AGE-STRUCTURED POPULATION DYNAMICS: AGE-DEPENDENT DIFFUSION AND DEATH RATES, AND THEIR APPLICATIONS TO THE CELL POPULATION

MOHAMMADKHEER M. AL-JARARHA

Age-structured Population Dynamics: Age-dependent Diffusion and Death Rates, and Their Applications to the Cell Population

by

©Mohammadkheer M. Al-Jerarha

A thesis submitted to the School of Graduate Studies in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

Department of Mathematics and Statistics
Memorial University of Newfoundland

Memorial University of Newfoundland

August 2011

St. John's Newfoundland

Abstract

Age-structured models play a major role in mathematical biology, ecology, and epidemiology. Therefore, it is important and interesting to investigate these models and their dynamics. In first part of this thesis, we consider the standard age-structure model with diffusion:

$$\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} = D(a)\frac{\partial^2 u}{\partial x^2} - d(a)u,$$

where $u(t, a, x)$ is the population density of the species at time t, age a, and location x in Ω ($\Omega = \mathbb{R}$ or $\Omega = [a, b] \subseteq \mathbb{R}$). The age-functions $D(a)$ and $d(a)$ are the age-dependent diffusion and death rates, respectively. For this case, we constructed a completely new model in terms of an integral equation. To investigate the new model, we consider two cases, the unbounded spatial domain case as well as the bounded domain case. For the unbounded domain case, we investigate the existence of traveling wave solution and the existence of spreading speed c^*, for different choices of birth functions. For the bounded spatial domain case, we investigate the existence and stability of positive steady state solution for different choices of birth functions. As a by-product, we also prove rigorously the existence of real principal eigenvalue with strongly positive eigenfunctions.

In the second part of this thesis, we present an age-size structured model to represent the dynamics of cell population in two comparative phases G_0 − Phase (the resting phase) and $P-$ Phase (the proliferation phase), during the cell-division cycle. Using this model, we derive a non-linear delay differential equation with a non-local term to represent the density of cell population in the resting phase (G_0- Phase). We also investigate the local stability of the zero solution of this delay differential equation. To do this, we investigate the analogous variational linear delay differential equation around the zero solution. Conclusively, we show that the linear delay differential equation admits a real eigenvalue, as well as a strongly positive real eigenfunctions. To support our mathematical results, we present a numerical simulation for each case.

Acknowledgements

First and foremost, I would like to express my sincere appreciation for my supervisor Dr. Chunhua Ou, for his encouragement, guidance and support during my Ph.D. program. Also, my thanks go to the supervising committee Dr. P. Heath, Dr. A. Foster, and Dr. B. Watson, as well as my thanks and appreciation go to the members of committee for their valuable and suggestive remarks.

Also, I would like to thank my teachers in MUN, especially, Dr. X.-Q. Zhao for teaching me the infinite dynamical systems course, and for his kind help. My thanks also are for the Math and Stat department staff members, and for my colleges in the department.

Finally, I would like to thank all my honest and truly friends here in Canada or at home; as well as my deepest thanks and appreciation are for my parents, for brothers and sisters.

Table of Contents

List of Figures

Chapter 1

Introduction

1.1 Age-structured Models in Biological Populations

Simple models often provide a good understanding about a simple population, or useful information about large and complicated populations. In 1798, T. R. Malthus proposed a simple model of population dynamics. In this model, Malthus assumed that the population growth rate is proportional to the size of the population. More precisely, if $N(t)$ represents the size of the population at time t, the governed differential equation is given as

$$\frac{d}{dt}N(t) = r \cdot N(t), \; t \geq 0, \; N(0) = N_0, \tag{1.1.1}$$

where the parameter r is the Malthusian's parameter of the given population. In fact, $r = b - d$, where b and d are the birth and death rates of the given population. The above equation is a linear ordinary differential equation. The solution of this equation is given by

$$N(t) = N_0 \cdot e^{rt} = N_0 \cdot e^{(b-d)t}. \tag{1.1.2}$$

It is easy to see that if $b > d$, then the population grows exponentially, while if $b < d$, then the population dies out. This model does not take in account the effects of the crowding or the limitation of the resources. Frankly, this model is unrealistic. A more realistic model was proposed by P. F. Verhulst in 1838. In this model, Verhulst allowed the Malthusian's parameter to depend on the size of the total population itself. Verhulst's model is given by the following differential equation:

$$\frac{d}{dt}N(t) = r \cdot N(t)\,(1 - \frac{N(t)}{K}),\ t \geq 0,\ N(0) = N_0, \tag{1.1.3}$$

where r and K are positive constants. The birth rate $r \cdot (1 - \frac{N(t)}{K})$ depends on $N(t)$. The constant K is the carrying capacity of the environment. Usually, the carrying capacity is determined by the available sustaining resources. The constant r is known as the interact growth constant. Usually, the above equation is called the logistic equation. The above logistic equation is a simple non-linear ordinary differential equation, and is easily solved by the separation of variables. The explicit solution of this equation is given by:

$$N(t) = \frac{N_0\,K\,e^{rt}}{K + N_0\,(e^{rt} - 1)}. \tag{1.1.4}$$

From this formula, it is easy to see that the solution $N(t)$ converges to K when t is large. In fact, if $N_0 < K$, then $\frac{dN}{dt} > 0$ and so the solution increases to K; while if $N_0 > K$, then $\frac{dN}{dt} < 0$ and so the solution decreases to K. Commonly, we observe that if $N_0 < k/2$, then the solution $N(t)$ has a typical sigmoid character (see Figure 1.1).

In biology and ecology, one of the most important effects on the population dy-

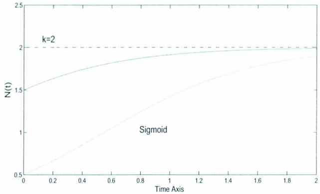


Figure 1.1: The solution, $N(t)$, of the logistic differential equation for different initial values. The carrying capacity $K = 2$.

namics is the age distribution within the population. In fact, to include the age effects in the mathematical models, to describe the dynamics of the populations, is more realistic approach. For example, removing all women in the age between 15-40 years from the human population not only reduces the size of the population, but it also reduces the birth rate to almost zero. Moreover, many animals cannot reproduce until the individuals reach a certain maturity level (certain age). Another example is the predation of animals; the predation could be heavier on some certain age groups. For instance, in the population of fish, the larvae of fish or the mollusks have a very low survival rate. Sometimes, in other species, the mature individuals' surviving rate becomes very low. An example of this is African elephants, which become attractive to the ivory poachers when they are old enough to have grown tusks.

In epidemiology, age is also one of the most important characteristics in the modeling of populations and infectious diseases. In fact, the disease may have different infection rates for different age groups. An example of this would be sexually-transited diseases (STDs) which are spread through individuals of a certain age; for instance, most AIDS cases occur in young adults. In another case, childhood diseases, such as measles, chicken pox, and rubella are spread mainly by contact between children among themselves (see Chapter 9 in [19] and the references therein).

In the cell population, a cell could be characterized by its age, its volume (size), and the maturity of the cell [18, 39]. Therefore, the age-structured models are playing a major role in describing the dynamics of the cell growth, and in describing the dynamics of the cells' proliferation process in many different comparative phases (see chapter 5 of this thesis).

Conclusively, many species have overlapping generations. Also, the fecundities and survival rates of the species are completely age dependent. Therefore, in many cases, the age structure should be taken into account, in order to have more realistic mathematical models. The earliest mathematical studies to incorporate the age effects in mathematical models were made by Sharpe and Lottka in 1907-1911 [10]. Mckendrick in 1926 [91], formulated a mathematical modal that is incorporating the age effects. Later, in 1959 [39], Von Foerster investigated Mckendrick's model to study the effects of age in cell population. To describe the Mckendrick model (Sharpe-Lottka-Mckendrick model, or Mckendrick-Von Foerster model), we let $n(t, a)$ be the distribution function of the population. Then $n(t, a)\,da$ is the approximate number of the individuals at time t in the age interval $[a,\ a + da]$. Hence, the total number of the population at time t is given by

$$N(t) = \int_0^\infty n(t, a)da. \tag{1.1.5}$$

Here, we consider the age a to be ranging over $[0, \infty)$, even though the age at death is finite. Then by using the preserving law, we have

The rate of change of the number of individuals

= the number of individuals that enter at age a

−the number of individuals that leave at age a

−the mortality rate.

Mathematically, we express this by

$$\frac{d}{dt}\left[n(t,a)\,da\right] = n(t,a) - n(t,a+da) - d(a)n(t,a)da, \tag{1.1.6}$$

where $d(a)$ is the age-dependent death rate. By dividing the above equation by da, we get

$$\frac{d}{dt}n(t,a) = \frac{n(t,a) - n(t,a+da)}{da} - d(a)n(t,a). \tag{1.1.7}$$

If we let da tend to zero, we get

$$n_t(t,a) + n_a(t,a) = -d(a)n(t,a). \tag{1.1.8}$$

At time $t = 0$, we assume that the population distribution is given by:

$$n(0,a) = f(a), \qquad a \geq 0.$$

Moreover, we let $b(t,a)$ be a nonnegative fecundity rate of females at time t and age a (maternity function). More precisely, the function $b(t,a)$ is the average number of the offspring per female at time t and age a. Then, the total number of offspring produced by females over all ages at time t is given by:

$$n(t,0) = B(t) = \int_0^\infty b(t,a)n(t,a)da, \tag{1.1.9}$$

which represents the boundary condition at age $a = 0$. This kind of boundary condition is called a non-local boundary condition, because it depends on the integral unknown solution in the problem.

In summary, if we assume that the maternity function $b(t,a)$ is time independent, then the age-structured model is given by:

$$\begin{cases} n_t(t,a) + n_a(t,a) = -d(a)n(t,a), & a > 0, \quad t > 0, \\ n(0,a) = f(a), & a \geq 0, \\ n(t,0) = \displaystyle\int_0^\infty b(a)n(t,a)da, & t \geq 0. \end{cases} \tag{1.1.10}$$

One of the observations of this model is that if $a > t$, then $n(t,a)$ is affected by the initial population $f(a)$ while if $t < a$, then $n(t,a)$ is affected by the entire population and fecundity rate $B(t)$ [82, 92, 118] (see Figure 1.2). To have some analysis for this model, we use the method of similarity [28, 81]. Therefore, we assume that

$$n(t,a) = U(a)\,e^{rt}, \tag{1.1.11}$$

where r is a parameter. In fact, the age structure $n(t,a)$ is affected by r, which either grows or decays with the time t, according to the sign of r. If we substitute this in Equation (1.1.10), we get

$$U'(a) = -(b(a) + r)U(a),$$

where the $'$ means $\frac{d}{da}$. The above ordinary differential equation is linear, and can

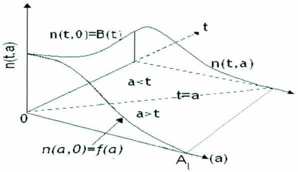


Figure 1.2: Age-Structured Model, we observe that if $a > t$, then $n(t,a)$ is affected by the initial population $f(a)$ while if $t < a$, then $n(t,a)$ is affected by the entire population and fecundity rate $B(t)$.

easily be solved. The solution of this equation is given by:

$$U(a) = c\,\Gamma(a)\,e^{-ra},$$

where c is the integration constant, and $\Gamma(a) = \exp\left\{-\int_0^a d(s)ds\right\}$. The function $\Gamma(a)$ is called the survivor-ship function, and it represents the probability of a population member surviving to age a. If we substitute $U(a)$ in equation (1.1.11), then we get

$$n(t,a) = c\,e^{(t-a)r}\Gamma(a).$$

Substituting $n(t,a)$ in the non-local boundary condition, we get

$$1 = \int_0^\infty b(a)\Gamma(a)e^{-ra}da := \Phi(r). \tag{1.1.12}$$

In fact, it is hard to solve the above integral equation explicitly to evaluate the parameter r. However, the function $\Phi(r)$ is decreasing function over the interval $[0, \infty]$. Therefore, the above integral differential equation has a unique solution (for more analysis of this model, one can see [24, 27, 30, 70, 82, 90, 118, 128]).

As we mentioned, the age-structured models are playing a major role in biological populations, epidemiology, ecology, and cell populations. The above linear age-structured model is one of the basic examples of the applications of the age-structured models in population demography (for non-linear age-structured models and there analysis, we refer the reader to an excellent book by Webb [128]). To ensure the importance of age-structured models in cell population, ecology, and epidemiology; we present some examples of age-structured models in these areas.

Example. (Cell Population, Mckendrik's-Von Foerster Model): As we mentioned before, Von Foerster investigated Mckendric's age-structured model to incorporate the effects of age in cell population. To describe Mckendrik's-Von Foerster age-structured model for cell population, we let $N(t, a)$ be the density of the cell population at time t and age a. Then Mckendrik's-Von Foerster equation (shortly, Mckendrik's equation) is given by:

$$n_t(t, a) + n_a(t, a) = -\lambda\, n(t, a),$$

where,

$$\lambda = \lambda_b + \lambda_s.$$

In fact, we write λ in this form to emphasize that the loss of the cells occurs due to the death of the cells (in the resting phase), and the synthesis of the cells (in the proliferation phase). The non-local boundary condition at age $a = 0$ is given by:

$$n(t) = n(t, 0) = 2\int_0^\infty \lambda_s(a) n(t, a) da,$$

which represents the cellular birth rate. The multiplication by λ_s gives the fraction of these cells that are dividing [106]. The number two appears to the left side of the integral, due to the fact that the mother cell divides into two new daughter cells. To impose the problem with an initial condition, we consider

$$n(0, a) = n_0(a).$$

Finally, the total cell population at any time t is given by:

$$N(t) = \int_0^\infty n(t, a)da.$$

For more models and analysis for the cell population, one can see [25, 90, 106].

Example. (Ecology, Age-Structured Predator-Prey Model): Let $n(t, a)$ be the population density of the prey at time t and age a, and let d be an age-independent death rate for the prey. This governs the age-time equation, which is

$$n_t(t, a) + n_t(t, a) = -d\, n(t, a).$$

We consider the maternity function

$$b(a) = b_0\, a\, e^{-\gamma a}, \quad b_0 > 0, \quad \gamma > 0. \tag{1.1.13}$$

Then the total number of offspring (eg. the prey eggs) is given by

$$B(t) = \int_0^\infty b_0\, a\, e^{-\gamma a}\, n(t, a)da.$$

Now, let P(t) be the age-independent population density of the predator. We assume that the predator eats only the prey eggs (i.e., at age $a = 0$). This will effect the number of offspring $n(t, 0) = B(t)$ (the egg number will decrease). Therefore, we consider

$$n(t, 0) = B(t) - kB(t)P(t),$$

where the constant k is the predation rate. Since the right hand side could be negative, then we let

$$M(t) := \max \{B(t) - kB(t)P(t), 0\}.$$

For the predator population, we impose the well-known Lotka-Voltera equation. i.e.,

$$\frac{dP}{dt}(t) = -\delta P(t) + cB(t)P(t),$$

where δ is the death rate. In summary, the governed age-structured predator-prey model is given as:

$$\begin{cases} n_t(t,a) + n_a(t,a) = -dn(t,a), & t, a \geq 0, \\ P_t = -\delta P(t) + cB(t)P(t), & t \geq 0, \\ n(t,0) = M(t), & t \geq 0, \\ P(0) = P_0. \end{cases} \tag{1.1.14}$$

For more analysis of this model, we refer the reader to [81, 82, 92, 93].

Example. (Epidemiology, Age-Structured SIR Model): Let $S(t, a)$, $I(t, a)$, and $R(t, a)$ be the population density at time t and age a of the susceptible, infective, and removed members, respectively. Then, the total population density is given by

$$n(t, a) = S(t, a) + I(t, a) + R(t, a).$$

The system of differential equations that describes the age-structured SIR-model is given as:

$$\begin{cases} S_t(t,a) + S_a(t,a) = -(\mu(a) + \lambda(t,a))S(t,a), & t,a \geq 0, \\ I_t(t,a) + I_a(t,a) = \lambda(t,a)S(t,a) - (\mu(a) + \gamma(a) + \delta(a))I(t,a), & t,a \geq 0, \\ R_t(t,a) + R_a(t,a) = -\mu(a)R(t,a) + \gamma(a)I(t,a), & t,a \geq 0, \end{cases} \tag{1.1.15}$$

where $\mu(a)$ is the death rate of susceptible, $\delta(a)$ is the disease death rate infection, $\gamma(a)$ is the recovery rate, and $\lambda(t,a)$ is the infection rate. The initial conditions at time $t = 0$ are given by

$$S(0,a) = \phi(a), \quad I(0,a) = \psi(a), \quad R(0,a) = 0.$$

The renewal condition (i.e., new births) is given by

$$S(t,0) = \int_0^\infty b(a)n(t,a)da.$$

This is true, since all the new borns are susceptible (i.e., No infection or removed among the new borns). The infection term $\lambda(t,a)$ could be selected to be intracohort mixing

$$\lambda(t,a) = f(a)I(t,a).$$

This means that the infection can be transmitted only between the individuals of the same age. The other choice is intercohort mixing

$$\lambda(t,a) = \int_0^\infty \beta(a,\alpha)I(t,a)d\alpha,$$

where $\beta(a,\alpha)$ is the rate of infection from contact between an infective of age α with susceptible of age a. For more a realistic approach, we consider $\beta(a,\alpha) = \beta_1(\alpha)\beta_2(a)$ is of separable kind [19, 88].

Finally, we remark that the non-local boundary condition (1.1.9) involves a birth function (maternity function). One of the most popular birth functions is the Nicholson's birth function. A special case of this function is the birth function that is given in Equation (1.1.13). The general case of Nicolson's birth function is given in the following formula:

$$b_1(u) = p\,u\,\exp\{-a\,u^q\}\,, \tag{1.1.16}$$

where the parameters a, p and q are positive constants. This function was first proposed by Nicolson to describe the oscillatory fluctuations in population density of the sheep blowfly "Lucilia cuprina" [95, 96]. Other popular birth functions are the spruce-budworms birth function and the logistic type birth function. These functions are given as:

$$b_2(u) = \frac{p\,u}{1 + a\,u^q}, \tag{1.1.17}$$

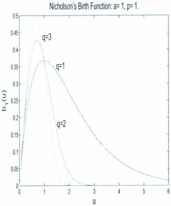
and

$$b_3(u) = \begin{cases} p\,u\,(1 - \frac{u^q}{K_c^q}), & 0 \le u \le K_c\,; \\ 0, & u > K_c\,; \end{cases} \tag{1.1.18}$$

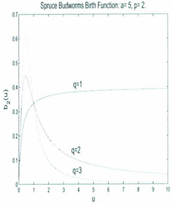
respectively. The parameters a, b, q and K_c appear above are positive constants. In cell population, we can regard the transition rate of cells from the resting phase to the proliferation phase as a birth function of cells (see Chapter 5 of this thesis). Mostly, this function is considered to be the Hill function. This function is given by the following formula:

$$b_4(u) = \frac{\beta\theta^n\,u}{\theta^n + u^n}, \tag{1.1.19}$$

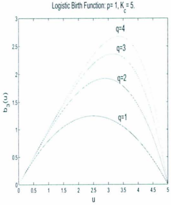
where β and θ are positive constants, whereas n is a positive integer. The graphs of these functions are given in Figure 1.3.



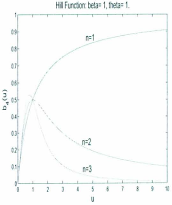
(a) The Nicholson's Birth Function.



(b) The Spruce Budworms Birth Function.



(c) The Logistic Birth Function.



(d) The Hill Function.

Figure 1.3: Different kinds of birth function.

1.2 Traveling Wave Solutions and Spreading Speed

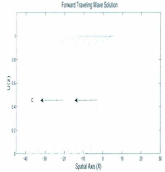
A very basic element in a vast number of phenomena in biology, ecology, and epidemiology is the appearance of the traveling waves in the spatial domain. For example, waves of chemical concentrations, spread of pest outbreak, spatial spread of epidemics (eg. The spreading of rabies across Europe [98]), traveling waves in the predator-prey models, and traveling wavefronts of a growing population and multispecies dynamics with dispersal [92].

A traveling wave solution is a special kind of solution of the reaction-diffusion models, integro-differential equations, delayed-differential equations, and integral equations [21, 52, 92, 93, 108, 126, 134]. In fact, it is taken to be a wave which travels in spatial domain without any change in its shape (see Figure 1.4). To have a better understanding of traveling waves concept, we consider the following reaction-diffusion equation

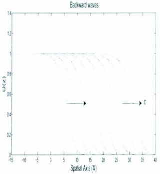
$$\frac{\partial u}{\partial t}(t,x) = D\Delta u(t,x) + f(u), \tag{1.2.1}$$

where D is the diffusion coefficient, Δ is the Laplacian's operator, and the function $f : \mathbb{R}^+ \to \mathbb{R}^+$ is the kinetics function. For instant, we assume that $f(u)$ admits two stationary points E_1 and E_2 (i.e., $f(E_1) = f(E_2) = 0$), and $E_2 > E_1$. Also, we assume that $f'(E_1) > 0$. A solution $u(t,x)$ of Equation (1.2.1) is called a traveling wave solution, if it is of the form $u(t,x) = U(x \pm ct) = U(z)$, where $z = x \pm ct$, $c \geq 0$, $x \in \mathbb{R}$, and $t > 0$. The constant c is called the wave speed (traveling wave speed, or the speed of propagation), and the veritable z is called the wave variable.

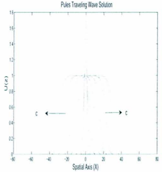
In particular, the traveling wave solution, if it exists, is a wave traveling to the right (forward traveling wave), to the left (backward wave), or for both sides (pulse waves). A traveling wave solution $U(z)$ is called a periodic traveling wave solution, if there exists a positive constant ω such that $U(z+\omega) = U(z)$, for each $z \in \mathbb{R}$. These different kinds of traveling waves are shown in Figure 1.4 [1].



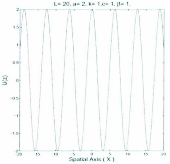
(a) The forward traveling waves (Wavefronts).



(b) The backward traveling waves (Back waves).



(c) The pulse traveling waves.



(d) Periodic traveling waves.

Figure 1.4: A figure shows the different kinds of traveling waves.

[1]The graph in Figure 1.4(d) is the graph of the traveling wave solution of the linear partial differential equation $u_t + cu_x + \beta u_{xxx} = 0$. In fact, this linear equation results from the linearization of Korteweg-DeVries equation (KDV-equation), which is given by $u_t + (c+u)u_x + \beta u_{xxx} = 0$). The solution of this linear problem is $u(t,x) = a\cos(kx - \omega t)$, where $\omega = ck - \beta k^3$ and k is the wave number [140].

The forward and backward traveling wave solutions satisfy the following asymptotic relations:

$$\lim_{t \to -\infty} U(z) = E_1 \quad ; \quad \lim_{t \to +\infty} U(z) = E_2,$$

and

$$\lim_{t \to -\infty} U(z) = E_2 \quad ; \quad \lim_{t \to +\infty} U(z) = E_1,$$

respectively. The pulse traveling wave solution satisfies the following asymptotic relation:

$$\lim_{t \to \pm\infty} U(z) = E_1 \text{ (or } E_2).$$

In general, the traveling wave solution does not necessarily exist. To show this, we illustrate the following example.

Example. We reconsider the above reaction diffusion equation, and we assume that the kinetics function $f(u)$ is identically zero. If we substitute $u(t,x) = U(x - ct) = U(z)$ in the resulting equation, then we get the following second order ordinary differential equation:

$$DU''(z) + cU'(z) = 0,$$

where the prime means the derivative with respect to the variable z. The solution of this homogeneous second order differential equation is given by

$$U(z) = A + Be^{-\frac{c}{D}z},$$

where the constants A and B are the integration constants. The above solution, $U(z)$, is bounded if $B = 0$. Therefore, $U(z) = A$, $\forall c \geq 0$. This solution is a constant and cannot represent a traveling wave solution. In many cases, There exists a constant $c^* > 0$, such that the traveling wave solution exists when $c \geq c^*$, while the traveling wave solution does not exist when $0 \leq c < c^*$. In this case, we call c^* the minimum wave speed. To prove the existence of the traveling wave solution of a given model is not easy in the general case. Some of the common techniques to prove the existence of the traveling wave solution are the phase plane analysis technique, asymptotic analysis techniques (perturbation methods), monotone operators and the existence of the upper and lower-solutions technique. To have a good understanding about these techniques, we present the following demonstration example:

Example. (Fisher's-Kolmogoroff Reaction-Diffusion Equation): Fisher's-Kolmogoroff (commonly, Fisher's equation) reaction diffusion equation is given by

$$\frac{\partial}{\partial t}u(t,x) = \frac{\partial^2}{\partial x^2}u(t,x) + u(t,x)(1 - u(t,x)). \tag{1.2.2}$$

This equation was first proposed by Fisher in 1937 [38], to study the spatial spread of a favored gene in a population. Later the traveling wave solution of this equation was investigated by Kolgomoroff et al. in 1937 [68]. Indeed, they proved that Fisher's equation admits a traveling wave solution for each $c \geq c^* = 2$. Next, we apply some techniques to show the existence of the traveling wave solution for Fisher's equation. First, we start them by the phase plane analysis technique:

(1) Phase Plane Analysis: We substitute $u(t,x) = U(x + ct) = U(z)$ in (1.2.2), then we get following problem:

$$\begin{cases} U''(z) - cU'(z) + U(z)(1 - U(z)) = 0, \quad z \in \mathbb{R}, \\ \lim\limits_{t \to -\infty} U(z) = 0, \qquad \lim\limits_{t \to \infty} U(z) = 1, \\ U'(\pm\infty) = 0. \end{cases} \tag{1.2.3}$$

Let $V = U'$, then $V' = U''$. Hence, we get the following system of differential equations:

$$\begin{cases} U'(z) = V(z) & := f_1(U, V), \\ V'(z) = cV - U(z)(1 - U(z)) & := f_2(U, V). \end{cases} \tag{1.2.4}$$

The above system has two equilibrium points, $(0, 0)$ and $(1, 0)$. To analyze the linear stability for the above system, we find the Jacobian's matrix of this system. The Jacobian's matrix is given by

$$J(U, V) = \begin{pmatrix} 0 & 1 \\ 2V - 1 & c \end{pmatrix}.$$

The eigenvalues of $J(0, 0)$ are

$$\lambda_{1,2} = \frac{c \pm \sqrt{c^2 - 4}}{2}.$$

Therefore, if $c \geq 2$, then the equilibrium point $(0, 0)$ is unstable node, whereas, if $c < 2$, then $(0, 0)$ is an unstable spiral. The eigenvalues of $J(1, 0)$ are

$$\lambda_{1,2} = \frac{c \pm \sqrt{c^2 + 4}}{2}.$$

Hence, the equilibrium point $(1, 0)$ is a saddle node. Therefore, If $c \geq 2$, Then there exists a positive orbit connecting the two equilibrium points $(0, 0)$ and $(1, 0)$. This orbit leaves out the equilibrium points $(0, 0)$, and it is connecting the equilibrium point $(1, 0)$ along with its stable manifold. Hence, the asymptotic limits $\lim_{t \to -\infty} U(z) = 0$, and $\lim_{t \to \infty} U(z) = 1$ hold (see Figure 1.5). As we mentioned above, if $0 < c < 2$, then $(0, 0)$ is an unstable spiral. Hence, the solution is oscillating and we cannot get a positive orbit which is connecting $(0, 0)$ and $(0,1)$ (see Figure 1.6).

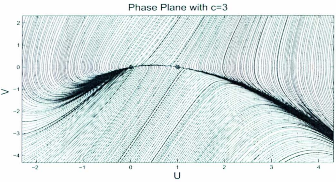


Figure 1.5: The phase plane analysis of Equation (1.2.4) when $c = 3$. The equilibrium point $(0, 0)$ is an unstable node while $(1, 0)$ is a saddle point. This figure is generated by the function PPlane8 using Matlab.

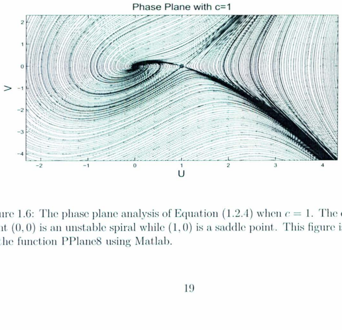


Figure 1.6: The phase plane analysis of Equation (1.2.4) when $c = 1$. The equilibrium point $(0, 0)$ is an unstable spiral while $(1, 0)$ is a saddle point. This figure is generated by the function PPlane8 using Matlab.

(2) Perturbation methods: We reconsider the equation

$$\begin{cases} U''(z) - cU'(z) + U(z)(1 - U(z)) = 0, & z \in \mathbb{R},\ c \geq 2; \\ \lim_{t \to -\infty} U(z) = 0, & \lim_{t \to \infty} U(z) = 1. \end{cases} \tag{1.2.5}$$

We remark that if $U(z)$ is a solution of the above equation, then $U(z + z_0)$ is again a solution of this equation. This is true since the above equation is autonomous equation. Therefore, without loss of generality, we may assume that $U(0) = \frac{1}{2}$. To introduce a small perturbation in the above equation, we introduce a new variable $s = z/c$, and a new function $g(s) = U(\frac{s}{\sqrt{\epsilon}})$ in the above equation. Using this change of variables, equation (1.2.5) reduces to

$$\begin{cases} \epsilon g''(s) - g'(s) + g(s)(1 - g(s)), & s \in \mathbb{R}, \\ g(-\infty) = 0, \quad g(0) = \frac{1}{2}, \quad g(\infty) = 1, \end{cases} \tag{1.2.6}$$

where $\epsilon = \frac{1}{c^2} \leq \frac{1}{4}$. The perturbed series of the solution $g(s)$ is given by

$$g(s) = g_0(s) + g_1(s)\epsilon + g_2(s)\epsilon^2 + \cdots . \tag{1.2.7}$$

Substituting this form in Equation (1.2.6) and then setting the coefficients of $\epsilon^n, n = 0, 1, 2, \cdots$, we get

$$\begin{cases} g_0'(s) = g_0(s)(1 - g_0(s)), & s \in \mathbb{R}, \\ g_0(-\infty) = 0, \quad g_0(0) = \frac{1}{2}, \quad g_0(\infty) = 1, \end{cases} \tag{1.2.8}$$

and

$$\begin{cases} g_1'(s) = g_0'' + g_1(s)(1 - 2g_0(s)), & s \in \mathbb{R}, \\ g_1(-\infty) = g_1(0) = g_1(\infty) = 0. \end{cases} \tag{1.2.9}$$

By solving Equation (1.2.8), we get the following solution

$$\begin{aligned} g_0(s) &= \left(1+e^{-s}\right)^{-1} \\ &= \frac{e^s}{1+e^s} \end{aligned}$$

We substitute this formula into Equation (1.2.9), and then we solve the resulting equation, to get

$$\begin{aligned} g_1(s) &= e^{-s}(1+e^{-s})^{-2}\log\frac{4e^{-s}}{(1+e^{-s})^2} \\ &= \frac{e^s}{(1+e^s)^2}\log\frac{4e^s}{(1+e^s)^2}. \end{aligned}$$

If we substitute this in Equation (1.2.6) and substitute $s = z/c$, then we get

$$U(z) = \frac{e^{z/c}}{1+e^{z/c}} + \frac{1}{c^2}\frac{e^{z/c}}{(1+e^{z/c})^2}\log\frac{4e^{z/c}}{(1+e^{z/c})^2} + O(\epsilon^2),$$

where $z = x + ct$, $x \in \mathbb{R}$, $t > 0$. If we consider $z = x - ct$, then the asymptotic solution for this case is

$$U(z) = \frac{1}{1+e^{z/c}} + \frac{1}{c^2}\frac{e^{z/c}}{(1+e^{z/c})^2}\log\frac{4e^{z/c}}{(1+e^{z/c})^2} + O(\epsilon^2).$$

The numerical simulation for these two solutions is given in Figure 1.7 and Figure 1.8, respectively (for more details see, for example, [94, 133]).

(3) Monotone Operators and Upper-Lower Solutions Technique:

We re-consider Equation (1.2.2), To apply the upper-lower solutions technique to this equation, we wish to define a monotone operator T on the space of bounded and continuous functions on $\mathbb{R}$ (i.e., on the space $\mathcal{C} = BC(\mathbb{R}, \mathbb{R})$). To do this, we rewrite

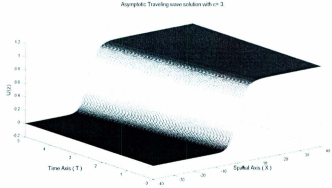


Figure 1.7: The asymptotic solution for Fisher's equation, the wave variable $z = x+ct$.

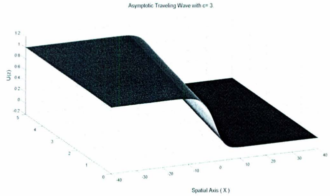


Figure 1.8: The asymptotic solution for Fisher's equation, the wave variable $z = x-ct$.

Equation (1.2.2) as

$$\begin{aligned} u_t &= u_{xx} - \beta u + [\beta u + u(1-u)] \\ &= u_{xx} - \beta u + F(u), \end{aligned} \tag{1.2.10}$$

where $\beta > 0$ is sufficiently large so that $F(u)$ is a monotone increasing function. Substitute $u(t,x) = U(x+ct) = U(z)$ in the above equation, we get

$$cU'(z) = U''(z) - \beta U(z) + F(U(z)). \tag{1.2.11}$$

The homogeneous part of the previous equation is given by

$$U''(z) - cU'(z) - \beta U(z) = 0.$$

The roots of the corresponding characteristic equation are

$$r_{1,2} = \frac{c \pm \sqrt{c^2 + 4\beta}}{2}.$$

These roots are real and distinct with opposite signs. Using the constant variation formula, the non-homogeneous solution of Equation (1.2.11) is given by

$$(T\phi)(z) = \frac{1}{\sqrt{c^2+4\beta}} \left[\int_{-\infty}^{z} e^{r_1(z-y)} F(\phi(y))dy + \int_{z}^{\infty} e^{r_2(z-y)} F(\phi(y))dy \right]. \tag{1.2.12}$$

Since $F(u)$ is monotone, then the operator T is monotone, i.e.,

$$T\phi \geq T\psi \quad \text{whenever} \quad \phi \geq \psi.$$

To show that Equation (1.2.11) has a solution, it is enough to show that the operator

T has a fixed point [83]. This is true since $T\phi$ satisfies

$$(T\phi)'' - c(T\phi)' - \beta(T\phi) + F(\phi) = 0. \qquad (1.2.13)$$

To show that T has a fixed point, we try to find an upper and lower-solution ($\overline{\phi} \in \mathcal{C}$ is called an upper solution of T, if $T\overline{\phi} \leq \overline{\phi}$. Similarly, $\underline{\phi} \in \mathcal{C}$ is called a lower solution of T, if $\underline{\phi} \leq T(\underline{\phi})$). If such a pair of solutions exists, then we can perform the following scheme:

$$\phi^0 := \overline{\phi}, \quad \phi^m := T\phi^{m-1}, \quad \forall m \geq 1.$$

By the monotonicity of T, we have

$$0 \leq \underline{\phi} \leq \cdots \leq \phi^m \leq \phi^{m-1} \leq \cdots \leq \phi_0 := \overline{\phi}.$$

Since this sequence is a monotone decreasing sequence, then it has a limit ϕ^*(i.e., $\lim_{m\to\infty} \phi^m = \phi^*$). Hence, by applying the Lesbesgue Dominated Convergence Theorem, T has a fixed point. To show the existence of a monotone traveling wave solution of (1.2.11), we are looking for a special kind of upper and lower solutions. In fact, we require $\overline{\phi}$ to be a non-decreasing function, and satisfies the following asymptotic relations:

$$\lim_{z\to-\infty} \overline{\phi} = 0 \quad \text{and} \quad \lim_{z\to\infty} \overline{\phi} = 1$$

This condition implies that ϕ^* is monotone. Also, we require $\underline{\phi}$ to be non-zero. This condition implies that ϕ^* is not identically zero. To show that T admits a pair of upper and lower solutions, it is sufficient to show that the original differential equation (1.2.2) admits a pair of upper and lower solutions (super-subsolutions) (see Lemma 2.5 and Lemma 2.6 [83]). A function $\overline{\phi} \in \mathcal{C}$ is called an upper solution of (1.2.2), if $\overline{\phi}$ is twice continuously differentiable on $\mathbb{R}$ except at finite points $z_1, z_2, \cdots, z_n$, $\overline{\phi}'(z_i^+) \leq \overline{\phi}'(z_i^-)$, and $\overline{\phi}''(z) - c\overline{\phi}'(z) + \overline{\phi}(z)(1 - \overline{\phi}(z)) \leq 0$, $\forall z \neq z_i$, $i = 1, 2, \cdots, n$. A similar definition holds for the lower solution $\underline{\phi}$, if we reverse the inequalities. To construct a pair of upper and lower solutions of Fisher's equation, we consider the linearized equation

$$U''(z) - cU'(z) + U(z).$$

The roots of the characteristic equation of this second order differential equation are

$$\lambda_{1,2} = \frac{c \pm \sqrt{c^2 - 4}}{2}.$$

If $c > 2$, then $0 < \lambda_2 < \lambda_1$. Let $0 < \epsilon \ll 1$ and $M \gg 1$, then

$$\overline{\phi}(z) = \min\left\{1,\ e^{\lambda_1 z}\right\},$$

and

$$\underline{\phi}(z) = \max\left\{0,\ (1 - Me^{\epsilon z})e^{\lambda_1 z}\right\}$$

are a pair of upper and lower solutions of Fishers equation (eg. see [31]). For more analysis of the existence and stability of the traveling wave solution for different mathematical models, we refer the reader to [3, 7, 8, 31, 35, 36, 38, 46, 47, 55, 79, 83, 84, 97, 98, 99, 100, 101, 109, 114, 115, 116, 119, 123, 124, 136, 138, 146, 148].

Asymptotic Spreading Speed.

To clarify the concept of spreading speed, we reconsider the reaction diffusion equation (1.2.1); i.e., we consider the reaction-diffusion equation

$$\frac{\partial u}{\partial t}(t, x) = D\Delta u(t, x) + f(u), \tag{1.2.14}$$

where $(t, x) \in \mathbb{R}^+ \times \mathbb{R}$ and the kinetic function $f : \mathbb{R}^+ \to \mathbb{R}^+$ satisfies $f(0) = f(1) = 0$, and $f'(0) > 0$. During their study of the above reaction-diffusion equation in 1975 [7], Aronson and Weinberger introduced the concept of asymptotic spreading speed (shortly, spreading speed). Indeed, in 1978 [8], Aronson and Weinberger proved the following theorem:

Theorem 1.2.1. *Let $u(t, x)$ be a non-zero solution of the reaction diffusion equation (1.2.14) with initial condition $u(0, x)$ which has a compact support. Then the following assertions hold:*

i) $\lim_{t\to\infty,\,|x|\geq ct} u(t, x) = 0, \qquad \forall c \in (c^*, \infty),$

ii) $\lim_{t\to\infty,\,|x|\leq ct} u(t, x) = 1, \qquad \forall c \in (0, c^*).$

They called c^* the asymptotic spreading speed. Also, they proved that $c^* = 2$ for Fisher's equation. As a result of this theorem, we observe that if $\rho \in (0, 1)$, then

$$\lim_{t\to\infty} \frac{x_\pm^\rho}{t} = c^* = 2$$

uniformly for each $\rho \in [a, b] \subseteq [0, 1]$. The quantities $x_\pm^\rho$ satisfy the relation $u(t, x_\pm^\rho) = \rho$, and they represent the distance from the origin to the right and to the left, respectively. That why it is reasonable to call c^* the asymptotic spreading speed (see Figure 1.9). We also observe that if $u(t, x)$ represents a population (eg. an infected population) at spatial point x and one leaves with a speed $c > c^*$, then he will outrun the population (will not be infected); while if one leaves with a speed $c < c^*$, then the population will overtake the observer (will be infected)[31]. Figure 1.9 shows the evolution of the solution with the time t in one dimensional spatial space. To demonstrate the evolution of the solution, and the spreading of the solution in higher dimensional spaces; we illustrate the following example:

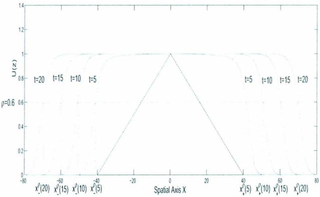


Figure 1.9: The asymptotic spreading speed.

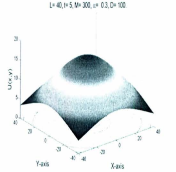
Example. (A Linear Reaction-diffusion Equation in two Dimensional Space, Target Waves). In this example, we consider the following linear reaction-diffusion equation in two dimensional space:

$$\begin{cases} \frac{\partial}{\partial t}u(t,x) = D\Delta u(t,x) + \alpha u(t,x), \quad \alpha > 0, \quad x \in \mathbb{R}^2; \\ u(0,x,y) = M\delta(x)\delta(y), \end{cases} \tag{1.2.15}$$

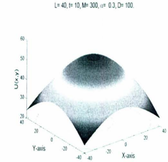
where $\delta(x)$ is the derac-delta function. Fortunately, we can apply the Fourier transformation technique (eg. see [28]) to this linear RD-equation. Therefore, the analytical solution for this equation is given by:

$$u(t,x,y) = \frac{M}{2\sqrt{\pi Dt}} \exp\left\{\alpha t - \frac{x^2+y^2}{4Dt}\right\},$$

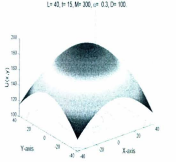
where M is a constant. The graph of the solution is a series of circular waves, which propagate from the origin (see Figure 1.10). This kind of waves travel in all directions of the spatial space, and it is called the target waves (target pattrens)[50, 69].



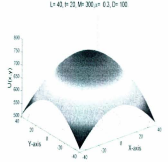
(a) The solution of Equation (1.2.15) for t=5.



(b) The solution of Equation (1.2.15) for t=10.



(c) The solution of Equation (1.2.15) for t=5.



(d) The solution of Equation (1.2.15) for t=20.

Figure 1.10: The evolution of Equation (1.2.15) solution with the time t.

Finally, we remark that after the early work of Aronson and Wieberger in 1975, the concept of spreading speed has been considered in many studies (eg. [32, 35, 65, 66, 75, 76, 77, 78, 119, 120, 127, 129, 130, 131, 132, 145]).

1.3 Thesis Layout

We divided the thesis into six chapters. In the first chapter, the introduction, we presented some basic concepts about the age-structured models and their application in mathematical biology. Also, we presented some basic concepts about the traveling waves, and the asymptotic spreading speed. In the following chapters, we present in chapter 2 some useful concepts and results. In chapter 3, we derived a new age structured model in terms of an integral equation. We show that this integral equation admits a unique (up to translation) traveling wave solution. Also, we show the existence of spreading speed c^*. In Chapter 5, we consider an age-size structured model over a bounded domain in $\Omega \subset \mathbb{R}$. We derived a new model in terms of an integral equation. We show that this integral equation admits a principle eigenvalue and a principle eigenfunction when the given birth function is linear. Also, we show the existence of positive steady state solution for this integral equation when the birth function is non-linear. In addition, we prove that the positive steady state solution is stable, provided that the principle eigenvalue λ_0 is positive. In chapter 5, we construct an age-structured model related to the cell cycle differentiation. From this model, we derive a delay differential equation with a nonlocal term. We show that the resulting linear delay differential equation admits a unique principle eigenvalue, as well as a principle eigenfunction. For the nonlinear delay differential equation we show that this equation admits a positive steady state solution, we also show that this steady state solution is stable provided that the principle eigenvalue λ_0 is positive and the transition function is monotone. In the last chapter, we present a nonlocal reaction diffusion model related to the cells adhesion phenomena. we present a numerical simulation for this reaction diffusion equation, and present some future work.

Chapter 2

Preliminaries

2.1 Introduction

In this chapter, we present some useful concepts and theorems that we use in this thesis. These concepts involve the ordered cones and Krien-Rotman Theorem, some concepts from infinite dynamical systems and monotone dynamical systems, the parabolic maximum principle and comparison theorems. We start this chapter by introducing the concept of ordered Banach spaces and ordered cones.

2.2 Ordered Cones and Krien-Rotman Theorem

At the beginning of this section, we recall some basic concepts from functional analysis. We start by defining the metric space and the complete metric space:

Definition 2.2.1. *(Metric space): A metric space is a pair (X, d), where X is a set and d is a metric on X. By a metric d on the set X, we mean the real valued function $d : X \times X \to \mathbb{R}^+$, such that for any $x, y, z \in X$, the following properties hold:*

(1) ***(Positivity)****: $d(x, y) \geq 0$, and $d(x, y) = 0$ if and only if $x = y$.*

*(2) **(Symmetry)**: $d(x, y) = d(y, x)$.*

*(3) **(Triangle inequality)**: $d(x, y) + d(y, z) \leq d(x, z)$.*

Sometimes, d is called a distance function.

Definition 2.2.2. *(A limit of a sequence): A sequence $\{x_n\}_{n=1}^{\infty}$ in a metric space X is said to be convergent if there is $x \in X$, such that*

$$\lim_{n \to \infty} d(x_n, x) = 0.$$

In this case, we call x the limit of x_n, and shortly, we write

$$\lim_{n \to \infty} x_n = x.$$

Definition 2.2.3. *(Cauchy sequence): A sequence $\{x_n\}_{n=1}^{\infty}$ in a metric space X is said to be a Cauchy sequence if for each $\epsilon > 0$ there exists natural number $N(\epsilon)$, such that*

$$d(x_n, x_m) < \epsilon \quad \text{whenever} \quad n, m > N(\epsilon).$$

Definition 2.2.4. *(A complete metric space): A metric space X is called complete metric space if and only if every Cauchy sequence in X is convergent in X (that is the limit is in X).*

Definition 2.2.5. *(Norm): Let X be a real (or, complex) vector space. The norm on X is a real valued function $\|.\| : X \to \mathbb{R}^+$, which satisfies the following conditions:*

*(1) **(Positivity)**: $\|x\| \geq 0$, and $\|x\| = 0$ if and only if $x = 0$.*

*(2) **(Scalar multiplication)**: $\|\alpha x\| = |\alpha| \, \|x\|$, $\alpha \in \mathbb{R}$ (or, $\alpha \in \mathbb{C}$).*

*(3) **(Triangle inequality)**: $\|x + y\| \leq \|x\| + \|y\|$, $\forall x, y \in X$.*

Definition 2.2.6. *(Banach-space): A normed space X is a vector space X with a norm defined on it. A Banach space X is a complete normed space.*

Let "$\leq$" be a partially ordered relation on the space X. We recall that the relation "$\leq$" is partially ordered if and only if

(1) (**reflexive**): $x \leq x$ for all $x \in X$.

(2) (**antisymmetric**): If $x \leq y$ and $y \leq x$, then $x = y$.

(3) (**Transitive**): If $x \leq y$ and $y \leq z$, then $x \leq z$.

Definition 2.2.7. *(Ordered metric space and ordered Banach space): An ordered metric space X is a metric space X with an order relation defined on it. Similarly, an ordered Banach space X is a Banach space with an order relation defined on it.*

Definition 2.2.8. *(Order Cone)[141]: Let X be an ordered Banach space and let K be a subset of X. Then K is called an order cone if and only if*

(i) K is closed, nonempty, and $K \neq \{0\}$.

(ii) for $a, b \in \mathbb{R}$, $a, b \geq 0$, $x, y \in K \Rightarrow ax + by \in K$.

(iii) $x \in K$ and $-x \in K \Rightarrow x = 0$.

As a notation, we mean by $x \leq y$ if and only if $y - x \in K$, $x < y$ if and only if $y - x \in K \setminus \{0\}$, and $x \ll y$ if and only if $y - x \in K^o$ (K^o is the interior of the cone K). Also, we denoted by $[a, b]_X$ to the ordered interval $[a, b]_X = \{x \in X | \, a \leq x \leq b\}$.

Definition 2.2.9. *(Generating, total, and solid ordered cones): An ordered cone K is called generating if and only if $X = span(K)$ (i.e., $X = K - K$), K is called total if and only span(X) is a dense subset in X (i.e., $X = \overline{K - K}$), and K is called solid if it has a non-empty interior (i.e., $K^o \neq \phi$).*

Definition 2.2.10. *(Normal cone): Let X be an ordered Banach space, and let K be a ordered cone in X. Then K is called normal if and only if there exists a number $c > 0$ such that,*

$$\|x\| \leq c\|y\| \quad \textit{whenever} \quad 0 \leq x \leq y, \ \forall x, y \in X.$$

Example 2.2.1. *In the applications and throughout this thesis, we are interested in the space of continuous functions $X = C(\overline{M})$ (with the supremum norm, i.e., $\|\phi\|_\infty = \sup_{x \in \overline{M}} |\phi(x)|$), where $\overline{M} = [0, \pi]$ and its positive ordered cone $C_+(\overline{M})$ which consists of all nonnegative real valued functions over the closed interval $[0, \pi]$, i.e., $C_+(\overline{M}) = \left\{f \in C(\overline{M}) : f(x) \geq 0 \text{ on } \overline{M}\right\}$. The relations "$f \leq g$", "$f < g$", and "$f \ll g$" are define on this space as follows:*

$$f \leq g \ \textit{ if and only if } \ f(x) \leq g(x) \ \textit{ for all } x \in \overline{M},$$

$$f < g \ \textit{ if and only if } \ f(x) \leq g(x) \textit{ for some } x \in \overline{M},$$

and

$$f \ll g \ \textit{ if and only if } \ f(x) < g(x) \ \textit{ for all } x \in \overline{M}.$$

respectively. Moreover, the positive cone $K = C_+([0, \pi])$ is a generating, solid, and normal cone.

Definition 2.2.11. *[141].*

(1) The operator $T : D(T) \subseteq X \to Y$ is called monotone increasing if and only if

$$x < y \quad \textit{implies that} \quad Tx \leq Ty, \ \forall x, y \in D(T).$$

The operator is called strictly (resp., strongly) monotone increasing if and only if the symbol "$\leq$" is replaced by "$<$" (resp., "$\ll$").

(2) *The operator T is called positive if and only if $T(0) \geq 0$ and*

$$x > 0 \quad \textit{implies that} \quad Tx \geq 0, \ \forall x, y \in D(T).$$

The operator is strictly (resp., strongly) positive if and only if "$\geq$" is replaced by "$>$" (resp., "$\gg$").

Theorem 2.2.1. *(Krien-Rotman Theorem) [141]. Let X be a real Banach space with an order cone $X_+ \subset X$. Let $T : X \to X$ be a linear compact operator with spectrum $\sigma(T)$, and let $\lambda_0 = r(T) = \sup((\sigma(T))$ be the spectral radius of T. Then the following hold:*

(i) *Assume that T is positive and that T has a nonzero point in its spectrum. Then $\lambda_0 > 0$ and $\lambda_0 \in \sigma(T)$. Moreover, there exists an eigenvector $x \in X_+$ corresponding to λ_0.*

(ii) *Assume that $X_+^o \neq \phi$ and T is a strongly positive operator. Then T has exactly one eigenvector with $x > 0$ and $\|x\| = 1$; the corresponding eigenvalue is λ_0 which is algebraically simple. Furthermore, $x \gg 0$. Also, $|\lambda| \leq \lambda_0$ for every $\lambda \in \sigma(T)$.*

Definition 2.2.12. *A linear operator T from a Banach space X to a Banach space Y is called compact if and only if it maps every bounded set in X to a relatively compact set in Y. A set B is said to be relatively compact in a Banach space X if and only if $\overline{B} = X$.*

Definition 2.2.13. *The operator T is a completely continuous operator if and only if it is continuous and compact.*

Remark 2.2.1. *We know that the operator $T : X \to Y$ is compact if and only if it maps every bounded sequence in X to a sequence in Y which has a convergent subsequence. Therefore, when the operator T is defined on the space of continuous functions over a compact set $C([a,b])$, we use the Ascole-Arzela's Theorem to prove that T is a compact operator. The Ascole-Arzela's Theorem is given in the following theorem.*

Theorem 2.2.2. *(Ascole-Arzela's Theorem) Let K be a compact subset in $\mathbb{R}$ and let $\mathfrak{F}$ be a family of functions in $C(K,\mathbb{R})$. Then $\mathfrak{F}$ is uniformly bounded and equicontinuous on K if and only if every bounded sequence in $\mathfrak{F}$ has a convergent subsequence.*

The definition of "uniformly bounded" and "equicontinuous" are given in the following definition:

Definition 2.2.14. *A set of functions $\mathfrak{F}$ is called uniformly bounded if and only if there exists $M > 0$, such that $\|f\|_\infty \leq M$, $\forall f \in \mathfrak{F}$. Moreover, the set $\mathfrak{F}$ is equicontinous if and only if for each $\epsilon > 0$, there exists $\delta(\epsilon) > 0$ such that*

$$|f(x) - f(y)| < \epsilon, \quad whenever \quad |x - y| < \delta(\epsilon), \ and\ f \in \mathfrak{F}.$$

Remarks:

(i) Throughout this thesis, we mean by $X = C([a,b])$ the space of all continuous real valued functions over a closed interval $[a,b]$ with the supremum norm $\|.\|_\infty$. Moreover, we mean by $X_+ = C_+([a,b])$ its positive ordered cone. This cone consists of all nonnegative functions in X and it has a non-empty interior ($X_+^o \neq \phi$). The interior of X_+ consists of all strictly positive function in X.

(ii) We mean by $Y = C_0([a,b])$ the space of all continuous real valued functions over a closed interval $[a,b]$, that vanish at the boundary, i.e., at a and b. We equipped this space with the supremum norm $\|.\|_\infty$. Moreover, we mean by $Y_+ = C_+([a,b])$ its positive ordered cone. This cone consists of all the nonnegative functions in Y. Since the functions in this space vanish at the boundary, this cone has an empty interior.

(iii) Since the interior of the cone Y_+ is empty. To define a strongly positive relation, we need a different space from Y, so that its positive cone has a non-empty interior. Therefore, we consider the space $Z = C_0^1[a,b]$, the space of continuous real valued functions which vanish at the boundary (at a and b), and have a continuous first derivative. Also, we consider its positive ordered cone $Z_+ = C_{0+}^1[a,b]$. This cone consists of all nonnegative functions in Z. This cone, Z_+, has a non-empty interior. In fact, The interior of this cone consists of all strictly positive functions on (a,b), vanish at the boundary a and b, and have a strictly finite positive derivative at a and a strictly finite negative derivative at b. We equipped this space with the following norm:

$$\|\phi\|_Z = \max_{x\in[a,b]} |\phi(x)| + \max_{x\in[a,b]} |\phi'(x)| .$$

2.3 Infinite Dynamical Systems

We begin this section by presenting some basic definitions. Let (X,d) be a metric space and $T : X \to X$ be a continuous map. For any $x \in X$, the positive orbit through x is defined by:

$$\gamma^+(x) = \bigcup_{n\geq 0} T^n(x).$$

Similarly, the negative orbit through x is defined by:

$$\gamma^-(x) = \bigcup_{n \le 0} T^n(x).$$

The full orbit in x is $\gamma(x) = \gamma^+(x) \cup \gamma^-(x)$. The ω-limit set at x, $\omega(x)$, is

$$\omega(x) = \{y \in X | \; T^{n_k}(x) \to y, \text{ as } n_k \to \infty\}.$$

Similarly, the α-limit set at x, $\alpha(x)$, is

$$\alpha(x) = \{y \in X | \; T^{n_k}(x) \to y \text{ as } n_k \to -\infty\}.$$

A set A is called positively invariant if $T(A) \subset A$, and A is called invariant if $T(A) = A$.

Definition 2.3.1. *(Attractor, Global attractor) A bounded set A is said to attract B in X if*

$$\lim_{n \to \infty} \sup_{x \in B} \{d(T^n(x), A)\} = 0.$$

A subset A in X is called an attractor for T if A is a nonempty, compact, and invariant, and A attracts some open neighborhood U of itself. A global attractor for T is an attractor that attracts every point in X.

Definition 2.3.2. *(Dissipative maps)[56]. Let X be a complete metric space, and let $T : X \to X$ be a continuous map. Then*

(1) T is called point dissipative on X if there exists a bounded set B attracts each point in X under T.

(2) T is called compact dissipative on X if there exists a bounded set B attracts each compact set in X under T.

Definition 2.3.3. *(Measure of non-compactness and Kuratowski measure of non-compactness)[122]. Let X be a complete metric space X. A function $\beta : B \subseteq_{bdd} X \to \mathbb{R}_+$ ($B \subseteq_{bdd} X$ means that B is a bounded subset of X) is called a a measure of non-compactness if it satisfies the following conditions:*

*(1) **(Regularity)** $\beta(A) = 0$ if and only if A is precompact ($\overline{A}$ is compact).*

*(2) **(Invariant under closer)** $\beta(A) = \beta(\overline{A})$.*

*(3) **(Semi-additivity)**$\beta(A \cup B) = max\{\beta(A), \beta(B)\}$.*

The Kuratowski measure of non-compactness is defined as follows:

$$\alpha(A) = \inf\{r : \ A \text{ has a cover of diameter } < r\}.$$

For more properties of the measure of non-compactness, one can see [122].

Definition 2.3.4. *(α-condensing and α-contraction maps). Let X be a metric space, and let $T : X \to X$ be a continuous map. Then T is called α-condensing if T maps the bounded sets to the bounded sets, and $\alpha(T(A)) < \alpha(A)$ for any nonempty closed bounded set A in X with $\alpha(A) > 0$. The same definition holds for the α-contraction maps of order $k \in [0, 1)$, if we replace the statement $\alpha(T(A)) < \alpha(A)$ by $\alpha(T(A)) < k\alpha(A)$.*

Notation 2.3.1. *Let X be a metric space, throughout this thesis, we mean by X_0 be an open set in X and ∂X_0 be its complement. i.e., $X = X_0 \cup \partial X_0$ (roughly speaking, ∂X_0 is the boundary of X_0 in X).*

Theorem 2.3.1. *(Theorem 3.4.8 [56]). Let $T : X \to X$ be a compact and point dissipative map. Then there is a connected global attractor A.*

Definition 2.3.5. *[144]. A function $T : X \to X$ is said to be uniformly persistent with respect to $(X_0, \partial X_0)$ if there exists $\eta > 0$ such that $\lim_{n\to\infty} d(T^n(x, \partial X_0)) \geq \eta$ for all $x \in X_0$. $T : X \to X$ is said to be weakly uniformly persistent with respect to $(X_0, \partial X_0)$ if we replace "inf" with "sup" in the limit.*

Theorem 2.3.2. *(Theorem 1.3.3 [144]). Let $T : X \to X$ be a compact map, and assume that X_0 is positively invariant. Also, assume that T has a global attractor A. Then weak uniform persistence implies uniform persistence.*

Definition 2.3.6. *[56] A semiflow on a space X is a continuous map $\Phi(t) : X \times \mathbb{R}^+ \to X$, which satisfies the following conditions:*

(i) $\Phi_0 = I_X$ where I_X is the identity on X.

(ii) $\Phi_t \circ \Phi_s = \Phi_{t+s}$.

(iii) $\Phi_t : X \to X$ is continuous in (t, x).

Theorem 2.3.3. *(Theorem 1.3.7 [144]). Let $\Phi(t) : X \to X$, $t \geq 0$, be an autonomous semiflow with $\Phi(t)X_0 \subset X_0$, for all $t \geq 0$. Assume that*

(1) $\Phi(t) : X \to X$ is point dissipative.

(2) $\Phi(t) : X \to X$ is compact for each $t > 0$; or alternatively, $\Phi(t) : X \to X$ is α-contraction with its contraction function $k(t) \in [0, 1), \forall t > 0$, and $\gamma^+(U)$ is strongly bounded in X_0 provided that U is strongly bounded in X_0;

(3) $\Phi(t) : X \to X$ is uniformly persistent with respect to $(X_0, \partial X_0)$.

Then there exists a global attractor A_0 for $\Phi(t)$ in X_0 that attracts strongly bounded sets in X_0. Moreover, $\Phi(t)$ has a stationary coexistence state x_0 in A_0 (i.e., $x_0 \in X_0$ and $\Phi(t)x_0 = x_0$, $\forall t \geq 0$).

For the existence of a global attractor A_0, see also Theorem 3.2 [57].

Definition 2.3.7. *Let K be a subset of an ordered space X. Then K is called order convex if $[u,v]_X \subset K$ whenever $u, v \in K$, and $u < v$.*

Definition 2.3.8. *Let $f : U \to U$ be a continuous map (U is nonempty, closed, and convex set). Then*

(1) *f is said to be subhomogeneous if $f(\lambda x) \geq \lambda f(x)$ for all $x \in U$ and $\lambda \in [0, 1]$.*

(2) *f is said to be strictly subhomogeneous if $f(\lambda x) > \lambda f(x)$ for all $x \in U, x \gg 0$ and $\lambda \in (0, 1)$.*

(3) *f is said to be strongly subhomogeneous if $f(\lambda x) \gg \lambda f(x)$ for all $x \in U, x \gg 0$ and $\lambda \in (0, 1)$.*

Theorem 2.3.4. *(Lemma 1 [143]) Let either $V = [0, b]_X$ with $b \gg 0$ or $V = P$ (P is the positive cone of X). If $f : V \to V$ is continuous, strongly positive, and strictly subhomogeneous on V, then f admits at most one positive fixed point in V.*

Theorem 2.3.5. *(Hirsch Attractively Theorem, Theorem 3.3 [62]). Let X be an ordered Banach space. Assume that monotone semiflow $\Phi(t)$ on X admits an attractor K, such that K contains one equilibrium point p. Then every trajectory attracted to K converges to p.*

2.4 Maximum Principle and Parabolic Comparison Theorems

In this section, we define the uniformly parabolic operators and we state the Maximum Principle, in addition to the comparison principle. We start by the meaning of uniformly parabolic operator.

Definition 2.4.1. *[104]. The differential operator*

$$L[u] = a(x,t)\frac{\partial^2 u}{\partial x^2} + b(x,t)\frac{\partial u}{\partial x} - \frac{\partial u}{\partial t}$$

is said to be parabolic at the point (x,t) if $a(x,t) > 0$. The operator L is uniformly parabolic in a domain D of the $x,t-$plane, if there is a positive constant μ such that $a(x,t) \geq \mu$ for all (x,t) in D.

Definition 2.4.2. *[102] The boundary of an open set Ω is said to have the outside strong sphere property if for every point $x_0 \in \partial\Omega$ there exists a closed ball B outside Ω such that $B \cap \partial\Omega = \{x_0\}$. A similar definition holds for the inside strong sphere property.*

Notation 2.4.1. *[102] Let Ω be a bounded subset of $\mathbb{R}^n$. Then Define $D_T := \Omega \times (0,T]$ and $S_T := \partial\Omega \times (0,T]$. On the other hand, by $C^{1,2}(D_T)$ we mean the set of functions with continuous first derivative with respect to t, and continuous second derivative with respect to x.*

Theorem 2.4.1. *(Maximum Principle)[102]. Let $w \in C^{1,2}(D_T)$ such that*

$$w_t - Lw \geq 0 \quad (x,t) \in D_T.$$

If w attains a minimum value m_0 at some point in D_T, then $w(t,x) = m_0$ throughout D_T. If $\partial\Omega$ has the inside strong sphere property and w attains a minimum at some point (t_0, x_0) on S_T, then the normal derivative $\partial w/\partial n < 0$ at (t_0, x_0) whenever w is not a constant.

Remark 2.4.1. *If we let $D_T = (0,T] \times (a,b)$, then the normal derivative of the solution $w(t,x)$ at the boundary points should be strictly negative, in case they are* *local minimum. This equivalent to* $w_x > 0$ *at* $x = a$ *and* $w_x < 0$ *at* $x = b$ *(when* $\Omega = (a, b)$*).*

Theorem 2.4.2. *(Comparison Principle). Let* $u,\ v \in C^{1,2}(D_T)$ *be two solutions to the equation:*

$$w_t - Lw = f(t, x, w).$$

If $u(0, x) \leq v(0, x)$*, then* $u(t, x) \leq v(t, x)$ *throughout* D_T*.*

For more details about the maximum principle and comparison theorems, one can see [102, 104].

Chapter 3

Populations Dynamics with Age-dependent Diffusion and Death Rates on Unbounded Domains

3.1 Introduction

Spatial movement and temporal maturation are two important characters in most of biological systems; modeling the interaction between them has attracted considerable attention recently [2, 46, 47, 48, 49, 64, 66, 80, 97, 98, 99, 100, 113, 115, 119, 139]. One of the most important methods applied is the Smith-Thieme age-structure technique [113]. In this approach, species population is divided into two groups: mature and immature. At different ages, the standard model with age structure and diffusion is incorporated (see [90]):

$$\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} = D(a)\frac{\partial^2 u}{\partial x^2} - d(a)u. \tag{3.1.1}$$

Here $u(t, a, x)$ denote the density of population of the species at time $t \geq 0$, age $a \geq 0$, and location $x \in \mathbb{R}$. $D(a)$ and $d(a)$ are the diffusion and death rates, respectively, at age a. Let $r \geq 0$ be the maturation time for the species and $A_l > 0$ be the life span of the species. The total matured population at time t and location x is given by

$$w(t, x) = \int_r^{A_l} u(t, a, x)da. \tag{3.1.2}$$

Since only the mature can reproduce, one can assume

$$u(t, 0, x) = b(w(t, x)), \tag{3.1.3}$$

where $b(.)$ is the birth function. In [115], So, Wu, and Zou assume that the diffusion and death rates, $D(a)$ and $d(a)$, of the mature population are age independent. i.e.,

$$D(a) = D_m \quad \text{and} \quad d(a) = d_m.$$

Based on this assumption, they substitute (3.1.1) into (3.1.2) to derive

$$\frac{\partial w}{\partial t} = D_m\frac{\partial^2 w}{\partial x^2} - d_m w + u(t, \tau, x), \tag{3.1.4}$$

where $u(t, \tau, x)$ is called the maturation rate and it can be solved from (3.1.1) and the boundary condition (3.1.3), with a formula given by

$$u(t, \tau, x) = \epsilon\int_{-\infty}^{\infty} b(w(t - r, y))f_\alpha(x - y)dy,$$

where

$$\epsilon = \exp\left[-\int_0^r d_I(a)da\right], \quad \alpha = \int_0^r D_I(a)da,$$

and

$$f_\alpha(x) = \frac{\exp^{(-x^2/4\alpha)}}{\sqrt{4\pi\alpha}},$$

where $D_I(a)$ and $d_I(a)$ are the age-dependent diffusion and death rates of the immature individuals. As such, a non-local reaction diffusion with delay can be obtained:

$$\frac{\partial w}{\partial t} = D_m \frac{\partial^2 w}{\partial x^2} - d_m w + \epsilon \int_{-\infty}^{\infty} b(w(t-r,y)) f_\alpha(x-y)dy. \tag{3.1.5}$$

In their paper, they investigated the existence of traveling wave solution for the above equation when the birth function is taken as the Nicholson's blowflies birth function ($b(u) = pue^{-u}$). Recently, there have been some further studies on this model. In [89], Mei and So investigated the stability of traveling wave solution in the case of Nicholson's blowflies birth function. Liang and Wu in [76] investigated the existence of traveling wave solutions for different birth functions. Thieme and Zhao in [119] considered the following general stage-structure model

$$\begin{cases} \partial_t u + \partial_a u = d_I(a)\Delta_x u - \mu_I(a)u, & 0 < a < r, \ x \in \mathbb{R}^n \\ u(t,0,x) = f(u_m(t,x)), & t \geq -r, \ x \in \mathbb{R}^n, \\ \partial_t u_m = d_m \Delta_x u_m - g(u_m) + u(t,r,x), & t > 0, \ x \in \mathbb{R}^n, \end{cases}$$

where $f(u_m)$ and $g(u_m)$ are the birth and death functions, $D_I(a)$ and $d_I(a)$ are the diffusion and death rates of the immature population, and D_m and d_m are age independent diffusion and death rates of the mature population. They investigated the existence of traveling wave solutions of this model, when the spatial domain is the whole real line $\mathbb{R}$. For more studies of these models over unbounded domains, we mention Al-Omari and Gourley [2], Gourley and Kuang in [46], Gourley and So in [49], Gourley, So, and Wu in [48], and Ou and Wu in [99].

Overall, all the above papers study the models with a crucial assumption that *the diffusion and death rates of the mature population are constants* so that Equation (3.1.5) can be easily derived . Actually, all models above seem to fail if $D_m(a)$ and $d_m(a)$ are not constants, because *equation (3.1.5) is not valid anymore if both* $D_m(a)$ *and* $d_m(a)$ *are age-dependent.* Therefore, a natural question to ask is how to study the population dynamics if the coefficients are not constants. We aim in this chapter to answer this question when the spatial domain is unbounded while the next chapter is devoted to answer this equation for the bounded domain case.

The chapter is organized as follows. We start in section 2 by establishing the new model, and obtain the global existence of the solution in section 3. In section 4, we investigate the existence of traveling wave solutions. In section 5, We investigate the existence of spreading speed c^*. Finally, in section 6, we present a numerical simulation.

3.2 The Derivation of the New Model

To derive the model, we re-consider equations (3.1.1)–(3.1.3). We fix $s > 0$ and define a function v by $v(s, a, x) = u(s + a, a, x)$. Then we obtain the following

$$\begin{aligned} \frac{\partial v}{\partial a} &= \left[\frac{\partial u}{\partial t}(t, a, x) + \frac{\partial u}{\partial a}(t, a, x)\right]_{t=a+s} \\ &= D(a)\frac{\partial^2 u}{\partial x^2}(a + s, a, x) - d(a)u(a + s, a, x) \\ &= D(a)\frac{\partial^2 v}{\partial x^2}(s, a, x) - d(a)v(s, a, x). \end{aligned} \tag{3.2.1}$$

By applying the Fourier transformation to the following equation:

$$\frac{\partial v}{\partial a} = D(a)\frac{\partial^2 v}{\partial x^2}(s,a,x) - d(a)v(s,a,x), \tag{3.2.2}$$

we get

$$\frac{d}{da}\overline{V}(s,a,\omega) = -\left[D(a)\omega^2\overline{V}(s,a,\omega) + d(a)\overline{V}(s,a,\omega)\right].$$

Hence,

$$\overline{V}(s,a,\omega) = K(s,\omega)\,\exp\left[-\int_0^a \left(D(\xi):\omega^2 + d(\xi)\right)d\xi\right] = \beta(a)K(s,\omega)e^{-\alpha(a)\omega^2},$$

where

$$\alpha(a) = \int_0^a D(\xi)d\xi, \quad \beta(a) = \exp\left[-\int_0^a d(\xi)d\xi\right],$$

and $K(s,\omega) = \mathcal{F}\{b(w(s,x)\}$. By taking the inverse transformation, we then obtain

$$\begin{aligned} v(r,a,x) &= \mathcal{F}^{-1}\{\overline{V}(r,a,\omega)\} \\ &= \beta(a)\left[\mathcal{F}^{-1}\{K(r,\omega)\} * \mathcal{F}^{-1}\{e^{-\alpha(a)\omega^2}\}\right] \\ &= \frac{\beta(a)}{\sqrt{4\pi\alpha(a)}}\int_{-\infty}^{\infty} b(w(s,y))\,e^{-\frac{(x-y)^2}{4\alpha(a)}}\,dy, \end{aligned}$$

where for the last equality, we have made use of the relation

$$\mathcal{F}^{-1}\left\{e^{-\alpha(a)\,\omega^2}\right\} = \frac{1}{\sqrt{4\pi\alpha(a)}}\,e^{\frac{-x^2}{4\alpha(a)}}.$$

Thus, it follows

$$u(t,a,x) = v(t-a,a,x) = \frac{\beta(a)}{\sqrt{4\pi\alpha(a)}}\int_{-\infty}^{\infty} b(w(t-a,y))\,e^{-\frac{(x-y)^2}{4\alpha(a)}}\,dy. \tag{3.2.3}$$

Then we substitute Equation (3.2.3) into Equation(3.1.2) to get

$$w(t,x) = \int_r^{A_l} \int_{-\infty}^{\infty} b\left(w(t-s,y)\right) \frac{e^{-(x-y)^2/4\alpha(s)}}{\sqrt{4\pi\alpha(s)}} \beta(s)\, dy\, ds, \tag{3.2.4}$$

which is an integral equation.

Remark 3.2.1. *Equation (3.2.3) is only valid for $t \geq a$. As such, equation (3.2.4) is technically true for $t \geq A_l$. However, we will concentrate on the long-time behavior of (3.2.4), and it is meaningful to study this equation for all $t \geq 0$.*

3.3 Global Existence of the Solution

In this section, we investigate the global existence of the solution of the integral equation (3.2.4). To simplify the equation, we change the variables in Equation (3.2.4). Hence, we get

$$\begin{aligned} w(t,x) &= \int_r^{A_l} \int_{-\infty}^{\infty} b\left(w(t-s,x-y)\right) \frac{e^{-y^2/4\alpha(s)}}{\sqrt{4\pi\alpha(s)}} \beta(s)\, dy\, ds \qquad (3.3.1) \\ &= \int_0^{\infty} \int_{-\infty}^{\infty} b\left(w(t-s,x-y)\right) K(s,y)\, dy\, ds\,, \end{aligned}$$

where

$$K(s,x) = \begin{cases} 0\,, & s < r \text{ or } s > A_l,\ x \in \mathbb{R} \\ \dfrac{\beta(s)}{\sqrt{4\pi\alpha(s)}} \exp\{-x^2/4\alpha(s)\}\,, & r \leq s \leq A_l,\ x \in \mathbb{R}\,, \end{cases} \tag{3.3.2}$$

$$\beta(s) = \exp\left\{-\int_0^s d(\xi)d\xi\right\},$$

and

$$\alpha(s) = \int_0^s D(\xi)d\xi.$$

So, Equation (3.3.1) can be written in the following form:

$$w(t,x) = \int_0^\infty \int_{-\infty}^\infty F\left(w(t-s, x-y), s, y\right) dy\, ds \,. \tag{3.3.3}$$

In the following sections, we shall study the above integral equation and investigate the existence of the traveling wave solution as well as the uniqueness of the traveling wave solution. In fact, we will consider three kinds of birth function $b(.)$. First, as an illustration, we will consider the Nichlson's blowflies birth function

$$b_0(u) = f(u) = pue^{-au^q},$$

where p, q, and a are positive constants.

To start, we may first choose $q = 1$. In this case, for simplicity, we may assume $a = p = 1$ after some scalings of the variables. Now, $F(u, s, y) = f(u)K(s, y)$, where $K(s, y)$ is the kernel given in Equation (3.3.2) and $f(u) = ue^{-u}$. We now use the properties of two functions $f(u)$, $K(s, u)$, and some results in [119] to prove the existence, as well as the uniqueness of the traveling wave solution of Equation (3.3.1) for each $c > c^*$, where c^* is the minimal wave speed.

Now, to obtain the global existence of solutions of (3.3.1), we introduce the known results in [119]. Suppose that the following conditions (A) are assumed:

(A1) $\int_0^\infty \int_{-\infty}^\infty K(s,y)dx\, dy < \infty$; in this case define $k^* = \int_0^\infty \int_{-\infty}^\infty K(s,y)dx\, dy$.

(A2) $0 \leq F(u, s, x) \leq u\, K(s, x)$, $\forall u, s \geq 0$, $x \in \mathbb{R}$.

(A3) For every compact interval I in $(0, \infty)$, there exists an $\epsilon > 0$ such that $F(u, s, x) \geq \epsilon\, K(s, x)$, $\forall u \in I$, $s > 0$, and $x \in \mathbb{R}$.

(A4) For every $\epsilon > 0$, there exists a $\delta > 0$ such that

$$F(u, s, x) \geq (1 - \epsilon)\, u\, K(s, x)\ ,$$

for all $u \in [0, \delta]$, $s \geq 0$, and $x \in \mathbb{R}$.

(A5) For every $w > 0$, there exists a $\Lambda > 0$ such that

$$|F(u, s, x) - F(v, s, x)| \leq \Lambda\, |u - v|\, K(s, x)\ ,$$

for each $u, v \in [0, w]$, $s \geq 0$, and $x \in \mathbb{R}$.

Then the following proposition from [119] holds.

Proposition 1. *[119] Let (A) hold. Then, for every Boreal measurable, nonnegative, and bounded function $u_0(t, x)$, there exists a unique measurable solution $u : \mathbb{R}_+ \times \mathbb{R} \to \mathbb{R}_+$ of the nonlinear equation $u(t, x) = u_0(t, x) + \int_0^t \int_{-\infty}^{\infty} F(u(t - s, x - y), s, y)\, dy\, ds$ and u is bounded on $[0, r] \times \mathbb{R}$, for every $r > 0$. Furthermore, the following results hold under additional assumptions:*

a) The solution u is bounded if there exist $c_1, c_2 > 0$ such that $c_1 k^* < 1$ and $F(u, s, x) \leq (c_1 + c_2 u)\, K(s, x)$, for all $u, s \geq 0$ and $x \in \mathbb{R}$.

b) If $r > 0$ and $\lim_{|x| \to \infty} u_0(x, t) = 0$ uniformly for $t \in [0, r]$, then the same holds for u.

Remark 3.3.1. *The kernel $K(x, y)$ which is given in Equation (3.2.3) satisfies*

$$\int_0^{\infty} \int_{-\infty}^{\infty} K(s, x)\, dx\, ds < \infty$$

.

In fact,

$$\int_0^\infty \int_{-\infty}^\infty K(s,x)\,ds\,dx = \int_r^{A_l}\int_{-\infty}^\infty \frac{\beta(s)}{\sqrt{4\pi\alpha(s)}} e^{\frac{-x^2}{4\alpha(s)}}\,ds\,dx$$
$$= \int_r^{A_l} \beta(s)\,ds < \infty.$$

Now, we turn to prove the existence of solution for the integral equation in (3.3.1) for the given birth function $b(u) = ue^{-u}$.

Theorem 3.3.1. *With the birth function given by $b(u) = ue^{-u}$, Equation (3.3.1) has a unique bounded solution.*

Proof. To prove this result, we have to check the satisfaction of conditions (A).

(A1): In fact (A1) holds by the assumptions and by Remark (3.3.1).

(A2): Since $0 < e^{-u} \leq 1$ for every $u \geq 0$, we have $0 < u\,e^{-u} \leq u$. Thus, $0 < u\,e^{-au}K(s,x) \leq uK(s,x)$, $\forall u, s \geq 0$ and $x \in \mathbb{R}$.

(A3): Let $I = [a,b]$ be a compact interval in $(0,\infty)$. We have $f'(u) = e^{-u}(1-u)$. So, f takes its maximum at $u = 1$, since $f(u)$ is increasing on the interval $[0,1]$ and decreasing on the interval $[1,\infty]$. If $b \leq 1$, let $\epsilon = f(a)$; if $a \geq 1$, let $\epsilon = f(b)$; and if $a < 1$ and $b > 1$, let $\epsilon = \min\{f(b), f(c)\}$. Hence, $f(u) = ue^{-au} \geq \epsilon$, for all $u \in I$. Therefore, $F(u,x,s) = f(u)K(s,x) \geq \epsilon K(s,x)$, for all $u \in I$, $s \geq 0$, and $x \in \mathbb{R}$.

(A4): Notice that $F(u,s,x) \geq 0$, for all $u, s \geq 0$, and $x \in \mathbb{R}$. Thus, the inequality in (A4) holds for every $\epsilon \geq 1$. Now, let $\epsilon < 1$ and $\delta = \ln\left(\frac{1}{1-\epsilon}\right) > 0$. Since e^{-u} is decreasing on $[0,\delta]$, we get the result directly.

(A5): $f(u)$ is continuous and its derivative exists for all $u \geq 0$. Therefore the inequality in (A5) holds by applying the mean value theorem. Since $f(u) = u\,e^{-u}$ takes its maximum value at $u = 1$, we have $u\,e^{-u} \leq \frac{1}{e}$, for $u \geq 0$. Therefore, $u\,e^{-u} \leq \frac{1}{e} + c_2 u$, where $c_2 > 0$ and satisfies $c_2 k^* < 1$. Indeed such c_2 exists since k^* is finite in our assumption. This completes our proof. ∎

The global existence of solutions of (3.3.1) for other birth functions in the sections below can be obtained by a similar approach. We will omit the details.

3.4 Existence and Uniqueness of Traveling Wave Solutions

3.4.1 Case 1: $b(u) = ue^{-u}$

At the beginning of this section, we introduce the following assumptions:

(B) Let $k : \mathbb{R}_+ \times \mathbb{R} \to \mathbb{R}_+$ be a Boreal measurable function such that

(B1) $k^* := \int_0^\infty \int_{-\infty}^\infty K(s,y)dyds \in (1, \infty)$.

(B2) $\exists\, \lambda_0$, such that $\int_0^\infty \int_{-\infty}^\infty e^{\lambda_0 y} K(s,y)dy\,ds < \infty$.

(B3) $\exists\, \sigma_2 > \sigma_1 > 0, \rho > 0$ such that $K(s,x) > 0$, for $s \in (\sigma_1, \sigma_2)$ and $x \in [0, \rho]$.

(B4) $K(s,x)$ is isotropic in x, in the sense $\psi(x) = \psi(y)$ whenever $|x| = |y|$, where $\psi : \mathbb{R}^n \to \mathbb{R}$.

Remark 3.4.1. *The kernel $K(s,x)$ which is given in Equation (3.2.3)satisfies the conditions (B2), (B3) and (B4). It is easy to see that (B1) holds if $1 < k^* = \int_0^{A_l} \beta(s)\,ds$.*

Definition 3.4.1. *(Traveling Wave Solutions). $u(x,t)$ is called a traveling wave solution of the integral equation in (3.3.3), if $u(x,t) = v(x+ct)$. The constant c is called the wave speed and the solution $v(.)$ is called the traveling wave front solution or traveling wave profile.*

Tto prove our main theorem in this section, we introduce the following conditions [119]:

(C) Let $f : \mathbb{R}_+ \to \mathbb{R}_+$ be a continuous function such that

(C1) $f(0) = 0$ and $\exists u^* > 0$ solution of $u = k^* f(u)$ such that $k^* f(u) > u$, for $u \in (0, u^*)$.

(C2) $f(u)$ is differentiable at $u = 0$, $f'(0) = 1$, and $f(u) \leq u$ for any $u \in [0, u^*]$.

Also, we introduce the following theorems:

Theorem 3.4.1. *[119] Let $F(u, s, x) = f(u)K(s, x)$, and assume that the conditions (B) and (C) hold. Suppose that f is increasing on $[0, u^*]$, and $f(u) \geq u - au^2$, $\forall u \in [0, u^*]$, for some $a > 0$. Then there is a constant $c^* > 0$ so that for any $c > c^*$, the equation*

$$u(t,x) = \int_0^\infty \int_{-\infty}^\infty F\left(u(t-s, x-y), s, y\right) dy\, ds$$

has a traveling monotone wave solution connecting 0 and u^* with speed c.

Theorem 3.4.2. *[119] Let $F(u, s, x) = f(u)K(s, x)$, and assume that the conditions (B) and (C) hold. Suppose that f is increasing on $[0, u^*]$, and*

$$|f(u) - f(v)| \leq |u - v|, \forall u, v \in [0, u^*] \,.$$

Then, for $c > c^*$ the equation

$$u(t,x) = \int_0^\infty \int_{-\infty}^\infty F\left(u(t-s, x-y), s, y\right) dy\, ds$$

admits at most one increasing traveling wave solution $u(x + ct)$ connecting 0 and u^* up to translation.

See also references [31] and [33] for the results similar to the above two theorems. Now, we can directly apply these two theorems to study the existence and uniqueness of an increasing traveling wave solution for our equation in the case $b(u) = ue^{-u}$. We can obtain the following theorem.

Theorem 3.4.3. *There is a constant $c^* > 0$ so that for $c > c^*$, equation (3.3.1) has a unique, up to translation, monotone traveling solution connecting $u = 0$ and $u^* = \ln(k^*)$, provided that $1 < k^* \le e$.*

Proof. Existence: To prove the existence, we apply Theorem 3.4.1. Notice that the conditions (B) hold by the assumption. To check the satisfaction of conditions in (C). We notice $f(u) = u\, e^{-u}$ is continuous, $f(0) = 0$, and $u^* = \ln(k^*)$ is a solution for $u = k^*\, f(u)$. Moreover, for every $u \in (0, u^*) = (0, \ln(k^*))$, we have

$$u < \ln(k^*) \Leftrightarrow e^u < k^* \Leftrightarrow \frac{1}{k^*} < e^{-u} \Leftrightarrow 1 < k^*\, e^{-u} \Leftrightarrow u < k^*\, u\, e^{-u} = k^*\, f(u)\,.$$

Therefore, condition (C1) holds. Next, for the condition (C2), it is obvious to see that f is differentiable at $u = 0$ with $f'(0) = 1$, and $f(u) = u\, e^{-u} \le u$, for all $u \in [0, u^*]$, since $e^{-u} \le 1$, for $u \in [0, u^*]$.Moreover, f is increasing provided that $k^* \le e$ which implies that $f(u)$ is increasing in $u \in [0, u^*]$. Also, if we let $g(u) = e^{-u} + u - 1$, then $g'(u) \ge 0$ for all $u \ge 0$. This implies that$f(u) \ge u - u^2$, $\forall u \in [0, u^*]$. This completes our proof for the existence part.

Uniqueness: To prove the uniqueness, we need to check the validity of the following inequality

$$|f(u) - f(v)| \le |u - v|,\ \forall u, v \in [0, u^*]\,.$$

To do this we notice that $f(u)$ is continuous and differentiable on $[0, u^*]$. So, it suffices to show that $|f'(u)| \le 1$. Actually, $f'(u) = (1-u)e^{-u}$, and $f''(u) = (u-2)e^{-u}$. So, $f'(u)$ is decreasing on $[0, 2]$. However, $1 < k^* \le e$, implies that $0 < \ln(k^*) \le 1$, and so $f'(u)$ is decreasing and positive on $[0, u^*] \subseteq [0, 1]$. Therefore, $0 \leq f'(u^*) \leq f'(u) \leq f'(0) = 1$, $\forall u \in [0, u^*]$. Hence, the inequality holds by applying the mean value theorem. ∎

Theorem 3.4.4. *[119] Let the conditions (A) and (B) hold. Then for each $c \in (0, c^*)$, there exists no traveling wave solution of the equation*

$$u(t,x) = \int_0^{\infty} \int_{-\infty}^{\infty} F\left(u(t-s, x-y), s, y\right) dy\, ds$$

with speed c.

3.4.2 Case 2: $b_1(u) = pue^{-au^q}$.

Now, we consider other cases of birth function in our model. To prove the existence and uniqueness of traveling wave solution, we state first the following theorem.

Theorem 3.4.5. *[119] Let (A2) and (B) hold. Assume that $F(.,s,x)$ is increasing in $[0, u^*]$ for each $(s,x) \in \mathbb{R}_+ \times \mathbb{R}$, and $F(u,s,x) \geq (u - bu^{\sigma})K(s,x), \forall u \in [0, \delta]$, $(s,x) \in \mathbb{R}_+ \times \mathbb{R}$ for appropriate $\delta \in (0, u^*]$, $\sigma > 1$ and $b > 0$. Then for each $c > c^*$, there exists a monotone traveling wave solution of the equation*

$$u(t,x) = \int_0^{\infty} \int_{-\infty}^{\infty} F\left(u(t-s, x-y), s, y\right) dy\, ds\,.$$

connecting 0 and u^* with speed c.

Consider the birth function $b(u) = p\,u\,e^{-au^q}$, where a, p, and $q > 0$. In condition (C_2), we require $f'(0) = 1$. Therefore, we denote $f(u) = u\,e^{-au^q}$. The constant coefficient p in the birth function can be included into the kernel function $K(s,x)$. After this setting, for $b(u) = p\,u\,e^{-au^q}$ we still can prove the following theorem which gives the existence and uniqueness, up to translation, of traveling wave solution of Equation (3.3.1).

Theorem 3.4.6. *There exists a constant $c^* > 0$ so that equation (3.3.1) has a unique monotone traveling wave solutions with speed $c > c^*$, connecting $u = 0$ and $u^* = \left[\frac{1}{a}\ln(pk^*)\right]^{1/q}$, provided that $1 < pk^* \leq e^{1/q}$.*

Proof. We notice that $F(u, s, x)$ is increasing in u on the interval $[0, u^*]$, since $f_1(u)$ is increasing on $[0, u^*]$. Furthermore, $F(u, s, x) \geq (u - bu^\sigma)\ K(s, x)$, $\forall u \in [0, \delta]$, $(s, x) \in \mathbb{R}_+ \times \mathbb{R}$, and for any $\delta \in (0, u^*]$, where $\sigma = q + 1$ and $b = a$. Moreover, conditions (A2) and (B) hold. Thus, by Theorem 3.4.5 there exists a monotone traveling wave solution of Equation (3.3.1). The uniqueness, up to translation, of the monotone traveling wave solution comes by applying Theorem 3.4.2. We remark here that the inequality in Theorem 3.4.2 holds by the Mean Value Theorem. Indeed, we have $|f_1'(u)| \leq 1$. ∎

3.4.3 Case 3: $b_2(u) = \frac{pu}{1+au^q}$

In this subsection we consider the birth function $b(u) = \dfrac{pu}{1 + au^q}$, where $a, p,$ and $q > 0$. In fact we let $f(u) = \dfrac{u}{1 + au^q}$ so that $f(0) = 0, f'(0) = 1$. The coefficient p is again put into the kernel function k. Similarly we have the following theorem for this case.

Theorem 3.4.7. *There is a constant $c^* > 0$ so that for each $c > c^*$, equation (3.3.1) admits a unique, up to translation, increasing traveling wave solution connecting $u = 0$ and $u^* = \left[\dfrac{pk^* - 1}{a}\right]^{1/q}$, provided that $1 < pk^* < \infty$ if $q \leq 1$ and $1 < pk^* < \dfrac{q}{q-1}$ if $q > 1$. On the other side, for $c \in (0, c^*)$, equation (3.3.1) has no positive traveling waves.*

Proof. Again the proof comes by applying Theorem 3.4.5 and Theorem 3.4.2. ∎

3.4.4 Case 4: $b_3(u) = pu(1 - \frac{u^q}{K^q})$

Now we Consider

$$b(u) = \begin{cases} pu(1 - \frac{u^q}{K^q}) \,, & 0 \leq u \leq K \\ 0 \,, & u > K \,, \end{cases}$$

and we let

$$f(u) = \begin{cases} u(1 - \frac{u^q}{K^q}) \,, & 0 \leq u \leq K \\ 0 \,, & u > K \,. \end{cases}$$

For this case we have the following theorem:

Theorem 3.4.8. *There is a constant $c^* > 0$, so that for $c > c^*$, equation (3.3.1) with the birth function $b_3(u)$ has a unique, up to translation, monotone traveling solution connecting $u = 0$ and $u^* = K\left(1 - \frac{1}{pk^*}\right)^{1/q}$, where $1 < pk^* \leq \frac{1+q}{q}$. On the other side, for $c \in (0, c^*)$, equation (3.3.1) has no positive traveling waves.*

Proof. Again the proof comes by applying Theorem 3.4.5 and Theorem 3.4.2. ∎

Remark 3.4.2. *To show that* (3.3.1) *admits a monotone traveling wave solution with speed $c = c^*$, we apply Theorem 3.4 [119]. As a direct result of this theorem, we have the following results:*

Theorem 3.4.9. *For $c = c^*$, and the birth function $b_1(u)$, Equation (3.3.1) admits a monotone traveling wave solutions connecting $u = 0$ and $u^* = \left[\frac{1}{a}\ln(pk^*)\right]^{1/q}$, provided that $1 < pk^* \leq e^{1/q}$.*

Theorem 3.4.10. *For $c = c^*$, and the birth function $b_2(u)$, Equation (3.3.1) admits a monotone traveling wave solution connecting $u = 0$ and $u^* = \left[\frac{pk^* - 1}{a}\right]^{1/q}$, provided that $1 < pk^* < \infty$ if $q \leq 1$ and $1 < pk^* < \frac{q}{q-1}$ if $q > 1$.*

Theorem 3.4.11. *For $c = c^*$, , and the birth function $b_3(u)$, Equation (3.3.1)admits a monotone traveling solution connecting $u = 0$ and $u^* = K\left(1 - \frac{1}{pk^*}\right)^{1/q}$, where $1 < pk^* \leq \frac{1+q}{q}$.*

Remark 3.4.3. *We consider the above birth functions due to their wide use in Mathematical Biology, especially, for the cases $q = 1$ in $b_1(u)$, $q = 2$ in $b_2(u)$, and $q = 1$ in $b_3(u)$. For example, see [125]. Moreover, when the diffusion and death functions are age independent, i.e. $D(a)$ and $d(a)$ are constant rates, it is easy to see that the conditions (A) and (B) hold for the above four cases. In fact, this case was studied in [79, 115] and our results can cover this particular case.*

3.5 Non-monotone Traveling Wave Solutions

In the previous section we showed that the integral equation (3.3.1) admits a monotone traveling wave solution which connecting $u = 0$ and $u = u^*$, for all $c \geq c^*$, provided that $f(u)$ (the birth function) is monotone increasing function on $[0, u^*]$. The case is different when the birth function $f(u)$ is non-monotone. In this case, the resulting integral operator is non-monotone operator, and therefore, we can not get the existence of monotone traveling wave solutions. In fact, the numerical simulation for this case shows the existence of a non-monotone traveling wave solution connecting $u = 0$ and $u = u^*$ (with a spike at $u = u^*$) for some cases. Analytically, Fang and Zaho [36] proved, using Schauder's Fixed Point Theorem, the existence (as well as the uniqueness up to translation) of a such traveling solution which connecting $u = 0, \forall c > c^*$. (see Theorem 3.1 [36]). This traveling wave solution exists provided that the conditions (A) and (B) hold, in addition to the conditions in Theorem 3.4.5 and Theorem 3.4.2. Also, they showed that such a solution does not exist provided that $c \in (0, c^*)$ (see Theorem 2.2 [36]). For the case $c = c^*$, they showed that for a positive small number β, there exists a traveling wave profile (U, c^*) connecting $u = 0$ with $U(0) = \beta$ and $U(\xi) \leq \beta$, $\forall \xi < 0$. Moreover, they showed that all these traveling wave solutions connecting $u = 0$ and $u = u^*$ under certain conditions. To apply their results to our model, we need first to put some assumptions on the birth function $f(u)$. We assume that $f(u)$ satisfies the following conditions:

(F) Assume there exists a positive constant M such that

(F1) $f \in C([0, M], [0, M])$, $f(0) = 0$, $f'(0) > 0$, and f is Lipschitz continuous on $[0, M]$.

(F2) $f(u) \leq f'(0)u$, $\forall u \in [0, M]$, and there exists $u^* \in [0, M]$ such that $k^* f(u^*) = u^*$, $k^* f(u) > u$, $\forall u \in (0, u^*)$, and $k^* f(u) < u$, $\forall u \in (u^*, M]$.

(F3) $\frac{f(u)}{u}$ is strictly increasing for $u \in (0, M]$, and $f(u)$ satisfies the property (P): that is for any $v, w \in (0, M]$ and $v \leq u^* \leq w$, $v \geq k^* f(w)$, and $w \leq k^* f(v)$, we have $v = w$.

Remark 3.5.1. *We remark that a function $f(u)$ satisfies the property (P) if one of the following holds (see Lemma 2.2 [65] and Lemma 3.1 [147]):*

(P0) $f(u)$ is non-decreasing on $[0, M]$.

(P1) $uf(u)$ is strictly increasing on $(0, M]$.

(P3) $f(u)$ is non-increasing for $u \in [u^*, M]$, and $\frac{f(k^* f(u))}{u}$ is strictly decreasing for all $u \in (0, u^*]$.

Following the same argument in [65], we define the following continuous functions:

$$f^+(u) = \max_{0 \leq v \leq u} f(v), \ \forall u \in [0, M] \quad \text{and} \quad f^-(u) = \min_{u \leq v \leq M} f(v), \ \forall u \in [0, M].$$

Moreover, we denote by u_+^* to the positive solution of $k^* f^+(u) = u$, and by u_-^* to the positive solution of $k^* f^-(u) = u$. Then we have the following inequality:

$$0 < u_-^* \leq u^* \leq u_+^* \leq M.$$

Theorem 3.5.1. *Let $f(u)$ in Equation (3.3.1) be the birth function $b_1(u)$, and assume that $1 < k^* p \leq e^{2/q}$. Then the following assertions hold:*

(I) For any $c > c^*$, Equation (3.3.1) admits a unique (up to translation) traveling wave solution connecting $u = 0$ and $u^* = \left[\frac{1}{a}\ln(pk^*)\right]^{1/q}$.

(II) For $c = c^*$, and for a small positive number β, there exists a traveling wave profile (U, c^*) connecting $u = 0$ and $u = u^*$ with $U(0) = \beta$ and $U(\xi) \leq \beta$, $\forall \xi < 0$.

(III) For $c \in (0, c^*)$ there is no traveling wave solution (U, c).

Proof. To prove this theorem, we need to check the validity of condition (F). In the proof of Theorem 3.4.5, we showed that conditions (F1) and (F2) hold. To check the validity of condition (F3), first, we remark that $f(u)/u$ is strictly decreasing on $[0, \infty]$. Moreover, $f'(0) = p > 0$, and $f(u)$ takes its maximum at $\overline{u} = (\frac{1}{aq})^{\frac{1}{q}}$ and $f(\overline{u}) = p(\frac{1}{aqe})^{\frac{1}{q}}$. Assume that $1 < k^* p \leq e^{\frac{1}{q}}$, then $f(u)$ is monotone increasing on $[0, u^*]$. Hence, we consider $M = u^*$, and therefore, (P0) holds. Now, we assume $k^* p > e^{\frac{1}{q}}$. In this case, we consider $M = f(\overline{u})$, and hence, $u_+^* = M$, $u_-^* = f(M) = \frac{p^2}{aqe} e^{-\frac{p}{qe}}$. Let

$$h(u) := \frac{f(k^* f(u))}{u} = p^2 k^* \exp\left\{-a\left(u^q + (pk^* u)^q e^{-aqu^q}\right)\right\}.$$

Then by elementary calculations, the function $h(u)$ is strictly decreasing on $[0, u^*]$ if $e^{\frac{1}{q}} < pk^* \leq e^{\frac{2}{q}}$. Therefore, (P2) holds. Hence, the above assertions hold by Theorem 2.2 and Theorem 3.1 [36]. ∎

Theorem 3.5.2. *Let $f(u)$ in Equation (3.3.1) be the birth function $b_2(u)$, and assume that $q \in \left(0, \max\left(2, \frac{pk^*}{pk^*-1}\right)\right]$, or $q > \max\left(2, \frac{pk^*}{pk^*-1}\right)$ and $k^* f(\overline{u}) \leq \left(\frac{2}{a(q-2)}\right)^{\frac{1}{q}}$; where $pk^* > 1$ and $\overline{u}$ is the value where $f(u)$ takes its maximum. Then the following assertions hold:*

(I) For any $c > c^*$, Equation (3.3.1) admits a unique (up to translation) traveling wave solution connecting $u = 0$ and $u^* = \left(\frac{pk^*-1}{a}\right)^{1/q}$.

(II) For $c = c^*$, and for a small positive number β, there exists a traveling wave profile (U, c^*) connecting $u = 0$ and $u^* = \left(\frac{pk^*-1}{a}\right)^{1/q}$ with $U(0) = \beta$ and $U(\xi) \leq \beta$, $\forall \xi < 0$.

(III) For $c \in (0, c^*)$ there is no traveling wave solution (U, c).

Proof. To prove this theorem, again, we need to check the validity of the condition (F). In the proof of Theorem 3.4.6, we showed that conditions (F1) and (F2) hold. To check the validity of condition (F3), first, we remark that $f(u)/u$ is strictly decreasing on $[0, \infty]$. Moreover, $f'(0) = p > 0$, and $f(u)$ takes its maximum at $\overline{u} = \left(\frac{1}{a(q-1)}\right)^{\frac{1}{q}}$ and $f(\overline{u}) = \frac{p(q-1)}{q}\overline{u}$. Assume that $q \in (0, 1]$, then $f(u)$ is monotone increasing on $[0, \infty)$, and hence, (P0) holds if we consider $M = u^*$. Now, if we assume $1 < q \leq 2$, then $uf(u)$ is increasing function on $[0, \infty)$. Hence (P1) holds with $M = u^*$. Moreover, if $1 < pk^* \leq \frac{q}{q-1}$ (i.e., $q \in \left(1, \frac{pk^*}{pk^*-1}\right)$), then $u^* \leq \overline{u}$. Hence, if we let $M = u^*$, then (P0) holds. conclusively, if $q \in \left(0, \max\left(2, \frac{pk^*}{pk^*-1}\right)\right]$, then either (P0) or (P1) holds. If $q > \max\left(2, \frac{pk^*}{pk^*-1}\right)$, then $h(u) := uf(u) = \frac{pu^2}{1+au^q}$ is monotone increasing on $\left[0, \left(\frac{2}{a(q-2)}\right)^{\frac{1}{q}}\right]$. Hence, if we consider $M = k^* f(\overline{u})$, then (P1) holds provided that $k^* f(\overline{u}) \leq \left(\frac{2}{a(q-2)}\right)^{\frac{1}{q}}$. Hence, the above assertions hold as a result of Theorem 2.2 and Theorem 3.1 [36]. ∎

In the following theorem, we consider the logistic birth function $b_3(u)$ with $q = 1$.

Theorem 3.5.3. *Let $f(u)$ in Equation (3.3.1) be the birth function $b_3(u)$ with $q = 1$, and assume that $1 < pk^* \leq 3$. Then the following assertions hold:*

(I) For any $c > c^*$, Equation (3.3.1) admits a unique (up to translation) traveling wave solution connecting $u = 0$ and $u^* = K\left(1 - \frac{1}{pk^*}\right)$.

(II) For $c = c^*$, and for a small positive number β, there exists a traveling wave profile (U, c^*) connecting $u = 0$ and $u^* = K\left(1 - \frac{1}{pk^*}\right)$ with $U(0) = \beta$ and $U(\xi) \leq \beta$, $\forall \xi < 0$.

(III) For $c \in (0, c^*)$ there is no traveling wave solution (U, c).

Proof. The proof of this theorem is similar to the proof of the above two theorems. First, we remark that the validity of the conditions (F1) and (F2) have been shown in Theorem 3.4.7. To check the validity of condition (F3), we remark that $f(u)/u$ is strictly decreasing on $(0, K]$. Moreover, $f'(0) = p > 0$, and $f(u)$ takes its maximum at $\overline{u} = \frac{K}{2}$ with $f(\overline{u}) = \frac{pK}{4}$. Assume that $1 < pk^* \leq 2$, then $f(u)$ is monotone increasing on $[0, \frac{2}{K}]$, and hence, (P0) holds if we consider $M = u^*$. If $2 < pk^* < 4$, we let $M = \frac{pk^*}{4}K$, and we define

$$h(u) := \frac{f(k^* f(u))}{u} = \frac{p^2 k^*}{K^3}\left(K^2 (K - u) - pk^* u (K - u)^2\right).$$

Then by elementary calculations, the function $h(u)$ is strictly decreasing on $[0, u^*]$ provided that $2 < pk^* \leq 3$, and hence, (P2) holds. Therefore, the above assertions hold by Theorem 2.2 and Theorem 3.1 [36]. ∎

3.6 Asymptotic Spreading Speed

In this section, we prove that the integral equation (3.3.1), with the birth functions $b_1(u)$, $b_2(u)$, and $b_3(u)$, admits a spreading speed c^*. The spreading of speed is defined as follows:

Definition 3.6.1. *[120]. A number $c^* > 0$ is called the asymptotic spreading speed (spreading speed) for a function $u(t,x) : \mathbb{R}_+ \times \mathbb{R} \to \mathbb{R}_+$, if the following statements hold:*

(1) $\lim_{t\to\infty, |x|\geq ct} u(t,x) = 0, \quad \forall c > c^*.$

(2) $\lim \inf_{t\to\infty, |x|\geq ct} u(t,x) > \epsilon, \quad \forall c < c^*,$ *and for some* $\epsilon > 0$.

Remark 3.6.1. *(Spreading Speed) [120]. The spreading speed is given by*

$$c^* = \inf\left\{c \geq 0 : \mathcal{K}(c,\lambda) < 1, \text{ for some } \lambda > 0\right\},$$

where

$$\mathcal{K}(c,\lambda) = \int_0^\infty \int_{-\infty}^\infty e^{-\lambda(y+cs)} K(s,y) dy ds.$$

For our model $\mathcal{K}(c,\lambda)$ is given by

$$\begin{aligned}\mathcal{K}(c,\lambda) &= \int_0^\infty \int_{-\infty}^\infty e^{-\lambda(y+cs)} K(s,y) dy ds \\ &= \int_r^{A_l} \int_{-\infty}^\infty \frac{\beta(s)}{\sqrt{4\pi\alpha(s)}} \exp\{-y^2/4\alpha(s)\}\, e^{-\lambda(y+cs)} dy ds.\end{aligned}$$

Remark 3.6.2. *If we assume that (B) holds, then there exists c^* and λ^* solve the equation $\mathcal{K}(c^*,\lambda^*) = 1$. Moreover, c^* and λ^* can be uniquely determined by solving the following system (see Lemma 2.2 and Proposition 2.3 [120]):*

$$\begin{cases} \mathcal{K}(c,\lambda) = 1, \\ \frac{d}{d\lambda}\mathcal{K}(c,\lambda) = 0. \end{cases}$$

Definition 3.6.2. *[119]: A function $u_0(t,x) : \mathbb{R}_+ \times \mathbb{R} \to \mathbb{R}_+$ is admissible if for each* *c and* λ *satisfy that* $\mathcal{K}(c, \lambda) < 1$*, we have*

$$u_0(t, x) \leq \gamma e^{\lambda(ct-|x|)}, \forall t \geq 0,\ \forall x \in \mathbb{R},\ \text{and some } \gamma > 0.$$

Remark 3.6.3. *For the given birth functions* $b_1(u)$, $b_2(u)$, *and* $b_3(u)$, *we showed that the conditions (A) and (B) hold. Moreover, we showed in the previous section that the condition (F) holds under certain conditions. Therefore, by applying Theorem 2.1 [36], we have the following results:*

Theorem 3.6.1. *Let* $f(u)$ *in Equation* (3.3.1) *be the birth function* $b_1(u)$, *and assume that* $1 < pk^* \leq e^{\frac{1}{q}}$. *Then the following assertions hold:*

(I) For every admissible function $u_0(t, x)$, $u(t, x)$ *satisfies*

$$\lim_{t \to \infty, |x| \geq ct} u(t, x) = 0, \quad \forall c > c^*.$$

(II) Assume that $u_0(t, x)$ *satisfies the property that* $u_0(t, x) \geq \eta > 0$, $\forall t \in (t_1, t_2), |x| \leq \eta$, *where* $t_2 > t_1 \geq 0$. *Then,*

$$\lim_{t \to \infty, |x| \leq ct} u(t, x) = u^*, \quad \forall c < c^*,$$

where $u^* = \left[\frac{1}{a} \ln(pk^*)\right]^{\frac{1}{q}}$.

Theorem 3.6.2. *Let* $f(u)$ *in Equation* (3.3.1) *be the birth function* $b_2(u)$, *and assume that* $q \in \left(0, \max\left(2, \frac{pk^*}{pk^*-1}\right)\right]$, *or* $q > \max\left(2, \frac{pk^*}{pk^*-1}\right)$ *and* $k^* f(\overline{u}) \leq \left(\frac{2}{a(q-2)}\right)^{\frac{1}{q}}$; *where* $pk^* > 1$ *and* $\overline{u}$ *is the value where* $f(u)$ *takes its maximum. Then the following assertions hold:*

(I) For every admissible function $u_0(t,x)$, $u(t,x)$ satisfies

$$\lim_{t\to\infty, |x|\geq ct} u(t,x) = 0, \quad \forall c > c^*.$$

(II) Assume that $u_0(t,x)$ satisfies the property that $u_0(t,x) \geq \eta > 0$, $\forall t \in (t_1, t_2), |x| \leq \eta$, where $t_2 > t_1 \geq 0$. Then,

$$\lim_{t\to\infty, |x|\leq ct} u(t,x) = u^*, \quad \forall c < c^*,$$

where $u^* = \left(\frac{pk^*-1}{a}\right)^{\frac{1}{q}}$

Theorem 3.6.3. *Let $f(u)$ in Equation (3.3.1) be the birth function $b_3(u)$ with $q = 1$, and assume that $1 < pk^* \leq 3$. Then the following assertions hold:*

(I) For every admissible function $u_0(t,x)$, $u(t,x)$ satisfies

$$\lim_{t\to\infty, |x|\geq ct} u(t,x) = 0, \quad \forall c > c^*.$$

(II) Assume that $u_0(t,x)$ satisfies the property that $u_0(t,x) \geq \eta > 0$, $\forall t \in (t_1, t_2), |x| \leq \eta$, where $t_2 > t_1 \geq 0$. Then,

$$\lim_{t\to\infty, |x|\leq ct} u(t,x) = u^*, \quad \forall c < c^*,$$

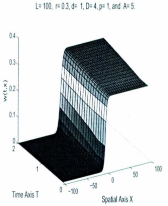
where $u^* = K(1 - \frac{1}{pk^*})$.

Remark 3.6.4. *From the above theorems and the results in the previous section, we remark that the minimum wave speed coincide with the spreading speed c^*.*

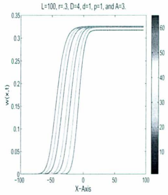
3.7 Numerical Simulation

In this section, we present a numerical simulation to investigate the long time behavior of the solution $w(t, x)$. In this simulation, we consider the Nichelson's blow-flies function $f(u) = pue^{-u}$. By applying the composite Simpson's rule, we can evaluate the integral in Equation (3.1.2). To evaluate the solution $u(t, a, x)$ at the mesh points $a_i, i = 1, 2, \cdots, N$, we solve the reaction diffusion equation (3.2.2) using the method of lines. In this simulation, we distinguish two cases: the constant case (death and diffusion rates are age independent), and the age-dependent case.

Case 1: In this case, we consider the diffusion and death rates to be constants. This numerical simulation shows that Equation (3.3.3) admits a monotone traveling wave solution. We apply our technique for the values $L = 100$, $r = 0.3$, $A = 3$, $p = 1$, $D = 4$, and $d = 1$ (see Figure 3.1(a) and Figure 3.1(b)).



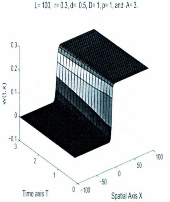
(a) Traveling wave solution. The values of the parameters are $L = 100$, $r = 0.3$, $A = 3$, $p = 1$, $D = 4$, and $d = 1$.



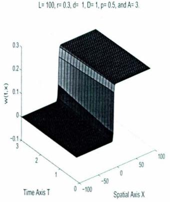
(b) A Two dimensional graph shows the traveling wave solution. The values of the parameters are $L = 100$, $r = 0.3$, $A = 3$, $p = 1$, $D = 4$, and $d = 1$.

Figure 3.1: Traveling wave fronts for the constant case.

Case 2: To investigate the effect of age dependence on the solution we add an exponential variation to the diffusion and death rates. Indeed, we consider $D(a) = D + e^{-a^2}$ and $d(a) = d + e^{-a^2}$. In this case, we choose $L = 100$, $r = 0.3$, $A = 3$, $p = 0.5$, $D = 1$, and $d = 1$ (see Figure 3.2(a)). Also, we consider $\alpha(a) = e^{-Da^2}$ and $\beta(a) = e^{-da^2}$ (i.e., the diffusion and death rates are linear) with the parameters $L = 100$, $r = 0.3$, $A = 3$, $p = 0.5$, $D = 1$, and $d = 1$ (see Figure 3.2(b)). Figure 3.3 shows a non-monotone traveling wave solution for the above two cases, and Figure 3.4 shows the spreading of the solution in both direction.

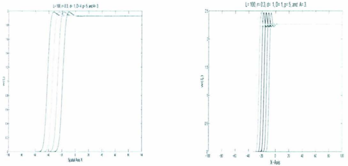


(a) Traveling wave solution when $D(a) = D + e^{-a^2}$ and $d(a) = d + e^{-a^2}$. The values of the parameters are $L = 100$, $r = 0.3$, $A = 3$, $p = 1$, $D = 1$, and $d = 0.5$.



(b) Traveling wave solutions when $\alpha(a) = e^{-Da^2}$ and $\beta(a) = e^{-da^2}$. The values of the parameters are $L = 100$, $r = 0.3$, $A = 3$, $p = 0.5$, $D = 1$, and $d = 1$.

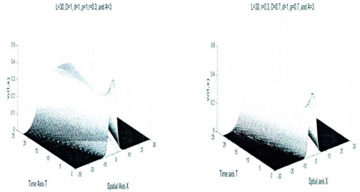
Figure 3.2: Traveling wave fronts for age-dependente case.



(a) Non-monotone traveling wave solution when $D(a) = D$ and $d(a) = d$. The values of the parameters are $L = 100$, $r = 0.3$, $A = 3$, $p = 5$, $D = 4$, and $d = 1$.

(b) Non-monotone traveling wave solutions when $\alpha(a) = e^{-Da^2}$ and $\beta(a) = e^{-da^2}$. The values of the parameters are $L = 100$, $r = 0.3$, $A = 3$, $p = 5$, $D = 1$, and $d = 1$.

Figure 3.3: Non-monotone traveling wave solution. The initial condition is $\phi(x) = 0,\ -L \le x < 0;\ \phi(x) = 1,\ 0 \le x < L$.



(a) Spreading of the solution when $D(a) = D$ and $d(a) = d$. The values of the parameters are $L = 30$, $r = 0.3$, $A = 3$, $p = 1$, $D = 1$, and $d = 1$.

(b) Spreading of the solution when $\alpha(a) = e^{-Da^2}$ and $\beta(a) = e^{-da^2}$. The values of the parameters are $L = 100$, $r = 0.3$, $A = 3$, $p = 0.5$, $D = 1$, and $d = 1$.

Figure 3.4: The spreading of the solution $w(t, x)$ in both directions.The initial condition is $\phi(x) = \frac{3}{\sqrt{\pi}} \exp\{-x^2/4\}$.

Chapter 4

Populations Dynamics with Age-dependent Diffusion and Death Rates on Bounded Domains

4.1 Introduction

In this chapter, we reconsider the age-dependent structured model

$$\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} = D(a)\frac{\partial^2 u}{\partial x^2} - d(a)u. \tag{4.1.1}$$

Again $u(t, a, x)$ represents the density of population of the species at time $t \geq 0$, age $a \geq 0$, and location $x \in [a, b] \subset \mathbb{R}$. The functions $D(a)$ and $d(a)$ are the diffusion and death rates, respectively, at age a. The total matured population at time t and location x is given by

$$w(t, x) = \int_r^{A_l} u(t, a, x)da, \tag{4.1.2}$$

and the initial data at $a = 0$, is given by

$$u(t, 0, x) = b(w(t, x)), \tag{4.1.3}$$

where $r \geq 0$ is the maturation time of the species, $A_l > 0$ is the life span of the species, and $b(.)$ is the birth function.

Under the assumption that the diffusion and death rates of mature population are constants, Liang, So, Zhang, and Zou [80], considered the above model on a bounded domain. In their paper, they investigated the long time behavior of the solution using numerical simulation. Xu and Zhao in [139] considered the following stage-structure model:

$$\begin{cases} \partial_t u + \partial_a u = d_I(a)\Delta_x u - \mu_I(a)u, & 0 < a < r, \quad x \in \Omega \subset \mathbb{R}^n \\ u(t, 0, x) = f(u_m(t, x)), & t \geq -r, \quad x \in \Omega \subset \mathbb{R}^n, \\ \partial_t u_m = d_m \Delta_x u_m - g(u_m) + u(t, r, x), & t > 0, \quad x \in \Omega \subset \mathbb{R}^n, \end{cases}$$

where $f(u_m)$ and $g(u_m)$ are the birth and death functions, $D_I(a)$ and $d_I(a)$ are the diffusion and death rates of the immature population, and D_m and d_m are age independent diffusion and death rates of the mature population. In this paper, the authors investigated the existence and the stability of a strongly positive steady-state solution.

In this chapter, we investigate the model (4.1.1)–(4.1.3) when the spatial domain is bounded, and the diffusion and death rates are age dependent. We organize this chapter as follows: We start in section 2 by establishing the new model on bounded domain. In section 3, we investigate the existence of principal eigenvalue and the corresponding eigenfunction when the birth function is linear. In section 3, we investigate the existence of a steady state solution when the birth function is nonlinear. In section 5, we concentrate on the long time behavior of the solution, i.e., we investigate the stability of the solution. In section 6, we present a numerical simulation. Finally, section 7 is devoted to show the existence of positive steady state solution when the birth function $f(u)$ is nonlinear positive function.

4.2 Age-Structured Model on Bounded Domains

In this section, we consider the model (4.1.1)–(4.1.3) when the spatial domain Ω is a finite and closed interval in $\mathbb{R}$. Let $u(t, a, x)$ denote to the density of species population at time $t \geq 0$, age $a \geq 0$, and location $x \in \Omega = [0, \pi]$. We rewrite the model (4.1.1)–(4.1.3) in the following equations:

$$\frac{\partial u}{\partial t} + \frac{\partial u}{\partial a} = D(a)\frac{\partial^2 u}{\partial x^2} - d(a)u, \tag{4.2.1}$$

$$w(t, x) = \int_r^{A_l} u(t, a, x)da \tag{4.2.2}$$

and

$$u(t, 0, x) = b(w(t, x)) \,. \tag{4.2.3}$$

To derive new models for this case, we should impose the above model with boundary conditions. For this study, we consider the Neumann boundary conditions as well as the Dirichlet boundary conditions. In the following analysis, we derive a new model subject to the Neumann boundary conditions. Since the same analysis can be done for the derivation of a new model subject to the Dirichlet boundary conditions, we omit the details. Now, we consider the model (4.2.1)–(4.2.3) subject to the Neumann boundary conditions:

$$\frac{\partial}{\partial x}u(t, a, 0) = 0 \text{ and } \frac{\partial}{\partial x}u(t, a, \pi) = 0, \; t \geq 0, \; a \geq 0. \tag{4.2.4}$$

We fix $s > 0$ and then we define a function $v(s,a,x) = u(s+a,a,x)$. Hence, we obtain

$$\begin{aligned} \frac{\partial v}{\partial a} &= \left[\frac{\partial u}{\partial t}(t,a,x) + \frac{\partial u}{\partial a}(t,a,x)\right]_{t=a+s} \\ &= D(a)\frac{\partial^2 u}{\partial x^2}(a+s,a,x) - d(a)u(a+s,a,x) \\ &= D(a)\frac{\partial^2 v}{\partial x^2}(s,a,x) - d(a)v(s,a,x). \end{aligned}$$

We re-arrange the above equation with the Neumann boundary conditions as:

$$\frac{\partial v}{\partial a} = D(a)\frac{\partial^2 v}{\partial x^2}(s,a,x) - d(a)v(s,a,x), \tag{4.2.5}$$

$$\frac{\partial}{\partial x}v(s,a,0) = 0, \text{ and } \frac{\partial}{\partial x}v(s,a,\pi) = 0. \tag{4.2.6}$$

To solve the above BVP (Boundary Value Problem), we apply the separation of variables technique. Therefore, we let $v(s,a,x) = A(a)X(x)$ and then substitute it into (4.2.5) to get

$$A'(a)X(x) = D(a)A(a)X''(x) - d(a)A(a)X(x). \tag{4.2.7}$$

The corresponding eigenvalue problem for the BVP in (4.2.5)–(4.2.6) is

$$\frac{d^2X}{dx^2} + \lambda^2 X = 0, \quad 0 < x < \pi, \tag{4.2.8}$$

$$X'(0) = 0, \quad X'(\pi) = 0. \tag{4.2.9}$$

The solutions of (4.2.8) and (4.2.9) are

$$X_n(x) = \cos nx, \quad n = 0, 1, 2, \cdots$$

and their corresponding eigenvalues are

$$\lambda_n = n, \quad n = 0, 1, 2 \cdots .$$

Moreover, the solutions of the differential equation

$$A'(a) + \Big(d(a) + n^2 D(a)\Big) A(a) = 0 \tag{4.2.10}$$

are given by

$$A_n(a) = c_n(s)\beta(a) \exp\Big\{-n^2\alpha(a)\Big\}, \quad n = 0, 1, 2, \cdots , \tag{4.2.11}$$

where

$$\alpha(a) = \int_0^a D(\xi)d\xi, \quad \beta(a) = \exp\Big\{-\int_0^a d(\xi)d\xi\Big\}.$$

Thus, we have

$$v(s, a, x) = \sum_{n=0}^{\infty} c_n(s)\beta(a) \exp\Big\{-n^2\alpha(a)\Big\} \cos nx. \tag{4.2.12}$$

To evaluate the coefficients $c_n(s)$ in the above equation, we use the initial condition $v(s, 0, x) = b(w(s, x))$. Let $a = 0$ in (4.2.12), then we have

$$b(w(s, x)) = v(s, 0, x) = \sum_{n=0}^{\infty} c_n(s) \cos nx.$$

Therefore, it follows

$$c_0 = \frac{1}{\pi}\int_0^{\pi} b(w(s, x))dx,$$

and

$$c_n = \frac{2}{\pi}\int_0^{\pi} b(w(s, x)) \cos nx\, dx, \quad n = 1, 2, 3, \cdots$$

On the other hand,

$$\begin{aligned}
u(t,a,x) &= v(t-a,a,x) \\
&= \beta(a)\sum_{n=0}^{\infty} c_n(t-a)\exp\left\{-n^2\alpha(a)\right\}\cos nx \\
&= \frac{\beta(a)}{\pi}\int_0^{\pi} b(w(t-a,y))\left(1+2\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\cos nx\,\cos ny\right)dy \\
&= \frac{\beta(a)}{\pi}\int_0^{\pi} b(w(t-a,y)) \\
&\times \left\{1+\sum_{n=1}^{\infty}\left[\cos n(x-y)+\cos n(x+y)\right]e^{-n^2\alpha(a)}\right\}dy \\
&= \int_0^{\pi} b(w(t-a,y))\overline{K}_1(a,x,y)dy,
\end{aligned}$$

where

$$\begin{aligned}
\overline{K}_1(a,x,y) &= \frac{\beta(a)}{\pi}\left(1+2\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\cos nx\,\cos ny\right) \\
&= \frac{\beta(a)}{\pi}\left\{1+\sum_{n=1}^{\infty}\left[\cos n(x-y)+\cos n(x+y)\right]e^{-n^2\alpha(a)}\right\}.
\end{aligned}$$

If we substitute this into Equation (4.2.2), we get the following integral equation:

$$w(t,x)=\int_r^{A_l}\int_0^{\pi} b(w(t-a,y))\overline{K}_1(a,x,y)dyda, \quad t\geq A_l. \tag{4.2.13}$$

Now, we consider Equation (4.2.1) subject to the Dirichlet boundary conditions:

$$u(t,a,0)=0, \quad u(t,a,\pi)=0, \quad t\geq 0, \quad a\geq 0. \tag{4.2.14}$$

Similarly, we apply the separation of variables technique to the following boundary value problem,

$$\frac{\partial v}{\partial a}=D(a)\frac{\partial^2 v}{\partial x^2}(s,a,x)-d(a)v(s,a,x), \tag{4.2.15}$$

subject to the boundary conditions

$$v(s,a,0)=0, \quad v(s,a,\pi)=0. \tag{4.2.16}$$

Then, we obtain

$$\begin{aligned}
u(t,a,x) &= v(t-a,a,x) \\
&= \beta(a)\sum_{n=1}^{\infty} c_n(t-a)\exp\left\{-n^2\alpha(a)\right\}\sin nx \\
&= \frac{\beta(a)}{\pi}\int_0^{\pi} b(w(t-a,y))\left(\sum_{n=1}^{\infty}\sin nx\,\sin ny\right)dy \\
&= \frac{2\beta(a)}{\pi}\int_0^{\pi} b(w(t-a,y)) \\
&\times \sum_{n=1}^{\infty}\left[\cos n(x-y)-\cos n(x+y)\right]e^{-n^2\alpha(a)}dy \\
&= \int_0^{\pi} b(w(t-a,y))\overline{K}_2(a,x,y)dy,
\end{aligned}$$

where

$$\begin{aligned}
\overline{K}_2(a,x,y) &= \frac{2\beta(a)}{\pi}\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\sin nx\,\sin ny \\
&= \frac{\beta(a)}{\pi}\sum_{n=1}^{\infty}\left[\cos n(x-y)-\cos n(x+y)\right]e^{-n^2\alpha(a)}.
\end{aligned}$$

If we substitute $\overline{K}_2$ into Equation (4.2.2), we get the following integral equation:

$$w(t,x)=\int_r^{A_t}\int_0^{\pi} b(w(t-a,y))\overline{K}_2(a,x,y)dyda. \tag{4.2.17}$$

4.3 The Existence of a Principal Eigenvalue and Principal Eigenfunction

In this section, we show that the integral equations (4.2.13) and (4.2.17) admit a positive (nonnegative and not identically zero) temporal-spatial steady state solution with a form $e^{\lambda t}W(x)$ when the birth function is linear i.e., $f(w) = pw$. To do this, we assume that $w(t,x) = e^{\lambda t}W(x)$ and we substitute it into Equation (4.2.13) and Equation (4.2.17), we get

$$W(x) = \int_r^{A_l} \int_0^{\pi} e^{-\lambda a} W(y) \overline{K}_1(a,x,y) dy da \tag{4.3.1}$$

and

$$W(x) = \int_r^{A_l} \int_0^{\pi} e^{-\lambda a} W(y) \overline{K}_2(a,x,y) dy da, \tag{4.3.2}$$

respectively. Now, we define

$$K_1(x,y) = \frac{p}{\pi} \left(\Gamma_0(\lambda) + 2 \sum_{n=1}^{\infty} \Gamma_n(\lambda) \cos nx \cos ny \right), \tag{4.3.3}$$

where

$$\Gamma_n(\lambda) = \int_r^{A_l} e^{-\left(\lambda a + \gamma(a) + n^2 \alpha(a)\right)} da, \quad \gamma(a) = \int_0^a d(\xi) d\xi; \quad n = 0, 1, 2, \cdots. \tag{4.3.4}$$

Similarly, we define

$$K_2(x,y) = \frac{2p}{\pi} \sum_{n=1}^{\infty} \Gamma_n(\lambda) \sin nx \sin ny, \tag{4.3.5}$$

where $\Gamma_n(\lambda)$, $n = 1, 2, \cdots$, is given in Equation (4.3.4). Moreover, we interchange the order of the integrals in Equation (4.3.1) and Equation (4.3.2) to get

$$W(x) = T_1(W)(x) = K_1 * W = \int_0^{\pi} W(y) K_1(x, y) dy, \tag{4.3.6}$$

and

$$W(x) = T_2(W)(x) = K_2 * W = \int_0^{\pi} W(y) K_2(x, y) dy, \tag{4.3.7}$$

where $K_1(x, y)$ and $K_2(x, y)$ are given in Equation (4.3.3) and Equation (4.3.5), respectively.

Assumptions and Notations: We assume that the diffusion function $D(a)$ is a continuous, positive, and bounded function on its domain. Let m_D and M_D be its infimum and supremum, respectively. i.e., $m_D = \inf_{A_l \geq a \geq 0} D(a)$ and $M_D = \sup_{A_l \geq a \geq 0} D(a)$. Similarly, we assume the death function $d(a)$ is a continuous and nonnegative bounded function on its domain. Also, we let m_d and M_d be its infimum and supremum, respectively. Moreover, we assume that $\lambda > -m_d$ in the case of Neumann boundary conditions and $\lambda > -(m_d + m_D)$ in the case of Dirichlet boundary conditions.Under these assumptions, we have the following notes:

(1) $\Gamma_n(\lambda)$ satisfies the inequality

$$\frac{e^{-(\lambda + M_d + n^2 M_D)r}}{\lambda + M_d + n^2 M_D} \leq \Gamma_n(\lambda) \leq \frac{e^{-(\lambda + m_d + n^2 m_D)r}}{\lambda + m_d + n^2 m_D}. \tag{4.3.8}$$

(2) By using the right inequality above and the boundedness of the sine and cosine functions, it is easy to see that the series in Equation (4.3.3) and Equation (4.3.5) converge uniformly and absolutely (For the convergence of the Fourier series, one can see Chapter 2 [22]).

Our goal now is to show that the linear operators in Equations (4.3.6) and (4.3.7) are compact and strongly positive operators over appropriate function-spaces, so that we can apply the Krien-Rutman Theorem (see Theorem 2.2.1). The proof of compactness will be given for T_2 while we omit the proof of T_1. First, we introduce the following useful concepts and results:

Definition 4.3.1. *(Degenerate Kernels) The Kernel $K(x,y) = \sum_{j=1}^{m} a_j(x)b_j(y)$ is said to be degenerate. If $a_j(x)$ and $b_j(x)$ belongs to $L_2[a,b]$, and $\{a_j(x)\}_{j=1}^{m}$ is linearly independent. A similar assumption hold for $\{b_j(x)\}_{j=1}^{m}$.*

Theorem 4.3.1. *[63] Consider the $L_2[a,b]$ space, and let K be a degenerate kernel. Then the integral operator*

$$K\phi = \sum_{j=1}^{m} a_j(x) \int_a^b b_j(y)\phi(y)dy.$$

is compact operator if $a_j(x)$ and $b_j(x)$ are in $L_2[a,b]$ for all j.

Therefore, we state and prove the following theorem.

Theorem 4.3.2. *Assume that $\lambda > -m_d$ in the case of Neumman boundary conditions and $\lambda > -(m_d + m_D)$ in the case of Dirichlet boundary conditions. Then the operators in Equation (4.3.6) and Equation (4.3.7) are compact linear operators:*

Proof. The proof will be for T_2 define the following sequence of compact operators:

$$K_m\phi = \frac{2}{\pi}\sum_{j=1}^{m} \Gamma_n(\lambda) \sin nx \int_0^{\pi} \sin ny\, \phi(y)dy.$$

Indeed, it is compact by the above theorem.

Claim: $K_m\phi \to T_2\phi$.

$$
\begin{aligned}
|K_m\phi - T_2\phi| &= \frac{2}{\pi}\left|\int_0^{\pi}\left(\sum_{n=1}^{m}\Gamma_n(\lambda)\sin nx\ \sin ny\phi(y) - \sum_{n=1}^{\infty}\Gamma_n(\lambda)\sin nx\ \sin ny\phi(y)dy\right)\right| \\
&\le \frac{2}{\pi}\int_0^{\pi}\left|\left(\sum_{n=1}^{m}\Gamma_n(\lambda)\sin nx\ \sin ny\phi(y) - \sum_{n=1}^{\infty}\Gamma_n(\lambda)\sin nx\ \sin ny\phi(y)\right)\right|dy \\
&\le \frac{2}{\pi}\left(\int_0^{\pi}\left|\sum_{n=1}^{m}\Gamma_n(\lambda)\sin nx\ \sin ny - \sum_{n=1}^{\infty}\Gamma_n(\lambda)\sin nx\ \sin ny\right|^2 dy\right)^{\frac{1}{2}} \\
&\times \ \|\phi(y)\|_{L_2}.
\end{aligned}
$$

The last inequality comes by Holders' inequality. Moreover, The above integrand is dominated by an integrable function for each m, this is true by using Inequality (4.3.8). Hence, by the dominated convergence theorem, we have

$$|K_m\phi - T_2\phi| \to 0 \quad as \quad m \to \infty.$$

Thus, the set of compact operators $\{K_m\phi\}_{m\in\mathbb{N}}$ converge to T_2. This implies that T_2 is a compact linear operator. Similarly, we can show that T_1 is compact. ∎

Remark 4.3.1. *To prove that T_1 is a strongly positive operator, we consider the space of functions $X = C([0,\pi])$, with its positive cone $K = X_+ = \{\phi(x) \in X \,|\phi(x) \ge 0\}$. The cone K has a nonempty interior, and its interior consists of strictly positive functions over $[0,\pi]$. i.e., $K^o = X_+^o = \{\phi(x) \in X_+ \,|\phi(x) > 0\}$. In the following theorem, we show that T_1 is positive, i.e., $T_1X_+ \subset X_+$. Moreover, we show that T_1 is a strongly positive operator, i.e., $T_1X_+ \setminus \{0\} \subset X_+^o$.*

Theorem 4.3.3. *Assume that $\lambda > -m_d$. Then the linear operator T_1 is a strongly positive operator over the space X_+.*

Proof. The proof will be in two parts. In the first part, we show that T_1 is positive. In the second part, we show that T_1 is a strongly positive operator.

From Equation (4.2.17), we have

$$\begin{aligned} T_1\phi &= \int_r^{A_l}\int_0^{\pi} \frac{p\beta(a)\,e^{-\lambda a}}{\pi}\left[1+2\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\cos nx\,\cos ny\right]\phi(y)\,dy\,da \\ &= \int_r^{A_l} p\beta(a)\,e^{-\lambda a}\left(\frac{1}{\pi}\int_0^{\pi}\left[1+2\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\cos nx\,\cos ny\right]\phi(y)\,dy\right)da. \end{aligned}$$

Since $p\beta(a)\,e^{-\lambda a} > 0$, it is enough to show that

$$V(x,a) = L\phi = \frac{1}{\pi}\int_0^{\pi}\left[1+2\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\cos nx\,\cos ny\right]\phi(y)\,dy \tag{4.3.9}$$

is positive (resp., strongly positive). We notice that the expression (4.3.9) is the explicit solution of the following boundary value problem:

$$\begin{cases} \dfrac{\partial V}{\partial a} = D(a)\dfrac{\partial^2 V}{\partial x^2} \\ \dfrac{\partial V}{\partial x}(0,a) = \dfrac{\partial V}{\partial x}(\pi,a) = 0, & a \in [0,\infty)\,; \\ V(x,0) = \phi(x), & x \in [0,\pi],\ \phi(x) \in X_+. \end{cases}$$

Positivity: Let $\phi(x) \in X_+$ be a nonnegative, we want to show that $V(x,a)$ has no negative values on $\overline{D} = [0,\pi] \times [0,A_l]$ (where $D = (0,\pi) \times (0,A_l)$). The proof is by contradiction. Suppose $V(x,a)$ has a negative value at some points $q = (\overline{x},\overline{a}) \in [0,\pi] \times [0,A_l]$, then $V(x,a)$ has a negative minimum at some points $p = (x_0,a_0) \in [0,\pi] \times [0,A_l]$. It is easy to see that $a_0 \neq 0$ (as well as $\overline{a}$), since this contradicts the assumption $\phi(x) \geq 0$. Moreover, $p \notin (0,\pi) \times (0,A_l]$, since this contradicts the maximum principle in Theorem 2.4.1. Therefore, $p = (x_0,a_0) \in \{0,\pi\} \times (0,A]$.

However, such choice contradicts the boundary conditions. In fact,

$$\frac{dV}{dn}\bigg|_{x=0} = \frac{\partial V}{\partial x}\bigg|_{x=0} = 0 \text{ and } \frac{dV}{dn}\bigg|_{x=\pi} = -\frac{\partial V}{\partial x}\bigg|_{x=\pi} = 0,$$

which contradicts the maximum principle (Theorem 2.4.1). In fact, the normal derivative at such points shall be strictly negative (by Theorem 2.4.1). Therefore, there is no such point $q = (\overline{x}, \overline{a}) \in [0, \pi] \times [0, A_l]$ and $V(q) < 0$. So T_1 maps the cone $K = X_+$ into itself i.e., $T_1 X_+ \subseteq X_+$.

Strong Positivity: In this part, we want to show that $V(x, a)$ is strictly positive provided that the initial data $\phi(x)$ is not identically zero. i.e., $\phi(\overline{x}) \neq 0$ for some $\overline{x} \in [0, \pi]$. Again, the proof is by contradiction. First, we assume that $V(x_0, a_0) = 0$ for some points $p = (x_0, a_0) \in [0, \pi] \times (0, A_l]$. In the above paragraph we showed that $V(x, a)$ cannot have negative values. So, if such a point exists then it would be local minimum. According to the maximum principle this point cannot be in $(0, \pi) \times (0, A_l]$. Moreover, if $p = (x_0, a_0) \in \{0, \pi\} \times (0, A_l]$, then the normal derivative at p should be strictly negative according to Theorem 2.4.1, which contradicts the boundary conditions (the normal derivative at $x = 0$ and $x = \pi$ is zero). Therefore, $V(x, a) > 0$ for each $(x, a) \in [0, \pi] \times (0, A_l]$. Moreover, we notice that $V(x, a)$ cannot be identically zero if $\phi(x)$ is not identically zero due to the Fourier series representation of the solution (not all the coefficients are zeros in the Fourier representation). In addition, it cannot be constant if $\phi(x)$ is not constant due the same reason. Hence, L maps the continuous functions that are not identically zero to a strictly positive function. i.e., T_1 maps $X_+ \setminus \{0\}$ into X_+^0. This implies that T_1 is a strongly positive operator. ∎

As a consequence of the above two theorems we have the following theorem:

Theorem 4.3.4. *Assume that $\lambda > -m_d$. Then the operator $T_1 : C([0, \pi]) \to C([0, \pi])$ has a positive principal eigenvalue $p(\lambda)$ which depends on λ. The eigenvalue is simple* *and the corresponding eigenfunction is strictly positive.*

Proof. The proof is a direct result from Theorem 4.3.2, Theorem 4.3.3, and the second part of Krein-Rutman Theorem. ∎

Next, we prove that T_1 varies continuously in λ. This leads $p(\lambda)$ to vary continuously with λ. In fact, this allows us to find $\lambda_0 > -m_d$ such that its corresponding principal eigenvalue satisfies $p(\lambda_0) = 1$. Moreover, the principal eigenvalue $p(\lambda_0) = 1$ has a positive eigenfunction $\phi(x)$. Therefore, the equation $(T_1\phi)(x) = \phi(x)$ hold. To find such λ_0, we wish to find λ_1 and λ_2 such that $p(\lambda_1) < 1$ and $p(\lambda_2) \geq 1$. Then by the Intermediate Value Theorem we can find λ_0 such that $p(\lambda_0) = 1$.

Theorem 4.3.5. *Assume that $\lambda > -m_d$. Then the operator $T_1(\lambda)$ varies continuously with λ.*

Proof. Recall that

$$T_1\phi = \int_0^\pi K_1(x, y)\phi(y)\, dy,$$

where

$$K_1(x, y) = \frac{p}{\pi}\left(\Gamma_0(\lambda) + 2\sum_{n=1}^{\infty}\Gamma_n(\lambda)\cos nx \cos ny\right).$$

To show that T_1 varies continuously with λ, it suffices to show that

$$F(\lambda) = \frac{1}{\pi}\left(\Gamma_0(\lambda) + 2\sum_{n=1}^{\infty}\Gamma_n(\lambda)\cos nx \cos ny\right)$$

is continuous in λ. First, we show that $\Gamma_n(\lambda)$ is continuous in λ, for each $n = 0, 1, 2, \cdots$.

Re-call that

$$\Gamma_n(\lambda) = \int_r^{A_l} \exp\left\{-\left(\lambda a + \gamma(a) + n^2\alpha(a)\right)\right\} da$$

for any given $\lambda > -m_d$. We can choose $\delta > 0$ such that $\lambda - \delta > -m_d$. Let $\epsilon > 0$, and choose λ and $\overline{\lambda}$ such that $\left|\lambda - \overline{\lambda}\right| < \delta$. Therefore,

$$\begin{aligned}
\left|\Gamma_n(\lambda) - \Gamma_n(\overline{\lambda})\right| &= \\
&= \left|\int_r^{A_l} \exp\left\{-(\lambda a + \gamma(a) + n^2\alpha(a))\right\} - \exp\left\{-(\overline{\lambda} a + \gamma(a) + n^2\alpha(a))\right\} da\right| \\
&\leq \int_r^{A_l} \left|\exp\left\{-(\lambda a + \gamma(a) + n^2\alpha(a))\right\} - \exp\left\{-(\overline{\lambda} a + \gamma(a) + n^2\alpha(a))\right\}\right| da \\
&= \int_r^{A_l} \exp\left\{-(\gamma(a) + n^2\alpha(a))\right\} \left|e^{-\lambda a} - e^{\overline{\lambda} a}\right| da \\
&\leq M_n \int_r^{A_l} \left|e^{-\lambda a} - e^{\overline{\lambda} a}\right| da \qquad (4.3.10)
\end{aligned}$$

for each $n = 0, 1, 2, \cdots$, where $M_n = \exp\left\{-(m_d + n^2 m_D)r\right\}$.

Now, $f(\lambda, a) = \exp\left\{-\lambda a\right\}$ is continuous on the compact set $[\lambda - \delta, \lambda + \delta] \times [r, A_l]$. Thus, it is uniformly continuous. Therefore, for $\epsilon/2M_n(A_l - r)$ there exists a $\delta_0 > 0$ such that $\delta_0 < \delta$ and

$$\left|e^{-\lambda a} - e^{-\overline{\lambda} a}\right| < \frac{\epsilon}{2M_n(A_l - r)}, \quad \text{whenever} \quad \left|\lambda - \overline{\lambda}\right| < \delta_0.$$

Combining this and (4.3.10), we get

$$\left|\Gamma_n(\lambda) - \Gamma_n(\overline{\lambda})\right| < \epsilon, \quad \text{whenever} \quad \left|\lambda - \overline{\lambda}\right| < \delta_0.$$

Since the sum in $F(\lambda)$ converges uniformly in λ, then it is continuous. Also, $\Gamma_0(\lambda)$ is continuous, which implies the continuity of $F(\lambda)$. To finish the proof, we let $\phi(x) \in C_+([0, \pi])$ be such that $\|\phi(x)\| = \sup_{x\in[0,\pi]} \phi(x) = 1$. $F(\lambda)$ is continuous, so for each $\epsilon > 0$, there exists a $\delta > 0$ such that

$$\left|F(\lambda) - F(\overline{\lambda})\right| < \frac{\epsilon}{\pi}, \quad \text{whenever} \quad \left|\lambda - \overline{\lambda}\right| < \delta.$$

Moreover,

$$\begin{aligned}
\left|T_1(\lambda)\phi - T_1(\overline{\lambda})\phi\right| &= \left|\int_0^\pi \left(F(\lambda)\phi(y) - F(\overline{\lambda})\phi(y)\right) dy\right| \\
&\leq \int_0^\pi \left|F(\lambda)\phi(y) - F(\overline{\lambda})\phi(y)\right| dy \\
&\leq \left(\int_0^\pi \left|F(\lambda) - F(\overline{\lambda})\right|^2 dy\right)^{1/2} \left(\int_0^\pi (\phi(y))^2 dy\right)^{1/2} \\
&\leq \pi\frac{\epsilon}{\pi} = \epsilon,
\end{aligned}$$

whenever

$$\left|\lambda - \overline{\lambda}\right| < \delta.$$

Thus,

$$\left\|T_1(\lambda) - T_1(\overline{\lambda})\right\| < \epsilon \quad \text{whenever} \quad \left|\lambda - \overline{\lambda}\right| < \delta.$$

Therefore, $T_1(\lambda)$ is continuous in λ. ∎

Now, we turn to prove that T_2 is a strongly positive operator. To do this we consider the space of continuous real valued functions that vanishes at the boundary and have a continuous first derivative. Indeed, we consider the space $Y = C_0^1([0,\pi])$. We also consider its positive order cone $Y_+ = \{\phi(x) \geq 0 \mid \phi(x) \in Y\}$. In fact, the cone Y_+ has a nonempty interior. The interior of Y_+ (as a notation Y_+^o) contains all the functions that are strongly positive on $(0,\pi)$, vanish at the boundary, and have a strictly negative normal derivative at the boundary (see [62], page 43).

Remark 4.3.2. *We consider the space $Y = C_0^1([0,\pi])$ with the following norm*

$$\|\phi(x)\|_Y = \max_{x\in[0,\pi]} |\phi(x)| + \max_{x\in[0,\pi]} |\phi'(x)| \tag{4.3.11}$$

Theorem 4.3.6. *Assume that $\lambda > -(m_d + m_D)$. Then the operator T_2 in Equation (4.3.7) is a strongly positive operator over the space Y_+.*

Proof. Re-call T_2 as:

$$\begin{aligned} T_2\phi &= \int_r^{A_l}\int_0^{\pi} \frac{p\beta(a)\,e^{-\lambda a}}{\pi}\left[2\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\sin nx\,\sin ny\right]\phi(y)\,dy\,da \\ &= \int_r^{A_l} p\beta(a)\,e^{-\lambda a}\left(\frac{2}{\pi}\int_0^{\pi}\left[\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\sin nx\,\sin ny\right]\phi(y)\,dy\right)da, \end{aligned}$$

since $p\beta(a)\,e^{-\lambda a} > 0$, it suffices to show that

$$L\phi = V(x,a) = \frac{2}{\pi}\int_0^{\pi}\left[\sum_{n=1}^{\infty} e^{-n^2\alpha(a)}\sin nx\,\sin ny\right]\phi(y)\,dy \tag{4.3.12}$$

is strongly positivity. To this end, we consider the space $Y = C_0^1([0,\pi])$ and its positive order cone $K = Y_+$. Moreover, we notice that the expression in Equation (4.3.12) is the explicit solution of the following boundary value problem:

$$\begin{cases} \dfrac{\partial V}{\partial a} = D(a)\dfrac{\partial^2 V}{\partial x^2}; & \\ V(0,a) = V(\pi,a) = 0, & a \in [0,\infty); \\ V(x,0) = \phi(x), & x \in [0,\pi],\ \phi(x) \in X_+. \end{cases} \tag{4.3.13}$$

Positivity: Let $\phi(x) \in Y_+$ be a nonnegative function. We want to show that $V(x,a)$ has no negative values in $\overline{D} = [0,\pi] \times [0,A_l]$ (where $D = (0,\pi) \times (0,A_l)$). The proof is by contradiction. Suppose that $V(x,a)$ has a negative value at some points $q = (\overline{x},\overline{a}) \in [0,\pi] \times [0,A_l]$, then $V(x,a)$ has a negative minimum at some points $p = (x_0,a_0) \in [0,\pi] \times (0,A_l]$. It is easy to see that $a_0 \neq 0$, since this contradicts the initial data. Moreover, $p \notin (0,\pi)\times(0,A_l]$, since otherwise, it contradicts the maximum principle (Theorem 2.4.1). Therefore, $p = (x_0,a_0) \in \{0,\pi\} \times (0,A_l]$. However, This choice contradicts the boundary conditions. In fact, we have $V(0,a) = V(\pi,a) = 0$. Hence, there is no point $q = (\overline{x},\overline{a}) \in [0,\pi] \times (0,\infty)$ such that $V(\,q\,) < 0$. Therefore, T_2 maps $K = Y_+$ into itself, i.e. $T_2 Y_+ \subseteq Y_+$.

Strong Positivity: To prove that T_2 is a strongly positive operator. We want to prove that $V(x,a)$ is strictly positive on $(0,\pi)\times(0,A_l]$, provided that the initial data $\phi(x)$ is not identically zero. i.e., $\phi(\overline{x})\neq 0$ for some $\overline{x}\in[0,\pi]$. Again, the proof is by contradiction. Assume that $V(x_0,a_0)=0$ for some $p=(x_0,a_0)\in(0,\pi)\times(0,A_l]$. In the above paragraph, we showed that $V(x,a)$ cannot have a negative values. So, if such a point exists, then it would be a local minimum. By the maximum principle this point cannot be in $(0,\pi)\times(0,A_l]$. In fact, if $(x_0,a_0)\in(0,\pi)\times(0,A_l]$, then the solution is identically zero on $[0,\pi]\times(0,A_l]$ due to the maximum principle, but this contradicts the initial data and the continuity of the explicit form of the solution. Indeed, the above series representation cannot be zero if $\phi(x)$ is not identically zero. Also, the solution cannot be a constant since the solution $V(x,a)$ is continuous and zero at the boundary. Moreover, the normal derivative of $V(x,a)$ is strictly negative according to the maximum principle. Since $V(x,a)$ is a solution of (4.3.13), then $V_x(x,a)$ is continuous. Therefore, T_2 maps Y_+ into its interor. Hence, T_2 is a strongly positive operator. ∎

Theorem 4.3.7. *Assume that $\lambda\geq-(m_d+m_D)$. Then the operator T_2 has a positive principal eigenvalue $p(\lambda)$; the corresponding eigenfunction is nonnegative and not identically zero.*

Proof. The proof is a direct result from Theorem 4.3.2, Theorem 4.3.6 and the second part of Krein-Rutman Theorem. ∎

Theorem 4.3.8. *Assume that $\lambda\geq-(m_d+m_D)$. Then the operator T_2 varies continuously with λ.*

Proof. The proof is similar to the proof of Theorem 4.3.5. ∎

Discussion and Examples: Following the same argument in [15], we wish to find λ_1 and λ_2 such that $p(\lambda_1)<1$ and $p(\lambda_2)\geq 1$. If we can do that, then by the Intermediate

Value Theorem we can find λ_0 such that $\lambda_1 \leq \lambda_0 \leq \lambda_2$ and $p(\lambda_0) = 1$. This is true since $p(\lambda)$ varies continuously in λ. Using inequality (4.3.8), $\Gamma_n(\lambda) \to 0$ as $\lambda \to \infty$; $\forall n = 0, 1, 2, \cdots$, and so $T_1(\lambda) \to 0$ as $\lambda \to \infty$. Therefore, $\|T_1\| \to 0$ as $\lambda \to \infty$. Hence, $p(\lambda) \to 0$, and so there exists a λ_1 such that $p(\lambda_1) < 1$. To find λ_2 such that $p(\lambda_2) \geq 1$ is not easy in the general case. Therefore, we consider the following examples.

Example 4.3.1. *We consider the death and diffusion rates to be constants, i.e., $d(a) = d$ and $D(a) = D$. Then*

$$\Gamma_n(\lambda) = \frac{\exp\{-(\lambda + d + n^2 D)r\}}{(\lambda + d + n^2 D)}, \quad \forall n = 0, 1, 2, \cdots .$$

It is easy to see that $\Gamma_0(\lambda) \to \infty$ as $\lambda \to -d^+$ (resp. $\Gamma_1(\lambda) \to \infty$ as $\lambda \to -(d+D)^+$). Therefore, the operators $T_1(\lambda)$ ($T_2(\lambda)$) is unbounded. Thus, $p(\lambda) \to \infty$ as $\lambda \to -d^+$ (resp. as $\lambda \to -(d+D)^+$). Therefore, there exists λ_2 such $p(\lambda_2) \geq 1$. Since there exists $p(\lambda_1) < 1$, as a consequence of the above discussion, there exists λ_0 such that $p(\lambda_0) = 1$. Thus the equations $T_1(\phi)(x) = \phi(x)$ ($T_2(\phi)(x) = \phi(x)$) holds. Also, the function $\phi(x)$ is positive (resp. nonnegative and not identically zero).

Example 4.3.2. *Assume that $\lambda > 0$, and re-call that*

$$\gamma(a) = \int_0^a d(s)\, ds.$$

Moreover, let m_γ and M_γ to be its infimum and supremum, respectively. Then

$$\exp\{-M_\gamma\} \leq \exp\{-\gamma(a)\} \leq \exp\{-m_\gamma\}.$$

Therefore, $\Gamma_0(\lambda)$ is bounded below by

$$\exp\{-(\lambda r + M_\gamma)\}/\lambda.$$

Hence, $\Gamma_0(\lambda)$ is unbounded as $\lambda \to 0$. Therefore, there exists λ_2 near 0 such that $p(\lambda_2) \geq 1$. This implies the existence of $\lambda_0 \in (\lambda_1, \lambda_2]$ such $p(\lambda_0) = 1$. Therefore, the equation $T_1\phi(x) = \phi(x)$ holds, where $\phi(x)$ is positive. Similarly, the operator equation $T_2\phi(x) = \phi(x)$ holds, where $\phi(x)$ is nonnegative and not identically zero.

In the previous analysis, we showed the existence of a principal eigenvalue λ_0. To determine λ_0, we have the following theorems.

Theorem 4.3.9. *Equation (4.3.1) admits a principal eigenvalue λ_0 with a corresponding eigenfunction $W(x) = 1$. The eigenvalue λ_0 can be determined by solving the following equation:*

$$p\Gamma_0(\lambda) = 1,$$

where

$$\Gamma_0(\lambda) = \int_r^{A_l} \exp\{-(\lambda a + \gamma(a))\}\, da,$$

and

$$\gamma(a) = \int_0^a d(\xi)d\xi$$

Proof. Let $W(x) = 1, x \in [0, \pi]$, in Equation (4.3.1). By using the fact that the functions $\{\cos nx\}_{n=0}^{\infty}$ are orthogonal, we get the result directly. ∎

Theorem 4.3.10. *Equation (4.3.2) admits a principal eigenvalue λ_0 with a corresponding eigenfunction $W(x) = \sin nx, x \in [0, \pi]$. The eigenvalue λ_0 can be determined by solving the following equation:*

$$p\Gamma_1(\lambda) = 1,$$

where

$$\Gamma_1(\lambda) = \int_r^{A_l} \exp\{-(\lambda a + \gamma(a) + \alpha(a))\}\, da.$$

The functions $\gamma(a)$ *and* $\alpha(a)$ *are given in the following formula:*

$$\gamma(a) = \int_0^a d(\xi)d\xi, \quad \textit{and} \quad \alpha(a) = \int_0^a D(\xi)d\xi,$$

respectively.

Proof. let $W(x) = \sin nx, x \in [0, \pi]$, in Equation (4.3.2). Again, by using the fact that the functions $\{\sin nx\}_{n=1}^{\infty}$ are orthogonal, we get the result directly. ∎

4.4 Existence of Steady State Solution for Nonlinear Case

In this section, we consider Equation (4.2.13) and Equation (4.2.17) with a nonlinear birth function $b(u)$ (eg. $b(w) = pwe^{-sw^q}$, where p, q, and s are positive constants). To show the existence of steady state solution, we assume that $w(t, x)$ is free of the time variable t, i.e., $w(t, x) = w(x)$. Substitute this into Equation (4.2.13) and Equation (4.2.17), to get

$$w(x) = \int_r^{A_l} \int_0^{\pi} b(w(y))\overline{K}_1(a, x, y)dyda,$$

and

$$w(x) = \int_r^{A_l} \int_0^{\pi} b(w(y))\overline{K}_2(a, x, y)dyda.$$

For the special case $b(w(x)) = pw(x)e^{-s(w(x))^q}$, we have we get

$$w(x) = \int_r^{A_l} \int_0^{\pi} pw(y)e^{-s(w(y))^q}\overline{K}_1(a, x, y)dyda,$$

and

$$w(x) = \int_r^{A_l} \int_0^\pi pw(y) e^{-s(w(y))^q} \overline{K}_2(a, x, y) dy da.$$

By integrate the above equations with respect to the variable a, we get

$$w(x) = \int_0^\pi pw(y) e^{-s(w(y))^q} K_1^*(x, y) dy, \tag{4.4.1}$$

and

$$w(x) = \int_0^\pi pw(y) e^{-s(w(y))^q} K_2^*(x, y) dy. \tag{4.4.2}$$

The kernel functions $K_1^*(x, y)$ and $K_2^*(x, y)$ are given by

$$K_1^*(x, y) = \frac{p}{\pi} \left(c_0 + 2 \sum_{n=1}^{\infty} c_n \cos nx \cos ny \right),$$

and

$$K_2^*(x, y) = \frac{2p}{\pi} \sum_{n=1}^{\infty} c_n \sin nx \sin ny,$$

where

$$c_n = \int_r^{A_l} e^{-\left(\gamma(a) + n^2 \alpha(a)\right)} da, \quad \gamma(a) = \int_0^a d(\xi) d\xi, \quad n = 0, 1, 2, \cdots.$$

As a remark, we notice that the constants c_n, $n = 0, 1, 2, \cdots$, satisfy the inequality

$$\frac{e^{-(M_d + n^2 M_D)r}}{M_d + n^2 M_D} \leq c_n \leq \frac{e^{-(m_d + n^2 m_D)r}}{m_d + n^2 m_D}. \tag{4.4.3}$$

Therefore, the above two series converge uniformly and absolutely. Hence, $K_1^*(x, y)$ and $K_2^*(x, y)$ are continuous in the variables x and y.

Remark 4.4.1. *As we showed in Theorem 4.3.3 and Theorem 4.3.6, we can show that the corresponding linear integral operators with the kernel functions $K_1^*(x, y)$ and $K_2^*(x, y)$ are strongly positive. Therefore, $K_1^*(x, y)$ is positive on $[0, \pi] \times [0, \pi]$ and*

$K_2^*(x,y)$ *is positive on* $(0,\pi)\times(0,\pi)$.

We rewrite the nonlinear integral equations (4.4.1) and (4.4.2) in abstract form as the following:

$$w(x) = N_1(w)(x) := \int_0^\pi w(y)e^{-s(w(y))^q}K_1^*(x,y)dy, \tag{4.4.4}$$

and

$$w(x) = N_2(w)(x) := \int_0^\pi w(y)e^{-s(w(y))^q}K_2^*(x,y)dy. \tag{4.4.5}$$

Our aim now, is to show that the above integral equations admit a positive (resp. a nonnegative and non-zero) solution. For this purpose, we consider the following general nonlinear integral equation:

$$u = N(u) := \int_0^\pi K(x,y)f(u(y))dy, \tag{4.4.6}$$

where $K(x,y)$ and $f(u)$ are the kernel functions and the birth function, respectively.

Now, we assume that $f(0)=0$. In this case, $u=0$ is a solution for the nonlinear integral equation (4.4.6). To prove that N has a positive solution we wish to apply Krasnosel'skii's Fixed-point Theorem. The Krasnosel'skii's Fixed-point Theorem is given in the following theorem:

Theorem 4.4.1. *(Krasnosel'skii Fixed-point Theorem) [53, 67] Let* X *be a Banach space, and let* $K\subset X$ *be a cone in* X. *Assume that* Ω_1,Ω_2 *are two open subsets of* X *with* $0\in\Omega_1$, $\overline{\Omega}_1\subset\Omega_2$ *and let* $T: K\cap(\Omega_2\setminus\overline{\Omega}_1)\to K$ *be a completely continuous operator, such that either*

(i) $\|Tu\|\le\|u\|$, $u\in K\cap\partial\Omega_1$, *and* $\|Tu\|\ge\|u\|$, $u\in K\cap\partial\Omega_2$; *or*

(ii) $\|Tu\|\ge\|u\|$, $u\in K\cap\partial\Omega_1$, *and* $\|Tu\|\le\|u\|$, $u\in K\cap\partial\Omega_2$.

Then T has at least one fixed point in $K \cap (\overline{\Omega}_2 \setminus \Omega_1)$.

For a generalization of Krasnosel'skii's Fixed-point Theorem, one can see [71]. To go further in our proofs, we need to impose the kernel function $K(x, y)$ and the birth function $f(u)$ by some assumptions. Hence, we assume the following:

Assumptions:

(K) We assume that $K(x, y)$ satisfies one of the following conditions:

(K1) $K(x, y)$ is a continuous and positive function on $[0, \pi] \times [0, \pi]$, or

(K2) $K(x, y)$ is a continuous and nonnegative function on $[0, \pi] \times [0, \pi]$.

(F) We assume that $f(u)$ satisfies the following condition:

(F1) $f(u)$ is a continuous, nonnegative and bounded function. Moreover, we assume that $f(u)$ is differentiable on $u \in [0, \infty)$, $f(0) = 0$, $f'(0) = 1$, and $\lim_{u \to \infty} f(u)/u = 0$.

Lemma 4.4.1. *Assume that K1 (or K2) and F1 hold. Then the operator in Equation (4.4.6) is positive. i.e., it maps the cone of positive functions $X_+ = \{\phi(x) \in X \,|\phi(x) \geq 0\}$ into itself.*

Proof. First, we show that N maps $C([0, \pi])$ into itself. Let x_n be a sequence in $[0, \pi]$ such that x_n converges to x. Then

$$\begin{aligned} |N\phi(x_n) - N\phi(x)| &= \left| \int_0^\pi K(x_n, y) f(\phi(y)) dy - \int_0^\pi K(x, y) f(\phi(y)) dy \right| \\ &\leq \int_0^\pi |K(x_n, y) f(\phi(y)) - K(x, y) f(\phi(y))| \, dy \\ &\leq \|f\|_\infty \int_0^\pi |K(x_n, y) - K(x, y)| \, dy. \end{aligned}$$

Now,

$$|K(x_n, y) - K(x, y)| \leq |K(x_n, y)| + |K(x, y)| \leq 2M$$

where $M = \max_{x,y\in[0,\pi]} |K(x,y)|$. Using the Dominated Convergence Theorem, we have

$$\begin{aligned}\lim_{n\to\infty} |N\phi(x_n) - N\phi(x)| &\leq \|f\|_\infty \lim_{n\to\infty} \int_0^\pi |K(x_n,y) - K(x,y)|\, dy \\ &= \|f\|_\infty \int_0^\pi \lim_{n\to\infty} |K(x_n,y) - K(x,y)|\, dy \\ &= 0.\end{aligned}$$

The last equality comes by the continuity of $K(x,y)$. The positivity of the operator N comes directly from the assumptions on $K(x,y)$ and $f(u)$ to be nonnegative functions.

∎

Lemma 4.4.2. *Assume that K1 (or K2) and F1 hold. Then the operator* $N : C_+([0,\pi]) \to C_+([0,\pi])$ *is a continuous operator.*

Proof. Let $(\phi_n)_{n\in\mathbb{N}}$ converges uniformly to $\phi(x)$. Then $\phi(x) \in C_+([0,\pi])$. This is true since $C_+([0,\pi])$ is a closed subset of the complete Banach space $C([0,\pi])$. Therefore, $C_+([0,\pi])$ is complete. Next, for each $x \in [0,\pi]$, we have

$$\begin{aligned}|N\phi_n(x) - N\phi(x)| &= \left|\int_0^\pi K(x,y)f(\phi_n(y))dy - \int_0^\pi K(x,y)f(\phi(y))dy\right| \\ &\leq \int_0^\pi |K(x,y)f(\phi(y)) - K(x,y)f(\phi(y))|\, dy \\ &\leq M \int_0^\pi |f(\phi_n(y)) - f(\phi(y))|\, dy \\ &\leq const. \|\phi_n - \phi\|_\infty .\end{aligned}$$

The last inequality comes by applying the Mean Value Theorem on $f(u)$. Therefore,

$$\|N\phi_n - N\phi\| \leq const. \|\phi_n - \phi\| ,$$

which implies the continuity of N. ∎

Remark 4.4.2. *To prove the compactness of the operator* N*, we apply the well-known*

Ascoli-Arzela's Theorem. i.e., we have to show that $T(B)$ is uniformly bounded and equicontinuous in Y, where B is any bounded subset of X. In our case, $X = C([0, \pi]$.

Lemma 4.4.3. *Assume that K1 (or K2) and F1 hold. Then the operator N : $C_+([0, \pi]) \to C_+([0, \pi])$ is compact.*

Proof To prove this result, we apply Ascoli-Arzela's Theorem. So, let $(\phi_n)_{n \in \mathbb{N}}$ be a uniformly bounded sequence in $C_+([0, \pi])$. i.e., there exists $\overline{M}$ such that $\|\phi_n(x)\| \leq \overline{M}$ for each $n \in \mathbb{N}$ and for each $x \in [0, \pi]$. Consider the family $\mathcal{F} = \{N\phi_n \, | n \in \mathbb{N}\}$. To apply Ascoli-Arzela's Theorem, we need to show that $\mathcal{F}$ is uniformly bounded and eqicontinuous. To prove that $\mathcal{F}$ is uniformly bounded is obvious. In fact, it comes from the boundedness of the functions $K(x, y)$ and $f(u)$. Indeed, we have $|N\phi_n| \leq \pi M \|f\|_\infty$. To prove that $\mathcal{F} = \{N\phi_n \, | n \in \mathbb{N}\}$ is equicontinuous, for given $x_1, x_2 \in [0, \pi]$, we estimate

$$\begin{aligned} |N\phi_n(x_2) - N\phi_n(x_1)| &= \left| \int_0^\pi [K(x_2, y) - K(x_1, y)] \, f(\phi_n(y)) dy \right| \\ &\leq \|f\|_\infty \int_0^\pi |K(x_2, y) - K(x_1, y)| \, dy. \end{aligned} \tag{4.4.7}$$

Re-call that $K(x, y)$ is continuous on the compact set $[0, \pi] \times [0, \pi]$. Therefore, $K(x, y)$ is uniformly continuous. Thus, for each $y \in [0, \pi]$ and for each $\epsilon > 0$, there exists $\delta > 0$, such that

$$|K(x_2, y) - K(x_1, y)| < \frac{\epsilon}{\pi \|f\|_\infty}, \quad \text{whenever } \|(x_2, y) - (x_1, y)\| < \delta.$$

Combining this and (4.4.7), we get the result. ∎

Using the above sequance of lemmas, we can prove the following theorem:

Theorem 4.4.2. *Assume that K1 (or K2) and F1 hold. Then the operator N : $C_+([0, \pi]) \to C_+([0, \pi])$ is completely continuous.*

Proof. The proof is a direct result from Lemma 4.4.2 and Lemma 4.4.3. ∎

Remark 4.4.3. *The Kernel function $K(x, y)$ is positive by assumption (K2) on $[0, \pi] \times [0, \pi]$. Therefore, it takes its maximum and minimum in $[0, \pi] \times [0, \pi]$. As a notation, we let $m = \min_{x,y \in [0,\pi]} K(x, y) > 0$ and $M = \max_{x,y \in [0,\pi]} K(x, y)$.*

Theorem 4.4.3. *Assume that $K1$ and $F1$ hold. Moreover, assume $\frac{m^2}{M} \geq 1$. Then there exist two distinct positive real numbers r and R and a positive solution $u(x)$ of Equation (4.4.6). Furthermore, this solution satisfies the inequality $r \leq \|u\| \leq R$.*

Proof. To prove this theorem, we apply Krasnosel'skii's Fixed-point Theorem. We have showed in Theorem 4.4.2 that N is a completely continuous operator from $C_+[0, \pi]$ into itself. To complete the proof we need to check the validity of one of the conditions in Theorem 4.4.1. In fact, we cannot apply Krasnosel'skii's Fixed-point Theorem on the cone $K = C_+([0, \pi])$. Therefore, we define a smaller cone (see [9]):

$$K_0 = \left\{ u(x) \in K \,\middle|\, \min_{x \in [0,\pi]} u(x) \geq \frac{m}{\pi M} \|u\| \right\}.$$

Claim: The operator N maps the cone K_0 into itself. In fact, we have

$$\begin{aligned}
Nu(x) &\geq m \int_0^\pi f(u(y))dy \\
&\geq \frac{m}{M} \int_0^\pi f(u(y)) \max_{x \in [0,\pi]} K(x, y)dy \\
&\geq \frac{m}{M} \max_{x \in [0,\pi]} \int_0^\pi f(u(y))K(x, y)dy \\
&\geq \frac{m}{M\pi} \max_{x \in [0,\pi]} \int_0^\pi f(u(y))K(x, y)dy \\
&= \frac{m}{M\pi} \|Nu\|.
\end{aligned}$$

Hence,

$$\min_{x \in [0,\pi]} Nu(x) \geq \frac{m}{M\pi} \|Nu\|.$$

Therefore, the operator N maps K_0 into itself. Since $\lim_{u\to\infty} \frac{f(u)}{u} = 0$, then there exists a sufficiently large positive real number R such that

$$f(u) \le \frac{1}{M\pi}u, \quad \forall u \in [R, \infty).$$

Let

$$\Omega_2 = \{u(x) \in K_0 \mid \|u\| < R\}.$$

Then $\forall u \in \partial\Omega_2$, $\|u\| = R$, we have

$$\begin{aligned} Nu(x) &\le M\int_0^\pi f(u(y))dy \\ &\le M\frac{1}{M\pi}\int_0^\pi u(y)dy \\ &\le \|u\|. \end{aligned}$$

Therefore, $\|Nu\| \le \|u\|$.

According to the assumptions, we have $\lim_{u\to+0} \frac{f(u)}{u} = 1$, and $\frac{M}{m^2} < 1$. Therefore, there exists a sufficiently small positive real number r such that $f(u) \ge \frac{M}{m^2}u$; $\forall u \in [0, r]$. Let

$$\Omega_1 = \{u(x) \in K_0 \mid \|u\| < r\}.$$

Then $\forall u \in \partial\Omega_1$, $\|u\| = r$, we have

$$\begin{aligned} Nu(x) &\ge m\int_0^\pi f(u(y))dy \\ &\ge \frac{M}{m}\int_0^\pi u(y)dy \\ &\ge \frac{M}{m} \times \frac{m}{M\pi}\|u\|\int_0^\pi dy \\ &= \|u\|. \end{aligned}$$

Therefore, $\|Nu\| \geq \|u\|$. Thus, by Krasnosel'skii's Fixed-point Theorem, N has a positive solution $u(x)$. This solution satisfies $r \leq \|u\| \leq R$. ∎

Corollary 4.4.1. *Assume that $m^2/M \geq 1$. Then the integral equation in (4.4.4) has a positive solution.*

Proof. The proof is a direct result from Theorem 4.4.3 and Remark 4.4.1. ∎

In the case that $K(x, y)$ is nonnegative, then $m = 0$ is the minimum value of $K(x, y)$, and hence, the above result is not applicable anymore. Therefore, we make the following modification remark to show the existence of a nonnegative and not identically zero solution.

Remark 4.4.4. *Assume that $K(x, y)$ is symmetric and positive on $(0, \pi) \times (0, \pi)$. Then $K(x, y)$ takes its maximum on $(0, \pi) \times (0, \pi)$. Moreover, we assume that $K(x, y)$ takes its maximum at a point of the form (x_0, x_0). Then there exists a closed neighborhood at (x_0, x_0), say $G := [x_0 - \delta, x_0 + \delta] \times [x_0 - \delta, x_0 + \delta]$ such that*

$$K(x, y) \geq \frac{m}{M} K(w, y); \; \forall x \in G = [x_0 - \delta, x_0 + \delta], \; \forall y, w \in [0, \pi],$$

where $m = \min_{x,y \in G} K(x, y)$ (see [53]).

Consider the space

$$C_0 = \{\phi(x) \in C([0, \pi]) \mid \phi(0) = \phi(\pi) = 0\},$$

and its positive cone

$$K = C_0^+([0, \pi]) = \{\phi(x) \in C_0 \mid \phi(x) \geq 0\}.$$

Define the cone

$$K_0 = \left\{ \phi(x) \in K \,\middle|\, \min_{x \in G} \phi(x) \geq \frac{m}{M} \|\phi\| \right\},$$

and assume that $2\delta \frac{m^2}{M} \geq 1$. Then we can prove the following theorem.

Theorem 4.4.4. *Assume that $K2$ and $F1$ hold. Moreover, assume that $K(x, y)$ satisfies the conditions in Remark 4.4.4 and $\frac{2\delta m^2}{M} \geq 1$. Then there exist two distinct positive real numbers r and R such that the integral equation in (4.4.6) has a nonnegative non-zero solution $u(x)$. This solution satisfies the inequality $r \leq \|u\| \leq R$.*

Proof. First, we show that N maps the cone K_0 into itself. In fact,

$$\begin{aligned} \phi(x) = Nu(x) &= \int_0^\pi K(x, y) f(u(y)) dy \\ &\geq \frac{m}{M} \int_0^\pi K(z, y) f(u(y)) dy \\ &= \frac{m}{M} Nu(z), \quad \forall x \in G,\ \forall z \in [0, \pi]. \end{aligned}$$

Therefore,

$$\min_{x \in G} \phi(x) = \min_{x \in G} Nu(x) \geq \frac{m}{M} \|Nu\|.$$

Hence, N maps K_0 into itself.

According to the assumptions, $\lim_{u \to \infty} f(u)/u = 0$. Therefore, there exists a sufficiently large real number R such that $f(u) \leq \frac{1}{\pi M} u, \ \ \forall u \in [R, \infty]$.

Let

$$\Omega_2 = \{u(x) \in K_0 \mid \|u\| < R\}.$$

Then $\forall u \in \partial\Omega_2$, $\|u\| = R$, we have

$$\begin{aligned} Nu(x) &\leq M\int_0^\pi f(u(y))dy \\ &\leq M\frac{1}{M\pi}\int_0^\pi u(y)dy \\ &\leq \|u\| = R. \end{aligned}$$

Hence, $\|Nu\| \leq \|u\|$. Also, by the assumptions, we have $\lim_{u\to+0}\dfrac{f(u)}{u} = 1$ and $\frac{2\delta m^2}{M} \geq 1$. Therefore, there exists a sufficiently small positive real number r such that $f(u) \geq \frac{M}{2\delta m^2}u$, $\forall u \in [0, r]$. Let

$$\Omega_1 = \{u(x) \in K_0 \mid \|u\| < r\}.$$

Then for all $u \in \partial\Omega_1$, $\|u\| = r$, we have

$$\begin{aligned} Nu(x) &= \int_0^\pi K(x,y)f(u(y))dy \\ &\geq \int_G K(x,y)f(u(y))dy \\ &\geq m\int_G f(u(y))dy \\ &\geq \frac{mM}{2\delta m^2}\int_G u(y)dy \\ &= \frac{M}{2\delta m}\int_G u(y)dy \\ &\geq \frac{M}{2\delta m}\times\frac{m}{M}\|u\|\int_G dy \\ &= \|u\|. \end{aligned}$$

Hence, $\|Nu\| \geq \|u\|$. Therefore, by Krasonel'skii's Fixed-point Theorem there exists a positive solution $u(x) \in K_0$. This solution satisfies $r \leq \|u\| \leq R$. ∎

Corollary 4.4.2. *The integral operator in Equation (4.4.5) has a nonnegative non-zero solution solution provided that $2\delta m^2/M \geq 1$, where δ is described in Remark 4.4.4.*

proof The proof is a direct result from Theorem 4.4.4 and Remark 4.4.1. In fact, the kernel $K_2^*(x, y)$ is symmetric and takes its maximum at $(\frac{\pi}{2}, \frac{\pi}{2})$. ∎

Now, we re-consider the integral equation (4.4.6), and we assume $f(0) \neq 0$. In this case, $u = 0$ is not a solution for this integral equation. Therefore, we can apply Schaefer's Fixed-point Theorem (see Theorem 4.4.5) to prove the existence of a nonnegative solution for this integral equation. To do this, we impose the kernel function $K(x, y)$ and the birth function $f(u)$ by the following assumptions:

(K1) The kernel $K(x, y)$ is continuous and positive on $[0, \pi] \times [0, \pi]$, or

(K1') The kernel $K(x, y)$ is continuous and nonnegative on $[0, \pi] \times [0, \pi]$.

(F1) Assume that $f(0) \neq 0$, $f(u)$ is continuous, nonnegative, and bounded function. Moreover, we assume that $f(u)$ is differentiable function on $u \in [0, \infty)$.

The Schaefer's Fixed-Point Theorem is given in the following theorem:

Theorem 4.4.5. *(Schaefer's Fixed-Point Theorem)[111] Let X be a Banach space and let $T : X \to X$ be a completely continuous operator. Then one of the following hold:*

(i) The equation $x = \lambda Tx$ has a solution for $\lambda = 1$, or

(ii) The set $\mathfrak{S} = \{x \in X \,| x = \lambda Tx, \lambda \in (0, 1)\}$ is unbounded.

Theorem 4.4.6. *Assume that K1 (or K1') and F1 hold. Then the integral equation in (4.4.6) has a positive (nonnegative and not identically zero).*

Proof. To prove this result, we apply Schaefer's Fixed-point Theorem. We showed in Lemma 4.4.1 that N maps $C_+([0, \pi])$ into itself. Moreover, N is a completely continuous operator by Theorem 4.4.2. To complete the proof, we need to show that

$$\mathfrak{S} = \{\phi(x) \in C_+([0, \pi]) \,|\phi(x) = \lambda(T\phi)(x), \lambda \in (0, 1)\}$$

is bounded. Let $\phi(x) \in \mathfrak{S}$ and let $\lambda \in (0, 1)$. Then for each $x \in [0, \pi]$, we have

$$\begin{aligned} |\phi(x)| &= |\lambda(N\phi)(x)| \\ &\leq |(N\phi)(x)| \\ &\leq \int_0^\pi |K(x, y)f(\phi(y))|\,dy \\ &\leq \pi M \|f\|_\infty . \end{aligned}$$

Therefore, the first condition of Theorem 4.4.5 holds. So, N has a fixed point in $C_+([0, \pi])$. i.e., it has a positive (nonnegative and not identically zero) solution. ∎

In the next section, by using the infinite dynamical systems approach, we will extended the existence results of a nonnegative and not identically zero steady state solution of the previous nonlinear integral operators, as well as its stability.

4.5 Stability

In this section, we investigate the long time behavior of the solution. Following the same argument in [139], we will prove that the positive steady state solution exists and is stable, provided that the principal eigenvalue λ_0 of the corresponding linear integral equation is positive. In fact, we will consider the nonlinear integral operator that correspond to the Dirichlet boundary conditions. i.e., the nonlinear integral equation (4.4.5). Similarly, we can prove the same result for the nonlinear integral equation that corresponds to the Neumann boundary conditions. i.e., the nonlinear integral equation (4.4.4).

Let $X = C_0^1([0, \pi])$ be the space of continuous functions that vanishes at the boundary and have a continuous first derivative with the norm defined as in (4.3.11).

Also, we let

$$X_+ = \{\phi(x) \in X \mid \phi(x) \geq 0\}$$

be its positive cone. X_+ has a nonempty interior and so we can define a strongly positive relation on this space (see section (3)). Let $Y = C([t_0 - A_l, t_0], X)$, where $t_0 \geq A_l$ is fixed (Technically, we may assume $t_0 = 0$). Let Y_+ be its positive cone. i.e., $Y_+ = C([t_0 - A_l, t_0], X_+)$. For convenience, we identify each $\phi \in Y_+$ as a function from $[t_0 - A_l, t_0] \times [0, \pi]$ to $\mathbb{R}$ as follows: $\phi(s, x) = \phi(s)(x)$. In the following analysis we consider the Nichelson's blowflies function. i.e., $f(w) = pwe^{-sw}, p > 0, s > 0$. Using the method of steps (see [134]) we can show that the solution $w(t, x, \phi)$ of

$$\begin{cases} w(t,x) = \displaystyle\int_r^{A_l}\int_0^{\pi} f(w(t-a,y))\overline{K_2}(a,x,y)dyda \\ w(t,0) = w(t,\pi) = 0 \quad , & t \geq t_0 \\ w(s,x) = \phi(s,x) \geq 0 \quad , & t_0 - A_l \leq s \leq t_0, \;\; x \in [0,\pi] \end{cases}$$

globally exists for any $\phi \in Y_+$. Moreover, this solution is unique since $f(w)$ is a Lipschitz function. So, we can define the semiflow $\Phi(t) = w(t, x, \phi) : Y_+ \to Y_+$. Moreover, the birth function $f(w)$ and the kernel function $\overline{K}_2(a, x, y)$ are continuous and bounded for $\forall t \geq t_0$. Hence the semiflow $\Phi(t) : Y_+ \to Y_+$ is compact for $\forall t \geq t_0$.

To prove the main result in this section, we introduce a sequence of concepts and lemmas. We start with the following lemma:

Lemma 4.5.1. *For any $\phi \in Y_+$ the semiflow solution $w(t, x, \phi)$ is uniformly bounded. Furthermore, the semiflow $\Phi(t) : Y_+ \to Y_+$ admits a connected global attractor on Y_+.*

Proof. The proof is a direct result from the boundedness of the birth function and the kernel function. Indeed, we have

$$\left\| \int_r^{A_l}\int_0^{\pi} f(w(t-a,x))\overline{K_2}(a,x,y)dyda \right\| \leq \|f\|_\infty M\pi(A_l - r) = \overline{M}.$$

Therefore, $\limsup_{t\to\infty} w(t,x,\phi) \le \overline{M}$, $\forall\phi \in Y_+$, $\forall t > t_0 - A_l$. Hence, the semiflow $\Phi(t): Y_+ \to Y_+$ is point dissipative. Therefore, the semiflow $\Phi(t): Y_+ \to Y_+$ admits a connected global attractor on Y_+, which attracts every bounded set in Y_+ (by Theorem 2.3.1). ∎

Re-consider the linear eigenvalue problem

$$\begin{aligned} w(x) &= \int_r^{A_l}\int_0^{\pi} pe^{-\lambda a} w(y)\overline{K_2}(a,x,y)dyda \\ &= \int_0^{\pi} w(y)K_2(\lambda,x,y)dy \end{aligned} \tag{4.5.1}$$

with its corresponding principal eigenvalue λ_0. Then, we have the following remark:

Remark 4.5.1. *Since the birth function $f(w)$ satisfies $f(w) = pwe^{-sw} \le pw$. Then the nonlinear integral equation*

$$w(t,x) = \int_r^{A_l}\int_0^{\pi} f(w(t-a,y))\overline{K_2}(a,x,y)dyda$$

is dominated by the linear integral equation. Therefore, If λ_0 is negative, then $\lim_{t\to 0}\|w(t,\phi)\| = 0$.

Lemma 4.5.2. *Let $Y_0 = \{\phi \in Y_+ \mid \phi \not\equiv 0\}$ and assume $\lambda_0 > 0$. Then the semiflow is uniformly persistent. i.e., there exists $\delta_1 > 0$ such that*

$$\liminf_{t\to\infty} dist(\Phi(t)\phi, \partial Y_0) \ge \delta_1,\ \forall\phi \in Y_0.$$

Proof. According to Theorem 4.6 in [121], it suffices to show that zero is a uniform weak repeller for Y_0. i.e., there exists a $\delta_0 > 0$ such that

$$\liminf_{t\to\infty} \|\Phi(t)\phi\| \ge \delta_0, \qquad \forall\phi \in Y_0.$$

To prove this we follow the same argument in the proof of Theorem (3.1) [139]. The proof is by contradiction. Let us consider the eigenvalue problem (4.5.1). Since this equation admits a positive eigenvalue λ_0 (see section (3)), then there exists a sufficiently small number $\epsilon > 0$, such that the following eigenvalue problem

$$w(x) = (1-\epsilon)\int_0^{\pi} w(y)K_2(\lambda, x, y)dy$$

admits a positive eigenvalue λ_ϵ with a corresponding eigenfunction $\phi_\epsilon(x)$. Moreover, $f'(0) = p$. Therefore, there exists δ_ϵ such that

$$f(w) > p(1-\epsilon)w, \quad \forall w \in (0, \delta_\epsilon).$$

Let $\delta_0 = \delta_\epsilon$. Assume there exists $\phi_0 \in Y_0$ such that

$$\limsup_{t\to\infty} \|\Phi(t)\phi_0\| < \delta_0.$$

Then there exists a $t' > t_0$ such that

$$\|w(t, ., \phi_0)\| < \delta_0, \quad \forall t \geq t' - t_0. \tag{4.5.2}$$

Therefore, $w(t, x, \phi_0) \in (0, \delta_\epsilon)$ and so $w(t, x)$ satisfies

$$f(w(t, x)) > p(1-\epsilon)w(t, x), \ t \geq t', x \in [0, \pi].$$

Since $w(t, x, \phi_0) > 0$, $\forall t > t_0, \forall x \in (0, \pi)$, then there exists $\eta > 0$ such that $w(t' + s, x, \phi_0) \geq \eta w_\epsilon(s, x), s \in [t_0 - A_l, t_0]$ and $x \in [0, \pi]$, where $w_\epsilon(t, x)$ is the solution of the following linear problem:

$$\begin{cases} w(t,x) = (1-\epsilon)\int_0^{A_l}\int_0^{\pi} w(t-a,y)\overline{K}_2(a,x,y)\,dy\,da, & \\ \phi_0(t,0) = \phi_0(t,\pi) = 0, & t > t', \\ w(s,x) = \phi_0(s,x), & s \in [t_0 - A_l, t_0],\ x \in [0,\pi]. \end{cases}$$

Using the Inequality (4.5.2) and the comparison principle (see Lemma 3.2 [120]), we have

$$w(t,x,\phi_0) \geq \eta w_\epsilon(t-t') = \eta e^{\lambda_\epsilon(t-t')w(x)},$$

which is unbounded when $t \to \infty$. This is a contradiction. ∎

Theorem 4.5.1. *Assume that $\lambda_0 > 0$, then*

$$\begin{cases} w(t,x) = \int_r^{A_l}\int_0^{\pi} f(w(t-a,y))\overline{K_2}(a,x,y)\,dy\,da & \\ w(t,0) = w(t,\pi) = 0 \quad , & t \geq t_0 \geq A_l \\ w(s,x) = \phi(s,x) \quad , & x \in (0,\pi), s \in [t_0 - A_l, t_0]. \end{cases}$$

admit at least one positive steady state $\phi_s(x)$.

Proof. Consider the following problem

$$\begin{cases} w(t,x) = \int_r^{A_l}\int_0^{\pi} f(w(t-a,y))\overline{K_2}(a,x,y)\,dy\,da & \\ w(t,0) = w(t,\pi) = 0 \quad , & t \geq t_0 \geq A_l \\ w(t_0,x) = \phi(x) \quad , & x \in [0,\pi]. \end{cases} \tag{4.5.3}$$

Let $\Phi_0(t) : X_+ \to X_+$ be its corresponding semiflow. Then $\Phi_0(t)$ is compact, point dissipative, and uniformly persistent. Therefore, by Theorem 2.3.3, $\Phi_0(t)$ has an equilibrium solution $\phi_s(x) \in X_+ \setminus \{0\}$ and satisfies $\Phi_0(\phi_s(x)) = \phi_s(x)$. ∎

Remark 4.5.2. *Using the maximum principle, we showed in Theorem 4.3.6 that we* *can generate a strongly positive relation on the space* $X = C_0^1([0, \pi])$. *Therefore, the semiflow* $\Phi(t) : Z \to Z$ $(Z = \left\{\phi(x) \in Y_+ \middle| \|\phi\|_\infty \leq \frac{1}{a}\right\})$ *is strongly positive* $\forall t > A_l$. *Moreover,* $f(w)$ *is increasing in* w, *for each* $w \in [0, \frac{1}{a}]$. *Hence, the semiflow* $\Phi(t) : Y_+ \to Y_+$ *is strongly monotone.*

Remark 4.5.3. *The function* $f(w)$ *is a strict sublinear function. i.e.,* $f(\alpha w) \leq \alpha f(w)$, $\forall \alpha \in (0, 1)$. *Therefore,* $\Phi_0(t) : X_+ \to X_+$ *is strictly sublinear. Since* $\Phi_0(t) : X_+ \to X_+$ *is strongly monotone. Then the steady state solution* $\phi_s(.)$ *is unique (see Lemma 1 [143]).*

Remark 4.5.4. *Since* $\Phi(t) : Y_+ \to Y_+$ *is compact, point dissipative, and uniformly persistence with respect to* Y_0. *Then, by Theorem 1.3.9 [144], there exists* $e^* \in int(Y_+)$ *and* $\delta > 0$, *such that* $\forall \phi \in Y_+$, $w(t, x, \phi) \geq \delta e(x)$, $\forall t \geq t(\phi)$, $x \in [0, \pi]$ *for some* $t(\phi)$.

Theorem 4.5.2. *Assume that* $\lambda_0 > 0$. *Then the unique positive steady state solution* $\phi_s(x)$ *satisfies* $lim_{t\to\infty} \|w(t, ., \phi) - \phi_s(.)\|_Y = 0$ *for any non-zero* $\phi \in Y_+$.

Proof. The steady state solution $\phi_s(x)$ is unique by Remark 4.5.3. Moreover, $\Phi(t) : Y_+ \to Y_+$ is compact for $t > t_0$, uniformly persistent and point dissipative. Moreover, $\Phi(t)$ admits a connected global attractor, say A_0. As a consequence of the proof of Theorem 3.2 [139], the global attractor A_0 contains only the unique equilibrium point $\phi_s(x)$. Therefore, by Hirsch attractive theorem (see Theorem 2.3.5), every solution converges to the unique equilibrium point. Moreover, every omega limit $\omega(\phi)$ is an equilibrium point for all $\phi \in Y_+$ and $\phi(t_0, .) \not\equiv 0$. Hence, $\omega(\phi) = \phi_s$. ∎

4.6 Numerical Simulation

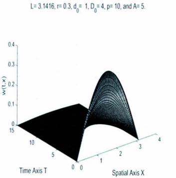
In this section, we present a numerical simulation to investigate the long time behavior of the solution $w(t, x)$. In this simulation, we consider the Nichelson's blow-flies birth function $f(u) = pue^{-u}$. We present this simulation for the Dirichlet boundary conditions case, and Neumann's boundary conditions case. This simulation shows that the solution $w(t, x)$ either converges to the zero solution or to a nonnegative and not identically zero solution in the case of Dirichlet boundary conditions case. Also, it shows that the solution $w(t, x)$ either converges to the zero solution or to a positive homogeneous solution in the case of Neummann boundary conditions.

For the numerical scheme, we apply the composite Simpson's rule to evaluate the integral in Equation (4.2.2). To evaluate the solution $u(t, a, x)$ at the mesh points $a_i, i = 1, 2, \cdots, N$, we solve the reaction diffusion equations (4.2.5) using the method of lines. Here, we also distinguish two cases: the constant case (death and diffusion rates are constants), and the age dependent case. In each case we consider the Dirichlet boundary conditions and the Neumann boundary conditions.

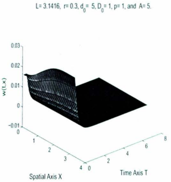
Case 1 (The constant case). We consider the diffusion and death rates to be constants. The numerical simulation for this case takes place in Figure (4.1). This simulation shows that the solution converges to the zero solution or to a nonnegative and nonzero solution (resp. positive solution).

Case 2 (The age dependence case). In this case, we consider $D(a) = D + e^{-a^2}$ and $d(a) = d + e^{-a^2}$. The simulation for this consideration takes place in Figure (4.2). Also, we consider the diffusion and death rates to be linear function (i.e., $D(a) = Da$ and $d(a) = da$). Hence, $\alpha(a) = e^{-Da^2}$ and $\beta(a) = e^{-da^2}$. The simulation for this case takes place in Figure (4.3).

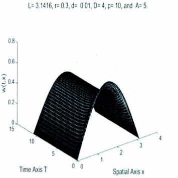
Remark 4.6.1. *In the case of age dependence, we considered the death rate $d(a) = d\,a$, since it represents a rough attempt to estimate the human population death rate. Indeed, the original formula is given by $d(a) = \frac{100}{A_l}\left(\frac{a}{A_l}\right)$, where A_l is the life limit (see [64]).*



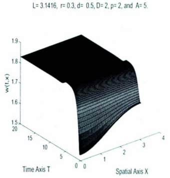
(a) Dirichlet boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 5$, $p = 1$, $D = 1$, and $d = 5$. The initial condition is $\phi(s, x) = \sin x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to the zero solution for large time t.



(b) Neumann boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 3$, $p = 0.5$, $D = 1$, and $d = 1$. The initial condition is $\phi(s, x) = 1 - \cos x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to the zero solution for large time t.

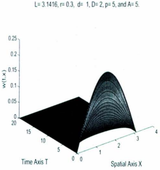


(c) Dirichlet boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 5$, $p = 10$, $D = 4$, and $d = 0.01$. The initial condition is $\phi(s, x) = \sin x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to a nonnegative and not identically zero solution for large time t.

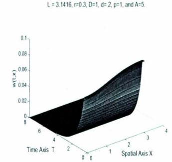


(d) Neumann boundary conditions case.The values of the parameters are $L = \pi$, $r = 0.3$, $A = 5$, $p = 2$, $D = 2$, and $d = 0.5$. The initial condition is $\phi(s, x) = 1 - \cos x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to a positive solution for large time t.

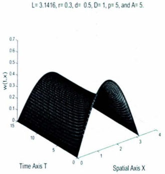
Figure 4.1: The behavior of the mature population $w(t, x)$ for large time t.



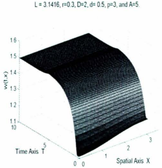
(a) Dirichlet boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 3$, $p = 5$, $D = 1$, and $d = 1$. The initial condition is $\phi(s, x) = \sin x$, $0 \le x \le \pi$; $0 \le s \le 0.3$. In this case, the solution $w(t, x)$ converges to the zero solution for large time t.



(b) Neumann boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 3$, $p = 1$, $D = 1$, and $d = 2$. The initial condition is $\phi(s, x) = 1 - \cos x$, $0 \le x \le \pi$; $0 \le s \le 0.3$. In this case, the solution $w(t, x)$ converges to the zero solution for large time t.

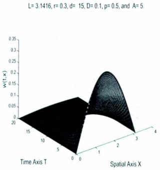


(c) Dirichlet boundary conditions. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 5$, $p = 5$, $D = 1$, and $d = 0.005$. The initial condition is $\phi(s, x) = \sin x$, $0 \le x \le \pi$; $0 \le s \le 0.3$. In this case, the solution $w(t, x)$ converges to a nonnegative and not identically zero solution for large time t.

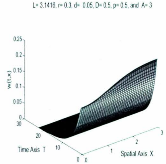


(d) Neumann boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 5$, $p = 3$, $D = 2$, and $d = 0.5$. The initial condition is $\phi(s, x) = 1 - \cos x$, $0 \le x \le \pi$; $0 \le s \le 0.3$. In this case, the solution $w(t, x)$ converges to a positive solution for large time t.

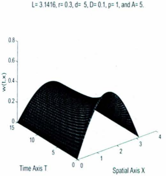
Figure 4.2: The behavior of the mature population $w(t, x)$ for large time t.



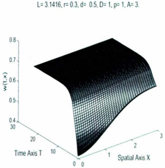
(a) Dirichlet boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 3$, $p = 5$, $D = 2$, and $d = 1$. The initial condition is $\phi(s, x) = \sin x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to the zero solution for large time t.



(b) Neumann boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 3$, $p = 1$, $D = 1$, and $d = 2$. The initial condition is $\phi(s, x) = 1 - \cos x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to the zero solution for large time t.



(c) Dirichlet boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 5$, $p = 1$, $D = 0.1$, and $d = 5$. The initial condition is $\phi(s, x) = \sin x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to a nonnegative and not identically zero solution for large time t.



(d) Neumann boundary conditions case. The values of the parameters are $L = \pi$, $r = 0.3$, $A = 5$, $p = 1$, $D = 1$, and $d = 0.5$. The initial condition is $\phi(s, x) = 1 - \cos x$, $0 \leq x \leq \pi$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to a positive solution for large time t.

Figure 4.3: The behavior of the mature population $w(t, x)$ for large time t.

Chapter 5

Age-size Structure Model of Cell Cycle and its Applications to the Human Tumor and Periodic Hematological Diseases

5.1 Introduction

Throughout the years, many mathematical models (and their numerical simulations) were derived to investigate the dynamics of periodic hematological diseases, due to the fact that they exhibit interesting dynamic behaviors. The most familiar hematological diseases are periodic auto-immune hemolytic anemia (AIHA), cyclical thrombocytopenia (CT), cyclical neutropenia (CN), and periodic chromic myelogenous leukemia (PCML). The auto-immune hemolytic anemia (AIHA) results from an abnormality in the production of auto-antibodies, which in turn attack and destroy the red blood cells (RBC). AIHA is characterized by the oscillations in the erythrocyte count, with an oscillation period of 16-17 days (see [16, 40, 85, 105]). Cyclical thrombocytopenia (CT) results from the reduction in the number of platelets in the blood. CT is characterized by oscillations in platelets number, usually ranging from 1×10^9 platelets/L to $150 - 450 \times 10^9$ platelets/L (the normal values). The oscillation period for CT is within 20-40 day [26, 40, 117]. Comparatively, cyclical neutropenia (CN) results from the reduction in the number of neutrophils present in the blood, usually ranging from the normal values 2×10^9 cells/L to less than 0.5×10^9 cells/L. The oscillation period for CN is about 3 weeks (see [40, 59, 60, 61, 86]). One of the most interesting dynamics of hematological diseases is seen in the dynamics of leukemia, which is the cancer of the blood or bone marrow. Leukemia is characterized by an abnormality in the proliferation of blood cells. Particularly of interest is periodic chronic myelogenous leukemia (PCML), which is characterized by periodical oscillations in circulating cell numbers that occur in leukocytes. Usually, the oscillations in the number of leukocytes ranges between 30×10^9 cells/L and 200×10^9 cells/L with an oscillation period of 40-80 days (see [40, 41]). A remarkable characteristic seen in these hematological diseases is that they are characterized by oscillations in the number of one or more circulating blood cells, with periods that can last from days to months (see [40, 59]).

In an attempt to provide better understanding of the dynamics of hematological diseases and the mechanism of human tumor growth in general, it is important to study the dynamics of the human cell division cycle. Basically, the cell division cycle is divided into two main phase: the resting phase ($G_0 -$ Phase) and the proliferation phase ($P -$ Phase). The Proliferation phase is divided into further four phases: the first growth phase ($G_1 -$ Phase), the synthesis phase ($S -$ Phase), the second growth phase ($G_2 -$ Phase), and the mitosis phase ($M -$ Phase)[5]. The real change of the cell size occurred in the proliferation phase ($P -$ Phase), which is due to the DNA duplication in the synthesis phase (see Figure 5.1).

Since a good mathematical understanding and modeling of tumors plays a major rule in clinical data analysis and manipulating relevant treatment protocols, many previous and current formulated mathematical models have investigated the cell division cycle, [4, 5, 11, 12, 13, 14, 23, 25, 29, 43, 58, 73, 86, 87, 90, 106, 107]. One of the earliest mathematical models derived to investigate the cell division cycle was developed by Bell and Anderson [17]. This model is given as:

$$\frac{\partial N(t,a,x)}{\partial t} + \frac{\partial N(t,a,x)}{\partial a} + \frac{\partial (F(a,x)N(t,a,x))}{\partial x} = -(P(a,x) + D(a,x)), \quad a > 0.$$

The total cell population at age $a = 0$ is given by

$$N(t,0,x) = 4\int_0^{\infty} P(a,2x)N(t,a,2x)da.$$

$N(t,a,x)$ is the total population of the cells at time t, age a, and volume (size) x. The functions $F(a,x)$, $P(a,x)$, and $D(a,x)$ represent the rate of cell growth, the proliferation rate, and the death rate of the cells at age a and size x, respectively. This model was also investigated by Beyer [18], where he considered the function $F(a,x)$ to be linear and age independent. Since this model does not take in account the four comparative phases in the proliferation phase, or even between the proliferation phase and the resting phase, many mathematical models have recently been created to deal with this. Basse et al. [12] derived a model to describe the cell division cycle in the comparative phases (G_1, S, G_2, and M-Phases). This model is given as:

$$\begin{cases} \frac{\partial G_1(x,t)}{\partial t} = 4bM(2x,t) - (k_1 + \mu_{G_1})G_1(x,t), \\ \frac{\partial S(x,t)}{\partial t} = D\frac{\partial^2 S}{\partial x^2} - g\frac{\partial S(x,t)}{\partial x} - \mu_s S(x,t) + k_1 G_1(x,t) - I(x,t;T_S), \\ \frac{\partial G_2(x,t)}{\partial t} = I(x,t;T_S) - (k_1 + \mu_{G_2})G_2(x,t), \\ \frac{\partial M(x,t)}{\partial t} = k_2 G_2(x,t) - bM(x,t) - \mu_M M(x,t), \end{cases}$$

where $G_1(x,t)$, $S(x,t)$, $G_2(x,t)$, and $M(x,t)$ are the density of cells at time t and size x in the phases G_1, S, G_2, and M, respectively. The symbols μ_{G_1}, μ_S, μ_{G_2}, and μ_M represent the death rates of the cells in the phases G_1, S, G_2, and M, respectively. The symbols b, D, g, k_1, and k_2 are the division rate, diffusion rate, the growth rate of cells, transition rate from G_1- Phase to $S-$ Phase, and the transition rate from $S-$ Phase to G_2- Phase, respectively. The term $I(x,t;T_S)$ represents the sub-population of cells entering the $S-$phase (T_S represents the time that the cell spends in the $S-$ Phase in hours) and are ready to exit to G_2- Phase (see section 2.1 [12]). Begg et al. [15] modified the above model in three comparative phases, G_1, S, and G_2, to be age dependent. In fact, they considered the following model:

$$\begin{cases} \frac{\partial G_1(x,a,t)}{\partial t} + \frac{\partial G_1(x,t)}{\partial a} = -(k_{G_1}(x,a) + \mu_{G_1})G_1(x,a,t), \\ \frac{\partial S(x,a,t)}{\partial t} + \frac{\partial S(x,a,t)}{\partial a} = D\frac{\partial^2 S(x,a,t)}{\partial x^2} - g\frac{\partial S(x,a,t)}{\partial x} - \mu_s S(x,a,t), \\ \frac{\partial G_2(x,a,t)}{\partial t} + \frac{\partial G_2(x,a,t)}{\partial a} = -(k_{G_2}(x,a) + \mu_{G_2})G_1(x,a,t), \end{cases}$$

subject to the following initial and boundary conditions:

$$\begin{cases} G_1(x,0,t) = 4\int_0^\infty k_{G_2}(2x,a)G_2(2x,a,t)dt, \\ S(x,0,t) = \int_0^\infty k_{G_1}(x,a)G_1(x,a,t)dt, \\ G_2(x,0,t) = S(x,T_s,t), \\ DS_x(0,a,t) - gS(0,a,t) = DS_x(l,a,t) - gS(l,a,t) = 0, \end{cases}$$

where the parameters D, g, μ_{G_1}, μ_S, and μ_{G_2} are the diffusion rate, the growth rate of cells, the death rate in G_1-phase, the death rate in $S-$phase, and the death rate in G_2- phase, respectively. The size-time dependent functions $k_1(x,t)$ and $k_2(x,t)$ are the transition rates from G_1-phase to $S-$phase, and the transition rate from $S-$phase to G_2-phase, respectively. In this paper, the authors investigated the existence of the age-size steady state solution (SASD). In these two studies, the authors considered the cell cycle in the proliferation phase. In fact, they did not consider the full cells' division cycle, nor the relation between the resting phase and the proliferation phase. Drobnjak et al. [34] presented a mathematical model to represent the blood cells' division cycle in humans. In their model, they consider two comparative phases, G_0 − phase and P − phase. They consider the blood cells population to be age-time-size dependent, i.e., $N(t, x,)$ (the density of cells population in G_0 − phase) and $P(t, x, m)$ (the density of cells population in P − phase) are age-time-size functions. In their study, they neglect the effect of the diffusion term, as well as the cells' growth term.

In this study, we derive a new age-size model to describe the cells' division cycle between the two comparative phases, which are the resting phase and the proliferation phase. Using this model, we derive a delay deferential equation with a non-local term to represent the total population of cells in the resting phase. Since it is important to know when the number of cells decay to the zero solution (for example, the tumor cells in humans), we investigate the stability of the zero solution for the resulting delay differential equation with a non-local term. Indeed, we show the existence of a Principal eigenvalue with a corresponding nonnegative eigenfunction for the analogous variational linear differential equation. We organize this chapter as follows: in section 2, we describe the new model. In section 3, we derive a delay differential equation with a non-local term. In section 4, we show the existence of a Principal eigenvalue, as well as the existence of the Principal eigenfunction for the analogous variational linear differential equation. In section 5, we investigate the existence and stability of the positive steady state solution. In section 6, we present a numerical simulation.

5.2 The New Mathematical Model

In this section, we present a mathematical model of cell production to describe the development of cells through the cells division cycle. In this model, we describe the development of the age and the size of the cells in the two distinguished phases, G_0-Phase and P-Phase, during the cells' division cycle (see Figure 5.1).

Introductory and Symbols

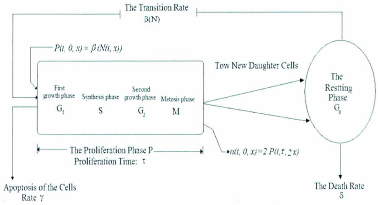


Figure 5.1: A graph shows the life cycle of a human cell.

- $n(t, a, x)$ is the density of cell population in G_0 − phase at time t, age a, and size x.
- $P(t, a, x)$ is the density of cell population in P − phase at time t, age a, and size x.
- δ is the death rate of cells in G_0 − phase.
- γ is the death rate (due to apoptosis) of cells in P − phase.

- τ is the time that the cell spends in $P-$ phase.

- $N(x,t)$ is the total cell population in the resting phase at time $t \geq 0$ and size $x \in [0, \pi/2]$. In fact, $N(t,x)$ is given by the following equation:

$$N(t,x) = \int_0^\infty n(t,a,x)da. \tag{5.2.1}$$

- $\beta(N)$ is the transition rate of the cells from the resting phase to the proliferation phase. In this study, we consider this rate to be a function of N. In particular, we consider the Hill function $\tilde{\beta}(N) = \frac{\beta\theta^n}{\theta^n + N^n}$. More precisely, we consider $\beta(N) = \frac{\beta}{1+N^n}$ since the function $\tilde{\beta}(N)$ can be scaled to $\beta(N)$ by changing the variables. Indeed, we can let $N = \frac{N}{\theta}$.

Assumptions

- We assume that $n(t,0,x) = 2P(t,\tau,2x)$;

- Due to the reality we have $n(t,\infty,x) = 0$;

- we assume that $P(t,0,x) = \beta(N)N$;

- We assume that the size of the cell does not change in the resting phase. In fact, this is a biological reality, since the size of the cell and the DNA doubling occur in the proliferation phase. Indeed, in the first growth phase (G_1-phase), Synthesis phase (S-phase), and second growth phase (G_2-phase);

- We assume that the cells with very small size are not present and cannot differentiate. We express this mathematically by the boundary condition $P(t,a,0) = 0$. Moreover, we assume that the cells in the proliferation phase cannot live to a size L. We express this mathematically by the boundary condition $P(a,t,L) = 0$.

- To ensure that the cells always have a positive DNA content, we consider the zero flux boundary conditions [12], i.e.,

$$D\frac{\partial P}{\partial x}(t,a,0) - gP(t,a,0) = 0.$$

- For mathematical analysis, we may consider

$$D\frac{\partial P}{\partial x}(t,a,L) - gP(t,a,L) = 0,$$

or

$$\frac{\partial P}{\partial x}(t,a,L) = 0.$$

- Also, for mathematical analysis, we may consider the Neumann boundary conditions

$$\frac{\partial P}{\partial x}(t,a,0) = \frac{\partial P}{\partial x}(t,a,L) = 0.$$

The symbols D and g appear in the above boundary conditions represent the diffusion and the growth rates of the cells, respectively.

Under these assumptions, the partial differential equation that is governed by the P-phase is the following reaction diffusion equation [12]:

$$\frac{\partial P}{\partial t}(t,a,x) + \frac{\partial P}{\partial a}(t,a,x) = D\frac{\partial^2 P}{\partial x^2}(t,a,x) - g\frac{\partial P}{\partial x}(t,a,x) - \gamma P(t,a,x). \qquad (5.2.2)$$

The term $D\frac{\partial^2 P}{\partial x^2}(t,a,x)$ is introduced here to compare the model outputs DNA profile directly with those obtained experimentally [12]. To simplify the mathematical calculation, we assume $L = \pi$. Therefore, the above equation holds $\forall t \geq 0$, $\forall a \in [0,\tau]$, and $\forall x \in [0,\pi]$.

Due to conservation law, the partial differential equation that is governed by the resting phase is

$$\frac{\partial n}{\partial t}(t,a,x) + \frac{\partial n}{\partial a}(t,a,x) = -\delta n(t,a,x) - \beta(N)n(t,a,x); \qquad (5.2.3)$$

and it is valid $\forall t \geq 0$, $\forall a \geq 0$, and $\forall x \in \left[0, \frac{\pi}{2}\right]$. Moreover, we assume that the cell size in the G_0 phase cannot exceed $\frac{\pi}{2}$. Therefore, we assume that $N(t,x) = 0, \forall x \in \left[\frac{\pi}{2}, \pi\right]$.

5.3 The Delay Differential Equation with a Non-local Term

To derive the required equation, we re-consider the model in equations (5.2.2) -(5.2.3). i.e.,

$$\frac{\partial P}{\partial t}(t,a,x) + \frac{\partial P}{\partial a}(t,a,x) = D\frac{\partial^2 P}{\partial x^2}(t,a,x) - g\frac{\partial P}{\partial x}(t,a,x) - \gamma P(t,a,x), \qquad (5.3.1)$$

and

$$\frac{\partial n}{\partial t}(t,a,x) + \frac{\partial n}{\partial a}(t,a,x) = -\delta n(t,a,x) - \beta(N)n(t,a,x), \qquad (5.3.2)$$

where equation (5.3.1) holds $\forall t \geq 0$, $\forall a \in [0,\tau]$, and $\forall x \in [0,\pi]$. Equation (5.3.2) holds $\forall t \geq 0$, $\forall a \geq 0$, and $\forall x \in \left[0, \frac{\pi}{2}\right]$. As a part of the discussion above we equipped (5.3.1) with one of the following boundary conditions:

1. Dirichlet boundary conditions:

$$P(t,a,0) = P(t,a,\pi) = 0 \qquad (5.3.3)$$

2. Roben's boundary conditions:

(a)

$$\begin{cases} D\dfrac{\partial P}{\partial x}(t,a,0) - gP(t,a,0) = 0, \\ \\ D\dfrac{\partial P}{\partial x}(t,a,\pi) - gP(t,a,\pi) = 0. \end{cases} \tag{5.3.4}$$

(b)

$$\begin{cases} D\dfrac{\partial P}{\partial x}(t,a,0) - gP(t,a,0) = 0, \\ \\ \dfrac{\partial P}{\partial x}(t,a,\pi) = 0. \end{cases} \tag{5.3.5}$$

3. Neumann boundary conditions:

$$\frac{\partial P}{\partial x}(t,a,0) = \frac{\partial P}{\partial x}(t,a,\pi) = 0. \tag{5.3.6}$$

First, we consider the model in equations (5.3.1)–(5.3.2) subject to the Dirichlet boundary conditions. To derive a new delay differential equation with a non-local term, we integrate (5.3.2) with respect to the age variable a over the interval $[0, \infty)$. Then, by using $N(t, x)$ form (Equation (5.2.1)) and the biological reality that $n(t, \infty, x) = 0$, we get

$$\begin{aligned} N_t(t,x) &= -(\delta + \beta(N))N + n(t,0,x) \\ &= -(\delta + \beta(N))N + 2P(t,\tau,2x). \end{aligned} \tag{5.3.7}$$

To find a formula for $P(t, \tau, 2x)$, we fix $s \geq 0$ and define the function $u^s(a,x) = P(a+s, a, x)$. By substituting $u^s(a,x)$ in Equation (5.3.1), We get:

$$\begin{aligned} u_a^s(a,x) &= P_t(a+s,a,x) + P_a(a+s,a,x) \\ &= DP_{xx}(a+s,a,x) - gP_x(a+s,a,x) - \gamma P(a+s,a,x) \\ &= Du_{xx}^s(a,x) - gu_x^s(a,x) - \gamma u^s(a,x). \end{aligned}$$

Equivalently,

$$u_a^s(a,x) = Du_{xx}^s(a,x) - gu_x^s(a,x) - \gamma u^s(a,x). \tag{5.3.8}$$

To simplify the above equation, we consider the following transformation:

$$u^s(a,x) = w^s(a,x)h(a,x) = w^s(a,x)\exp\left\{\frac{g}{2D}x - \left(\frac{g^2}{4D} + \gamma\right)a\right\}.$$

This transforms Equation (5.3.8) to the heat equation:

$$\begin{cases} w_a^s(a,x) = Dw_{xx}^s(a,x) \\ w^s(a,0) = w^s(a,\pi) = 0. \end{cases} \tag{5.3.9}$$

To find a closed formula for $w^s(a,x)$, we apply the separation of variables technique to (5.3.9). We let $w(a,x) = A(a)X(x)$ (for simplicity, we quit the symbol s). Then we get the following Boundary Value Problem (BVP):

$$\begin{cases} X''(x) + \mu^2 X(x) = 0 \\ X(0) = X(\pi) = 0. \end{cases}$$

The eigenvalues for this problem are

$$\mu = n; \quad n = 1, 2, 3, \cdots$$

and the corresponding eigenfunctions are

$$X_n(x) = \sin nx; \quad n = 1, 2, 3, \cdots .$$

The resulting IVP (Initial Value Problem) in the age variable a is:

$$A'(a) = -\mu^2 DA(a) = -n^2 DA(a),$$

where the solution of this problem is $A_n(a) = C_n(s)\, e^{-n^2 Da}$, $n = 1, 2, 3\cdots$. Therefore, $w^s(a, x)$ can be written in Fourier series representation as:

$$w^s(a, x) = \sum_{n=1}^{\infty} C_n(s) e^{-n^2 Da} \sin nx. \tag{5.3.10}$$

Using the initial condition $P(t, 0, x) = \beta(N)N$ we have

$$w^s(0, x) = \beta(N(s, x))N(s, x)\, e^{\frac{-g}{2D}x} = f(N(s, x))\, e^{\frac{-g}{2D}x}.$$

Therefore, the coefficients $C_n(s)$ are given by:

$$C_n(s) = \frac{2}{\pi}\int_0^{\pi} f(N(s, y))e^{\frac{-g}{2D}y}\ \sin nydy.$$

So,

$$w^s(a, x) = \frac{2}{\pi}\sum_{n=1}^{\infty} e^{-n^2 Da} \sin nx \int_0^{\pi} f(N(s, y))e^{\frac{-g}{2D}y}\ \sin nydy.$$

Recall that

$$P(t, a, x) = u^{t-a}(a, x) = \frac{2}{\pi}h(a, x)\sum_{n=1}^{\infty} e^{-n^2 Da} \sin nx \int_0^{\pi} f(N(t - a, y))e^{\frac{-g}{2D}y}\ \sin nydy.$$

Hence,

$$P(t,\tau,2x) = \frac{2}{\pi}h(\tau,2x)\sum_{n=1}^{\infty} e^{-n^2D\tau}\sin 2nx \int_0^{\pi} f(N(t-\tau,y))e^{\frac{-g}{2D}y}\ \sin nydy.$$

Since $f(0) = 0$ and $N(t,x) = 0,\ \forall x \in \left[\frac{\pi}{2},\pi\right]$. Then the above equation can be written as:

$$\begin{aligned} P(t,\tau,2x) &= \frac{2}{\pi}h(\tau,2x)\sum_{n=1}^{\infty} e^{-n^2D\tau}\sin 2nx \int_0^{\pi/2} f(N(t-\tau,y))e^{\frac{-g}{2D}y}\ \sin nydy \\ &= \frac{2}{\pi}h(\tau,2x)\int_0^{\pi/2} K_\tau^1(x,y)e^{-n^2D\tau}f(N(t-\tau,y))dy. \end{aligned}$$

By substituting this in Equation (5.3.7), we get the following delay differential equation with a nonlocal term:

$$N_t(t,x) = -(\delta + \beta(N(t,x)))N(t,x) + 2\Psi_\tau^1(t,x), \tag{5.3.11}$$

where the nonlocal term is given in the following formula:

$$\Psi_\tau^1(t,x) = \frac{2}{\pi}h(\tau,2x)\int_0^{\pi/2} K_\tau^1(x,y)\ e^{\frac{-g}{2D}y}\ f(N(t-\tau,y))dy, \tag{5.3.12}$$

$$K_\tau^1(x,y) = \sum_{n=1}^{\infty} e^{-n^2D\tau}\ \sin 2nx\ \sin ny, \tag{5.3.13}$$

and

$$h(\tau,2x) = \exp\left\{\frac{g}{D}x - \left(\frac{g^2}{4D}+\gamma\right)\tau\right\}. \tag{5.3.14}$$

Applying the same technique to Equation (5.3.1) subject to the boundary conditions (5.3.4), (5.3.5), and (5.3.6), we have the following delay differential equations (DDE) with a nonlocal term:

$$N_t(t,x) = -(\delta + \beta(N(t,x)))N(t,x) + 2\Psi_\tau^i(t,x), \quad i = 2,3,4, \tag{5.3.15}$$

where

$$\Psi_\tau^i(t,x) = h(\tau,\ 2x)\int_0^{\pi/2} K_\tau^i(x,y)\, e^{\frac{-g}{2D}y}\, f(N(t-\tau,y))dy, \ \ i = 2,3,4. \tag{5.3.16}$$

The kernel functions $K_\tau^i(x,y),\ i = 2,3,4$ are given in the following equations:

$$K_\tau^2(x,y) = \sum_{n=0}^{\infty} \frac{e^{-\alpha_n^2 D\tau}}{\|\eta_n(x)\|_{L^2[0,\pi]}^2}\ \eta_n(2x)\ \eta_n(y), \tag{5.3.17}$$

where

$$\alpha_n^2 = \begin{cases} \frac{g^2}{4D^2}, & n = 0, \\ n^2, & n = 1,2,3,\cdots \end{cases}$$

and

$$\eta_n(x) = \begin{cases} e^{\frac{gx}{2D}}, & n = 0, \\ \cos nx + \frac{g}{2nD}\sin nx, & n = 1,2,3,\cdots; \end{cases}$$

in the case $i = 3$,

$$K_\tau^3(x,y) = \sum_{n=1}^{\infty} \frac{e^{-\alpha_n^2 D\tau}}{\|\eta_n(x)\|_{L^2[0,\pi]}^2}\ \eta_n(2x)\ \eta_n(y), \tag{5.3.18}$$

where $\alpha_n' s$ are the solutions of the following equation:

$$\tan\alpha_n\pi = \frac{g}{2D\alpha_n}$$

and

$$\eta_n(x) = \cos\alpha_n x + \frac{g}{2\alpha_n D}\sin\alpha_n x, \qquad n = 1,2,3,\cdots;$$

and lastly, in the case of $i = 4$,

$$K_\tau^4(x,y) = \frac{1}{\pi}\left(1 + 2\sum_{n=1}^{\infty} e^{-n^2 D\tau} \cos 2nx \ \cos ny\right). \tag{5.3.19}$$

5.4 Existence of a Principal Eigenvalue and the Local Stability of the Zero Solution

In this section, we investigate the stability of the zero solution of the non-linear delay differential equation with a non-local term (5.3.11) as well as the delay differential equations with a non-local term that are given in Equation (5.3.15). To do this, we study the dynamics of the corresponding variational linear differential equation (see Equation (5.4.3)). In fact, we show that the variational linear equation admits a principal eigenvalue with a corresponding positive (nonnegative and not identically zero) eigenfunction. Re-consider the following nonlinear delay differential equation with a nonlocal term:

$$\begin{cases} N_t(t,x) = -\delta N(t,x) - f(N(t,x)) & \\ +\frac{4}{\pi} h(\tau, 2x) \displaystyle\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, f_\tau(N(t,y))dy, & t > 0,\ x \in (0, \frac{\pi}{2}), \\ N(t,0) = N(t,\frac{\pi}{2}) = 0, & t > 0, \\ N(s,x) = \xi(s,x) \geq 0, & s \in [-\tau, 0],\ x \in (0,\frac{\pi}{2}). \end{cases} \tag{5.4.1}$$

where $f_\tau(N(t,x)) = f(N(t-\tau,x))$ and $K_\tau^1(x,y)$ is given in Equation (5.3.13).

The variational equation about zero is given in the following equation:

$$\begin{cases} N_t(t,x) = -\delta N(t,x) - f'(0)N(t,x) \\ +\frac{4}{\pi}h(\tau,2x)f'(0)\displaystyle\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, N(t-\tau,y)dy, & t>0,\ x\in(0,\frac{\pi}{2}), \\ N(t,0) = N(t,\frac{\pi}{2}) = 0, & t>0, \\ N(s,x) = \xi(s,x) \geq 0, & s\in[-\tau,0],\ x\in(0,\frac{\pi}{2}). \end{cases} \tag{5.4.2}$$

We notice that $f'(0)=\beta$. Moreover, if we assume that $N(t,x) = \theta + \phi(x)\exp(\lambda t)$ (θ is the zero solution), then we have the following eigenvalue problem:

$$\begin{cases} \lambda N(x) = -(\delta+\beta)N(x) \\ +\frac{4\beta}{\pi}h(\tau,2x)e^{-\lambda\tau}\displaystyle\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, N(y)dy, & x\in(0,\frac{\pi}{2}), \\ N(0) = N(\frac{\pi}{2}) = 0. \end{cases} \tag{5.4.3}$$

For simplicity, we also consider the following linear differential equation:

$$\begin{cases} N_t(t,x) = -\delta N(t,x) - f'(0)N(t,x) \\ +\frac{4}{\pi}h(\tau,2x)f'(0)\displaystyle\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, N(t,y)dy, & t>0,\ x\in(0,\frac{\pi}{2}), \\ N(t,0) = N(t,\frac{\pi}{2}) = 0, & t>0, \\ N(0,x) = \xi(x) \geq 0, & x\in(0,\frac{\pi}{2}). \end{cases} \tag{5.4.4}$$

The linear eigenvalue problem of (5.4.4) is given by

$$\begin{cases} \lambda N(x) = -(\delta+\beta)N(x) \\ +\frac{4\beta}{\pi}h(\tau,2x)\displaystyle\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, N(y)dy, & x\in(0,\frac{\pi}{2}), \\ N(0) = N(\frac{\pi}{2}) = 0. \end{cases} \tag{5.4.5}$$

Remark 5.4.1. *In the later analysis, we will show that the linear equation* (5.4.3), *as well as the linear equation* (5.4.5), *admits a unique eigenvalue with a corresponding* *nonnegative and not identically zero eigenfunction (In the case of Dirichlet boundary conditions). Moreover, we will show that these two eigenvalues have the same sign. Hence, these two equations have the same dynamics at the zero solution. In fact, this simplifies the investigation of the stability of the zero solution (see section 5).*

To go further in our analysis, We re-write the linear equations (5.4.3) and (5.4.5) as

$$N(x) = \frac{4}{\pi} h(\tau, 2x) F(\lambda) \int_0^{\pi/2} K_\tau^1(x, y)\, e^{\frac{-g}{2D} y}\, N(y) dy,$$

and

$$N(x) = \frac{4}{\pi} h(\tau, 2x) \widetilde{F}(\lambda) \int_0^{\pi/2} K_\tau^1(x, y)\, e^{\frac{-g}{2D} y}\, N(y) dy,$$

where $F(\lambda) = \frac{\beta e^{-\lambda\tau}}{\lambda+\delta+\beta}$ and $\widetilde{F}(\lambda) = \frac{\beta}{\lambda+\delta+\beta}$. To analyze the above two linear integral equations, we write them in abstract form as:

$$L_\tau^1(\phi)(x) = \frac{4}{\pi} h(\tau, 2x) F(\lambda) \int_0^{\pi/2} K_\tau^1(x, y)\, e^{\frac{-g}{2D} y}\, \phi(y) dy, \tag{5.4.6}$$

and

$$L_0^1(\phi)(x) = \frac{4}{\pi} h(\tau, 2x) \widetilde{F}(\lambda) \int_0^{\pi/2} K_\tau^1(x, y)\, e^{\frac{-g}{2D} y}\, \phi(y) dy. \tag{5.4.7}$$

To show that the above linear integral operators admit principal eigenvalues λ_0 and $\widetilde{\lambda}_0$, respectively, we apply the Krien-Rotman Theorem (see Theorem 2.2.1). Therefore, we need to prove L_τ^1 and L_0^1 are compact and strongly positive operators on appropriate function spaces. We start by the following lemma:

Lemma 5.4.1. *Assume that $\lambda > -(\delta + \beta)$. Then the linear operators L_τ^1 and L_0^1 map the space $X = C([0, \pi/2])$ into itself. Moreover, the linear operators L_τ^1 and L_0^1 map* *the space* $Z = C_0^1([0,\pi/2])$ *into itself.*

proof The proof will be for L_τ^1 while the proof for L_0^1 is similar. Let x_n be a sequence in $[0,\pi/2]$ and x_n converges to x in $([0,\pi/2])$. Then

$$\begin{aligned}
\left|L_\tau^1\phi(x_n) - L_\tau^1\phi(x)\right| &\leq \frac{4}{\pi}F(\lambda)\left|h(\tau,2x_n) - h(\tau,2x)\right|\left|\int_0^{\pi/2} K_\tau^1(x,y)e^{\frac{-g}{2D}y}\,\phi(y)dy\right| \\
&+ \left|\int_0^{\pi/2} K_\tau^1(x_n,y)e^{\frac{-g}{2D}y}\,\phi(y)dy - \int_0^{\pi/2} K_\tau^1(x,y)e^{\frac{-g}{2D}y}\,\phi(y)dy\right| \\
&\times \frac{4}{\pi}F(\lambda)\left|h(\tau,2x)\right| \\
&\leq 2MF(\lambda)\left\|\phi(y)\right\|_\infty \left|h(\tau,2x_n) - h(\tau,2x)\right| \\
&+ \frac{4}{\pi}F(\lambda)\left\|h(\tau,2x)\right\|_\infty \left\|\phi(y)\right\|_\infty \int_0^{\pi/2}\left|K_\tau^1(x_n,y) - K_\tau^1(x,y)\right|dy
\end{aligned}$$

The kernel function $K_\tau^1(x,y)$ is a continuous function on the compact set $\left[0,\frac{\pi}{2}\right]\times\left[0,\frac{\pi}{2}\right]$. Therefore, it is bounded. Let $M = \max_{x,y\in\left[0,\frac{\pi}{2}\right]} K_\tau^1(x,y)$. Then $|K_\tau^1(x_n,y) - K_\tau^1(x,y)| \leq 2M$. Hence, the integrand above is dominated by an integrable function. Moreover, the function $h(\tau,x)$ is continuous. Therefore, by the continuity of h and Dominated Convergence Theorem, the right hand side in the above inequality is zero when $n\to\infty$. This shows that L_τ^1 maps the space $X = C(\left[0,\frac{\pi}{2}\right])$ into itself.

Now, we prove that L_τ^1 maps the space $Z = C_0^1(\left[0,\frac{\pi}{2}\right])$ into itself. First, we notice that $K_\tau^1(0,y) = K_\tau^1(\frac{\pi}{2},y) = 0$. Therefore, $\psi(x) := L_\tau^1(\phi)(x)$, $\phi\in Z$, $\lambda > -(\delta+\beta)$; vanishes at the boundary. To complete the proof, we need to show that $\psi'(x)$ exists and continuous on $[0,\frac{\pi}{2}]$. Let

$$\theta(x) := \int_0^{\pi/2} K_\tau^1(x,y)\,e^{\frac{-g}{2D}y}\,\phi(y)dy.$$

Then,

$$\theta'(x) = \int_0^{\pi/2} \frac{\partial}{\partial x}K_\tau^1(x,y)\,e^{\frac{-g}{2D}y}\,\phi(y)dy.$$

exists and is continuous. In fact, it is exist since $\frac{\partial}{\partial x}K_\tau^1(x,y)$ exists and is bounded. To prove the continuity we follow the same argument above. Therefore,

$$\psi(x) = \frac{4}{\pi}h(\tau, 2x)F(\lambda)\theta(x)$$

has a continuous derivate. ∎

Theorem 5.4.1. *Assume that $\lambda > -(\delta + \beta)$. Then the linear operators L_τ^1 and L_0^1 are compact operators over $X = C(\left[0, \frac{\pi}{2}\right])$. Moreover, L_τ^1 and L_0^1 are compact over the space $Z = C_0^1([0, \pi/2])$.*

proof We prove that L_τ^1 is compact. To do this we apply Ascole-Arzela Theorem. Therefore, we want to show that for each uniformly bounded set $\mathcal{B}$ in $X = C(\left[0, \frac{\pi}{2}\right])$. Then $L_\tau^1\mathcal{B}$ is uniformly bounded and equicontinuous in X. First, we show that $L_\tau^1\mathcal{B}$ is a uniformly bounded set, provided that $\mathcal{B}$ is uniformly bounded. Since $\mathcal{B}$ is uniformly bounded, then there exists $\overline{M}$ such that $\|\phi\|_\infty < \overline{M}$, $\forall \phi \in \mathcal{B}$. Now, we have

$$\begin{aligned}
\left|L_\tau^1(\phi(x))\right| &= \frac{4}{\pi}F(\lambda)h(\tau, 2x)\left|\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, \phi(y)dy\right| \\
&\leq 2\, M\, \overline{M}\, F(\lambda)\, \|h(\tau, .)\|_\infty \left\|e^{\frac{-g}{2D}(.)}\right\|_\infty \\
&= 2\, M\, \overline{M}\, F(\lambda)\, \|h(\tau, .)\|_\infty = \widetilde{M}.
\end{aligned}$$

Therefore, $L_\tau^1\mathcal{B}$ is uniformly bounded. Second, we prove that $L_\tau^1\mathcal{B}$ is equicontinuous set. Given $x_1,\ x_2 \in \left[0, \frac{\pi}{2}\right]$, $\phi \in \mathcal{B}$, and let $\epsilon > 0$. Then

$$\begin{aligned}
\left|L_\tau^1(\phi(x_1)) - L_\tau^1(\phi(x_2))\right| &= \frac{4}{\pi}F(\lambda)\left|h(\tau, 2x_1) - h(\tau, 2x_2)\right| \\
&\times \left|\int_0^{\pi/2} K_\tau^1(x_1, y)\, e^{\frac{-g}{2D}y}\, \phi(y) - K_\tau^1(x_2, y)\, e^{\frac{-g}{2D}y}\, \phi(y)\right| dy \\
&\leq 2\overline{M}\left|h(\tau, 2x_1) - h(\tau, 2x_2)\right|\left|K_\tau^1(x_1, y) - K_\tau^1(x_2, y)\right| \\
&\leq 2\overline{M}\epsilon_1\epsilon_2 = \epsilon, \quad \text{whenever} \quad |x_1 - x_2| < \delta.
\end{aligned}$$

For the last equality, we choose ϵ_1 and ϵ_2 to be $\frac{\sqrt{\epsilon}}{2}$ and $\frac{\sqrt{\epsilon}}{M}$, respectively. This is true by the uniform continuity of the functions $h(x)$ and $K_\tau^1(x,y)$. Therefore, L_τ^1 is compact operator over the space X. To complete the proof, Let $\mathcal{B}$ be a uniformly bounded set in the space Z, and let $\overline{\overline{M}}$ be its uniform bound (i.e., $\|\phi\|_Z < \overline{\overline{M}}$, for all $\phi \in \mathcal{B}$). We showed in the previous lemma that $\psi'(x)$ exists and continuous on $[0, \pi/2]$, where $\psi(x) := L_\tau^1(\lambda)(\phi(x)), \phi \in \mathcal{B}, \lambda > -(\delta + \beta)$. First, we show that L_τ^1 is uniformly bounded in Z-norm. As we showed in the first part, we have

$$|\psi(x)| = \left|L_\tau^1(\lambda)(\phi(x))\right| \leq 2M\overline{\overline{M}}F(\lambda)\left\|h(\tau,.)\right\|_\infty := \widetilde{M}_1$$

Also, we have

$$\begin{aligned} |\psi'(x)| &= \frac{4}{\pi}F(\lambda)\left|h(\tau,2x)\theta'(x) + \theta(x)h'(\tau,2x)\right| \\ &\leq 2\overline{\overline{M}}F(\lambda)\left[\left\|h(\tau,.)\right\|_\infty M' + \left\|h'(\tau,.)\right\|_\infty M\right] := \widetilde{M}_2, \end{aligned}$$

where $M' := \max_{x,y\in[0,\pi/2]} \frac{\partial}{\partial x}K_\tau^1(x,y)$. Combining these two inequalities together, we get

$$\|\psi\|_Z = \|\psi\|_\infty + \|\psi'\|_\infty \leq \widetilde{M}_1 + \widetilde{M}_2 := \widetilde{M}_3.$$

Finally, we remark that $f(u)$ is continuous and bounded function. Moreover, the function $h(\tau, 2x)$ is continuous function over $[0, \pi/2]$, as well as its derivative. Hence, $h(\tau, 2x)$ and $h'(\tau, 2x)$ are uniformly continuous. In addition, the kernel function function $K_\tau^1(x, y)$ is of C^2-class in x and y on the compact set $[0, \pi/2] \times [0, \pi/2]$. Therefore, $\psi(x)$ and its derivative $\psi'(x)$ are uniformly continuous over $[0, \pi/2] \times [0, \pi/2]$. Therefore, by following the above procedure, we can show that $(L_\tau^1\mathcal{B})'$ (the $'$ means the derivative with respect to x) is equicontinuous family over the space Z. We showed in the previous lemma that L_τ^1 maps the space Z into itself (Indeed, it maps the space X into the space Z). Moreover, the space Z is a closed subspace of X (i.e., the convergence of any sequence in $L_\tau^1\mathcal{B}$ is again in Z). Hence, L_τ^1 is compact over Z. ∎

Now, we consider the heat equation

$$\begin{cases} w_a(a,x) = Dw_{xx}(a,x), & \\ w(a,0) = w(a,\pi) = 0, & a \in [0,\tau] \\ w(0,x) = \phi_0(x) \geq 0, & x \in [0,\pi], \end{cases} \tag{5.4.8}$$

and we let $w(a,x)$ be its solution. Then we have the following lemma:

Lemma 5.4.2. *Assume that $\phi_0(x) \in C_0^+([0,\pi])$. Then $w(a,x) \geq 0$, $\forall(a,x) \in [0,\tau] \times [0,\pi]$. Moreover, if $\phi_0 \in C_0^+([0,\pi])$ and not identically zero, then $w(a,x) > 0$, $\forall(a,x) \in (0,\tau] \times (0,\pi)$.*

proof. Let $\phi_0(x) \in Y_+ = C_0^+([0,\pi])$. First, we show that $w(a,x)$ cannot have negative values on $[0,\tau] \times [0,\pi]$, provided that the initial condition $\phi_0(x)$ is nonnegative. The proof is by contradiction. Let $\phi_0(x) \in Y_+$ be a nonnegative function and assume that $w(a,x)$ has a negative value at some points $q = (\bar{a},\bar{x}) \in [0,\tau] \times [0,\pi]$. Then, $w(a,x)$ has a negative minimum at some points $p = (a_0,x_0) \in [0,\tau] \times (0,\pi]$. It is easy to see that $a_0 \neq 0$, since this contradicts the assumption $\phi(x) \geq 0$. Moreover, $p \notin (0,\tau] \times (0,\pi)$, since this contradicts the maximum principle (Theorem 2.4.1). Therefore, $p = (a_0,x_0) \in (0,\tau] \times \{0,\pi\}$. However, such choice contradicts the boundary conditions, since $w(a,0) = w(a,\pi) = 0$. Therefore, there is no $q = (\bar{a},\bar{x}) \in [0,\tau] \times [0,\pi]$, and $w(q) < 0$.

Second, we show that $w(a,x)$ is positive $(0,\tau] \times (0,\pi)$, provided that the initial condition $\phi_0(x)$ is a nonnegative function and not identically zero. The proof is by contradiction. Let $\phi_0(x) \in Y_+$ be a nonnegative function, and not identically zero. Let $p = (a_0,x_0) \in [0,\tau] \times (0,\pi)$ be such that $w(a_0,x_0) = 0$. In the above paragraph we showed that $w(x, a)$ cannot have negative values. Therefore, if such a point exists then it is a local minimum. According to the maximum principle, this point cannot be in $(0, \tau] \times (0, \pi)$. In fact, if $p = (a_0, x_0) \in (0, \tau] \times (0, \pi)$, then the solution is identically zero on $(0, \tau] \times [0, \pi]$. This contradicts the initial data and the continuity of $w(a, x)$. This completes the proof. ∎

In the next theorem, we will show that the operators L_τ^1 and L_0^1 are strongly positive operators. In fact, the cone $Y_+ = C_0^+[0, \pi/2]$ has an empty interior. Therefore, we consider the space $C_0^1[0, \pi/2]$ and its positive cone $Z_+ = C_{0+}^1[0, \pi/2]$. This cone has a non-empty interior, and so we can define a strong positive relation on this cone (see the assumptions above).

Theorem 5.4.2. *Let $\lambda > -(\delta + \beta)$. Then the integral operators L_τ^1 and L_0^1 are strongly positive operators over the space Z.*

Proof. The proof will be for the operator L_τ^1 while the proof of L_0^1 is similar. We showed in Lemma 5.4.1 that L_τ^1 maps the space Z into itself. Next, we show that L_τ^1 is positive. i.e., L_τ^1 maps Z_+ into itself. We re-call that

$$L_\tau^1(\phi)(x) = \frac{4}{\pi} h(\tau, 2x) F(\lambda) \int_0^{\pi/2} K_\tau^1(x, y)\, e^{\frac{-g}{2D}y}\, \phi(y) dy.$$

Since $\frac{4}{\pi} h(\tau, 2x) F(\lambda) > 0$. Then it is enough to show that

$$\hat{L}\phi(x) = \int_0^{\pi/2} K_\tau^1(x, y)\, e^{\frac{-g}{2D}y}\, \phi(y) dy$$

is a nonnegative provided that $\phi(x) \in Z_+$ is nonnegative, or equivalently, to show that

$$w(\tau, x) = \sum_{n=1}^{\infty} e^{-n^2 D\tau} \sin nx \int_0^{\frac{\pi}{2}} e^{-\frac{g}{2D}y} \sin ny\, \phi(y) dy \tag{5.4.9}$$

is nonnegative. To do this, we consider th following expression:

$$w(a,x) = \sum_{n=1}^{\infty} e^{-n^2 Da} \sin nx \int_0^{\frac{\pi}{2}} e^{-\frac{g}{2D}y} \sin ny\, \phi(y) dy, \tag{5.4.10}$$

where $\phi(x) \in Z_+$. The above expression is the explicit solution to the heat equation (5.4.8) with the following initial function:

$$w_0(x) = \begin{cases} \phi(x) \exp\{-\frac{g}{2D}x\}, & x \in \left[0, \frac{\pi}{2}\right], \\ 0, & x \in \left[\frac{\pi}{2}, \pi\right]. \end{cases} \tag{5.4.11}$$

This function belongs to the cone $C_0^+([0,\pi])$, and satisfies the Dirichlet boundary conditions. According to Lemma 5.4.2 the expression (5.4.10) is nonnegative on $[0,\pi]$. Hence, it is nonnegative on $[0, \frac{\pi}{2}]$, and so the expression (5.4.9) is nonnegative on $[0, \frac{\pi}{2}]$. Therefore, L_τ^1 is positive.

To prove that L_τ^1 is strongly positive we need to show that L_τ^1 maps the non-zero elements in Z_+ into its interior. Let $\phi(x) \in Z_+$ and $\phi(x) \not\equiv 0$. Then the function

$$w_0(x) = \begin{cases} \phi(x) \exp\{-\frac{g}{2D}x\}, & x \in \left[0, \frac{\pi}{2}\right], \\ 0, & x \in \left[\frac{\pi}{2}, \pi\right]. \end{cases} \tag{5.4.12}$$

belongs to the cone $C_0^+([0,\pi])$ and not identically zero. Using the same argument above and Lemma 5.4.2, the expression

$$w(\tau,x) = \sum_{n=1}^{\infty} e^{-n^2 D\tau} \sin nx \int_0^{\frac{\pi}{2}} e^{-\frac{g}{2D}y} \sin ny\, \phi(y) dy,$$

is strictly positive on $(0, \frac{\pi}{2})$. Moreover, the normal derivative at the boundary points is strictly negative according to the maximum principle. Therefore, L_τ^1 maps Z_+ into its interior. Hence, the operator L_τ^1 is strongly positive. ∎

Theorem 5.4.3. *Let $\lambda > -(\delta+\beta)$. Then the operator L_τ^1 admits a principal eigenvalue $p(\lambda)$ with a corresponding nonnegative and not identically eigenfunction $\phi(x) \in Z_+ = C_{0+}^1([0,\frac{\pi}{2}])$. Similarly, the operator L_0^1 admits a principal eigenvalue $\tilde{p}(\lambda)$ with a corresponding nonnegative and not identically eigenfunction $\tilde{\phi}(x) \in Z_+ = C_{0+}^1([0,\frac{\pi}{2}])$.*

Proof. The proof is a direct result from Theorem 5.4.1, Theorem 5.4.2, and the second part of the Krien-Rotman Theorem. ∎

Remark 5.4.2. *We remark that the principal eigenvalues $p(\lambda)$ and $\tilde{p}(\lambda)$ are algebraically simple due to the Krien-Rotman Theorem. Moreover, $p(\lambda)$ and $\tilde{p}(\lambda)$ are depending on λ. In the next theorem, we will show that L_τ^1 and L_0^1 vary continuously with λ. In fact, this allows $p(\lambda)$ and $\tilde{p}(\lambda)$ to vary continuously with λ, see [1].*

Theorem 5.4.4. *Let $\lambda > -(\delta+\beta)$. Then the operators L_τ^1 and L_0^1 vary continuously with λ over the space Y. Moreover, L_τ^1 and L_0^1 vary continuously with λ over the space Z.*

Proof. The proof will be for L_τ^1 while the proof of L_0^1 is similar. Let $\lambda, \lambda' > -(\delta+\beta)$ and $\phi(x) \in Y_+$. Then

$$\begin{aligned}\left|L_\tau^1(\lambda)\phi(x) - L_\tau^1(\lambda')\phi(x)\right| &= \left|\frac{4}{\pi}h(\tau,2x)\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\,\phi(y)dy\right| \\ &\times\ |F(\lambda)-F(\lambda')| \\ &\le 2M\ \|h\|_\infty\ \|\phi\|_\infty\ |F(\lambda)-F(\lambda')|\,.\end{aligned}$$

$F(\lambda)$ is continuous in λ. Therefore, for $\epsilon > 0$ with $\frac{\epsilon}{2M\|h\|_\infty}$, there exists $\delta_0 > 0$ such that

$$|F(\lambda)-F(\lambda')| < \frac{\epsilon}{2M\,\|h\|_\infty}, \quad \text{whenever} \quad |\lambda-\lambda'| < \delta_0.$$

Hence,

$$\left|L_\tau^1(\lambda)\phi(x) - L_\tau^1(\lambda')\phi(x)\right| < \epsilon \, \|\phi\|_\infty, \quad \text{whenever} \quad |\lambda - \lambda'| < \delta_0.$$

Therefore,

$$\left\|L_\tau^1(\lambda) - L_\tau^1(\lambda')\right\| < \epsilon, \quad \text{whenever} \quad |\lambda - \lambda'| < \delta_0.$$

This completes the proof of the first part. To prove the second part, that is L_τ^1 varies continuously with λ over the space Z, we define $\psi_\lambda(x) := L_\tau^{(1)}\phi(x) = \frac{4}{\pi}h(\tau, 2x)\theta(x)$, for a given $\phi(x) \in Z$. The C^1- function $\theta(x)$ is defined as in the proof of Lemma 5.4.1. We denote by $\psi'_\lambda(x)$ the first derivative of $\psi_\lambda(x)$ with respect to x. Using these notations and following the above argument, we have

$$|\psi_\lambda(x) - \psi_{\lambda'}(x)| \le 2M \, \|h\|_\infty \, \|\phi\|_Z \, |F(\lambda) - F(\lambda')| \, .$$

Hence, for $\epsilon > 0$, and by the continuity of $F(\lambda)$, there exists $\delta_1 > 0$ such that

$$|\psi_\lambda(x) - \psi_{\lambda'}(x)| < \frac{\epsilon}{2} \, \|\phi\|_Z \quad \text{whenever} \quad |\lambda - \lambda'| < \delta_1. \tag{5.4.13}$$

We also have

$$|\psi'_\lambda(x) - \psi'_{\lambda'}(x)| \le 2 \left(M \, \|h'\|_\infty + M' \, \|h\|_\infty\right) \|\phi\|_Z \, |F(\lambda) - F(\lambda')| \, ,$$

where $M' = \max\limits_{[0,\pi/2]} \dfrac{\partial}{\partial x} K_\tau^1(x, y)$. Hence, by the continuity of $F(\lambda)$, there exists δ_2 such that

$$|\psi'_\lambda(x) - \psi'_{\lambda'}(x)| < \frac{\epsilon}{2} \, \|\phi\|_Z \quad \text{whenever} \quad |\lambda - \lambda'| < \delta_2. \tag{5.4.14}$$

Let $\delta = \min\{\delta_1, \delta_2\}$, and by taking the maximum over $[0, \pi/2]$ of Equation (5.4.13) and Equation (5.4.14), we have

$$\max_{x\in[0,\pi/2]} |\psi_\lambda(x) - \psi_{\lambda'}(x)| < \frac{\epsilon}{2} \|\phi\|_Z \quad \text{whenever} \quad |\lambda - \lambda'| < \delta, \tag{5.4.15}$$

and

$$\max_{x\in[0,\pi/2]} |\psi'_\lambda(x) - \psi'_{\lambda'}(x)| < \frac{\epsilon}{2} \|\phi\|_Z \quad \text{whenever} \quad |\lambda - \lambda'| < \delta. \tag{5.4.16}$$

Combine Equation (5.4.15) and Equation (5.4.16) together and re-write $\psi_\lambda(x)$ in L^1_τ form, we get

$$\left\| L^1_\tau(\lambda)\phi(x) - L^1_\tau(\lambda')\phi(x) \right\|_Z < \epsilon \; \|\phi\|_Z \quad \text{whenever} \quad |\lambda - \lambda'| < \delta.$$

Hence,

$$\left\| L^1_\tau(\lambda) - L^1_\tau(\lambda') \right\|_Z < \epsilon \quad \text{whenever} \quad |\lambda - \lambda'| < \delta.$$

This completes the proof. ∎

Remark 5.4.3. *We remark that $F(\lambda) \to 0$, as $\lambda \to \infty$, and $F(\lambda) \to \infty$, as $\lambda \to -(\delta+\beta)$. Therefore, $p(\lambda) \to 0$, as $\lambda \to \infty$, and $p(\lambda) \to \infty$, as $\lambda \to -(\delta+\beta)$. This is true, since $p(\lambda)$ varies continuously with λ (Remark 5.4.2) and the relation $L^1_\tau\phi(x) = p(\lambda)\phi(x)$ hold. Hence, there exists λ_1 and λ_2 such that $p(\lambda_1) \geq 1$ and $p(\lambda_2) < 1$. So, there exists $\lambda_0 > -(\delta+\beta)$ such that $p(\lambda_0) = 1$, this is true by the Mean Value Theorem. Hence, there exists a nonnegative and not identically zero solution $\phi(x)$, such that $L^1_\tau(\lambda_0)\phi(x) = p(\lambda_0)\phi(x) = \phi(x)$. Similarly, the same conclusion holds for the operator L^1_0. i.e., there exists $\tilde{\lambda}_0 > (\delta+\beta)$ such that $\tilde{p}(\tilde{\lambda}_0) = 1$ with a corresponding nonnegative and not identically zero eigenfunction $\tilde{\phi}(x)$. Moreover, the eigenfunction $\tilde{\phi}(x)$ satisfies the equation $L^1_0(\tilde{\lambda}_0)\tilde{\phi}(x) = \tilde{p}(\lambda_0)\tilde{\phi}(x) = \tilde{\phi}(x)$.*

Remark 5.4.4. *Since the functions $F(\lambda)$ and $\tilde{F}(\lambda)$ are decreasing functions in λ.*

Then $p(\lambda)$ and $\tilde{p}(\lambda)$ are decreasing functions in λ. This true by using the comparison principle of the spectrum (see Corollary 7.28 [141]).

These two remarks allow us to state the following theorem:

Theorem 5.4.5. *There exists a unique $\lambda_0 > -(\delta+\beta)$ (resp. $\tilde{\lambda}_0 > -(\delta+\beta)$) corresponding to a principal eigenvalues $p(\lambda_0)$ (resp. $\tilde{p}(\tilde{\lambda}_0)$) of magnitude one. The corresponding eigenfunction $\phi(x)$ (resp. $\tilde{\phi}(x)$) is nonnegative and not identically zero, and it satisfies the operator equation $L_\tau^1(\lambda_0)\phi(x) = p(\lambda_0)\phi(x) = \phi(x)$ (resp. $L_0^1(\tilde{\lambda}_0)\tilde{\phi}(x) = \tilde{p}(\lambda_0)\tilde{\phi}(x) = \tilde{\phi}(x)$).*

Proof. The existence of λ_0 comes from Remark 5.4.3 while the uniqueness of λ_0 comes from Remark 5.4.4. ∎

Theorem 5.4.6. *Let λ_0 and $\tilde{\lambda}_0 > -(\delta+\beta)$ as describe in Theorem 5.4.5. Then λ_0 and $\tilde{\lambda}_0$ have the same sign.*

Proof. First, we remark that $F(0) = \tilde{F}(0)$. Therefore, L_τ^1 and L_0^1 share the same principal eigenvalue at $\lambda = 0$. i.e., $p(\lambda = 0) = \tilde{p}(\lambda = 0)$. This is true according to the uniqueness of the principal eigenvalue. In fact, if $p(\lambda = 0)$, $\tilde{p}(\lambda = 0) > 1$, then λ_0, $\tilde{\lambda}_0$ are positive. Moreover, if $p(\lambda = 0)$, $\tilde{p}(\lambda = 0) < 1$, then λ_0, $\tilde{\lambda}_0$ are negative. This is completes the proof. ∎

Now, we consider the delay differential equations in (5.3.15). We let L_τ^i, $i = 2, 3, 4$ to be their corresponding linear operators with delay and we let L_0^i, $i = 2, 3, 4$ to be their corresponding linear operators without delay. In the following analysis we follow the same argument above to analyze these operators. In fact, we have almost the same results, but we have a slightly difference in the proofs of the theorems and the choice of the the function space. We start by the following lemma:

Lemma 5.4.3. *Assume that $\lambda > -(\delta+\beta)$. Then the linear operators L_τ^i and L_0^i, for $i = 2, 3, 4$, map the space $X = C(\left[0, \frac{\pi}{2}\right])$ into itself.*

Proof. The proof is similar to the proof of Lemma 5.4.1 ∎

Theorem 5.4.7. *Assume that $\lambda > -(\delta + \beta)$. Then the linear operators L_τ^i and L_0^i, for $i = 2, 3, 4$ are compact operators over the space $X = C(\left[0, \frac{\pi}{2}\right])$.*

Proof. The proof of this Theorem is similar to the proof of Theorem 5.4.1. ∎

Now, we re-consider the heat equation

$$w_a(a,x) = Dw_{xx}(a,x), \quad \text{where } (a,x) \in [0,\tau] \times [0,\pi] \tag{5.4.17}$$

subject to one of the Robin's boundary conditions,

$$\begin{cases} w_x(a,0) - \frac{g}{2D} w(a,0) = 0, & a \in [0,\tau], \\ w_x(a,\pi) - \frac{g}{2D} w(a,\pi) = 0, & a \in [0,\tau], \end{cases} \tag{5.4.18}$$

$$\begin{cases} w_x(a,0) - \frac{g}{2D} w(a,0) = 0, & a \in [0,\tau], \\ w_x(a,\pi) = 0, & a \in [0,\tau], \end{cases} \tag{5.4.19}$$

or the Neumann boundary conditions

$$\begin{cases} w_x(a,0) = 0, & a \in [0,\tau], \\ w_x(a,\pi) = 0, & a \in [0,\tau]. \end{cases} \tag{5.4.20}$$

Let $w(a,x)$ be the solution of the heat equation (5.4.17), subject to one of the above boundary conditions and to an initial data $w(0,x) = \phi_0(x) \in X = C([0,\pi])$. Then, we have the following lemma for $w(a,x)$:

Lemma 5.4.4. *Suppose that $\phi_0(x) \geq 0$. Then $w(a,x) \geq 0$, $\forall (a,x) \in [0,\tau] \times [0,\pi]$. Moreover, If $\phi_0(x) \geq 0$ and not identically zero, then $w(a,x) > 0$, $\forall (a,x) \in [0,\tau] \times [0,\pi]$.*

Proof. Let $\phi_0(x) \in X_+ = C^+([0,\pi])$. First, we show that $w(a,x)$ cannot have negative values on $[0,\tau] \times [0,\pi]$, provided that the initial condition $\phi_0(x)$ is nonnegative. The proof is by contradiction. Let $\phi_0(x) \in X_+$ be a nonnegative function and assume $w(a,x)$ has a negative value at some points $q = (\bar{a}, \bar{x}) \in [0,\tau] \times [0,\pi]$. Then, $w(a,x)$ has a negative minimum at some points $p = (a_0, x_0) \in [0,\tau] \times (0,\pi]$. It is easy to see that $a_0 \neq 0$, since this contradicts the assumption $\phi(x) \geq 0$. Moreover, $p \notin (0,\tau] \times (0,\pi)$, since this contradicts the maximum principle (Theorem 2.4.1). Therefore, $p = (x_0, a_0) \in \{0,\pi\} \times (0,\tau]$. If $p = (x_0, a_0) \in \{0\} \times (0,\tau]$, then the derivative at this point is strictly positive, according to the maximum principle. However, this choice contradicts the boundary conditions, since $w_x(a,0) = \frac{g}{2D} w(a,0) \leq 0$. Therefore, $p = (x_0, a_0) \in \{\pi\} \times (0,\tau]$. If this is true, then there exists a' such that $0 < a' < a_0$ and $w(a', x_0) = 0$. Now, the initial condition $\phi(x)$ is nonnegative, and the solution $w(a,x)$ is continuous and nonnegative on $[0,a'] \times [0,\pi]$. Therefore, this point (a', x_0) is a local minimum of $w(a,x)$ on $[0,a'] \times [0,\pi]$. Hence, the derivative at this point must be negative but we have $w_x(a', x_0) = \frac{g}{2D} w(a', x_0) = 0$, which is a contradiction. Therefore, there is no point $q = (\bar{a}, \bar{x}) \in [0,\tau] \times [0,\pi]$, and $w(q) < 0$.

Second, we show that $w(a,x)$ is positive on $[0,\tau] \times [0,\pi]$, provided that the initial condition $\phi_0(x)$ is nonnegative and not identically zero. Again, the proof is by contradiction. Let $\phi_0(x) \in Y_+$ be a nonnegative and not identically zero function in X_+. Let $p = (a_0, x_0) \in (0,\tau] \times [0,\pi]$ be such that $w(p) = w(a_0, x_0) = 0$. In the above paragraph we showed that $w(x,a)$ cannot have a negative value on $[0,\tau] \times [0,\pi]$. Therefore, if such a point exists then it would be a local minimum. According to the Maximum Principle, this point cannot be in $(0,\tau] \times (0,\pi)$. In fact, if $p = (a_0, x_0) \in (0,\tau] \times (0,\pi)$, then the solution is identically zero on $(0,\tau] \times [0,\pi]$ but this is incorrect unless $\phi_0(x)$ is zero. Moreover, the point $p = (a_0, x_0)$ cannot be on $\{0,\pi\} \times (0,\tau]$. In fact, this contradicts the boundary conditions, since $w_x(a_0, 0) = \frac{g}{2D} w(a_0, 0) = 0 = \frac{g}{2D} w(a_0, \pi) = w_x(a_0, \pi)$;

but $w_x(a_0, 0) > 0$ and $w_x(a_0, 0) < 0$ according to the maximum principle. Therefore, there is no point $p = w(a_0, x_0) \in [0, \tau] \times [0, \pi]$ and $w(p) = w(a_0, x_0) = 0$. Similarly, we can prove the result for Robin's boundary conditions (5.4.19), and the Neumann boundary conditions (5.4.20). ∎

Again, we re-consider the heat equation (5.4.17) subject to Robin's or the Neumann boundary conditions that are given in equations (5.4.18), (5.4.19), and (5.4.20). Moreover, we let $\phi(x) \in X_+ = C_+([0, \frac{\pi}{2}])$ and we assume that $\phi(x)$ satisfies one of the boundary conditions (5.4.18), (5.4.19), or (5.4.20) at $x = 0$. Then the function

$$\hat{w}_0(x) = \begin{cases} \phi(x)\exp\{-\frac{a}{2D}x\}, & x \in \left[0, \frac{\pi}{2}\right], \\ 0, & x \in \left[\frac{\pi}{2}, \pi\right], \end{cases} \tag{5.4.21}$$

is a nonnegative function and satisfies the required boundary conditions. This function could be discontinuous at $x = \pi/2$. Let $\hat{w}(a, x)$ be the solution of heat equation (5.4.17) on $(0, \tau] \times [0, \pi]$ with initial data $\hat{w}(a, x)$. Then, by applying the above lemma, and by using the same argument in the proof of prove Theorem 5.6 in [15], we have the following result for $\hat{w}(a, x)$.

Lemma 5.4.5. *Suppose that $\phi_0(x) \in C_+([0, \pi/2])$. Then $\hat{w}(a, x) \geq 0$, $\forall (a, x) \in [0, \tau] \times [0, \pi/2]$. Moreover, If $\phi_0(x) \geq 0$ and not identically zero, then $w(a, x) > 0$, $\forall (a, x) \in (0, \tau] \times [0, \pi/2]$.*

Theorem 5.4.8. *Let $\lambda > -(\delta + \beta)$. Then the integral operators L_τ^i and L_0^i are strongly positive operators on the space $C_+\left(\left[0, \frac{\pi}{2}\right]\right)$, for each $i = 2, 3, 4$.*

Proof. The proof will be for the operator L_τ^2 while the proofs of $L_\tau^3, L_\tau^4, L_0^2, L_0^3$, and L_0^4 are similar. We showed in lemma 5.4.3 that L_τ^2 maps the space $X = C(\left[0, \frac{\pi}{2}\right])$ into itself. Next, we show that L_τ^2 is positive. i.e., L_τ^2 maps X_+ into itself. We re-call that

$$L_\tau^2(\phi)(x) = \frac{4}{\pi} h(\tau, 2x) F(\lambda) \int_0^{\pi/2} K_\tau^2(x, y)\, e^{\frac{-g}{2D}y}\, \phi(y) dy.$$

Since $\frac{4}{\pi} h(\tau, 2x) F(\lambda) > 0$. Then it is enough to show that

$$\hat{L}\phi(x) = \int_0^{\pi/2} K_\tau^2(x, y)\, e^{\frac{-g}{2D}y}\, \phi(y) dy$$

is nonnegative provided that $\phi(x) \in X_+$ is nonnegative, or equivalently, to show that

$$w(\tau, x) = \sum_{n=0}^{\infty} \frac{e^{-n^2 D\tau}}{\|\eta_n(x)\|^2_{L_2[0,\pi]}} \eta_n(x) \int_0^{\frac{\pi}{2}} e^{-\frac{g}{2D}y} \eta_n(y)\, \phi(y) dy \tag{5.4.22}$$

is nonnegative. To do this, we consider th following expression:

$$w(a, x) = \sum_{n=0}^{\infty} \frac{e^{-n^2 Da}}{\|\eta_n(x)\|^2_{L_2[0,\pi]}} \eta_n(x) \int_0^{\frac{\pi}{2}} e^{-\frac{g}{2D}y} \eta_n(y)\, \phi(y) dy, \tag{5.4.23}$$

where $\phi(x) \in X_+$. The above expression is the explicit solution to the heat equation (5.4.17) with the following initial function:

$$\hat{w}_0(x) = \begin{cases} \phi(x) \exp\{-\frac{g}{2D}x\}, & x \in \left[0, \frac{\pi}{2}\right], \\ 0, & x \in \left[\frac{\pi}{2}, \pi\right]. \end{cases} \tag{5.4.24}$$

Therefore, $w(a, x)$ is nonnegative on $[0, \tau] \times [0, \pi]$ due to Lemma 5.4.4. Hence, $w(a, x)$ is nonnegative on $[0, \tau] \times [0, \pi/2])$, and so $w(\tau, x)$ is nonnegative on $[0, \pi/2]$. Hence, L_τ^2 is positive. Similarly, $w(\tau, x)$ is strictly positive on $[0, \pi/2]$ provided that $\phi(x)$ is nonnegative and not identically zero. So, the operator L_τ^2 is a strongly positive operator. i.e., L_τ^2 maps the nonnegative and not identically zero functions in X_+ into its interior. This completes the proof. ∎

Theorem 5.4.9. *Let $\lambda > -(\delta+\beta)$. Then for each $i = 2,3,4$, the operator L_τ^i admits a principal eigenvalue $p_i(\lambda)$ with a corresponding positive eigenfunction $\phi_i(x) \in X_+ = C_+([0, \frac{\pi}{2}])$. Similarly, for each $i = 2,3,4$, the operator L_0^i admits a principal eigenvalue $\tilde{p}(\lambda)$ with a corresponding positive eigenfunction $\tilde{\phi}(x) \in X_+ = C_+([0, \frac{\pi}{2}])$.*

Proof. The proof is a direct result from Theorem 5.4.7, Theorem 5.4.8, and the second part of the Krien-Rotman Theorem. ∎

Theorem 5.4.10. *Let $\lambda > -(\delta+\beta)$. Then for each $i = 2,3,4$, the operators $L_\tau^i(\lambda)$ and $L_0^i(\lambda)$ vary continuously with λ.*

Proof. The proof of this theorem is similar to the proof of Theorem 5.4.4. ∎

Theorem 5.4.11. *For each $i = 2,3,4$, there exists $\lambda_0^i > -(\delta+\beta)$ such that the corresponding principal eigenvalue $p(\lambda_0^i) = 1$. Moreover, the corresponding positive eigenfunction $\phi_i(x)$ satisfies the equation $L_\tau^i(\lambda_0^i)\phi(x) = p(\lambda_0^i)\phi(x) = \phi(s)$ for each $i = 2,3,4$. The same result holds for the operators L_0^i for each $i = 2,3,4$.*

Proof. The proof of this theorem is a direct result from Theorem 5.4.10 and Remark 5.4.3. ∎

Theorem 5.4.12. *Let λ_0^i and $\tilde{\lambda}_0^i$, for each $i = 2,3,4$, as described in the above theorem. Then for each $i = 2,3,4$, λ_0^i and $\tilde{\lambda}_0^i$, have the same sign.*

Proof. The proof is similar to the proof of Theorem 5.4.6 ∎

Remark 5.4.5. *As a conclusion of Theorem 5.4.5 and Theorem 5.4.11. We remark that if λ_0^i for all $i = 1,2,3,4$ (resp. λ_τ^i for all $i = 1,2,3,4$) is negative, then the zero solution is locally stable.*

5.5 Existence and Stability of Steady-State Solution

In this section, we present our conjuncture for the existence and stability of steady state solutions of the Equations (5.3.11) and (5.3.15), respectively. First, we remark if the transition rate from G_0- phase to P-phase is constant, then the resulting delay differential equations (5.3.11) and (5.3.15) are linear. As a result of the above analysis, Equation (5.3.11) (resp. Equation (5.3.15)) admits a nonnegative and not identically zero (resp. positive) steady state solution $\phi_s(x)$. Due to the properties of the solution of these linear equations, if λ_0^i (or equivalently, $\widetilde{\lambda}_0^i$) is negative for each $i = 1, 2, 3, 4$, then the total cell population $N(t, x)$ converges locally to the zero solution for large time t. If $f(N)$ is non-linear and λ_0^i (or equivalently, $\widetilde{\lambda}_0^i$) is positive for each $i = 1, 2, 3, 4$. We conjecture the existence of a nonnegative and not identically zero (resp. positive) steady state solution $\phi_s(x)$, $x \in [0, \pi/2]$, for the Equations (5.3.11) and (5.3.15), respectively. Moreover, we conjuncture that $\phi_s(x)$ is globally stable under some certain conditions.

To show the existence of steady state solution for the non-linear case, i.e., when $f(N)$ is a non-linear function is not easy. This problem is still open. In the following analysis, we present a technique to show the existence of a such steady state solution and its stability. The main problem in the following analysis is the lack of the compactness of the semiflow solution $\Phi(t)$ (due to the absence of the diffusion term) of Equations (5.3.11) and (5.3.15), respectively. The results in the following analysis are correct if we can show that the semiflow $\Phi(t)$ is α-contraction with a contraction function $k(t) \in (0, 1), \forall t \geq \tau$ (see Definition 2.3.4). However, to show that $\Phi(t)$ is α-contraction this is not easy. Therefore, we keep this as an open problem. Instantly, if we assume this is correct, i.e., the semiflow $\Phi(t)$ is α-contraction, then the following analysis shows the existence and the stability of a unique strongly positive steady state solution under some certain conditions. To go further in our analysis, we impose the function $f(N)$ with the following assumptions:

Assumption

F1: Assume that $f(N) \in C^1(\mathbb{R}^n, \mathbb{R}^n)$, $f(0) = 0$, $f'(0) > 0$, and $f(N)$ is a sublinear function. i.e., $f(\delta N) \geq \delta f(N)$, for all $N \geq 0$, and $\delta \in (0,1)$.

We re-consider the space of continuous functions $X = C_0^1(\left[0, \frac{\pi}{2}\right])$, with its positive cone:

$$X_+ = \{\phi(x) \in X \,|\phi(x) \geq 0\} .$$

Also, we consider the space of functions $Y = C([-\tau, 0], X)$, with its positive cone $Y_+ = C([-\tau, 0], X_+)$.

Remark 5.5.1. *Using the same argument in the proof of theorem 2.1 in [139], we can show that Equation* (5.4.1) *admits a unique solution $N(t, x, \phi)$ on $[-\tau, \infty)$, for all $\phi \in Y_+$. Moreover, by applying Corollary 8.1.3 in [134], Y_+ is positively invariant. i.e., for any $\phi \in Y_+$ the unique solution $N(t, x, \phi) \in Y_+$. Hence, we can define a semiflow $\Phi(t) : Y_+ \to Y_+$ by $(\Phi(t)\phi)(s, x) = u(t + s, x, \phi), \forall s \in [-\tau, 0]$, $x \in [0, \pi/2]$. As we mentioned above, the semiflow $\Phi(t) : Y_+ \to Y_+$ is not compact for all $t > \tau$. Under the assumption that $\Phi(t)$ is α-contraction, we can prove our main results in this section.*

Remark 5.5.2. *Let $g(N) = \delta N + f(N)$, where $f(N)$ satisfies the assumption F1. Then $g \in C^1(\mathbb{R}^+, \mathbb{R}^+)$, $g(0) = 0$, and $g'(0) > 0$. Moreover, there exists a non-negative number M, such that for all $L > M$, $\overline{f}(L) - g(L) < 0$, where $\overline{f}(N) = \exp\left\{-(\frac{g^2}{4D} + \gamma)\tau\right\} \max_{\nu \in [0,N]} f(\nu)$. Using the same technique in the proof of Theorem 2.1 in [139], we can show that $\limsup_{t\to\infty} N(t, x, \phi) \leq M$ for all $x \in [0, \frac{\pi}{2}]$. Hence, $\Phi(t) : Y_+ \to Y_+$ is point dissipative.*

Remark 5.5.3. *Since $\Phi(t) : Y_+ \to Y_+$ is α-contraction for all $t > \tau$, and point dissipative. Then, by the above remarks, the semiflow $\Phi(t)$ admits a connected global attractor which attracts each bounded set in Y_+ (by the continuous time version of Theorem 1.1.2 [144], see also the proof of Theorem 3.1 in [142]).*

In the following lemma, we show that the zero solution is a weak repeller for

$$Y_0 = \left\{ \phi \in Y^+ : \phi(0,.) \not\equiv \theta \right\},$$

in the sense that there exists δ_0 such that $\limsup_{t\to\infty} \|\Phi(t)\phi\|_X \geq \delta_0$, $\forall \phi \in Y_0$. In fact, this implies that $\Phi(t)$ is uniformly persistent with respect to Y_0 (See Theorem 4.6 in [121]). We mean by the uniform persistence of the semiflow $\Phi(t)$ with respect to Y_0, that there exists $\delta_1 > 0$ such that

$$\liminf_{t\to\infty} dist(\Phi(t)\phi, \partial Y_0) \geq \delta_1, \quad \forall \phi \in Y_0,$$

where $\partial Y_0 := Y \setminus Y_0$.

Lemma 5.5.1. *Let Y_0 as described above and assume that $\tilde{\lambda}_0^1 > 0$. Then the semiflow $\Phi(t) : Y_+ \to Y_+$ is uniformly persistent.*

Proof. To show that $\Phi(t)$ is uniformly persistent it is enough to show that the zero is uniform weak repeller for Y_0, see Theorem 4.6 in [121]. i.e., we have to show that there exists a $\delta_0 > 0$ such that

$$\liminf_{t\to\infty} \|\Phi(t)\phi\| \geq \delta_0, \qquad \forall \phi \in Y_0.$$

We can prove this by following the same argument in the proof of Theorem 3.1 in [139]. The proof is by contradiction. Let us consider the eigenvalue problem (5.4.3).

Since this equation admits a positive eigenvalue λ_0^1, see section (4), then there exists a sufficiently small number $\epsilon > 0$, such that the following eigenvalue problem

$$\begin{cases} \lambda N(t,x) = -\delta N(t,x) - (f'(0)+\epsilon)N(t,x) + \frac{4\beta}{\pi}h(\tau,2x)e^{-\lambda\tau} \\ \times(f'(0)-\epsilon)\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, N(y)dy \quad x\in(0,\pi/2), \\ N(0)=N(\pi/2)=0, \end{cases} \tag{5.5.1}$$

admits a positive eigenvalue λ_ϵ with a corresponding eigenfunction $\phi_\epsilon(x)$. Moreover, $f'(0)=\beta$. So, there exists $\delta_\epsilon > 0$ such that

$$f(N) > (f'(0)-\epsilon)N \quad \text{and} \quad f(N) < (f'(0)+\epsilon)N, \quad \forall N \in (0,\delta_\epsilon).$$

Let $\delta_0 = \delta_\epsilon/k$ (k is a positive constant that satisfies the relation $\|.\|_\infty \le k\|.\|_X$). Assume there exists $\phi_0 \in Y_0$ such that

$$\limsup_{t\to\infty} \|\Phi(t)\phi\|_X < \delta_0.$$

Then there exists a $t' > \tau$ such that

$$\|N(t,.,\phi_0)\|_\infty \le k\|N(t,.,\phi_0)\|_X < \delta_\epsilon, \quad \forall t \ge t'-\tau. \tag{5.5.2}$$

Therefore, $N(t,x,\phi_0) \in (0,\delta_\epsilon)$, $\forall t \ge t'-\tau$. Hence, $N(t,x,\phi)$ satisfies the following inequality:

$$\begin{aligned} \frac{dN(t,x)}{dt} &> -\delta N(t,x) - (f'(0)+\epsilon)N(t,x) + \frac{4\beta}{\pi}h(\tau,2x)e^{-\lambda\tau} \\ &\times \ (f'(0)-\epsilon)\int_0^{\pi/2} K_\tau^1(x,y)\, e^{\frac{-g}{2D}y}\, N(y)dy, \quad t\ge t' \quad x\in(0,\pi/2). \end{aligned} \tag{5.5.3}$$

Since $N(t,x,\phi_0) > 0$, $\forall t > 0, \forall x \in (0,\pi/2)$, then there exists $\eta > 0$ such that

$N(t'+s,x,\phi_0) \geq \eta N_\epsilon(s,x)$, $s \in [-\tau, 0]$ and $x \in [0,\pi]$, where $N_\epsilon(t,x) = \phi_\epsilon(x)e^{\lambda_\epsilon t}$ is the solution of the linear differential equation (5.5.1). Using the Inequality (5.5.3) and the comparison principle, we have

$$N(t,x,\phi_0) \geq \eta N_\epsilon(t-t') = \eta\phi_(x)\epsilon e^{\lambda_\epsilon(t-t')},$$

which is unbounded when $t \to \infty$. This is a contradiction. ∎

Remark 5.5.4. *We remarked (Remark 1) that the semiflow $\Phi(t) : Y_+ \to Y_+$ is α-contraction (assumption), and point dissipative. Also, we showed in the previous lemma that the semiflow $\Phi(t)$ is uniformly persistent for Y_0. Similarly, we can show that $\Phi_0(t) : X_+ \to X_+$ is α-contraction (assumption), point dissipative, and uniformly persistent. Hence, by 2.3.3 there exists at least one steady state solution. Following the same argument in the proof of Theorem 3.2 in [139]. The strongly positive steady state solution $\phi_s(x)$ is unique provided that $f(N)$ is a strictly subhomogeneous function; and Therefore, we have the following existence theorem.*

Theorem 5.5.1. *Assume that F1 holds, and $\tilde{\lambda}_0^1 > 0$. Then the non-linear delay differential equation* (5.4.1) *admits a unique steady state solution $\phi_s(x)$ with $\phi_s(x) \in (0, M], \forall x \in (0, \pi/2)$.*

Remark 5.5.5. *If we assume that $\tilde{\lambda}_0^1 > 0$, and the transition function $f(N)$ is a strictly monotone function on $[0,\infty)$, then the semiflow $\Phi(t)$ is strongly monotone. Similar to the proof of Theorem 3.2 [142], we can show that the unique steady state solution $\phi_s(x)$ is globally stable; and Hence, we have the following result.*

Theorem 5.5.2. *Assume that $\tilde{\lambda}_0^1 > 0$, and $f(N)$ satisfies the condition (F1). Moreover, assume that $f(N)$ is monotone increasing function on $[0,\infty)$. Then the unique* *positive steady state solution $\phi_s(x)$ satisfies*

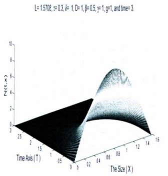
$$lim_{t\to\infty} \|N(t,.,\phi) - \phi_s(.)\|_X = 0$$

for any non-zero $\phi \in Y_+ \setminus \{0\}$.

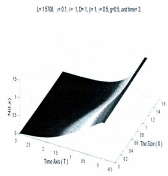
Remark 5.5.6. *The above results hold for the delay differential equations that are given in Equation* (5.3.15).

5.6 Numerical Simulation

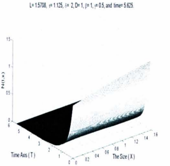
In this section, we present a numerical simulation to investigate the long time behavior of the solution $N(t,x)$. In this simulation, we consider the Hill function $f(N) = \frac{\beta N}{1+N}$. To evaluate the non-local term that is given in the Equations (5.3.11) and (5.3.15), we apply the composite Simpson's rule. To estimate the solution $N(t,x)$ at the mesh points $x_i, i = 1, 2, \cdots, N$, we solve the the delay differential equation that is given in Equation (5.3.11) and Equation (5.3.15) using the method of lines. This numerical simulation shows that the solution $N(t,x)$ either converges to the zero solution (see Figure 5.2), or to a positive solution (nonnegative and not identically zero in Dirichlet boundary conditions case)(see Figure 5.3).



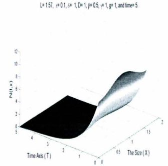
(a) Case I: The values of the parameters are $L = \frac{\pi}{2}$, $\tau = 0.3$, $D = 1$, $\delta = 0.5$, $\beta = 0.5$, $\gamma = 1$, and $g = 1$. The initial condition is $\phi(s, x) = \sin 2x$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $N(t, x)$ converges to the zero solution for large time t



(b) Case II. The values of the parameters are $L = \frac{\pi}{2}$, $\tau = 0.1$, $D = 1$, $\beta = 0.5$, $\delta = 1$, $\gamma = 1$, and $g = 1$. The initial condition is $\phi(s, x) = \exp\left\{-(\frac{g}{2D})x\right\}$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $N(t, x)$ converges to the zero solution for large time t.

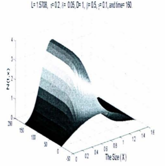


(c) Case III: The values of the parameters are $L = \frac{\pi}{2}$, $\tau = 1.125$, $\delta = 2$, $D = 1$, $\beta = 1$, $\gamma = 0.5$, and $g = 0.5$. The initial condition is $\phi(s, x) = \cos \alpha_1 x + \frac{g}{2\alpha_1 D} \sin \alpha_1 x$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $N(t, x)$ converges to the zero solution for large time t.

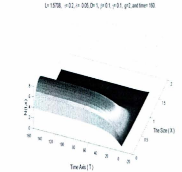


(d) Case IV: The values of the parameters are $L = \frac{\pi}{2}$, $\tau = 0.3$, $D = 1$, $\delta = 1$, $D = \beta = 0.5$, $\gamma = 1$, and $g = 1$. The initial condition is $\phi(s, x) = 1 - \cos 2x$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $N(t, x)$ converges to the zero solution for large time t

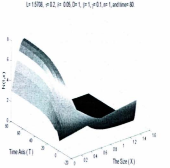
Figure 5.2: For large time t the total cell population $N(t, x)$ in G_0 − phase converges to the zero solution.



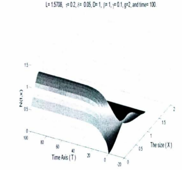
(a) Case I. The values of the parameters are $L = \frac{\pi}{2}$, $\tau = 0.2$, $\delta = 0.05$, $D = 5$, $\beta = 0.5, \gamma = 0.1$, and $g = 1$. The initial condition is $\phi(s, x) = \sin 2x$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $N(t, x)$ converges to a nonnegative and not identically zero for large time t.



(b) Case II. The values of the parameters are $L = \frac{\pi}{2}$, $\tau = 0.2$, $\delta = 0.05$, $D = 1$, $\beta = 0.1$, $\gamma = 0.1$, and $2 = 2$. The initial condition is $\phi(s, x) = \exp\left\{-(\frac{g}{2D})x\right\}$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $N(t, x)$ converges to a positive solution for large time t.



(c) Case III. The values of the parameters are $L = \frac{\pi}{2}\pi$, $\tau = 0.2$, $\delta = 0.05$, $D = 1$, $\beta = 1$, $\gamma = 0.1$ and $g = 2$. The initial condition is $\phi(s, x) = \phi(s, x) = \cos \alpha_1 x + \frac{g}{2\alpha_1 D} \sin \alpha_1 x$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to a nonnegative and not identically zero solution for large time t.



(d) Neumann boundary conditions case. The values of the parameters are $L = \frac{\pi}{2}$, $\tau = 0.2$, $\delta = 0.05$, $D = 1$, $\beta = 2$, $\gamma = 0.1$, and $g = 2$. The initial condition is $\phi(s, x) = 1 - \cos 2x$, $0 \leq x \leq \frac{\pi}{2}$; $0 \leq s \leq 0.3$. In this case, the solution $w(t, x)$ converges to a positive solution for large time t.

Figure 5.3: For large time t the total cell population $N(t, x)$ in G_0 − phase converges a to positive solution.

Chapter 6

A Non-local Reaction Diffusion Model for Adhesion in Cell Aggregation and Cancer Invasion

6.1 Introduction

It is thought that the selective adhesion is responsible for certain types of tissue breakdown, as well as it is recognized as a factor in the invasion and metastasis of tumor cells. Basically, a cell-cell adhesion is a biological phenomenon describing the binding of one cell to another through cell surface proteins known as adhesion molecules (CAMs) [6, 42]. The earliest mathematical studies for this phenomenon were done by Graner and Galzier in 1992-1993 [45, 51], where they adopted the Pott model in physics to a biological cell population. Recently, in 2006, Armstrong et al. have derived mathematical model to describe the cell adhesion phenomenon. This model is given in the following non-local reaction diffusion equation:

$$\frac{\partial}{\partial t}n(t,x) = D\frac{\partial^2}{\partial x^2}n(t,x) - \frac{\partial}{\partial x}(n(t,x)\,K(n(t,x))), \tag{6.1.1}$$

where

$$K(n(t,x)) = \frac{\alpha\phi}{R}\int_{-R}^{R} g(n(t,x+y))\omega(y)dy.$$

Here, ϕ is a constant of proportionality related to viscosity, D is the diffusion rate, α is a positive parameter reflecting the strength of adhesion force between the cells, and R describes the radius over which cells can sense their surroundings. The function $g(n)$ is given in the following formula:

$$g(n) = \begin{cases} n(1-n/M), & n < M, \\ 0, \quad o.w., & \end{cases} \tag{6.1.2}$$

here the constant M represents the crowding capacity of the population. The function $\omega(y)$ is considered to be an odd function with

$$\omega(y) = \begin{cases} > 0, \; y > 0, \\ < 0, \; y < 0. \end{cases}$$

For the simplicity, we consider

$$\omega(y) = \begin{cases} 1, \; -R < y < 0, \\ -1, \; 0 < y < R. \end{cases} \tag{6.1.3}$$

Using the following scaling

$$x^* = \frac{x}{R}, \quad t^* = \frac{Dt}{R^2}, \quad n^* = \frac{n}{n_0}, \quad \alpha^* = \frac{\alpha\phi RM}{D},$$

Equation(6.1.1) is non-dimesionalised to

$$\frac{\partial}{\partial t}n(t,x) = \frac{\partial^2}{\partial x^2}n(t,x) - \frac{\partial}{\partial x}(n(t,x)\, K(n(t,x))), \quad (6.1.4)$$

where

$$K(n(t,x)) = \alpha \int_{-1}^{1} g(n(t,x+y))\omega(y)dy,$$

and the non-dimensionalise logistic force function $g(n)$ is $g(n) = n(1-n)$. Using the linear stability, the authors showed that the homogeneous steady state solution U is unstable provided that

$$\frac{1}{2\alpha U}k^2 < 1 - cos(k),$$

where the constant k is the wave number.

Since the above model does not take into account the cell division as well as the cell lose. Sherratt et al. [110] modified Armstrong model by adding a cell kinetics function $f(n)$ ($f(n)$ represents the cell division and cell lose). The new model is given by the following non-local reaction diffusion equation:

$$\frac{\partial}{\partial t}n(t,x) = D\frac{\partial^2}{\partial x^2}n(t,x) - \frac{\partial}{\partial x}(n(t,x)\, K(n(t,x))) + f(n), \quad (6.1.5)$$

where

$$K(n(t,x)) = \frac{\alpha\phi}{R}\int_{-R}^{R} g(n(t,x+y))\omega(y)dy.$$

The parameters ϕ, D, α and R are as described above. The functions $g(n)$ and $\omega(y)$ were given in Equation (6.1.2) and Equation (6.1.3), respectively. The standard choice of the function $f(n)$ is the logistic function. i.e., $f(n) = \mu\, n\,(1 - n/n_0)$, where μ is a positive constant. Again, to non-dimensionalise this equation the authors used the following scaling:

$$x^* = \frac{x}{R}, \quad t^* = \frac{Dt}{R^2}, \quad n^* = \frac{2n}{M}, \quad \alpha^* = \frac{\alpha\phi M}{4D}, \mu^* = \frac{\mu R^2}{D}, \quad n_0^* = \frac{2n_0}{M}.$$

The non-dimensionalise problem is given as:

$$\begin{aligned}\frac{\partial n(t,x)}{\partial t} &= \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha\frac{\partial}{\partial}\left[n(t,x)\int_{-1}^{1} \max\{n(t,x+y)(2-n(t,x+y)),0\}\, sign(y)\,dy\right] \\ &+ \mu n(1-n/n_0). \end{aligned} \tag{6.1.6}$$

If $n_0 < 2$, then $n = n_0$ is a homogeneous steady state solution for this equation. The linear stability shows that $n = n_0$ is unstable provided that

$$4\alpha n_0(1-n_0) > \frac{4\theta^2+\mu}{2\sin^2\theta},$$

where $\theta \in (0, \pi/2)$ is the solution of $\tan\theta = \frac{4\theta^2+\mu}{4\theta}$ [110]. In this paper, the authors also supported their results by a numerical simulation (see section 3, [110]). Now, it is natural to ask the following questions:

1. How the solution pattern looks if we replace the Numann's boundary conditions by Dirichlet boundary conditions? Do we have a nonnegative and not identically zero solution for this problem?

2. If R is large, what about the existence of traveling wave solution for this model?

6.2 Numerical Simulation

In this section, we present a numerical simulation to the reaction diffusion equation (6.1.6). If we assume that $n_0 < 2$, then Equation (6.1.6) becomes as the following:

$$\begin{aligned}
\frac{\partial n(t,x)}{\partial t} &= \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha \frac{\partial}{\partial x}\left[n(t,x)\int_{-1}^{1}[n(t,x+y)(2-n(t,x+y))]\, sign(y)\, dy\right] \\
&+ \mu n(1-n/n_0) \\
&= \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha \frac{\partial}{\partial x}\left[n(t,x)\int_{-1}^{1} f(n(t,x)) sign(y)\, dy\right] + \mu n(1-n/n_0) \\
&= \frac{\partial^2 n(t,x)}{\partial x^2} - \alpha \frac{\partial}{\partial x}[n(t,x)K(n(t,x))] + \mu n(1-n/n_0). \qquad (6.2.1)
\end{aligned}$$

In this numerical simulation, we use the method of lines to approximate the solution $n(t,x)$ of the above equation. To have more description to our numerical scheme, we let $x_0 = -1, \cdots, x_{N+1} = 1$ be $(N+2)$-discretization of the interval $[-1,1]$. Then the difference formula for Equation (6.2.1) is given by:

$$\begin{aligned}
n_t(t,x_k) &= \frac{n(t,x_{k+1}) - 2n(t,x_k) + n(t,x_{k-1})}{h^2} \\
&- \alpha\left[\frac{n(t,x_{k+1}) - n(t,x_{k-1})}{2h} K(t,x_k) + n(t,x_k)\frac{K(t,x_{k+1}) - K(t,x_{k-1})}{2h}\right] \\
&+ \mu\left[n(t,x_k)\left(1 - \frac{n(t,x_k)}{n_0}\right)\right], \qquad (6.2.2)
\end{aligned}$$

where

$$K(t,x_k) = \int_{-1}^{1} f(n(t,x_k+y))\, sign(y)\, dy. \qquad (6.2.3)$$

To approximate the above integral, we expand $f(n(t,x+y))$ at x using Taylor's expansion (eg. see [44]). Then we have

$$f(n(t,x+y)) = \sum_{j=0}^{s} \frac{y^j}{j!}\frac{d^j}{dx^j} f(n(t,x)) + O(y^{s+1}),$$

where s is an even integer. Multiply this equation by $sign(y)$, and then integrate over the interval $[-1,1]$ (recall that $sign(y)$ is odd function). we get

$$\begin{aligned}\int_{-1}^{1} f(n(t,x+y))\, sign(y)\, dy &\approx \int_{-1}^{1}\left(\sum_{j=0}^{s}\frac{y^j}{j!}\frac{d^j}{dx^j}f(n(t,x))\right) sign(y)dy \\ &= 2\sum_{j=0}^{\frac{s}{2}-1}\frac{d^{(2j+1)}}{dx^{(2j+1)}}\left(f(n(t,x))\right)\int_0^1\frac{y^{2j+1}}{(2j+1)!}dy \\ &= 2\sum_{j=0}^{\frac{s}{2}-1}\frac{1}{(2j+2)!}\frac{d^{(2j+1)}}{dx^{(2j+1)}}\left(f(n(t,x))\right). \qquad (6.2.4)\end{aligned}$$

Consider the first term of the above approximation, and then substitute in Equation (6.2.2), to get the following difference formula:

$$\begin{aligned}n_t(t,x_k) &= \frac{n_{k+1}-2n_k+n_{k-1}}{h^2} \\ &- \frac{\alpha}{2h^2}\left[(1-n_k)\left(n_{k+1}-n_{k-1}\right)^2\right] \\ &- \frac{\alpha}{2h^2}\left[n_k\left(1-n_{k+1}\right)\left(n_{k+2}-n_k\right)\right] \\ &- \frac{\alpha}{2h^2}\left[n_k\left(1-n_{k-1}\right)\left(n_k-n_{k-2}\right)\right] \\ &+ \mu\left[n(t,x_k)\left(1-\frac{n(t,x_k)}{n_0}\right)\right], \qquad (6.2.5)\end{aligned}$$

where $k=2,\cdots,N-1$. We can evaluate $n(t,x_k)$ at $k=0,1,N,N+1$ by using the boundary conditions at $x=-1$ and $x=1$. To solve this non-linear ODE system, we use the function ODE15S in MATLAB. The results of this simulation take place in Figure 6.1, Figure 6.2, Figure 6.3, and Figure 6.4.

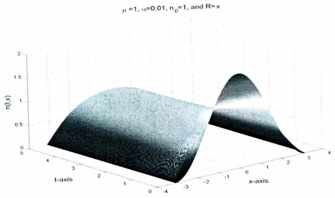


Figure 6.1: Dirichlet boundary conditions case. The values of the parameters are $R = \pi$, $\mu = 1$, $\alpha = 0.01$, and $n_0 = 1$. The initial condition is $\phi(x) = 1 + \sin(\frac{\pi}{2} - x)$, $-\pi \leq x \leq \pi$. In this case, the solution $n(t, x)$ converges to a nonnegative and not identically zero solution for large time t.

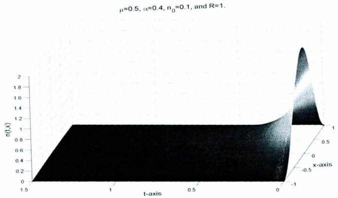


Figure 6.2: Dirichlet boundary conditions case. The values of the parameters are $R = \pi$, $\mu = 0.5$, $\alpha = 0.4$, and $n_0 = 0.1$. The initial condition is $\phi(x) = 1 + \sin(\frac{\pi}{2} - \pi x)$, $-1 \leq x \leq 1$. In this case, the solution $n(t, x)$ converges the zero solution for large time t.

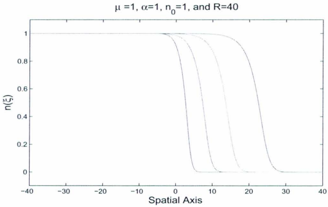


Figure 6.3: Traveling wave solution. The values of the parameters are $R = 40$, $\mu = 1$, $\alpha = 1$, and $n_0 = 1.$. The initial data is $\phi(x) = 0$, $x \geq 0$, and $\phi(x) = 1$, $x < 0$,

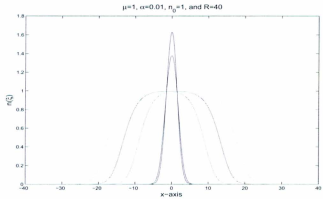


Figure 6.4: Traveling wave solution. The values of the parameters are $R = 40$, $\mu = 1$, $\alpha = 0.01$, and $n_0 = 1$. The initial data is $\phi(x) = \frac{3}{\sqrt{\pi}} \exp\{-x^2/4\}$.

As a conclusion, the numerical simulation shows that the reaction diffusion equation (6.1.6) admits a nonnegative and not identically zero steady state solution, as well it shows that Equation (6.1.6) admits a traveling wave solution.

6.3 Discussion and Future Work

As we mentioned in the previous section. The numerical simulation shows that the non-local reaction diffusion equation (6.1.6) admits a nonnegative and not identically zero steady state solution, when the boundary conditions are of the Dirichlet type. Also, it shows that (6.1.6) admits a traveling wave solution. Therefore, for the future work, we expect to prove this analytically. In fact, we wish to investigate the following problems:

1. The existence and stability of a nonnegative steady state solution for Equation (6.1.6), when the boundary conditions are of Dirichlet type.

2. The existence of a traveling wave solution of Equation (6.1.6), provided that R is large (i.e., The domain is unbounded).

Bibliography

[1] M. Al-Jorarha, C. Ou, *Population dynamics with age-dependent diffusion and death rates*, submitted.

[2] J. F. M. Al-Omari, S. A. Gourley, *Monotone traveling fronts in an age-structured reaction-diffusion model of a single species*, J. of Math. Biol., **45**(2002), pp. 294–312.

[3] F. M. Al-Omari, S. A. Gourley, *Monotone wave-fronts in a structured population model with distributed maturation delay*, IMA J. Appl. Math., **70** (2005), 858-879.

[4] J. C. Arciero, T. L. Jackson, D. E. Kirschner, *A mathematical model of tumor-immune evasion and siRNA treatment*, Discrete and Continuous Dynamical Systems-series, **4**(2004), No. 1, pp. 39-58.

[5] O. Arino, E. Sánchez, *A survey of cell population dynamics*, Computational and Mathematical Methods in Medicine, **1** (1997), pp. 35–51.

[6] N. J. Armstrong, K. J. Painter, J. A. Sherratt, *A continuum Approach to Modeling Cell-cell Adhesion*, Journal of Theoretical Biology, **243**(2006), pp. 98–113.

[7] D. G. Aronson and H. F. Weinberger, *Nonlinear diffusion in population genetics, combustion, and nerve pulse propagation*, Lecture notes in Mathematics, **446** (1975), Springer-Verlag, pp. 5-49.

[8] D. G. Aronson and H. F. Weinberger, *Multidimentional nonlinear diffusion arising in population genetics*, Adv. Math., **30** (1978), pp. 33-76.

[9] F. M. Atici, G. S. Guseinov, *On the existence of positive solutions for nonlinear differential equations with periodic boundary conditions*, Journal of Computational and Applied Mathematics, **132**(2001), pp. 341–356.

[10] N. Bacaer , *A Short History of Mathematical Population Dynamics* , Springer-Verlag London Limited, London, 2011.

[11] B. Basse, B. C. Baguley, E. S. Marshall, W. R. Joseph, G. Wake, D. J. N. Wall, *Modeling the flow of cytometric data obtained from unperturbed human tumour cell lines: parameter fitting and comparison*, Bulletin of Mathematical Biology, **67**(2005), pp. 815–830.

[12] B. Basse, B. C. Baguley, E. S. Marshall, W. R. Joseph, B. V. Brunt, G. Wake, D. J. N. Wall, *A mathematical model for analysis of the cell cycle in human tumours*, J. Math. biology, **47**(2003), pp. 295–312.

[13] B. Basse, B. C. Baguley, E. S. Marshall, W. R. Joseph, B. V. Brunt, G. Wake, D. J. N. Wall, *Modelling cell death in human tumour cell lines exposed to the anticancer drug paclitaxel*, J. Math. biology, **49**(2004), pp. 329–357.

[14] B. Basse, P. Ubezio, *A generalised age- and phase-structured model of human tumour cell populations both unpertubed and exposed to a range of cancer therapies*, Bulletin of Mathematical Biology, **69**(2007), pp. 1673–1690.

[15] R. E. Begg, D. J. N. Wall, G. C. Wake, *The steady-state of a multi-compartment, age-size distribution model of cell-growth*, Eurc. Jnl of Applied Mathematics , **19**(2008), pp. 435–458.

[16] J. Belair, M. C. Mackey, J. M. Mahaffy, *Age-structured and two delay models for erythpoiesis*, Math. Biosci., **128**(1995), pp. 317–346.

[17] G. I. Bell, E. C. Anderson, *Cell Growth and division I. A mathematical model with applications to cell volume distribution im mammalian suspension cultures*, Biophysical Journal, **7**(1967), pp. 329–351.

[18] W. A. Beyer, *Solutions to a mathematical model of cell growth, division, and death*, Mathematical Biosciences, **6**(1970), pp. 431–436.

[19] F. Brauer, P. van den Driessche, J. Wu, *Mathematical Epidemiology*, Lecture Notes in Mathematics, Mathematical Biosciences Subseries. Springer-Verlag, Berlin, 2008.

[20] F. Brauer, C. C. Chávez, *Mathematical Models in Population Biology and Epidemiology*, Springer, New York, 2001.

[21] N. F. Britton, *Reaction-Diffusion Equations and Their Applications to Biology*, Academic Press, New York, 1986.

[22] J. W. Brown, R.V. Churchill, *Fourier series and boundary value problems*, 7^{th} Edition, McGraw Hill, 2008.

[23] S. J. Chapman, M. J. Plank, A. James, b. Basse, *A nonlinear model of age and size-structured population with applications to cell cycles*, ANZIAM J., **49**(2007), No. 1, pp. 151-169.

[24] B. Charlesworth, *Evolution in Age-Structured Population*, Second Edition, Cambridge University Press, UK, 1994.

[25] A. Chauviére, L. Prezios, C. Verdier, *Cell mechanics from single-based models to multiscale modeling*,Champan and Hall, UK, 2010

[26] T. Cohen, D. P. Cooney, *Cyclical thrombocytopenia: case report and review of literature*, Scand. J. Haematol., **16**(1974), pp. 133–138.

[27] J. M. Cushing, *An introduction to structured Population Dynamics*, Society for Industrial and Applied Mathematics, USA, 1998.

[28] L. Debanth, *Nonlinear Partial Differential Equations for Scientist and Engineers*, Second Edition, Birkhäuser, USA, 2006.

[29] O. Diekmann, H. J. A. M. Heijmans, H. R. Thieme, *On the stability of the cell size distribution*, J. Math. biology, **19**(1984), pp. 227–248.

[30] O. Diekmann, J. A. P. Heesterbeek, *Mathematical Epidemiology of Infectious Diseases*, John Wiley and Sons Ltd, UK, 2000.

[31] O. Diekmaann, *Thresholds and traveling waves for the geographical spread of infection*, J. Math. Biol, **6** (1978), pp. 109-130.

[32] O. Diekmann, *Run for your life, A note on the asymptotic speed of propagation of an epidemic*, J. Differential Equations, **33** (1979), pp. 58-73.

[33] O. Diekmann, H. G. Kapper, *On the bounded solutions of a nonlinear convolution equations*, Nonlinear Analysis, Theory, Method and applications, **2** (2003), pp. 721–737.

[34] I. Drobnjak, A. C. Fowler, M .C. Mackey, *Oscillations in a maturation model of blood cell production*, SIAM J. Appl. Math., **66**(2006), No. 6, pp. 2027–2048.

[35] J. Fang, X.-Q. Zhao, *Spreading speeds and traveling waves for non-monotone time-delayed lattice equations*, Proceedings of The Royal Society of London Series A Mathematical, Physical and Engineering Sciences, **466** (2010), pp. 1919-1934.

[36] J. Fang , X.-Q. Zhao, *Existence and uniqueness of traveling waves for non-monotone integral equations with applications*, Journal of Differential Equations, **248** (2010), pp. 2199-2226.

[37] J. Fang, X.-Q. Zhao, *Monotone wavefronts for partially degenerate reaction-diffusion systems*, Journal of Dynamics and Differential Equations, **21** (2009), pp. 663-680.

[38] R. A. Fisher, *The wave of advance of advantageous genes*, Annals of Eugenics, **7** (1937), pp. 355-369.

[39] H. Von Foerster, Some remarks on changing populations, *The Kinetics of Cellular Proliferation*, Grune & Stratton, New York, (1959) 384-407.

[40] C. Foley, M. C. Mackey, *Dynamics hematological disease: a review*, J. Math. Biol., **58**(2009), pp. 285–322.

[41] P. Fortin, M. C. Makey, *Periodic chronic myelogenous leukemia: spectral analysis of blood cell counts and etiological implications*, Brit. J. Haematol., **104** (1999), pp. 336–345.

[42] R. A. Foty, M. S. Steinberg, *The Differential Adhesion Hypothesis: A Direct Evaluation*, Developmental Biology, **278** (2005), pp. 255-263.

[43] A. C. Fowler, M .C. Mackey, *Relaxation Oscillations in a class of delay differential equations*, SIAM J. Appl. Math., **63**(2002), No. 1, pp. 299–323.

[44] A. Gerisch, M. A. J. Chaplain, *Mathematical modeling of cancer cell invasion of tissue: local and non-local models and the effect of adhesion*, J. of Theoretical biology, **250**(2008), pp. 684–704.

[45] J. A. Glazier, F. Graner, *Simulation of Biological Cell Sorting Using a Two-dimensional Extended Potts Model*, Phys. Rev., **47** (1993), pp 2128-2154.

[46] S. A. Gourley and Y. Kuang, *Wavefronts and global stability in a time-delayed population model with stage structure*, Proc. R. Soc. Lond., Ser., **459** (2003), pp. 1563-1579.

[47] S. A. Gourley and J. Wu, *Delayed non-local diffusive systems in biological invasion and disease spread*, Fields Inst. Commun., **48** (2006), pp. 137-200.

[48] S. A. Gourley, J. W.-H. So, and J. Wu, *Non- locality of reaction-diffusion equations induced by delay: biological modeling and nonlinear dynamics*, Journal of Mathematical Science, **124** (2004), No. 4, pp. 5119–5153.

[49] S. A. Gourley, J. W.-H. So, *Extinction and wavefront propagation in a reaction-diffusion model of a structured population with distributed maturation delay*, Proceedings of the Royal Society of Edinburgh, **133A** (2003), pp. 527–548.

[50] M. Golubitsky, E. Knobloch, I. Stewart, *Target patterns and spirals in planar reaction-diffusion systems*, J. Nonlinear Sci., **10** (2000), pp. 333Ű-354.

[51] F. Graner, J. A. Glazier, *Simulation of the Differential Adhesion Driven Rearrangement of Biology Cells*, Phys. Rev. Lett., **69** (1992), pp 2013-2016.

[52] P. Grindrod, *The Theory and Applications of Reaction-Diffusion Equations, Patterns and Waves*, Oxford University Press, New York, 1996.

[53] D. Guo, V. Lakshmikantham, Nonlinear problems in abstract cones, Acadimic Press Inc., London, 1988.

[54] M. Gyllenberg, H. J. A. M. Heijmans, *An Abstract delay-differential equation modelling size dependent cell growth and division*, SIAM J. Math. Anal., **18**(1987), No. 1, pp. 74-88.

[55] K. P. Hadeler, F. R. Tübingen, *Traveling Fronts in Nonlinear Diffusion Equations*, J. Math. Biol., **2** (1975), pp. 251 - 263.

[56] J. K. Hale, *Asymptotic behavior of dissipative systems*, Math. Survey and Monographs 25, AMS, providence, RI, 1988.

[57] J. K. Hale, Paul Waltman, *Persistence in infinite dimensional systems*, SIAM Journal of Mathematical Analysis, **20** (1989), No. 2, pp. 338–395.

[58] K. B. Hannsgen, J. J. Tyson, *Stability of the steady-state size distribution in a model of cell growth and division*, J. Math. biology, **22**(1985), pp. 293–301.

[59] C. Haurie, D. C. Dale, M. C. Makey, *Cyclical neutropenia and other periodic hematological diseases: a review of mechanisms and mathematical models*, Blood, **92** (1998), pp. 2629–2640.

[60] C. Haurie, D. C. Dale, R. Rudnicki., M. C. Makey, *Modeling complex neutrophil dynamics in the grey collie*, J. Theor. Biol., **204** (2000), pp. 504–519.

[61] T. Hearn, C. Haurie, M. C. Makey, *Cyclical neutropenia and the peripheral control of white blood cells production*, J. Theor. Biol., **192** (1998), pp. 167–181.

[62] M. W. Hirsch, *The dynamical systems approach to differential equations*, AMS, **11** (1984), no. 1, pp. 1–64.

[63] H. Hochstadt, *Integral Equations*, John Wiley and Sons, New Yourk, 1973.

[64] J. V. Huddleston, *Population dynamics with Age and time-dependent birth and death rates*, Bulletin of Mathematical biology, **45**(1983), No. 5, pp. 827–836.

[65] S. Hsu, X.-Q. Zhao, *Spreading speeds and traveling waves for non-monotone integrodifference equations*, SI AM J. Math. Anal, **40** (2008), pp. 776-789.

[66] Y. Jin, X.-Q. Zhao, *Spatial dynamics of a nonlocal periodic reaction-diffusion model with stage structure*. SIAM J. Math. Anal. **40** (2009), No. (6), pp. 2496–2516.

[67] M. A. Krasnosel'skii, *Positive Solutions of Operator Equation*, P. Noordhoff, Groningen, The Netherlands, 1964.

[68] A. Kolgomorov, N. Petrovsky, N. S. Picoounov, *A study of the equation of diffusion with increase in thequantity of matter, and its application to a biological problem*, Moscow Bulletin of Mathematics, **1** (1937), pp. 1-25.

[69] N. Kopell, *Target pattern solutions to reaction-diffusion equations in the presence of impurities*, Adv. Appl. Math., **2** (1981), pp. 389Ű-399.

[70] M. Kot, *Elements of Mathematical ecology*, Cambridge University Press, UK, 2001.

[71] M. K. Kwong, *On Krasnoselskii's Cone Fixed Point Theorem*, Fixed Point Theory and Applications, Hindawi Publishing Corporation, Volume 2008, PP 1-18.

[72] M. K. Kwong, C. Ou, *Existence and nonexistence of Monotone Traveling Waves for the Delayed Fisher Equation*, Journal of Differential Equations, **249**, Issue 3 (2010), pp. 728-745.

[73] A. Lasota, M. C. Mackey, *Cell division and the stability of cellular populations*, J. Math. biology, **38**(1999), pp. 241–261.

[74] B. Li, M. A. Lewis and H. F. Weinberger, *Existence of traveling waves for integral recursions with nonmonotone growth functions*, Journal of Mathematical Biology **58** (2009), pp. 323-338.

[75] B. Li, H. F. Weinberger and M. A. Lewis, *Spreading speeds as slowest waves speeds for cooperative systems*, Math. Biosci., **196** (2005), pp. 82-98.

[76] X. Liang, Y. Yi and X.-Q. Zhao, *Spreading speeds and traveling waves for periodic evolution systems*, J. Differential Equations, **231** (2006), pp. 57-77.

[77] X. Liang and X.-Q. Zhao, *Asymptotic speeds of spread and traveling waves for monotone semiflows with applications*, Coram. Pure Appl. Math., **60** (2007), pp. 1-40. Erratum: 61(2008), pp. 137-138.

[78] X. Liang, X.-Q. Zhao, *Spreading speeds and traveling waves for abstract monostable evolution systems*, Journal of Functional Analysis, **259**(2010), pp. 857-903.

[79] D. Liang, J.Wu, *Travelling waves and numerical approximations in a reaction advection diffusion equation with nonlocal delayed effects*, J. Nonlinear Sci., **13** (2003), 289–310.

[80] D. Liang, J. W.-H So, F. Zhang, X. Zou, *Population dynamics models with nonlocal delay on bounded domains and their numerical computation*, Differential Equations and Dynamical Systems, Vol. **11**(2003), Nos. 1&2, pp. 117–139.

[81] J. D. Logan, *An Introduction to Nonlinear Partial Differential Equations*, Second Edition, John Wiley and Sons, USA, 2008.

[82] J. D. Logan, W. R. Wolesensky, *Mathematical Methods in Biology*, John Wiley and Sons, New York, 2009.

[83] S. Ma *Traveling Wavefron for Delayed Reaction-Diffusion Systems via a Fixed Point Theorem*, Journal of Differential Equations, **171** (2001), pp. 294-314.

[84] S. Ma, J. Wu, *Existence, uniqueness and asymptotic stability of traveling wavefronts in non-local delayed diffusion equation*, J. Dynam. Differential Equations, **19** (2007), No. (2), pp. 391-Ű436.

[85] M. C. Mackey, *Periodic auto-immune hemolytic anemia: An induced dynamical disease*, Bull. Math. Biol., **41**(1979), pp. 829–834.

[86] M. C. Mackey, *Unified hypothesis for the origin of aplastic anemia and periodic hematopoiesis*, Blood, **51**(1978), No. 5, pp. 941-956.

[87] M. C. Mackey, C. Ou, L. Pujo-Menjouet, J. Wu, *Periodic oscillations of blood cell populations in chronic myelgenous leukemia*, SIAM J. Math. Anal., **38**(2006), No. 1, pp. 166-187.

[88] H. Malchow, S. V. Pertrovskii, E. Venturino, *Spatiotemporal Patterns in Ecology and Epidemiology, Theory, Models, and Simulation*, Chapman and Hall, USA, 2008.

[89] M. Mei, J. W.-H So, *Stability of strong traveling waves for non-local time-delayed reaction diffusion equation*, Proceedings of the Royal society of Edinburgh, **138A** (2008), pp. 551–568.

[90] J. A. J. Metz, Dekmann, O., *The dynamics of physiologically structured populations*, (edited by J. A. J. Metz and O. Dekmann), Springer, 1986.

[91] A. G. Mckendrick, *Applications of Mathematics to Medical Problems*, Proc. Edinb. Math. Soc., **44**(1926), pp. 98–130.

[92] J. D. Murray, *Mathematical Biology I: An Introduction*, Third Edition, Springer-Verlag, Berlin, 2002.

[93] J. D. Murray, *Mathematical Biology II: Spatial Models and Biomedical Applications*, Third Edition, Springer-Verlag, Berlin, 2002.

[94] D. J. Needham, *Matched Asymptotic Expansions in Reaction-Diffusion Theory*, Springer-Verlag London Limited, London, 1991.

[95] A.J. Nicholson, *An outline of the dynamics of animal populations*, Austral. J. Zool, **2** (1955), pp. 9Ű65.

[96] A.J. Nicholson, *The self adjustment of populations to change*, Cold Spring Harb. Symp. Quant. Biol.,**22** (1957), pp. 153-173.

[97] C. Ou, J. Wu, *Existence and Uniqueness of a Wavefront in a Delayed Hyperbolic-parabolic Model*, Nonlinear Analysis Theory and Methods, **63** (2005), No. 3, pp. 364-387.

[98] C. Ou, J. Wu *Spatial Spread of Rabies Revisited: Influence of Age-dependent Diffusion on Nonlinear Dynamics*. SIAM Journal on Applied Mathematics,**67** (2006), No. 1, pp. 138-163.

[99] C. Ou, J. Wu *Persistence of Wavefronts in Delayed Nonlocal Reaction-diffusion Equations*, Journal of Differential Equations,**235** (2007), No. 1, pp. 219-261.

[100] C. Ou, J. Wu, *Traveling Wavefronts in a Delayed food-limited Population Model*, SIAM Journal on Mathematical Analysis,**39** (2007), No. 1, pp. 103-125.

[101] C. Ou, W. Yuan, *Traveling Wavefronts in a Volume-filling Chemotaxis Model*. SIAM Journal on Applied Dynamical Systems, **8**, (2009), No. 1, pp. 390-416.

[102] C. V. Pao, *Nonlinear Parabolic and Elliptic Equations*, Plenum Press, 1992.

[103] L. Priori, P. Ubezio, *Mathematical modeling and computer simulation of cell synchrony*, Methods in Cell Science, **18**(1996), pp. 83-91.

[104] M. H. Protter, H. F. Weinberger, *Maximum Principles in Differential Equations*, Springer, 1984.

[105] P. Ranlov, A. Videbaek, *Cyclic haemoltic anemia synchronous with Pel-Ebstein fever in a case of Hodgkin's disease*,Acta Med. Scand., **174** (1963), pp. 583–588.

[106] L. A. Segel, *Mathematical Models in Molecular and Cellular biology*, Cambridge University Press, UK, 1980.

[107] G. Sena, C. Onado, P. Cappella, F. Montalenti, P. Ubezio, *Measuring the complexity of cell cycle arrest and killing of drugs: Kinetics of phase-specific effects induced by taxol*, Cytometry, **37**(1999), pp. 113–124.

[108] K. Schumacher, *Traveling-front solutions for integro-differential equations II, Biological Growth and Spread: Mathematical Theories and Applications*, Lecture Notes in Biomath. **38**, Springer, Berlin, 1980.

[109] W. Shen, *Traveling waves in time periodic lattice differential equations*, Nonlinear Anal, **54** (2003), pp. 319-339.

[110] J. A. Sherratt, S. A. Gourley, N. J. Armstrong, K. J. Painter, *Boundedness of Solutions of a Non-local Reaction-diffusion Model for Adhesion in Cell Aggregation and Cancer Invasion*, Euro. Jnl of Applied Mathematics, **20**(2008), pp. 123–144.

[111] D. R. Smart, *Fixed Point Theorems*, Cambridge University Press, New Yourk, 1974.

[112] H. L. Smith, *Monotone Dynamical Systems: An introduction to the Theory of competitive and Cooperative Systems*, American Mathematical society, Mathematical Surveys and Monographs, Volume **41**, USA, 1995.

[113] H. Smith and H. Thieme, *Strongly order preserving semiflows generated by functional differential equations*, J. Differential Equations, **93** (1991), pp. 332–363.

[114] H. Smith, X.-Q. Zhao, *Traveling waves in a bio-reactor model*, Nonlinear Analysis Real World Applications An International Multidisciplinary Journal, **5**(2004), pp. 895-909.

[115] W.-H So , J. Wu, J. X. Zou, *A reaction-diffusion model for a single species with age structure. I Traveling wavefronts o unbounded domains*, Proc. R. Soc. Lond. A, **457** (2001), pp. 1841-1853.

[116] J.W.-H. So, X. Zou (2001) *Traveling waves for the diffusive Nicholsons blowflies equation.* Appl. Math.Compt., **122** (2001), pp. 385-392.

[117] J. Swinburne, M. C. Makey, *Cyclical thrombocytopenia: characterization by spectral analysis and a review*, J. Theor. Med., **2** (2000), pp. 81–91.

[118] H. R. Thieme, *Mathematics in Population biology*, Princeton University Press, United Kingdom, 2003.

[119] H. R. Thieme and X.-Q. Zhao, *Asymptotic speeds of spread and traveling waves for integral equations and delayed reaction-diffusion models*, J. Differential Equations, **195** (2003), pp. 430-470.

[120] H. R. Thieme, *Asymptotic estimates of the solutions of nonlinear integral equations and asymptotic speeds for the spread of populations*, J. Reine Angew. Math. 306 (1979), pp. 94-121.

[121] H. R. Thieme, *Persistence under relaxed point-disspativity with applications to an endemic model*, SIAM Journal of Mathematical Analysis, **24** (1993), No. 2, pp. 407–435.

[122] J. M. A. Toledano, T. D. Benavides, G. L. Acedo, *Measure of noncompactness in metric fixed point theory*, birkhäuser verlag, Switzerland, 1997.

[123] J. Tsai, J. Sneyd, *Existence and stability of traveling waves in buffered systems*, SIAM J. Appl. Math., **66** (2005), pp. 237-265.

[124] J. Tsai, *Global exponential stability of traveling waves in monotone bistable systems*, Discrete Contin. Dyn. Syst,**21**(2008), pp. 601-623.

[125] N. K. Vaidya, J. Wu, *Modeling spruce budworm population revisited: Impact of physiological structure on outbreak control*, Bulletin of Mathematical Biology, **70**(2008), pp. 769–784.

[126] A. I. Volpert, V. A. Volpert, V. A. Volpert, *Traveling Wave Solutions of Parabolic Systems*, Translations of Mathematical Monographs, Vol. **140**, American Mathematical Society, 1994.

[127] Q. Wang, X.-Q. Zhao, *Spreading speed and traveling waves for the diffusive logistic equation with a sedentary compartment, Dyn. Contin. Discrete Impuls. Syst.* Ser. A Math. Anal.,**13** (2006), pp. 231-246.

[128] G. F. Webb, *Theory of Non-linear Age-Dependent Population Dynamics*, Marcel Dekker Inc., New York, 1985.

[129] P. Weng, X.-Q. Zhao, *Spreading speed and traveling waves for a multi-type SIS epidemic model*, J. Differential Equations, **229** (2006), pp. 270-296.

[130] H. F. Weinberger, On spreading speeds and traveling waves for growth and migration models in a periodic habitat, J. Math. Biol., **45** (2002), pp. 511-548.

[131] H. F. Weinberger, K. Kawasaki and N. Shigesada, *Spreading speeds of spatially periodic integro-difference models for populations with nonmonotone recruitment functions*, Math. Biol., **57** (2008), pp. 387-411.

[132] H Weinberger, X.-Q. Zhao. *An extension of the formula for spreading speeds*, Mathematical Biosciences and Engineering MBE, **7**(2010), pp. 187-194.

[133] T. P. Witelski, *An asymptotic solution for traveling waves of a nonlinear-diffusion Fisher's equation*, J. Math. Biol., **33** (1994), 1 - 16.

[134] J. Wu, Theory and Applications of Partial Functional Differential Equations, Applied Math. Sci. **119**, Springer-Verlag, New Yourk, 1996.

[135] J. Wu, X. Zou, *Traveling wave fronts of reaction-diffusion systems with delay, J. Dynam. Differential Equations*, **13**(3) (2001), pp. 651-687. Erratum: **20** (2008), 531-533.

[136] J. Wu, X. Zou, *Traveling Wave Front of Reaction-Diffusion Systems with Delay*, Journal of Dynamics and Differential Equations, **13** (2001), No. (3), pp. 651–687.

[137] D. Xu, X.-Q. Zhao, *Asymptotic speed of spread and traveling waves for a nonlocal epidemic model*, Discrete and Continuous Dynamical Systems Series B A Journal Bridging Mathematics and Sciences, **5** (2005), pp. 1043-1056.

[138] D. Xu, X.-Q. Zhao, *Bistable waves in an epidemic model, J. Dynam. Differential Equations*, **16**(2004), pp. 679-707.

[139] D. Xu, X.-Q. Zhao, *A nonlocal reaction-diffusion population model with stage structure*. Can. Appl. Math. Q. **11** (2003), No. 3, pp. 303–319.

[140] E. Zauderer, *Partial Differential Equations of Applied Mathematics*, Second edition, John Wiley and Sons, New York, 1988.

[141] E. Zeidler, *Nonlinear Functional Analysis and its Applications*, V. I, (Translated by Peter R. Wadsack), Springer-Verlag, 1985.

[142] K. F. Zhang, X.-Q. Zhao, *Asymptotic behaviour of a reaction-deffusion model with a quiescent stage*, Proc. R. Soc., **A 463**(2007), pp. 1029–1043.

[143] X.-Q. Zhao, *Global attractivity and stability in some monotone discrect dynamical systems*, Bull. Austral. Math Soc.,**53** (1996), pp. 305–324.

[144] X.-Q. Zhao, *Dynamical Systems in Population Biology*, Springer-Verlag, New York, 2003.

[145] X.-Q. Zhao, D. Xiao, *The asymptotic speed of spread and traveling waves for a vector disease model*, Journal of Dynamics and Differential Equations, **18** (2006), pp. 1001-1019.

[146] X.-Q. Zhao, W. Wang, *Fisher waves in an epidemic model*, Discrete Contin. Dyn. Syst. Ser., **4** (2004), pp. 1117-1128.

[147] X.-Q. Zhao, *Global attractivity in a class of nonmonotone reaction-diffusion equations with time delay* , Canadian Applied Mathematics Quarterly, **17** (2009), No. 1, pp. 271–281.

[148] H. Zuh, W. Yuan, C. Ou. *Justification for Wavefront Propagation in a Tumour Growth Model with Contact Inhibition.* Proceedings of the Royal Society of London Series: A Mathematical, Physical and Engineering Sciences, **464** (2008), pp. 1257-1273.