormous changes in the mathematical methods. Using computers to handle the model equations may never lead to elegant results, but it is much more robust against alterations.

■ Modeling is a process that uses mathematics to make, analyze, make predictions, or provide insight into real-world phenomena such as "What is the best climate conservation program for my city Setif, my country Algeria, or the world?" "How will the outbreak of the Corona virus affect Algeria or the world?", or any other question related to climate, weather, pollution, environment, epidemics or other. After defining the problem statement, designers must make assumptions to reduce the number of factors affecting the model. Defining variables tells designers exactly which units they are looking for. This creates the basis for the next part of the process - getting a solution to your mathematical model. Here's where you'll first find out if you've really answered your original problem in the real world.

2.1.2 Why study modeling ?

The importance of mathematical modeling in physics, chemistry, economics, even industry, and the various natural sciences, especially biology, ecology and medicine, cannot be ignored. Mathematical modeling in basic sciences is gaining popularity, especially in biological and medical sciences, and this is what we are witnessing in recently published research on the spread of infectious diseases (Corona, Hepatitis, AIDS, Malaria, Ebola,...), the spread of pollution in the world, global warming. , climate, weather, industry, economy, and others.

2.1.3 Modeling steps

i. Make assumptions about the phenomenon studied.

ii. The assumptions are translated mathematically into a model.

iii. We study the mathematical model; we draw qualitative or quantitative consequences and we make forecasts.

iv. Predictions are compared to experimental realities.

v. We eventually come back to the assumptions to modify the model, and the cycle continues.

2.2 About the mathematical modeling in Epidemiology

The study of infectious disease data began with the work of John Graunt (1620–1674) in his 1662 book "Natural and Political Observations made upon the Bills of Mortality." The Bills of Mortality were weekly records of numbers and causes of death in London parishes. The records, beginning in 1592 and kept continuously from 1603 on, provided the data that Graunt used to begin to understand or identify possible causes of observed mortality patterns. He analyzed the various causes of death and gave a method of estimating the comparative risks of dying from various diseases, giving the first approach to a theory of competing risks.

In the eighteenth century smallpox was endemic and, perhaps not surprisingly, the first model in mathematical epidemiology was tied in to the work that Daniel Bernoulli (1700–1782) carried out on estimating the impact of inoculation against smallpox. Variolation, essentially inoculation with a mild strain, was introduced as a way to produce lifelong immunity against smallpox, but with a small risk of infection and death. There was heated debate about variolation, and Bernoulli was led to study the question of whether variolation was beneficial. His approach was to calculate the increase in life expectancy if smallpox were to be eliminated as a cause of death. His approach to the question of competing risks led to the publication of a brief outline in 1760 [19] followed in 1766 by a more complete exposition [18]. His work received a mainly favorable reception; research that has become known in the actuarial literature rather than in the epidemiological literature. More recently his approach has been generalized [30].

Another valuable contribution to the understanding of infectious diseases prior to our understanding of disease transmission processes was gained from the study of the temporal and spatial pattern of cholera cases during the 1855 epidemic in London carried out by John Snow. He was able to pinpoint the Broad Street water pump as the source of the infection [49, 108]. In 1873,William Budd was able to gain a similar understanding of the spread of typhoid [22]. Statistical theory also moved forward with William Farr's study of statistical returns in 1840, a study that had as its goal the discovery of the laws that underlie the rise and fall of epidemics [35].

Many of the early developments in the mathematical modeling of communicable diseases are due to public health physicians. The first known result in mathematical epidemiology, as noted before, is a defense of the practice of inoculation against smallpox in 1760 by Daniel Bernoulli, a member of a famous family of mathematicians (eight spread over three generations) who had been trained as a physician. The first contributions to modern mathematical epidemiology are due to P.D. En'ko between 1873 and 1894 [34], and the foundations of the entire approach to epidemiology based on compartmental models were laid by public health physicians such as Sir R.A. Ross,W.H. Hamer, A.G. McKendrick, and W.O. Kermack between 1900 and 1935, along with important contributions from a statistical perspective by J. Brownlee.

2.2.1 Compartmental Models

In order to describe a mathematical model for the spread of a communicable disease, it is necessary to make some assumptions about the means of spreading infection. The idea of invisible living creatures as agents of disease goes back at least to the writings of Aristote (384–322 BC). The existence of microorganisms was demonstrated by van Leeuwenhoek (1632–1723) with the aid of the first microscopes. The first expression of the germ theory of disease by Jacob Henle (1809–1885) came in 1840 and was developed by Robert Koch (1843–1910), Joseph Lister (1827–1912), and Louis Pasteur (1822–1875) in the late nineteenth and early twentieth centuries. The modern view is that many diseases are spread by contact through a virus or bacterium. We focus in this work on the problem of understanding the spread of disease at a population level. Similar modeling approaches can be used to study the dynamics of infection within a host for diseases including HIV. This area is the backbone of the field of mathematical and computational immunology and viral dynamics. An introduction to immunology may be found in the book by Nowak and May [88].

In 1906, W.H. Hamer argued that the spread of infection should depend on the number of susceptible individuals and the number of infective individuals [45]. He suggested a mass action law for the rate of new infections, and this idea has been basic in the formulation of compartmental models since that time. It is worth noting that the foundations of the entire approach to epidemiology based on compartmental models were laid, not by mathematicians, but primarily by public health physicians such as Sir R.A. Ross,W.H. Hamer, A.G. McKendrick, and W.O. Kermack between 1900 and 1935.

A particularly instructive example is the work of Ross on malaria. Sir Ronald Ross was awarded the second Nobel Prize in Medicine in 1902 for his demonstration of the dynamics of the transmission of malaria between mosquitoes and humans. He discovered the malarial parasite in the gastrointestinal tract of the Anopheles mosquito from which he was able to characterize the life cycle of malaria. He concluded that this vector-borne disease was transmitted by the Anopheles mosquito and in the process he developed a program for controlling or eliminating it at the population level.

It was generally believed that, so long as mosquitoes were present in a population, malaria could not be eliminated. Ross introduced a simple compartmental model [98] that included mosquitoes and humans. He showed that reducing the mosquito population below a critical level would be sufficient to eliminate malaria. This was the first introduction of the concept of the basic reproduction number, a central idea in mathematical epidemiology since that time. Field trials supported Ross' conclusion leading sometimes to brilliant successes in malaria control.

The basic compartmental models to describe the transmission of communicable diseases are contained in a sequence of three papers by W.O. Kermack and A.G. McKendrick in 1927, 1932, and 1933 [55, 56]. The first of these papers described epidemic models.

The Kermack–McKendrick epidemic model, included dependence on age of infection, that is, the time since becoming infected, and can be used to provide a unified approach to compartmental epidemic models. Various disease outbreaks including the SARS epidemic of 2002–2003, the concern about a possible H5N1 influenza epidemic in 2005, the H1N1 influenza pandemic of 2009, and the Ebola outbreak of 2014 have reignited interest in epidemic models, with the reformulation of the Kermack–McKendrick model by Diekmann, Heesterbeek, and Metz [29]. In the work of Ross and Kermack and McKendrick there is a threshold quantity, the basic reproduction number, which is now almost universally denoted by R_0. Neither Ross nor Kermack and McKendrick identified this threshold quantity or gave it a name. It appears that the first person to name the threshold quantity explicitly was MacDonald [67] in his work on malaria.

The basic reproduction number, R_0 (referred to as the basic reproductive number by some authors), is defined as the expected number of disease cases (secondary infections) produced by a "typical" infected individual in a wholly susceptible population over the full course of the disease outbreak. In an epidemic situation, in which the time period is short enough to neglect demographic effects and all infected individuals recover with full immunity against reinfection, the threshold $R_0 = 1$ is the dividing line between the infection dying out and the onset of an epidemic. In a situation that includes a flow of new susceptible individuals, either through demographic effects or recovery without full immunity against reinfection, the threshold $R_0 = 1$ is the dividing line between an approach to a disease-free equilibrium and an approach to an endemic equilibrium, in which the disease is always present.

Since 1933, there has been a great deal of work on compartmental disease transmission models, with generalizations in many directions. In particular, it is assumed in [55, 56] that stays in compartments are exponentially distributed.

2.2.2 Endemic Disease Models

The analytic approaches to models for endemic diseases and epidemics are quite different. The analysis of a model for an endemic disease, begins with the search for equilibria, which are, by definition, constant solutions of the model. Usually there is a disease-free equilibrium and there are one or more endemic equilibria, with a positive number of infected individuals. The next step is to linearize about each equilibrium and determine the stability of each equilibrium. Usually, if the basic reproduction number is less than 1, the only equilibrium is the disease-free equilibrium and this equilibrium is asymptotically stable. If the basic reproduction number is greater than 1, the usual situation is that the disease free equilibrium is unstable and there is a unique endemic equilibrium which is asymptotically stable. This approach also covers diseases in which there is vertical transmission, which is direct transmission from mother to offspring at birth [23].

However, more complicated behavior is possible. For example, if there are two strains of the disease being studied it is common to have regions in the parameter space in which there is an asymptotically stable equilibrium with only one of the strains present and a region in which there is an asymptotically stable equilibrium with both strains coexisting. Another possibility is that there is a unique endemic equilibrium but it is unstable. In this situation, there is often a Hopf bifurcation and an asymptotically stable periodic orbit around the endemic equilibrium. An example of such behavior may be found in an SIRS model, with a temporary immunity period of fixed length following recovery [46] and in an SV $\mathbb{R}$ model [36]. If there is a periodic orbit with large amplitude and a long period, data must be gathered over a sufficiently large time interval to give an accurate picture.

Another possible behavior is a backward bifurcation. As R_0 increases through1 there is an exchange of stability between the disease-free equilibrium, which is asymptotically stable for $R_0 < 1$ and unstable for $R_0 > 1$, and the endemic equilibrium which exists if $R_0 > 1$. The usual transition is a forward, or transcritical, bifurcation at $R_0 = 1$, with an asymptotically stable endemic equilibrium and an equilibrium infective population size depending continuously on R_0.

The behavior at a bifurcation may be described graphically by the bifurcation curve, which is the graph of the infective population size I at equilibrium as a function of the basic reproduction number R_0. It has been noted [31, 43, 44, 58] that in epidemic models with multiple groups and asymmetry between groups or multiple interaction mechanisms it is possible to have a very different bifurcation behavior at $R_0 = 1$. There may be multiple positive endemic equilibria for values of $R_0 < 1$ and a backward bifurcation at $R_0 = 1$. The qualitative behavior of a system with a backward bifurcation differs from that of a system with a forward bifurcation and the nature of these changes has been described in [7]. Since these behavioral differences are important in planning how to control a disease, it is important to determine whether a system can have a backward bifurcation. In the presence of two modes of sexually transmitted HIV, it was shown that multiple endemic equilibrium could be supported [48].

2.2.3 Diseases Transmitted by Vectors

Many diseases are transmitted from human to human indirectly, through a vector. Vectors are living organisms that can transmit infectious diseases between humans. Many vectors are bloodsucking insects that ingest disease-producing microorganisms during blood meals from an infected (human) host, and then inject it into a new host during a subsequent blood meal. The best known vectors are mosquitoes for diseases including malaria, dengue fever, chikungunya, Zika virus, Rift Valley fever, yellow fever, Japanese encephalitis, lymphatic filariasis, and West Nile fever, but ticks (for Lyme disease and tularemia), bugs (for Chagas' disease), flies (for onchocerciasis), sandflies (for leishmaniasis), fleas (for plague, transmitted by fleas from rats to humans), and some freshwater snails (for schistosomiasis) are vectors for some diseases.

Every year there are more than a billion cases of vector-borne diseases and more than a million deaths. Vector-borne diseases account for over 17% of all infectious diseases worldwide. Malaria is the most deadly vector-borne diseases, causing an estimated 627,000 deaths in 2012. The most rapidly growing vector-borne disease is dengue, for which the number of cases has multiplied by 30 in the last 50 years. These diseases are found more commonly in tropical and sub-tropical regions where mosquitoes flourish, and in places where access to safe drinking water and sanitation systems is uncertain.

Some vector-borne diseases such as dengue, chikungunya, and West Nile virus are emerging in countries where they were unknown previously because of globalization of travel and trade and environmental challenges such as climate change. A troubling new development is the Zika virus, which has been known since 1952 but has developed a mutation in the South American outbreak of 2015 [107] which has produced very serious birth defects in babies born to infected mothers. In addition, the current Zika virus can be transmitted directly through sexual contact as well as through vectors.

Many of the important underlying ideas of mathematical epidemiology arose in the study of malaria begun by Sir R.A. Ross [98]. Malaria is one example of a disease with vector transmission, the infection being transmitted back and forth between vectors (mosquitoes) and hosts (humans). It kills hundreds of thousands of people annually, mostly children and mostly in poor countries in Africa. Among communicable diseases, only tuberculosis causes more deaths. Other vector diseases include West Nile virus, yellow fever, and dengue fever. Human diseases transmitted heterosexually may also be viewed as diseases transmitted by vectors, because males and females must be viewed as separate populations and disease is transmitted from one population to the other.

Vector-transmitted diseases require models that include both vectors and hosts. For most diseases transmitted by vectors, the vectors are insects, with a much shorter life span than the hosts, who may be humans as for malaria or animals as for West Nile virus, although there is malaria (not human malaria) in various animal populations and West Nile virus has infected humans as far as Arizona in the USA. The compartmental structure of the disease may be different in host and vector species; for many diseases with insects as vectors an infected vector remains infected for life so that the disease may have an SI or SEI structure in structure in the vectors and an SIR or $SEIR$ structure in the hosts.

2.3 Reaction-diffusion systems and modeling

► Reaction-diffusion equations describe distributions of temperature, concentrations or of some other variables in space and in time. These equations are characterized by the presence of diffusion and production terms. Originally, diffusion was understood as random motion of atoms and molecules and described by the Laplace operator. Heat conduction was described by similar differential expressions. This simplest description of heat and mass transport was later completed by other mechanisms. Among them cross diffusion, anomalous diffusion, other mechanisms of heat conduction. Next, similar models were applied to biological processes such as displacement of biological cells or individuals in biological populations. The mechanisms of motion become more complex. However, in some cases, this motion is random and it can be described by conventional diffusion terms. In some other cases, more complex models of motion should be used. For example, biological cells can move in a random or in a directed way with the whole spectrum of intermediate patterns between these two limiting cases.

► It should be noted that diffusion and other transport processes can occur in various spaces. First of all, it is the usual physical space mostly used in chemical and physical applications. However, it can also be the spaces of different parameters which characterize biological populations. For example, intracellular concentrations p of some proteins. In this case the cell population can be characterized by the distribution $u(p,t)$ of cells as a function of the concentration p and of time t. The second property, which characterizes reaction-diffusion processes, is production. In the case of chemical reactions, it is production of chemical compounds or heat production. They are described by equations of chemical kinetics, often based on the mass action law, though other models also exist. Cell division and birth of biological individuals determine production in biological populations Their simplest description is based on the same assumption as for chemical reaction, that the rate of production is proportional to the population density. In more detailed models, time delay and various specific mechanisms are taken into account. In the case of biological cells, it can be cell cycle and various intracellula and extracellular regulatory mechanisms.

2.3.1 What can reaction-diffusion models tell us ?

Reaction-diffusion models can explain three types of spatial phenomena that are relevant in ecology: waves of invasion by exotic species, the formation of patterns in homogeneous space, and the effects of the size, shape, and heterogeneity of the spatial environment on the persistence of species and the structure of communities. The idea that reaction-diffusion models can support traveling waves was introduced by Fisher (1937) in the context of models for the spatial spread of an advantageous gene. The idea that adding diffusion to a nonspatial model (with two or more components) can destabilize spatially homogenous equilibria and lead to the formation of patterns was introduced by Turing (1952) in the context of models for morphogenesis. The idea that reaction-diffusion models predict the minimal patch size needed to sustain a population was introduced by Skellam (1951) and Kierstead and Slobodkin (1953), specifically in the context of spatial ecology. (Skellam also extended Fisher's idea of a traveling wave to the spread of populations, as opposed to genes within a population.) In what follows we focus our attention almost exclusively. Traveling waves in reaction-diffusion models are discussed from a mathematical viewpoint by Fife (1979), Smoller (1982), and Grindrod (1996). They are discussed from the viewpoint of biological applications by Murray (1993). Models for biological invasions, including but not limited to reaction-diffusion models, are discussed by Kawasaki and Shigesada (1997). Pattern formation is discussed by Grindrod (1996) and, again in the biological context, by Murray (1993). There are some general treatments of reaction-diffusion systems in bounded spatial domains, including Lotka-Volterra models with diffusion, for example Leung (1989) and Pao (1992), and in the time periodic case (Hess, 1991), but those treatments are essentially mathematical in nature and generally do not attempt to make close connections with specific applications in ecology. Also, the material we present includes a number of methods and applications which to our knowledge have only appeared in journal articles.

The phenomena that can be described via reaction-diffusion models can often be treated via other types of models. If highly detailed specific predictions are required, it is probably best to use simulations, perhaps via individual based models, cellular automata, or interacting particle systems. Some of these sorts of approaches are discussed by Tilman et *al*. (1997). A limitation of simulation models is that it is usually difficult to analyze them mathematically and extract general properties which can provide insights into the mechanisms underlying their predictions. However, they can be used in numerical experiments to construct artificial data sets from which general properties can be inferred.

In particular, cellular automata models have been observed to generate spatial patterns analogous to those produced by reaction-diffusion models (Comins et *al*., 1992; Hassell et *al*., 1994). It is sometimes possible to obtain information about the rate at which a population expands its range from interacting particle systems; see Ellner and et *al*. (1998).

Traveling waves can be shown to exist in island chain models; see Zinner (1991,1992). A limitation of reaction-diffusion models for the propagation of traveling waves is that diffusion equations on unbounded domains predict that an initial density which is zero except on some bounded set will be positive everywhere for all positive times. This seems to be at odds with the notion that organisms move with finite speed. That could be resolved by replacing reaction-diffusion models with models based on the telegraph equation

$$2\frac{\partial^2 u}{\partial t^2}+\frac{\partial u}{\partial t}=\frac{\partial^2 u}{\partial x^2}+f(u)$$

However, it turns out that for parameter values that occur in natural systems, the predictions of the telegraph equation are very close to those of the corresponding reaction diffusion model (Holmes, 1993). A more serious problem is that diffusion models do not account for long-distance movement, e.g. for the movement of an insect that "hitch-hikes" on a car or truck instead of crawling on its own. More generally, diffusion predicts that a population which is initially concentrated at a single point will develop a normal (i.e. Gaussian) distribution in space as time passes. Other patterns are certainly possible, and these can be examined by using models based on integral kernels. It turns out that the details of how the kernel decays at infinity can have profound effects on wave propagation; see Lewis (1997). Thus, there are sometimes good reasons to use such models instead of reaction-diffusion models in the study of biological invasions.

However, in a finite habitat patch the issue of long distance dispersal is much less important, especially if the primary goal is to understand the long term effects of local dispersal and habitat geometry on population dynamics. Thus, while it is possible to use integral kernels to study long term persistence in habitat patches (Hardin et *al*., 1988, 1990; VanKirk and Lewis, 1997, 1999), it is also reasonable to use reaction-diffusion models. Metapopulation models, especially as formulated by Hanski and his co-workers (1997, 1999) and Tilman (1994) can address the issue of persistence in finite habitats, but those models treat networks of patches and treat local population dynamics implicitly, in terms of presence or absence of populations. Thus, they are typically appropriate models for spatial effects on a different set of spatial scales than reaction-diffusion models. Discrete diffusion models, i.e. island chain models, can also be used to model patch networks. To describe systems where different species operate on different spatial scales, it may be necessary to combine reaction-diffusion models and patch network models. An example is discussed in Cantrell and Cosner (1996).

The phenomena of traveling waves and pattern formation differ from that of minimal patch in a fundamental way: they can occur in homogeneous space, while the very notion of "patch" requires at least enough spatial heterogeneity to distinguish the patch from its surroundings. A defining feature of any finite habitat is that it has a boundary, or edge. Edges can mediate numerous effects in population dynamics (Fagan et *al.*, 1999). Habitat edges can be created by physical features such as rivers, roads, or (for aquatic systems) shorelines; they can also arise from interfaces between different types of ecological communities such as forests and grasslands. Edges can influence population dynamics in various ways. They can affect movement patterns, act as a source of mortality or resource subsidy, or function as a unique environment with its own rules for population interactions (Fagan et *al.*, 1999). Edges can have different effects on different species; for example, a road may act as a barrier for some species and a source of mortality for others. Thus, because edges can exert different effects on different species, the presence of edges can influence community structure in ways that are not completely obvious from the ways in which they affect each species. Reaction-diffusion models provide a natural framework for the study of edge effects, because to correctly formulate a reaction-diffusion model in a finite patch it is necessary to specify boundary conditions. In other words, we must describe not only how individuals disperse throughout a patch, but also what they do when they reach the edge of the patch. An advantage of reaction-diffusion models is that they can readily incorporate simple rules about the effects of edges. They can also incorporate effects of internal heterogeneity within a patch. We will use those features of reaction-diffusion models to study how environmental heterogeneity affects populations.

2.4 Principal uses of reaction-diffusion theory in ecology

There are three principal uses of reaction-diffusion theory in ecology as we indicated in the previous section namely in the study of ecological invasions (dating from the work of Fisher in the 1930s) and in the study of pattern formation (dating from the work of Turing in the 1950s). Skellam in particular examined reaction-diffusion models for the population density of a species in a bounded habitat, employing both linear (Malthusian) and logistic population growth rate.

2.4.1 Reaction-diffusion models and spatial ecology

The “origin of this species” lies in the pages of the journal Biometrika and precedes the birth of either of the authors. There, in his remarkable landmark 1951 paper “Random dispersal in theoretical populations,” J.G. Skellam made a number of observations that have profoundly affected the study of spatial ecology. First, he made the connection between random walks as a description of movement at the scale of individual members of some theoretical biological species and the diffusion equation as a description of dispersal of the organism at the scale of the species’ population density, and demonstrated the plausibility of the connection in the case of small animals using field data for the spread of the muskrat in central Europe. Secondly, he combined the diffusive description of dispersal with population dynamics, effectively introducing reaction-diffusion equations into theoretical ecology, paralleling Fisher’s earlier contribution to genetics. Thirdly, Skellam in particular examined reaction-diffusion models for the population density of a species in a bounded habitat, employing both linear (Malthusian) and logistic population growth rate terms, oneand two-dimensional habitat geometries, and various assumptions regarding the interface between the habitat and the landscape surrounding it. His examinations lead him to conclude that “[just] as the area/volume ratio is an important concept in connection with continuance of metabolic processes in small organisms, so is the perimeter/area concept (or some equivalent relationship) important in connection with the survival of a community of mobile individuals. Though little is known from the study of field data concerning the laws which connect the distribution in space of the density of an annual population with its powers of dispersal, rates of growth and the habitat conditions, it is possible to conjecture the nature of this relationship in simple cases. The treatment shows that if an isolated terrestrial habitat is less than a certain critical size the population cannot survive. If the habitat is slightly greater than this the surface which expresses the density at all points is roughly dome-shaped, and for very large habitats this surface has the form of a plateau.”

The most general equation for a population density u mentioned in Skellam’s paper has the form

$$\frac{\partial u}{\partial t} = d\nabla^2 u + c_1(x,y)u - c_2(x,y)u^2$$

Writing in 1951, Skellam observed that “orthodox analytic methods appear in adequate” to treat the equation, even in the special case of a one-dimensional habitat. The succeeding half-century since Skellam’s paper has seen phenomenal advances in many areas of mathematics, including partial differential equations, functional analysis, dynamical systems, and singular perturbation theory. That which Skellam conjectured regarding reaction-diffusion models (and indeed much more) is now rigorously understood mathematically and has been employed to provide new ecological insight into the interactions of populations and communities of populations in bounded terrestrial (and, for that matter, marine).

2.4.2 Spatial pattern formation with reaction-diffusion systems

▶ In spite of the enormous amount of research and the exploding growth of genetics, the development of spatial pattern and form is still one of the central issues in embryology. In the past 20–30 years, it has spawned exciting, important and genuine interdisciplinary research between theoreticians and experimentalists, the common aim of which is the elucidation of the underlying mechanisms involved in embryology and medicine; most of these mechanisms are essentially still unknown.

▶ By way of illustration, we shall describe some specific biological problems and their modelling. We shall point out some of the limitations of Turing-type reaction–diffusion mechanisms which necessitated a new, and more experimentally verifiable, approach to biological pattern formation, known as the mechanical theory of biological pattern formation proposed by Oster et *al*. [90], Murray et *al*. [83] and Murray & Oster [82]. A large body of research has been developed on tumour growth, such as brain tumours (see [78] for a survey): it is now being used medically to quantify the efficacy of individual patient treatment scenarios prior to their use.

▶ The first genuine experimentally based reaction–diffusion system which produced steady-state chemical spatial patterns in line with Turing's predictions was developed by Thomas [113].

The suggestion here was that tumor cells create an environment which allows certain mutations to be selected and hence the evolution of mutant cell populations to occur within the body; this is called somatic evolution. The authors analyzed somatic evolution in this context and showed a number of evolutionary pathways in ductal carcinoma in situ. Colleagues suggested that different mutant clones would emerge in a well-defined temporal sequence, while the mathematical simulations showed that this was highly unlikely.

▶ The basic concept, which Turing demonstrated mathematically, was that if you have two chemicals, in later studies (such as [42] referred to as an activator and an inhibitor, which react together and at the same time diffuse, crucially at different rates with the inhibitor having the larger diffusion coefficient, it is possible for such a coupled system of reaction–diffusion equations to produce steady-state spatial patterns in chemical concentrations of the reactants. In the early to mid- 1970s Turing's paper was rediscovered by more theoreticians with an increasing number of publications starting to appear. Closely related, but not specifically to Turing's work, is the seminal experimental work on the importance of chemical gradients in embryonic development by Wolpert [119], who introduced the concept of 'positional information', where cells in a chemical gradient react to a chemical concentration with which they are associated. His work initiated a huge amount of experimental and theoretical work, often controversial, that is still going on. For a review of his work and his views on development, seeWolpert's [118] book on the principles of development.

▶ **Reaction-diffusion (Turing) Mechanisms**

Density dependent proliferation is taken into account by introduction of cell concentration in the denominator. Diffusion term in the equation for promoter is Turing (1952) suggested that, under certain conditions, chemicals can react and diffuse in such a way as to produce steady state heterogeneous spatial patterns of chemical or morphogen concentration. which is in the form:

$$\frac{\partial \mathbf{c}}{\partial t} = \mathbf{f}(\mathbf{c}) + D\nabla^2 \mathbf{c}$$

where $\mathbf{c}$ is the vector of morphogen concentrations, $\mathbf{f}$ represents the reaction kinetics and D is the diagonal matrix of positive constant diffusion coefficients. With models for two chemical species, $A(\mathbf{r},t)$ and $B(\mathbf{r},t)$ say. The equations system is then of the form

$$\begin{cases} \dfrac{\partial A}{\partial t} = F(A,B) + D_A \nabla^2 A \\ \dfrac{\partial B}{\partial t} = G(A,B) + D_B \nabla^2 B \end{cases}$$

where F and G are the kinetics, which will always be nonlinear.

Turing's (1952) idea is a simple but profound one. He said that, if in the absence of diffusion (effectively $D_A = D_B = 0$), A and B tend to a linearly stable uniform steady state then, under certain conditions, which we shall derive, spatially inhomogeneous patterns can evolve by diffusion driven instability if $D_A = D_B$. Diffusion is usually considered a stabilising process which is why this was such a novel concept.

Consider a field of dry grass in which there is a large number of grasshoppers which can generate a lot of moisture by sweating if they get warm. Now suppose the grass is set alight at some point and a flame front starts to propagate. We can think of the grasshopper as an inhibitor and the fire as an activator. If there were no moisture to quench the flames the fire would simply spread over the whole field which would result in a uniform charred area. Suppose, however, that when the grasshoppers get warm enough they can generate enough moisture to dampen the grass so that when the flames reach such a pre-moistened area the grass will not burn. The scenario for spatial pattern is then as follows. The fire starts to spread—it is one of the 'reactants,' the activator, with a 'diffusion' coefficient D_F say. When the grasshoppers, the inhibitor 'reactant,' ahead of the flame front feel it coming they move quickly well ahead of it; that is, they have a 'diffusion' coefficient, D_G say, which is much larger than D_F. The grasshoppers then sweat profusely and generate enough moisture to prevent the fire spreading into the moistened area. In this way the charred area is restricted to a finite domain which depends on the 'diffusion' coefficients of the reactants—fire and grasshoppers—and various 'reaction' parameters. If, instead of a single initial fire, there were a random scattering of them we can see how this process would result in a final spatially heterogeneous steady state distribution of charred and uncharred regions in the field and a spatial distribution of grasshoppers, since around each fire the above scenario would take place. If the grasshoppers and flame front 'diffused' at the same speed no such spatial pattern could evolve.

2.4.3 Reaction-diffusion models in population dynamics

Population dynamics is one of the oldest areas of mathematical modelling. Already in 1202 Leonard Fibonacci introduced special sequences of numbers (Fibonacci sequences) in order to describe growth of rabbit population. In 1748 Euler used geometrical sequences (exponential growth) to study human societies.

Malthus wrote in [68]: "It is an obvious truth, which has been taken notice of by many writers, that population must always be kept down to the level of the means of subsistence; but no writer that the Author recollects has inquired particularly into the means by which this level is effected: and it is a view of these means which forms, to his mind, the strongest obstacle in the way to any very great future improvement of society".

Malthus described two types of populations with preventive and destructive ways to control the rate of growth. He also observed that the destructive mode could be accompanied by oscillations in the population size and conditions (price of labour, etc.), though these oscillations were difficult to observe in human societies. As we will see below, these two modes of population growth correspond to logistic and prey-predator models which were introduced later by Verhulst and Lotka–Volterra.

A important question raised by Malthus concerned help to the poor and redistribution of wealth. "The poor laws of England tend to depress the general condition of the poor in these two ways. Their first obvious tendency is to increase population without increasing the food for its support. A poor man may marry with little or no prospect of being able to support a family in independence. They may be said therefore in some measure to create the poor which they maintain, and as the provisions of the country must, in consequence of the increased population, be distributed to every man in smaller proportions, it is evident that the labour of those who are not supported by parish assistance will purchase a smaller quantity of provisions than before and consequently more of them must be driven to ask for support.

Secondly, the quantity of provisions consumed in workhouses upon a part of the society that cannot in general be considered as the most valuable part diminishes the shares that would otherwise belong to more industrious and more worthy members, and thus in the same manner forces more to become dependent. If the poor in the workhouses were to live better than they now do, this new distribution of the money of the society would tend more conspicuously to depress the condition of those out of the workhouses by occasioning a rise in the price of provisions" ([68], Chapter 5). The question about how redistribution of wealth acts on society is more complex for modelling.

According to Malthus, growth rates for populations and for resources are different, then there is a constant pressure on the population to control its rate of growth. So the next step is to analyze how this pressure acts inside a population or species and between them. Here we enter the area of "struggle for life", as Darwin called it. The model of competition of species has been known for a long time. However, modelling of intra-specific competition is more recent. Similar models can also be used to describe economical populations.

Many problems modeling the evolution of populations involve several different physical effects. These include: Birth and death rates as functions of the populations, intra-species competition, i.e., when the birthrate decreases as the population increases, due to crowding and competition for scarce resources, inter-species competition, when two or more species compete for the same resources Diffusive spreading, non-local interactions, i.e., the evolution of a population at a location depends not just on local conditions but also on resources in a neighborhood of the location, etc...

2.5 Reaction-diffusion in chemical physics

A chemical reaction is a transformation of matter during which the chemical species that make up matter are modified: the species that are consumed are called reactants.

The species formed during the reaction are called reaction products. Since the work of Lavoisier (1777), scientists know that the chemical reaction takes place without measurable variation in mass: "Nothing is lost, nothing is created, everything is transformed", which reflects the conservation of mass. The aluminothermic reaction is a spectacular redox. We will cite some examples in this context in the next chapter. for more information, see Duvaut [32].

2.5.1 Laws of behavior

2.5.1.1 Diffusion

When you put a colored substance, such as a drop of ink, in a container filled with water, what is called a diffusion phenomenon takes place. The substance is first separated from the water by a clear border, then the molecules of the substance are distributed uniformly in the water under the action of a concentration gradient. Where the concentration is high, the molecules tend to decrease in number; and conversely, in places of low concentration their number increases.

2.5.1.2 Lois de Fick

This law qualitatively expresses that the particles move towards the regions with lower density. Concentration $\varrho = \varrho(t,x)$. We will assume that ρ is differentiable with respect to t and x. The amount of diffusing matter, flowing through one square centimeter per second in a given direction where the concentration will decrease is expressed in a system of Cartesian coordinates by the formula

$$J = -d\frac{\partial \varrho}{\partial x}$$

J is the transfer or transport rate per unit area of section in one direction x normal to the section and d is a proportionality factor, it is the diffusion coefficient, considered as a positive constant. This law can be generalized to three or more dimensions

$$J = -d\nabla\varrho \tag{2.1}$$

where J is the diffusion flux of the substance. The flux is defined as the quantity of material which per second crosses the unit area of a surface normal to the transfer movement. $\nabla\varrho$ it is the concentration gradient ϱ. The relation (2.1) bears the name of **Fick's first law**.

We have Ω the reactor or the reaction takes place, it is a bounded region in $\mathbb{R}^3$, so we have by definition $M(t) = \int_\Omega \left(\varrho t, x dx\right)$ the mass of the substance in Ω in time t. $M_e(t)$ the mass of the substance flowing outward from Ω during the time interval $[0,t.[$ We have by definition:

$$\frac{dM_e(t)}{dt} = \int_{\partial\Omega} J.d\sigma$$

As $M(t) + M_e(t) = constante$, we get then

$$\frac{d}{dt}(M(t) + M_e(t)) = \frac{d}{dt}\int_\Omega \left(\int_\Omega \varrho(t,x)dx + \int_{\partial\Omega} J.d\sigma\right) = 0$$

Gauss's divergence theorem gives us

$$\int_\Omega \left(\varrho_t + \nabla.J\right)dx = 0$$

As this last equality is true for any region Ω, we conclude

$$\varrho_t + \nabla.J = 0$$

And according to Fick's first law, we get

$$\varrho_t = \nabla.\left(d\nabla\varrho\right) \tag{2.2}$$

This is **Fick's second law of diffusion**.

For more details, see for example, Coirier [26], Duvaut [32], Royis [99] and Salençon [105].

2.5.2 Derivation of equations

Consider a region (which can be a test tube or a living cell) in which chemical reactions take place (the living cell is the site of thousands of simultaneous chemical reactions).

Either $u_i = u_i(x,t), i = 1,\ldots,n$ the concentration of the i-th species E_i taking part in the reactions, and either $f_i = f_i(x,t,u)$ the rate of formation of this species in this reaction. here $u = (u_1,\ldots,u_n)$ is the vector of concentrations, x is the locus and t is the time.

Either $\phi_i = \phi_i(x,t),\ i = 1,\ldots,n$,the flow of the i-th species due to the diffusion with the usual convention is that ϕ_i is positive if the flow of the i-th species is from the interior of the region to the exterior.

Either Ω the considered surface region $S = \partial\Omega$. So, the rate of formation of the amount of E_i in Ω is equal to the amount formed by the reaction minus the flux across the surface S. In mathematical terms:

$$\frac{\partial}{\partial t}\int_{\Omega} u_i dx = \int_{\Omega} f_i dx - \int_S \phi_i d\sigma$$

Using the divergence theorem, it comes

$$\int_{\Omega}\left(\frac{\partial u_i}{\partial t} - f_i + \nabla.\phi_i\right)dx = 0$$

As this relation is true for any region we draw from it for each i

$$\frac{\partial u_i}{\partial t} + \nabla.\phi_i = f_i$$

According to Fick's first law, the flow ϕ_i of E_i is given by the expression

$$\phi_i = -D_i \nabla u_i$$

where D_i is the diffusion coefficient of the species E_i. Thus, from the last two relations we derive

$$\frac{\partial u_i}{\partial t} = \nabla.(D_i \nabla u_i) + f_i \tag{2.3}$$

for $i = 1, \ldots, n$

It is also possible that the flux ϕ_i of the density u_i may depend on the gradients of the concentrations of other species not only on ∇u_i the gradient of u_i, i.e.

$$\phi_i = -\sum_{1 \le j \le n} D_{ij} \nabla u_j$$

or in matrix form

$$\phi = -D\nabla u$$

where $D = \left(D_{ij}\right)$ is an $n \times n$ non-diagonal matrix, its terms are the diffusion coefficients. D_{ij} characterizes the diffusion of u_i in u_j.

In this case we have what we call a diffusion crossing between the densities u_i.

It should be noted here that:

(i) Diffusion coefficients are not always positive.

(ii) If the reaction term $f_i > 0$, there is a source or mass production for the i-th species. Otherwise $f_i < 0$, there is mass annihilation.

(iii) The diffusion coefficient D is constant if the region Ω is a homogeneous medium.

2.5.3 Modeling of the evolution of reaction

2.5.3.1 Speed of a reaction, conservation of matter

Note $[A]$ the concentration of a component A in a given system, that is to say the quantity of this constituent per unit of volume. The mole per liter is generally used as the unit of concentration. Consider in a general way the following equation in equilibrium

$$n_1A_1 + n_2A_2 + ... + n_pA_p \longrightarrow m_1B_1 + m_2B_2 + ... + m_qB_q$$

The constituents A_i are called reactants, and the constituents B_j produced. In general, an equilibrium reaction is not only made up of an elementary reaction, but several parallel or successive reactions, for example of the following type

$$A \longrightarrow B \quad , \quad B \longrightarrow C$$

or

$$A \rightleftharpoons B$$

or

$$A + B \rightleftharpoons X \quad , \quad X \rightleftharpoons C + D$$

We will suppose that, in the reactions called "elementary", The reaction rate is assumed to be proportional to the product of the concentrations of the reactants.

2.5.3.2 Elementary reactions

We will assume that the elementary reactions satisfy the law of mass action. The study of the speed of a chemical reaction is done by chemical kinetics. In the following two experiments we study some of the factors influencing the speed of a chemical reaction. Most chemical reactions take place in several stages, that is to say, they evolve by successive elementary chemical reactions. For example, the overall reaction

$$A + B + C \rightarrow D + E$$

could happen in two stages

$$\begin{aligned} A + B &\rightarrow D + X \\ X + C &\rightarrow E \end{aligned}$$

Both stages are elementary reactions. Each step will have its own speed and the speed of the overall reaction will be a function of these two speeds. The series of steps through which the reaction takes place is called the reaction mechanism. In some cases one of the steps will be much slower than the others, so the speed of the overall reaction will be essentially equal to the speed of the slower reaction.

The speed of a chemical reaction depends on several parameters:

- Concentration of reagents,
- Temperature,
- Solvent used,
- Possible presence of a catalyst.

A catalyst is a substance which, added to a reaction mixture, accelerates the reaction without being consumed in it. This acts by reducing the activation energy of the reaction considered. In biological media, it is the enzymes that play the role of catalyst. An enzyme is a proteinaceous substance that allows metabolic reactions to take place at a sufficient rate at body temperature. see Duvaut [32]. Either the reaction

$$A + B \rightarrow C$$

the speed v of the reaction is given by the variation in the concentrations of A, B or C as a function of time:

$$V = \frac{-d\,[A]}{dt} = \frac{-d\,[B]}{dt} = \frac{-d\,[C]}{dt}\;[ms^{-1}]$$

We find, experimentally, that the speed depends on the concentration of the reactants according to the law of speed:

$$V = \frac{-d\,[A]}{dt} = k\,[A]^x\,[B]^y$$

where

k is the rate constant for the reaction considered (attention: k depends on temperature and solvent).

x and y are the partial orders of the reaction with respect to A and B respectively.

The global order is given by $(x + y)$.

The expressions of the speed law for different orders are then:

- Zero order: speed $= k$ (constant independent of the concentration).
- first global order: speed$= k\,[A]$ or $k\,[B]$
- second global order: speed $= k\,[A][A].[B]$ or $k[A]^2$ or $k\,[B]^2$
- third global order: speed $= k\,[A].[B].[C]$ or $k[A]^2\,[B]$ etc.

The variation in the concentration of the reactants as a function of time can be obtained by integrating the differential equation giving the law of speed.

Zero order

$$\begin{aligned} V &= \frac{-d[A]}{dt} = k \\ d[A] &= -kt \end{aligned}$$

Integration between 0 and t donne : $[A]_t = [A]_0 - kt$ (t = time), where $[A]_0$ is the concentration of A at time $t = 0$, and $[A]_t$ is the concentration of A at time t.

A zero-order reaction is characterized by a linear dependence of the concentration: $[A]$ as a function of time. The constant k is measured in $[m.s^{-1}]$.

First order

$$\begin{aligned} V &= \frac{-d[A]}{dt} = k[A]^2 \\ \frac{d[A]}{[A]^2} &= -kdt \end{aligned}$$

After integration we find

$$\frac{1}{[A]_t} - \frac{1}{[A]_0} = kt$$

A second order reaction is characterized by a linear dependence of $\frac{1}{[A]}$ as a function of time. The constant is measured in $[m^{-1}s^{-1}]$.

Law of order two Consider the example of ammonia

$$N_2 + 3H_2 \longrightarrow 2NH_3$$

whose mechanism can be explained by the introduction of an intermediate state X

$$\begin{aligned} &N_2 + 3H_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} X \\ &X \xrightarrow{k_2} NH_3 + NH_3 \end{aligned}$$

CHAPTER 3

Some reaction-diffusion models in bioscience

This chapter presents several models involving reaction diffusion systems in biology, medicine, ecology, biochemistry and engineering. The models were collected from published articles and specialist books. Most of them are similar to the models studied in the last three chapters of this thesis.

3.1 Reaction-diffusion models in chemical physics

3.1.1 The Belousov-Zhabotinskii model

The Belousov-Zhabotinskii reaction consists of the metal-ion-catalyzed oxidation by bromate ion of brominated organic materials. This reaction is a visually dramatic phenomenon for that a mathematical model of ten chemical reactions with seven intermediates has been developed (cf. [41]). The chemical reaction scheme of this simplification is given by

$$\begin{aligned} &A_1+Y\to X, \quad X+Y\to P_1, \quad A_2+X\to 2X+Z \\ &2X\to P_2, \qquad Z\to \gamma Y, \end{aligned}$$

Here A_1 and A_2 are reactants that are considered as known constants, P_1 and P_2 are products, γ is the stoichiometric factor, and X, Y and Z are the concentrations of the intermediates $HBrO_2$ (Bromous acid), Br^-(Bromide Ion) and Ce (IV) (Cerium), respectively. If we apply the law of mass action to reaction-diffusion the resulting equations describing the dynamics of the oregonator model are given by

$$\begin{cases} \dfrac{\partial X}{\partial t} - D_1 \nabla^2 X = -k_1 XY + k_2 A_2 X - 2k_3 X^2 + k_4 A_1 Y \\ \dfrac{\partial Y}{\partial t} - D_2 \nabla^2 Y = -k_1 XY + \gamma k_5 Z - k_4 A_1 Y \\ \dfrac{\partial Z}{\partial t} - D_3 \nabla^2 Z = k_2 A_2 X - k_5 Z \end{cases}$$

where D_i are the diffusion coefficients and k_i, $1 \le i \le 5$, are the forward rate constants. Some numerical values of A_1, A_2, and k_i are given by $A_1 = A_2 = 0.06\ M$, $k_1 = 1.6 \times 10^9\ Ms^{-1}$, $k_2 = 8 \times 10^3 Ms^{-1}$, $k_3 = 4 \times 10^7 Ms^{-1}$ and $k_4 = 1.34\ Ms^{-1}$. The constants k_5 and γ are expendable.

3.1.2 A gas-liquid interaction model

Consider a dissolved gas A and a dissolved reactant B that interact in a bounded diffusion medium Ω. The chemical reaction scheme is given by $A + k_1 B \rightarrow k_2 P$ and is called the second order reaction, where k_1 and k_2 are the rate constants and P is the product. Denote by $u \equiv u(x)$ and $v \equiv v(x)$ the concentrations of the dissolved gas A and the reactant B, respectively. Then the above reaction scheme leads to the coupled reaction-diffusion system

$$\begin{cases} u_t - D_1 \nabla^2 u = f_1(x,u,v) \\ v_t - D_2 \nabla^2 v = f_2(x,u,v) \end{cases} \quad \text{in } D$$

The boundary condition is given either in the form

$$\mathbf{B}_1 u = h_1(x), \quad \mathbf{B}_2 v = h_2(x) \quad \text{on } \partial D$$

or in the special form $\mathbf{B}_1 = \mathbf{B}_2 \equiv \mathbf{B}$, that is

$$\mathbf{B} u = h_1(x), \quad \mathbf{B} v = h_2(x), \quad \text{on } \partial D$$

with

$$f_1(u,v) = -\sigma_1 uv, \quad f_2(u,v) = -\sigma_2 uv$$

where σ_1 is the rate constant and $\sigma_2 = k_1 \sigma_1$. In a more general reaction scheme called the (m,n) the order reaction, f_1 and f_2 are given by

$$f_1(x,u,v) = -\sigma_1 u^m v^n + q_1(x), \quad f_2(x,u,v) = -\sigma_2 u^m v^n + q_2(x)$$

where $m \ge 1, n \ge 1$ are constants and $q_i(x) \ge 0$, $i = 1,2$, are possible internal sources.

Remark 3.1. *This model, as well as the following models similar to it; has been studied in detail by K.I. Saffidine and S. Mesbahi, and the results obtained are the subject of an article sent for publication in the journal "MATHEMATICAL COMMUNICATIONS".*

3.1.3 Heat-Mass transfer in chemical reactors

In the process of chemical reactions as well as in the theory of combustion, where both temporal and spatial variations are taken into consideration the equations for the mass concentration and temperature. In the case of a single irreversible chemical reaction in a porous medium as well as in the classical problem of thermal ignition the equations for the chemical concentration (or combustible material) u and the temperature v become

$$\begin{cases} u_t - D_1\nabla^2 u = -\sigma_1 u^p f(v) \\ v_t - D_2\nabla^2 v = \sigma_2 u^p f(v) \end{cases} \text{in } D$$

where σ_1, σ_2 are positive constants, $p \geq 1$ is the order of reaction, and

$$f(v) = \exp(\gamma - \frac{\gamma}{v}) \quad (\gamma > 0)$$

The physical meaning of the constants σ_1, σ_2, γ and the derivation of the reaction function $f(v)$ have been discussed in [94].

3.1.4 A diffusion model with temperature feedback

One of the fundamental problems of reactor physics is the determination of neutron density and temperature distribution as a function of time and space. Because of the complexity of the problem various simplified models have been proposed. In this section we consider the adiabatic case with or without the diffusion effect on temperature. This leads to the consideration of the system

$$\begin{cases} u_t - D_1\nabla^2 u = u(a - bv) \\ v_t - D_2\nabla^2 v = cu \end{cases} \text{in } D$$

where a, b, and c are constants and $c > 0$ temperature is neglected we set $D_2 = 0$ and ignore the boundary condition for v.

$$f_1(u,v) = u(a - bv) \quad , \quad f_2(u,v) = cu$$

3.2 Reaction-diffusion models in biomedical

3.2.1 Cell dynamics with extracellular regulation

We will assume in this section that cell density is sufficiently small such that cells do not prevent random motion of each other and convective motion of the medium does not occur. Cell adhesion is also neglected, so that they move independently of each other. Let $C = (C_1,\dots,C_n)$ be the vector of cell concentrations and $u = (u_1,\dots,u_m)$ the vector of concentrations of extracellular substances. Assuming that the rates of self-renewal, differentiation and apoptosis depend on cell concentrations and extracellular variables, we get the reaction-diffusion system

$$\frac{\partial C}{\partial t} = D_c \Delta C + F(C,u) \tag{3.1}$$

$$\frac{\partial u}{\partial t} = D_u \Delta u + G(C,u) \tag{3.2}$$

where $F = (F_1,\dots,F_n)$ are the rates of cell production, $G = (G_1,\dots,G_n)$ are the rates of production of extracellular species. By the rate of cell production we understand the overall rate of change of cell concentration taking into account their self-renewal, proliferation, apoptosis. Similarly, the functions G_i take into account production, consumption and destruction of the corresponding biochemical species. We will assume for simplicity that the matrices of diffusion coefficients are diagonal.

Self-renewal and apoptosis Consider a cell population which consists of a single cell type and denote its concentration by C. These cells can divide and give similar cells (self-renewal) or die by apoptosis. Suppose that there exists one extracellular variable u. We consider equations (3.1), (3.2) with the functions

$$F(C,u) = (k_s(u) - k_a(u))C, \quad G(C,u) = qC - \sigma u$$

where $k_s(u)$ and $k_a(u)$ are the rates of self-renewal and apoptosis, which depend on the extracellular variable, q and σ are positive numbers. We suppose that k_s and k_u are sufficiently smooth positive functions. The extracellular species is produced by cells themselves, so that the first term in the function G is proportional to the cell concentration.

Consumption of nutrients As before, we consider a cell population which consists of cells of the same type. Cells can consume nutrients and divide. The concentration of nutrients is denoted by u. where the functions F and G are given by the equalities:

$$F(C,u) = k_1 uC, \quad G(C,u) = -k_2 uC$$

k_1 and k_2 are some positive constants. Here we assume that cell proliferation is proportional to the cell concentration and to the concentration of nutrients, and consumption of nutrients is also proportional to the same concentrations. For more details, see Chapter10 in [116].

3.2.2 An enzyme model

Biochemical reactions are continually taking place in all living organisms and most of them involve proteins called enzymes, which act as remarkably efficient catalysts. Enzymes react selectively on definite compounds called substrates. For example, haemoglobin in red blood cells is an enzyme and oxygen, with which it combines, is a substrate. Enzymes are important in regulating biological processes, for example, as activators or inhibitors in a reaction. To understand their role we have to study enzyme kinetics which is mainly the study of rates of reactions, the temporal behavior of the various reactants and the conditions which influence them. Introductions with a mathematical bent are given in the books by Rubinow (1975), Murray (1977) and the one edited by Segel (1980). Biochemically oriented books, such as Laidler and Bunting (1977) and Roberts (1977), go into the subject in more depth.

There are enzyme reaction models governed by the coupled reaction-diffusion equations. One of these models describes a substrate S_1 and a cosubstrate S_2 in an enzyme membrane that separates two reservoirs along the longitudinal axis of a cylindrical domain Ω. In an artificial membrane proposed in [54] the enzyme is taken as uricase and the substrate and cosubstrate are uric acid and oxygen. The kinetics are those of the enzyme uricase, which catalyzes an irreversible reaction involving the two substrates. An empirical expression for the reaction rate is given by

$$R(S_1, S_2) = K_1 S_1 S_2 \left(K_2 + S_1 + K_3 S_1^2\right)^{-1}$$

where K_i, $i = 1,2,3$, are positive constants related to the various reaction rates. Let $S_1^{(o)}, S_2^{(o)}$ be the fixed concentrations of the two substrates S_1, S_2 in the surrounding reservoirs. Under the assumption of a possible linear absorption from the reservoir the law of conservation of mass yields the following balance relation:

$$\begin{cases} (S_1)_t - D_1\nabla^2 S_1 = -R(S_1,S_2) + K_1'\left(S_1^{(o)} - S_1\right) \\ (S_2)_t - D_2\nabla^2 S_2 = -R(S_1,S_2) + K_2'\left(S_2^{(o)} - S_2\right) \end{cases}$$

where K_1' and K_2' represent the rates of absorption, including the case of no absorption when $K_1' = K_2' = 0$. By letting $u = \frac{S_1}{K_2}$, $v = \frac{S_2}{K_2}$ the above system is reduced to the form

$$\begin{cases} u_t - D_1\nabla^2 u = -\sigma_1 uv\left(1+u+b_1u^2\right)^{-1} + a_1(\rho_1 - u) \\ v_t - D_2\nabla^2 v = -\sigma_2 uv\left(1+u+b_2u^2\right)^{-1} + a_2(\rho_2 - v) \end{cases} \quad \text{in } D$$

where σ_i, b_i, and ρ_i are positive constants and $a_i \geq 0$, $i = 1,2$. These physical constants are related to the constants K_i, K_i', $S_1^{(0)}$ and $S_2^{(0)}$ in an obvious way. See [94].

3.2.3 Model in protein networks

The following reaction-diffusion system models protein-protein interactions in a signaling network that regulates the actin cytoskeleton in a malignant breast cell

$$\begin{cases} \dfrac{\partial u_i}{\partial t} - d_i\Delta u_i = r_i(u,k) & \text{in } \Omega\times(0,T) \\ \dfrac{\partial u_i}{\partial t} = 0 & \text{on } \partial\Omega\times(0,T) \\ u_i(x,0) = u_i^0(x) & \text{in } \Omega\times(t=0) \end{cases}, \quad 1 \leq i \leq N$$

Assume that the domain Ω is an open, bounded and connected subset of $\mathbb{R}^\eta$, where $u_1(x,t),\ldots,u_N(x,t)$ are the concentration levels of N proteins, $d_1,\ldots,d_N \in (0,+\infty)^N$ are the mass diffusivities, and $k_1,\ldots,k_M \in (0,+\infty)^M$ are the rate constants. Assume that the initial value $u^0 \in L^\infty(\Omega)^N$ and $u^0(x) > 0$ for all $x \in \Omega$. We call r_i the reaction function of the i-th protein. The structure of the reaction function is determined by two factors: the reaction kinetics model and the protein network topology. For more details see [120].

3.3 Reaction-diffusion systems in physiology

3.3.1 Model for glioma tumor growth

Mathematical modelling of tumor growth is one of the most useful and inexpensive approaches to determine and predict the stage, size and progression of tumors in realistic geometries. Moreover, these models has been used to get an insight into cancer growth and invasion and in the analysis of tumor size and geometry for applications in cancer treatment and surgical planning. The following model presents a general perspective of the use of models based on reaction-diffusion equations not only for the description of tumor growth in gliomas, addressing for processes such as tumor heterogeneity, hypoxia, dormancy and necrosis, but also its potential use as a tool in designing optimized and patient specific therapies.

$$\begin{cases} \dfrac{\partial C}{\partial t} = D_C \dfrac{\partial^2 C}{\partial x^2} + F(C,P,I) - \sigma C \\ \dfrac{\partial I}{\partial t} = D_I \dfrac{\partial^2 I}{\partial x^2} + a_{11} C - a_{12} I \\ \dfrac{\partial P}{\partial t} = a_{21} C - a_{22} P \end{cases}$$

Here C is the concentration of cells, I is the concentration of inhibitor and P of promoter, a_{ij} and σ are positive constants, F is the rate of cell division given by the expression

$$F(C,P,I) = \frac{rC}{\epsilon C + 1} \cdot \frac{P}{I+1}$$

3.3.2 Model in Atherosclerosis

Atherosclerosis is an inflammatory disease. The atherosclerosis process starts when low-density lipoproteins (LDLs) enter the intima of the blood vessel, where they are oxidized (ox-LDLs). The anti-inflammatory response triggers the recruitment of monocytes. Once in the intima, the monocytes are transformed into macrophages and foam cells, leading to the production of inflammatory cytokines and further recruitment of monocytes. This auto-amplified process leads to the formation of an atherosclerotic plaque and, possibly, to its rupture. In this paper we develop two mathematical models based on reaction-diffusion equations in order to explain the inflammatory process. This model explains the inflammatory process and shows that atherosclerosis develops as a reaction-diffusion wave, see [116] page 516.

Two-dimensional model is formulated for the concentration M of cells in the intima and for the concentration A of cytokines [33]

$$\frac{\partial M}{\partial t} = d_1 \Delta M - \beta M \tag{3.3}$$

$$\frac{\partial A}{\partial t} = d_2 \Delta A + f(A) M - \gamma A + b \tag{3.4}$$

This system is considered in the two-dimensional domain $\Omega = \{-\infty < x < \infty, 0 < y < L\}$, which corresponds to the longitudinal cross section of the blood vessel wall. Here $y = L$ corresponds to the boundary between blood flow and intima. The boundary conditions are as follows:

$$y = 0 : \frac{\partial M}{\partial y} = \frac{\partial A}{\partial y} = 0, \quad y = L : \frac{\partial M}{\partial y} = g(A), \quad \frac{\partial A}{\partial y} = 0$$

3.3.3 Model applied to HIV infection

The basic model of virus dynamics as proposed by Nowak and Bangham to study HIV infection [88], and later adapted to HBV [89] and HCV [87] infection. The basic model can be formulated as a system of three differential equations

$$\begin{aligned}
\dot{T}(t) &= \lambda - dT - \beta V T \\
\dot{I}(t) &= \beta V T - aI \\
\dot{V}(t) &= kI - mV
\end{aligned}$$

where susceptible host cells (T) are produced at a rate λ, die at a rate dT and become infected by virus at a rate βVT. Infected cells (I) die at a rate all. Free virus (V) is produced by infected cells at a rate kI and decays at a rate mV.

K. Wang and W. Wang [117] assumed that susceptible host cells and infected cells are hepatocyte and cannot move under normal conditions and neglected their mobility, while viruses can move freely and their motion follows a Fickian diffusion. They proposed the following model:

$$\begin{aligned}
\frac{\partial T}{\partial t} &= \lambda - dT(x,t) - \beta V(x,t)T(x,t) \\
\frac{\partial I}{\partial t} &= \beta V(x,t)T(x,t) - aI(x,t) \\
\frac{\partial V}{\partial t} &= d_v \Delta V + kI(x,t) - mV(x,t)
\end{aligned}$$

where $T(x,t), I(x,t)$, and $V(x,t)$ represent the densities of uninfected cells, infected cells, and free virus at location x and time t, respectively, d_V is the diffusion coefficient. They assumed that the domain is the whole real line and proved the existence of traveling waves.

3.3.4 Model for viral infection and immune response

It is a model for model for virus infection and immune response to account for the spatial effects of processes, such as diffusion transport of virions, biomolecules, and cells. This leads to two different models of nonlinear EDP, a first where cells and biomolecules diffuse (which we call the reaction-diffusion model) and a second where only biomolecules can diffuse (the hybrid model).

Let $\Omega \subset \mathbb{R}^N$ $(N = 2,3)$ be a bounded domain with Lipschitz boundary Γ, and let $T > 0$. We consider in $\Omega \times [0,T]$ a reaction-diffusion system

$$\begin{cases} \partial_t W = d\Delta W - iW - vW \\ \partial_t I = d\Delta I - \mu_I I + vW \\ \partial_t R = d\Delta R + iW \\ \partial_t v = d_v \Delta v - \mu_v v + \alpha_v I - \alpha_4 vW \\ \partial_t i = d_i \Delta i - \mu_i i + \alpha_i I - \alpha_3 iW \end{cases}$$

where W wild-type cells, I infected cells, R resistant cells, v virions and i interferons, with boundary conditions

$$\begin{cases} \nabla W.n(\sigma,t) = 0 & \text{on } \Gamma \times [0,T] \\ \nabla I.n(\sigma,t) = 0 & \text{on } \Gamma \times [0,T] \\ \nabla R.n(\sigma,t) = 0 & \text{on } \Gamma \times [0,T] \\ \nabla v.n(\sigma,t) = 0 & \text{on } \Gamma \times [0,T] \\ \nabla i.n(\sigma,t) = 0 & \text{on } \Gamma \times [0,T] \end{cases}$$

and initial conditions

$$\begin{cases} W(x,0) = W_0(x) \\ I(x,0) = I_0(x) \\ R(x,0) = R_0(x) \\ v(x,0) = v_0(x) \\ i(x,0) = i_0(x) \end{cases}$$

For more details see [69].

3.3.5 The Fitz Hugh-Nagumo model in Neurophysiology

When study of nerve impulses on nerve axons Hodgkin and Huxley proposed a set of differential equations to describe the ionic and electrical events occurring during the transmission of an impulse along an axon, which is usually the filament carrying signals from the nerve cell body to other parts of the organism. Their formulation is based on the assumption that an axon behaves like a cylindrical electrical cable with conducting core and partially insulating sheath. A simplified formulation has been suggested by FitzHugh ; and by Nagumo, Arimoto and Yoshizawa which appears to preserve most of the qualitative features of the original system, and yet is more amenable to analytical manipulation. This simplification leads to the so-called FitzHugh-Nagumo equations, which are given by the following coupled system of two equations where u denotes the electrical potential across the axonal membrane and v represents a pair of variables in the original Hodgkin-Huxley model and

$$\begin{cases} u_t - D_1\nabla^2 u = \sigma u(u-\theta)(1-u) - bv & (t>0,\ x\in\Omega) \\ v_t = cu - av & (t>0,\ x\in\Omega) \end{cases}$$

where u denotes the electrical potential across the axonal membrane and v represents a pair of variables in the original Hodgkin-Huxley model. The physical constants D_1, σ, a, b, c, and θ are all positive, and $0<\theta<1$. This system has been given considerable attention in relation to the qualitative property of the solution, including the traveling wave solution in $\mathbb{R}$. See Murray [79].

3.3.6 Model of Calcium ions in dendritic spines

Ca^{2+} ions inside the dendritic spine play a crucial role in the twitching motion and synaptic plasticity, and therefore in cognitive processes like learning and memory. We consider calcium ions interacting with some proteins that have 4 binding sites for the ions. Both calcium ions and proteins diffuse all within a moving domain Ω (a dendritic spine) full of cytoplasm. Let M be the concentration of calcium ions, U the total number of binding sites and W the total number of free sites and V the cytoplasmic flow field. If we suppose that the proteins are fixed in the cytoplasm (i.e. they do not diffuse) then the model is

$$\begin{cases} \partial_t M = \nabla\cdot[D\nabla M - VM] - k_1[A-U] \\ \partial_t U = -k_1 MU + k_{-1}[A-U] \\ V = \nabla\Phi, \quad \Delta\Phi = 0 \end{cases}$$

with initial conditions

$$\begin{cases} M(x,0) = m_0(x) \\ U(x,0) = A(x) \end{cases}$$

and boundary conditions

$$\begin{cases} M(\sigma,t) = 0 & \text{on} \quad \Gamma_a\times[0,T] \\ (D\nabla M - VM).n(\sigma,t) = 0 & \text{on} \quad \Gamma_r\times[0,T] \\ \nabla\Phi.n(\sigma,t) = a(\sigma)\lambda(t) & \text{on} \quad \Gamma\times[0,T] \end{cases}$$

For a better understanding see [69].

3.4 Reaction-diffusion systems applied in ecology

3.4.1 The Volterra-Lotka Competition Model

The competition between two competing species in an ecological system has been traditionally formulated in relation to time evolution with uniform population distributions in the habitat. This leads to the well-known Volterra-Lotka competition model. If the presence of the u -population species encourages the growth of the v -population species and vice versa then the governing equations for u and v become

$$-D_1\nabla^2 u = u(a_1 - b_1 u + c_1 v)$$
$$-D_2\nabla^2 v = v(a_2 + b_2 u - c_2 v)$$

where a_i, b_i, and c_i are positive constants, $i = 1,2$. See [94]. This model is a good example of the problem studied in chapter 4.

3.4.2 The Volterra prey-predator model

When the two competing species in the previous model are replaced by a prey and a predator species the equations governing the prey population u and the predator population v are given by

$$\begin{cases} u_t - D_1\nabla^2 u = u(a_1 - b_1 u - c_1 v) \\ v_t - D_2\nabla^2 v = v(a_2 + b_2 u - c_2 v) \end{cases} \text{in } D$$

where a_i, b_i, and $c_i, i = 1,2$, are positive constants. The physical meaning is that in the presence of the prey u the population of the predator increases in u with an increasing rate $b_2 u$.

3.4.3 A competition model

The following two-species Lotka-Volterra competition model is

$$\begin{cases} u_t - d_1(x)\nabla^2 u^{\alpha_1} = u(a_1 - b_1 u - c_1 v) \\ v_t - d_2(x)\nabla^2 v^{\alpha_2} = v(a_2 - b_2 u - c_2 v) \quad (t > 0, x \in \Omega) \end{cases}$$

under the boundary and initial conditions specific, where for each $i = 1,2, \alpha_i, a_i, b_i$ and c_i are positive constants with $\alpha_i > 0, d_i(x) > 0$ on $\bar{\Omega}$ and $(u_0, v_0) > (0,0)$ in Ω. It is known that in the density independent case $\alpha_1 = \alpha_2 = 1$,the solution (u,v) converges to a positive steady-state solution for a certain class of initial functions if some additional condition is satisfied.

3.5 Reaction-diffusion systems applied in epidemiology

3.5.1 An SIS epidemic model

Allen et *al*. in [9] proposed a frequency-dependent SIS (susceptible-infected-susceptible) reaction-diffusion model for a population living in a continuous spatial habitat, which reads as follows

$$\begin{cases} \dfrac{\partial S}{\partial t} - d_S \Delta S = -\dfrac{\beta(x)SI}{S+I} + \gamma(x)I & x \in \Omega,\ t > 0 \\ \dfrac{\partial I}{\partial t} - d_I \Delta I = \dfrac{\beta(x)SI}{S+I} - \gamma(x)I & x \in \Omega,\ t > 0 \\ \dfrac{\partial S}{\partial \nu} = \dfrac{\partial I}{\partial \nu} = 0 & x \in \partial\Omega,\ t > 0 \\ S(x,0) = S_0(x) \geq 0,\ I(x,0) = I_0(x) \gneqq 0 & x \in \Omega \end{cases} \tag{3.5}$$

Here, S and I represent the density of susceptible and infected individuals at location x and time t respectively; d_S and d_I are positive constants for the susceptible and infected populations respectively; and β and γ are positive Hölder continuous functions on $\bar{\Omega}$ that represent the rates of disease transmission and recovery at x respectively. The habitat $\Omega \subset \mathbb{R}^n$ is a bounded domain with smooth boundary $\partial\Omega$, and the homogeneous Neumann boundary conditions mean that no population flux crosses the boundary $\partial\Omega$.

3.5.2 An SIS epidemic model with spontaneous infection in a spatially heterogeneous environment

The heterogeneity of spatial environment and the movement of the individual play an important role in the theory of epidemiology. The following model is one among many mathematical models for studying the effects of migration and spatial heterogeneity on disease transmission

$$\begin{cases} \dfrac{\partial S}{\partial t} - d_S \Delta S = -\dfrac{\beta(x)SI}{S+I} + \gamma(x)I, & x \in \Omega,\ t > 0 \\ \dfrac{\partial I}{\partial t} - d_I \Delta I = \dfrac{\beta(x)SI}{S+I} - \gamma(x)I, & x \in \Omega,\ t > 0 \\ \dfrac{\partial S}{\partial \nu} = \dfrac{\partial I}{\partial \nu} = 0, & x \in \partial\Omega,\ t > 0 \\ S(x,0) = S_0(x) \geq 0,\ I(x,0) = I_0(x) \gneqq 0 & x \in \Omega \end{cases}$$

where d_S, d_I, β, γ, S and I have the same epidemiological interpretation as in (3.5). Here we also assume that the spontaneous infection rate η depends on spatial location x, is positive and Hölder continuous functions on $\bar{\Omega}$. The function η models the propagation of the disease due to imported cases of the infection. In order to know how to study it see [114].

3.5.3 A model of transmission of the HIV virus within a population

This system may be viewed as a model of a diffusive epidemic, which describes the HIV virus transmission within a population. The population considered contains susceptible individuals S_1, S_2 and infected ones U_1, U_2 divided into two groups, where indices 1 and 2 indicate which group they belong to. The constants Λ_1 and Λ_2 represent the influx rates of new susceptible individuals in each group. μ is the mortality rate, the ratio of the number of deaths from the disease to the total number of cases per unit of time of that disease. The parameters β_i describe the rate at which the disease is spread among the individuals per unit of time, and T is the total population.

$$\begin{cases} \dfrac{\partial S_1}{\partial t} - d_1 \Delta S_1 = \Lambda_1 - \beta_1 \frac{S_1 \varphi(U_1)}{T} - \beta_2 \frac{S_1 \varphi(U_2)}{T} - \mu S_1 & \text{in } \mathbb{R}^+ \times \Omega \\ \dfrac{\partial U_1}{\partial t} - d_2 \Delta U_1 = \beta_1 \frac{S_1 \varphi(U_1)}{T} + \beta_2 \frac{S_1 \varphi(U_2)}{T} - \sigma_1 U_1 & \text{in } \mathbb{R}^+ \times \Omega \\ \dfrac{\partial S_2}{\partial t} - d_3 \Delta S_2 = \Lambda_2 - \beta_3 \frac{S_2 \varphi(U_1)}{T} - \beta_4 \frac{S_2 \varphi(U_2)}{T} - \mu S_2 & \text{in } \mathbb{R}^+ \times \Omega \\ \dfrac{\partial U_2}{\partial t} - d_4 \Delta U_2 = \beta_3 \frac{S_2 \varphi(U_1)}{T} + \beta_4 \frac{S_2 \varphi(U_2)}{T} - \sigma_2 U_2 & \text{in } \mathbb{R}^+ \times \Omega \end{cases}$$

with the homogeneous Neumann boundary conditions

$$\frac{\partial S_i}{\partial v} = \frac{\partial U_i}{\partial v} = 0 \quad \text{on } \mathbb{R}^+ \times \partial\Omega, \quad i = 1, 2$$

and the continuous initial data $S_{1,0}, U_{1,0}, S_{2,0}, U_{2,0}$

$$S_i(0,x) = S_{i,0}(x) \geq 0, \quad U_i(0,x) = U_{i,0}(x) > 0 \quad \text{in } \Omega, \quad i = 1, 2$$

Here, Ω is a bounded domain of class C^1 in $\mathbb{R}^n$, with boundary $\partial\Omega$. The nonlinearity φ is assumed to be a nonnegative and continuously differentiable function on $[0, +\infty)$. For more details, see [115].

3.5.4 SIR epidemic reaction-diffusion model

We consider the following delayed SIR epidemic model with nonlinear incidence rate and spatial diffusion where S,I and R are susceptible, infectious and recovered classes, respectively. B is the recruitment rate of new individuals is into the susceptible class. μ_1,μ_2 and μ_3 are positive constants representing the death rates of the classes, respectively. The average time spent in class I before recovery is $\frac{1}{\gamma}, \beta$ is the contact number and α determines the level at which the force of infection saturates and the positive constants d_S, d_l and d_R denote the corresponding diffusion rates for the susceptible, infected and removed populations, respectively.

$$\begin{cases} \dfrac{\partial S}{\partial t} = d_S \Delta S + B - \mu_1 S(x,t) - \dfrac{\beta S(x,t) I(x,t-\tau)}{1+\alpha I(x,t-\tau)} \\ \dfrac{\partial I}{\partial t} = d_I \Delta I + \dfrac{\beta S(x,t) I(x,t-\tau)}{1+\alpha I(x,t-\tau)} - \left(\mu_2+\gamma\right) I(x,t) \\ \dfrac{\partial R}{\partial t} = d_R \Delta R + \gamma I(x,t) - \mu_3 R(x,t) \end{cases}$$

assumed that $d_S = d_I = d_R$ and proved the existence of traveling waves solutions for the model. with homogeneous Neumann boundary conditions

$$\frac{\partial S}{\partial v} = \frac{\partial I}{\partial v} = 0, \quad \text{on } \partial\Omega \times (0,+\infty)$$

and initial conditions

$$S(x,s) = S_0(x,s) \geq 0, \quad I(x,s) = I_0(x,s) \geq 0, \quad (x,s) \in \Omega \times [-\tau, 0]$$

For more details see [120]

3.5.5 The Kermack-McKendrick model with diffusion

In the description of the spread of infection in some epidemic problems a classical model for the susceptible and infective populations is the well-known Kermack-McKendrick equation. When the effect of diffusion is taken into consideration an extended version of this model is given by

$$\begin{cases} u_t - D_1 \nabla^2 u = -a_1 u - b_1 u \int_\Omega K(x,\xi) v(t,\xi) d\xi \\ v_t - D_2 \nabla^2 u = -a_2 u - b_2 u \int_\Omega K(x,\xi) v(t,\xi) d\xi \end{cases} \quad \text{in} \quad D$$

where u and v represent the susceptible and infective populations, respectively; a_i and $b_i, i = 1,2$, are the rate constants; and $K(x,\xi)$ is a transfer function. The inclusion of the diffusion terms allows the migration of both infective and susceptible populations, and the integral term gives a transfer mechanism of infection governed by a nonlocal law: the presence of infective population at $x \in \Omega$ influences both populations in a small region surrounding x. This interpretation leads to the assumption that $a_i \geq 0, b_i > 0$, and $K(x,\xi)$ is bounded nonnegative Hölder continuous in $\Omega \times \Omega$. this system becomes $(u_1,u_2) = (u,v) \equiv \mathbf{u}$ and

$$\begin{cases} f_1(t,x,\xi,u_1,\mathbf{u}) = -b_1 K(x,\xi)u(t,x)v(t,\xi) \\ f_1(t,x,\xi,u_2,\mathbf{u}) = -b_2 K(x,\xi)u(t,x)v(t,\xi) \end{cases}$$

where $\mathbf{u} \equiv \mathbf{u}(t,\xi)$. By the nonnegative property of $K(x,\xi)$ the reaction function $f = (f_1, f_2)$ is mixed quasi-monotone reaction-diffusion systems in Neurophysiology.

The study of synapses is a very recurrent and important topic that lies in the intersection of Medicine, Neurology, Biology and Chemistry. The current technology of microscopes has shown that the dendritic spines, the smallest structures of the neuron and the part responsible of the synapses, possess a twitching motion.

CHAPTER 4

Existence Result for Positive Solution of a Degenerate Reaction-Diffusion System via a Method of Upper and Lower Solutions

The aim of this paper is to prove the existence of positive maximal and minimal solutions for a class of degenerate elliptic reaction-diffusion systems, including the uniqueness of the positive solution. To answer these questions, we use a technique described by Pao based on the method of upper and lower solutions, its associated monotone interactions and various comparison principles.

The work constituting this chapter is the subject of an article published in an international journal specialized in Mathematics (Nonlinear Dynamics and Systems Theory), in collaboration with S. Mesbahi.

4.1 Introduction

Reaction-diffusion systems are widely used in biology, ecology, engineering, physics and chemistry. What we observe in modern scientific studies is the great interest of scientists in studying this type of systems; this confirms once again its importance in the development of applied and technological sciences. Various models and real examples can be found in various scientific fields, see Murray [78, 79]. The propagation of epidemics (Coronavirus, Hepatitis,...), population dynamics, migration of biological species are among many examples of such phenomena. There are many methods and techniques for studying these issues. The reader can see some of them in the works of Alaa and Mesbahi [5, 6, 73, 74], Abbassi et *al*. [1], Lions [65], Raheem [96] and the references therein.

In recent years, special attention has been paid to degenerate systems. However, most of the discussions relate to systems of two equations of the porous reaction medium type diffusion and with diffusion coefficients and specific reaction functions. This is because of their wide applications in various sciences. Among the important works on degenerate systems, we mention, for example, Alaa et *al*. [6], Al-Hdaibat et *al*. [8], Anderson [13], where we find techniques and methods of treatment.

The aim of this paper is to show the existence of positive maximal and minimal solutions for a quasilinear elliptic degenerate system, including the uniqueness of the positive solution. The two elliptic operators of the system under consideration can degenerate in the sense that $D_1(0) = 0$ or $D_2(0) = 0$. To answer these questions, we use a technique described by Pao, based on the upper and lower solutions. For more details on this technique, see Pao et *al*. [94]-[95]. So, we need to construct suitable upper and lower solutions. We are therefore interested in studying the following system:

$$\begin{cases} -\mathbf{div}(D_1(u)\nabla u) = f(x,u,v) & \text{in } \Omega \\ -\mathbf{div}(D_2(v)\nabla v) = g(x,u,v) & \text{in } \Omega \\ u(x) = u_0(x)\ ,\ v(x) = v_0(x) & \text{on } \partial\Omega, \end{cases} \tag{4.1}$$

where Ω is a bounded domain in $\mathbb{R}^n$ $(n \geq 2)$ with the boundary $\partial\Omega$. D_1, D_2, f and g are prescribed functions satisfying the conditions in hypotheses (H_1) and (H_3). We remark that these two functions f and g verify simple properties, this allows us to choose them from a wide range. Below we will denote $C^\alpha(\Omega)$ to the space of Hölder continuous functions in Ω.

The results obtained in this paper can be applied to a large number of reaction-diffusion models, which arise in various fields of the applied science such as theory of shells, Brownian motion theory and many problems of physics and biology. In addition to the classical problems in the fields of mass-heat transfer, chemical reactors, and nuclear reactor dynamics, there are many recently developed models from enzyme kinetics, population growth, nerve axion problems, and others.

The system (4.1) can model the circulation of an ideal gas in a homogeneous porous medium with an isentropic flow. It can also model the steady-state of phenomena such as the heat propagation in a two-components combustible mixture, chemical processes, the interaction of two non-self-limiting biological groups, etc. We send the reader to see many models and applications in Friedman [39], Ladyženskaja et *al*. [60], Lei and Zheng [62], especially Pao [91, 93] and the references therein. For example, the steady-state of the Gas-Liquid Interaction Problem, when considering a dissolved gas **A** and a dissolved reactant **B** that interact in a bounded diffusion medium, is a special case of (4.1) with the reaction terms $f(u,v) = -\sigma_1 uv$, $g(u,v) = -\sigma_2 uv$, where σ_1 is the rate constant and $\sigma_2 = k_1\sigma_1$. In a more general reaction scheme called the (m,n) order reaction, the resulting equations are given by (4.1) with $f(x,u,v) = -\sigma_1 u^m v^n + q_1(x)$, $g(x,u,v) = -\sigma_2 u^m v^n + q_2(x)$, $m,n \geq 1$ are constants and $q_1(x), q_2(x) \geq 0$ are possible internal sources.

In the problems of molecular interactions and subsonic flows, a simple model for the density function u is given by (4.1) with the reaction function $f(u) = \sigma u^p$, with $\sigma > 0$, $p \geq 1$.

This model also describes the temperature in radiating bodies or gases and in nuclear reactors with positive temperature feedback. For more information on this model, and also to see other models, we refer the reader to Pao [91].

The rest of this paper is organized as follows. In the next section, we state our main result. In the third section, we provide some preliminary results on the scalar problem which we need in the proof of the main theorem. Next, we give some results concerning the approximate problem. The fifth section is devoted to proving the main result. Finally, we give an application to the problem under study. The paper ends with a concluding remarks and some perspectives.

4.2 Statement of the Main Result

In all that follows, we denote $\mathbf{u} \equiv (u,v)$, $\tilde{\mathbf{u}}_s \equiv (\tilde{u},\tilde{v})$, $\hat{\mathbf{u}}_s \equiv (\hat{u},\hat{v})$. The inequality $\hat{\mathbf{u}}_s \leq \tilde{\mathbf{u}}_s$ means that $\hat{u} \leq \tilde{u}$ and $\hat{v} \leq \tilde{v}$.

4.2.1 Assumptions

First, we have to clarify in which sense we want to solve our problem.

Definition 4.1. A pair of functions $\tilde{\mathbf{u}}_s \equiv (\tilde{u}, \tilde{v})$, $\hat{\mathbf{u}}_s \equiv (\hat{u}, \hat{v})$ in $C^2(\Omega) \cap C(\bar{\Omega})$ are called ordered upper and lower solutions of (4.1) if $\hat{\mathbf{u}}_s \leq \tilde{\mathbf{u}}_s$ and

$$\begin{cases} -\mathbf{div}(D(\hat{u})\nabla\hat{u}) \leq f(x,\hat{u},\hat{v}) & \text{in } \Omega \\ -\mathbf{div}(D(\hat{v})\nabla\hat{v}) \leq g(x,\hat{u},\hat{v}) & \text{in } \Omega \\ \hat{u}(x) \leq u_0(x)\ ,\ \hat{v}(x) \leq v_0(x) & \text{on } \partial\Omega \end{cases} \tag{4.2}$$

and $\tilde{u}$, $\tilde{v}$ satisfies (4.2) with inequalities reversed.

For a given pair of ordered upper and lower solutions $\tilde{\mathbf{u}}_s$ and $\hat{\mathbf{u}}_s$, we define

$$\begin{aligned} S_1^* &= \left\{u \in C(\bar{\Omega}) \mid \hat{u} \leq u \leq \tilde{u}\right\} \ ,\ S_2^* = \left\{v \in C(\bar{\Omega}) \mid \hat{v} \leq v \leq \tilde{v}\right\} \\ S^* &= \left\{\mathbf{u} = (u,v) \in \left(C(\bar{\Omega})\right)^2 \mid \hat{\mathbf{u}}_s \leq \mathbf{u} \leq \tilde{\mathbf{u}}_s\right\}. \end{aligned}$$

Now, we make the following assumptions:

(H_1) $f(x,.)$, $g(x,.) \in C^\alpha(\bar{\Omega})$ and $u_0(x)$, $v_0(x) \in C^\alpha(\partial\Omega)$.

(H_2) $D_1(u) \in C^2([0,M_1])$, $D_1(u) > 0$ in $(0,\ M_1]$, and $D_1(0) \geq 0$ with $M_1 = \|\tilde{u}\|_{C(\bar{\Omega})}$.
$D_2(v) \in C^2([0,M_2])$, $D_2(v) > 0$ in $(0,\ M_2]$, and $D_2(0) \geq 0$ with $M_2 = \|\tilde{v}\|_{C(\bar{\Omega})}$.

(H_3) $f(.,\mathbf{u})$, $g(.,\mathbf{u}) \in C^1(S^*)$, and

$$\frac{\partial f}{\partial v}(.,\mathbf{u}) \geq 0 \quad \text{and} \quad \frac{\partial g}{\partial u}(.,\mathbf{u}) \geq 0 \quad \text{for all } \mathbf{u} \in S^*.$$

(H_4) There exists a constant $\delta_0 > 0$ such that for any $x_0 \in \partial\Omega$ there exists a ball $\mathbf{K}$ outside of Ω with radius $r \geq \delta_0$ such that $\mathbf{K} \cap \bar{\Omega} = \{x_0\}$.

In the above system, we further assume $D_1(0) = 0$ or $D_2(0) = 0$.

Let $\gamma_1(x)$ and $\gamma_2(x)$ be smooth positive functions satisfying

$$\gamma_1(x) \geq \max\left\{-\frac{\partial f}{\partial u}(x,\ \mathbf{u})\ ;\ \mathbf{u} \in S^*\right\} \text{ and } \gamma_1(x) \geq C_1(x) + \delta_1 \tag{4.3}$$

$$\gamma_2(x) \geq \max\left\{-\frac{\partial g}{\partial v}(x,\ \mathbf{u})\ ;\ \mathbf{u} \in S^*\right\} \text{ and } \gamma_2(x) \geq C_2(x) + \delta_2 \tag{4.4}$$

for some constants δ_1, $\delta_2 > 0$, where $C_1(x)$ and $C_2(x)$ are analogous to $C(x)$ defined in Section 3 by the relations (4.11), i.e.,

$$\begin{aligned} C_1(x) &= -\mathbf{div}\nabla(\tilde{u})D_1'(\theta_1) - f_u(x,\theta_2) \\ C_2(x) &= -\mathbf{div}\nabla(\tilde{v})D_2'(\bar{\theta}_1) - g_v\left(x,\bar{\theta}_2\right). \end{aligned}$$

We define for all $\mathbf{u} \in S^*$

$$F(x,\mathbf{u}) = \gamma_1(x)u + f(x,\mathbf{u}) \quad \text{and} \quad G(x,\mathbf{u}) = \gamma_2(x)v + g(x,\mathbf{u}). \tag{4.5}$$

A typical example where the result of this paper can be applied is

$$\begin{cases} -\Delta u^{\lambda} = p(x)u^j v^k & \text{in } \Omega \\ -\Delta v^{\mu} = q(x)u^{\ell} v^m & \text{in } \Omega \\ u = v = 0 & \text{on } \partial\Omega, \end{cases} \tag{4.6}$$

where $\lambda,\ \mu > 1,\ j,\ k,\ \ell,\ m > 0$ and $p(x),\ q(x) > 0$ in Ω.

It is obvious that the problem (4.6) is a special case of (4.1) with

$$\begin{aligned} D_1(u) &= \lambda u^{\lambda-1} \ ,\ D_2(v) = \mu u^{\mu-1} \ ,\ u_0(x) = v_0(x) = 0 \\ f(x,u,v) &= p(x)u^j v^k \ ,\ g(x,u,v) = q(x)u^{\ell} v^m. \end{aligned}$$

Lemma 4.1. *$F(x,\mathbf{u})$ and $G(x,\mathbf{u})$ are nondecreasing functions in $\mathbf{u}$ for all $\mathbf{u} \in S^*$.*

Proof. According to (H_3) and (4.5), we have for all $\mathbf{u} \in \mathbf{S}^*$

$$\frac{\partial F}{\partial v}(x,\mathbf{u}) = \frac{\partial f}{\partial v}(x,\mathbf{u}) \geq 0 \ \text{ and } \ \frac{\partial G}{\partial u}(x,\mathbf{u}) = \frac{\partial g}{\partial u}(x,\mathbf{u}) \geq 0.$$

By (4.3) − (4.5), we obtain

$$\frac{\partial F}{\partial u}(x,\mathbf{u}) = \gamma_1(x) + \frac{\partial f}{\partial u}(x,\mathbf{u}) \geq 0 \ \text{ and } \ \frac{\partial G}{\partial v}(x,\mathbf{u}) = \gamma_2(x) + \frac{\partial g}{\partial v}(x,\mathbf{u}) \geq 0,$$

which implies the desired result. ∎

4.2.2 The main result

Now, we can state the main result of this paper.

Theorem 4.1. *Let $\tilde{\mathbf{u}}_s$, $\hat{\mathbf{u}}_s$ be ordered positive upper and lower solutions of (4.1), and let hypotheses (H_1)–(H_4) hold. Then problem (4.1) has a minimal solution $\underline{\mathbf{u}}_s$ and a maximal solution $\overline{\mathbf{u}}_s$ such that $\hat{\mathbf{u}}_s \leq \underline{\mathbf{u}}_s \leq \overline{\mathbf{u}}_s \leq \tilde{\mathbf{u}}_s$. If $\underline{\mathbf{u}}_s = \overline{\mathbf{u}}_s \left(\equiv \mathbf{u}_s^*\right)$, then $\mathbf{u}_s^*$ is the unique positive solution in S^*.*

4.3 Preliminary Results for the Scalar Problem

To illustrate our basic approach to the coupled system (4.1), we first consider the following scalar quasilinear elliptic boundary problem:

$$\begin{cases} -\mathbf{div}(D(w)\nabla w) = h(x,w) & \text{in } \Omega \\ u(x) = h(x) & \text{on } \partial\Omega, \end{cases} \tag{4.7}$$

where D and h are prescribed functions satisfying hypotheses $(H_1)-(H_4)$ above.

The following theorem ensures the existence of positive solutions to the scalar problem (4.7). For the proof, we refer to Friedman [39], Ladyženskaja et *al*. [60], Pao and Ruan [94].

Theorem 4.2. *Let $\tilde{w}_s(x)$, $\hat{w}_s(x)$ be a pair of upper and lower solutions of (4.7) such that $\tilde{w}_s(x) \geq \hat{w}_s(x) > 0$ in Ω, and let hypotheses (H_1) and (H_3) hold. Then problem (4.7) has a classical solution $w_s(x)$ such that $\hat{w}_s(x) \leq w_s(x) \leq \tilde{w}_s(x)$ in $\overline{\Omega}$. Furthermore, there are maximal and minimal solutions $\overline{w}_s(x)$ and $\underline{w}_s(x)$ such that every solution $w_s \in S_0^*$ satisfies $\underline{w}_s(x) \leq w_s(x) \leq \overline{w}_s(x)$.*

Remark 4.1. *We consider the scalar problem (4.7) for w. In this case, we can write*

$$-\mathbf{div}(D(\hat{w})\nabla\hat{w}) \leq h(x,\hat{w}) \text{ in } \Omega \tag{4.8}$$

$$-\mathbf{div}(D(\tilde{w})\nabla\tilde{w}) \geq h(x,\tilde{w}) \text{ in } \Omega. \tag{4.9}$$

Subtracting (4.9) from (4.8), we find

$$\begin{aligned} &-\mathbf{div}\left[D_1(\hat{w})\nabla(\hat{w}-\tilde{w}) + \nabla\tilde{w}\left(\frac{D(\hat{w})-D(\tilde{w})}{\hat{w}-\tilde{w}}(\hat{w}-\tilde{w})\right)\right] \\ \leq\ & \frac{h(x,\hat{w})-h(x,\tilde{w})}{\hat{w}-\tilde{w}}(\hat{w}-\tilde{w}). \end{aligned}$$

According to the mean value theorem, there exist $\theta_1, \theta_2 \in [0,M]$, where $M = \|\tilde{w}\|_{C(\bar{\Omega})}$, such that

$$-\mathbf{div}\left[D(\hat{w})\nabla z + \nabla\tilde{w}\left(D'(\theta_1)z\right)\right] \leq h_w(x,\theta_2)z$$

with $z = \hat{w} - \tilde{w}$*, then*

$$-\mathbf{div}(\nabla z)(D(\hat{w})) - \nabla(D(\hat{w}))\nabla z$$
$$-\mathbf{div}\left(\nabla \tilde{w}\left(D'(\theta_1)z\right)\right) - \nabla(\tilde{w})D'(\theta_1)\nabla z - h_w(x,\theta_2)z \leq 0.$$

We get

$$-D(\hat{w})\Delta z + \left[-\nabla D(\hat{w}) - D'(\theta_1)\nabla(\tilde{w})\right]\nabla z + \left[-\nabla.\nabla(\tilde{w})D'(\theta_1) - h_w(x,\theta_2)\right]z \leq 0.$$

We denote

$$B(x) = -\nabla D(\hat{w}) - D'(\theta_1)\nabla(\tilde{w}) \tag{4.10}$$

$$C(x) = -\mathbf{div}\nabla(\tilde{w})D'(\theta_1) - h_w(x,\theta_2). \tag{4.11}$$

To understand the calculations well, see Friedman [39], Ladyženskaja et *al*. [60], Pao and Ruan [94].

Another important result is the following.

Lemma 4.2. *If* $\underline{z}$*,* $\overline{z}$ *are in* $C^2(\Omega) \cap C\left(\bar{\Omega}\right)$ *and satisfy the relation*

$$\begin{cases} -\Gamma\left[\underline{z}\right] + \gamma\underline{z} \leq -\Gamma\left[\overline{z}\right] + \gamma\overline{z} & \text{in } \Omega \\ \underline{z}(x) \leq \overline{z}(x) & \text{on } \partial\Omega \end{cases}$$

with $\Gamma[u] = \mathbf{div}(D(w)\nabla w)$*, then* $\underline{z}(x) \leq \overline{z}(x)$ *on* $\overline{\Omega}$*.*

Proof. Let $z(x) = \underline{z}(x) - \overline{z}(x)$. Firstly, we have

$$-\Gamma\left[\underline{z}\right] + \gamma\underline{z} \leq -\Gamma\left[\overline{z}\right] + \gamma\overline{z} = \gamma\overline{z} + h(x,\bar{z}) \equiv F(x,\bar{z}),$$

then

$$-\Gamma\left[\underline{z}\right] + \gamma\left(\underline{z} - \bar{z}\right) - h(x,\bar{z}) \leq 0. \tag{4.12}$$

On the other hand, we have

$$\Gamma\left[\overline{z}\right] + \gamma\left(\underline{z} - \overline{z}\right) + h\left(x,\underline{z}\right) \leq 0. \tag{4.13}$$

Adding (4.12) and (4.13), we obtain

$$\begin{gathered}-\mathbf{div}\left[D\left(\underline{z}\right)\nabla\left(\underline{z}-\overline{z}\right)+\nabla\overline{z}\left(\frac{D(\underline{z})-D(\overline{z})}{\underline{z}-\overline{z}}\left(\underline{z}-\overline{z}\right)\right)\right] \\ +2\gamma\left(\underline{z}-\bar{z}\right)+\frac{h(x,\underline{z})-h(x,\overline{z})}{\underline{z}-\overline{z}}\left(\underline{z}-\overline{z}\right)\leq 0.\end{gathered}$$

According to the mean value theorem, $\exists\, \theta_1, \theta_2 \in [0, M]$ such that

$$-\mathbf{div}\left[D\left(\underline{z}\right)\nabla z+\nabla\overline{z}\left(D'(\theta_1)z\right)\right]+2\gamma\left(\underline{z}-\bar{z}\right)+\frac{h\left(x,\underline{z}\right)-h\left(x,\overline{z}\right)}{\underline{z}-\overline{z}}\left(\underline{z}-\overline{z}\right)\leq 0$$

with $z=\underline{z}-\overline{z}$, then we get

$$\begin{gathered}-\mathbf{div}(\nabla z)\left(D\left(\underline{z}\right)\right)-\nabla\left(D\left(\underline{z}\right)\right)\nabla z \\ -\mathbf{div}\left(\nabla\overline{z}\left(D'(\theta_1)z\right)\right)-\nabla(\overline{z})D'(\theta_1)\nabla z+h_w(x,\theta_2)z\leq 0\end{gathered}$$

We obtain then

$$\begin{gathered}-D\left(\underline{z}\right)\Delta z-\left[\nabla D\left(\underline{z}\right)-D'(\theta_1)\nabla(\overline{z})\right]\nabla z \\ -\mathbf{div}\nabla(\overline{z})D'(\theta_1)z+2\gamma z+h_w(x,\theta_2)z\leq 0 \\ -D\left(\underline{z}\right)\Delta z+\left[-\nabla D\left(\underline{z}\right)-D'(\theta_1)\nabla(\overline{z})\right]\nabla z+ \\ \left[\gamma+\mathbf{div}\nabla(\overline{z})D'(\theta_1)+h_w(x,\theta_2)\right]z\leq 0.\end{gathered}$$

We come to

$$-D\left(\underline{z}\right)\Delta z+(\mathbf{B}(x))\nabla z+\left(\gamma-\mathbf{C}(x)\right)z\leq 0,$$

where $\mathbf{B}(x)$ and $\mathbf{C}(x)$ are defined in the same way as $B(x)$ and $C(x)$ of relations (4.10) and (4.11), i.e.,

$$\begin{aligned}\mathbf{B}(x) &= -\nabla D\left(\underline{z}\right)-D'(\theta_1)\nabla(\overline{z}) \\ \mathbf{C}(x) &= -\mathbf{div}\nabla(\overline{z})D'(\theta_1)+h_w(x,\theta_2).\end{aligned}$$

Assume, by contradiction, that $z(x)$ has a positive maximum at some point $x_0 \in \overline{\Omega}$. Then $x_0 \in \Omega$ and $\Delta z(x_0) \leq 0$, $\nabla z(x_0) = 0$. This implies that $\left(\gamma - C\right) z(x_0) \leq 0$, which is a contradiction because $\gamma - C = \delta > 0$. ■

4.4 Approximating Scheme

To prove the main theorem, we use the method of upper and lower solutions and its associated monotonic iteration. The basic idea of this method is that when using an upper solution or a lower solution as the initial iteration in a suitable iterative process, the resulting sequence of iterations is monotone and converges to a solution of the problem. Using then either $\hat{\mathbf{u}}_s$ or $\tilde{\mathbf{u}}_s$ as the initial iteration, we construct a sequence $\left\{\mathbf{u}_s^{(m)}\right\}$ from the iteration process

$$\left\{\begin{array}{ll} -\Phi\left[u^{(m)}\right]+\gamma_1 u^{(m)}=F\left(x,\mathbf{u}_s^{(m-1)}\right) & \text{in } \Omega \\ -\Psi\left[v^{(m)}\right]+\gamma_2 v^{(m)}=G\left(x,\mathbf{u}_s^{(m-1)}\right) & \text{in } \Omega \\ u^{(m)}(x)=u_0(x)\ ,\ v^{(m)}(x)=v_0(x) & \text{on } \partial\Omega \end{array}\right. \tag{4.14}$$

with

$$\Phi[u]=\mathbf{div}(D_1(u)\nabla u)\quad,\quad \Psi[v]=\mathbf{div}(D_2(v)\nabla v).$$

We denote the sequence by $\{\underline{\mathbf{u}}_s^{(m)}\}$ if $\mathbf{u}_s^{(0)}=\hat{\mathbf{u}}_s$, and by $\left\{\overline{\mathbf{u}}_s^{(m)}\right\}$ if $\mathbf{u}_s^{(0)}=\tilde{\mathbf{u}}_s$. We call them minimal and maximal sequences, respectively. The existence of these sequences is ensured by the previous Lemma 5.2.

Lemma 4.3. *The minimal and maximal sequences* $\{\underline{\mathbf{u}}_s^{(m)}\}$, $\left\{\overline{\mathbf{u}}_s^{(m)}\right\}$ *exist and possess the monotone property*

$$\hat{\mathbf{u}}_s\le\underline{\mathbf{u}}_s^{(m)}\le\underline{\mathbf{u}}_s^{(m+1)}\le\overline{\mathbf{u}}_s^{(m+1)}\le\overline{\mathbf{u}}_s^{(m)}\le\tilde{\mathbf{u}}_s\ \ \textit{for all } m\ge 1. \tag{4.15}$$

Proof. Firstly, we consider the scalar problem

$$\left\{\begin{array}{ll} -\Phi\left[u^{(m)}\right]+\gamma_1 u^{(m)}=F\left(x,\mathbf{u}_s^{(m-1)}\right) & \text{in } \Omega \\ u^{(m)}(x)=u_0(x) & \text{on } \partial\Omega. \end{array}\right. \tag{4.16}$$

We prove by induction. Start from $m=1$ and $\mathbf{u}_s^{(0)}=\hat{\mathbf{u}}_s$. By Definition 5.1, the components $\hat{u}$ of $\hat{\mathbf{u}}_s$ satisfy the relation

$$\left\{\begin{array}{ll} -\Phi[\hat{u}]+\gamma_1\hat{u}\le F(x,\hat{\mathbf{u}}_s)=F\left(x,\underline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ \hat{u}(x)\le u_0(x) & \text{on } \partial\Omega \end{array}\right. \tag{4.17}$$

and the components $\tilde{u}$ of $\tilde{\mathbf{u}}_s$ satisfy the above inequalities (4.17) in revers order, i.e.,

$$\left\{\begin{array}{ll} -\Phi[\tilde{u}]+\gamma_1\tilde{u}\ge F(x,\tilde{\mathbf{u}}_s)\ge F\left(x,\underline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ \tilde{u}(x)\ge u_0(x) & \text{on } \partial\Omega. \end{array}\right.$$

Similarly, by considering the case $m = 1$ and $\mathbf{u}_s^{(0)} = \tilde{\mathbf{u}}_s$, we have

$$\begin{cases} -\Phi[\hat{u}] + \gamma_1 \hat{u} \leq F(x, \hat{\mathbf{u}}_s) \leq F(x, \tilde{\mathbf{u}}_s) = F\left(x, \overline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ \hat{u}(x) \leq u_0(x) & \text{on } \partial\Omega \end{cases} \tag{4.18}$$

and the components $\tilde{u}$ of $\tilde{\mathbf{u}}_s$ satisfy the above inequalities (4.18) in revers order, i.e.,

$$\begin{cases} -\Phi[\tilde{u}] + \gamma_1 \tilde{u} \geq F(x, \tilde{\mathbf{u}}_s) = F\left(x, \overline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ \tilde{u}(x) \geq u_0(x) & \text{on } \partial\Omega. \end{cases}$$

We see that $\tilde{u}$ and $\hat{u}$ are ordered upper and lower solutions of (4.16) for the case $m = 1$. By Theorem 5.1, problem (4.16) has also a minimal solution $\underline{u}$ and a maximal solution $\overline{u}$ such that $\hat{u} \leq \underline{u} \leq \overline{u} \leq \tilde{u}$. We choose $\underline{u}$ (or $\overline{u}$) as $\underline{u}^{(1)}$ if $\mathbf{u}_s^{(0)} = \hat{\mathbf{u}}_s$ and $\overline{u}$ (or $\underline{u}$) as $\overline{u}^{(1)}$ if $\mathbf{u}_s^{(0)} = \tilde{\mathbf{u}}_s$. So, we get $\hat{u} \leq \underline{u}^{(1)} \leq \overline{u}^{(1)} \leq \tilde{u}$.

The same works if we consider the problem

$$\begin{cases} -\Psi\left[v^{(m)}\right] + \gamma_2 v^{(m)} = G\left(x, \mathbf{u}_s^{(m-1)}\right) & \text{in } \Omega \\ v^{(m)}(x) = v_0(x) & \text{on } \partial\Omega, \end{cases}$$

which gives $\hat{v} \leq \underline{v}^{(1)} \leq \overline{v}^{(1)} \leq \tilde{v}$.

This shows that $\underline{\mathbf{u}}_s^{(1)} \equiv \left(\underline{u}^{(1)}, \underline{v}^{(1)}\right)$ and $\overline{\mathbf{u}}_s^{(1)} \equiv \left(\overline{u}^{(1)}, \overline{v}^{(1)}\right)$ are solutions of (4.14) for $m = 1$ and satisfy $\hat{\mathbf{u}}_s \leq \underline{\mathbf{u}}_s^{(1)} \leq \overline{\mathbf{u}}_s^{(1)} \leq \tilde{\mathbf{u}}_s$.

Assume, by induction, that $\underline{\mathbf{u}}_s^{(m-1)} \leq \underline{\mathbf{u}}_s^{(m)} \leq \overline{\mathbf{u}}_s^{(m)} \leq \overline{\mathbf{u}}_s^{(m-1)}$ for some $m > 1$. Then by the nondecreasing property of $F(.,\mathbf{u})$ for $\mathbf{u} \in S^*$ we have

$$\begin{cases} -\Phi\left[\underline{u}^{(m)}\right] + \gamma_1 \underline{u}^{(m)} = F\left(x, \underline{\mathbf{u}}_s^{(m-1)}\right) \leq F\left(x, \underline{\mathbf{u}}_s^{(m)}\right) \\ -\Phi\left[\overline{u}^{(m)}\right] + \gamma_1 \overline{u}^{(m)} = F\left(x, \overline{\mathbf{u}}_s^{(m-1)}\right) \geq F\left(x, \overline{\mathbf{u}}_s^{(m)}\right) \\ \underline{u}^{(m)} = \overline{u}^{(m)} = u_0(x). \end{cases}$$

This implies that $\overline{u}^{(m)}$, $\underline{u}^{(m)}$ are ordered upper and lower solutions of (4.16) when $(m-1)$ is replaced by m and $\mathbf{u}_s^{(m)}$ is either $\underline{\mathbf{u}}_s^{(m)}$ or $\overline{\mathbf{u}}_s^{(m)}$. Again, by Theorem 5.1, problem (4.16) has a minimal solution $\underline{u}$ and a maximal solution $\overline{u}$. We choose $\underline{u}$ (or $\overline{u}$) as $\underline{u}^{(m+1)}$ if $\mathbf{u}_s^{(m)} = \underline{\mathbf{u}}_s^{(m)}$ and $\underline{u}$ (or $\overline{u}$) as $\overline{u}^{(m+1)}$ if $\mathbf{u}_s^{(m)} = \overline{\mathbf{u}}_s^{(m)}$, which gives us $\underline{u}^{(m)} \leq \underline{u}^{(m+1)} \leq \overline{u}^{(m+1)} \leq \overline{u}^{(m)}$.

This choice ensures that $\underline{\mathbf{u}}_s^{(m+1)} \equiv \left(\underline{u}^{(m+1)}, \underline{v}^{(m+1)}\right)$ and $\overline{\mathbf{u}}_s^{(m+1)} \equiv \left(\overline{u}^{(m+1)}, \overline{v}^{(m+1)}\right)$ are solutions of (4.14) and possess the monotone property (4.15), which implies, by induction, the truth of the relation (4.15). ■

4.5 Proof of the Main Result

We are now ready to prove the main result of this work.

Proof of Theorem Th1 In view of Lemma 5.3 the pointwise limits

$$\lim_{m \longrightarrow \infty} \underline{\mathbf{u}}_s^{(m)} = \underline{\mathbf{u}}_s \quad , \quad \lim_{m \longrightarrow \infty} \overline{\mathbf{u}}_s^{(m)} = \overline{\mathbf{u}}_s \tag{4.19}$$

exist and satisfy $\hat{\mathbf{u}}_s \leq \underline{\mathbf{u}}_s \leq \overline{\mathbf{u}}_s \leq \tilde{\mathbf{u}}_s$. To prove that $\underline{\mathbf{u}}_s$ and $\overline{\mathbf{u}}_s$ are, respectively, the minimal and maximal solutions of (4.1), we first consider the minimal sequence $\{\underline{\mathbf{u}}_s^{(m)}\} \equiv \{\underline{u}^{(m)}, \underline{v}^{(m)}\}$. Define for each m

$$\begin{cases} \underline{w}_1^{(m)}(x) = I_1\left(\underline{u}^{(m)}\right) = \int_0^{\underline{u}^{(m)}} D_1(s)\,ds \\ \underline{Q}_1^{(m)}(x) = -\gamma_1(x)\underline{u}^{(m)} + F\left(x, \underline{\mathbf{u}}^{(m-1)}\right) \end{cases}$$

and

$$\begin{cases} \underline{w}_2^{(m)}(x) = I_2\left(\underline{v}^{(m)}\right) = \int_0^{\underline{v}^{(m)}} D_2(s)\,ds \\ \underline{Q}_2^{(m)}(x) = -\gamma_2(x)\underline{v}^{(m)} + F\left(x, \underline{\mathbf{u}}^{(m-1)}\right). \end{cases}$$

We remark that $I_1'\left(\underline{u}\right) = D_1\left(\underline{u}\right)$ and $I_2'\left(\underline{v}\right) = D_2\left(\underline{v}\right)$. The inverse of $I_1\left(\underline{u}\right)$ and $I_2\left(\underline{v}\right)$ exist and are denoted, respectively, by $q_1\left(\underline{w}_1\right)$ and $q_2\left(\underline{w}_2\right)$.

The quasilinear problem (4.14) may be written as the scalar linear problem

$$\begin{cases} -\nabla^2 \underline{w}_1^{(m)} = \underline{Q}_1^{(m)}(x) & \text{in } \Omega \\ -\nabla^2 \underline{w}_2^{(m)} = \underline{Q}_2^{(m)}(x) & \text{in } \Omega \\ \underline{w}_1^{(m)}(x) = u_0^*(x) \ , \ \underline{w}_2^{(m)}(x) = v_0^*(x) & \text{on } \partial\Omega, \end{cases}$$

where $u_0^*(x) = I_1(u_0) \geq 0$ and $v_0^*(x) = I_2(v_0) \geq 0$. It is clear from (4.19) and (4.5) that $\underline{w}_1^{(m)} \to \underline{w}_1 \equiv I_1\left(\underline{u}\right)$, $\underline{w}_2^{(m)} \to \underline{w}_2 \equiv I_2\left(\underline{v}\right)$ and $\underline{Q}_1^{(m)} \to f\left(x, \underline{\mathbf{u}}_s\right)$, $\underline{Q}_2^{(m)} \to g\left(x, \underline{\mathbf{u}}_s\right)$ as $m \to \infty$.

By the argument in the proof for the scalar problem (4.7), $\underline{w}_1$ is the unique solution of the linear problem

$$\begin{cases} -\nabla^2 \underline{w}_1^{(m)}(x) = \underline{Q}_1^{(m)}(x) \\ \underline{w}_1^{(m)}(x) = u_0^*(x) \end{cases}$$

and $\underline{w}_2$ is the unique solution of the linear problem

$$\begin{cases} -\nabla^2 \underline{w}_2^{(m)}(x) = \underline{Q}_2^{(m)}(x) \\ \underline{w}_2^{(m)}(x) = v_0^*(x). \end{cases}$$

This shows that $\underline{\mathbf{u}}_s \equiv \left(\underline{u}, \underline{v}\right)$, where $\underline{u} = q_1\left(\underline{w}_1\right)$ and $\underline{v} = q_2\left(\underline{w}_2\right)$ are solutions of (4.1) and $\underline{\mathbf{u}}_s \in S^*$.

Now, we show that $\overline{\mathbf{u}}_s$ is a solution of (4.1) in S^*, for this we consider the maximal sequence $\left\{\overline{\mathbf{u}}_s^{(m)}\right\} \equiv \left\{\overline{u}^{(m)}, \overline{v}^{(m)}\right\}$. Define for each m

$$\begin{cases} \overline{w}_1^{(m)}(x) = I_1\left(\overline{u}^{(m)}\right) = \int_0^{\overline{u}^{(m)}} D_1(s)\,ds \\ \overline{Q}_1^{(m)}(x) = -\gamma_1(x)\overline{u}^{(m)} + F\left(x, \overline{\mathbf{u}}^{(m-1)}\right) \end{cases}$$

and

$$\begin{cases} \overline{w}_2^{(m)}(x) = I_2\left(\overline{v}^{(m)}\right) = \int_0^{\overline{v}^{(m)}} D_2(s)\,ds \\ \overline{Q}_2^{(m)}(x) = -\gamma_2(x)\overline{v}^{(m)} + G\left(x, \overline{\mathbf{u}}^{(m-1)}\right). \end{cases}$$

Then the quasilinear problem (4.14) may be written as the scalar linear problem

$$\begin{cases} -\nabla^2 \overline{w}_1^{(m)} = \overline{Q}_1^{(m)}(x) & \text{in } \Omega \\ -\nabla^2 \overline{w}_2^{(m)} = \overline{Q}_2^{(m)}(x) & \text{in } \Omega \\ \overline{w}_1^{(m)}(x) = u_0^*(x)\ ,\ \overline{w}_2^{(m)}(x) = v_0^*(x) & \text{on } \partial\Omega. \end{cases}$$

It is clear from (4.19) and (4.5) that $\overline{w}_1^{(m)} \to \overline{w}_1 \equiv I_1\left(\underline{u}\right)$, $\overline{w}_2^{(m)} \to \overline{w}_2 \equiv I_2(\overline{v})$ and $\overline{Q}_1^{(m)} \to f\left(x, \overline{\mathbf{u}}_s\right)$, $\overline{Q}_2^{(m)} \to g\left(x, \overline{\mathbf{u}}_s\right)$ as $m \to \infty$.

By the argument in the proof for the scalar problem, $\overline{w}_1$ is the unique solution of the linear problem

$$\begin{cases} -\nabla^2 \overline{w}_1^{(m)}(x) = \overline{Q}_1^{(m)}(x) \\ \overline{w}_1^{(m)}(x) = u_0^*(x) \end{cases}$$

and $\overline{w}_2$ is the unique solution of the linear problem

$$\begin{cases} -\nabla^2 \overline{w}_2^{(m)}(x) = \overline{Q}_2^{(m)}(x) \\ \overline{w}_2^{(m)}(x) = v_0^*(x). \end{cases}$$

This shows that $\overline{\mathbf{u}}_s \equiv (\overline{u}, \overline{v})$, where $\overline{u} = q_1(\overline{w}_1)$ and $\overline{v} = q_2(\overline{w}_2)$ are solutions of (4.1) and $\overline{\mathbf{u}}_s \in S^*$.

To show that $\underline{\mathbf{u}}_s$ and $\overline{\mathbf{u}}_s$ are, respectively, minimal and maximal solutions of (4.1) in S^*, we observe that every solution $\mathbf{u} = (u, v)$ of (4.1) in S^* satisfies

$$\begin{cases} -\Phi[u] + \gamma_1 u = F(x, \mathbf{u}_s) \geq F\left(x, \underline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ u(x) = u_0(x) & \text{on } \partial\Omega \end{cases}$$

and

$$\begin{cases} -\Psi[v] + \gamma_1 v = G(x, \mathbf{u}_s) \geq G\left(x, \underline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ v(x) = v_0(x) & \text{on } \partial\Omega. \end{cases}$$

By (4.14) (with $m = 1$ and $u^{(1)} = \underline{u}^{(1)}$ and $v^{(1)} = \underline{v}^{(1)}$) we have

$$\begin{aligned} F\left(x, \underline{\mathbf{u}}_s^{(0)}\right) &= -\Phi\left[\underline{u}^{(1)}\right] + \gamma_1 \underline{u}^{(1)} \\ G\left(x, \underline{\mathbf{u}}_s^{(0)}\right) &= -\Psi\left[\underline{v}^{(1)}\right] + \gamma_1 \underline{v}^{(1)}, \end{aligned}$$

then

$$\begin{aligned} -\Phi[u] + \gamma_1 u &\geq -\Phi\left[\underline{u}^{(1)}\right] + \gamma_1 \underline{u}^{(1)} \\ -\Psi[v] + \gamma_1 v &\geq -\Psi\left[\underline{v}^{(1)}\right] + \gamma_1 \underline{v}^{(1)}. \end{aligned}$$

By Lemma 5.2 we have $u \geq \underline{u}^{(1)}$ and $v \geq \underline{v}^{(1)}$, i.e. $\mathbf{u} \geq \underline{\mathbf{u}}_s^{(1)}$. This implies, by Lemma 5.1, that $F(x, \mathbf{u}) \geq F\left(x, \underline{\mathbf{u}}_s^{(1)}\right)$ and $G(x, \mathbf{u}) \geq G\left(x, \underline{\mathbf{u}}_s^{(1)}\right)$. It follows by an induction argument that

$$\begin{aligned} F(x, \mathbf{u}) &\geq F\left(x, \underline{\mathbf{u}}_s^{(1)}\right) \geq F\left(x, \underline{\mathbf{u}}_s^{(2)}\right) \geq \ldots \geq F\left(x, \underline{\mathbf{u}}_s^{(m)}\right) \\ G(x, \mathbf{u}) &\geq G\left(x, \underline{\mathbf{u}}_s^{(1)}\right) \geq G\left(x, \underline{\mathbf{u}}_s^{(2)}\right) \geq \ldots \geq G\left(x, \underline{\mathbf{u}}_s^{(m)}\right), \end{aligned}$$

then $\mathbf{u} \geq \underline{\mathbf{u}}_s^{(m)}$, for every $m \geq 1$.

In the same way, we observe that every solution $\mathbf{u} = (u, v)$ of (4.1) in S^* satisfies

$$\begin{cases} -\Phi[u] + \gamma_1 u = F(x, \mathbf{u}) \leq F\left(x, \overline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ u(x) = u_0(x) & \text{on } \partial\Omega \end{cases}$$

and

$$\begin{cases} -\Psi[v] + \gamma_1 v = G(x, \mathbf{u}) \leq G\left(x, \overline{\mathbf{u}}_s^{(0)}\right) & \text{in } \Omega \\ v(x) = v_0(x) & \text{on } \partial\Omega. \end{cases}$$

By (4.14) (with $m = 1$ and $u^{(1)} = \overline{u}^{(1)}$ and $v^{(1)} = \overline{v}^{(1)}$) we have

$$\begin{aligned} F\left(x, \overline{\mathbf{u}}_s^{(0)}\right) &= -\Phi\left[\overline{u}^{(1)}\right] + \gamma_1 \overline{u}^{(1)} \\ G\left(x, \overline{\mathbf{u}}_s^{(0)}\right) &= -\Psi\left[\overline{v}^{(1)}\right] + \gamma_1 \overline{v}^{(1)}, \end{aligned}$$

then

$$\begin{aligned} -\Phi[u] + \gamma_1 u &\leq -\Phi\left[\overline{u}^{(1)}\right] + \gamma_1 \overline{u}^{(1)} \\ -\Psi[v] + \gamma_1 v &\leq -\Psi\left[\overline{v}^{(1)}\right] + \gamma_1 \overline{v}^{(1)}. \end{aligned}$$

By Lemma 5.2, we have $u \leq \overline{u}^{(1)}$ and $v \leq \overline{v}^{(1)}$, i.e., $u_s \leq \overline{\mathbf{u}}_s^{(1)}$. This implies, by Lemma 5.1, that $F(x, \mathbf{u}) \leq F\left(x, \overline{\mathbf{u}}_s^{(1)}\right)$ and $G(x, \mathbf{u}) \leq G\left(x, \overline{\mathbf{u}}_s^{(1)}\right)$. It follows by an induction argument that

$$\begin{aligned} F(x, \mathbf{u}) &\leq F\left(x, \overline{\mathbf{u}}_s^{(1)}\right) \leq F\left(x, \overline{\mathbf{u}}_s^{(2)}\right) \leq \ldots \leq F\left(x, \overline{\mathbf{u}}_s^{(m)}\right) \\ G(x, \mathbf{u}) &\leq G\left(x, \overline{\mathbf{u}}_s^{(1)}\right) \leq G\left(x, \overline{\mathbf{u}}_s^{(2)}\right) \leq \ldots \leq G\left(x, \overline{\mathbf{u}}_s^{(m)}\right), \end{aligned}$$

which implies $u_s \leq \overline{\mathbf{u}}_s^{(m)}$.

Letting $m \to \infty$ and using relation (4.19) lead to $\underline{\mathbf{u}}_s \leq \mathbf{u} \leq \overline{\mathbf{u}}_s$. This proves the minimal and maximal property of $\underline{\mathbf{u}}_s$ and $\overline{\mathbf{u}}_s$. Finally, if $\underline{\mathbf{u}}_s = \overline{\mathbf{u}}_s \; (\equiv \mathbf{u}_s^*)$, then this maximal-minimal property ensures that $\mathbf{u}_s^*$ is the unique positive solution in S^*. ■

4.6 Application

As an application of the obtained theorem, we give a model concerning the type of diffusion in porous media, where the diffusion coefficients are degenerate; it is the following two-species Lotka–Volterra competition steady-state model:

$$(4.20)\qquad \begin{cases} -D_1(x)\nabla^2 u^{\alpha} = u\,(a_1 - b_1 u - c_1 v) \\ -D_2(x)\nabla^2 v^{\beta} = v\,(a_2 - b_2 u - c_2 v) & ,\ t > 0,\ x \in \Omega \\ u\,(x) = u_0(x) > 0\ ,\ v\,(x) = v_0(x) > 0, \end{cases}$$

where for each $i = 1,\ 2,\ \alpha,\ \beta,\ a_i,\ b_i,\ c_i$ are positive constants, and $\alpha > 1,\ \beta > 1$, with $D_i(x) > 0$ on $\bar{\Omega}$. For more details on this model, we refer the reader to Pao in [91, 93].

4.7 Concluding Remarks and Perspectives

This work has mainly focused on the question of the existence and the uniqueness of positive maximal and minimal solutions for a class of degenerate reaction-diffusion systems. It should be noted that the results obtained can be applied to a number of models arising from biology, ecology and biochemistry as well as to models in several fields of applied sciences and engineering. We have developed original methods to overcome certain difficulties, and despite the complexity of the model studied, we have succeeded in obtaining an existence result.

There are many additional important open problems, which we hope to address in the near future, they are: Numerical simulation, Generalization to the parabolic case, Generalization to the case of a higher order system. This list of questions corresponds to a work in progress or prospective work. Some are a continuation of the work already done, and some are new research projects. This not only makes it possible to delve deeper into the theoretical study, but also goes beyond the theoretical framework by developing models and techniques.

CHAPTER 5

ON THE EXISTENCE AND UNIQUENESS OF POSITIVE SOLUTION FOR A DEGENERATE REACTION-DIFFUSION PROBLEM

The objective of this paper is to show the existence and uniqueness of positive solutions for a class of quasilinear degenerate parabolic reaction-diffusion problems defined in a bounded domain, which have many applications in various applied sciences. Its specificity lies in the introduction of degenerate diffusion. Our approach towards our goal is mainly based on the method of upper and lower solutions. The result obtained is applied to the Lotka-Volterra model.

The work constituting this chapter is the subject of an article published in an international journal specialized in Mathematics (IEEE International Conference on Recent Advances in Mathematics and Informatics), in collaboration with S. Mesbahi.

5.1 Introduction

Many problems and phenomena in science, engineering, and biology are modeled in the form of reaction-diffusion equations, which gives great importance to this type of equations. This is what prompted many researchers to take an interest in the study of reaction-diffusion systems, whether in terms of modeling like what we find, for example, in Hritonenko and Yatsenko [47] and in Murray's books [78, 79], where we find many examples and models in economics, biology, environment and various applied sciences; or in terms of mathematical study in many ways and various techniques depending on the situation. This is what we find, for example, in the works of Alaa and Mesbahi et *al*. [5, 6, 50, 73, 74, 104], and the references contained therein.

In recent years, special attention has been given to degenerate models due to their wide applications. We find many models and applications in Alaa et *al*. [4], Anderson [13], Desvillettes et *al*. [28], Floridia et *al*. [37], Liang [64], Murakawa [77], Murray [78, 79], Pao and Ruan [94], Sabri et *al*. [101], Saffidine and Mesbahi [104], and the references therein, where we find techniques and methods of treatment; in addition to what was previously mentioned.

The work that we will do in this paper is in this context, we will be interested in the study of a quasilinear parabolic degenerate reaction-diffusion model. The elliptical operator of the considered system can degenerate.

We will use a technique described by Pao, based on the construction of the upper and lower solutions. In Pao [94], we find important details about this technique. We are therefore interested in the study of the following system:

$$\begin{cases} \dfrac{\partial u}{\partial t} - \mathbf{div}(D(u)\nabla u) = f(t,x,u) & \text{in } Q_T \\ u(t,x) = u_0(t,x) & \text{on } \Sigma \\ u(0,x) = h(x) & \text{in } \Omega, \end{cases} \tag{5.1}$$

where Ω is a bounded domain in $\mathbb{R}^n$ $(n \geq 2)$ with boundary $\partial\Omega$. $D(u)$ and f are prescribed functions satisfying the conditions in hypotheses (H_1)-(H_3) that we will mention later in the next section.

System (5.1) can model the circulation of an ideal gas in a homogeneous porous medium with an isentropic flow. It can also model the heat propagation in a combustible mixture, chemical processes, etc. For example, the problem of the enzyme-substrate model discussed in Pao [94] is a special case of (5.1) with the reaction term

$$f(u) = \frac{-\sigma u}{1 + au + bu^2}, \text{ with } \sigma,\ a,\ b > 0.$$

The rest of this paper is organized as follows. In the next section, we present the assumptions under which we will study our problem. Next, we present some preliminary results that we will need later. In the fourth section, we prove an important and necessary result related to the approached problem. In the fifth section, we state our main result and also present its proof. In the penultimate section, we present an application of the obtained result. The paper ends with a conclusion remarks and perspectives.

5.2 Assumptions and notations

Below we will denote $\mathbf{C}^{\ell}(Q_T)$ to the space of all continuous functions whose partial derivatives up to the ℓ-th order are continuous in Q_T, $\mathbf{C}^{\alpha}(Q_T)$ to the space of Hölder continuous functions in Q_T, and $\mathbf{C}^{\ell+\alpha}(Q_T)$ to the space of functions in $\mathbf{C}^{\ell}(Q_T)$ that are Hölder continuous in Q_T with exponent $\alpha \in (0,1)$. Let also $\mathbf{C}^{\ell,m}(Q_T)$ the space of functions whose ℓ-times derivatives in t and m-times derivatives in x are continuous in Q_T. In particular, the space $\mathbf{C}^{1,2}(Q_T)$ consists of all functions that are once continuously differentiable in t and twice continuously differentiable in x for $(t,x) \in Q_T$. When $\ell = 0$, we denote by $\mathbf{C}(Q_T)$ the set of continuous functions in Q_T. Similar notations are used if Q_T is replaced by another set.

Now, we introduce the definition of upper and lower solutions.

Definition 5.1. A pair of functions $\tilde{u}$, $\hat{u}$ in $\mathbf{C}\left(\overline{Q}_T\right) \cap \mathbf{C}^{1,2}(Q_T)$ are called ordered upper and lower solutions of (4.1) if $\hat{u} \leq \tilde{u}_s$ and

$$\begin{cases} \dfrac{\partial \hat{u}}{\partial t} - \mathbf{div}(D(\hat{u})\nabla \hat{u}) \leq f(t,x,\hat{u}) & \text{in } Q_T \\ \hat{u}(t,x) \leq u_0(t,x) & \text{on } \Sigma \\ u(0,x) \leq h(x) & \text{in } \Omega, \end{cases} \tag{5.2}$$

and $\tilde{u}$ satisfies (5.2) with inequalities reversed.

For a given pair of ordered upper and lower solutions $\tilde{u}$ and $\hat{u}$, we define

$$S = \left\{ u \in \mathbf{C}^{\alpha}(Q_T) \cap \mathbf{C}\left(\overline{Q}_T\right) \mid \hat{u} \leq u \leq \tilde{u} \right\}.$$

Now, we make the following assumptions:

(H_1) $f(t,x,.) \in \mathbf{C}^{\frac{\alpha}{2},\alpha}\left(\overline{Q}_T\right)$, $f(t,x,0) \geq 0$ in Q_T, $u_0(t,x) \in \mathbf{C}^{\frac{\alpha}{2},\alpha}(\Sigma)$ and $h(x) \in \mathbf{C}^{\alpha}\left(\overline{\Omega}\right)$, where $\alpha \in (0,1)$.

(H_2) $f(.,u) \in \mathbf{C}^1(\Sigma)$ and $\dfrac{\partial f}{\partial u}(.,u) \geq 0$ for $u \in \Sigma$.

(H_3) $D(u) \in \mathbf{C}^1([0,M])$, $D(0) \geq 0$ and $D(u) > 0$ in $(0,\ M]$, with $M = \|\tilde{u}\|_{\mathbf{C}\left(\overline{Q}_T\right)}$.

(H_4) $u_0(t,x) \geq 0$ on Σ, $h(x) > 0$ in Ω and $h(x) = u_0(0,x)$ on $\partial\Omega$.

(H_5) There exists a constant $\delta_0 > 0$ such that for any $x_0 \in \partial\Omega$, there exists a ball $\mathbf{K}$ outside of Ω with radius $r \geq \delta_0$ such that $\mathbf{K} \cap \overline{\Omega} = \{x_0\}$.

For the functions $D(u)$, we will assume that $D(0) = 0$. This is why we say that system (5.1) is degenerate, this is exactly the main difficulty in this work.

Remark 5.1. *The assumption* (H_5) *is a powerful property of* Ω*, this means that it is not necessary to assume the usual smooth state to have a classical solution, and it is useful in applications such as rectangles or polygons .*

Let $\gamma \equiv \gamma(t,x)$ be any smooth non-negative function satisfying

$$\gamma(t,x) \geq \max\left\{-\frac{\partial f}{\partial u}(t,x,u) \mid \hat{u} \leq u \leq \tilde{u}\right\}, \tag{5.3}$$

and define

$$F(t,x,u) = \gamma u + f(t,x,u). \tag{5.4}$$

Hypothesis (H_2) leads directly to the following lemma.

Lemma 5.1. $F(t,x,\cdot)$ *is nondecreasing function in* S.

5.3 Preliminary results

An important comparison relation between a lower solution and an upper solution, we summarize it in the following lemma.

Lemma 5.2. *Let* $\tilde{u}(t,x)$*,* $\hat{u}(t,x)$ *be a pair of upper and lower non-negative solutions of* (4.1)*. Then* $\tilde{u}(t,x) \geq \hat{u}(t,x)$ *in* Q_T*. Moreover, problem* (4.1) *has at most one solution in* Q_T*.*

Proof. We can write

$$\frac{\partial \hat{u}}{\partial t} - \mathbf{div}(D(\hat{u})\nabla\hat{u}) \leq f(t,x,\hat{u}) \text{ , in } \Omega \tag{5.5}$$

$$\frac{\partial \tilde{u}}{\partial t} - \mathbf{div}(D(\tilde{u})\nabla\tilde{u}) \geq f(t,x,\tilde{u}) \text{ , in } \Omega. \tag{5.6}$$

Subtracting (5.6) from (5.5), we find

$$\frac{\partial(\hat{u}-\tilde{u})}{\partial t}- \mathbf{div}\left[D(\hat{u})\nabla(\hat{u}-\tilde{u})+\nabla\tilde{u}\left(\frac{D(\hat{u})-D(\tilde{u})}{\hat{u}-\tilde{u}}(\hat{u}-\tilde{u})\right)\right] \leq \frac{f(t,x,\hat{u})-f(t,x,\tilde{u})}{\hat{u}-\tilde{u}}(\hat{u}-\tilde{u}).$$

According to the mean value theorem, there exist two functions θ_1, θ_2 between $\hat{u}$ and $\tilde{u}$ such that

$$z_t - \mathbf{div}\left[D(\hat{u})\nabla z + \nabla\tilde{u}\left(D'(\theta_1)z\right)\right] \leq f_u(t,x,\theta_2)z,$$

with $z = \hat{u} - \tilde{u}$, then

$$\begin{gathered} z_t - \mathbf{div}(\nabla z)(D(\hat{u})) - \nabla(D(\hat{u}))\nabla z \\ -\mathbf{div}\left(\nabla\tilde{u}\left(D'(\theta_1)z\right)\right) - \nabla(\tilde{u})D'(\theta_1)\nabla z \\ -f_u(x,\theta_2)z \leq 0. \end{gathered}$$

We obtain

$$\text{(5.7)} \qquad \begin{cases} z_t - D(\hat{u})\Delta z + \left[-\nabla D(\hat{u}) - D'(\theta_1)\nabla(\tilde{u})\right]\nabla z & \\ \quad + \left[-\nabla.\nabla(\tilde{u})D'(\theta_1) - f_u(t,x,\theta_2)\right]z \leq 0 & \text{in } Q_T \\ z(t,x) \leq 0 & \text{on } \Sigma \\ z(0,x) \leq 0 & \text{in } \Omega. \end{cases}$$

We denote

$$\text{(5.8)} \qquad \begin{aligned} B(t,x) &= -\nabla(D(\hat{u})) - D'(\theta_1)\nabla(\tilde{u}) \\ C(t,x) &= -\mathbf{div}\left(D'(\theta_1)\nabla(\tilde{u})\right) - f_u(t,x,\theta_2) \end{aligned}$$

We find many explanations and important details about this part in Friedman [39] and Ladyženskaja et al. [60]. Let $k \geq |C|_{L^\infty(Q_T)}$ be a constant and let $w(t,x) = z(t,x)e^{-kt}$. Then, the maximum of w in $\overline{Q}_T$ is also positive and by (4.9), we have

$$\text{(5.9)} \qquad \begin{cases} w_t - D(t,x)\Delta w + & \\ B(t,x)\cdot\nabla w + (k + C(t,x))w \leq 0 & \text{in } Q_T \\ w(t,x) \leq 0 & \text{on } \Sigma \\ w(0,x) \leq 0 & \text{in } \Omega. \end{cases}$$

Assume that the maximum of w in $\overline{Q}_T$ is achieved at (t_0, x_0). Then, by the last two inequalities of (5.9), $(t_0, x_0) \in Q_T$. Hence $w_t(t_0, x_0) \geq 0$, $\Delta w(t_0, x_0) \leq 0$, $\nabla w(t_0, x_0) = \mathbf{0}$, and

$$\begin{aligned} &w_t - D(w)\Delta w + B(t,x) \cdot \nabla w + (k + C(t,x))w \\ &\geq \left(k - |C|_{L^\infty(Q_T)}\right) w(t_0, x_0) > 0, \end{aligned}$$

this contradicts the first inequality of (5.9) which leads to $\tilde{u} \geq \hat{u}$. According to Definition 5.1, every solution of (5.1) is an upper solution as well as a lower solution, the above conclusion ensures that there is at most one solution in S. ∎

Another important result that we find proven in Pao [94]. This is the following theorem.

Theorem 5.1. *Let $\tilde{u}(t,x)$, $\hat{u}(t,x)$ be a pair of upper and lower solutions of* (5.1) *such that $\tilde{u}(t,x) \geq \hat{u}(t,x) > 0$ in Q_T, and let hypotheses $(H_1)-(H_3)$ hold. Then problem* (5.1) *has a unique classical solution $u(t,x)$ in Q_T that satisfies the relation $\hat{u}(t,x) \leq u(t,x) \leq \tilde{u}(t,x)$ in Q_T.*

5.4 Approximating scheme

Here, we will use the method of upper and lower solutions and its associated monotonic iteration. Using then either $\hat{u}$ or $\tilde{u}$ as the initial iteration, we construct a sequence $\{u^{(m)}\}$ from the iteration process

$$(5.10) \qquad \begin{cases} \left(u^{(m)}\right)_t - \Phi\left[u^{(m)}\right] + \gamma u^{(m)} = F\left(t, x, u^{(m-1)}\right) & \text{in } Q_T \\ u^{(m)}(t,x) = u_0(t,x) & \text{on } \Sigma \\ u(0,x) = h(x) & \text{in } \Omega, \end{cases}$$

with $\Phi[u] = \mathbf{div}(D(u)\nabla u)$. We denote $\{\underline{u}^{(m)}\}$ to the minimal sequence if $u^{(0)} = \hat{u}$, and $\left\{\overline{u}^{(m)}\right\}$ to the maximal sequence if $u^{(0)} = \tilde{u}$. The following lemma confirms the existence of these sequences.

Lemma 5.3. *The minimal and maximal sequences $\{\underline{u}^{(m)}\}$, $\left\{\overline{u}^{(m)}\right\}$ exist and possess the monotone property*

$$(5.11) \qquad \hat{u} \leq \underline{u}^{(m)} \leq \underline{u}^{(m+1)} \leq \overline{u}^{(m+1)} \leq \overline{u}^{(m)} \leq \tilde{u} \quad \textit{in } \overline{Q}_T,$$

for all $m \geq 1$.

Proof. We consider the following problem

$$(5.12) \qquad \begin{cases} \dfrac{\partial u}{\partial t} - \Phi[u] + \gamma u = F(t,x,u) & \text{in } Q_T \\ u(t,x) = u_0(t,x) & \text{on } \Sigma \\ u(0,x) = h(x) & \text{in } \Omega \end{cases}$$

We will take the method of proof by induction. Starting from $m = 1$ and $u^{(0)} = \hat{u}$. By Definition 5.1, the component $\hat{u}$ satisfy

$$(5.13) \qquad \begin{cases} \dfrac{\partial \hat{u}}{\partial t} - \Phi[\hat{u}] + \gamma \hat{u} \leq F(t,x,\hat{u}) = F\left(t,x,\underline{u}^{(0)}\right) & \text{in } Q_T \\ \hat{u}(t,x) \leq u_0(t,x) & \text{on } \Sigma \\ \hat{u}(0,x) \leq h(x) & \text{in } \Omega \end{cases}$$

and the component $\tilde{u}$ satisfy the above inequalities (5.13) in reversed order, i.e.,

$$\begin{cases} \dfrac{\partial \tilde{u}}{\partial t} - \Phi[\tilde{u}] + \gamma \tilde{u} \geq F(t,x,\tilde{u}) \geq F\left(t,x,\underline{u}^{(0)}\right) & \text{in } Q_T \\ \tilde{u}(t,x) \geq u_0(t,x) & \text{on } \Sigma \\ \tilde{u}(0,x) \geq h(x) & \text{in } \Omega. \end{cases}$$

Similarly, by considering $u^{(0)} = \tilde{u}$, we have

$$(5.14) \qquad \begin{cases} \dfrac{\partial \hat{u}}{\partial t} - \Phi[\hat{u}] + \gamma \hat{u} \leq F(x,\hat{u}) \leq & \text{in } Q_T \\ F(t,x,\tilde{u}) = F\left(t,x,\overline{u}^{(0)}\right) & \\ \hat{u}(t,x) \leq u_0(t,x) & \text{on } \Sigma \\ \hat{u}(0,x) \leq h(x) & \text{in } \Omega, \end{cases}$$

and the component $\tilde{u}$ satisfy the above inequalities (5.14) in reversed order, i.e.,

$$\begin{cases} \dfrac{\partial \tilde{u}}{\partial t} - \Phi[\tilde{u}] + \gamma \tilde{u} \geq F(t,x,\tilde{u}) = F\left(t,x,\overline{u}^{(0)}\right) & \text{in } Q_T \\ \tilde{u}(t,x) \geq u_0(t,x) & \text{on } \Sigma \\ \tilde{u}(0,x) \geq h(x) & \text{in } \Omega. \end{cases}$$

For the case $F(t,x,u) = F\left(t,x,\underline{u}^{(0)}\right)$. It is easy to see from Definition 5.1 and $F(t,x,\tilde{u}) \geq F\left(t,x,\underline{u}^{(0)}\right)$ that $\tilde{u}$ and $\hat{u}$ are upper and lower solutions of (5.12). Theorem 5.1 ensures the existence of a unique solution $\underline{u}^{(1)}$ to (5.12) satisfying $\hat{u} \leq \underline{u}^{(1)} \leq \tilde{u}$ in $\overline{Q}_T$. Similarly, by considering $F(t,x,u) = F(t,x,\tilde{u})$ in (5.12), there exists a unique solution $\overline{u}^{(1)}$ to (5.12) satisfying $\hat{u} \leq \overline{u}^{(1)} \leq \tilde{u}$ in $\overline{Q}_T$. Moreover, as in the proof of Theorem 5.1 in Pao [94], using $z = \underline{u}^{(1)} - \overline{u}^{(1)}$, we obtain $\underline{u}^{(1)} \leq \overline{u}^{(1)}$. This shows that $\hat{u} \leq \underline{u}^{(1)} \leq \overline{u}^{(1)} \leq \tilde{u}$ in $\overline{Q}_T$.

Assume, by induction, that $\underline{u}^{(m-1)} \leq \underline{u}^{(m)} \leq \overline{u}^{(m)} \leq \overline{u}^{(m-1)}$ for some $m > 1$. Then, the component $\underline{u}^{(m)}$ satisfy the boundary and initial conditions in (5.10) and the relations

$$\begin{aligned}\left(\underline{u}^{(m)}\right)_t - \Phi\left[\underline{u}^{(m)}\right] + \gamma\underline{u}^{(m)} &= \\ F\left(t,x,\underline{u}^{(m-1)}\right) &\leq F\left(t,x,\underline{u}^{(m)}\right).\end{aligned}$$

which proves that $\underline{u}^{(m)}$ is a lower solution of (5.12) when $F(t,x,u) = F\left(t,x,\underline{u}^{(m)}\right)$. Depending on the inequality $F\left(t,x,\overline{u}^{(m-1)}\right) \geq F\left(t,x,\underline{u}^{(m)}\right)$, we also find easily that $\overline{u}^{(m)}$ is an upper solution. By Theorem 5.1, problem (5.12) has a unique solution $\left(\underline{u}^{(m+1)}, \overline{u}^{(m+1)}\right)$ satisfying $\underline{u}^{(m)} \leq \underline{u}^{(m+1)} \leq \overline{u}^{(m)}$ and $\underline{u}^{(m)} \leq \overline{u}^{(m+1)} \leq \overline{u}^{(m)}$. As in the proof of Theorem 5.1, using $z = \overline{u}^{(m+1)} - \underline{u}^{(m+1)}$, we get $\underline{u}^{(m+1)} \leq \overline{u}^{(m+1)}$. This shows that $\underline{u}^{(m)} \leq \underline{u}^{(m+1)} \leq \overline{u}^{(m+1)} \leq \overline{u}^{(m)}$, which proves the monotonic property. ■

5.5 The main result

The main result of this paper is what the following theorem states.

Theorem 5.2. *Let $\tilde{u}$, $\hat{u}$ be a pair of upper and lower solutions of* (5.1) *such that $\tilde{u} \geq \hat{u} > 0$ in Q_T, and let hypotheses $(H_1)-(H_5)$ hold. Then problem* (5.1) *has a unique positive solution u^* that satisfies $\hat{u} \leq u^* \leq \tilde{u}$. Moreover, the sequences $\left\{\underline{u}^{(m)}\right\}, \left\{\overline{u}^{(m)}\right\}$ governed by* (5.10) *with $\underline{u}^{(0)} = \hat{u}$ and $\overline{u}^{(0)} = \tilde{u}$ converge monotonically to u^* and satisfy the relation*

$$\begin{aligned}\hat{u} &\leq \underline{u}^{(m)} \leq \underline{u}^{(m+1)} \leq u^* \leq \\ &\leq \overline{u}^{(m+1)} \leq \overline{u}^{(m)} \leq \tilde{u} \quad \text{in } \overline{Q}_T,\end{aligned}$$

for every $m \geq 1$.

Proof. In view of Lemma 5.3 the pointwise limits

$$\lim_{m\to\infty} \underline{u}^{(m)}(t,x) = \underline{u}(t,x) \quad \text{and} \quad \lim_{m\to\infty} \overline{u}^{(m)}(t,x) = \overline{u}(t,x), \tag{5.15}$$

exist and satisfy $\underline{u}^{(m)} \leq \underline{u} \leq \overline{u} \leq \overline{u}^{(m)}$ for every m. Depending on the previous results, we conclude that $\underline{u}$ and $\overline{u}$ satisfy the relations of (5.1). For a clearer detail on this point, see Friedman [39] or Pao [94].

To show the uniqueness of the solution, we let $w(t,x) = e^{-kt}(\underline{u}(t,x) - \overline{u}(t,x))$ for a sufficiently large constant k. Then, by (5.1), (5.4), $F(t,x,\underline{u}) \leq F(t,x,\overline{u})$, $w(t,x)$ satisfies the relations

$$\begin{cases} (w)_t - D(w)\Delta w + B(t,x)\cdot\nabla w + \\ (k + C(t,x))w \leq 0 \text{ in } Q_T \\ \\ w(t,x) = 0 \quad \text{ on } \Sigma \\ w(0,x) = 0 \quad \text{ in } \Omega, \end{cases}$$

where B and C are given in the form of (5.8) with respect to $D(u)$, and with $\hat{u}$, $\tilde{u}$ replaced by $\underline{u}$, $\overline{u}$ respectively, i.e.,

$$\begin{aligned} B(t,x) &= -\nabla D\left(\underline{u}\right) - D'(\theta_1)\nabla(\overline{u}) \\ C(t,x) &= -\mathbf{div}\left(D'(\theta_1)\nabla(\overline{u})\right) - f_w(t,x,\theta_2). \end{aligned}$$

Since B and C are bounded in $\overline{Q}_T$. The argument in the proof of Theorem 5.1 in Pao [94] shows that $w \leq 0$. It follows from $\underline{u} \leq \overline{u}$ that $\underline{u} = \overline{u}$. This proves that $\underline{u} = \overline{u} \equiv u^*$ in Q_T and $\overline{u}^*$ is the unique solution of (5.1) which completes the proof of our theorem. ■

5.6 Application

As an application of the obtained result, we give a two-species Lotka-Volterra competition model with polynomial growth, where the diffusion coefficient is degenerated; it is the following

$$(5.16) \qquad \begin{cases} u_t - d(x)\Delta u^{\alpha} = u(a + bu^{\nu}) & \text{in } Q_T \\ u(t,x) = 0 & \text{on } \Sigma \\ u(0,x) = \Psi(x) & \text{in } \Omega, \end{cases}$$

where α, a, b and ν are positive constants, and d is a positive smooth function on $\overline{\Omega}$. It is obvious that problem (5.16) is special case of (5.1) with

$$\begin{aligned} D(u) &= \alpha u^{\alpha-1} \\ f(u) &= u\left(a + bu^{\nu}\right) \\ u_0(t,x) &= 0. \end{aligned}$$

This model is well studied in Pao [94], where we also find other models similar to problem (5.1).

5.7 Conclusion

Despite the difficulties encountered in this study, we managed to obtain important results; It can be applied to other similar models. There are many other important open problems that we hope to study in the near future, the first of which is to study the same problem numerically using one of the well-known numerical methods. We also hope to study the asymptotic behavior of solutions.

Chapter 6

On the existence of weak periodic solutions for a class of quasilinear parabolic problems

In this paper, we are interested in the study of a quasilinear parabolic problem with an arbitrary growth nonlinearity in gradient and nonlinear boundary conditions. This model appears in the modeling of many diffusion phenomena in various sciences. Using techniques of functional analysis based on Schauder's fixed point theorem; we prove an existence result of weak periodic solutions.

Several partial results were obtained with additional hypotheses justifying a paper accepted for publication in an international journal specialized in Mathematics (Journal of Applied Mathematics and Computational Mechanics), in collaboration with S. Mesbahi and N. Alaa.

6.1 Introduction

In our lived reality we find many periodic physical, environmental, biological phenomena, which can be mathematically modeled by reaction diffusion systems. As is the case, for example, in problems arising from the population ecology, where the data depend periodically on time according to seasonal or daily variations. We can also find many other models in this context in the works of Murray [78, 79]. We mention that many mathematicians have been interested in the study of this type of phenomena, whether in terms of mathematical modeling, the existence of solutions or their behavior, or otherwise, using different methods depending on the situation. This is what we can find in [4], [121] and references given there; where we find other models in addition to what was previously mentioned.

Our work will be in this context. More precisely, we will prove the existence of weak periodic solutions for a class of quasilinear parabolic reaction-diffusion models. For this we will use a technique based on Schauder's fixed point theorem. We are then interested in the following problem

$$\begin{cases} \dfrac{\partial u}{\partial t} - d\Delta u + \sigma |\nabla u|^p = 0 & \text{in } Q_T \\ u(0,.) = u(T,.) & \text{in } \Omega \\ -\dfrac{\partial u}{\partial \eta} = \beta(x,t)u + g(t,x,u) & \text{on } \Sigma_T \end{cases} \tag{6.1}$$

where Ω is an open regular bounded subset of $\mathbb{R}^N$, $N \geq 1$, with the smooth boundary $\partial\Omega$, $T > 0$ is the period, $Q_T =]0,T[\times\Omega$, $\Sigma_T =]0,T[\times\partial\Omega$, $p \geq 1$, $d > 0, \sigma > 0$ and η denote the unit normal vector to the boundary $\partial\Omega$.

Our work is mainly focused on research of periodic solutions in an appropriate space of T-periodic functions. To achieve our goal, we will rely on the following theorem for maximal monotone mappings joint with a suitable fixed point argument.

Theorem 6.1 (for maximal monotone mappings)**.** *Let L be a linear closed, densely defined operator from the reflexive space $\mathcal{V}$ to $\mathcal{V}^*$, L maximal monotone and let A be a bounded hemicontinuous monotone mapping from $\mathcal{V}$ to $\mathcal{V}^*$, then $L+A$ is maximal monotone in $\mathcal{V}\times\mathcal{V}^*$. Moreover, if $L+A$ is coercive, then $Range(L+A) = \mathcal{V}^*$.*

For the proof of this theorem as well as for some applications, see Browder [21] and Lions [65].

The rest of this paper is organized as follows. In the next section, we formulate the necessary assumptions, we choose the functional framework in which we search periodic solutions to our problem, we also introduce the idea of a weak periodic solution, and then we state our main result. In the third section, we prove the existence and uniqueness of a periodic solution for an abstract problem formulated by means of maximal monotone mappings. The penultimate section is devoted to proving the main result. The paper ends with a conclusion.

6.2 Statement of the main result

In this section, we will formulate the necessary assumptions for our problem and then establish our main result.

6.2.1 Assumptions

Throughout this work, we consider the following assumptions:

$(H1)$ β is a periodic positive continuous and bounded function such that

$$0 < \beta_1 \leq \beta(t,x) \leq \beta_2, \ \forall (t,x) \in \Sigma_T$$

$(H2)$ $g : \Sigma_T \times \mathbb{R}^+ \to \mathbb{R}$ is a periodic Caratheodory function in time, $s \mapsto g(t,x,s)$ is nondecreasing with respect to s for a.e. $(t,x) \in \Sigma_T$ and

$$\begin{array}{rcl} s.g(t,x,s) & \geq & 0 \\ |g(t,x,s)| & \leq & \xi(t,x) + |s| \ \text{ where } \xi \in L^2(\Sigma_T) \end{array}$$

6.2.2 Functional framework and definitions

Here, we present our functional framework for the periodic solutions of our problem. We define $\mathbf{v} = \{\psi \in D(\Omega), \mathbf{div}\psi = 0\}$, and we will denote V to the adherence of $\mathbf{v}$ in $H^1(\Omega)$, V' to the topological dual space of V, H to the adherence of $\mathbf{v}$ in $L^2(\Omega)$ and X' to the topological dual space of H.

We have $V \subset H \subset V'$ with continuous and dense injection.

$$\begin{array}{rcl} \mathcal{V} & = & L^2\left(0,T;H^1(\Omega)\right) \cap L^\infty\left(0,T;H \cap W^{1,q}(\Omega)\right) \\ \mathcal{V}^* & = & L^2\left(0,T;\left(H^1(\Omega)\right)^*\right) + L^1\left(0,T;X'\right) \end{array}$$

with $q = 2p$, and we denote by $\left(H^1(\Omega)\right)^*$ the topological dual space of $H^1(\Omega)$ and $\langle \cdot,\cdot \rangle$ present the duality pairing between $\mathcal{V}$ and $\mathcal{V}^*$. For more details and information, see (Lions [65]). The standard norm of $L^2\left(0,T;H^1(\Omega)\right)$ is defined by

$$\|u\|_{L^2(0,T;H^1(\Omega))} := \left(\int_{Q_T} |\nabla u(t,x)|^2 \, dt dx + \int_{Q_T} |u(t,x)|^2 \, dt dx\right)^{\frac{1}{2}}$$

Throughout this paper, we equipped $\mathcal{V}$ with the norm

$$\|u\|_{\mathcal{V}} := \left(\int_{Q_T} |\nabla u(t,x)|^2 \, dt dx + \int_{\Sigma_T} \beta(t,\sigma) |\tilde{u}(t,\sigma)|^2 \, dt d\sigma\right)^{\frac{1}{2}}$$

which is equivalent to the standard norm of $L^2\left(0,T;H^1(\Omega)\right)$. We denote by $\tilde{u}$ the trace of u on Σ_T. Let us define the set

$$\mathscr{W}(0,T) := \left\{ u \in \mathscr{V} \mid \frac{\partial u}{\partial t} \in \mathscr{V}^* \text{ and } u(0) = u(T) \right\}$$

equipped with the norm $\|u\|_{\mathscr{W}(0,T)} := \|u\|_{\mathscr{V}} + \left\|\frac{\partial u}{\partial t}\right\|_{\mathscr{V}^*}$.

It is obvious that $\mathscr{W}(0,T)$ is dense in $\mathscr{V}$ due to the density of $C^\infty\left(\overline{Q}\right) \subset \mathscr{W}(0,T)$ in $\mathscr{V}$. For more details on this point, the reader can refer to Lions [65].

Now, we present the concept of a weak periodic solution of our problem.

Definition 6.1. A function u is said to be a weak periodic solution of the problem (6.1), if $u \in \mathscr{V}$ and for all $\varphi \in \mathscr{W}(0,T) \cap L^\infty(Q_T)$, we have

$$-\left\langle u, \frac{\partial \varphi}{\partial t} \right\rangle + d\int_{Q_T} \nabla u \nabla \varphi + \sigma \int_{Q_T} |\nabla u|^p \varphi + \int_{\Sigma_T} \beta(t,x)\tilde{u}\tilde{\varphi} + \int_{\Sigma_T} g(t,x,\tilde{u})\tilde{\varphi} = 0$$

6.2.3 The main result

Now, we can state the main result of this paper, it is the following theorem.

Theorem 6.2. *Under hypotheses* $(H1)$ *and* $(H2)$*, the problem* (6.1) *admits a weak periodic solution* $u \in \mathscr{W}(0,T)$.

6.3 Abstract problem

Using Theorem 6.1, we will prove the existence and uniqueness of a periodic solution for an abstract problem formulated by means of maximal monotone mappings.

Having fixed $w \in \mathscr{V}$, we consider the problem

$$-\left\langle u, \frac{\partial \varphi}{\partial t} \right\rangle + d\int_{Q_T} \nabla u \nabla \varphi + \sigma \int_{Q_T} |\nabla w|^p \varphi + \int_{\Sigma_T} \beta(t,x)\tilde{u}\tilde{\varphi} + \int_{\Sigma_T} g(t,x,\tilde{u})\tilde{\varphi} = 0 \tag{6.2}$$

In order to use Theorem 6.1, we must define two mappings L and A:

L is the linear operator defined by

$$L : \mathscr{W}(0,T) \to \mathscr{V}^* \quad \text{with} \quad \langle Lu, \varphi \rangle = \int_{Q_T} u_t \varphi \, dt\, dx, \ \forall \varphi \in \mathscr{W}(0,T)$$

This operator is closed, skew-adjoint (i.e., $L = -L^*$) and maximal monotone (see Lemma 1.1, p 313 and Section 2.2 of Chapter 3 in Lions [65]). As for the operator A, it is defined as follows:

$$\begin{array}{rcl} A & : & \mathcal{V} \to \mathcal{V}^* \\ \langle Au, \varphi \rangle & = & d\displaystyle\int_{Q_T} \nabla u \nabla \varphi + \int_{\Sigma_T} \beta(t,x)\tilde{u}\tilde{\varphi} + \int_{\Sigma_T} g(t,x,\tilde{u})\tilde{\varphi}, \ \forall \varphi \in \mathcal{W}(0,T) \end{array}$$

The following proposition summarizes the properties of the operator A.

Proposition 6.1. *If the assumptions* $(H1)$ *and* $(H2)$ *are fulfilled, then the mapping A is (i) hemicontinuous, (ii) monotone and (iii) coercive.*

Proof. **(i)** The hemicontinuity follows from the Hölder inequality. In fact,

$$\left|\langle Au, \varphi \rangle\right| \le \left| d\int_{Q_T} \nabla u \nabla \varphi \right| + \left| \int_{\Sigma_T} \beta(t,x)\tilde{u}\tilde{\varphi} \right| + \left| \int_{\Sigma_T} g(t,x,\tilde{u})\tilde{\varphi} \right|$$

which implies

$$\begin{array}{rcl} \left|\langle Au, \varphi \rangle\right| & \le & \left[\left(d + 1 + \dfrac{1}{\beta_1} \right) \|u\|_{\mathcal{V}} + \dfrac{1}{\sqrt{\beta_1}} \|\xi\|_{L^2(Q_T)} \right] \|\varphi\|_{\mathcal{V}} \\ \|Au\|_* & \le & \left(d + 1 + \dfrac{1}{\beta_1} \right) \|u\|_{\mathcal{V}} + \dfrac{1}{\sqrt{\beta_1}} \|\xi\|_{L^2(\Sigma_T)} \end{array}$$

(ii) According to $(H2)$, the function $s \mapsto g(t,x,s)$ is nondecreasing with respect to s for a.e. (t,x). So,

$$\int_{\Sigma_T} [g(t,x,\tilde{u}) - g(t,x,\tilde{u})](\tilde{u} - \tilde{v}) > 0$$

then $\langle Au - Av, u - v \rangle > 0$, which shows the strict monotony of A.

(iii) According to $(H2)$, we have $g(t,x,\tilde{u})\tilde{u} \ge 0$. Then

$$\langle Au, u \rangle \ge d\int_{Q_T} |\nabla u|^2 + \int_{\Sigma_T} \beta(t,x)|\tilde{u}|^2$$

which implies $\lim\limits_{\|u\|_{\mathcal{V}} \to +\infty} \frac{\langle Au, u \rangle}{\|u\|_{\mathcal{V}}} = +\infty$; hence the coercivity. ■

Besides that, let $G \in \mathcal{V}^*$ be the linear functional defined as follows.

$$\langle G, \varphi \rangle = -\sigma \int_{Q_T} |\nabla w|^p \varphi, \ \forall \varphi \in \mathcal{W}(0,T)$$

then, problem (6.2) can be reformulated in the following abstract form

$$Lu + Au = G \tag{6.3}$$

Now we state the main result of this section, it is the following proposition.

Proposition 6.2. *Let $w \in \mathcal{V}$ be given and assuming $(H1)$ and $(H2)$,then the problem (6.3) has a unique weak periodic solution.*

Proof. The existence of weak periodic solution descends from Theorem 6.1. Uniqueness is a consequence of the strict monotonicity. Indeed, suppose that u_1, u_2 are solutions of problem (6.3). So, $Lu_1 + A(u_1) = G$ and $Lu_2 + A(u_2) = G$, which implies $\langle Lu_1 + A(u_1) - Lu_2 - A(u_2), u_1 - u_2 \rangle = 0$. It is a contradiction because of the strict monotonicity. ■

6.4 Proof of the main result

Now we can prove Theorem 6.2 based on previous results.

of Theorem 6.2 The existence of weak solutions to (6.1) will be based on the research of fixed points for the following mapping

$$\Psi : \mathcal{V} \to \mathcal{V} \quad \text{with} \quad w \mapsto \Psi(w) = u$$

where u is the unique weak periodic solution of the following problem

$$\begin{cases} \dfrac{\partial u}{\partial t} - d\Delta u + \sigma |\nabla w|^p = 0 & \text{in } Q_T \\ u(0,.) = u(T,.) & \text{in } \Omega \\ -\dfrac{\partial u}{\partial \nu} = \beta(x,t)u + g(t,x,u) & \text{on } \Sigma_T \end{cases} \tag{6.4}$$

The existence and uniqueness of the weak periodic solution is clear, which shows that the application is well defined.

(i) Continuity of Ψ : We will prove some very important estimates and convergences. Let $w_n \in \mathcal{V}$ be a sequence strongly converges to w in $\mathcal{V}$. Moreover, let u_n denote the weak periodic solution of the problem

$$\begin{aligned} -\left\langle u_n, \frac{\partial \varphi}{\partial t}\right\rangle + d\int_{Q_T} \nabla u_n \nabla \varphi + \\ +\sigma \int_{Q_T} |\nabla w_n|^p \varphi + \int_{\Sigma_T} \beta(t,x) u_n \varphi + \int_{Q_T} g(t,x,u_n)\varphi = 0 \end{aligned} \tag{6.5}$$

Setting $\varphi = u_n$ as a test function in (6.5), we have

$$\begin{aligned} d\int_{Q_T} |\nabla u_n|^2 + \int_{\Sigma_T} \beta(t,x)|u_n|^2 &\le \frac{\sigma}{2\varepsilon}\int_{Q_T} \left(|\nabla w_n|^p\right)^2 + \frac{\varepsilon}{2}\int_{Q_T} |u_n|^2 \\ &\le \frac{\sigma}{2\varepsilon}\int_{Q_T} \left(|\nabla w_n|^p\right)^2 + \frac{\varepsilon}{2}\|u_n\|_{L^2(0,T;H^1(\Omega))} \end{aligned}$$

and taking into account the equivalence of the norms in $\mathcal{V}$, we have

$$d\int_{Q_T} |\nabla u_n|^2 + \int_{\Sigma_T} \beta(t,x)|u_n|^2 - \frac{\varepsilon}{2}c(T,\Omega)\|u_n\|_{\mathcal{V}} \le \frac{\sigma}{2\varepsilon}\int_{Q_T} \left(|\nabla w_n|^p\right)^2$$

which give

$$\left(\min\{1,d\} - \frac{\varepsilon}{2}c(T,\Omega)\right)\|u_n\|_{\mathcal{V}} \le \frac{\sigma}{2\varepsilon}\int_{Q_T} \left(|\nabla w_n|^p\right)^2 \le c'(\varepsilon)$$

We choose ε small enough to obtain the following classical energy estimate

$$\|u_n\|_{\mathcal{V}} \le c'' \tag{6.6}$$

where the positive real constant c'' is independent of n. From (6.5) and the energy estimate (6.6), we get that $\left(\frac{\partial u_n}{\partial t}\right)$ is bounded in the $\mathcal{V}^*$ norm; which proves the boundedness of u_n in $\mathcal{W}(0,T)$, i.e., $\|u_n\|_{\mathcal{W}(0,T)} \le c''$, for all $n \in \mathbb{N}$. Thus, we can extract a subsequence denoted u_n such that $u_n \rightharpoonup u$ weakly in $\mathcal{V}$ as $n \to +\infty$. By Aubin's theorem in [112], the sequence u_n is precompact in $L^2(Q_T)$. So, $u_n \to u$ in $L^2(Q_T)$ and a.e. in Q_T. Furthermore, according to the trace theorem, see (Morrey [75], Theorem 3.1.4), we have $u_n \to u$ in $L^2(\Sigma_T)$ and a.e. in Σ_T.

Now, we prove that the sequence ∇u_n strongly converges to ∇u in $L^2(Q_T)$.

We have

$$d\lim_{n\to+\infty}\int_{Q_T} |\nabla u_n|^2 = -\int_{\Sigma_T} \beta(t,x)u^2 - \int_{Q_T} g(t,x,u)u - \sigma\int_{Q_T} |\nabla w|^p u \tag{6.7}$$

Moreover, setting $\varphi = u$ as a test function in (6.5), it comes

$$d\int_{Q_T} |\nabla u|^2 = -\int_{\Sigma_T} \beta(t,x)u^2 - \int_{Q_T} g(t,x,u)u - \sigma\int_{Q_T} |\nabla w|^p u \tag{6.8}$$

and by comparing (6.7) and (6.8), it results $\lim\limits_{n\to+\infty} \int_{Q_T} |\nabla u_n|^2 = \int_{Q_T} |\nabla u|^2$. Consequently, the mapping Ψ is continuous.

(ii) Compactness of Ψ : Let (w_n) be a bounded sequence in $\mathcal{V}$ and we denote $u_n = \Psi(w_n)$. As in the previous step (up to a subsequence), we have

$$\begin{array}{rcl}
w_n & \rightharpoonup & w \text{ weakly in } \mathcal{V} \\
u_n & \rightharpoonup & u \text{ weakly in } \mathcal{V} \\
\dfrac{\partial u_n}{\partial t} & \rightharpoonup & \dfrac{\partial u}{\partial t} \text{ weakly in } \mathcal{V}^* \\
u_n & \to & u \text{ strongly in } L^2(Q_T) \text{ and a.e. in } Q_T \\
u_n & \to & u \text{ strongly in } L^2(\Sigma_T) \text{ and a.e. in } \Sigma_T
\end{array}$$

It suffices to prove the strong convergence of (∇u_n) in $L^2(Q_T)$. Note that the absence of almost everywhere convergence of (∇w_n) in Q_T poses a difficulty, but we can overcome it. It is obvious that

$$\lim_{n\to+\infty} \int_{Q_T} \nabla u(\nabla u_n - \nabla u) = 0$$

Now, let (w_n) be a bounded sequence in $\mathcal{V}$ and we denote $u_n = \Psi(w_n)$. By the same reasoning of the first step, we have

$$\begin{array}{rcl}
w_n & \rightharpoonup & w \text{ weakly in } \mathcal{V} \\
u_n & \rightharpoonup & u \text{ weakly in } \mathcal{V} \\
\dfrac{\partial u_n}{\partial t} & \rightharpoonup & \dfrac{\partial u}{\partial t} \text{ weakly in } \mathcal{V}^*
\end{array}$$

$$\begin{array}{rcl}
u_n & \longrightarrow & u \text{ strongly in } L^2(Q_T) \text{ and a.e. in } Q_T \\
u_n & \longrightarrow & u \text{ strongly in } L^2(\Sigma_T) \text{ and a.e. in } \Sigma_T
\end{array}$$

To get the compactness of Ψ, it suffices to prove the strong convergence of (∇u_n) in $L^2(Q_T)$, noting that the difficulty is presented by the absence of the almost everywhere convergence of (∇w_n) in Q_T , but we can overcome this problem by observing that

$$\int_{Q_T} |\nabla u_n - \nabla u|^2 = \int_{Q_T} \nabla u_n (\nabla u_n - \nabla u) - \int_{Q_T} \nabla u (\nabla u_n - \nabla u)$$

Thanks to the weak convergence of (u_n) in $\mathcal{V}$, we get

$$-\left\langle u_n, \frac{\partial u_n}{\partial t} \right\rangle + \int_{Q_T} |\nabla u_n|^2 + \int_{Q_T} |\nabla w_n|^p u_n + \int_{\Sigma_T} \beta(t,x) u_n^2 + \int_{Q_T} g(t,x,u_n) u_n = 0$$

which leads to

$$\begin{aligned} \sigma \int_{Q_T} \left| |\nabla w_n|^p (u_n - u) \right| &\leq \sigma \left(\int_{Q_T} \left(|\nabla w_n|^p \right)^2 \right)^{\frac{1}{2}} \left(\int_{Q_T} |u_n - u|^2 \right)^{\frac{1}{2}} \\ &= \sigma \left(\int_{Q_T} \left(|\nabla w_n|^p \right)^2 \right)^{\frac{1}{2}} \|u_n - u\|_{L^2(Q_T)} \end{aligned}$$

then

$$\lim_{n \to +\infty} \int_{Q_T} \left| |\nabla w_n|^p (u_n - u) \right| = 0$$

Note that $\left(\int_{Q_T} (|\nabla w_n|^p)^2 \right)^{\frac{1}{2}}$ is convergent because $w_n \in \mathcal{V}$. Also note that the periodicity and the weak convergence of $\left(\frac{\partial u_n}{\partial t} \right)$ in $\mathcal{V}^*$ yields

$$\lim_{n \to +\infty} \left\langle \frac{\partial u_n}{\partial t}, u_n - u \right\rangle = - \lim_{n \to +\infty} \left\langle \frac{\partial u_n}{\partial t}, u_n \right\rangle - \lim_{n \to +\infty} \left\langle \frac{\partial u_n}{\partial t}, u \right\rangle = 0$$

Now, we pass to the limit, it results

$$\lim_{n \to +\infty} \int_{Q_T} \nabla u_n (\nabla u_n - \nabla u) = 0$$

which ensures the compactness of Ψ.

(iii) Ψ send the ball of $\mathcal{V}$ of R radius to itself. Indeed, we get the existence of a constant $R > 0$ such that $\Psi(B(0,R)) \subset B(0,R)$ where $B(0,R)$ is the ball of $\mathcal{V}$ with radius R. Let $w \in \mathcal{V}$ and $u = \Psi(w)$, by taking u as test function in the equation satisfied by u, we easily find

$$\|u\|_{\mathcal{V}} \leq \left(\int_{Q_T} \left(|\nabla w_n|^p \right)^2 \right)^{\frac{1}{2}} := R$$

This is what ends the proof of our theorem. ■

APPENDIX

A

CONCLUSION AND PERSPECTIVES

This study focuses on the analysis and mathematical modeling of reaction-diffusion systems that are frequently used in the modeling of diffusion phenomena in various natural sciences, especially in biology, ecology and medicine.

- **The aim of this thesis was to study several biological and medical problems via reaction-diffusion systems in order to assess their effect to the resolution of problems despite the complexity of the matter, presence of many constraints and multitude of parameters. We choose the quasilinear and degenerate problem because it's the closer to reality biological and medical.**

- **Many important results have been obtained with additional assumptions that can be applied to several models in biology, ecology, physics and others as appropriate.**

- **We have developed original methods to overcome certain difficulties, and despite the complexity of the models studied, we have managed to obtain several important results, original and solve very difficult news problems.**

In addition to this work, we can address the following interesting questions :

(i) The mathematical analysis of anisotropic system, which consists in adding diffusion coefficients to the studied system depending on (t,x) or more generally depending on $(t,x,u,\nabla u)$.

(ii) The asymptotic behavior of the solutions of the studied problems.

(iii) We would like to implement some numerical simulations in order to get a better understanding of the solutions at large times

(iv) It is important to study the same model with other conditions.

(v) We would like to develop work on modeling the diffusion of the Coronavirus.

This list of loose themes corresponds to work in progress or prospective. Some are a continuation of the work already done, and some are new research projects.

This not only makes it possible to tackle current reality and its fears, but also to go beyond the theoretical framework by developing models and tools that can be used and transferred to different sciences.

APPENDIX B

KNOWN NAMES IN THE FIELD OF REACTION-DIFFUSION SYSTEMS

The purpose of this page is to present some mathematicians who, through their works, have contributed to the development of reaction-diffusion systems.

J**acques-Louis Lions**, (born in Grasse on May 3, 1928 and died in Paris on May 17, 2001) is a French mathematician, member of the Academy of Sciences. He was a lecturer then professor at the Faculty of Sciences of Nancy (1954-1963), professor at the Faculty of Sciences of Paris (1963-1972), professor of digital analysis at the École Polytechnique (1966-1986) and finally professor at the college of France (1973-1998). His work mainly focused on the theory of partial differential equations and their applications, and in particular on variational problems, control theory and systems of partial differential inequalities.

J**ames Dickson Murray**, (born January 2, 1931 in Moffat, Scotland) is a British mathematician, Professor Emeritus of Applied Mathematics at the University of Washington and the University of Oxford. He is best known for his authoritative book “Mathematical Biology”. Its research is characterized by its great variety and depth: an early example is its fundamental contribution to understanding the biomechanics of the human body when launched from an aircraft into an ejection seat. He has contributed to many other areas, ranging from understanding and preventing severe scarring; the formation of fingerprints; the determination of the sex, the modeling of the animal’s coat and the formation of the territory of populations in interaction wolf-deer.

M**ichel Pierre**, is a french mathematician, born in 1949 in France. Professor at ENS Cachan Bretagne (since 1996) and researcher at IRMAR, Digital Analysis team. Research topics: optimization of forms and reaction-diffusion systems. He is author and co-author of a very large number of scientific papers in various branches of applied mathematics. He has greatly contributed to the development of many methods of dealing with reaction-diffusion systems.

N**oureddine Alaa**, is a moroccan mathematician, born in 1961 in Marrakesh. He is the pupil of Michel Pierre. He has numerous scientific publications in various branches of mathematics, in particular reaction-diffusion systems and its applications. He is currently a mathematics professor in the Marrakesh university. He is credited with the development of several analytical and numerical methods in applied mathematics.

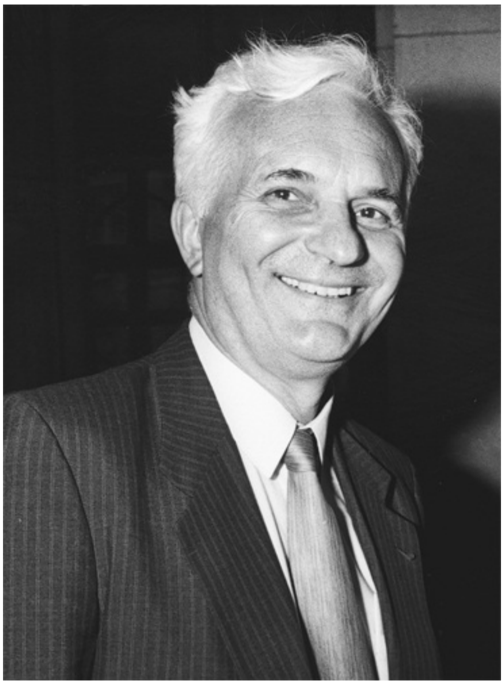

FIGURE B.1. Jacques-Louis Lions (1928-2001).

M**okhtar Kirane**, is an algerian mathematician, received a PhD in Mathematics from the University of Pierre et Marie Curie, Paris VI, France in 1983, and a Habilitation to conduct research from the University of Picardie, France, in 2000. He is currently a mathematics professor in La Rochelle University, France. He has a very large number of scientific papers in various branches of applied mathematics. He is well known for his works on reaction-diffusion systems.

A**mmar Youkana**, is an algerian mathematician, born June 11, 1958 in Batna, Algeria. He graduated in applied mathematics from the Jacques-Louis Lions Laboratory, Pierre and Marie Curie University - Paris VI, France in 1986. He is well known for his works on reaction-diffusion systems and its applications. He is currently a mathematics professor in the Mathematics Department of the Mustapha Ben Boulaïd University of Batna.

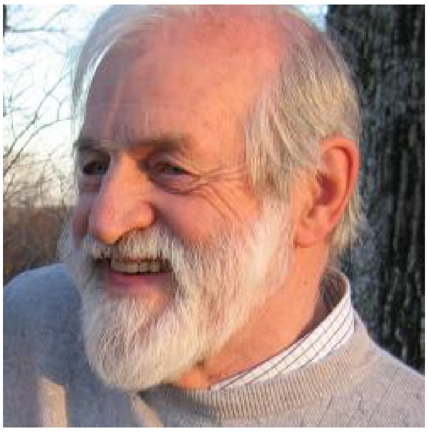

FIGURE B.2. James Dickson Murray (1931).

FIGURE B.3. Michel Pierre (1949).

FIGURE B.4. Noureddine Alaa (1961).

FIGURE B.5. Mokhtar Kirane.

FIGURE B.6. Ammar Youkana (1958).

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Doctoral thesis

in Mathematics Applied to Biological and Medical Sciences

Presented by : **Khaoula Imane SAFFIDINE**
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العنوان : النمذجة والتحليل الرياضي لبعض أنظمة تفاعل-انتشار المستمدة من علم الأحياء والطب.

ملخص : العمل الذي يشكل هذه الأطروحة هو مساهمة في النمذجة والتحليل الرياضي لأنظمة تفاعل-انتشار المستمدة من علم الأحياء والطب. نحن مهتمون بدراسة وجود حلول لبعض النماذج المكافئة والناقصة؛ باستخدام تقنيات تعتمد على التحليل الوظيفي وطريقة الحلول العلوية والسفلية. يتكون هذا العمل من ستة فصول مستقلة، مسبوقة بمقدمة عامة تسلط الضوء على فن الموضوع والمشكلات التي تم تناولها.

كلمات مفتاحية : أنظمة تفاعل-انتشار ، الأنظمة المكافئة المتدهورة ، الحلول العلوية والسفلية ، نمذجة ظواهر الانتشار.

Titre : MODÉLISATION ET ANALYSE MATHÉMATIQUE DE CERTAINS SYSTÈMES DE RÉACTION-DIFFUSION ISSUS DE LA BIOLOGIE ET DE LA MÉDECINE.

Résumé :

Le travail constituant cette thèse est une contribution à la modélisation et l'analyse mathématique de systèmes de réaction-diffusion issus de la biologie et de la médecine. Nous nous intéressons à l'étude de l'existence de solutions de certains modèles paraboliques et elliptiques ; utilisant des techniques basées sur l'analyse fonctionnelle et la méthode de sous et sur solutions. Ce travail est alors composé de six chapitres indépendants, précédés d'une introduction générale qui met en évidence l'art du sujet et les problèmes abordés.

Mots-clés : systèmes de réaction-diffusion, systèmes paraboliques dégénérés, sous et sur solutions, modélisation des phénomènes de diffusion.

Title : MODELING AND MATHEMATICAL ANALYSIS OF SOME REACTION-DIFFUSION SYSTEMS DRIVEN FROM BIOLOGY AND MEDICINE.

Abstract : The work constituting this thesis is a contribution to the modeling and mathematical analysis of reaction-diffusion systems driven from biology and medicine. We are interested in studying the existence of solutions of some parabolic and elliptical models; using techniques based on functional analysis and the method of upper and lower solutions. This work is then composed of six independent chapters, preceded by a general introduction which highlights the art of the subject and the problems addressed.

Keywords : reaction diffusion systems, degenerate parabolic systems, upper and lower solutions, modeling of diffusion phenomena.