FUNCTIONAL PARTIAL DIFFERENTIAL EQUATIONS

a space-time odyssey

A thesis presented in partial fulfillment of the requirements for the degree of

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by

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Abstract

We study functional partial differential equations (FPDEs) involving one and two nonlocal terms for certain constant and variable coefficients. First, we generalize the first order FPDE with one nonlocal term, studied by Perthame and Rhyzik, to the two nonlocal term case. We show the large time convergence of solutions to the separable solution.

We then solve a model that entails an initial boundary value problem involving a second-order parabolic partial differential equation with two nonlocal terms, the presence of which is a consequence of asymmetry in cell division. The solution techniques for solving such problems are rare due to the nonlocal terms. We obtain a separable solution, as well as the general solution to the partial differential equation, and show that the solutions converge to the separable solution for large time. The dispersion term does not affect the rate of convergence to the separable solution.

We establish the existence of solutions to an initial boundary value problem that involves a certain class of nonhomogeneous FPDEs, with one and two nonlocal terms, of the pantograph type with singular time dependent coefficients. The problem is motivated from a cell division equation.

We also consider FPDEs with one and two nonlocal terms involving time dependent coefficients. The existence of a steady size distribution (SSD) solution is established and is shown to be the large time attracting solution for a certain class of time dependent coefficients. The rate of convergence of solutions towards the SSD solution is affected by the choice of coefficients

and remains unaffected by the number of nonlocal terms. The uniqueness of solutions to the initial boundary value problem is also established.

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Contents

Chapter 1

Introduction and Literature review

The principle of causality is an underlying phenomenon in systems considered in applied sciences. This phenomenon dictates that any future predictions about the system under consideration be independent of the past and solely dependent on the present [1]. An ordinary differential equation (ODE) or a partial differential equation (PDE) governs the systems based on the current state and the rate with which the state changes. Nonetheless, there are systems that are not completely independent of the past and take into consideration not just the present state of the system but previous states as well. These equations are either differential difference equations or functional differential equations.

Even though this was known for quite some time, the theory to tackle such systems has been developed rather recently. Laplace, Bernoulli, and Condorcet were among the first ones to encounter differential difference equations in the later half of the eighteenth century but very little progress was accomplished until the twentieth century. The subject progressed rapidly and has been under continuous investigation after the mid of the twentieth century. Focus has primarily been in the areas of control theory, mathematical applications in economics and mathematical biology [38].

One of the modern time investigators is Minorsky [37], who was one of the first ones to study the differential difference equation (DDE)

$$\frac{dx}{dt} = F(t, x(t), x(t-r)), \tag{1.1}$$

where $r > 0$. The feedback control system he studied could not neglect the communication time.

While studying the distribution of primes, Lord Cherwell [39] encountered the differential difference equation

$$\frac{dx}{dt} = -\alpha x(t-1)(1 + x(t)). \tag{1.2}$$

The theory of growth has used variants of the above equation as models in different studies. Cunningham [40] studied the delay equation in growth

$$\frac{dN(t)}{dt} = [k - aN(t-\tau)]N(t), \tag{1.3}$$

where $N(t)$ and $N(t-\tau)$ are populations at times t and $t-\tau$, and k, a and τ are positive real constants. Studying the predator-prey model, Volterra [41] studied the distributed delay equations

$$\begin{aligned} \frac{dN_1(t)}{dt} &= \left(\epsilon_1 - \gamma_1 N_2(t) - \int_{-r}^{0} F_1(-\theta) N_2(t+\theta) d\theta\right) N_1(t) \\ \frac{dN_2(t)}{dt} &= \left(-\epsilon_2 + \gamma_2 N_1(t) - \int_{-r}^{0} F_2(-\theta) N_1(t+\theta) d\theta\right) N_2(t), \end{aligned} \tag{1.4}$$

where $N_1(t)$ represents the number of prey and $N_2(t)$ shows the number of predators. The constants $\theta, \gamma_1, \gamma_2, \epsilon_1$ and ϵ_2 are all positive, as well as the functions, F_1 and F_2.

For similar predator-prey models, Wangersky and Cunningham [42] used the delay equations

$$\begin{aligned} \frac{d}{dt}N_1(t) &= \alpha(N_1(t))\left(\frac{A_1 - N_1(t)}{A_1}\right) - bN_1(t)y(t) \\ \frac{d}{dt}N_2(t) &= -\beta N_2(t) + pN_1(t-r)N_2(t-r), \end{aligned} \tag{1.5}$$

where $N_1(t)$ and $N_2(t)$ are the prey and predator populations respectively. α is increasing rate of prey, A_1 is the limitation on growth of prey, b denotes the effect of predation on N_1, p is the effect of predation on N_2 and β is the death rate of N_2 and $r > 0$.

Levin and Nohel [44] studied, in detail, the delay equation

$$\frac{dx(t)}{dt} = -\frac{1}{a}\int_{t-a}^{t}(a-(t-u))k(y(u))du, \tag{1.6}$$

where $a, u > 0$, $k(y)$ is spring restoring force and $0 \leq t < \infty$. When studying the circulating-fuel reactor, this model was studied by Ergen [43] where x denoted the rate of change of neutron density. In viscoelasticity of one dimension, the same model can be implemented where strain and relaxation function are represented by x and a respectively.

Brayton [45] studied lossless transmission lines and encountered a delay differential equation given as

$$\frac{dv(t)}{dt} = G(\dot{v}(t), \dot{v}(t-r)) + F(v(t), v(t-r)), \tag{1.7}$$

where G and F are linear difference-differential and nonlinear operators respectively, and $\dot{v}$ represents the derivative with respect to time t. Rubanik [46] studied a second order delay-differential equation with delay term in the second derivative in his study of elastic bars with vibrating masses attached to them.

Several other models have been studied including Driver's [47] collision problem in electrodynamics and El'sgol'tz and Hughes [49, 48] variational (minimization) problem.

The several examples above show equations of different types. Some models are based on the past states, whereas some are based on future states. There are some examples of systems incorporating the rates of change of a past state. Hale described in detail the significant differences in the behavior of solutions for each type [50]. Bellman and Cooke [51] classified the differential difference equations as retarded (based on past state), neutral, and advanced (involve a non-local term). In this thesis, we primarily deal with functional partial differential equations of the advanced type.

Earlier models, discussed above, invovled ordinary differential equations with functional (nonlocal) terms. Nonlocal terms arise in partial differential equations as well. Such PDEs are known as functional partial differential equations (FPDE's). It is the representation of our understanding of the complex processes that take place in our daily lives. A partial differential equation can express the flow of heat difference over the length of a rod over time, the motion of mechanical and EM waves, or the population size of a specie over time. Population models were formally studied in the late 18th century when Malthus analyzed the human population growth. However, the obvious shortcomings of the model that overlooked several relevant variables, such as age, led to the use of structured population models. Age structured population models have been studied by several mathematicians and detailed accounts can be found in [68, 69, 67].

Functional PDEs arise in a number of applications such as the fragmentation process in polymers and droplets [2, 8], internet protocols [3] and more recently cell division models [31]. Living cells are usually structured on size because they grow and divide simultaneously. The size of a certain cell is any quantifiable physical property, for example, mass, volume or DNA content of the cell. Several researchers have studied a size structured model for cell populations. In 1962, Collins and Richmond [52] studied the growth rate of "*Bacillus cereus*" and developed a method to find the growth rate at any given length of the bacterium. In the same year, Koch and Schaechter [53] came up with a model for the statistics of the cell division process. Powell [54], in 1964 then published the consequences of the hypothesis provided by Koch and Schaechther. It was not until 1967, when Sinko and Streifer [16] constructed a deterministic model, structured on size, for the species reproducing by fission. In the model, they accounted for the continuous changes in mass and accounted for the influx from the growth of smaller organisms and the division of larger organisms and neonates.

During the 1980s, O.Diekman et al. [55] studied a related linear problem, whereas Heijmans [56] developed a nonlinear model, structured on size, to describe asymmetric cell division. Hall and Wake [10], then built on the works of O. Diekman et al., Heijmans and others to study solutions to a symmetric, size structured cell population model. A symmetric size structured model studies the process where α daughter cells of size $\frac{x}{\alpha}$ are obtained after a cell of size x divides. The resulting equation is an advanced first order functional

PDE of the form

$$\frac{\partial}{\partial t}(n(x,t)) + \frac{\partial}{\partial x}(g(x,t)n(x,t)) = -b(x,t)n(x,t) + \alpha^2 b(\alpha x,t)n(\alpha x,t), \quad (1.8)$$

with $n(x,t)$ denoting the number of cells of size x at time t and $g(x,t)$ is the growth rate of cell which is always positive. The rate of division of cells into α daughter cells is $b(x,t) > 0$. Hall and Wake [72] observed that the steady size distributions (where the size distribution of cell population maintains its shape irrespective of the overall population growth or decay [11]) is of interest to biologists. The observation was motivated by the experimental data obtained in [66]. The key observation in the data was that cell size distribution acquired a certain shape irrespective of the initial distribution $n_0(x) = n(x,0)$. A separable solution of the form

$$n(x,t) = N(t)y(x) \quad (1.9)$$

was assumed where $y(x)$ is a probability density function (pdf). Hall and Wake [10] assumed growth and division rate to be dependent on x, (the size) alone, whereas in general these rates are dependent on both x and t. The separable solution substitution into the equation (1.8) yields

$$\frac{1}{N(t)}\frac{d}{dt}N(t) = \lambda, \quad (1.10)$$

where λ is a separation constant and equation (1.10) becomes

$$N(t) = \Lambda e^{\lambda t}, \quad (1.11)$$

where Λ is a constant. Using the separation constant λ, we get the functional differential equation

$$\frac{d}{dx}(g(x)y(x)) + (b(x) + \lambda)y(x) = \alpha^2 b(\alpha x)y(\alpha x), \tag{1.12}$$

with boundary conditions

$$y(0) = 0, \quad \lim_{x\to\infty} y(x) = 0. \tag{1.13}$$

Integrating equation (1.12) from 0 to ∞ and using the probability density function (pdf) property of $y(x)$ yields

$$\lambda = (\alpha - 1)\int_0^\infty b(x)y(x)dx. \tag{1.14}$$

In the above equation (1.14), it is assumed that $b(x) \in L^1[0, \infty)$. Hall and Wake [10] studied the constant division and growth rate case for the equation (1.8) where $b(x) = b > 0$ and $g(x) = g > 0$. For the constant case,

$$\lambda = b(\alpha - 1), \tag{1.15}$$

and equation (1.12) reduces to the following pantograph-type equation

$$gy'(x) + b\alpha y(x) = b\alpha^2 y(\alpha x). \tag{1.16}$$

There are several applications of the pantograph-type equation in physics and engineering. It appears in the light absorption models in the Milky Way [57] and current accumulation in an electric locomotive [58]. It also has applications in probability and arises in a ruin problem [59]. The cell growth variation of the pantograph equation is different from the aforementioned applications due to the existence of an eigenvalue and boundary conditions in the problem. As shown in [35] and [36], the higher eigenvalues of the pantograph equation, that arise in cell growth modeling, do not correspond to eigenfunctions that are pdf. Hall and Wake [10] showed that the equation (1.16) has a positive, unique solution for positive x and can be represented as a Dirichlet series of the form

$$y(x) = \frac{1}{\prod_{m=1}^{\infty}(1-\alpha^{-m})}\left(e^{\frac{-b\alpha x}{g}} + \sum_{k=1}^{\infty}\frac{(-1)^k e^{\frac{-b\alpha^{k+1}x}{g}}}{\alpha^{k(k-1)/2}\prod_{j=1}^{k}(1-\alpha^{-j})}\right). \tag{1.17}$$

It was shown that the solution is uni-modal [60]. That is the graphical representation of the solution in (1.17) had only one local and global maximum.

As the choice of division and growth rates vary, the nature of the solution to the pantograph equation varies too. When van Brunt and Hulstman [35] studied pantograph equation with non-constant coefficients of the form

$$y'(x) + bx^d y(x) = \lambda\alpha^d x^d y(\alpha x), \tag{1.18}$$

along with the boundary conditions as in (1.13) and the pdf condition (1.14) for $d \geq 0$. They obtained a spectrum of eigenvalues. The corresponding eigenvectors are

$$y_m(x) = C_m\left(e^{\frac{-bx^{d+1}}{d+1}} + \sum_{k=1}^{\infty} p_k(\lambda_m)e^{\frac{-b\alpha^{k(d+1)}x^{d+1}}{d+1}}\right), \tag{1.19}$$

where $\lambda_m = b\alpha^{m(d+1)+1}$ and m is a non-negative integer. It was further established that these eigenfunctions are unique. Perthame and Rhyzik [15] showed that for constant growth rate g, (1.16) has a unique solution under certain conditions on the size-dependent division rate. They also showed the for constant growth and division rates, large time solutions map on to the separable solution. In this thesis, we generalize Perthame and Ryzhik's work to asymmetric division of cells and to a certain class of time dependent division and growth rates.

The deterministic model (1.8) may not reflect the significant variations in growth rates, as supported by experimental data [11]. Hall [11], in his thesis, derived a second order functional partial differential equation in the form of a Fokker Planck equation obtained by Cox and Miller [61]. Hall considered the growth rate to be a stochastic process. Using a probability distribution of increase in the size x of a cell, Hall introduced the dispersion coefficient, $D(x,t) > 0$, into the equation. The equation has the form

$$\begin{aligned}\frac{\partial^2}{\partial x^2}(D(x,t)n(x,t)) + \frac{\partial}{\partial t}n(x,t) + \frac{\partial}{\partial x}(G(x,t)n(x,t)) + B(x,t)n(x,t)\\ = \alpha^2 B(\alpha x,t)n(\alpha x,t).\end{aligned} \tag{1.20}$$

Here, $G(x,t) > 0$ in this model is the approximation of the mean growth rate and $B(x,t) > 0$ is the division rate. This model is supplemented with decay conditions

$$\begin{aligned}\lim_{x\to\infty} n(x,t) = 0,\\ \lim_{x\to\infty} \frac{\partial}{\partial x}n(x,t) = 0,\end{aligned} \tag{1.21}$$

and no-flux conditions

$$\begin{aligned}\lim_{x\to 0^+}\left(\frac{\partial}{\partial x}(D(x,t)n(x,t)) - G(x,t)n(x,t)\right) = 0,\\ \lim_{x\to\infty}\left(\frac{\partial}{\partial x}(D(x,t)n(x,t)) - G(x,t)n(x,t)\right) = 0.\end{aligned} \tag{1.22}$$

The problem is subject to an initial cell size distribution

$$n(x,0) = n_0(x), \tag{1.23}$$

for all $x \geq 0$. The initial cell size distribution $n_0(x)$ may be regarded as a probability density function (pdf). Consequently, $n_0(x) \geq 0$ for all $x \geq 0$ and $\int_0^\infty n_0(x)dx = 1$.

A separable solution to the problem (1.20), subject to conditions (1.21)-(1.22), was studied by van Brunt and Wake [62] for $D(x,t) = Dx$ and constant $G > 0$ and $B > 0$. The problem involves the equation

$$(Dxy(x))'' - (Gy(x))' - (B+\lambda)y(x) + \alpha^2 By(\alpha x) = 0. \tag{1.24}$$

Using appropriate substitutions, (1.24) becomes

$$xy''(x) - k_1 y'(x) - k_2 y(x) + k_2 \alpha y(\alpha x) = 0, \tag{1.25}$$

where

$$k_1 = \left(\frac{G}{D} - 2\right),$$

and

$$k_2 = \frac{\alpha B}{D}.$$

They showed the uniqueness and positivity of solution subject to the normalizing condition ($\int_0^\infty y(x)dx = 1$) with existence in $L^1[0,\infty)$. The solution was obtained using Mellin transforms and expressed in terms of modified Bessel functions. In this thesis, we use Mellin transform to determine the existence of a dispersion problem with time dependent singular coefficients with a source term. The existence of solution is subject to certain conditions on the source term.

A related problem

$$y''(x) + ay'(x) + by(x) + cy(\alpha x) = 0, \tag{1.26}$$

was studied by Kim [63]. Wake et al. [19] had found the separable solutions to the problem for constant coefficients. Basse et al. [64], while studying plankton's symmetric cell division, used constant dispersion and growth rate, with a generalized division rate $b(x)$. Begg et al. [65] used the entropy method to study the above problem for constant dispersion and growth rate. However, they studied it for $B(x) = b\delta(l - x)$, with $l > 0$ and $b > 0$. Recently, Efendiev et al. [31] came up with a technique to solve the Dispersion Problem (1.20) for constant dispersion, growth and division rates. In this thesis, we build on this technique to find analytic solution and long time asymptotics of the cell growth model with asymmetric division. Recall that asymmetric division in cells refer to the situation when daughter cells of different sizes are obtained after a parent cell divides.

Lately, van Brunt et al [33] studied a size-structured cell division model. More specifically the following model was studied

$$n_t(x,t) + g(xn(x,t))_x + bx^r n(x,t) = b\alpha^{2+r} x^r n(\alpha x, t), \tag{1.27}$$

satisfying the conditions

$$\lim_{x \to 0^+} gxn(x,t) = 0, \quad \lim_{x \to \infty} gxn(x,t) = 0, \text{ for } t \geq 0 \tag{1.28}$$

along with

$$n(x,0) = n_0(x), \tag{1.29}$$

where g and b are positive constants and gx and bx^r and size dependent growth and division rates respectively and $n(x,t)$ represents the number density of cells of size x at time t. Certain transformations reduce the PDE (1.27) to

$$\varphi_t(x,t) + gx\varphi_x(x,t) + bx\varphi(x,t) = b\alpha x\varphi(\alpha x,t), \tag{1.30}$$

where $\varphi(x,0) = \varphi_0(x) = x^2 n_0(x)$. Conditions (1.28)-(1.29) give

$$\lim_{x\to 0^+} \frac{\varphi(x,t)}{x} = 0, \quad \lim_{x\to\infty} \frac{\varphi(x,t)}{x} = 0. \tag{1.31}$$

A Mellin transform technique was used to find the solution of the PDE (1.30). The solution is

$$\varphi(x,t) = \omega_0(xe^{-gt})e^{-\eta x(1-e^{-gt})} + \sum_{k=1}^{\infty} a_k \omega_0(\alpha^k xe^{-gt})e^{-\eta\alpha^k x(1-e^{-gt})}, \tag{1.32}$$

where $\eta = b/g$, $a_k = \frac{(-1)^k \alpha^k}{\prod_{i=1}^{k}(\alpha^i - 1)}$ and ω_0 is found to be bounded on $(0,\infty)$. Furthermore $\omega_0' \in C^1(0,\infty)$, and ω_0' is bounded on $[p_0,\infty)$ for any $p_0 > 0$. Although these results are obtained for the transformed equation, it can be shown that the method holds for any $r > 0$ in (1.27).

The above work is a generalization of a simpler problem with constant growth and division rate. Zaidi et al. [22] developed a novel technique to solve the problem

$$n_t(x,t) + gn_x(x,t) = \alpha^2 bn(\alpha x,t) - bn(x,t) - \mu n(x,t), \tag{1.33}$$

which, using certain transformations, reduces to

$$n_t(x,t) + n_x(x,t) = b\alpha^2 n(\alpha x, t), \tag{1.34}$$

where b is a positive constant and n is the number density of cells of size x at time t. Zaidi et al. first obtained the solution for $x \geq t$. The solution obtained was of the form

$$S(x,t) = \sum_{k=0}^{\infty} L_k(x,t), \tag{1.35}$$

where $L_k(x,t) = \sum_{j=0}^{k} a_{k,j} V_k(u_{k,j}(x,t))$. Here

$$a_{k,j} = \frac{b\alpha^2 a_{k-1,j-1}}{\alpha^{k-j}(\alpha^j - 1)}, \quad V_0(u) = \mathfrak{n}_0(u), \quad V'_{k+1}(u) = V_k(u).$$

In addition,

$$a_{k,0} = -\sum_{j=1}^{k} a_{k,j}, \quad a_{0,0} = 1, \quad \text{and } u_{k,j}(x,t) = \alpha^{k-j}(\alpha^j x - t).$$

With the above conditions, the non-negativity of $S(x,t)$ is established for $\mathbb{W}_0 = \{(x,t) : x \geq t\}$. The solution is then extend to $0 \leq x < t$ by constructing wedges which takes care of the functional terms in $\mathbb{W}_k$ if solution is known in $\mathbb{W}_{k-1}$, where

$$\mathbb{W}_k = \{(x,t) : \frac{t}{\alpha^k} \leq x \leq \frac{t}{\alpha^{k-1}}\}.$$

A piecewise solution is obtained for all $x \geq 0$ and $t \geq 0$ by finding solutions in each wedge. Continuity is then imposed on the boundary of wedges. The solution obtained for the n^{th} wedge, $\mathbb{W}_n$, is of the form

$$z_n = L_n + J_0(u_{0,0}) + \sum_{k=1}^{n-1} \frac{(b\alpha)^k}{\prod_{m=1}^{k}(\alpha^m - 1)} J_k(u_{k,k}),$$

where J_0 is an arbitrary function and $J'_{k+1}(w) = J_k(w)$ for $k \geq 1$.

This approach by Zaidi et al. [22] inspired the work of Mohsin and Zaidi [34], who showed that a solution to a problem with two non-local terms exists and is unique. The problem is given below

$$\frac{\partial}{\partial t} n(x,t) + \frac{\partial}{\partial x} n(x,t) = \alpha b n(\alpha x, t) + \beta b n(\beta x), \tag{1.36}$$

where $\frac{1}{\alpha} + \frac{1}{\beta} = 1$. Their work mainly focuses on the construction of wedges and solutions are shown to exist in a wedge $\mathbb{W}_n$, if solutions exist in the wedge $\mathbb{W}_{n-1}$, for $n \geq 1$. The second nonlocal term adds complexity that makes the construction of wedges formidable.

The case involving two non-local terms, i.e., asymmetric division was studied by Suebcharoen et al. [30]. They developed a model for asymmetric cell division arising in *Drosophila* and *C. elegans*. In particular they devised the model

$$\frac{\partial}{\partial t} n(x,t) = -g \frac{\partial}{\partial x} n(x,t) - Q n(x,t) + \sum_{i=1}^{2} a_i \alpha_i^2 n(\alpha_i x, t), \tag{1.37}$$

where x/α_i is the size of the cell after a cell of size x divides, and a_i is the rate of division. The constant $g > 0$ is the rate of growth, and the constants a_i and α_i are positive reals for $i = 1, 2$. Suebcharoen et al. [30] considered an

SSD solution of the form $n(x,t) = N(t)y(x)$, where y satisfies

$$y'(x) + Ay(x) = \sum_{i=1}^{2} C_i y(\alpha_i x). \tag{1.38}$$

Here, $A = \frac{a_1\alpha_1 + a_2\alpha_2}{g}$ and $C_i = \frac{a_i\alpha_i^2}{g}$. The unique solution to (1.38) is of the form

$$f(z) = \sum_{i=0}^{\infty}\sum_{j=0}^{\infty} K_{i,j} e^{-\alpha_1^i \alpha_2^j z},$$

where $z = xA$, and $K_{i,j} = \frac{-1}{(\alpha_1^i\alpha_2^j - 1)}(d_1 K_{i-1,j} + d_2 K_{i,j-1})$. Further,

$$K_{i,0} = \frac{(-1)^i d_1^i}{\prod_{k=1}^{i}(\alpha_1^k - 1)} K_{0,0} \quad \text{and} \quad K_{0,j} = \frac{(-1)^j d_2^j}{\prod_{k=1}^{j}(\alpha_2^k - 1)} K_{0,0},$$

where

$$K_{0,0} = 1 + \sum_{k=1}^{\infty} \frac{d_1(\frac{1}{\alpha_1})^{k+1} + d_2(\frac{1}{\alpha_2})^{k+1}}{\prod_{n=1}^{k}\left(1 - \frac{d_1}{\alpha_1^{n+1}} - \frac{d_2}{\alpha_2^{n+1}}\right)},$$

which is convergent and $d_i = \frac{a_i\alpha_i}{Ag}$, for $i = 1, 2$.

In this thesis, we build on the theory of functional partial differential equations arising in cell growth models. Chapter 2 is the generalization of Perthame and Ryzhik's work [15] to the asymmetric case (2.1.2)-(2.1.4). In chapter 3, we tackle the dispersion equation (3.1.7) and find the exact solution to the asymmetric dispersion problem. Also, large time asymptotics are established in chapter 3. After solving the dispersion equation for the constant case, we discuss the second order dispersion equation for symmetric case with inhomogeneous time dependent coefficients. In particular, we study equation (4.1.1) and establish that a unique solution to the problem exists. In chapter 5 we generalize the work done in chapter 4 for asymmetric case. In chapter 6, Perthame and Ryzhik's [15] work is considered for time dependent division and growth rates and their results are generalized for a certain class of growth and division rates.

Chapter 2

Large time asymptotics for asymmetric division

2.1 Introduction

Perthame and Ryzhik [15] considered the symmetric division of cells for constant and linear growth rates and established the existence of a steady size distribution for a broad class of division rates. In this chapter, we extend Perthame and Ryzhik's analysis to the case of asymmetric cell division.

Perthame and Ryzhik considered the PDE

$$\frac{\partial}{\partial t}n(x,t) + \frac{\partial}{\partial x}n(x,t) + b(x)n(x,t) = k^2 b(kx)n(kx,t), \tag{2.1.1}$$

where $k = 2, \quad t > 0$, and $x \geq 0$. Equation (2.1.1) is supplemented with conditions

$$n(0,t) = 0, \quad t > 0 \;\text{ and }\; n(x,0) = n_0(x) \in L^1(\mathbb{R}^+).$$

Perthame and Ryzhik, showed that $\|e^{\lambda t}n(x,t) - y(x)\| \to 0$ as $t \to \infty$, where λ is a unique eigenvalue and $y(x)$ is the corresponding eigenfunction.

In this chapter we extend the method for asymmetric equation with $\alpha > 2 > \beta > 1$ such that $\frac{1}{\alpha} + \frac{1}{\beta} = 1$. We consider the differential equation

$$\frac{\partial}{\partial t}n(x,t) + \frac{\partial}{\partial x}n(x,t) + B(x)n(x,t) = \alpha B(\alpha x)n(\alpha x,t) + \beta B(\beta x)n(\beta x,t), \tag{2.1.2}$$

along with boundary condition

$$n(0,t) = 0, \quad t > 0, \tag{2.1.3}$$

and the initial condition

$$n(x,0) = n_0(x) \in L^1[0,\infty). \tag{2.1.4}$$

Equation (2.1.2) models asymmetric cell division (or growth-fragmentation) where mass is conserved and particles divide into two unequal parts.

Let us consider a separable solution

$$n(x,t) = y(x)N(t). \tag{2.1.5}$$

Upon substitution of (2.1.5) into (2.1.2), we get

$$\frac{d}{dx}y(x) + (\lambda + B(x))y(x) = \alpha B(\alpha x)y(\alpha x) + \beta B(\beta x)y(\beta x), \quad x \geq 0, \tag{2.1.6}$$

where λ is a constant and $y(x) \geq 0$ for all $x \geq 0$. The boundary conditions for the above problem are

$$\lim_{x \to 0^+} y(x) = 0, \tag{2.1.7}$$

$$\lim_{x \to \infty} y(x) = 0, \tag{2.1.8}$$

coupled with the pdf condition

$$\int_0^\infty y(x)dx = 1. \tag{2.1.9}$$

2.1.1 Adjoint equation

Using $\Phi(x)$ to be the adjoint function for $y(x)$ and $\mathbb{L}^*$ be the corresponding adjoint operator, we get the condition for the adjoint operator as

$$\int_0^\infty \Phi(x)\mathbb{L}(y)dx = \int_0^\infty y(x)\mathbb{L}^*(\Phi)dx, \tag{2.1.10}$$

which gives the adjoint equation

$$\frac{d}{dx}\Phi(x) - (\lambda + B(x))\Phi(x) = -B(x)\Phi(\frac{x}{\alpha}) - B(x)\Phi(\frac{x}{\beta}), \quad x \geq 0, \tag{2.1.11}$$

along with the conditions

$$\Phi(x) > 0 \quad \text{and} \int_0^\infty y(x)\Phi(x)dx = 1. \tag{2.1.12}$$

2.2 The case of constant division rate

We first consider a constant division rate $B(x) = b > 0$. Integrating w.r.t x from 0 to ∞, the equation (2.1.10), gives

$$\lambda = b. \tag{2.2.1}$$

Substituting (2.2.1) in equation (2.1.5) and (2.1.11), we get

$$\frac{d}{dx}y(x) + 2by(x) = b\alpha y(\alpha x) + b\beta y(\beta x), \quad x \geq 0, \tag{2.2.2}$$

and

$$\frac{d}{dx}\Phi(x) - 2b\Phi(x) = -b\Phi(\frac{x}{\alpha}) - b\Phi(\frac{x}{\beta}), \quad x \geq 0, \tag{2.2.3}$$

with conditions (2.1.7), (2.1.8) and (2.1.9).

It is easily verified that the function $\Phi = 1$ satisfies (2.2.3) with constant coefficients. The solutions to (2.2.2) have been discussed in detail. Thus we apply the technique of Perthame and Rhyzik, using signum function to determine the uniqueness of the given problem with constant coefficients.

Let $sgn(\xi)$ denote the signum function, then multiplying $sgn(y(x))$ to equation (2.2.2) yields

$$sgn(y(x))\frac{d}{dx}y(x) + 2by(x)sgn(y(x)) = b\alpha y(\alpha x)sgn(y(x)) + b\beta y(\beta x)sgn(y(x)). \tag{2.2.4}$$

Using the fact that $|\xi| = \xi sgn(\xi)$, we get

$$\frac{d}{dx}|y(x)| + 2b|y(x)| = b\alpha y(\alpha x)sgn(y(x)) + b\beta y(\beta x)sgn(y(x)), \tag{2.2.5}$$

for all $x \in \mathbb{R}$. Integrating the above equation from 0 to ∞ we get

$$2b\int_0^\infty |y(x)|dx = b\alpha\int_0^\infty y(\alpha x)sgn(y(x))dx + b\beta\int_0^\infty y(\beta x)sgn(y(x))dx. \tag{2.2.6}$$

Using the substitutions $\alpha x = u_1$ and $\beta x = u_2$ in the second and third integral terms respectively of the above expression, we get

$$2b\int_0^\infty |y(x)|dx = b\int_0^\infty y(x)sgn(y(x/\alpha))dx + b\int_0^\infty y(x)sgn(y(x/\beta))dx. \tag{2.2.7}$$

Dividing the above by b yields

$$sgn(y(x)) = \frac{sgn(y(x/\alpha)) + sgn(y(x/\beta))}{2}. \tag{2.2.8}$$

Theorem 2.2.1. *For $B(x) = b$, with $b > 0$, all solutions to* (2.1.2) *satisfy*

$$||n(x,t)e^{-bt} - \langle n_0\rangle y(x)||_{L^1[0,\infty)} \leq e^{-bt}\Big[||n_0(x) - \langle n_0\rangle y(x)||_{L^1[0,\infty)} + 2b||\Upsilon^0||_{L^1[0,\infty)}\Big],$$

where

$$\langle n_0\rangle = \int_0^\infty n_0(x)dx,$$

and

$$\Upsilon^0(x) = \int_0^x [n_0(\xi) - \langle n_0\rangle y(\xi)]d\xi \to 0 \quad as \quad x \to \infty.$$

Proof. Equation (2.1.2), when multiplied by e^{-bt}, becomes

$$e^{-bt}\frac{\partial}{\partial t}n(x,t) + e^{-bt}\frac{\partial}{\partial x}n(x,t) + e^{-bt}bn(x,t) = e^{-bt}(\alpha bn(\alpha x,t) + \beta bn(\beta x,t). \tag{2.2.9}$$

Since

$$e^{-bt}\frac{\partial}{\partial t}n(x,t) = \frac{\partial}{\partial t}[e^{-bt}n(x,t)] + be^{-bt}n(x,t),$$

equation (2.2.9) becomes

$$\frac{\partial}{\partial t}[e^{-bt}n(x,t)]+\frac{\partial}{\partial x}[e^{-bt}n(x,t)]+2be^{-bt}n(x,t) = \alpha be^{-bt}n(\alpha x,t)+\beta be^{-bt}n(\beta x,t). \tag{2.2.10}$$

Let

$$\varrho(x,t) = n(x,t)e^{-bt} - \langle n_0\rangle y(x).$$

The equation (2.2.10) yields

$$\begin{aligned}\frac{\partial}{\partial t}\varrho(x,t) \quad &+ \quad \frac{\partial}{\partial x}\varrho(x,t) + 2b\varrho(x,t) - \alpha b\varrho(\alpha x,t) - \beta b\varrho(\beta x,t) + \frac{\partial}{\partial t}\langle n_0\rangle y(x)\\ &= \quad -\langle n_0\rangle\left(\frac{d}{dx}y(x) + 2by(x) - \alpha by(\alpha x) - \beta by(\beta x)\right),\end{aligned} \tag{2.2.11}$$

where the t derivative of $\langle n_0\rangle y(x) = 0$. Using (2.2.2), the above equation becomes

$$\frac{\partial}{\partial t}\varrho(x,t) + \frac{\partial}{\partial x}\varrho(x,t) + 2b\varrho(x,t) = \alpha b\varrho(\alpha x,t) + \beta b\varrho(\beta x,t). \tag{2.2.12}$$

The conditions satisfied by (2.2.12) are

$$\varrho(0,t) = 0, \qquad \int_0^\infty \varrho(x,t)dx = 0, \forall t > 0.$$

Integrating (2.2.12) gives

$$\frac{\partial}{\partial t}\int_0^x \varrho(\varsigma,t)d\varsigma+\frac{\partial}{\partial x}\int_0^x \varrho(\varsigma,t)d\varsigma+2b\int_0^x \varrho(\varsigma,t)d\varsigma = b\int_0^{\alpha x} \varrho(\varsigma,t)d\varsigma+b\int_0^{\beta x} \varrho(\varsigma,t)d\varsigma. \tag{2.2.13}$$

Let

$$\Upsilon(x,t) = \int_0^x \varrho(\varsigma,t)d\varsigma. \tag{2.2.14}$$

Then (2.2.13) reduces to

$$\begin{cases} \frac{\partial}{\partial x}\Upsilon(x,t) + \frac{\partial}{\partial t}\Upsilon(x,t) + 2b\Upsilon(x,t) = b\Upsilon(\alpha x,t) + b\Upsilon(\beta x,t) \quad t>0, x\geq 0 \\ \Upsilon(0,t) = 0, \quad \Upsilon(\infty,t) = 0, \qquad \forall t>0. \end{cases} \tag{2.2.15}$$

Equations (2.2.15) and (2.2.13) yield

$$\varrho(x,t) = -\frac{\partial}{\partial t}\Upsilon(x,t) - 2b\Upsilon(x,t) + b\Upsilon(\alpha x,t) + b\Upsilon(\beta x,t),$$

so that,

$$\frac{\partial}{\partial t}[e^{-bt}\Upsilon(x,t)] + \frac{\partial}{\partial x}[e^{-bt}\Upsilon(x,t)] + 2b[e^{-bt}\Upsilon(x,t)] = be^{-bt}[\Upsilon(\alpha x,t) + b\Upsilon(\beta x,t)].$$

Multiplying $sgn(\Upsilon(x,t))$, on both sides of the above, gives

$$\frac{\partial}{\partial t}|e^{-bt}\Upsilon(x,t)|+\frac{\partial}{\partial x}|e^{-bt}\Upsilon(x,t)|+2b|e^{-bt}\Upsilon(x,t)| = be^{-bt}[\Upsilon(\alpha x,t)+\Upsilon(\beta x,t)]sgn(\Upsilon(x,t)). \tag{2.2.16}$$

Integration from 0 to ∞, of (2.2.16), with respect to x and boundary conditions

(2.2.15), yield

$$\frac{\partial}{\partial t}\int_0^\infty |e^{-bt}\Upsilon(x,t)|dx + 2b\int_0^\infty |e^{-bt}(\Upsilon(x,t)|dx \leq \\ b\Big[\int_0^\infty e^{-bt}(\Upsilon(\alpha x,t)+\Upsilon(\beta x,t)) \;\; sgn(\Upsilon(x,t)\Big]dx, \tag{2.2.17}$$

which, using (2.2.8), gives

$$\frac{\partial}{\partial t}\int_0^\infty |e^{-bt}\Upsilon(x,t)|dx + 2b\int_0^\infty |e^{-bt}\Upsilon(x,t)|dx \\ \leq b\int_0^\infty |e^{-bt}\Upsilon(\alpha x,t)|dx + b\int_0^\infty |e^{-bt}\Upsilon(\beta x,t)|dx. \tag{2.2.18}$$

Using the substitution $\nu_1 = \alpha x$ and $\nu_2 = \beta x$ gives

$$\frac{\partial}{\partial t}\int_0^\infty |e^{-bt}\Upsilon(x,t)| + 2b\int_0^\infty |e^{-bt}\Upsilon(x,t)|dx \\ \leq \frac{b}{\alpha}\int_0^\infty |e^{-bt}\Upsilon(\nu_1,t)|d\nu_1 + \frac{b}{\beta}\int_0^\infty |e^{-bt}\Upsilon(\nu_2,t)|d\nu_2 \\ = 2b\int_0^\infty |e^{-bt}\Upsilon(x,t)|dx,$$

so that

$$\frac{\partial}{\partial t}\int_0^\infty |e^{-bt}\Upsilon(x,t)|dx \leq 0.$$

This gives

$$\int_0^\infty |\Upsilon(x,t)|dx \leq e^{-bt}\int_0^\infty |\Upsilon^0(x)dx|, \tag{2.2.19}$$

where $\Upsilon^0(x) = \int_0^x [n_0(\xi) - \langle n_0\rangle y(\xi)]d\xi$.

Let

$$\Delta(x,t) = \frac{\partial}{\partial t}\Upsilon(x,t). \tag{2.2.20}$$

Differentiating (2.2.15) yields

$$\begin{cases} \frac{\partial}{\partial x}\Delta(x,t) + \frac{\partial}{\partial t}\Delta(x,t) + 2b\Delta(x,t) = b\Delta(\alpha x,t) + b\Delta(\beta x,t) \quad t>0, \quad x \geq 0 \\ \Delta(0,t) = 0, \quad \Delta(\infty,t) = 0, \qquad \forall\ t > 0. \end{cases} \tag{2.2.21}$$

Also, (2.2.20) and (2.2.15) give

$$\Delta(x,t) = b\Upsilon(\alpha x,t) + b\Upsilon(\beta x,t) - 2b\Upsilon(x,t) - \frac{\partial}{\partial x}\Upsilon(x,t), \tag{2.2.22}$$

so that at $t = 0$, (2.2.22) gives

$$\Delta_0(x) = b\Upsilon^0(\alpha x) + b\Upsilon^0(\beta x) - 2b\Upsilon^0(x) - \varrho_0(x), \tag{2.2.23}$$

where $\varrho_0(x) = \varrho(x,0)$ and $\Delta_0(x) = \Delta(x,0)$. The earlier analysis can be employed to show that

$$\int_0^\infty |\Delta(x,t)|dx \leq e^{-bt}\int_0^\infty |\Delta_0(x)|dx, \tag{2.2.24}$$

so that

$$\int_0^\infty |\Delta(x,t)|dx \leq e^{-bt}\bigg(\int_0^\infty [|2b\Upsilon^0(x)| + |\varrho_0(x)|]dx\bigg). \tag{2.2.25}$$

Substituting $\frac{\partial}{\partial t}\Upsilon(x,t) = \Delta(x,t)$ in (2.2.15) and integrating with respect to x from 0 to ∞ yields

$$\int_0^\infty |\varrho(x,t)|dx \leq e^{-bt}\bigg(\int_0^\infty |\Delta(x,t)|dx + 2b\int_0^\infty |\Upsilon^0(x)|dx\bigg),$$

The inequality (2.2.25) yields

$$\int_0^\infty |\varrho(x,t)|dx \le e^{-bt}\Big(|h_0(x)|dx + 2b\int_0^\infty |\Upsilon^0(x)|dx\Big),$$

which establishes the Theorem 2.2.1. □

2.3 The variable asymmetric division case

We study the large time dynamics of (2.1.2)-(2.1.4) and show that solutions to problem converge to the solution of (2.1.6)-(2.1.9) in $L^1[0,\infty)$ norm as $t \to \infty$.

Theorem 2.3.1. *Let $B \in \mathbb{C}(\mathbb{R}^+)$, and let b_m, b_M and b_∞ be the minimum, maximum and limiting values of $B(x)$ for $x \in \mathbb{R}^+$. Furthermore, assume the existence of a unique solution (λ, y, Φ) to the (2.1.6) and (2.2.3), where $y, \Phi \in \mathbb{C}^1(\mathbb{R})$. Moreover, let the renormalized rate of division, $B(x)$, defined by*

$$\hat{B}(x) = B(x)\frac{(\Phi(x/\alpha) + \Phi(x/\beta))}{\Phi(x)},$$

satisfies

$$0 < \hat{b}_m \le \hat{B}(x) \le \hat{b}_M < \infty,$$

where $\hat{b}_m$ and $\hat{b}_M$ are some constants. In addition to the above, assume that Φ satisfies

$$\hat{p}(1 + x^{z_0}) \le \Phi(x) \le \hat{P}(1 + x^{z_0}),$$

where $\hat{p}, \hat{P}$ and z_0 are positive constants such that $\alpha^{z_0} = \frac{\alpha b_\infty}{\lambda + b_\infty}$. Furthermore, *it is also assumed that* $y(x)$ *decays rapidly, i.e., for all* $c > 0$,

$$\int_0^\infty x^c y(x)dx < \infty,$$

and the bounds on λ *are*

$$b_m \leq \lambda \leq b_M.$$

Then there exists a constant $W > 0$ *such that*

$$\kappa := \|\hat{B}(x) - W\|_{L^\infty[0,\infty)} < \frac{W}{k+W},$$

and the solution to (2.1.2) *satisfies*

$$\begin{aligned} &\|\big(n(x,t)e^{-\lambda t} - \langle n_0\rangle y(x)\big)\Phi(x)\|_{L^1[0,\infty)} \\ &\leq e^{-\mu t}(\alpha+\beta)\Bigg[\|(n_0(x) - \langle n_0\rangle y(x))\Phi(x)\| + (\alpha+\beta)E^3\|\Upsilon^0\|_{L^1_{[0,\infty)}}\Bigg], \end{aligned} \tag{2.3.1}$$

where $\mu = ((\alpha+\beta)^2(1+E^2\kappa) + (2-\alpha-\beta)E)$ *and* $\Upsilon^0(x) = \int_0^x [n_0(\zeta) - \langle n_0\rangle y(\zeta)]d\zeta \to 0$ *as* $x \to \infty$.

Proof. Equation (2.1.2) is multiplied by $e^{-\lambda t}$. This gives

$$\begin{aligned} e^{-\lambda t}\frac{\partial}{\partial t}n(x,t) + \frac{\partial}{\partial x}[e^{-\lambda t}n(x,t)] + B(x)[e^{-\lambda t}n(x,t)] \\ = \alpha e^{-\lambda t}B(\alpha x)n(\alpha x,t) + \beta e^{-\lambda t}B(\beta x)n(\beta x,t). \end{aligned} \tag{2.3.2}$$

Since

$$e^{-\lambda t}\frac{\partial}{\partial t}n(x,t) = \frac{\partial}{\partial t}[e^{-\lambda t}n(x,t)] + \lambda[e^{-\lambda t}n(x,t)],$$

equation (2.3.2) gives

$$\frac{\partial}{\partial t}[e^{-\lambda t}n(x,t)] + \frac{\partial}{\partial x}[e^{-\lambda t}n(x,t)] + (B(x)+\lambda)e^{-\lambda t}n(x,t)$$
$$= \alpha B(\alpha x)e^{-\lambda t}n(\alpha x,t) + \beta(\beta x)e^{-\lambda t}n(\beta x,t). \tag{2.3.3}$$

Let

$$\varrho(x,t) = n(x,t)e^{-\lambda t} - \langle n_0\rangle y(x).$$

Then (2.3.3) yields

$$\frac{\partial}{\partial t}\varrho(x,t) + \frac{\partial}{\partial x}\varrho(x,t) + (B(x)+\lambda)\varrho(x,t)$$
$$-\alpha B(\alpha x)\varrho(\alpha x,t) - \beta B(\beta x)\varrho(\beta x,t) + \frac{\partial}{\partial t}\langle n_0\rangle y(x)$$
$$= -\langle n_0\rangle\left(\frac{d}{dx}y(x) + (B(x)+\lambda)y(x) - \alpha B(\alpha x)y(\alpha x) - \beta B(\beta x)y(\beta x)\right), \tag{2.3.4}$$

where the t derivative of $\langle n_0\rangle y(x) = 0$. Since y satisfies (2.1.6), equation (2.3.4) reduces to

$$\frac{\partial}{\partial t}\varrho(x,t) + \frac{\partial}{\partial x}\varrho(x,t) + (B(x)+\lambda)\varrho(x,t) = \alpha B(\alpha x)\varrho(\alpha x,t) + \beta B(\beta x)\varrho(\beta x,t), \tag{2.3.5}$$

so that $\varrho(0,t) = 0$. Multiplying (2.3.5) with $\Phi(x)$ gives

$$\frac{\partial}{\partial t}\Phi(x)\varrho(x,t) + \frac{\partial}{\partial x}\Phi(x)\varrho(x,t) + (B(x)+\lambda)\varrho(x,t)\Phi(x) - \varrho(x,t)\Phi'(x)$$
$$= \alpha B(\alpha x)\varrho(\alpha x,t)\Phi(x) + \beta B(\beta x)\varrho(\beta x,t)\Phi(x), \tag{2.3.6}$$

which, using (2.1.11), implies

$$\frac{\partial}{\partial t}\Phi(x)\varrho(x,t) + \frac{\partial}{\partial x}\Phi(x)\varrho(x,t) + B(x)\big(\Phi(x/\alpha) + \Phi(x/\beta)\big)\varrho(x,t)$$
$$= \alpha B(\alpha x)\varrho(\alpha x,t)\Phi(x) + \beta B(\beta x)\varrho(\beta x,t)\Phi(x). \qquad (2.3.7)$$

Dividing (2.1.11) by $\Phi(x)$ and using the definition of $\hat{B}(x)$ gives

$$\lambda + B(x) = \frac{\Phi'(x)}{\Phi(x)} + \hat{B}(x).$$

Let

$$\psi(x,t) = \Phi(x)\varrho(x,t). \qquad (2.3.8)$$

Then (2.3.7) yields

$$\frac{\partial}{\partial t}\psi(x,t) + \frac{\partial}{\partial x}\psi(x,t) + B(x)\frac{\big(\Phi(x/\alpha) + \Phi(x/\beta)\big)}{\Phi(x)}\psi(x,t)$$
$$= \alpha B(\alpha x)\psi(\alpha x,t)\frac{\Phi(x)}{\Phi(\alpha x)} + \beta B(\beta x)\psi(\beta x,t)\frac{\Phi(x)}{\Phi(\beta x)},$$

so that

$$\frac{\partial}{\partial t}\psi(x,t) + \frac{\partial}{\partial x}\psi(x,t) + \hat{B}(x)\psi(x,t) = \alpha B(\alpha x)\psi(\alpha x,t)\frac{\Phi(x)}{\Phi(\alpha x)} +$$
$$\beta B(\beta x)\psi(\beta x,t)\frac{\Phi(x)}{\Phi(\beta x)}, \qquad (2.3.9)$$

Since $\varrho(0,t) = 0$, so $\psi(0,t) = 0$. In order to determine the large time convergence of solutions, we first establish the exponential decay of the antiderivative of $\psi(x,t)$. We begin by integrating (2.3.9) with respect to x from 0 to x. This gives

$$\frac{\partial}{\partial t}\int_0^x \psi(\xi,t)d\xi + \frac{\partial}{\partial x}\int_0^x \psi(\xi,t)d\xi + \int_0^x \hat{B}(\xi)\psi(\xi,t)d\xi$$
$$= \int_0^{\alpha x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\alpha)}{\Phi(\xi)}d\xi + \int_0^{\beta x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\beta)}{\Phi(\xi)}d\xi. \tag{2.3.10}$$

Let

$$\Upsilon(x,t) = \int_0^x \psi(\xi,t)d\xi. \tag{2.3.11}$$

Recasting (2.2.13) gives

$$\begin{cases} \frac{\partial}{\partial x}\Upsilon(x,t) + \frac{\partial}{\partial t}\Upsilon(x,t) + \int_0^x \hat{B}(\xi)\psi(\xi,t)d\xi = \int_0^{\alpha x} M_1 + \int_0^{\beta x} M_2 \quad t>0, x\geq 0 \\ \Upsilon(0,t)=0, \quad \Upsilon(\infty,t)=0, \quad \forall\, t>0, \end{cases} \tag{2.3.12}$$

where $M_1 = B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\alpha)}{\Phi(\xi)}d\xi$ and $M_2 = B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\beta)}{\Phi(\xi)}d\xi$. Splitting the integrals on the right hand side of (2.3.12) gives

$$\frac{\partial}{\partial t}\Upsilon(x,t) + \frac{\partial}{\partial x}\Upsilon(x,t) + \int_0^x \hat{B}(\xi)\psi(\xi,t)d\xi$$
$$= \int_0^{x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\alpha)}{\Phi(\xi)}d\xi + \int_0^{x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\beta)}{\Phi(\xi)}d\xi$$
$$+ \int_x^{\alpha x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\alpha)}{\Phi(\xi)}d\xi + \int_x^{\beta x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\beta)}{\Phi(\xi)}d\xi,$$

so that

$$\frac{\partial}{\partial t}\Upsilon(x,t) + \frac{\partial}{\partial x}\Upsilon(x,t) + \int_0^x \hat{B}(\xi)\psi(\xi,t)d\xi$$
$$= \int_0^x \hat{B}(\xi)\psi(\xi,t)d\xi + \int_0^{x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\alpha)}{\Phi(\xi)}d\xi + \int_0^{x} B(\xi)\psi(\xi,t)\frac{\Phi(\xi/\beta)}{\Phi(\xi)}d\xi.$$

This gives

$$\frac{\partial}{\partial t}\Upsilon(x,t)+\frac{\partial}{\partial x}\Upsilon(x,t)=\int_x^{\alpha x} M_1+\int_x^{\beta x} M_2,$$

where M_1 and M_2 are given by (2.3.12). Adding and subtracting $(\alpha+\beta)E\Upsilon(x,t)-\alpha E\Upsilon(\alpha x,t)-\beta E\Upsilon(\beta x,t)$ on both sides yields

$$\begin{aligned}&\frac{\partial}{\partial t}\Upsilon(x,t)+\frac{\partial}{\partial x}\Upsilon(x,t)+(\alpha+\beta)E\Upsilon(x,t)-\alpha E\Upsilon(\alpha x,t)-\beta E\Upsilon(\beta x,t)\\&=\int_x^{\alpha x} B_1(\xi)\psi(\xi)d\xi+\int_x^{\beta x} B_2(\xi)\psi(\xi)d\xi+(\alpha+\beta)E\Upsilon(x,t)\\&-\alpha E\Upsilon(\alpha x,t)-\beta E\Upsilon(\beta x,t),\end{aligned} \tag{2.3.13}$$

where $B_1(\xi)=B(\xi)\frac{\Phi(\xi/\alpha}{\Phi(\xi)}$ and $B_2(\xi)=B(\xi)\frac{\Phi(\xi/\beta}{\Phi(\xi)}$. Equation (2.3.13) gives

$$\begin{aligned}&\frac{\partial}{\partial t}\Upsilon(x,t)+\frac{\partial}{\partial x}\Upsilon(x,t)+(\alpha+\beta)E\Upsilon(x,t)-\alpha E\Upsilon(\alpha x,t)-\beta E\Upsilon(\beta x,t)\\&=\int_x^{\alpha x}(B_1(\xi)-\alpha E)\psi(\xi)d\xi+\int_x^{\beta x}(B_2(\xi)-\beta E)\psi(\xi)d\xi.\end{aligned} \tag{2.3.14}$$

Multiplying (2.3.14) by $sgn(\Upsilon)$ gives

$$\begin{aligned}&\frac{\partial}{\partial t}|\Upsilon(x,t)|+\frac{\partial}{\partial x}|\Upsilon(x,t)|+(\alpha+\beta)E|\Upsilon(x,t)|-\alpha E|\Upsilon(\alpha x,t)|\\&-\beta E|\Upsilon(\beta x,t)|\le\int_x^{\alpha x}|(B_1(\xi)-\alpha E)\psi(\xi)|d\xi+\int_x^{\beta x}|(B_2(\xi)-\beta E)\psi(\xi)|d\xi.\end{aligned}$$

Integrating from 0 to ∞ with respect to x and applying boundary conditions on Υ yields

$$\begin{aligned}
&\frac{\partial}{\partial t}\|\Upsilon(t)\| + (\alpha+\beta)E\|\Upsilon(t)\| - 2E\|\Upsilon(t)\| \\
&\leq \int_{x=0}^{\infty}\int_{\xi=x}^{\alpha x} |(B_1(\xi)-\alpha E)\psi(\xi)|d\xi dx + \int_{x=0}^{\infty}\int_{\xi=x}^{\beta x} |(B_2(\xi)-\beta E)\psi(\xi)|d\xi dx \\
&\leq \int_{x=0}^{\infty}\int_{\xi=0}^{\infty} |(B_1(\xi)-\alpha E)\psi(\xi)|d\xi dx + \int_{x=0}^{\infty}\int_{\xi=0}^{\infty} |(B_2(\xi)-\beta E)\psi(\xi)|d\xi dx,
\end{aligned}$$

where $\|\Upsilon(x,t)\|$ denotes the $L^1[0,\infty)$ norm of Υ with respect to x. The above inequality can be written as

$$\frac{\partial}{\partial t}\|\Upsilon(t)\| + (\alpha+\beta-2)E\|\Upsilon(t)\| \leq \kappa\|\psi(t)\|. \tag{2.3.15}$$

Multiplying (2.3.15) by $e^{E(\alpha+\beta-2)}$ and the integrating with respect to t from 0 to ∞ yields

$$\|\Upsilon(t)\| \leq e^{-E(\alpha+\beta-2)t}\|\Upsilon^0\| + \kappa\int_0^{\infty} e^{-E(\alpha+\beta-2)(t-s)}\|\psi(s)\|ds, \tag{2.3.16}$$

where Υ^0 is the value of $\Upsilon(t)$ at $t=0$. The analysis of the constant coefficient case is not applicable here due to the form of the integrand in (2.3.16). Consequently, we introduce

$$\omega(x,t) = \psi(x,t)e^{(\alpha+\beta)Et}. \tag{2.3.17}$$

Multiplying (2.3.9) by $e^{(\alpha+\beta)Et}$ gives

$$\frac{\partial}{\partial t}\omega(x,t) + \frac{\partial}{\partial x}\omega(x,t) = \alpha E\omega(\alpha x,t) + \beta E\omega(\beta x,t) + Q(x,t), \tag{2.3.18}$$

where

$$Q(x,t) = e^{(\alpha+\beta)Et}[\alpha(B_1(\alpha x) - E)\psi(\alpha x, t) + \beta(B_2(\beta x) - E)\psi(\beta x, t) \\ - (\hat{B}(x) - (\alpha+\beta)E)\psi(x,t)].$$

Let the characteristic variables be defined as ξ and η. Integration of (2.3.18) along the characteristic projection yields

$$\frac{\partial t}{\partial \xi} = 1, \quad t(0,\eta) = 0, \quad \frac{\partial x}{\partial \xi} = 1, \quad x(0,\eta) = \eta,$$

so that $x = \xi + \eta$ and $t = \xi$. Thus

$$\frac{\partial \omega}{\partial \xi} = \alpha E \omega(\alpha(\xi+\eta), \xi) + \beta E \omega(\beta(\xi+\eta), \xi) + Q(\xi+\eta, \xi), \quad \omega(\eta, 0) = \omega_0(\eta). \tag{2.3.19}$$

Integration of (2.3.19) with respect to ξ gives

$$\omega(\eta,\xi) = \omega_0(\eta) + E\alpha \int_0^\xi \omega(\alpha\sigma + \alpha\eta, \sigma)d\sigma + E\beta \int_0^\xi \omega(\beta\sigma + \beta\eta, \sigma)d\sigma \\ + \int_0^\xi Q(\sigma+\eta, \sigma)d\sigma.$$

In terms of x and t, we have

$$\omega(x,t) = \omega_0(x-t) + E\alpha \int_0^t \omega(\alpha\sigma + \alpha(x-t), \sigma)d\sigma + \\ E\beta \int_0^t \omega(\beta\sigma + \beta(x-t), \sigma)d\sigma + \int_0^t Q(\sigma + (x-t), \sigma)d\sigma. \tag{2.3.20}$$

Let $\sigma = t - u$. Then (2.3.20) implies

$$\omega(x,t) = \omega_0(x-t) - E\alpha \int_t^0 \omega(\alpha(x-u), t-u)du -$$
$$E\beta \int_t^0 \omega(\beta(x-u), t-u)du \int_t^0 Q(x-u, t-u)du,$$

i.e.,

$$\omega(x,t) = \omega_0(x-t) + E\alpha \int_0^t \omega(\alpha(x-u), t-u)du +$$
$$E\beta \int_0^t \omega(\beta(x-u), t-u)du + \int_0^t Q(x-u, t-u)du. \tag{2.3.21}$$

The first integral on the right hand side of (2.3.21), after iterating the formula for ω, can be expressed as

$$\int_0^t \omega(\alpha(x-u), t-u) = \int_0^t \omega_0(\alpha x - t - (\alpha - 1)u)du$$
$$+E\alpha \int_0^t \int_{s=0}^{t-u} \omega(\alpha^2(x-u) - \alpha s, t-u-s)dsdu$$
$$+E\beta \int_0^t \int_{x=0}^{t-u} \omega(\beta\alpha(x-u) - \alpha s, t-u-s)dsdu$$
$$+ \int_0^t \int_{s=0}^{t-u} Q((\alpha x - \alpha u - s), t-u-s)dsdu. \tag{2.3.22}$$

Similarly, the second integral in (2.3.21) can be expressed as

$$
\begin{aligned}
&\int_0^t \omega(\beta(x-u), t-u) = \int_0^t \omega_0(\beta x - t - (\beta-1)u)du \\
&+E\alpha \int_0^t \int_{s=0}^{t-u} \omega(\alpha\beta(x-u) - \beta s, t-u-s)dsdu \\
&+E\beta \int_0^t \int_{s=0}^{t-u} \omega(\beta^2(x-u) - \beta s, t-u-s)dsdu \\
&+ \int_0^t \int_{s=0}^{t-u} Q((\beta x - \beta u - s), t-u-s)dsdu.
\end{aligned}
\tag{2.3.23}
$$

Substituting (2.3.22) and (2.3.23) in (2.3.21) gives

$$
\begin{aligned}
&\omega(x,t) = \omega_0(x-t) + \int_0^t Q(x-u, t-u)du \\
&+E\alpha \int_0^t \omega_0(\beta x - t - (\beta-1)u)du + E\beta \int_0^t \omega_0(\alpha x - t - (\alpha-1)u)du \\
&+(E\alpha)^2 \int_0^t \int_{s=0}^{t-u} \omega(\alpha^2(x-u) - \alpha s, t-u-s)dsdu \\
&+E^2\alpha\beta \int_0^t \int_{s=0}^{t-u} \omega(\alpha\beta(x-u) - \alpha s, t-u-s)dsdu \\
&+E\alpha \int_0^t \int_{s=0}^{t-u} Q((\alpha x - \alpha u - s), t-u-s)dsdu \\
&+E^2\alpha\beta \int_0^t \int_{s=0}^{t-u} \omega(\alpha\beta(x-u) - \beta s, t-u-s)dsdu \\
&+(E\beta)^2 \int_0^t \int_{s=0}^{t-u} \omega(\beta^2(x-u) - \beta s, t-u-s)dsdu \\
&+E\beta \int_0^t \int_{s=0}^{t-u} Q((\beta x - \beta u - s), t-u-s)dsdu.
\end{aligned}
\tag{2.3.24}
$$

Integrating (2.3.24) with respect to x from 0 to ∞, we have

$$\|\omega(x,t)\| \leq \int_0^\infty |\omega_0(x-t)|dx + \int_0^\infty \int_0^t |Q(x-u,t-u)|dudx$$
$$+E\alpha \int_0^\infty \int_0^t |\omega_0(\beta x - t - (\beta-1)u)|dudx$$
$$+E\beta \int_0^\infty \int_0^t |\omega_0(\alpha x - t - (\alpha-1)u)|dudx$$
$$+(E\alpha)^2 \int_0^\infty \int_0^t \int_{s=0}^{t-u} |\omega(\alpha^2(x-u) - \alpha s, t-u-s)|dsdudx$$
$$+E^2\alpha\beta \int_0^\infty \int_0^t \int_{s=0}^{t-u} |\omega(\alpha\beta(x-u) - \alpha s, t-u-s)|dsdudx$$
$$+E\alpha \int_0^\infty \int_0^t \int_{s=0}^{t-u} |Q((\alpha x - \alpha u - s), t-u-s)|dsdudx$$
$$+E^2\alpha\beta \int_0^\infty \int_0^t \int_{s=0}^{t-u} |\omega(\alpha\beta(x-u) - \beta s, t-u-s)|dsdudx$$
$$+(E\beta)^2 \int_0^\infty \int_0^t \int_{s=0}^{t-u} |\omega(\beta^2(x-u) - \beta s, t-u-s)|dsdudx$$
$$+E\beta \int_0^\infty \int_0^t \int_{s=0}^{t-u} |Q((\beta x - \beta u - s), t-u-s)|dsdudx. \tag{2.3.25}$$

The bounds on each term of the above inequality give

$$\|\omega(x,t)\| \leq (1+E(\alpha+\beta)t)\|\omega_0\| + (E\alpha+E\beta)^2 \int_0^t \|\Upsilon(t-v)\|dv$$
$$+(\alpha+\beta)\int_0^t \|\omega(u)\|du + \alpha(\alpha+\beta)E\int_0^t (t-u)\|\omega(u)\|du.$$
$$+\beta(\alpha+\beta)E\int_0^t (t-u)\|\omega(u)\|du. \tag{2.3.26}$$

Using inequality (2.3.16), the first integral in (2.3.26) becomes

$$(E\alpha+E\beta)^2\int_0^t e^{(\alpha+\beta)Ev}\|\Upsilon(v)\|dv = (E\alpha+E\beta)^2\|\Upsilon^0\|\int_0^t e^{(\alpha+\beta)Ev}e^{-E(\alpha+\beta-2)v}dv$$
$$+(E\alpha+E\beta)^2\kappa\int_0^t e^{(\alpha+\beta)Ev}\int_0^v e^{-E(\alpha+\beta-2)(v-s)}\|\psi(s)\|dsdv, \qquad (2.3.27)$$

which, in terms of ω, the becomes

$$(E\alpha+E\beta)^2\int_0^t e^{(\alpha+\beta)Ev}\|\Upsilon(v)\|dv = (E\alpha+E\beta)^2\|\Upsilon^0\|(e^{2Et}-1)$$
$$+(E\alpha+E\beta)^2\kappa\int_0^t e^{2Ev}\int_0^v e^{-2Es}\|\omega(s)\|dsdv. \qquad (2.3.28)$$

The second term on the right hand side of the above equation, after changing the order of integration, becomes

$$(E\alpha{+}E\beta)^2\kappa\int_0^v e^{-2Es}\|\psi(s)\|\int_0^t e^{2Ev}dvds \le (E\alpha{+}E\beta)^2\kappa\int_0^v e^{-2E(t-s)}\|\omega(s)\|ds.$$

since $0\le v\le t$, we have

$$(E\alpha{+}E\beta)^2\kappa\int_0^v e^{-2Es}\|\omega(s)\|\int_0^t e^{2Ev}dvds \le (E\alpha{+}E\beta)^2\kappa\int_0^t e^{-2E(t-s)}\|\omega(s)\|ds.$$

Inequalities (2.3.28) and (2.3.26) give

$$\|\omega(x,t)\| \le (1+E(\alpha+\beta)t)\|\omega_0\| + (E\alpha+E\beta)^2(e^{2Et}-1)\|\Upsilon^0\|$$
$$+(\alpha+\beta)\int_0^t(1+(\alpha+\beta)E(t-u))\|\omega(u)\|du$$
$$+(E\alpha+E\beta)^2\kappa\int_0^t e^{2E(t-v)}\|\omega(v)\|dv.$$
$$(2.3.29)$$

Since $(1+E(\alpha+\beta)t) \leq (\alpha+\beta)e^{2Et}$ and $(E\alpha+E\beta)^2(e^{2Et}-1) \leq (\alpha+\beta)^2E^3e^{2Et}$, inequality (2.3.29) reduces to

$$\|\omega(x,t)\| \leq (\alpha+\beta)e^{2Et}\|\omega_0\| + (\alpha+\beta)^2E^3e^{2Et}\|\Upsilon^0\|$$
$$+(\alpha+\beta)^2(1+E^2\kappa)\int_0^t e^{2E(t-v)}\|\omega(v)\|dv, \tag{2.3.30}$$

so that

$$e^{-2Et}\|\omega(x,t)\| \leq (\alpha+\beta)\|\omega_0\| + (\alpha+\beta)^2E^3\|\Upsilon^0\|$$
$$+(\alpha+\beta)^2(1+E^2\kappa)\int_0^t e^{-2Ev}\|\omega(v)\|dv. \tag{2.3.31}$$

Let

$$f(t) = \int_0^t e^{-2Es}\|\omega(s)\|ds.$$

Then

$$f'(t) = e^{-2Et}\|\omega(s)\|, \tag{2.3.32}$$

where $f'(t) = \frac{df(t)}{dt}$. The inequality (2.3.31) in terms of f becomes

$$f'(t) \leq (\alpha+\beta)\|\omega_0\| + (\alpha+\beta)^2E^3\|\Upsilon^0\| + (\alpha+\beta)^2(1+E^2\kappa)f(t). \tag{2.3.33}$$

Using Gronwall's lemma [76], we have

$$f(t) \leq \frac{e^{(\alpha+\beta)^2(1+E^2\kappa)t}}{(\alpha+\beta)^2(1+E^2\kappa)}\big[(\alpha+\beta)\|\omega_0\| + (\alpha+\beta)^2E^3\|\Upsilon^0\|\big], \tag{2.3.34}$$

which, differentiating with respect to t, yields

$$f'(t) \leq e^{(\alpha+\beta)^2(1+E^2\kappa)t}\big[(\alpha+\beta)\|\omega_0\| + (\alpha+\beta)^2E^3\|\Upsilon^0\|\big]. \tag{2.3.35}$$

Equation (2.3.32) and inequality (2.3.35) give

$$\|\omega(t)\| = e^{2Et} f'(t) \le e^{(\alpha+\beta)^2(1+E^2\kappa)t} \big[(\alpha+\beta)\|\omega_0\| + (\alpha+\beta)^2 E^3 \|\Upsilon^0\|\big] e^{2Et},$$

which, in terms of ϱ and Φ, becomes

$$\|\varrho(t)\Phi(x)\| \le \big(e^{((\alpha+\beta)^2(1+E^2\kappa)+(2-\alpha-\beta)E)t} \big[(\alpha+\beta)\|\omega_0\| + (\alpha+\beta)^2 E^3 \|\Upsilon^0\|\big]\big).$$

Consequently, as t goes to infinity the solution, any solution $n(x,t)$ to (2.1.2)-(2.1.4) approaches the separable solution (2.1.5). □

Chapter 3

Asymmetric cell division with stochastic growth rate

3.1 Introduction

The first order hyperbolic functional partial differential equation (PDE) of the pantograph type

$$\frac{\partial n}{\partial t} + g\frac{\partial n}{\partial x} = b\alpha^2 n(\alpha x, t) - (b + \mu)n(x, t), \tag{3.1.1}$$

together with an initial cell distribution

$$n(x, 0) = n_0(x), \tag{3.1.2}$$

and the boundary condition

$$n(0, t) = 0, \tag{3.1.3}$$

for $t > 0$, arises in a size structured cell growth model in which cells grow at a constant rate $g > 0$ and divide into $\alpha > 1$ equal sized daughter cells at a constant rate $b > 0$. Here size is mass (or DNA content), $n(x,t)$ is the number density of cells of size x at time t and $\mu > 0$ is the per capita death rate. The cell growth model (3.1.1)-(3.1.3) is based on a model proposed by Sinko and Streifer [16, 17] for planarian worms. The functional PDE (3.1.1) was studied, among others, by Hall and Wake [10, 66], Begg *et al.* [65], Metz and Diekmann [70] and Zaidi *et al.* [22]. Perthame and Ryzhik [15] established the existence of a unique eigenvalue λ and the corresponding positive eigenfunction $y(x)$ towards which all solutions to (3.1.1) converge exponentially for large time, i.e.,

$$\|e^{-\lambda t}n(x,t) - < n_0 > y(x)\|_{L^1(\mathbb{R}^+)} \to 0,$$

as $t \to \infty$. Here $< n_0 >= \int_0^\infty n_0(x)dx$ is a normalization constant. Hall and Wake [10] determined the long time asymptotic solution to (3.1.1) by considering a separable solution of the form $n(x,t) = N(t)y(x)$, where y satisfies the pantograph equation

$$gy'(x) + b\alpha y(x) = \alpha^2 by(\alpha x).$$

They called it a Steady Size Distribution (SSD) solution and showed that y can be expressed as a certain Dirichlet series.

The functional PDE (3.1.1) models a symmetric cell division problem in which cells divide into α daughter cells of equal size. Cells, however, may divide asymmetrically [71]. The simplest case is when a cell divides into two daughters of different sizes, say size α and size β. It is assumed that there is no loss of mass (or DNA content) in the division. The sizes α and β are thus related by

$$\frac{1}{\alpha} + \frac{1}{\beta} = 1. \tag{3.1.4}$$

Asymmetrical division was studied, among others, by Diekmann *et al.* [55] and Heijmans [56]. This type of division leads to a functional partial differential equation with two non local terms

$$\frac{\partial n}{\partial t} + g\frac{\partial n}{\partial x} = \alpha bn(\alpha x, t) + \beta bn(\beta x, t) - (\mu + b)n(x, t), \tag{3.1.5}$$

where $\alpha > 2 > \beta > 1$. Suebcharoen *et al.* [30] found the separable solution to (3.1.5) subject to conditions (3.1.2) and (3.1.3) and Zaidi *et al.* [29] showed that this solution is unimodal.

A second order analogue of the functional PDE (3.1.1), involving symmetric division of cells, arises when dispersion is included by virtue of stochasticity in the growth rate of cells [32, 11]. This leads to a modified Fokker-Planck equation of the form

$$\frac{\partial n}{\partial t} + g\frac{\partial n}{\partial x} = D\frac{\partial^2}{\partial x^2}(n(x, t)) + b\alpha^2 n(\alpha x, t) - bn(x, t) - \mu n(x, t), \tag{3.1.6}$$

where $D = \frac{\sigma^2}{2} \geq 0$ is the constant dispersion coefficient and σ is the standard deviation. We thus assume a Gaussian "white noise" sharply peaked around g, which now represents the mean growth. This means, to leading order ϵ^2, D is a constant where ϵ is roughly the "width" of the Gaussian 'blip'. Wake *et al.* [19] derived the SSD solution to the equation and showed that the solution is positive and unique. They, however, did not establish that their

SSD solution was in fact the long time asymptotic solution. Efendiev *et al.* [31] solved PDE (3.1.6) and established that this SSD solution is the long time asymptotic solution. The first order cell growth problem and its second order generalization have also been studied for non-constant coefficients [72], [21], [62].

In this chapter, we generalize the work of Efendiev *et al.* [31] to the case of asymmetric division. Specifically, we study the PDE

$$\frac{\partial n}{\partial t} + g\frac{\partial n}{\partial x} = \frac{\partial^2}{\partial x^2}(Dn(x,t)) + b\alpha n(\alpha x,t) + b\beta n(\beta x,t) - bn(x,t) - \mu n(x,t). \tag{3.1.7}$$

This equation is supplemented by the no-flux conditions (1.22) and an initial number density (3.1.2). The boundary conditions (1.22) are Robbins type conditions which suggest that there is no flux of cells across the boundary at $x = 0$ and at infinity. In this model, the conservation of mass (or DNA content) during division is assumed so that α and β satisfy (3.1.4)

The PDE (3.1.7) is a special case of a more general coagulation-fragmentation equation for which there is a dearth of general solution techniques. Here, we solve (3.1.7) analytically and establish directly the long time asymptotic behaviour of solutions.

The PDE (3.1.7) can be reduced to a simplified form by using a sequence of transformations. The transformation

$$n(x,t) = e^{-(b+\mu)t}\tilde{n}(x,t)$$

reduces (3.1.7) to

$$\frac{\partial}{\partial t}\tilde{n}(x,t) + g\frac{\partial}{\partial x}\tilde{n}(x,t) = \frac{\partial^2}{\partial x^2}(D\tilde{n}(x,t)) + b\alpha\tilde{n}(\alpha x,t) + b\beta\tilde{n}(\beta x,t),$$

which, using the transformation $x = g\hat{x}$, can be further reduced to

$$-\frac{\partial^2}{\partial \hat{x}^2}(\hat{D}\hat{n}(\hat{x},t)) + \frac{\partial}{\partial t}\hat{n}(\hat{x},t) + \frac{\partial}{\partial \hat{x}}\hat{n}(\hat{x},t) = b\alpha\hat{n}(\alpha\hat{x},t) + b\beta\hat{n}(\beta\hat{x},t).$$

Here, $\hat{D} = \frac{D}{g^2}$ and $\hat{n}(\hat{x},t) = \tilde{n}(g\hat{x},t)$. The problem can thus be simplified, by dropping circumflexes and tildes of the above PDE, to

$$-\frac{\partial^2}{\partial x^2}(Dn(x,t)) + \frac{\partial}{\partial t}n(x,t) + \frac{\partial}{\partial x}n(x,t) = b\alpha n(\alpha x,t) + b\beta n(\beta x,t), \quad (3.1.8)$$

along with conditions (3.1.2) and (1.22). If, for any fixed $t > 0$ and for all $x \geq 0$, we assume that the solutions to (3.1.8) subject to conditions (3.1.2) and (1.22) are integrable with respect to x, then PDE (3.1.8) transforms to

$$-\frac{\partial^2}{\partial x^2}(Dm(x,t)) + \frac{\partial}{\partial t}m(x,t) + \frac{\partial}{\partial x}m(x,t) = b\{m(\alpha x,t) + m(\beta x,t)\}, \quad (3.1.9)$$

where

$$m(x,t) = \int_x^\infty n(\xi,t)d\xi.$$

To specify a boundary condition on (3.1.9), we integrate (3.1.8) with respect to x from 0 to ∞ and apply conditions (1.22). This gives

$$\frac{\partial}{\partial t}m(0,t) = 2bm(0,t),$$

so that the boundary condition is

$$m(0,t) = k_0 e^{2bt}, \tag{3.1.10}$$

for some constant k_0. The initial condition to (3.1.9) can be obtained by evaluating the expression for $m(x,t)$ at $t=0$. This yields

$$m_0(x) = m(x,0) = \int_x^\infty n_0(\xi) d\xi. \tag{3.1.11}$$

The no-flux conditions (1.22) become

$$\lim_{x \to 0^+} -D \frac{\partial^2}{\partial x^2} m(x,t) + \frac{\partial}{\partial x} m(x,t) = 0, \tag{3.1.12}$$

$$\lim_{x \to \infty} -D \frac{\partial^2}{\partial x^2} m(x,t) + \frac{\partial}{\partial x} m(x,t) = 0. \tag{3.1.13}$$

In the next section, we derive some qualitative results that concern the existence of a probability density function (pdf) eigenvalue, the steady size distribution (SSD) solution to the corresponding eigenfunction, its positivity and uniqueness. In section 3.3, we solve the full PDE (3.1.7) in the form of a certain series. In section 3.4, we show that the general solution obtained in section 3.3 approaches the SSD solution.

3.2 The Separable Solution

In this section, we determine separable solutions to the original PDE (3.1.6) subject to conditions (3.1.2) and (1.22). The separable solution to the transformed equation (3.1.9) subject to conditions (3.1.10)-(3.1.13) can be determined in a similar manner. The first order PDE (3.1.5) involving two non local terms was shown to have an eigenvalue and a corresponding SSD solution as a certain double Dirichlet series ([29]). The second order case involving a modified Fokker-Planck equation (3.1.6) with only one non local term was considered by Wake *et al.* [19] and they found the eigenvalue and the SSD solution as a certain single Dirichlet series. In both the instances, the eigenvalue and the SSD solution were found by considering a separable solution to the PDE. Motivated by this, we find the eigenvalue and the SSD solution to the second order equation (3.1.7) with two non local terms by first considering a solution of the form

$$n(x,t) = N(t)y(x), \tag{3.2.1}$$

where y is a pdf and $N(t) = \int_0^\infty n(x,t)dx$ is the total population at time t. The Solution form (3.2.1) and equation (3.1.7) yield

$$n(x,t) = e^{-\lambda t}y(x),$$

where λ is the constant of separation. In addition, y satisfies the ordinary functional differential equation

$$Dy''(x) - gy'(x) + \alpha by(\alpha x) + \beta by(\beta x) - (\mu + b - \lambda)y(x) = 0, \tag{3.2.2}$$

along with the no-flux condition

$$Dy'(0) - gy(0) = 0, \tag{3.2.3}$$

and the conditions

$$\lim_{x\to\infty} y(x) = 0, \quad \lim_{x\to\infty} y'(x) = 0. \tag{3.2.4}$$

Since y is a pdf, we require that $y(x) \geq 0$ for all $x \geq 0$ and

$$\int_0^\infty y(x)dx = 1. \tag{3.2.5}$$

The eigenvalue λ can be found by integrating (3.2.2) from 0 to ∞ and using conditions (3.2.3)-(3.2.5). This gives

$$\lambda = \mu - b, \tag{3.2.6}$$

and so,

$$N(t) = ke^{(b-\mu)t},$$

for some constant $k > 0$. This indicates an exponential growth in time if the rate of division b is greater than the mortality rate μ. We note that the λ given by (3.2.6) is independent of α and β in contrast with the symmetric cell division ([19]), where the value of λ is $\mu - b(\alpha - 1)$. It is also worth noting that the eigenvalue λ for the case $D = 0$ is the same as given in (3.2.6) (cf. [29]). The eigenvalue (3.2.6) reduces (3.2.2) to

$$Dy''(x) - gy'(x) + \alpha by(\alpha x) + \beta by(\beta x) - 2by(x) = 0. \tag{3.2.7}$$

Motivated by the observation that the PDE (3.1.6) involving only one non local term has an SSD solution in terms of a single Dirichlet series, and that the PDE (3.1.5) with two non local terms has an SSD solution in terms of a double Dirichlet series, we seek a solution to (3.2.7) of the form

$$y(x) = \sum_{k=0}^{\infty}\sum_{j=0}^{\infty} c_{k,j} e^{-\alpha^k \beta^j A x}, \tag{3.2.8}$$

where the coefficients $c_{k,j}$ and A are to be determined. From equation (3.2.8) we have

$$y'(x) = \sum_{k=0}^{\infty}\sum_{j=0}^{\infty}(-\alpha^k\beta^j A) c_{k,j} e^{-\alpha^k \beta^j A x}, \tag{3.2.9}$$

$$y''(x) = \sum_{k=0}^{\infty}\sum_{j=0}^{\infty}(\alpha^{2k}\beta^{2j} A^2) c_{k,j} e^{-\alpha^k \beta^j A x}, \tag{3.2.10}$$

$$y(\alpha x) = \sum_{k=0}^{\infty}\sum_{j=0}^{\infty} c_{k,j} e^{-\alpha^{k+1} \beta^j A x}, \tag{3.2.11}$$

$$y(\beta x) = \sum_{k=0}^{\infty}\sum_{j=0}^{\infty} c_{k,j} e^{-\alpha^k \beta^{j+1} A x}. \tag{3.2.12}$$

Equations (3.2.7) and (3.2.8)-(3.2.12) give

$$D\sum_{k=0}^{\infty}\sum_{j=0}^{\infty}\alpha^{2k}\beta^{2j}A^2 c_{k,j} e^{-\alpha^k \beta^j A x} - g\sum_{k=0}^{\infty}\sum_{j=0}^{\infty}(-\alpha^k\beta^j A) c_{k,j} e^{-\alpha^k \beta^j A x} +$$
$$\alpha b\sum_{k=0}^{\infty}\sum_{j=0}^{\infty} c_{k,j} e^{-\alpha^{k+1} \beta^j A x} + \beta b\sum_{k=0}^{\infty}\sum_{j=0}^{\infty} c_{k,j} e^{-\alpha^k \beta^{j+1} A x} - 2b\sum_{k=0}^{\infty}\sum_{j=0}^{\infty} c_{k,j} e^{-\alpha^k \beta^j A x} = 0. \tag{3.2.13}$$

Equating coefficients of e^{-Ax}, $e^{-\alpha^k Ax}$,$e^{-\beta^j Ax}$, and $e^{-\alpha^k\beta^j Ax}$ yields the indicial equation

$$DA^2 + gA - 2b = 0, \tag{3.2.14}$$

and

$$c_{k,0} = \frac{(-1)^k(\alpha b)^k c_{0,0}}{\prod_{s=1}^{k}(DA^2\alpha^{2s} + gA\alpha^s - 2b)}, \tag{3.2.15}$$

$$c_{0,j} = \frac{(-1)^j(\beta b)^j c_{0,0}}{(\prod_{s=1}^{j}(DA^2\beta^{2s} + gA\beta^s - 2b)}, \tag{3.2.16}$$

$$c_{k,j} = \frac{-b}{(DA^2\alpha^{2k}\beta^{2j} + gA\alpha^k\beta^j - 2b)}(\alpha c_{k-1,j} + \beta c_{k,j-1}), \tag{3.2.17}$$

for $k, j \in \mathbb{N}$. Since the series (3.2.8) diverges if $A < 0$, we choose A to be the positive root of (3.2.14). This gives

$$A = \frac{-g + \sqrt{g^2 + 8bD}}{2D}. \tag{3.2.18}$$

The coefficient $c_{0,0}$ is chosen so that $\int_0^\infty y dx = 1$. We note that (3.2.8) and (3.2.15)-(3.2.17) reduce to the results obtained by Zaidi *et al.* when $D = 0$ (cf. [29]).

The convergence of series (3.2.8) for the $c_{k,j}$ defined by (3.2.15)-(3.2.17) can be established in a way similar to that used by Zaidi *et al.* [21]. The positivity, uniqueness and unimodality of the double Dirichlet series solution can be proved by employing analysis, similar to the one used by Suebcharoen *et al.* [30] and Zaidi *et al.* [29].

We can determine the separable solution F to the transformed PDE (3.1.9) subject to conditions (3.1.10)-(3.1.13) by term by term integration of (3.2.8).

3.3 The General Solution

In this section, we find the general solution to the initial boundary value problem (3.1.9)-(3.1.13). In the next section, we show that this general solution approaches the SSD solution obtained in Section 3.2. Motivated by this, let

$$m(x,t) = e^{2bt}F(x) - v(x,t), \tag{3.3.1}$$

where $v(x,t)$ satisfies

$$-Dv_{xx}(x,t) + v_x(x,t) + v_t(x,t) = bv(\alpha x,t) + bv(\beta x,t), \tag{3.3.2}$$

along with the initial condition

$$v(x,0) = F(x) - m_0(x) = w_0(x). \tag{3.3.3}$$

Here, F satisfies

$$-DF''(x) + F'(x) + 2bF(x) = b(F(\alpha x) + F(\beta x)). \tag{3.3.4}$$

The above ordinary differential equation can be obtained from (3.1.9) by following a pattern similar to that used in Section 3.2 for equation (3.1.7), i.e., we assume a separable solution to (3.1.9) of the form $m(x,t) = M(t)F(x)$, where $M(t) = k_0 e^{bt}$, for some constant k_0, and F satisfies (3.3.4). Given the relation between m and n, equation (3.3.4) is in fact an "integrated" version of (3.2.7). We know the solution to (3.3.4) with mortality transformed out and $g = 1$ is given by the double Dirichlet series

$$F(x) = \sum_{k=0}^{\infty} \sum_{j=0}^{\infty} d_{k,j} e^{-\alpha^k \beta^j A x},$$

where

$$d_{k,0} = \frac{(-1)^k b^k c_{0,0}}{\prod_{s=1}^{k} (DA^2\alpha^{2s} + A\alpha^s - 2b)},$$

$$d_{0,j} = \frac{(-1)^j b^j c_{0,0}}{(\prod_{s=1}^{j} (DA^2\beta^{2s} + A\beta^s - 2b)},$$

$$d_{k,j} = \frac{-b}{(DA^2\alpha^{2k}\beta^{2j} + gA\alpha^k\beta^j - 2b)}(c_{k-1,j} + c_{k,j-1}),$$

and

$$A = \frac{-1 + \sqrt{1 + 8bD}}{2D}.$$

Note that

$$-DF''(0) + F'(0) + 2bF(0) = 2bF(0),$$

so that $e^{2bt}F(x)$ also satisfies the no-flux condition (3.1.12) at $x = 0$. The solution $v(x,t)$ to (3.3.2) can be obtained using the technique of Efendiev *et al.* [31]. In the absence of the functional term, equation (3.1.9) along with (3.1.11) corresponds to the Cauchy problem

$$-Du_{xx} + u_x + u_t = 0,$$

$$u(x, 0) = u_0(x).$$

The solution to the above problem is given by

$$u(x,t) = \int_0^\infty \psi(x,\xi,t) u_0(\xi) d\xi,$$

where

$$\psi(x,\xi,t) = \frac{e^{\frac{-t}{4D}} e^{\frac{-(\xi-x)}{2D}}}{2\sqrt{D\pi t}} \{ e^{\frac{-(x-\xi)^2}{4Dt}} - e^{\frac{-(x+\xi)^2}{4Dt}} \}. \tag{3.3.5}$$

The kernel ψ is the same as that in Efendiyev *at al.* [31], and has the properties

(a) $\lim_{t\to 0^+} \int_0^\infty \psi(x,\xi,t) u_0(\xi) d\xi = u_0(x)$.

(b) $\psi(0,\xi,t) = 0$ for all $t > 0$.

(c) $-D\psi_{xx} + \psi_x + \psi_t = 0$.

(d) $\int_0^\infty \psi(x,\xi,t) d\xi \leq 1$.

(e) $\int_0^\infty \psi(x,\xi,t) dx \leq 1$.

We seek a solution to (3.3.2) of the form

$$v(x,t) = \sum_{k=0}^\infty v_k(x,t), \tag{3.3.6}$$

where, if the differential operator L is defined by

$$L\phi = -D\phi_{xx} + \phi_x + \phi_t,$$

the v_k are defined by

$$Lv_{k+1} = b\{v_k(\alpha x,t) + v_k(\beta x,t)\}, \tag{3.3.7}$$

with

$$v_0(x,t) = \int_0^\infty \psi(x,\xi,t) w_0(\xi) d\xi, \tag{3.3.8}$$

and for $k \geq 0$,

$$v_{k+1}(x,t) = b \int_0^t \int_0^\infty \psi(x,\xi,t-\tau)\{v_k(\alpha\xi,\tau) + v_k(\beta\xi,\tau)\} d\xi d\tau. \tag{3.3.9}$$

We note that the v_k defined by (3.3.9) satisfy equation (3.3.7). Also from equation (3.3.9), it is clear that for $k \geq 1$

$$v_k(x,0) = 0, \tag{3.3.10}$$

and from equation (3.3.9) and property (b), that

$$v_k(0,t) = 0. \tag{3.3.11}$$

We show that the series solution (3.3.6) converges uniformly in $\Omega_T = \{(x,t) : x \geq 0, 0 \leq t \leq T\}$. Let

$$\|w_0\| = \sup_{x \geq 0} |w_0(x)|.$$

Then, using property (d) of ψ,

$$|v_0(x,t)| \leq \int_0^\infty |\psi(x,\xi,t)||w_0(\xi)| d\xi \leq \|w_0\|,$$

and

$$|v_1(x,t)| = b\int_0^t\int_0^\infty |\psi(x,\xi,t-\tau)|\{|v_0(\alpha\xi,\tau)| + |v_0(\beta\xi,\tau)|\}d\xi d\tau$$
$$\leq 2b\|w_0\|t,$$

since $\psi(x,\xi,t-\tau)$ also satsifies property (d). Continuing this process,

$$|v_2(x,t)| \leq b\int_0^t\int_0^\infty |\psi(x,\xi,t-\tau)|\{|v_1(\alpha\xi,\tau)| + |v_1(\beta\xi,\tau)|\}d\xi d\tau$$
$$\leq b\int_0^t 2b\|w_0\|\tau\int_0^\infty \psi(x,\xi,t-\tau)d\xi d\tau$$
$$\leq (2b)^2\|w_0\|\frac{t^2}{2},$$

and in general,

$$|v_k(x,t)| \leq (2b)^k\|w_0\|\frac{t^k}{k!};$$

hence,

$$|v(x,t)| \leq \sum_{k=0}^\infty |v_k(x,t)| \leq \|w_0\|e^{2bt},$$

so that the solution converges uniformly in Ω_T.

3.4 Large time asymptotics

In this section, we show that the solution v obtained in the Section 3.3 goes to zero in the L^1 norm as time goes to infinity. Let

$$\|f\|_1 = \int_0^\infty |\phi(x,t)|dx.$$

Then

$$\|v_{k+1}\|_1 = \int\limits_0^\infty |v_{k+1}(x,t)|dx = \int\limits_0^\infty |b\int\limits_0^t \int\limits_0^\infty \psi(x,\xi,t-\tau)\{v_k(\alpha\xi,\tau) + v_k(\beta\xi,\tau)d\xi d\tau|dx$$
$$\leq b\int\limits_0^t \int\limits_0^\infty \{\int\limits_0^\infty \psi(x,\xi,t-\tau)dx\}|v_k(\alpha\xi,\tau) + v_k(\beta\xi,\tau)|d\xi d\tau,$$

which, using property (d) of ψ, gives

$$\|v_{k+1}\|_1 \leq b\int\limits_0^t \int\limits_0^\infty (|v_k(\alpha\xi,\tau) + v_k(\beta\xi,\tau)|)d\xi d\tau,$$
$$= b\int\limits_0^t (\frac{1}{\alpha}\|v_k\|_1 + \frac{1}{\beta}\|v_k\|_1)d\tau,$$
$$= b\int\limits_0^t \|v_k\|_1 d\tau. \tag{3.4.1}$$

Now,

$$\|v_0\|_1 = \int\limits_0^\infty |v_0(x,t)|dx = \int\limits_0^\infty |\int\limits_0^\infty \psi(x,\xi,t)w_0(\xi)d\xi|dx,$$
$$\leq \int\limits_0^\infty \int\limits_0^\infty |\psi(x,\xi,t)||w_0(\xi)|d\xi dx,$$

which, using property (d), gives

$$\|v_0\|_1 \leq \int\limits_0^\infty |w_0(\xi)|d\xi;$$

thus,

$$\|v_0\|_1 \leq \|w_0\|_1. \tag{3.4.2}$$

Similarly, for $k = 0$, inequalities (3.4.1) and (3.4.2) give

$$\|v_1\|_1 \leq b\|w_0\|_1 t.$$

In general, for any $k \geq 0$,

$$\|v_k\|_1 \leq b^k \|w_0\|_1 \frac{t^k}{k!}.$$

Thus

$$\|v(x,t)\|_1 \leq e^{bt}\|w_0\|_1. \tag{3.4.3}$$

From equation (3.3.1), we have

$$|m(x,t)e^{-2bt} - F(x)| = e^{-2bt}|v(x,t)|,$$

so that

$$\int_0^\infty |m(x,t)e^{-2bt} - F(x)|dx = \int_0^\infty e^{-2bt}|v(x,t)|dx.$$

The above equation and inequality (3.4.3) thus give

$$\int_0^\infty |m(x,t)e^{-2bt} - F(x)|dx \leq e^{-bt}\|w_0\|_1.$$

It is evident from the above equation that the solution $m(x,t)$ converges to the separable solution $e^{2bt}F(x)$ for large time.

3.5 Conclusions

Solutions to the cell division equation (3.1.7) subject to conditions (1.22) were procured analytically, which is significant because there is a paucity of analytical solutions to most functional PDEs. The nonlocal PDE considered here with constant D, g and b has a dominant eigenvalue and a corresponding eigenfunction towards which solutions to the PDE converge exponentially in time. This is different from the case when $D = 0$ and $G(x) = x$ which, for instance, gives rise to time dependent oscillatory solutions [24].

The solution technique for the symmetric cell division case can be adapted to determine the general solution for the case of asymmetric cell division. We conclude that adding dispersion to the cell division problem (3.1.5) does not impact the shape and positivity the SSD solution in a substantial way (See Figure (3.1)), though it does increase the number density of smaller cells. We also conclude that shape of the SSD solution and its positivity remain largely unaffected by the mode of cell division. Even if cells divide asymmetrically, the SSD solution still remains positive and unimodal (see Figure 3.2). It has been mooted that cells under division do not always produce daughter cells of exactly same size [20]. The analysis here shows that the model is robust in that the same general behaviour occurs even under asymmetrical division.

The SSD solution is another name for the positive separable solution. This solution is important in simpler models because it also corresponds to the solution to which other solutions converge for large time. We have shown that

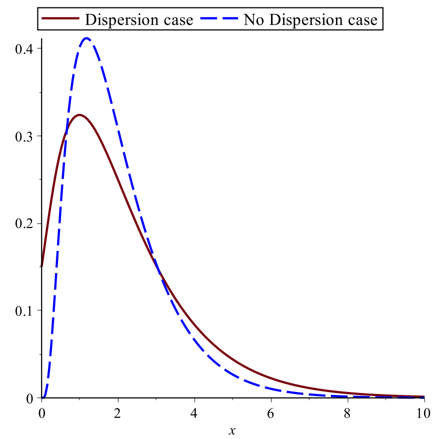

Figure 3.1: The solution obtained by Zaidi *et al.* [29] for the no dispersion case and the solution given by the Dirichlet series (3.2.8) for $D = 1$. Here, $\alpha = 3$, $\beta = \frac{3}{2}, b = 1$ and $g = 2$ units.

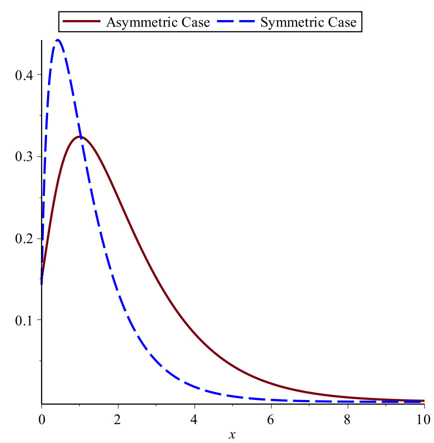

Figure 3.2: The solution obtained by Wake *et al.* [19] for the case of symmetric cell division and the solution given by the Dirichlet series (3.2.8) for binary asymmetric division. Here, $D = 1, \alpha = 3$, $\beta = \frac{3}{2}, b = 1$ and $g = 2$ units.

the SSD for this problem is the long time attracting solution for the model.

The cell division model considered in this chapter is a size structured model and is essentially one dimensional. It is the simplest version of the process, but underlying this is some of the biological assumptions. Certainly we can go up to higher dimensions with the model by bringing in, for example, age structure as well as size. This will be addressed in future work.

The more general case where $D = D(x, n)$ and $G = G(x, n)$ is also to be addressed in future work. Some work in this direction, for related models, has been done in [73, 74].

Chapter 4

Inhomogeneous Pantograph Type Equation with singular coefficients and symmetric cell division

4.1 Introduction

This chapter deals with the existence of solutions to a certain class of functional partial differential equations (PDEs) of the form

$$\begin{aligned} n_t(x,t) + (G(x,t)n(x,t))_x + B(x,t)n(x,t) =& (D(x,t)n(x,t))_{xx}(x,t) \\ &+ \alpha^2 B(\alpha x,t)n(\alpha x,t) + f(x,t), \end{aligned} \tag{4.1.1}$$

subject to the initial condition

$$\lim_{t \to 0^+} n(x,t) = n_0(x), \tag{4.1.2}$$

the boundary conditions (1.22), and the condition

$$\lim_{x \to \infty} n(x,t) = 0. \tag{4.1.3}$$

for $t > 0$. Here, $\alpha > 1$, and $f(x,t)$ is a known forcing term. If $f \equiv 0$, then (4.1.1) appears in a cell division model with stochastic growth rate, where $x \geq 0$ represents size and $t > 0$ denotes time. The coefficients $D(x,t)$, $G(x,t)$ and $B(x,t)$ represent the dispersion rate, growth rate and the frequency of division of cells respectively. Also, $n(x,t)$ denotes the number density of cells.

The homogeneous version of (4.1.1) has been studied for constant coefficients. Wake *et al.* [19] obtained separable solutions to this problem. Separable solutions are of interest since these usually correspond to the large time attracting solutions, referred to as steady size distribution (SSD) solutions. Wake *et al.*, however, did not show that their separable solutions are the large time attracting solutions to the problem. Efendiyev *et al.* [31] then solved the full PDE by developing a solution technique. They obtained exact solutions to the problem and showed that the separable solution obtained by Wake *et al.* was the SSD solution. Recently, Gul [9] studied the case of linear growth in size with constant dispersion and division rate, and showed that the problem does not have a steady size distribution solution as $t \to \infty$. Zaidi *et al.* [21] studied the homogeneous problem for $D(x,t) = ax^2$, $B(x,t) = bx^2$, $G(x,t) = gx$, where $a > 0, b, > 0$ and $g > 0$, and showed that there is a unique probability density function that solves the problem. Lo [12] then obtained the exact solution of the problem.

The homogeneous first order case ($D = 0$) has also been studied and has applications in fragmentation in polymers and droplets [2, 8, 13], internet protocols in telecommunication systems [3], planarian worm division [16, 17], and a cell division model [10]. For constant coefficients, Hall and Wake [10] obtained separable solutions to the problem. Perthame and Ryzhik [15] showed that the separable solutions of Hall and Wake are the SSD solutions to the problem as $t \to \infty$. The full problem was solved by Zaidi *et al.* [22] using a novel solution technique. The homogeneous first order case has also been studied for certain choices of size dependent coefficients. Hall and Wake studied separable solutions for $G(x,t) = ax$ and $B(x,t) = bx^k$, where a, b and k are positive numbers [72]. The full PDE problem was solved by van Brunt *et al.* [24]. The large time attracting solution, in this case, is periodic in time. The dynamics are thus different from the constant coefficient case. There has been much progress, however, on the local inhomogeneous equations with singular coefficients and explicit solutions have been obtained. For instance, Bizhanova [6] studied a Cauchy problem entailing a parabolic equation with singular coefficients and proved the existence and uniqueness of solutions to the problem. He also obtained explicit solutions to the problem along with the estimates of the solution.

There are no general methods for solving such initial boundary value problems even for a restricted class of coefficients. The inhomogeneous problem has not been solved hitherto. In this paper, we consider time dependent coefficients $D(x,t) = \frac{D}{t}$, $G(x,t) = \frac{g}{t}$, $B(x,t) = \frac{b}{t}$, where D, g and b are positive numbers, and show that for a certain class of functions $f(x,t)$, there exists solutions to the initial boundary value problem. With these choice of coefficients, equation (4.1.1) reduces to

$$-\frac{D}{t}n_{xx}(x,t)+\frac{g}{t}n_x(x,t)+n_t(x,t)+\frac{b}{t}n(x,t)=\frac{b}{t}\alpha^2 n(\alpha x,t)+f(x,t),$$

which can be simplified, using the transformation $x = g\tilde{x}$, to

$$-\frac{\tilde{D}}{t}\tilde{n}_{xx}(\tilde{x},t)+\frac{1}{t}\tilde{n}_x(\tilde{x},t)+\tilde{n}_t(\tilde{x},t)+\frac{b}{t}\tilde{n}(\tilde{x},t)=\frac{b}{t}\alpha^2\tilde{n}(\alpha\tilde{x},t)+f(\tilde{x},t),$$

where $\tilde{D}=\frac{D}{g^2}$ and $\tilde{n}(\tilde{x},t)=n(g\tilde{x},t)$. Dropping the tildes yields

$$-\frac{D}{t}n_{xx}+\frac{1}{t}n_x(x,t)+n_t(x,t)+\frac{b}{t}n(x,t)=\frac{b}{t}\alpha^2 n(\alpha x,t)+f(x,t). \quad (4.1.4)$$

We consider functions f and solutions n that are integrable with respect to x for any fixed t. The transformations

$$m(x,t)=\int_x^\infty n(\xi,t)d\xi, \qquad \text{and} \qquad q(x,t)=\int_x^\infty f(\xi,t)d\xi,$$

yield

$$-\frac{D}{t}m_{xx}+\frac{1}{t}m_x(x,t)+m_t(x,t)+\frac{b}{t}m(x,t)=\frac{b}{t}\alpha m(\alpha x,t)+q(x,t). \quad (4.1.5)$$

The boundary condition on m is specified by integrating (4.1.4) with respect to x from 0 to ∞ and using conditions (1.22). This gives

$$m_t(0,t)-\frac{b}{t}(\alpha-1)m(0,t)=q(0,t),$$

so that

$$m(0,t) = ct^{b(\alpha-1)} + t^{b(\alpha-1)} \int t^{-b(\alpha-1)} q(0,t)dt, \tag{4.1.6}$$

where c is the constant of integration. The initial condition on m is

$$m(x,0) = m_0(x) = \int_x^\infty n_0(\xi)d\xi. \tag{4.1.7}$$

In the next section, we obtain a Mellin transform solution to the problem. In Section 4.3, we show that the inverse Mellin transform exists for a certain class of source terms f. We conclude the discussion in Section 4.4

4.2 A Mellin transform Solution

In this section, we study the existence and uniqueness of a Mellin transform solution to equation (4.1.5) subject to conditions (4.1.6) and (4.1.7). The Mellin transform converts equation (4.1.5) to a nonhomogeneous ordinary differential equation, which can be solved using the Green's function. This leads to an integral equation that has a unique solution.

Applying the Mellin transform to equation (4.1.5) with respect to time yields

$$\begin{aligned} -DM_{xx}(x,s-1) - (s-1-b)M(x,s-1) + M_x(x,s-1) =& b\alpha M(\alpha x, s-1) \\ &+ F(x,s-1), \end{aligned} \tag{4.2.1}$$

where $s < 1$, and

$$M(x, s-1) = \int_0^\infty t^{s-2} m(x,t)dt \qquad \text{and} \qquad F(x, s-1) = \int_0^\infty t^{s-2} tq(x,t)dt,$$

so that, for $s < 0$, equation (4.2.1) yields

$$-DM_{xx}(x,s) + M_x(x,s) - (s-b)M(x,s) = b\alpha M(\alpha x, s) + F(x,s). \quad (4.2.2)$$

The boundary conditions are

$$\lim_{x\to\infty} M(x,s) = 0, \quad (4.2.3)$$

and

$$M(0,s) = \int_0^\infty t^{s-1} m(0,t)dt = -\frac{1}{s + b(\alpha - 1)} F(0, s+1)$$
$$= H(s), \quad (4.2.4)$$

where $s < -b(\alpha - 1)$. The problem can be converted to one with homogeneous boundary conditions using the transformation

$$V(x,s) = P(x)H(s) - kM(x,s),$$

and this requires

$$\lim_{x\to\infty} P(x) = 0,$$

and,

$$P(0) = k.$$

Equation (4.2.2) thus converts to

$$\begin{aligned} -DV_{xx}(x,s) + V_x(x,s) - (s-b)V(x,s) - b\alpha V(\alpha x,s) + kF(x,s) \\ +(s-b)P(x) + b\alpha P(x) = [-DP''(x) + P'(x) + b\alpha P(x) - b\alpha P(\alpha x)]H(s). \end{aligned} \tag{4.2.5}$$

We choose $P(x)$ such that it solves

$$-DP''(x) + P'(x) + b\alpha P(x) = b\alpha P(\alpha x),$$

subject to the boundary conditions

$$\lim_{x\to 0^+} (-DP'(x) + P(x)) = 0,$$
$$\lim_{x\to\infty} (-DP'(x) + P(x)) = 0,$$

and the condition

$$\lim_{x\to\infty} P(x) = 0.$$

Wake *et al.* [19] obtained such a solution $P(x)$, which is given as a certain Dirichlet series. With this choice of $P(x)$, equation (4.2.5) reduces to

$$-DV_{xx}(x,s) + V_x(x,s) - (s-b)V(x,s) = b\alpha V(\alpha x,s) + \eta(x,s), \tag{4.2.6}$$

where

$$\eta(x,s) = -P(x)F(0,s+1) - kF(x,s). \tag{4.2.7}$$

The corresponding Green's function satisfies

$$-DG'' + G' - (s-b)G = \delta(x-\xi),$$

where the derivative is with respect to x. Thus,

$$G(x,\xi,s) = \begin{cases} G_1(x,\xi,s) = \frac{e^{-m_1\xi}}{D(m_1-m_2)}\left(e^{m_1x} + \left(\frac{m_1D-1}{1-m_2D}\right)e^{m_2x}\right); & 0 < x < \xi \\ \\ G_2(x,\xi,s) = \frac{e^{m_2x}}{D(m_1-m_2)}\left(e^{-m_2\xi} + \left(\frac{m_1D-1}{1-m_2D}\right)e^{-m_1\xi}\right); & \xi < x < \infty \end{cases} \tag{4.2.8}$$

where m_1 and m_2 are given by

$$\begin{aligned} m_1 &= \frac{1+\sqrt{1-4(s-b)D}}{2D}, \\ m_2 &= \frac{1-\sqrt{1-4(s-b)D}}{2D}. \end{aligned} \tag{4.2.9}$$

The solution $V(x,s)$ thus satisfies

$$V(x,s) = b\alpha\int_0^\infty G(x,\xi,s)V(\alpha\xi,s)d\xi + h(x,s), \tag{4.2.10}$$

where $h(x,s)$ is a known function and is given by

$$h(x,s) = \int_0^\infty G(x,\xi,s)\eta(\alpha\xi,s)d\xi. \tag{4.2.11}$$

Let K and T be operators defined by $\mathrm{K}\,\phi = \mathrm{T}\,\phi + h$, where

$$\mathrm{T}\,\phi = b\alpha \int_0^\infty G(x,\xi,s)\phi(\alpha\xi,s)d\xi.$$

The work of Efendiev *et al.* [31] can be mimicked to show that

$$\|\,\mathrm{K}\,\phi_1 - \mathrm{K}\,\phi_2\| \leq \frac{b\alpha}{(-\operatorname{Re} s + b)}\|\phi\|_\infty,$$

so that T is a contraction mapping for $\operatorname{Re} s < -b(\alpha - 1)$. The solution V is thus given by

$$V = \sum_{j=0}^{\infty} \mathrm{T}^j\, h, \tag{4.2.12}$$

where $\mathrm{T}^0\, h = h$, and $\mathrm{T}^j\, h = \mathrm{T}^{j-1}\, h$.

4.3 Asymptotics as $|s| \to \infty$

In this section, we show that for a certain class of source terms f, the solution V obtained in Section 4.2 lies in a suitable space, so that the Paley-Wiener theorem can be invoked to establish the existence of an inverse Mellin transform. In the next lemma, we establish bounds on $h(x,s)$.

Lemma 4.3.1. *Let* $\operatorname{Re} s < -b(\alpha - 1)$ *and* F *be a function such that* $F(x,s) = R(x)Q(s)$, *where* $|Q(s)| \sim \mathrm{O}(\frac{1}{|s|^p})$, $p \geq 1$, *and* $R(x)$ *is bounded and* $R'(x) \in L^1[0,\infty)$, *then there exists an* $L > 0$, *such that*

$$|h(x,s)| < \frac{L}{|s|^2}. \tag{4.3.1}$$

as $|s| \to \infty$.

Proof. Let $h(x,s) = C_1 + C_2$, where

$$C_1 = \int_0^x G_2(x,\xi,s)\eta(\xi,s)d\xi,$$

and,

$$C_2 = \int_x^\infty G_1(x,\xi,s)\eta(\xi,s)d\xi.$$

Integrating C_1 and C_2 by parts gives

$$C_1 = [\eta(\xi,s)v_1(x,\xi,s)]|_{\xi=0}^{x} - \int_0^x v_1(x,\xi,s)\frac{\partial}{\partial\xi}\eta(\xi,s)d\xi, \tag{4.3.2}$$

and

$$C_2 = [\eta(\xi,s)v_2(x,\xi,s)]|_{\xi=x}^{\xi=\infty} - \int_x^\infty v_2(x,\xi,s)\frac{\partial}{\partial\xi}\eta(\xi,s)d\xi, \tag{4.3.3}$$

where

$$v_1(x,\xi,s) = \int_0^\xi G_2(x,\tau,s)d\tau,$$

and

$$v_2(x,\xi,s) = \int_\xi^\infty G_1(x,\tau,s)d\tau.$$

Since,

$$|v_2(\xi)| \leq \frac{1}{|Dm_1(m_1m_2)|} + \frac{|m_2|^2 + |m_1|^2}{D|m_1(m_1m_2)(m_1 - m_2)|},$$

and, from (4.2.8), $m_k \sim \mathrm{O}(|\sqrt{s}|)$ for $k = 1, 2$ as $|s| \to \infty$, so that there exists a constant γ_2 such that

$$|v_2(\xi)| \leq \frac{\gamma_2}{|s|}, \tag{4.3.4}$$

as $|s| \to \infty$. Similarly, for v_1, there exists a constant γ_1 such that, as $|s| \to \infty$,

$$|v_1(\xi)| \leq \frac{\gamma_1}{|s|}. \tag{4.3.5}$$

Since $P(x)$ is a positive decreasing function in $[0, \infty)$ ([19]) and R is bounded, equation (4.2.7) implies that there exists numbers k_1 and k_2 such that

$$|\eta(x, s)| \leq (|P(x)R(0)| + |kR(x)|)\frac{1}{|s|} \leq \frac{k_1}{|s|}, \tag{4.3.6}$$

and,

$$|\frac{\partial}{\partial x}\eta(x, s)| \leq (|P'(x)R(0)| + |kR'(x)|)\frac{1}{|s|} \leq \frac{k_2}{|s|}, \tag{4.3.7}$$

as $|s| \to \infty$. Equations (4.3.2)-(4.3.3) and inequalities (4.3.4)-(4.3.7) yield

$$|h(x, s)| \leq |C_1| + |C_2| < \frac{L}{|s|^2},$$

as $|s| \to \infty$, where $L = \max(\gamma_1, \gamma_2)(k_1 + k_2)$. □

Lemma 4.3.2. *Let $F(x, s)$ satisfy the assumptions of Lemma 4.3.1. Then for* *any* $\nu > b\alpha$,

$$|V(x,s)| < \frac{\tilde{L}}{|s|^2}, \tag{4.3.8}$$

where $\tilde{L} = \frac{L}{1-q}$ *and* $q = \frac{b\alpha}{\nu}$.

Proof. Since,

$$|V(x,s)| \le |h(x,s)| + \sum_{n=1}^{\infty} |\operatorname{T}^n h(x,s)|, \tag{4.3.9}$$

we compute the bounds on the terms of the Neumann series to get a bound on V. Now,

$$\begin{aligned} |\operatorname{T} h(x,s)| &\le b\alpha \int\limits_0^\infty |G(x,\xi,s)||h(\alpha\xi,s)|d\xi, \\ &\le b\alpha \frac{L}{|s|^2} \int\limits_0^\infty |G(x,\xi,s)|d\xi. \\ &\le b\alpha \frac{L}{|s|^2} \{ \int\limits_0^x |G_2(x,\xi,s)|d\xi + \int\limits_x^\infty |G_1(x,\xi,s)|d\xi \}. \end{aligned} \tag{4.3.10}$$

It is straightforward to show that

$$\int\limits_0^x |G_2(x,\xi,s)|d\xi \le \frac{1}{D\mu_2(\mu_1+\mu_2)}, \tag{4.3.11}$$

and

$$\int\limits_x^\infty |G_1(x,\xi,s)|d\xi \le \frac{1}{D\mu_1(\mu_1+\mu_2)}, \tag{4.3.12}$$

where $\mu_1 = \operatorname{Re} m_1 > 0$, and $-\mu_2 = \operatorname{Re} m_2 < 0$. Inequalities (4.3.10)-(4.3.12) yield

$$|\operatorname{T} h(x,s)| \leq \frac{L}{|s|^2}\frac{b\alpha}{D\mu_1\mu_2}. \tag{4.3.13}$$

Now,

$$\mu_1 = \operatorname{Re} m_1 = \frac{1}{2D}(1 + \operatorname{Re}\sqrt{1-4(s-b)D}),$$

and,

$$\mu_2 = -\operatorname{Re} m_2 = \frac{1}{2D}(\operatorname{Re}\sqrt{1-4(s-b)D} - 1),$$

so that,

$$\frac{1}{\mu_1\mu_2} \leq \frac{D}{(-\operatorname{Re} s + b)},$$

which, using inequality (4.3.13), gives

$$|\operatorname{T} h(x,s)| \leq \frac{L}{|s|^2}\frac{b\alpha}{(-\operatorname{Re} s + b)},$$

and since $\operatorname{Re} s < -b(\alpha - 1)$, the above inequality yields

$$|\operatorname{T} h(x,s)| \leq \frac{L}{|s|^2} q,$$

where $q = \frac{b\alpha}{\nu} < 1$. In general,

$$|\operatorname{T}^n h(x,s)| \leq q^n \frac{L}{|s|^2}, \tag{4.3.14}$$

so that, inequalities (4.3.1), (4.3.9) and (4.3.14), yield (4.3.8). □

The above Lemmas establish the following result.

Theorem 4.3.3. *Let $F(x,s)$ satisfy the assumptions of Lemma 4.3.1. There exists a solution m to equation (4.1.5) that satisfies conditions (4.1.6) and (4.1.7) for all $x > 0$ and $t > 0$.*

Proof. Since $|V(x,s)| < \frac{\tilde{L}}{|s|^2}$, the Paley-Wiener theorem ([9], [14], [18]) asserts the existence of a unique continuous function $v(x,t)$, such that

$$V(x,s) = \int_0^\infty t^{s-1} v(x,t) dt.$$

□

4.4 Concluding remarks

In this chapter, the existence of a unique solution to the inhomogeneous pantograph type equation (4.1.1), subject to conditions (4.1.2)-(4.1.3), is established for a restricted class of source terms f, and for a certain choice of coefficients. The Mellin transform $F(x,s)$ of the "integrated" version of the source term $f(x,t)$ is $O(\frac{1}{|s|^p})$, $p \geq 1$. The approach used here can also be employed for a more general class of dispersion, growth and division rates. The challenge, however, is finding the appropriate Green's function that satisfies the corresponding nonlocal differential equation (DE). The choice of coefficients, in this paper, makes the Green's function DE local and able to be solved easily. The inverse transform in the time domain is formidable to obtain and the Paley-Wiener theorem for Mellin transforms is employed to extract qualitative information about the solution. Some tools in this regard have been developed by Butzer and Stefan [5] and Bardaro *et al.* [4]. Future work will cover a more general class of functions f.

The homogeneous problem $f \equiv 0$ can be addressed using a similar approach. It, however, leads to a homogeneous Fredholm equation of the second kind and the analysis used here breaks down. Solution techniques for the homogeneous problem will be discussed in future work.

Chapter 5

Inhomogeneous Pantograph Type Equation with singular coefficients and asymmetric cell division

5.1 Introduction

This chapter is the asymmetric generlization of chapter 4 and deals with PDEs of the form

$$n_t(x,t) + (G(x,t)n(x,t))_x + B(x,t)n(x,t) = (D(x,t)n(x,t))_{xx}$$
$$+\alpha B(\alpha x,t)n(\alpha x,t) + \beta B(\beta x,t)n(\beta x,t) + f(x,t) \tag{5.1.1}$$

subject to the initial condition

$$\lim_{t\to 0^+} n(x,t) = n_0(x), \tag{5.1.2}$$

and the boundary conditions (1.22), and the condition

$$\lim_{x\to \infty} n(x,t) = 0, \tag{5.1.3}$$

for $t > 0$. Here $\alpha > 2 > \beta > 1$, and $f(x,t)$ is a known forcing term. Furthermore $\frac{1}{\alpha} + \frac{1}{\beta} = 1$. If $f \equiv 0$, then (5.1.1) appears in a cell division model with stochastic growth rate, where $x \geq 0$ represents size and $t > 0$ denotes time. The coefficients $D(x,t)$, $G(x,t)$ and $B(x,t)$ represents dispersion rate, growth rate and frequency of division of cells respectively. Furthermore, the number density of cells at a given time is denoted by $n(x,t)$.

As discussed prviously, general techniques for solving such initial boundary value problems lack, even for a restricted class of coefficients. The inhomogeneous problem, for symmetric case, has been discussed in detail in previous chapter, and here we tend to find the results for the asymmetric version of the problem in chapter 4. Here, we consider time dependent coefficients $D(x,t) = \frac{D}{t}, G(x,t) = \frac{g}{t}, B(x,t) = \frac{b}{t}$, where D, g and b are positive numbers, and show that for a certain class of functions $f(x,t)$, there exists solutions to the initial boundary value problem. With these coefficients, equation (5.1.1) becomes

$$-\frac{D}{t}n_{xx}(x,t)+\frac{g}{t}n_x(x,t)+n_t(x,t)+\frac{b}{t}n(x,t) = \frac{b}{t}\alpha n(\alpha x,t)+\frac{b}{t}\beta n(\beta x,t)+f(x,t),$$

which can be simplified, using the transformation $x = g\tilde{x}$, to

$$-\frac{\tilde{D}}{t}\tilde{n}_{xx}(\tilde{x},t)+\frac{1}{t}\tilde{n}_x(\tilde{x},t)+\tilde{n}_t(\tilde{x},t)+\frac{b}{t}\tilde{n}(\tilde{x},t) = \frac{b}{t}\alpha\tilde{n}(\alpha\tilde{x},t)+\frac{b}{t}\beta\tilde{n}(\beta\tilde{x},t+f(\tilde{x},t),$$

where $\tilde{D} = \frac{D}{g^2}$ and $\tilde{n}(\tilde{x},t) = n(g\tilde{x},t)$. Dropping the tildes yields

$$-\frac{D}{t}n_{xx}+\frac{1}{t}n_x(x,t)+n_t(x,t)+\frac{b}{t}n(x,t) = \frac{b}{t}\alpha n(\alpha x,t)+\frac{b}{t}\beta n(\beta x,t)+f(x,t). \tag{5.1.4}$$

We consider functions f and solutions n that are integrable with respect to x for any fixed t. The transformations

$$m(x,t) = \int_x^\infty n(\xi,t)d\xi, \quad \text{and} \quad q(x,t) = \int_x^\infty f(\xi,t)d\xi,$$

yield

$$-\frac{D}{t}m_{xx}+\frac{1}{t}m_x(x,t)+m_t(x,t)+\frac{b}{t}m(x,t) = \frac{b}{t}m(\alpha x,t)+\frac{b}{t}m(\beta x,t)+q(x,t). \tag{5.1.5}$$

The boundary conditions on m is specified by integrating (5.1.4) with respect to x from 0 to ∞ and using conditions (1.22). This gives

$$m_t(0,t) - \frac{b}{t}m(0,t) = q(0,t),$$

so that

$$m(0,t) = ct^b + t^b \int t^{-b}q(0,t)dt, \tag{5.1.6}$$

where c is a constant of integration. The initial condition on m is

$$m(x,0) = m_0(x) = \int_x^\infty n_0(\xi)d\xi. \tag{5.1.7}$$

In the next section, we obtain a Mellin transform solution to the problem. In section 5.2, we show that the inverse Mellin transform exists for a certain class of source terms f. We conclude the dicussion in section 5.3.

5.2 A Mellin transform solution

In this section, we study the existence and uniqueness of a Mellin transform solution to equation (5.1.5) subject to conditions (5.1.6) and (5.1.7). The Mellin transform converts equation (5.1.5) to a nonhomogeneous ordinary differential equation, which can be solved using the Green's function. This leads to an integral equation that has a unique solution.

Applying the Mellin transform to equation (5.1.5) with respect to time yields

$$\begin{aligned} &-DM_{xx}(x,s-1)-(s-1-b)M(x,s-1)+M_x(x,s-1) \\ &= bM(\alpha x,s-1)+bM(\beta x,s-1)+F(x,s-1), \end{aligned} \tag{5.2.1}$$

where $s<1$, and

$$M(x,s-1)=\int_0^\infty t^{s-2}m(x,t)dt \quad \text{and} \quad F(x,s-1)=\int_0^\infty t^{s-2}tq(x,t)dt,$$

so that, for $s<0$, equation (5.2.1) yields

$$-DM_{xx}(x,s)+M_x(x,s)-(s-b)M(x,s)=bM(\alpha x,s)+bM(\beta x,s)+F(x,s). \tag{5.2.2}$$

The boundary conditions are

$$\lim_{x\to\infty} M(x,s) = 0, \tag{5.2.3}$$

and

$$\begin{aligned} M(0,s) = \int_0^\infty t^{s-1} m(0,t)dt &= -\frac{1}{s+b}F(0,s+1) \\ &= H(s), \end{aligned} \tag{5.2.4}$$

where $s < -b$. The problem can be converted to one with homogeneous boundary conditions using the transformation

$$V(x,s) = P(x)H(s) - kM(x,s),$$

and this requires

$$\lim_{x\to\infty} P(x) = 0,$$

and,

$$P(0) = k.$$

Equation (5.2.2) thus converts to

$$\begin{aligned} &- DV_{xx}(x,s) + V_x(x,s) - (s-b)V(x,s) - bV(\alpha x,s) + bV(\beta x,s)kF(x,s) + 2bP(x) \\ &+ (s-b)P(x) = [-DP''(x) + P'(x) + 2bP(x) - bP(\alpha x) - bP(\beta x)]H(s). \end{aligned} \tag{5.2.5}$$

We choose $P(x)$ such that it solves

$$-DP''(x) + P'(x) + 2bP(x) = bP(\alpha x) + bP(\beta x),$$

subject to the boundary conditions

$$\lim_{x \to 0+} (-DP'(x) + P(x)) = 0,$$
$$\lim_{x \to \infty} (-DP'(x) + P(x)) = 0,$$

and the condition

$$\lim_{x \to \infty} P(x) = 0.$$

A Dirichlet series solution, $P(x)$, was obtained by Wake et al. [19]. Using a certain choice of $P(x)$, (5.2.5) reduces to

$$-DV_{xx}(x,s) + V_x(x,s) - (s-b)V(x,s) = bV(\alpha x, s) + bV(\beta x, s) + \eta(x,s), \tag{5.2.6}$$

where

$$\eta(x,s) = -P(x)F(0,s+1) - kF(x,s).$$

The corresponding Green's function satisfies

$$-DG'' + G' - (s-b)G = \delta(x-\xi),$$

where the derivative is with respect to x. Thus

$$G(x,\xi,s) = \begin{cases} G_1(x,\xi,s) = \frac{e^{-m_1\xi}}{D(m_1-m_2)}(e^{m_1 x} - (\frac{m_1 D-1}{1-m_2 D})e^{m_2 x}), & 0 < x < \xi \\ G_2(x,\xi,s) = \frac{e^{m_2 x}}{D(m_1-m_2)}(e^{-m_2\xi} - (\frac{m_1 D-1}{1-m_2 D})e^{-m_1\xi}), & \xi < x < \infty \end{cases} \tag{5.2.7}$$

where m_1 and m_2 are given by

$$m_1 = \frac{1+\sqrt{1-4(s-b)D}}{2D},$$

$$m_2 = \frac{1-\sqrt{1-4(s-b)D}}{2D}. \tag{5.2.8}$$

The solution to (5.2.6) thus satisfies

$$V(x,s) = b\int_0^\infty G(x,\xi,s)(V(\alpha\xi,s)+V(\beta\xi,s))d\xi + h(x,s), \tag{5.2.9}$$

where $h(x,s)$ is a known function and is given by

$$h(x,s) = \int_0^\infty G(x,\xi,s)(\eta(\alpha\xi,s)+\eta(\beta\xi,s))d\xi. \tag{5.2.10}$$

Let the operators K and T be defined by $K\phi = T\phi + h$, where

$$T\phi = b\int_0^\infty G(x,\xi,s)(\phi(\alpha\xi,s)+\phi(\beta\xi,s))d\xi.$$

Since,

$$|T\phi| \leq b\|\phi\|_\infty\{\Delta_1+\Delta_2\}, \tag{5.2.11}$$

$$\Delta_1 = \int_0^x \big|G_2(x,\xi/\alpha,s)+G_2(x,\xi/\beta,s)\big|d\xi,$$

and

$$\Delta_2 = \int_x^\infty \big|G_1(x,\xi/\alpha,s)+G_1(x,\xi/\beta,s)\big|d\xi,$$

a straightforward calculation shows that

$$|G_1(x,\xi/\alpha,s)| = |G_{1\alpha}| \leq \frac{2}{D(\zeta_1+\zeta_2)}\big[e^{-\zeta_1(\xi/\alpha-x)}\big],$$

$$|G_1(x,\xi/\beta,s)| = |G_{1\beta}| \le \frac{2}{D(\zeta_1+\zeta_2)}\left[e^{-\zeta_1(\xi/\beta - x)}\right],$$

$$|G_2(x,\xi/\alpha,s)| = |G_{2\alpha}| \le \frac{2}{D(\zeta_1+\zeta_2)}\left[e^{-\zeta_2(x-\xi/\alpha)}\right],$$

and

$$|G_2(x,\xi/\beta,s)| = |G_{2\beta}| \le \frac{2}{D(\zeta_1+\zeta_2)}\left[e^{-\zeta_2(x-\xi/\beta)}\right],$$

where $\zeta_1 = \text{Re } m_1 > 0$ and $-\zeta_2 = \text{Re } m_2 < 0$.

Also, it can be shown that

$$\Delta_1 \le \frac{2(\alpha+\beta)}{D\zeta_2(\zeta_1+\zeta_2)},$$

and

$$\Delta_2 \le \frac{2(\alpha+\beta)}{D\zeta_1(\zeta_1+\zeta_2)}.$$

Inequality (5.2.11), implies

$$|T\phi| \le \frac{2b(\alpha+\beta)}{D\zeta_1\zeta_2}\|\phi\|_\infty.$$

Since

$$\frac{1}{\zeta_1\zeta_2} \le \frac{D}{(-\text{Re}s+b)},$$

we have,

$$|T\phi| \le \frac{2b(\alpha+\beta)}{(-\text{Re}s+b)}\|\phi\|_\infty, \tag{5.2.12}$$

so that

$$\begin{aligned}\|K\phi_1 - K\phi_2\| &\le \|T(\phi_1-\phi_2)\| \\ &\le \frac{2b(\alpha+\beta)}{(-\text{Re}s+b)}\|\phi_1-\phi_2\|.\end{aligned}$$

Consequently, T is a contraction mapping for $\mathrm{Re}s < b(1-2(\alpha+\beta))$ and the solution is given by

$$V = \sum_{j=0}^{\infty} T^j h, \tag{5.2.13}$$

where $T^0 h = h$, and $T^j h = T^{j-1} h$.

5.3 Asymptotics as $|s| \to \infty$

In this section, we show that for a certain class of source terms f, the solution V obtained in Section 5.2 lies in a suitable space, so that the Paley-Wiener theorem can be invoked to establish that an inverse of the Mellin tranform exists. In the next lemma, we establish bounds on $h(x,s)$.

Lemma 5.3.1. *Let* $\mathrm{Re}\, s < b(1-2(\alpha+\beta))$ *and* F *be a function such that* $F(x,s) = R(x)Q(s)$, *where* $|Q(s)| \sim \mathrm{O}(\frac{1}{|s|^p})$, $p \geq 1$, *and* $R(x)$ *is bounded and* $R'(x) \in L^1[0,\infty)$, *then there exists an* $L > 0$, *such that*

$$|h(x,s)| < \frac{L}{|s|^2}. \tag{5.3.1}$$

as $|s| \to \infty$.

The analysis in Lemma 4.3.1 establishes Lemma 5.3.1.

Lemma 5.3.2. *Let* $F(x,s)$ *satisfy the assumptions of Lemma 5.3.1. Then for any* $\nu > 2(\alpha+\beta)$,

$$|V(x,s)| < \frac{\tilde{L}}{|s|^2}, \tag{5.3.2}$$

where $\tilde{L} = \frac{L}{1-q}$ *and* $q = \frac{2(\alpha+\beta)}{\nu}$.

Proof. Since,

$$|V(x,s)| \leq |h(x,s)| + \sum_{n=1}^{\infty} |\operatorname{T}^n h(x,s)|, \tag{5.3.3}$$

we compute the bounds on the terms of the Neumann series to get a bound on V. Now,

$$\begin{aligned} |\operatorname{T} h(x,s)| &\leq b \int_0^{\infty} |G(x,\xi,s)||h(\alpha\xi,s) + h(\beta\xi,s)|d\xi, \\ &\leq b\frac{L}{|s|^2} \int_0^{\infty} |G(x,\xi,s)|d\xi. \\ &\leq b\frac{L}{|s|^2}\{\int_0^{x} |G_2(x,\xi,s)|d\xi + \int_x^{\infty} |G_1(x,\xi,s)|d\xi\}. \end{aligned} \tag{5.3.4}$$

It is straightforward to show that

$$\int_0^{x} |G_2(x,\xi,s)|d\xi \leq \frac{2(\alpha+\beta)}{D\mu_2(\mu_1+\mu_2)}, \tag{5.3.5}$$

and

$$\int_x^{\infty} |G_1(x,\xi,s)|d\xi \leq \frac{2(\alpha+\beta)}{D\mu_1(\mu_1+\mu_2)}, \tag{5.3.6}$$

where $\mu_1 = \operatorname{Re} m_1 > 0$, and $-\mu_2 = \operatorname{Re} m_2 < 0$. Inequalities (5.3.4)-(5.3.6) yield

$$|\operatorname{T} h(x,s)| \leq \frac{L}{|s|^2}\frac{2(\alpha+\beta)}{D\mu_1\mu_2}. \tag{5.3.7}$$

Now,

$$\mu_1 = \operatorname{Re} m_1 = \frac{1}{2D}(1 + \operatorname{Re}\sqrt{1 - 4(s-b)D}),$$

and,

$$\mu_2 = -\operatorname{Re} m_2 = \frac{1}{2D}(\operatorname{Re}\sqrt{1 - 4(s-b)D} - 1),$$

so that,

$$\frac{1}{\mu_1 \mu_2} \leq \frac{D}{(-\operatorname{Re} s + b)},$$

which, using inequality (5.3.7), gives

$$|\,\mathrm{T}\, h(x,s)| \leq \frac{L}{|s|^2} \frac{2(\alpha + \beta)}{(-\operatorname{Re} s + b)},$$

and since $\operatorname{Re} s < b(1 - 2(\alpha + \beta))$, the above inequality yields

$$|\,\mathrm{T}\, h(x,s)| \leq \frac{L}{|s|^2} q,$$

where $q = \frac{2(\alpha+\beta)}{\nu} < 1$. In general,

$$|\,\mathrm{T}^n\, h(x,s)| \leq q^n \frac{L}{|s|^2}, \tag{5.3.8}$$

so that, inequalities (5.3.1), (5.3.3) and (5.3.8), yield (5.3.2). □

The above Lemmas establish the following result.

Theorem 5.3.3. *Let $F(x, s)$ satisfy the assumptions of Lemma 5.3.1. There* *exists a solution m to equation* (5.1.5) *that satisfies conditions* (5.1.6) *and* (5.1.7) *for all $x > 0$ and $t > 0$.*

Proof. Since $|V(x,s)| < \frac{\tilde{L}}{|s|^2}$, the Paley-Wiener theorem ([9], [14], [18]) asserts the existence of a unique continuous function $v(x,t)$, such that

$$V(x,s) = \int_0^\infty t^{s-1} v(x,t) dt.$$

□

Chapter 6

Time dependent growth and division rates

6.1 Introduction

In this chapter, we study the asymmetric cell division equation

$$\frac{\partial}{\partial t}n(x,t) + \frac{\partial}{\partial x}(G(x,t)n(x,t)) = \alpha B(\alpha x,t)n(\alpha x,t) + \beta B(\beta x,t)n(\beta x,t), \\ - b(x,t)n(x,t), \quad (6.1.1)$$

subject to an initial distribution

$$n(x,0) = n_0(x), \quad (6.1.2)$$

and the boundary condition

$$\lim_{x\to 0^+}(G(x,t)n(x,t)) = 0, \quad (6.1.3)$$

for a certain class of time dependent coefficients. The assumption that division does not cause any loss of DNA content or mass leads to

$$\frac{1}{\alpha} + \frac{1}{\beta} = 1. \tag{6.1.4}$$

The major focus, hitherto, has been on the cell growth PDEs where B and G are either constant or functions of x alone. This makes the separation of variables possible and the separable solution in most cases corresponds to the long time asymptotic solution. Time dependent coefficients classically appear in biology. Michel *et al.* [27] studied time varying coefficients in the context of renewal equation with $T-$periodic death and birth rates. Here, we investigate time dependent growth and division rates and show that, at least, for a certain class of time dependent functions $B(x,t)$ and $G(x,t)$, the separable solution to the initial boundary value problem (6.1.1), (6.1.2)-(6.1.3) exists and is in fact the long time asymptotic solution towards which solutions to the PDE converge in time.

In the next section, we determine a probability density function eigenvalue and a separable solution to the initial boundary value problem (6.1.1), (6.1.2)-(6.1.3) for a certain class of growth and division rates. In Section 6.3 we show that this separable solution is the long time asymptotic solution. In Section 6.4 we show that if the problem has a solution, then it is unique.

6.2 The Separable Solution

Separable solutions are of central interest since these usually correspond to the steady size distribution solutions which attract solutions to the PDE for large time. We show that if B and G are separable with same time dependence, i.e., $B(x,t) = br(t)m(x)$ and $G(x,t) = gr(t)h(x)$, where b and g are positive numbers and r, h and k are positive functions for all $t > 0$ and $x > 0$, then variables can be separated in principle. Consequently, we consider the PDE

$$\frac{\partial}{\partial t}n(x,t) + gr(t)\frac{\partial}{\partial x}(h(x)n(x,t)) = \alpha br(t)m(\alpha x)n(\alpha x,t) + \beta br(t)m(\beta x)n(\beta x,t) - br(t)m(x)n(x,t), \tag{6.2.1}$$

and solutions of the form

$$n(x,t) = N(t)y(x), \tag{6.2.2}$$

where y is required to be a probability density function with $\int_0^\infty y(x)dx = 1$, and $N(t)$ represents the total population of cells of all sizes at a given time t. The separable form (6.2.2) and PDE (6.2.1) give

$$N'(t)y(x) + gr(t)h'(x)N(t)y'(x) + gr(t)h(x)N(t)y'(x) + br(t)m(x)N(t)y(x) = \alpha br(t)m(\alpha x)N(t)y(\alpha x) + \beta br(t)m(\beta x)N(t)y(\beta x),$$

which, dividing by $r(t)N(t)y(x)$, yields

$$N(t) = ce^{-\Lambda R(t)},$$

for some constant $c > 0$, separation constant Λ (to be determined), and

$$R(t) = \int r(t)dt. \tag{6.2.3}$$

The function $y(x)$ satisfies

$$gh(x)y'(x) + (gh'(x) + bm(x) - \Lambda)y(x) = \alpha bm(\alpha x)y(\alpha x) + \beta bm(\beta x)y(\beta x), \tag{6.2.4}$$

along with the conditions

$$\lim_{x\to 0^+} gh(x)y(x) = 0, \tag{6.2.5}$$

$$\lim_{x\to\infty} gh(x)y(x) = 0. \tag{6.2.6}$$

Equation (6.2.4) is a pantograph type equation with two nonlocal terms. It appears in various applications including the absorption of light in the Milky Way [57] and internet protocols [3]. Although there are no general methods of solving (6.2.4), solutions have been obtained for constant coefficients [30] and for $h(x) = x$ and $m(x) = x^r$, where $r > 0$ [75]. In both instances, the solution entails a positive Dirichlet series of the form

$$\sum_{\kappa=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\kappa,\nu} \exp(-\alpha^{s\kappa}\beta^{s\nu} r f(x)), \tag{6.2.7}$$

where c_k are coefficients, s and r are constants and f satisfies

$$f(\alpha x) = \alpha^s f(x). \tag{6.2.8}$$

Zaidi and van-Brunt [75] also showed that for any positive solution to (6.2.4),

$\Lambda < 0$. Dirichlet series solutions are of central interest since these correspond to the long time asymptotic solution to (6.2.1) at least for constant coefficients.

We show that if h is not constant or h is not a linear monomial, then (6.2.4) does not possess a Dirichlet series solution of the form (6.2.7). To establish this, we suppose on the contrary that a Dirichlet series solution of the form (6.2.7) to the PDE (6.2.4) exists. Equations (6.2.4) and (6.2.7) give

$$\sum_{\kappa=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\kappa,\nu}\exp(-\alpha^{s\kappa}\beta^{s\nu}rf(x))gh'(x) \tag{6.2.9}$$
$$+\sum_{\kappa=0}^{\infty}\sum_{\nu=0}^{\infty}(-\alpha^{s\kappa}\beta^{s\nu}r)d_{\kappa,\nu}\exp(-\alpha^{s\kappa}\beta^{s\nu}rf(x))gh(x)f'(x)$$
$$+\sum_{\kappa=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\kappa,\nu}\exp(-\alpha^{s\kappa}\beta^{s\nu}rf(x))m(x)-\Lambda\sum_{\kappa=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\kappa,\nu}\exp(-\alpha^{s\kappa}\beta^{s\nu}rf(x))$$
$$=\alpha\sum_{\kappa=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\kappa,\nu}\exp(-\alpha^{s(\kappa+1)}\beta^{s\nu}rf(x))m(\alpha x) \tag{6.2.10}$$
$$+\beta\sum_{\kappa=0}^{\infty}\sum_{\nu=0}^{\infty} d_{\kappa,\nu}\exp(-\alpha^{s\kappa}\beta^{s(\nu+1)}rf(x))m(\beta x). \tag{6.2.11}$$

Balancing the coefficients yields

$$gh'(x) - rh(x)f'(x) + m(x) - \Lambda = 0,$$

so that

$$f(x) = \frac{1}{r}\left(g\int \frac{h'(x)}{h(x)}dx + \int \frac{m(x)}{h(x)}dx - \Lambda\int \frac{1}{h(x)}dx\right).$$

For constant h and m [29], $f(x) = a_1 x$, for some constant a_1, so that f satisfies (6.2.8). Also, for $h(x) = x$, and $m(x) = x^s$, $s > 0$ [75], the eigenvalue $\Lambda = -g$, so that $f(x) = a_2\frac{x^s}{s}$ for some constant a_2. Consequently, f satisfies

(6.2.8). It may be possible that $m(x) \sim -h'(x)$, but since $\Lambda < 0$, balancing coefficients in (6.2.11) requires $m(x)$ and $h'(x)$ to be constants. Consequently, if h is not constant or a linear monomial, the first of these integral yields a logarithmic function which is not a homogeneous function in general. Hence, $f(\alpha x) \neq \alpha^s f(x)$ for any $s \in \mathbb{Z}$, and equation (6.2.4) does not possess a Dirichlet series solution of the form (6.2.7).

For $h \equiv 1$ and $m \equiv 1$, the eigenvalue Λ and the corresponding solution to (6.2.4) have been determined [29]. The eigenvalue is

$$\Lambda = 2b,$$

and solution y to the corresponding eigenvalue is

$$y(x) = \sum_{\kappa=0}^{\infty} \sum_{\nu=0}^{\infty} d_{\kappa,\nu} e^{-\frac{2b}{g}\alpha^k \beta^j x}, \tag{6.2.12}$$

where $d_{\kappa,\nu}$'s are determined as in [29].

In the next section, we show that for this choice of h and m, the separable solution is the long time asymptotic solution to (6.2.1) at least for a certain class of functions r.

6.3 Large time asymptotics

In this section we show that the separable solution to (6.2.1),(6.1.2)-(6.1.3) obtained in Section 6.2 for $B(x,t) = br(t)$ and $G(x,t) = gr(t)$ is the large time attracting solution for a certain class of $r(t)$. For this choice of coefficients, PDE (6.1.1) reduces to

$$\frac{\partial}{\partial t}n(x,t) + gr(t)\frac{\partial}{\partial x}n(x,t) = \alpha br(t)n(\alpha x,t) + \beta br(t)n(\beta x,t) - br(t)n(x,t). \tag{6.3.1}$$

For constant coefficients and symmetric cell division, Zaidi *et al.* [22] derived the large time attracting solution from solutions to the PDE (1.33). The solution turned out to be the separable solution.

Since the full problem (6.3.1), (6.1.2)-(6.1.3) has not been solved for any choice of coefficients, we employ the tools developed by Perthame and Ryzhik [15] to study the long time dynamics. The analysis in [15], however, is valid for one non local term and for constant coefficients and certain arguments break down because of the t dependence of coefficients. We can, nonetheless, extend their analysis to a certain class of time dependent coefficients and asymmetric cell division.

Theorem 6.3.1. *Let n be a solution to (6.3.1) that satisfies (6.1.2) and (6.1.3) and $R(t)$ and y be defined by (6.2.3) and (6.2.12) respectively. If $r(t)$ is monotonically decreasing and $R(t)$ is bounded at t=0 and $R(t)$ goes to infinity as t tends to infinity, then*

$$\lim_{t\to\infty}\int_0^\infty |n(x,t)e^{-bR(t)} - ky(x)| = 0,$$

where $k = e^{-bR(0)}\int_0^\infty n_0(x)dx$.

Proof. Let

$$u(x,t) = n(x,t)e^{-bR(t)} - ky(x).$$

Then u satisfies the PDE

$$\frac{\partial}{\partial t}u(x,t) + gr(t)\frac{\partial}{\partial x}u(x,t) + 2br(t)u(x,t) = \alpha br(t)u(\alpha x,t) + \beta br(t)u(\beta x,t), \tag{6.3.2}$$

and the conditions

$$u(0,t) = 0,$$
$$\lim_{x\to\infty} u(x,t) = 0.$$

Also, the integration of (6.3.2) with respect to x from 0 to ∞, along with condition (6.1.2), yields

$$\int_0^\infty u(x,t)dx = 0. \tag{6.3.3}$$

The transformation

$$\tilde{S}(x,t) = \int_0^x u(s,t)ds \tag{6.3.4}$$

yields

$$\frac{\partial}{\partial t}\tilde{S}(x,t) + gr(t)\frac{\partial}{\partial x}\tilde{S}(x,t) + 2br(t)\tilde{S}(x,t) = br(t)\tilde{S}(\alpha x,t) + br(t)\tilde{S}(\beta x,t), \tag{6.3.5}$$

along with the conditions

$$\tilde{S}(0,t) = 0, \tag{6.3.6}$$

$$\lim_{x\to\infty} \tilde{S}(x,t) = 0. \tag{6.3.7}$$

Equation (6.3.5) gives

$$\frac{\partial}{\partial t}[\tilde{S}(x,t)e^{bR(t)}] + gr(t)\frac{\partial}{\partial x}[\tilde{S}(x,t)e^{bR(t)}] + br(t)[\tilde{S}(x,t)e^{bR(t)}] = br(t)[\tilde{S}(\alpha x,t)e^{bR(t)}] + br(t)[\tilde{S}(\beta x,t)e^{bR(t)}], \tag{6.3.8}$$

which, multiplication by sgn($\tilde{\mathrm{S}}$), yields

$$\frac{\partial}{\partial t}|\tilde{S}(x,t)e^{bR(t)}| + gr(t)\frac{\partial}{\partial x}|\tilde{S}(x,t)e^{bR(t)}| + br(t)|\tilde{S}(x,t)e^{bR(t)}| \leq br(t)|\tilde{S}(\alpha x,t)e^{bR(t)}| + br(t)|\tilde{S}(\beta x,t)e^{bR(t)}|. \tag{6.3.9}$$

Integrating (6.3.9) from 0 to ∞ with respect to x and using conditions (6.3.6), (6.3.7) and (6.1.4) yields

$$\frac{d}{dt}\int_0^\infty |\tilde{S}e^{bR(t)}|dx \leq 0,$$

which shows that $\int_0^\infty |\tilde{S}e^{bR(t)}|dx$ is a decreasing function in time, so that

$$\int_0^\infty |\tilde{S}e^{bR(t)}|dx \leq e^{bR_0}\int_0^\infty |\tilde{S}_0(x)|dx, \tag{6.3.10}$$

where $\tilde{S}_0(x) = \tilde{S}(x,0)$ and $R_0 = R(0)$. Let

$$\bar{P}(x,t) = \tilde{S}(x,t)e^{bR(t)}.$$

Then (6.3.8) becomes

$$\frac{\partial}{\partial t}\bar{P}(x,t) + gr(t)\frac{\partial}{\partial x}\bar{P}(x,t) + br(t)\bar{P}(x,t) = br(t)\bar{P}(\alpha x,t) + br(t)P(\beta x,t), \tag{6.3.11}$$

which, differentiating with respect to t, gives

$$\frac{\partial}{\partial t}K(x,t) + gr'(t)\frac{\partial}{\partial x}\bar{P}(x,t) + gr(t)\frac{\partial}{\partial t}\left(\frac{\partial \bar{P}}{\partial x}\right) + br'(t)\bar{P}(x,t) + br(t)K(x,t)$$
$$= br'(t)\bar{P}(\alpha x,t) + br'(t)\bar{P}(\beta x,t) + br(t)K(\alpha x,t) + br(t)K(\beta x,t), \tag{6.3.12}$$

where

$$K = \frac{\partial \bar{P}}{\partial t}.$$

Equations (6.3.12) and (6.3.11) give

$$\frac{\partial}{\partial t}K(x,t) + gr(t)\frac{\partial}{\partial x}K(x,t) - \frac{r'(t)}{r(t)}K(x,t) + br(t)K(x,t) = br(t)K(\alpha x,t)$$
$$+ br(t)K(\beta x,t). \tag{6.3.13}$$

Equation (6.3.13) can be multiplied with sgn(K). This gives

$$\frac{\partial}{\partial t}|K(x,t)| + gr(t)\frac{\partial}{\partial x}|K(x,t)| - \frac{r'(t)}{r(t)}|K(x,t)| + br(t)|K(x,t)| \le br(t)|K(\alpha x,t)| + br(t)|K(\beta x,t)|, \tag{6.3.14}$$

which, integrating with respect to x from 0 to ∞ and using (6.1.4) and the fact that $K(0,t) = 0 = K(\infty,t)$, yields

$$\frac{d}{dt}\int_0^\infty |K|dx \le 0,$$

which shows that $\int_0^\infty |K|dx \le 0$ is decreasing in t, so that

$$\int_0^\infty |K|dx \le \int_0^\infty |K_0(x)|dx, \tag{6.3.15}$$

where

$$K_0(x) = K(x,0) = \left.\frac{\partial \bar{P}}{\partial t}\right|_{t=0}.$$

Since $\bar{P} = \tilde{S}e^{bR(t)}$, we have

$$K_0(x) = \frac{\partial}{\partial t}[\tilde{S}e^{bR(t)}]\Big|_{t=0} = \tilde{S}_0(x)br_0e^{bR_0} + e^{bR_0}\left.\frac{\partial \tilde{S}}{\partial t}\right|_{t=0},$$

where $r_0 = r(0)$ and $R_0 = R(0)$. Equations (6.3.5) and (6.3.4) imply

$$\left.\frac{\partial \tilde{S}}{\partial t}\right|_{t=0} = r_0[-gu_0(x) - 2b\tilde{S}_0(x) + bS_0(\alpha x) + b\tilde{S}_0(\beta x)],$$

so that,

$$K_0(x) = e^{bR_0} r_0[-gu_0(x) - 2b\tilde{S}_0(x) + b\tilde{S}_0(\alpha x) + b\tilde{S}_0(\beta x) + b\tilde{S}_0(x)]. \quad (6.3.16)$$

Equations (6.3.15), (6.3.16) and (6.1.4) give

$$\begin{aligned}\int_0^\infty |K|dx &= \int_0^\infty \left|\frac{\partial}{\partial t}[\tilde{S}e^{bR(t)}]\right| dx \\ &\leq e^{bR_0} r_0 \int_0^\infty [|gu_0(x)| + |2b\tilde{S}_0(x)| + b|\tilde{S}_0(\alpha x)| + b|\tilde{S}_0(\beta x)| + |b\tilde{S}_0(x)|]dx \\ &= e^{bR_0} r_0 \left[\int_0^\infty |gu_0(x)| + 4b\int_0^\infty |\tilde{S}_0(x)|dx\right]. \quad (6.3.17)\end{aligned}$$

Equations (6.3.4) and (6.3.8) give

$$\begin{aligned}u(x,t) = \frac{\partial}{\partial x}\tilde{S}(x,t) = \frac{e^{-bR(t)}}{gr(t)}\{&-\frac{\partial}{\partial t}[\tilde{S}(x,t)e^{bR(t)}] - br(t)[\tilde{S}(x,t)e^{bR(t)}] \\ &+ br(t)[\tilde{S}(\alpha x,t)e^{bR(t)}] + br(t)[\tilde{S}(\beta x,t)e^{bR(t)}]\},\end{aligned}$$

so that

$$\begin{aligned}\int_0^\infty |u(x,t)|dx \leq \frac{e^{-bR(t)}}{gr(t)}\{&\int_0^\infty |\frac{\partial}{\partial t}[\tilde{S}(x,t)e^{bR(t)}]|dx + br(t)\int_0^\infty |\tilde{S}(x,t)e^{bR(t)}|dx \\ &+ br(t)\int_0^\infty |\tilde{S}(\alpha x,t)e^{bR(t)}|dx + br(t)\int_0^\infty |\tilde{S}(\beta x,t)e^{bR(t)}|dx\},\end{aligned}$$

which, using (6.1.4), gives

$$\int_0^\infty |u(x,t)|dx \leq \frac{e^{-bR(t)}}{gr(t)}\{\int_0^\infty |\frac{\partial}{\partial t}[\tilde{S}(x,t)e^{bR(t)}]|dx + 2br(t)\int_0^\infty |\tilde{S}(x,t)e^{bR(t)}|dx\}. \tag{6.3.18}$$

Inequalities (6.3.18), (6.3.17) and (6.3.10) give

$$\int_0^\infty |u(x,t)|dx \leq \frac{e^{-bR(t)}}{gr(t)}\{e^{bR_0}r_0[\int_0^\infty |gu_0(x)|dx + 4b\int_0^\infty |\tilde{S}_0(x)|dx] + 2br(t)e^{bR_0}\int_0^\infty |\tilde{S}_0(x)|dx\},$$

which goes to zero as t goes to infinity. □

The above analysis, for $r(t) = 1$ for all $t > 0$ and $\alpha = \beta = 2$, recovers the result of Perthame and Ryzhik [15]. As seen from the above equation, the asymmetry in cell division does not affect the rate of convergence to the separable solution.

6.4 Uniqueness

In this section we show that if there exists a solution to the problem (6.3.1),(6.1.2)-(6.1.3), then it is unique. The uniqueness of solutions to (1.33) for constant coefficients was established by Zaidi *et al.* [22]. Their analysis, however, breaks down for time dependent coefficients and asymmetric cell division equation.

To prove uniqueness, we simplify (6.3.1) using the transformation

$$\tilde{h}(x,t) = \int_x^\infty n(\zeta,t)d\zeta. \tag{6.4.1}$$

This yields

$$\frac{\partial}{\partial t}\tilde{h}(x,t) + gr(t)\frac{\partial}{\partial x}\tilde{h}(x,t) + br(t)\tilde{h}(x,t) = br(t)\tilde{h}(\alpha x,t) + br(t)\tilde{h}(\beta x,t). \tag{6.4.2}$$

Integrating (6.3.1) with respect to x from 0 to ∞, and using (6.1.4) and (6.1.3), gives

$$\frac{\partial}{\partial t}\tilde{h}(0,t) = br(t)\tilde{h}(0,t),$$

so that,

$$\tilde{h}(0,t) = ce^{bR(t)}, \tag{6.4.3}$$

for some constant c. Also, equations (6.1.2) and (6.4.1) give

$$\tilde{h}(x,0) = \tilde{h}_0(x) = \int_x^\infty n_0(\zeta)d\zeta. \tag{6.4.4}$$

Suppose that $\tilde{h}_1$ and $\tilde{h}_2$ are two distinct solutions to (6.4.2) that satisfy (6.4.3) and (6.4.4). Let $\bar{m}(x,t) = \tilde{h}_1(x,t) - \tilde{h}_2(x,t)$. Then m satisfies

$$\frac{\partial}{\partial t}\bar{m}(x,t) + gr(t)\frac{\partial}{\partial x}\bar{m}(x,t) + br(t)\bar{m}(x,t) = br(t)\bar{m}(\alpha x,t) + br(t)\bar{m}(\beta x,t), \tag{6.4.5}$$

and the conditions

$$\bar{m}(0,t) = 0, \tag{6.4.6}$$

$$\bar{m}(x,0) = 0. \tag{6.4.7}$$

The PDE (6.4.5) can be multiplied with sgn(m). This gives

$$\frac{\partial}{\partial t}|\bar{m}(x,t)| + gr(t)\frac{\partial}{\partial x}|\bar{m}(x,t)| + br(t)|\bar{m}(x,t)| \leq br(t)|\bar{m}(\alpha x,t)| + br(t)|\bar{m}(\beta x,t)|,$$

which, integrating with respect to x from 0 to ∞ and using (6.1.4) and (6.4.6)-(6.4.7), yields

$$\frac{d}{dt}\int_0^\infty |\bar{m}(x,t)|dx \leq 0,$$

which shows that $\int_0^\infty |\bar{m}(x,t)|dx$ is a decreasing function in t, so that

$$\begin{aligned}\int_0^\infty |\bar{m}(x,t)|dx &\leq \int_0^\infty |\bar{m}(x,0)|dx \\ &= 0 \end{aligned} \tag{6.4.8}$$

and consequently $\tilde{h}_1(x,t) = \tilde{h}_2(x,t)$.

We note that if $r(t) = 1$ for all $t > 0$, the above analysis establishes the uniqueness of solutions to (6.1.1) subject to conditions (6.1.2)-(6.1.3) for constant coefficients. It also endorses the result of Zaidi *at al.* [22] for $r(t) \equiv 1$ and $\alpha = \beta = 2$.

6.5 Conclusions

In this chapter we have determined the separable solution to the cell division equation (6.3.1) subject to conditions (6.1.2) and (6.1.3) and have shown that solutions to the PDE converge to this separable solution for large time, at least for a certain class of time dependent coefficients. The convergence of solutions to the separable solution is observed for constant coefficients but not for certain choice of variable coefficients [24]. The asymmetry in cell division does not affect the rate of convergence of solutions towards the SSD solution. We have also established the uniqueness of solutions to the problem (6.3.1),(6.1.2)-(6.1.3).

The shape of the SSD obtained for time dependent coefficients is a scaling, in time, of the shape of the SSD solution of the constant coefficients case (See Figure 6.1).

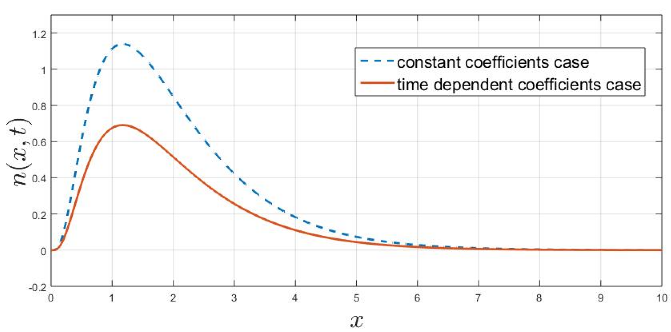

Figure 6.1: The SSD solution obtained by Zaidi *et al.* [29] for the constant coefficient case and the SSD solution given by the (6.2.2) for $t = 1$, $\alpha = 3$, $\beta = \frac{3}{2}$, $b = 1$, $g = 2$ units.

Chapter 7

Conclusion

This dissertation has supplemented a cell growth models for symmetric and asymmetric divisions with constant and time dependent growth and division rates [22, 11, 19]. Several models with constant and size-dependent growth and division rates have been studied in detail previously. Due to lack of analytical tools and solution techniques to solve functional PDEs, it is not easy to find a general solution for these models. Several techniques were developed to tackle symmetric and asymmetric growth models with constant division and growth rates. However, specific models with size-dependent growth and division rates and their solutions were discussed. Chapter 1 gives a detailed overview of the difference differential equations, their applications, and their evolution into advanced functional partial differential equations used in cell growth modeling.

Chapter 2 generalizes the work of Perthame and Ryzhik [15] for the asymmetric cell division model with $\alpha > 2 > \beta > 1$. The analysis holds for the first order asymmetric equation (2.1.2). Perthame and Ryzhik [15] had established this result for the symmetric case where $\alpha = 2$. The general solution to equation (2.1.2) converges in large-time to separable solutions for constant and size-dependent growth and division rates.

As discussed in chapter 1, the first order advanced functional PDE does not account for the stochasticity involved in the cell division process. For this purpose, Hall [11] in his thesis developed the Dispersion problem (1.20). Efendiev et al. [31] developed a technique to solve the Dispersion problem for the symmetric case. Chapter 3 generalizes the solution technique developed in [31] to the asymmetric cell division model (equation (3.1.7) with conditions (1.22)) with constant division and growth rates. This is a notable achievement because of the scarcity of analytical solutions to most functional PDEs with nonlocal terms. The analytic solution was obtained using Laplace transforms. The analytic solution was shown to converge to the separable solution for large-time. It was also shown that the mode of cell division had no effect on the positivity and unimodality of the solution, as shown in the figure 3.1.

So far, many cell growth models have been investigated [22, 19, 31]. They vary from first order functional PDEs with constant growth and division rates to second order functional PDEs with size-dependent growth and division rates. Few models have incorporated the time dependence of division and growth rates since it simplifies mathematics. In Chapters 4, 5, and 6, we have studied different models with time dependent growth and division rates. In chapter 4, a second order symmetric cell division equation (4.1.1) is studied with singular time dependent growth and division rates. In particular, the growth and division rates are given by $\frac{g}{t}$ and $\frac{b}{t}$ respectively. The equation (4.1.1) contains a source term $f(x,t)$ belonging to a restricted class. The integrated form of the source term has its Mellin transform of the order $O(\frac{1}{|s|^p}), \quad p > 1$. For this choice of source term and coefficients, we establish the existence and uniqueness of the solution to the problem. We find a solution in the transformed space using Mellin transform and find the suitable Green's function. Finding the inverse transform is challenging, but we use Paley-Wiener theorem for Mellin transform to establish the existence of the inverse transform. When $f \equiv 0$, the analysis leads to a homogeneous Fredholm equation of the second kind. Future work will deal with such problems as the analysis in this chapter breaks down for homogeneous cases. Chapter 5 employs the same analysis technique developed in chapter 4 and extends the work for asymmetric equation (5.1.1). The results obtained are promising since the tools used for the symmetric case also work for the asymmetric case.

The first order functional PDE with nonlocal terms (1.33) was solved, using a novel technique, by Zaidi et al. [22]. The explicit solution obtained converges to the separable solution of the equation. This thesis considers time dependent coefficients involved in first and second order functional PDEs with one and two nonlocal terms. To understand the behavior of the model with a certain class of time dependent coefficients, we use a technique motivated by the work of Perthame and Ryzhik [15]. In chapter 6, we find the separable solution to (6.1.1) and show that the solutions to this PDE converge to the separable solution. It is worth noting that the coefficients $G(x,t)$ and $B(x,t)$ have the same time dependence. In particular, both these coefficients involve the same function of t, i.e., $r(t)$. In addition to the above, we also establish that the solution to (6.1.1), (6.1.2)-(6.1.4) is unique.

We have furthered the theory of functional PDEs arising in cell growth models for most of the thesis. We have considered size-structured models in one dimension. Future work may involve higher dimensions by introducing age variable to the size-structured models.

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