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The Analysis of Fragmentation Type
Equation for Special Division
Kernels

A thesis presented in partial fulfillment of the
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Abstract

The growth fragmentation equation is a linear integro-differential equation describing the evolution of cohorts that grow, divide and die or disappear in the course of time. The general formula is of first or second order, depending whether the growth process is deterministic or stochastic, respectively. We focus on a particular choice of division kernel that models size-structured cell cohorts which divide into daughter cells of equal size. This problem reduces to an initial-boundary value type that involves a modified Fokker-Planck equation with an advanced functional term. There are no general techniques for solving these problems. The constant growth rate case has been studied by a number of researchers. In particular, it was shown that the limiting solutions converge to a special solution, the separable solution.

We consider the case when the growth rate is linear and deterministic. This problem can be solved analytically for monomial splitting rates. We show that the long time dynamics for this case differ markedly from the constant growth rate case. Specifically, the solutions approach a time dependent attracting solution that is periodic in time.

The qualitative features of solutions differ when the splitting rate is constant. There are two cases. The first is when the growth rate is deterministic; the second is when the growth rate is stochastic. This case involves a constant dispersion term. In both cases, the problem can be solved directly, and the classic properties of solutions can be adapted from the previous case (with non constant splitting rate). The main distinct trait is that there is no long time attracting solution in L^1 for probability distribution initial data. (This result in the dispersive case follows, provided the parameters g , b and α satisfy a certain inequality.) The long time asymptotic behaviour of solutions proves to be formidable to evaluate analytically for these cases. We use numerical methods to elucidate possible

behaviour and examine the influence of the dispersion term. We find numerical evidence that the dispersion term plays a prominent rôle as a smoothing effect on the oscillatory behaviour, spatially and time wise, encountered in the dispersion free examples with exponential growth.

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Published work

Most the materials in Chapter 3 appear in the paper “On a Cell Division Equation with a Linear Growth Rate”, authored by van Brunt, B., *et al.*, published in *the ANZIAM Journal*, vol. 59, no. 3, 2018, pp. 293–312 [66]. doi:10.1017/s1446181117000591.

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Abbreviations

ODE	Ordinary Differential Equation
PDE	Partial Differential Equation
LHS	Left-Hand Side
RHS	Right-Hand Side
PDF	Probability Density Function
FPE	Fokker Planck Equation
GRE	General Relative Entropy
SSD	Steady Size Distribution
PE	Pantograph Equation
IBVP	Initial-Boundary Value Problem
FTCS	Forward-Time Centred-Space
SODC	Second Order Degenerate Case

Symbols

$n(x, t)$	Number density	
x	Cell size	$[L]$
t	Time	$[s]$
$G(x)$	Cell growth rate	$\frac{[L]}{[s]}$
$\mu(x)$	Cell death rate	$\frac{1}{[s]}$
$\Delta(\xi, x)$	Cells' number modelling function	
$B(x)$	Division rate	
$D(x)$	Dispersion term	$\frac{[L]^2}{[s]}$

The notations L and s refer to size unit and second, respectively.

This thesis is dedicated to my parents, my wife and my daughter, with all my love.

Chapter 1

Introduction

1.1 Fragmentation process

The fragmentation process, roughly speaking, is a splitting process into small fragments, particles or individuals, constituting a population. Fragmentation finds its way in a wide array of scientific and technological disciplines including demography, biology, mass spectrometry, computing, economics, physics, astronomy, etc. Giving a rigorous definition requires *de facto* characterisation of the data and a fine understanding of the dynamical system that causes the fragmentation process (see [13] for a thorough explanation and examples). The fragmentation process in this study falls into a category of the evolutionary kind. The dynamics in this type of process exemplify an exponential growth problem.

1.2 Exponential growth modelling

The problem of modelling exponential growth has a long history and has passed through a number of stages of development. The Malthusian model [44] was one of the earliest attempts at modelling such a problem mathematically. In Malthus's

model, the growth rate is directly proportional to the population size and is defined by the difference between the birth and death rates of the individuals (intrinsic growth). Mathematically, if the total number of individuals in an area, town, environment, or culture is assigned by a single variable function, e.g., $N(t)$ at given time t with a time independent growth rate per capita, say, g , then the Malthusian growth model can be written as a linear ordinary differential equation (ODE) of the form

$$\frac{d}{dt}N(t) = (\beta - \zeta)N(t),$$

provided with an initial number of individuals $N(t_0) = N_0$ (an initial condition) at time $t = t_0$, where β and ζ are the birth and death rates, respectively. One critical aspect of this model is when the birth rate dominates over the death rate. It results in an unbounded population requiring unlimited space and resources, which makes the model realistic only for a short period of time. Also, the model neglects growth limitation factors such as competition between individuals (cf. [38]). In spite of that, and the severe criticisms received by William Godwin and others, the Malthusian model remains the foundation of many successful population growth models, for instance, the logistic equation by Verhulst (1844), in which he generalised Malthus's model and considered density dependent limitation factors such as competition between individuals. The rationale behind such a factor is that as the population growth increases, the individuals compete with each other for resources. This competition limits the population density, so it does not exceed the maximum capacity of an environmental system as time passes, leading to the logistic curve (see Figure 1.1). In the context of mathematics, the rate of change of the population size over time is described by

$$\frac{d}{dt}N(t) = gN(t)\left(1 - \frac{N(t)}{N_{\max}}\right),$$

where N_{\max} is the maximum size of the population, and the other parameters follow from the Malthusian model. The logistic equation is used in modelling

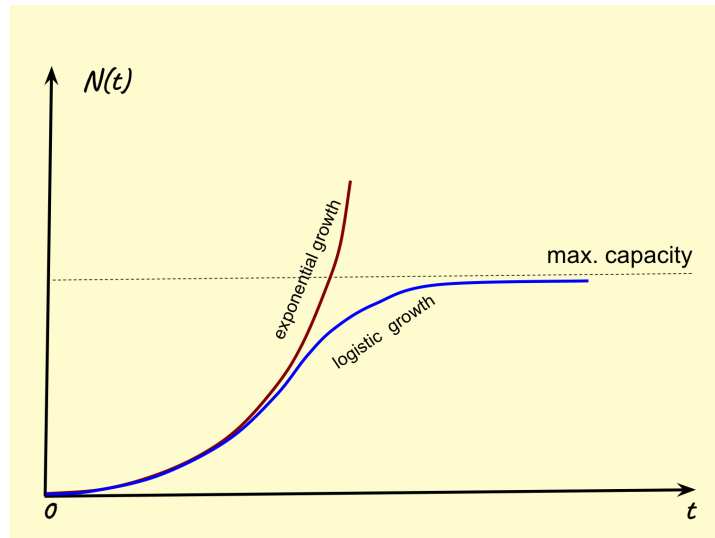


FIGURE 1.1: Examples of growth curves.

many applications ranging from statistics (the logistic distribution) and medicine (Gompertz curves) to chemistry and physics. More scholars have studied population dynamics with different factors and broader problems, but the models remained totally population dependent, regardless of the internal properties or the characteristics of individuals.

It is believed that Euler (cf. [35]) was the first to take the characteristics of individuals (structured population) into account based on age in an early study on human populations. Since the 18th century, there have been no records of structured population models until two centuries later, when Sharpe and Lotka [59] developed an age structured model, in 1911, building on the Euler study, addressing the question of asymptotic behaviour. These age models motivated researchers to consider other properties such as size, stage and saturation. The book by Metz and Dieckmann [46] gives a detailed account of physiologically structured populations. Assisted by the development of the microscope, structured models found applications in the study of microorganisms. Specifically, researchers were attracted to the unicellular organisms characterised by size as they dynamically produce fewer complications than their multicellular counterparts (cf. [30]). Another way cellular organisms may arise is by aggregation

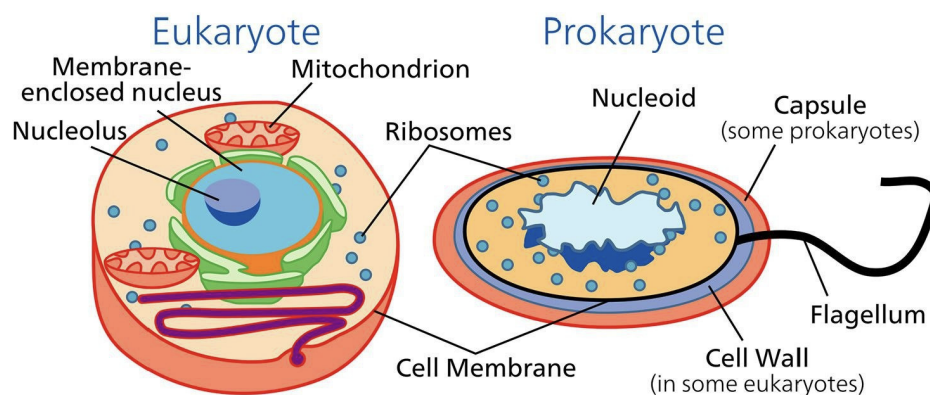
(such as myxobacteria) [31]: this case is excluded from our study. The models have been generalised to include multicellular organisms.

We study models that describe a fragmentation process caused by cellular organisms. Before we embark on that, we need to understand how the evolutionary process of cells occurs.

1.3 Cell fragmentation process

Describing the fragmentation process requires an understanding of the dynamical cause. In this model, the fragmentation process is caused by a cell division process (cell cycle). In general, the cell cycle is an ordered sequence of events in which a mother cell evolves until it reaches maturity and divides, to give two daughter cells of smaller size that can grow and divide in a similar manner to the mother cell.

Cells are of two types – eukaryotes and prokaryotes – based on a cellular structure which is depicted in a simple diagram (Figure 1.2). The former type includes

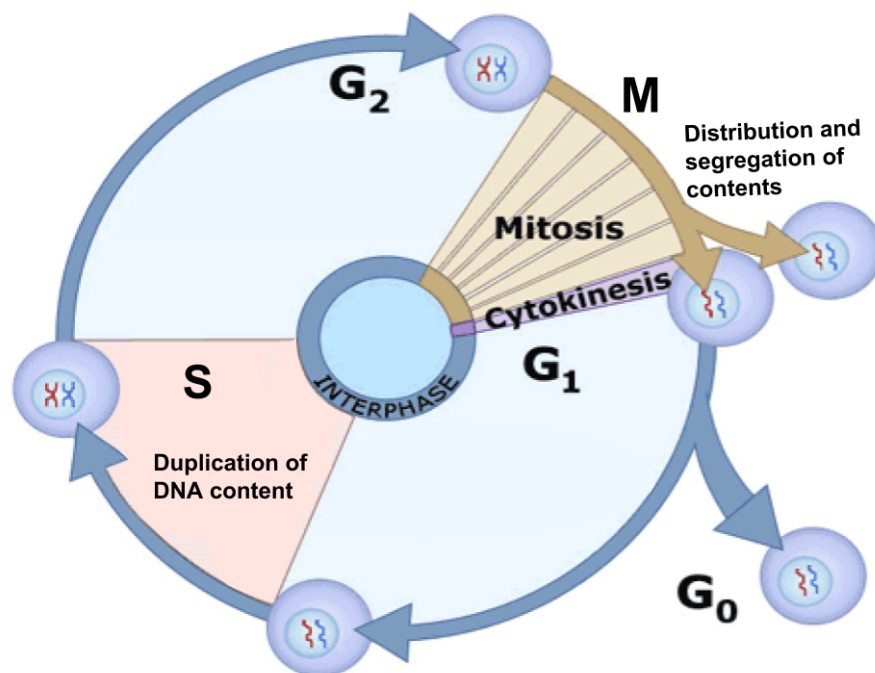


Taken from the Science Primer, a work of the National Center for Biotechnology Information, part of the National Institutes of Health, USA.

FIGURE 1.2: Prokaryotes vs Eukaryotes.

unicellular and multicellular organisms, while the latter represents unicellular organisms. Regardless of the differences, most cells replicate the DNA, segregate and distribute the contents, grow and divide [52]. The cell division in prokaryotes is known as binary fission (as in bacteria), while in eukaryotes (including animals, most plants and human cells) it falls into two classes: mitosis (as a result of an asexual reproduction process) and meiosis (as a result of a sexual reproduction process).

Consider the cell division process that occurs in eukaryotes (Figure 1.3). The



An edited image taken from the University of Leicester website (link: <https://www2.le.ac.uk/projects/vgec/highereducation/topics/cellcycle-mitosis-meiosis>).

FIGURE 1.3: Cell cycle in eukaryotes.

cell cycle is comprised of four discrete phases ([18, 49, 50, 52]): first gap (G_1), synthesis (S), second gap (G_2), and mitosis (M), respectively. The first three phases form the so-called interphase, which represents most of the cell's growth period. In a typical cell, the S and M phases are independently dedicated to

replication of the cell's contents and distribution, respectively, as well as segregation of the duplicated contents into two parts (daughter cells). The M phase technically consists of two simultaneous events: mitosis (nuclear division) and cytokinesis (complete division) at which the cell ends its cycle. The G_1 and G_2 feature a longer time frame than the two other phases, allowing for the cells to grow in size, but no DNA synthesis occurs.

In some cases, a cell may not initiate growth or division due to an environmental or functional reason. In such a scenario, the cell halts the progression and departs the cell cycle, entering into a state called G_0 (or *senescence*) for a prolonged period, perhaps for the entire remaining lifetime of an organism. Many cells in humans and adult animals typically enter G_0 but are still capable of re-entering the cell cycle when needed ([18, 50, 52]).

In some cells, it is observed that the daughter cells have exact copies of the DNA, but other cells' contents may be distributed asymmetrically, resulting in new cells of unequal size (such as budding yeast [50]). Another observation is that the cell cycle regulatory process described above differs between cell types and organisms [49, 50, 52].

For biologists, the DNA content and other quantities, like mass, length or volume among others, are vital parameters in describing a cell. These quantities can be measured by tools like flow cytometry for DNA [7, 65], or Coulter spectrometry for volume distribution [4].

From the above context, we comprehend that modelling the cell cycle is extensive and complex. The mathematical model introduced in the next section is an attempt to describe the cell division process based on certain factors and constraints that would make it easier to understand, mathematically, such complicated phenomena and compare results with experimental data.

1.4 Model formulation and terminologies

Cell size is the most fundamental cellular characteristic [65]. Consider a population of cells where individual cells are characterised by “size” x . Here, “size” may be mass or DNA content. It is a quantity that obeys a conservation law during the division process. For example, no DNA is created or destroyed during cell division.

Let L denote the unit of cell size, which is measured by its mass during its life cycle. Typically, the mass of a unit cell is defined by the number of polymers or particles times the mass of a single polymer/particle. The number of cells of size x at time t is described by the number density $n(x, t)$. In other words, $n(x, t)$ describes the density of the cell population such that the total number of cells between sizes a and b , $0 < a < b$, at time t is given by

$$\int_a^b n(x, t) dx.$$

The amount of population mass (mass density) is then defined by the number density times the mass of a single cell, *i.e.*,

$$\text{mass density} = x \times n(x, t),$$

which traditionally refers to the biomass. The total biomass, hence, is given by

$$\int_0^\infty xn(x, t) dx.$$

The increase in cell population means a gain in cell numbers and cell mass, and therefore an increase in biomass. The number of cells of size x may increase, due to the division of larger-sized cells into smaller daughter cells, and the mass of cells may increase due to the smaller cells growing to size x . The population may decrease owing to cell division to a smaller size or through mortality.

The change in the number of cells of size x at time t is described as follows:

1. New cells are added as a result of larger cells dividing;
2. Cells are lost as a result of division to smaller-sized cells;
3. Cells die;
4. Cells grow.

The balance law for the cells' distribution can be written as

$$\frac{\partial}{\partial t}n(x, t) + \frac{\partial}{\partial x}\left(G(x, t)n(x, t)\right) = (\text{new daughter cells}) \tag{1.1}$$

– (loss through division) – (death),

in which the terms on left-hand side (LHS) represent the net rate of change over time and the size growth rate, respectively. Here, $G(x, t)$ is the growth rate per capita per unit time $\left(\frac{[L]}{[s]}\right)$. Motivated by the work in [48], the rate at which the number of cells of size x is increasing in the interval $(x, x + dx)$ from the division of larger cells ξ in the size interval $(\xi, \xi + d\xi)$ is given by

$$\int_x^\infty B(\xi)\Delta(x, \xi)n(\xi, t)d\xi, \tag{1.1a}$$

where $0 \leq B(\xi)\Delta(x, \xi) \in L^\infty(\mathbb{R}^+; L^1 \cap L^\infty)$, $B(x)$ is the division rate and $\Delta(x, \xi) \geq 0$ is a time independent function which models division of a cell at size $\xi > x$ into a finite number of cells of size x . Division occurs only when ξ is a multiple of x such that $\Delta(x, \xi) = 0$ if $\xi < x$. As the reproduction process is assumed to yield finite α new cells, one can write

$$\int_0^\xi \Delta(x, \xi)dx = \alpha.$$

The rate of loss of individuals from cells of size x can be derived (see [1] for more general integral kernel) and is given by

$$B(x)n(x, t) \int_0^x \frac{\tau}{x} \Delta(\tau, x) d\tau. \quad (1.1b)$$

The integrand in (1.1b) indicates that the biomass of cells in the interval $(\tau, \tau + d\tau)$ produced by the division of x cell in the interval $(x, x + dx)$ into smaller cells of size τ is $\int_0^x \tau \Delta(\tau, x) d\tau$. Since the biomass is conserved, this means

$$\int_0^x \tau \Delta(\tau, x) d\tau = x. \quad (1.1c)$$

We assume that the rate at which cells of size x die is proportional to the population, and this leads to a mortality term of the form

$$\mu(x, t)n(x, t), \quad (1.1d)$$

where $\mu(x, t)$ is the per capita death rate with units of $\frac{1}{[s]}$. Further, the formulation of the model is governed by whether the functions $G(x, t)$, $B(x)$ and $\mu(x, t)$ are deterministic or whether they represent a stochastic process. We restrict our attention to deterministic and stochastic growth rates. The deterministic case leads to a first order equation; the stochastic case leads to a second order equation. We explain this in the following section.

We seek solutions that do not blow up spatially, and this leads to the conditions

$$\begin{aligned} \lim_{x \rightarrow \infty} n(x, t) &= 0, \\ \lim_{x \rightarrow \infty} \frac{\partial}{\partial x} n(x, t) &= 0, \end{aligned}$$

for all $t \geq 0$. We are interested in the transient behaviour of solutions from an initial distribution

$$n(x, 0) = n_0(x). \quad (1.2)$$

For the sake of mathematical analysis, we assume that the cell division is spontaneous, with continuous growth during the cell cycle, in the sense that the temporal

gap between the phases G_1 , G_2 and M is negligible.

1.4.1 The growth process

Cell growth and cell division are the essential mechanisms for the survival of any cell [17, 65]. Typically, the growth of a cell of mass $x(t)$ is not a constant process but evolves over time, either in a continuous or discrete manner. If this process is continuous and incorporates no random behaviour, then

$$\frac{d}{dt}x(t) = G(x, t).$$

Many studies have reported the existence of stochastic (random) process in living organisms and systems, including cell biology. In the latter, the stochastic process was observed in some cell cultures [35]. There are various ways to add stochasticity. In the framework of the generalised theory of stochastic process, one way the randomness can be modelled is by adding a noise term, $\omega(t)$, to the above differential equation (cf. [53]), which is to obtain diffusions [15]. This means that the exact behaviour of the stochastic process is unknown but its probability distribution is known. It can generally be described by the following ODE

$$\frac{d}{dt}x(t) = G(x(t), t) + \sigma(x(t), t)\omega(t),$$

where $G(x(t), t)$ and $\sigma(x(t), t)$ are given functions. It is reasonable to choose $\omega(t)$ as a white noise process (a generalised stochastic process) which is typically defined as the formal derivative of a Wiener process $W(t)$ (or Brownian motion), whose increments $dW(t) \stackrel{\text{def}}{=} W(t + dt) - W(t)$ have zero mean Gaussian distribution with a standard deviation $\sigma(x(t), t)$ and $dt = dW^2$. In the sense of Itô calculus, this leads to the form

$$dx(t) = G(x(t), t)dt + \sigma(x(t), t)dW(t).$$

Since the values of x are uncertain at a given time, let $\rho(x, t)$ be the probability density function describing the likelihood of the value of x in any given range at time t . For the last stochastic differential equation (SDE), the process is described by the Fokker-Planck equation (FPE) (cf. [7]):

$$\frac{\partial}{\partial t}\rho(x, t) = -\frac{\partial}{\partial x}\left(G(x(t), t)\rho(x, t)\right) + \frac{\partial^2}{\partial x^2}\left(\sigma(x(t), t)\rho(x, t)\right).$$

Following Begg [7], for a large number of particles in the system, we can multiply the last equation by the number of individuals (say, N) to formally get

$$\frac{\partial}{\partial t}n(x, t) - \frac{\partial^2}{\partial x^2}\left(D(x, t)n(x, t)\right) + \frac{\partial}{\partial x}\left(G(x, t)n(x, t)\right) = 0, \quad (1.3)$$

as time evolves, where $D(x, t) = \frac{\sigma^2(x, t)}{2}$ and $n(x, t)$ is equal to the probability density $\rho(x, t)$ times N . We refer to the added process resulting in the above PDE by the stochastic growth model after adding the birth, loss and death terms.

1.4.2 The general formula

The general cell division equation using (1.3) and (1.1a)-(1.1d) can be written as follows

$$\begin{aligned} \frac{\partial}{\partial t}n(x, t) - \frac{\partial^2}{\partial x^2}\left(D(x, t)n(x, t)\right) + \frac{\partial}{\partial x}\left(G(x, t)n(x, t)\right) \\ = \int_x^\infty B(\xi)\Delta(x, \xi)n(\xi, t)d\xi - \left(B(x) + \mu(x)\right)n(x, t), \end{aligned} \quad (1.4)$$

subject to the initial condition (1.2) and the boundary data

$$\lim_{x \rightarrow 0^+} \left[-\left(D(x, t)n(x, t)\right)_x + G(x, t)n(x, t) \right] = 0, \quad (1.5)$$

$$\lim_{x \rightarrow \infty} \left[-\left(D(x, t)n(x, t)\right)_x + G(x, t)n(x, t) \right] = 0, \quad (1.6)$$

Another derivation method for this model can be found in [35], including further references. The development of this formulation originated from age and age-size structured population models dating back to the 1900s to 1960s, which will be reviewed in the next chapter.

Our research revolves around developing solution techniques and studying qualitative properties, such as uniqueness and positivity, as well as related asymptotic properties to a class of cell division problems that stem from the formula (1.4) for particular choices of $D(x, t)$, $G(x, t)$, $B(x)$ and $\Delta(x, \xi)$. In most models, including this, the functions $D(x, t)$ and $G(x, t)$ appear as time independent parameters to simplify the problem. In this thesis, we focus on the case $G(x) = gx$, $B(x) = bx^r$ and constant $D(x) = D \geq 0$ such that g and b are some positive constants, $r \geq 0$ and $\alpha > 1$. We utilise numerical methods to study problems unsolved analytically.

1.5 Outline of the thesis

1.5.1 Chapter 2

In this chapter, we review the background of the growth fragmentation equation and its development. We survey the mathematical and biological motivations and lay out their connections to the model of study. We introduce the special case of interest,

$$\Delta(x, \xi) = \alpha \delta\left(\frac{\xi}{\alpha} - x\right),$$

where δ denotes the Dirac delta function. For this choice, the integro-differential equation (4.1) reduces to a linear advanced functional partial differential equation (PDE), and the cell division problem is either a first or a second order PDE with a functional term depending on whether the growth rate is deterministic or stochastic, respectively.

1.5.2 Chapter 3

In this chapter, we develop a solution technique and study related qualitative properties to the cell division equation (2.8) for general initial data with $D = 0$ (*i.e.*, no stochasticity in the growth process), $G(x) = gx$ and $B(x) = bx^r$ such that g, b and r are positive constants. The model was originally presented by Hall and Wake [33] and revolved around the study of separable solution. We recast the problem into what we call “Problem A” in order to simplify solving it for all $r > 0$ and $x \geq 0, t \geq 0$.

We show in Section 3.1 that the solution is unique and positive. We derive a general solution in Section 3.2 through the Mellin transform to Problem A, which involves an arbitrary function w_0 to be determined. We use the Mellin transform to glean a relationship for w_0 in Section 3.3. A key step is the identification of a partition function which is found in a number of pantograph type ODEs (e.g., [71], [76]). In Section 3.4, we derive the eigenvalues and eigenfunctions associated with Problem A by studying a class of non trivial solutions of the form $\bar{m} = A(t)y(x)$, where $y(x) \geq 0$ is required to be a PDF. The observation that

$$\int_0^\infty y(x)dx \neq 0,$$

$$\int_0^\infty \frac{y(x)}{x}dx \neq 0,$$

allows us to show there is precisely one real eigenvalue $\lambda_{0,0} = 0$. We show in fact there is no dominant eigenvalue, and this is the source of oscillatory terms in the long time asymptotic behaviour of solutions to Problem A. In Section 3.5, we prove that the solution to Problem A, defined by the series (3.22), converges in the domain of definition and satisfies the boundary conditions. We show that the long time asymptotic behaviour to Problem A converges to a product of the separable solution in [33] and some function that depends on time and the initial condition m_0 , with exponential convergence in the L^1 norm, and that the complete solution

converges in a weighted L^1 norm. We illustrate the solution behaviour with some examples of Gaussian type distribution initial data in Section 3.6.

1.5.3 Chapter 4

We note that if $r = 0$, the cell division problem cannot be solved by the methods in Chapter 3. In this chapter, we study two examples for this case subject to similar criteria as in Chapter 3. The first example is of a deterministic growth rate (Section 4.1); the second involves constant dispersion as a result of stochasticity in the growth process (Section 4.2).

We show in Section 4.1 that there is no PDF separable solution to the deterministic growth version in the $L^1[0, \infty)$ norm, and in fact a general solution can be gleaned directly if the initial condition is smooth and bounded. The solution technique is to construct a sequence of functions defined by a sequence of PDEs and exploit the hyperbolic character of the equation. The solution uniqueness and positivity proofs can be adapted from the case in Chapter 3. However, the study of long time asymptotic behaviour from the solution formula is not feasible. We instead provide an illustration to examine the influence of the initial data. We observe that the long time asymptotic solution exhibits periodic oscillations but different in character from the case in Chapter 3 and that it converges to a Dirac delta type solution. We notice that a generalised solution of the form

$$n(x, t) = e^{b(\alpha-1)t} \delta(x),$$

satisfies the equation (4.4).

In Section 4.2, we study the second order version. We first review in Section 4.2.1 the constant parameters case in [27] since the solution techniques and results for this case can be extended to the second order case in Section 4.2.2. Similar to the case in Section 4.1, we show in Section 4.2.2.1 that there are no classical PDF

separable solutions to this case in the $L^1[0, \infty)$ norm if the coefficients g and b satisfy the following inequality

$$g > \alpha b \ln \alpha. \quad (1.7)$$

It remains unclear if a PDF separable solution exists for the case when g and b satisfy

$$g < \alpha b \ln \alpha. \quad (1.8)$$

Motivated by the solution techniques and results in [27], we show in Section 4.2.2.2 that a general solution can be constructed for the second order equation. The uniqueness and positivity proofs of solution can also be adapted from the case in Chapter 3. It remains elusive to study the long time asymptotic behaviour of solution from the formulation in this case, neither a graph can be obtained at this time. We utilise numerical methods in Chapter 5 to study potential behaviours for this case.

1.5.4 Chapter 5

In this chapter we employ numerical methods using (forward-time centred-space) finite difference approximation to examine solution behaviour for the problems in Sections 4.2.2.1 and 4.2.2.2.

We introduce the numerical method and set up the scheme in Sections 5.1 and 5.2, respectively. We utilise the examples from Chapters 3 and 4 as well as four from the literature to validate the method in Section 5.3. We find that though this method exhibits some numerical errors and inaccurate approximation, particularly, in the first order degenerate case, it does manage to capture the main solution properties in general. We observe in Section 5.4 that the numerical solution agrees with the analytical argument for the inequality (1.7) only if the

dispersion term D is small enough (but $D \rightarrow 0^+$). For the inequality (1.8), the numerical approximation indicates that there is a PDF type solution for D large enough. The numerical evaluation for the long time asymptotic behaviour suggests that for any D a steady state does not appear when (1.7) is satisfied, while it does when (1.8) is imposed. We note from the numerical solutions that, in general, the oscillatory character seen in the dispersion free cases smooths out when allowing for large enough dispersion. These observations are limited to constant dispersion.

Chapter 2

The growth fragmentation equation

The cell fragmentation process models the evolution of the size distribution in time. This model can be described using a growth fragmentation equation accompanied by appropriate conditions. In general, the studies have been devoted to finding solutions to the discrete and continuous systems in order to understand general behaviour. Growth fragmentation equations have become central to the mathematical models from many fields such as phase transition, polymerisation processes, aerosols, prion proliferation, and cell growth. Cell growth modelling in itself is an extensive field that has made contributions to understanding problems like tumour cell growth. Like every study, the growth fragmentation model has historical roots.

2.1 Primary studies

The earliest mathematical structured model which arose in the literature was chronological age dependent. This model was proposed by Sharpe and Lotka [59]

in 1911 in a demography study and first appeared as a PDE by McKendrick [45] in 1926. In the model, the density of individuals of age $a \geq 0$ at time $t \geq 0$ is described by $n(a, t)$, such that the total number of individuals having ages between a_1 and a_2 ($a_1 \leq a_2$) in a population is given by

$$\int_{a_1}^{a_2} n(a, t) da.$$

The governing equation, thus, can be written as

$$\frac{\partial}{\partial t} n(a, t) + \frac{\partial}{\partial a} n(a, t) = -d(a, t)n(a, t), \quad (2.1)$$

along with an initial condition

$$n(a, 0) = n_0(a), \quad (2.2)$$

and a boundary condition (renewal condition)

$$n(0, t) = \int_0^{\infty} B(a)n(a, t) da, \quad (2.3)$$

where $d(a, t)$ and $B(a)$ are the rates of loss and birth of individuals, respectively. Many scientists contributed to the development of the linear age model, but no rigorous results were established until, according to Webb [74], Feller in 1941 followed by others. The age model was extended to the study of cell population growth by Scherbaum and Rasch [58] in 1957. Two years later, von Foerster [72] rediscovered equation (2.1) describing the age and size of cell populations. In some literature, von Foerster is credited for the derivation of equation (2.1). One of the most influential works in this sector was done by Bellman and Cooke. [11].

In 1967, a new approach by three groups (Bell and Anderson [9] using the Collins and Richmond equation [16]; Sinko and Streifer [61]; Frederickson *et al.* [30]) independently adopted a model with two physiological properties and derived

an equation analogous to (2.1). This model was driven by experimental data such as that conducted by Slobodkin (1954) on the *Daphnia obtusa* population, in which he found that a single property structured model was insufficient to describe the physiological behaviour of an animal, and concluded that “age and size taken together can be considered to define a class of physiologically identical animals until proven to the contrary” (cf. [64]). Generally, the derivation of the age size model relies on the principle that a small change in the system occurs in a small time interval. The resulting equation can be written as

$$\frac{\partial}{\partial t}n(x, a, t) + \frac{\partial}{\partial x}\left(G(x, a)n(x, a, t)\right) + \frac{\partial}{\partial a}n(x, a, t) = -d(x, a)n(x, a, t), \quad (2.4)$$

where $n(x, a, t)$ is the density of population at time t with age a and property x (x can be mass, volume, length, ... or, as here, the size of a cell). $G(x, a)$ is the growth rate per capita, $dx/dt = G(x, a)$ and $da/dt = 1$. The model can be supplemented with initial-boundary data. For instance, in the model of Bell and Anderson, the conditions are

$$\begin{aligned} n(x, a, 0) &= n_0(x, a), \\ n(x, 0, t) &= 4 \int_0^\infty B(2x, a)n(2x, a, t)da, \end{aligned}$$

for which B is the birth rate, and the term $2x$ indicates binary fission, which occurs for an individual with age a and property x . Note that when the rate d is caused by loss of individuals owing to birth (fission) and death, one can write

$$d(x, a) = B(x, a) + \mu(x, a),$$

such that μ is the death rate per capita per unit. Bell [?] and Anderson *et al.* [3] further developed and analysed the above model. It was also discussed in [46], including a paper by Heijmans (Chapter V, p. 185), and has been generalised to allow for age a and properties x_1, \dots, x_k , and studied in detail in [54]. Using a non linear system, the model was investigated by [64] as well as others.

It is known that age related models can be converted to a Volterra integral equation of convolution type and solved by the Laplace transform. Also, it is known that the general solution reaches a steady state exponentially through the Perron-Frobenius theorem after time re-normalisation, as long as the birth and death rates are independent of time. The reader is directed to [56], [63], or [74] for further results and literature profiles.

2.2 Introductory models

Age and age related models have proven useful in multicellular organism studies when the birth and death rates are associated with chronological age. However, this is not always the case. Evidence was found (1965) in cell populations indicating that the cell division is partially or probably completely size dependent, which can be dissociated from the chronological age of a cell (cf. [64]). In particular, the mass, the DNA content or the length of a cell among other biological properties are found, in unicellular organisms, to be more relevant than the age at mitosis. This perhaps prompted researchers to return to structured models characterised by a single property. Since then, studies have been increasingly focused on cell size property, partly due to advances in measuring instruments that led to cell size can be easily and precisely measured. Amongst models that investigated size structured populations by different groups with different approaches (e.g., [16, 22, 23, 32–34, 36, 37, 43, 46]) is the model studied by Sinko and Streifer [62] who first studied the deterministic version. The model at first considers a simple case of binary fission in which each individual parent, characterised by size x (which can be measured by one of the aforesaid properties above), gives birth to two new smaller individuals of equal size over time t . More recent researchers have investigated size structured models including [1, 6–8, 48, 55, 68, 76], and many more.

Consider $n(x, t)$ to denote the number density of cells of size x at time t , such that the total population number in the interval $[x_1, x_2]$ is calculated by the integral of the number density with respect to x within such interval. The balance law follows from (2.4), without age dependence but with an added birth term to the reproduction process side (the right-hand side (RHS)), resulting in

$$\frac{\partial}{\partial t} n(x, t) + \frac{\partial}{\partial x} \left(G(x)n(x, t) \right) = 4B(2x)n(2x, t) - d(x)n(x, t). \quad (2.5)$$

The explanation of the new term on the RHS can be found in [46], [35], or [7]. Sinko and Streifer (*op. cit.*) then applied the model to populations of the planarian worm *Dugesia tigrina*, and solved the problem numerically for a more complicated system. In fact, the modelling equation (2.5) can be written in a more general form known by “the growth fragmentation equation” such that individuals give birth to $\alpha > 1$ offspring. That is,

$$\begin{aligned} \frac{\partial}{\partial t} n(x, t) + \frac{\partial}{\partial x} \left(G(x)n(x, t) \right) = & \int_x^\infty B(\xi)\Delta(x, \xi)n(\xi, t)d\xi \\ & - \left(B(x) + \mu(x) \right) n(x, t), \end{aligned} \quad (2.6)$$

where $\Delta(x, \xi)$ models the number of cells when a parent cell with size ξ divides to form smaller cells with size x . One can recover equation (2.5) by choosing a suitable Δ in equation (2.6). The choice $\Delta(x, \xi) = 2\delta(\frac{\xi}{2} - x)$, which represents a symmetrical binary division, yields the desired equation (2.5) where

$$B(x) + \mu(x) = d(x),$$

and

$$\int_0^\xi \Delta(x, \xi)dx = 2.$$

In the framework of the growth fragmentation equation, much progress has been made on the long time asymptotic behaviour of solutions and the existence

of steady size distribution (SSD) type solutions for a broad class of functions $B(x)$ and constant growth rates [47], [48], [55], [26]. In these models, techniques from General Relative Entropy (GRE) are key tools, as well as the Krein-Rutman theorem to deal with the eigenvalue problem associated with the existence of SSD (e.g., [20]). The models have also been extended to a higher order fragmentation equation based on the FPE [6, 8, 27, 42, 70, 71, 75]. In a broader sense, the model is a growth fragmentation equation with an added stochastic process, as discussed in the previous chapter. Generically, the fragmentation equation is non local (functional) in character, arising from the birth term. The simple cell growth model produces a first order functional PDE, the general solution of which is unknown for all but a very special class of initial distributions. There are choices of interest, however, that result in PDEs. Here, there is a wealth of information and techniques.

2.3 Special cases

There are two choices of $\Delta(\xi, x)$ that arise in the literature. One represents symmetrical cell division and the other, asymmetrical cell division.

Symmetrical cell division

In this case, a cell of size $\xi > x$ divides into α daughter cells of the same size. This can be modelled by

$$\Delta(x, \xi) = \alpha \delta\left(\frac{\xi}{\alpha} - x\right), \quad (2.7)$$

where δ is the Dirac delta function. Hall and Wake [32] presented and studied this model in 1989 based on earlier work by Sinko and Streifer [61, 62]. The most realistic case is when $\alpha = 2$, which was considered earlier by Koch and Schaechter [43]. For such a choice of Δ , the growth fragmentation equation (2.6) reduces to

a first order PDE when the growth rate is deterministic, and to a second order version when the growth rate is stochastic. In both cases, a non local term arises from the birth term. The general equation is of the form

$$\begin{aligned} n_t(x, t) - \left(D(x)n(x, t) \right)_{xx} + \left(G(x)n(x, t) \right)_x \\ = \alpha^2 B(\alpha x)n(\alpha x, t) - \left(B(x) + \mu(x) \right) n(x, t), \end{aligned} \quad (2.8)$$

where the subscripts x and t indicate the partial derivatives with respect to the corresponding arguments. The cell division problem is thus a PDE with a functional term accompanied by conditions of the initial-boundary value type ((1.2), (1.5) and (1.6)). The analysis of such models poses non trivial and challenging mathematical problems.

If $\mu(x)$ is constant, then the transformation

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

results in an equation for \tilde{n} of the form (2.8) with $\mu = 0$. For this reason, we will neglect the mortality term, though we recognise that for non constant μ such a transformation is in general not available. Hall and Wake [32, 33], studied a special class of solutions to (2.8), the so-called SSD solutions for the case $D = 0$. Such solutions correspond to the separable solutions to equation (2.8) that satisfy condition (1.5) and (1.6) with $D = 0$. Their study was motivated by experimental data on size structure cell populations in certain plant tissues. The observation that motivated the study was that the cell size distribution (number density) evolved to a certain shape that did not depend on the initial distribution n_0 . In other words, for t sufficiently large, the distribution assumed the same shape, regardless of the initial distribution. At least for constant growth rates, the SSD solutions matched the experimental data. As long as the coefficients are independent of time, the SSD solutions are usually found by assuming a solution of the form

$$n(x, t) = N(t)y(x),$$

which, upon substitution into (2.8) with $D = \mu = 0$, yields

$$\frac{N'(t)}{N(t)} = -\frac{(G(x)y(x))'}{y(x)} - B(x) + \frac{\alpha^2 B(\alpha x)y(\alpha x)}{y(x)} = \lambda.$$

Here, λ is a constant of separation to be determined, and ' denotes the derivative with respect to the argument. Evidently,

$$N(t) = Ce^{\lambda t},$$

where C is some constant, and y satisfies

$$(G(x)y(x))' + (B(x) + \lambda)y(x) = \alpha^2 B(\alpha x)y(\alpha x). \quad (2.9)$$

The solution relies crucially on λ . If $\lambda < 0$, then the number density decays exponentially as $t \rightarrow \infty$; if $\lambda > 0$, then n increases exponentially as $t \rightarrow \infty$. For the cell growth model, the possible values of λ are limited by the boundary conditions,

$$\begin{aligned} \lim_{x \rightarrow 0^+} G(x)y(x) &= 0, \\ \lim_{x \rightarrow \infty} G(x)y(x) &= 0, \end{aligned} \quad (2.10)$$

and the requirement that $y(x)$ is a probability density function (PDF), *i.e.*,

$$\int_0^\infty y(x)dx = 1, \quad (2.11)$$

and $y(x) \geq 0$. An expression for λ can be obtained by integrating (2.9) from 0 to ∞ and using conditions (2.10)-(2.11), namely,

$$\begin{aligned}\lambda &= -\left[G(x)y(x)\right]_0^\infty + (\alpha - 1) \int_0^\infty B(x)y(x)dx \\ &= (\alpha - 1) \int_0^\infty B(x)y(x)dx,\end{aligned}\tag{2.12}$$

provided that $B(x)y(x) \in L^1[0, \infty)$. Hall and Wake [32] studied this problem where the functions $G(x)$ and $B(x)$ are positive constants. In this case, equation (2.9) reduces to the well-known ‘‘pantograph equation’’ (PE). Kato and McLeod [41] studied the PE extensively subject to an initial condition. They proved that the problem is well posed with a power series solution for the retarded case ($0 < \alpha < 1$), and ill posed for the advanced version ($\alpha > 1$). The PE is found in several applications (cf. [40], [69] for more details with references). Hall and Wake [32] constructed a PDF solution using the Laplace transform and showed that the solution is unique. Other solution properties have also been studied in [7]. Later, Hall and Wake studied the same problem in [33] for the case $G(x) = gx$ and $B(x) = bx^r$, where g , b and r are positive numbers. The constant λ cannot be determined directly from (2.12); however, one can multiply (2.9) by x and integrate to get

$$\begin{aligned}\lambda &= \frac{\int_0^\infty G(x)y(x)dx}{\int_0^\infty xy(x)dx} \\ &= g,\end{aligned}\tag{2.13}$$

assuming that $G(x)y(x)$ and $xy(x)$ are in $L^1[0, \infty)$. Hence, equation (2.9) reduces to

$$gxy'(x) + (bx^r + 2g)y(x) = b\alpha^{r+2}x^r y(\alpha x).\tag{2.14}$$

They ([33]) proved that this equation subject to (2.10)-(2.11) forms a well posed problem, and the solution can be deduced through a transformation which reduces (2.14) to the PE. Van Brunt and Vlieg-Hulstman [68] showed that this problem leads to a family of eigenvalues (a discrete spectrum) and corresponding eigenfunctions, which can be determined by Mellin transforms. The first eigenfunction turned out to be the PDF established in [32]. They showed there exist

higher eigenfunctions, but these are not PDFs. The open problem of the span of these eigenfunctions was reviewed recently by Zaidi [75], but it remains open. The problem can be interpreted as a Sturm-Liouville problem, and the solution can be represented as a Dirichlet series. The unimodality of solution was investigated for the constant coefficient case in [20]. We note that the case, when $B(x) = b$ and $G(x) = gx$, is problematic because λ can be determined by (2.12) and (2.13), and these expressions can produce different values for λ . In fact, we will show that this case possesses no PDF solutions. The long time asymptotic behaviour of solutions to the cell division equation for certain cases was studied prior to the work of Hall and Wake. For instance, Diekmann *et al.* [23] studied the long time asymptotics for the case where cells are limited by a maximum size and can divide only after a minimum size is reached. The semigroup theory and compactness arguments were employed to establish the existence of SSD. Finally, we note that although Hall and Wake produced a separable solution, they did not study the long time asymptotic behaviour of the general solutions. They did not show that their solutions were in fact SSDs. Perthame and Ryzhik [55] established this for the case $G(x) = g$, and we will show in Chapter 3 that for $G(x) = gx$, the Hall and Wake solution plays a prominent rôle, but it is not an SSD solution.

If $D \neq 0$, the boundary value problem arising from (2.8), (1.5) and (1.6) through the separable solution is given by

$$- \left(D(x)y(x) \right)'' + \left(G(x)y(x) \right)' + \left(B(x) + \mu(x) + \lambda \right) y(x) = B(\alpha x)y(\alpha x), \quad (2.15)$$

$$\lim_{x \rightarrow 0^+} \left[\left(D(x)y(x) \right)' - G(x)y(x) \right] = 0, \quad (2.16)$$

$$\lim_{x \rightarrow \infty} \left[\left(D(x)y(x) \right)' - G(x)y(x) \right] = 0. \quad (2.17)$$

This problem was studied for the constant coefficient case by Wake *et al.* [73]. They proved an SSD solution exists and that the problem is well posed. Kim [42] studied a special form of (2.15) for various choices of constant and non constant

coefficients outside cell growth models. Van Brunt *et al.* [70] investigated the constant coefficient case as a singular Sturm-Liouville problem. In the footsteps of the work in [70], Zaidi [75] incorporated the death term μ and showed there are more eigenfunction solutions corresponding to eigenvalues. Assuming that $y(x)$ is a PDF and satisfies (2.11), a value for λ , in this case, can be deduced in a similar manner to the first order case with constant coefficients and is given by (2.12). The solution to this case is inspired by the solution techniques to the first order case with constant coefficients. It can be found for certain values of λ by construction using a Dirichlet series ([68]), or through the Laplace transform ([27, 68, 75]) which involves further complications that require tools like the Paley-Wiener theorem to assert the inverse problem. Van Brunt and Wake [71] investigated the equation (2.15) with $D(x)$ given by a linear function, and $G(x)$ and $B(x)$ are positive constants. They found that the Mellin transform is a convenient technique to establish the solution. Of independent interest, Basse *et al.* [6] and Begg *et al.* [8] studied the second order boundary value problem where $D(x)$, $G(x)$ and $\mu(x)$ are positive constants, and $B(x)$ models cell division that occurs only at a critical size. In this scenario, the value of λ depends on the solution. Their analysis proved that the SSD solution is achieved only if the growth and division parameters satisfy a certain inequality and as long as the dispersion term $D(x)$ tends to zero as $x \rightarrow 0^+$.

Although much is known about SSD solutions to cell growth equations, there are few techniques for solving IBVPs that involve a functional argument. Certain general results for the Cauchy problem, such as uniqueness, are given in [14, 21] for a broad class of functional PDEs, but solution techniques for the IBVP are lacking. Recently, Zaidi *et al.* [76] developed a technique whereby the IBVP can be solved for general initial data for the case where $B(x)$ and $G(x)$ are constant functions and $D(x), \mu(x) = 0$. General solutions with non constant $G(x)$ and $B(x)$ are unknown, and this will be the case study in Chapter 3. Also, general solutions to the critical case when $B(x)$ is constant are unknown, which will

be investigated in Chapter 4 with deterministic and stochastic growth processes (with constant dispersion term).

Asymmetrical cell division

In the case of asymmetrical cell division, a parent cell of size ξ divides into two daughter cells of size α and size β . Here, the function Δ takes the following form

$$\Delta(x, \xi) = \delta\left(\frac{\xi}{\alpha} - x\right) + \delta\left(\frac{\xi}{\beta} - x\right).$$

This gives the following equation from (1.4),

$$\begin{aligned} n_t(x, t) - \left(D(x)n(x, t)\right)_{xx} + \left(G(x)n(x, t)\right)_x &= \alpha B(\alpha x)n(\alpha x, t) \\ &+ \beta B(x)n(\beta x, t) - \left(B(x) + \mu(x)\right)n(x, t). \end{aligned}$$

The conservation of size implies that

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

Since we focus only on the symmetrical division case in this thesis, we refer the reader to [75] for further details.

Chapter 3

A first order cell division equation with a linear growth rate and non constant splitting rates

In this chapter a study case on a cell size structured model derived from Section 1.4 is presented. Most of the material in this chapter appears in [66]. In particular, we study equation (2.8) along with the conditions (1.2), (1.5) and (1.6) for the case $G(x) = gx$, $B(x) = bx^r$ and $D(x) = 0$, where g , b and r are positive numbers, and $\alpha > 1$. This model was studied by Hall and Wake [33] for a special class of solutions; here, we study the problem for a general class of initial data. We thus consider the equation

$$n_t(x, t) + g \left(xn(x, t) \right)_x + bx^r n(x, t) = \alpha^{r+2} bx^r n(\alpha x, t), \quad (3.1)$$

subject to the conditions

$$\begin{aligned}\lim_{x \rightarrow 0^+} xn(x, t) &= 0, \\ \lim_{x \rightarrow \infty} xn(x, t) &= 0,\end{aligned}\tag{3.2}$$

and

$$n(x, 0) = n_0(x).\tag{3.3}$$

We first transform equation (3.1) into a simpler form. Let

$$n(x, t) = \frac{e^{gt}}{x^2} \theta(x, t),$$

then

$$\theta_t(x, t) + gx\theta_x(x, t) + bx^r\theta(x, t) = b\alpha^r x^r \theta(\alpha x, t).\tag{3.4}$$

Further, let

$$z = \frac{x^r}{r},$$

and

$$\psi(z, t) = \theta(x, t).$$

Then

$$\theta(\alpha x, t) = \psi(\alpha^r z, t),$$

and equation (3.4) yields

$$\psi_t(z, t) + \tilde{g}z\psi_z(z, t) + \tilde{b}z\psi(z, t) = \tilde{b}\beta z\psi(\beta z, t),\tag{3.5}$$

where $\tilde{g} = rg$, $\tilde{b} = rb$ and $\beta = \alpha^r > 1$. Equation (3.5) shows that it is sufficient to study the case $r = 1$. We thus focus on the equation

$$m_t(x, t) + gxm_x(x, t) + bxm(x, t) = b\alpha xm(\alpha x, t).\tag{3.6}$$

Conditions (3.2)-(3.3) under the transformations become

$$\begin{aligned} \lim_{x \rightarrow 0^+} \frac{m(x, t)}{x} &= 0, \\ \lim_{x \rightarrow \infty} \frac{m(x, t)}{x} &= 0, \end{aligned} \tag{3.7}$$

for any $t \geq 0$, and

$$m(x, 0) = m_0(x), \tag{3.8}$$

where

$$m_0(x) = x^2 n_0(x).$$

For succinctness, we will refer to this problem as “Problem A”.

The choice of the growth rate here corresponds to the “exponential growth” case, and the long time asymptotic behaviour of solutions differs markedly from the constant growth case. In particular, it can be shown (cf. [55], [56]) for a general class of functions $B(x)$ and constant $G(x)$ (linear increase in cell size) that there is a unique eigenvalue λ and a corresponding positive eigenfunction y such that for any initial distribution n_0 ,

$$\|e^{-\lambda t} n(x, t) - y(x)\| \rightarrow 0,$$

as $t \rightarrow \infty$. Here, $\|\cdot\|$ is a weighted L^1 norm that depends on $B(x)$. In contrast, it has been shown for the exponential growth case that there is no dominant eigenvector [23] and that long time asymptotic solutions may include time dependent oscillations [12]. In fact, there are choices for $B(x)$ (e.g., constant division rate) that lead to critical cases where there is no eigenvalue leading to a positive eigenfunction [25].

In the next section we show that if Problem A has a solution, then it is unique and non negative for non negative initial data. In Section 3.2, we derive a general solution to Problem A using the Mellin transform. This transform has been applied previously to related problems (e.g., [71]) and proved useful in separating the effect of the functional argument. The choices of $G(x)$ and $B(x)$ also motivate

the use of this transform. The solution contains an arbitrary function w_0 that is determined by the initial data m_0 . In Section 3.3, we obtain an explicit relation defining w_0 in terms of m_0 for $x > 0$, and show that the behaviour of w_0 as $x \rightarrow 0^+$ is oscillatory. We confirm that the solution constructed in Section 3.2 satisfies the boundary conditions in Section 3.5 and show that this solution converges in the L^1 norm to a certain “limiting” solution that contains time dependent oscillatory terms. We provide some examples of initial data in Section 3.6 to illustrate the solution behaviour.

3.1 Some qualitative results

In this section we show that if Problem A has a solution it is unique and that any such solution must be non negative if the initial function m_0 is non negative. Let $\Omega = \{(x, t) : 0 \leq x, 0 \leq t\}$ and let \mathcal{N} denote the set of functions $h : \Omega \rightarrow \mathbb{R}$ such that:

1. h_x and h_t are continuous on Ω ;
2. there is a positive number ℓ such that for any fixed $T \geq 0$

$$h(x, T) \sim O\left(\frac{1}{x^{1+\ell}}\right)$$

as $x \rightarrow \infty$; and

3. for any $\epsilon > 0$ and $T \geq 0$ there is a corresponding $\delta > 0$ and X such that

$$|xh(x, t)| < \epsilon,$$

whenever $0 < t - T < \delta$ and $x > X$.

Theorem 3.1.1 (Uniqueness). *Suppose that $m \in \mathcal{N}$ is a solution to Problem A. Then m is unique among functions in \mathcal{N} .*

Proof. We first transform equation (3.6). Let

$$m(x, t) = \frac{e^{gt}}{x} \tilde{m}(x, t),$$

then \tilde{m} satisfies

$$\tilde{m}_t(x, t) + gx\tilde{m}_x(x, t) + bx\tilde{m}(x, t) = bx\tilde{m}(\alpha x, t). \quad (3.9)$$

Suppose that there are two solutions m_1 and m_2 in \mathcal{N} , then there are two corresponding solutions \tilde{m}_1 and \tilde{m}_2 to equation (3.9). Let $u = \tilde{m}_1 - \tilde{m}_2$. The function u satisfies (3.9) along with the conditions

$$u(0, t) = 0, \quad (3.10)$$

$$u(x, 0) = 0. \quad (3.11)$$

Suppose that m_1 and m_2 are distinct. Then there is a point (\hat{x}_0, t_0) at which $u(\hat{x}_0, t_0) \neq 0$. Without loss of generality, we can assume that $u(\hat{x}_0, t_0) > 0$. Since m_1 and m_2 are in \mathcal{N} , we know that u , u_x and u_t are continuous on Ω and that, for any fixed $t \geq 0$, $u(x, t) \rightarrow 0$ as $x \rightarrow \infty$. Since $u(0, t_0) = 0$, we conclude that $u(x, t_0)$ must have a global maximum, say, $L_0 > 0$ at some $x > 0$, and the decay condition on $u(x, t_0)$ precludes $u(x, t_0)$ from achieving this value for arbitrarily large values of x . Let x_0 denote the largest value of x at which $u(x, t_0)$ achieves its global maximum. Thus, $u(x_0, t_0) = L_0$, $u_x(x_0, t_0) = 0$, and $u(x_0, t_0) > u(\alpha x_0, t_0)$; hence, equation (3.9) implies

$$u_t(x_0, t_0) < 0. \quad (3.12)$$

The above inequality indicates that $u(x_0, t) > u(x_0, t_0)$ for some $t < t_0$.

Consider now the compact set $\Omega_0 = \{(x, t) : 0 \leq x \leq \alpha x_0, 0 \leq t \leq t_0\}$. The function u must achieve a global maximum in Ω_0 , and it is clear from equations (3.10) and (3.11) that this maximum will not occur on the x or t axes. Inequality

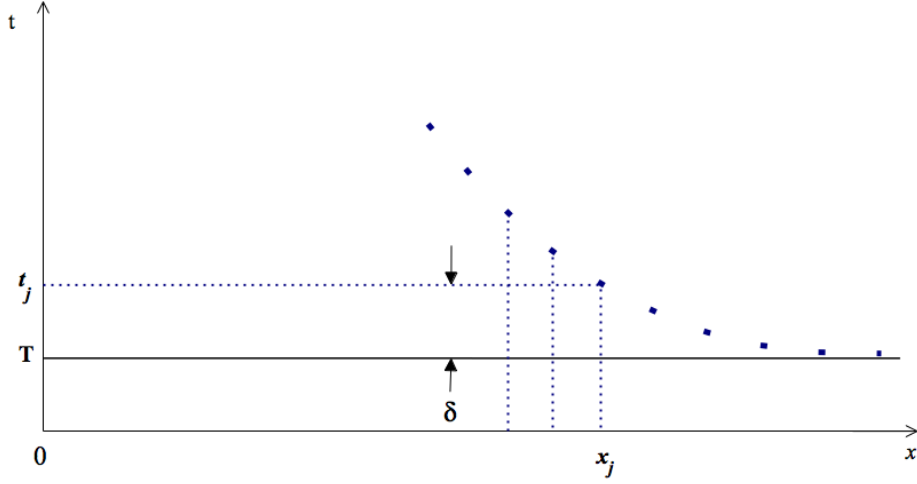


FIGURE 3.2: Solution uniformity for $0 < t - T < \delta$.

condition 3. If this condition is applied to the limit T of $\{t_j\}$ then u cannot meet this condition.

□

Theorem 3.1.2. (Non Negative Solution) *Suppose that $m \in \mathcal{N}$ is a solution to Problem A. If $m_0 \geq 0$, then $m(x, t) \geq 0$ for all $(x, t) \in \Omega$.*

Proof. Suppose that there is a point (\hat{x}, t_0) at which $m(\hat{x}, t_0) < 0$. Then $\tilde{m}(\hat{x}, t_0) < 0$, where \tilde{m} is as defined in the proof of Theorem 3.1.1. Clearly, the boundary and initial conditions preclude \tilde{m} taking negative values on the x and t axes. We can proceed much like we did for the proof of uniqueness to first note that the function $\tilde{m}(x, t_0)$ must have a global minimum $l_0 < 0$, and then let x_0 be the largest value at which $\tilde{m}(x, t_0)$ achieves this minimum. It thus follows that $\tilde{m}_t(x_0, t_0) > 0$. We can follow the construction in the proof of Theorem 3.1.1 and deduce the existence of infinite sequences $\{x_j\}$, $\{t_j\}$ such that $x_j \rightarrow \infty$ as $j \rightarrow \infty$ and $\{t_j\}$ converges to some limit T , where $0 \leq T < t_0$. For each $j \geq 1$, $\tilde{m}(x_j, t_j) < l_0 < 0$ and hence $\tilde{m}(x, T)$ cannot satisfy the uniform decay condition 3.

□

3.2 A Mellin transform solution

In this section we derive a solution to equation (3.6) that satisfies condition (3.7). The solution contains an arbitrary function that will be used in Section 3.3 to ensure the solution satisfies the initial condition (3.8).

The Mellin transform of m with respect to x is given by

$$M(s, t) = \int_0^\infty x^{s-1} m(x, t) dx.$$

Assuming that $m \in \mathcal{N}$ we know that $xm(x, t) \rightarrow 0$ as $x \rightarrow \infty$ for all $t \geq 0$, so that equation (3.6) yields the partial differential difference equation

$$M_t(s, t) - gsM(s, t) + b\left(1 - \frac{1}{\alpha^s}\right)M(s+1, t) = 0. \quad (3.13)$$

Let

$$M(s, t) = P(s)W(s, t),$$

where

$$P(s) = \prod_{k=0}^{\infty} \left(1 - \frac{1}{\alpha^{s+k}}\right). \quad (3.14)$$

The choice of P is strategic because

$$P(s) = \left(1 - \frac{1}{\alpha^s}\right)P(s+1).$$

In fact, the partition function P arises in a number of applications with pantograph type equations (cf. [71]). Equation (3.13) implies

$$W_t(s, t) - gsW(s, t) + bW(s+1, t) = 0. \quad (3.15)$$

Rather than solve equation (3.15), we solve the corresponding PDE in the original (x, t) space. This equation is not functional in character. Let $w(x, t)$ denote the

inverse Mellin transform of $W(s, t)$, then equation (3.15) corresponds to the PDE

$$w_t(x, t) + gxw_x(x, t) + bxw(x, t) = 0, \quad (3.16)$$

which is equation (3.6) without the functional term.

We now pose the Cauchy problem of solving (3.16) subject to an initial condition of the form

$$w(x, 0) = w_0(x).$$

The characteristic projections are

$$\begin{aligned} t &= \xi, \\ x &= \eta e^{g\xi}; \end{aligned}$$

hence, equation (3.16) has solutions of the form

$$w(x, t) = w_0(xe^{-gt})e^{-\gamma x(1-e^{-gt})}, \quad (3.17)$$

where $\gamma = b/g$.

The infinite product defining P can be converted into an infinite series using the Euler identity ([5], p. 17)

$$\prod_{k=0}^{\infty} (1 + zq^k) = 1 + \sum_{k=1}^{\infty} \frac{q^{\frac{k(k-1)}{2}} z^k}{\prod_{j=1}^k (1 - q^j)}, \quad (3.18)$$

which is valid for $|q| < 1$ and $z \in \mathbb{C}$. The Euler identity with $q = 1/\alpha$ and $z = -1/\alpha^s$ indicates that

$$P(s) = 1 + \sum_{k=1}^{\infty} c_k \left(\frac{1}{\alpha^s} \right)^k,$$

where

$$\begin{aligned}
 c_k &= \frac{(-1)^k \alpha^k}{\prod_{m=1}^k (\alpha^m - 1)} \\
 &= \frac{(-1)^k q^{\frac{k(k-1)}{2}}}{\prod_{j=1}^k (1 - q^j)}.
 \end{aligned} \tag{3.19}$$

The inverse of $P(s)$ is

$$p(x) = \delta(x - 1) + \sum_{k=1}^{\infty} c_k \delta(\alpha^k x - 1), \tag{3.20}$$

where δ denotes the Dirac delta function.

The inverse transform of $M(s, t) = P(s)W(s, t)$ is given by the Mellin convolution

$$m(x, t) = \int_0^{\infty} w\left(\frac{x}{\xi}, t\right) \frac{p(\xi)}{\xi} d\xi, \tag{3.21}$$

from which we get a solution of the form

$$m(x, t) = w_0(xe^{-gt})e^{-\gamma x(1-e^{-gt})} + \sum_{k=1}^{\infty} c_k w_0(\alpha^k x e^{-gt})e^{-\gamma \alpha^k x(1-e^{-gt})}. \tag{3.22}$$

3.3 The function w_0

The function w_0 is determined by the initial condition m_0 . Before we determine w_0 , a few conditions are placed on the function m_0 . These conditions ensure that m_0 , regarded as a function on Ω , is in the set \mathcal{N} introduced in Section 3.1 and that m_0 also satisfies (3.7) for consistency. We make the following assumptions:

1. $m_0(x) \geq 0$ for all $x \geq 0$ and m_0 is not identically zero on $[0, \infty)$;
2. $m_0''(x)$ is continuous for all $x \geq 0$;
3. there exists a positive number ℓ such that

- a. $m_0(x) \sim O(1/x^{1+\ell})$ as $x \rightarrow \infty$;
- b. $m_0(x) \sim O(x^{1+\ell})$ as $x \rightarrow 0^+$; and
- c. $m'_0(x) \sim O(1/x^{1+\ell})$ as $x \rightarrow \infty$.

We use the Mellin transform to deduce a relationship for w_0 . Conditions 3.a and 3.b ensure that the Mellin transform of m_0 is holomorphic in a strip that includes $\{s \in \mathbb{C} : -1 \leq \Re(s) \leq 1\}$.

Equation (3.21) implies

$$m_0(x) = \int_0^\infty w_0\left(\frac{x}{\xi}\right) \frac{p(\xi)}{\xi} d\xi, \quad (3.23)$$

and taking the Mellin transform of both sides of (3.23), noting that the integral is a Mellin convolution, yields

$$W_0(s) = \frac{M_0(s)}{P(s)}, \quad (3.24)$$

where W_0 and M_0 are the Mellin transforms of w_0 and m_0 , respectively, and P is given by (3.14). The function $1/P$ is a generalisation of a well-known partition function. Morgan [51] has studied this function and its special properties. We can use another partition identity ([5], p. 17) to show that

$$\frac{1}{P(s)} = \sum_{k=0}^{\infty} R_k(\alpha) \frac{1}{\alpha^{ks}}, \quad (3.25)$$

where

$$R_0(\alpha) = 1,$$

and, for all $k \geq 1$,

$$R_k(\alpha) = \prod_{j=1}^k \left(1 - \frac{1}{\alpha^j}\right)^{-1}.$$

Equation (3.24) thus gives

$$W_0(s) = M_0(s) \sum_{k=0}^{\infty} R_k(\alpha) \frac{1}{\alpha^{ks}},$$

for $\Re(s) > 0$, and, since the above series is uniformly convergent in $\{s \in \mathbb{C} : \Re(s) \geq \sigma\}$ for any $\sigma > 0$, the transform can be inverted term by term to get the inverse transform

$$w_0(x) = \sum_{k=0}^{\infty} R_k(\alpha) m_0(\alpha^k x). \quad (3.26)$$

Let

$$R(\alpha) = \prod_{k=1}^{\infty} \left(1 - \frac{1}{\alpha^k}\right)^{-1}.$$

The value of $R(\alpha)$ can be expressed in terms of elliptic integrals, theta functions, the Dedekind eta function, or Euler's pentagonal number series (cf. [51], [32] and [71]). Now, the sequence $\{R_k(\alpha)\}$ is monotonic increasing and bounded above by $R(\alpha)$. The decay condition 3.a on m_0 ensures that the series in equation (3.26) is uniformly convergent in $[x_0, \infty)$ for any $x_0 > 0$; however, the behaviour of $w_0(x)$ as $x \rightarrow 0^+$ is not clear. (Note that the series $\sum_{k=0}^{\infty} R_k(\alpha)$ diverges.)

The behaviour of $w_0(x)$ near zero can be gleaned directly from the Mellin transform using a well-known asymptotic relation (cf. [29], Theorem 4). Specifically, suppose F is the Mellin transform of a function f and that the strip of holomorphy for F is $a < \Re(s) < c$ and that F is meromorphic for $a \leq \Re(s) \leq c$. The leading order terms for f as $x \rightarrow 0^+$ are determined by the singularities on the line $\Re(s) = a$. In particular, suppose that F has the poles a_1, \dots, a_j on this line. Then,

$$f(x) = \sum_{k=1}^j \operatorname{Res}\left(F(s)x^{-s}, a_k\right) + O(x^{-A}),$$

as $x \rightarrow 0^+$, where A is some number less than a that depends on the position of the singularities of F with real part less than a . The formula can be refined to include more singularities (producing lower order terms), and it can be extended to the case where there are an infinite number of singularities on the line $\Re(s) = a$ provided the infinite series is convergent.

Now, $M_0(s)$ is holomorphic for $-1 \leq \Re(s) \leq 1$, and $P(s)$ is an entire function with first order zeros at $s = -\ell + i\tau_j$, where $\ell = 0, 1, 2, \dots$ and, for any integer j , $\tau_j = \frac{2\pi j}{\log \alpha}$. The function $W_0(s)$ is thus holomorphic in a strip that includes $\Re(s) = 1$ and has simple poles along the imaginary axis at $i\tau_j$. These poles will determine the behaviour of w_0 near 0.

The Mellin inverse formula gives

$$w_0(x) = \frac{1}{2\pi i} \int_{\gamma-i\infty}^{\gamma+i\infty} W_0(s)x^{-s}ds, \quad (3.27)$$

in which $\gamma > 0$ is taken inside the strip of holomorphy. The integrand in (3.27) can be evaluated using the calculus of residues applied to a limiting sequence of closed contours Λ_j oriented anticlockwise and defined by the lines $\Re(s) = \gamma$, $\Im(s) = \eta_j$, $\Re(s) = -\sigma_0$, $\Im(s) = -\eta_j$, where $\tau_j < \eta_j < \tau_{j+1}$ and $0 < \sigma_0 < 1$ (see Figure 3.3). Note that the “next” poles of W_0 in the left half plane are on the line $\Re(s) = -1$. Let Λ denote the “limiting rectangle” that consists of the lines ℓ and $\hat{\ell}$ defined by $\Re(s) = \gamma$, $\Re(s) = -\sigma_0$, respectively. Let ℓ_j , h_j , $\hat{\ell}_j$, \hat{h}_j be as in Figure 3.3. Now,

$$\frac{1}{2\pi i} \int_{\Lambda_j} W_0(s)x^{-s}ds = \sum_{k=-j}^j \text{Res}\left(W_0(s)x^{-s}, i\tau_j\right),$$

and

$$\begin{aligned} \text{Res}\left(W_0(s)x^{-s}, i\tau_j\right) &= \text{Res}\left(\frac{M_0(s)}{P(s)}x^{-s}, i\tau_j\right) \\ &= \frac{R(\alpha)}{\ln \alpha} M_0(i\tau_j)x^{-i\tau_j} \\ &= \frac{R(\alpha)}{\ln \alpha} M_0(i\tau_j) \left(\cos(\tau_j \log x) - i \sin(\tau_j \log x) \right). \end{aligned}$$

Now,

$$\int_{\Lambda_j} = \int_{\ell_j} + \int_{h_j} + \int_{\hat{\ell}_j} + \int_{\hat{h}_j},$$

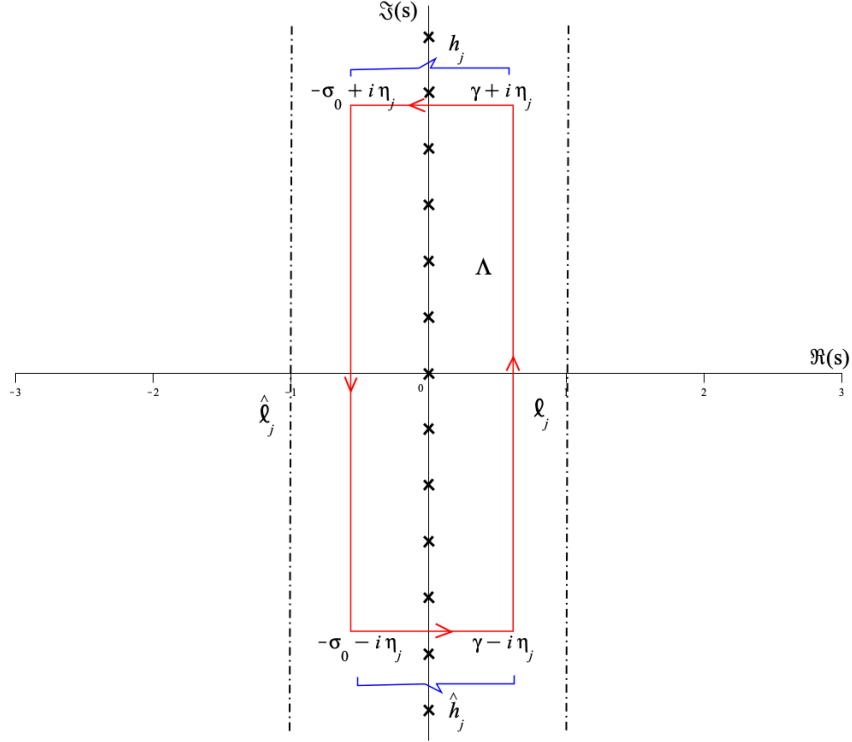


FIGURE 3.3: The fundamental strip of holomorphy.

and the Riemann Lebesgue lemma implies that the h_j and \hat{h}_j integrals vanish as $j \rightarrow \infty$; thus, we have

$$\begin{aligned} \lim_{j \rightarrow \infty} \int_{\Lambda_j} W_0(s)x^{-s} ds &= \int_{\Lambda} W_0(s)x^{-s} ds \\ &= \int_{\ell} W_0(s)x^{-s} ds + \int_{\hat{\ell}} W_0(s)x^{-s} ds, \end{aligned}$$

so that

$$\frac{1}{2\pi i} \int_{\gamma-i\infty}^{\gamma+i\infty} W_0(s)x^{-s} ds = \sum_{-\infty}^{\infty} \text{Res}\left(W_0(s)x^{-s}, i\tau_j\right) - \frac{1}{2\pi i} \lim_{\tau_j \rightarrow \infty} \int_{-\sigma_0+i\tau_j}^{-\sigma_0-i\tau_j} W_0(s)x^{-s} ds. \quad (3.28)$$

As $x \rightarrow 0^+$,

$$w_0(x) = \frac{R(\alpha)}{\log \alpha} \sum_{-\infty}^{\infty} M_0(i\tau_j) \left(\cos(\tau_j \log x) - i \sin(\tau_j \log x) \right) + O(x^{\sigma_0}), \quad (3.29)$$

where the term $O(x^{\sigma_0})$ arises from the contour integral in (3.28) along the line

$\Re(s) = -\sigma_0$. We have made the strong assumption that m_0 is twice continuously differentiable. Under this assumption, we can appeal to the Riemann Lebesgue lemma to assert that

$$|M_0(i\tau_j)| \sim o(|\tau_j|^{-2}),$$

as $j \rightarrow \pm\infty$ and this will ensure the convergence of the series $\sum_{-\infty}^{\infty} |M_0(i\tau_j)|$. Clearly, this condition can be relaxed but we will not pursue this. The Riemann Lebesgue lemma can also be used to refine the $O(x^{\sigma_0})$ term in (3.29). Now,

$$\begin{aligned} \left| \int_{-\sigma_0-i\infty}^{-\sigma_0+i\infty} W_0(-\sigma_0 + i\eta) x^{-(\sigma_0+i\eta)} d\eta \right| &\leq x^{\sigma_0} \int_{-\sigma_0-i\infty}^{-\sigma_0+i\infty} \left| \frac{M_0(-\sigma_0 + i\eta)}{P(-\sigma_0 + i\eta)} \right| d\eta \\ &\leq \rho_0 x^{\sigma_0}, \end{aligned}$$

where

$$\rho_0 = \frac{1}{|P(-\sigma_0)|} \int_{-\sigma_0-i\infty}^{-\sigma_0+i\infty} |M_0(-\sigma_0 + i\eta)| d\eta.$$

Equation (3.29) can thus be written

$$w_0(x) = h_0(x) + x^{\sigma_0} r_0(x), \tag{3.30}$$

where

$$h_0(x) = \frac{R(\alpha)}{\log \alpha} \sum_{-\infty}^{\infty} M_0(i\tau_j) \left(\cos(\tau_j \log x) - i \sin(\tau_j \log x) \right),$$

and

$$|r_0(x)| \leq \rho_0.$$

The asymptotic behaviour of w_0 as $x \rightarrow 0^+$ can be further refined by using a contour that also encloses the poles along the line $\Re(s) = -1$. We know that M_0 is holomorphic along the line $\Re(s) = -1$ so that there is a σ_1 , $1 < \sigma_1 < 2$ such that W_0 is holomorphic along the line $\Re(s) = -\sigma_1$. If we incorporate the poles on $\Re(s) = -1$, following the above approach, then w_0 can be expressed in the form

$$w_0(x) = h_0(x) + x h_1(x) + x^{\sigma_1} r_1(x), \tag{3.31}$$

where

$$h_1(x) = \frac{R(\alpha)}{(1-\alpha)\log\alpha} \sum_{-\infty}^{\infty} M_0(-1+i\tau_j) \left(\cos(\tau_j \log x) - i \sin(\tau_j \log x) \right), \quad (3.32)$$

and there is a constant

$$\rho_1 = \frac{1}{|P(-\sigma_0 - 1)|} \int_{-\sigma_0 - i\tau_j}^{-\sigma_0 + i\tau_j} |M_0(-\sigma_0 - 1 + i\eta)| d\eta,$$

such that

$$|r_1(x)| \leq \rho_1. \quad (3.33)$$

This form will be used later to show that m meets the boundary condition (3.7).

The next lemma summarises some of the important properties of w_0 that will be needed in Section 3.5.

Lemma 3.3.1. *Let w_0 be defined by equation (3.26). Under the conditions 1-3 on m_0 :*

1. w_0 is bounded on $(0, \infty)$;
2. $w'_0(x) \in C^1(0, \infty)$; and
3. $w'_0(x)$ is bounded on $[x_0, \infty)$ for any $x_0 > 0$.

Proof. The Mellin transform can also be used to examine the decay rate of $w_0(x)$ as $x \rightarrow \infty$. Briefly, $1/P$ is holomorphic in the right half plane and M_0 is holomorphic in the strip $-1 \leq \Re(s) \leq 1$. This means that the strip of holomorphy for the Mellin transform W_0 must include a strip of the form $0 < \Re(s) < c$, for some $c > 1$, and this implies

$$w_0(x) \sim O(x^{-c}), \quad (3.34)$$

as $x \rightarrow \infty$. Condition 3.c yields a similar result for w'_0 .

The decay conditions on m_0 as $x \rightarrow \infty$ show that in any interval of the form $I_0 = [x_0, \infty)$,

$$0 \leq m_0(x) \leq \frac{A}{x^{1+\ell}},$$

for all $x > X$, and any constants A and X . Choose $x_0 > 0$ and let $N \in \mathbb{Z}^+$ such that

$$\alpha^N x > \alpha^N x_0 > X,$$

hence,

$$N > \frac{\log(X) - \log(x_0)}{\log(\alpha)}.$$

The function m_0 is continuous, and conditions 3.a and 3.b show that it must be bounded. Let U be an upper bound for $m_0(\alpha^N x)$. Then, since $R_k(\alpha) < R(\alpha)$ and $\alpha^{N+1} x > X$ for all $x \in I_0$,

$$\begin{aligned} \sum_{k=0}^{\infty} R_k(\alpha) m_0(\alpha^k x) &= \sum_{k=0}^N R_k(\alpha) m_0(\alpha^k x) + \sum_{k=N+1}^{\infty} R_k(\alpha) m_0(\alpha^k x) \\ &\leq (N+1)R(\alpha)U + \frac{AR(\alpha)}{x_0^{1+\ell}} \sum_{k=N+1}^{\infty} \frac{1}{\alpha^k}, \end{aligned}$$

and consequently the series in (3.26) is uniformly convergent, and the continuity of m_0 implies that w_0 is also continuous in that interval. Relation (3.34) implies that w_0 must be bounded on that interval. Relation (3.29) shows that w_0 is bounded on the interval $(0, \infty)$.

To show that $w_0 \in C^1(0, \infty)$, we note that $m_0 \in C^1(0, \infty)$ and Condition 3.c ensures that the series $\sum_{k=0}^{\infty} R_k(\alpha) \alpha^k m_0'(\alpha^k x)$ is uniformly convergent in I_0 . The boundedness of w_0' in $[x_0, \infty)$ can be established in the same manner as done for w_0 . Evidently,

$$M\{w_0'(x); s\} = \sum_{-\infty}^{\infty} \text{Res} \left(\frac{M_0(s-1)}{P(s-1)} x^{-s}, i\tau_j \right) + \frac{1}{2\pi i} \lim_{\tau_j \rightarrow \infty} \int_{-\sigma_0 - i\tau_j}^{-\sigma_0 + i\tau_j} \frac{M_0(s-1)}{P(s-1)} x^{-s} ds,$$

in which $M\{w_0'(x); s\}$ represents the Mellin transform of the derivative with respect to the argument, $1/P(s-1)$ has zero of order 1 at $\text{Re}(s) = 0$, $M(s-1)$

is non trivial, and

$$\operatorname{Res}\left(\frac{M_0(s-1)}{P(s-1)}x^{-s}, i\tau_j\right) = \frac{R(\alpha)}{(1-\alpha)}M_0(i\tau_j-1)e^{-i\tau_j \ln(x)}.$$

As $x \rightarrow 0^+$,

$$w'_0(x) = \frac{R(\alpha)}{(1-\alpha)\log(\alpha)} \sum_{-\infty}^{\infty} M_0(i\tau_j-1)(\cos(\tau_j \log x) - i \sin(\tau_j \log x)) + O(x^{\sigma_0}).$$

Analogously, we can write

$$w'_0(x) = h_1(x) + x^{\sigma_0}r_1(x),$$

where $h_1(x)$ and $r_1(x)$ are given by (3.32) and (3.33), respectively. The Riemann Lebesgue lemma fulfils boundedness for $M_0(i\tau_j-1)$ as $j \rightarrow \pm\infty$.

□

3.4 Dominant eigenvalues and eigenfunctions

The eigenvalues and eigenfunctions associated with Problem A can be derived by studying the class of non trivial solutions of the form

$$\bar{m}(x, t) = A(t)y(x).$$

Substituting this solution form into equation (3.6) yields

$$\frac{A_t(t)}{A(t)} = \frac{1}{y(x)} \left(-xy'(x) - \gamma xy(x) + \gamma \alpha xy(\alpha x) \right) = \lambda,$$

where λ is a separation constant. The above expression implies,

$$A(t) = \kappa e^{\lambda t}, \tag{3.35}$$

where κ is a constant, and y satisfies the equation

$$xy'(x) + (\gamma x + \lambda)y(x) = \gamma\alpha xy(\alpha x), \quad (3.36)$$

where $'$ denotes the derivative with respect to the argument. There is precisely one *real* eigenvalue $\lambda_{0,0}$ such that $\bar{m} \in \mathcal{N}$ is non negative in Ω and satisfies condition (3.7). Since $\bar{m} \in \mathcal{N}$, we know that y is integrable on $[0, \infty)$; moreover, condition (3.7) indicates that

$$\lim_{x \rightarrow 0^+} \frac{y(x)}{x} = 0, \quad (3.37)$$

so that $y(0) = 0$ and $y(x)/x$ is also integrable on $[0, \infty)$. Since $\bar{m}(x, t) \geq 0$ is non trivial, we know that

$$\int_0^\infty y(x) dx \neq 0$$

and

$$\int_0^\infty \frac{y(x)}{x} dx \neq 0.$$

These observations allow us to glean a value for $\lambda_{0,0}$. Specifically, if we divide both sides of equation (3.36) by x and integrate from 0 to ∞ , we find that $\lambda_{0,0} = 0$; hence, equation (3.36) yields the PE

$$y'(x) + \gamma y(x) = \gamma\alpha y(\alpha x). \quad (3.38)$$

A detailed analysis of this equation can be found in [41] (cf. also [40]). The PDF solution to this equation is derived by Hall and Wake in [32], where they showed that there is a unique PDF solution y . In fact, they studied the exponential growth case [34] and used their solution to the PE to construct what they called an SSD solution to Problem A. Briefly, the solutions to equation (3.38) are of the form

$$y(x) = CD(x, \gamma), \quad (3.39)$$

where C is a positive constant, the c_k are given by equation (3.19), and

$$D(x, \gamma) = e^{-\gamma x} + \sum_{k=1}^{\infty} c_k e^{-\gamma \alpha^k x}.$$

The constant C is generally chosen to normalise the corresponding separable solution to the original equation (3.1) to be a PDF at $t = 0$. For the original PDE, however, the normalisation comes from the initial data.

Note that the value of $D(0, \gamma)$ can be determined from the Euler identity (3.18) with $z = -1$. This gives

$$\begin{aligned} D(0, \gamma) &= 1 + \sum_{k=1}^{\infty} c_k \\ &= \prod_{k=0}^{\infty} (1 - \alpha^{-k}) = 0. \end{aligned} \tag{3.40}$$

Since D is a solution to equation (3.38), it follows that all the derivatives of D with respect to x also vanish at $x = 0$. This can also be deduced directly from the Euler identity because

$$1 + \sum_{k=1}^{\infty} c_k \alpha^{jk} = \prod_{k=0}^{\infty} (1 - \alpha^{j-k}) = 0,$$

for any positive integer j . The next lemma gives a summary of some important properties of the Dirichlet series. The proof of these properties can be found in [32].

Lemma 3.4.1. *For any positive constant β , the Dirichlet series*

$$D(x, \beta) = e^{-\beta x} + \sum_{k=1}^{\infty} c_k e^{-\beta \alpha^k x}$$

is a solution to

$$D_x(x, \beta) + \beta D(x, \beta) = \beta \alpha D(\alpha x, \beta).$$

The function D has the following properties:

1. *D has derivatives of all orders with respect to x .*

2. D and all its derivatives with respect to x vanish at $x = 0$ and as $x \rightarrow \infty$.

3. $D(x, \beta) > 0$ for all $x > 0$.

Returning to equation (3.36), a complex eigenvalue $\lambda_{(0,j)}$ and corresponding eigenfunction y_j can be calculated as follows. Let

$$y_j(x) = u_j(x)y(x), \tag{3.41}$$

such that $y_j(x)$ is any function satisfying (3.36) with the properties $u_0(x) = 1$ and $u_j(x) = u_j(\alpha x)$. For all $j > 0$, we have

$$xu'_j(x)y(x) + xu_j(x)y'(x) + (\gamma x + \lambda_{(0,j)})u_j(x)y(x) = \gamma \alpha x u_j(\alpha x)y(\alpha x). \tag{3.42}$$

One can now apply (3.41) into (3.42) and solve to find an eigenfunction solution of the form

$$y_j(x) = x^{-\lambda_{(0,j)}}y(x),$$

in which $\lambda_{(0,j)} = i\tau_j$. (In fact, all the zeros of P are eigenvalues.) The dominant real eigenvalue is 0, but $\Re(\lambda_{(0,j)}) = 0$ for all integers j , so there is no dominant eigenvalue, and this is the source of oscillatory terms in the long time asymptotic behaviour of solutions to Problem A. Actually, the absence of a dominant eigenvalue associated with exponential growth was first noted by O. Diekmann [22].

3.5 The solution and long time dynamics

We first establish that equation (3.22) provides the solution to Problem A.

Theorem 3.5.1. *Let m_0 satisfy Conditions 1-3 of Section 3.3. Then the function m defined by (3.22), where w_0 is given by equation (3.26), is the solution to Problem A.*

Proof. The uniqueness and positivity of the solution was established in Section 3.1. Lemma 3.3.1 shows that the series in (3.22) is uniformly convergent in the quadrant $\{(x, t) \in [x_0, \infty) \times (0, \infty)\}$ for any $x_0 > 0$ and differentiable. By construction, the series satisfies the PDE (3.6) and initial condition (3.8). It remains, however, to show that the boundary conditions (3.7) are satisfied for $t > 0$.

Let

$$\Phi_0(x, t) = h_0(xe^{-gt}), \quad \frac{R(\alpha)}{\log \alpha} \sum_{-\infty}^{\infty} |M_0(i\tau_j)| = \Upsilon_0,$$

and

$$\Phi_1(x, t) = h_1(xe^{-gt}), \quad \frac{R(\alpha)}{(\alpha - 1) \log \alpha} \sum_{-\infty}^{\infty} |M_0(-1 + i\tau_j)| = \Upsilon_1,$$

and note that, for $k = 0, 1$,

$$\Phi_k(x, t) = \Phi_k(\alpha x, t).$$

Equation (3.30) implies that

$$m(x, t) = \Phi_0(x, t)D(x, \beta(t)) + x^{\sigma_0} e^{-\sigma_0 g t} R_0(x, t), \quad (3.43)$$

where $\beta(t) = \gamma(1 - e^{-gt})$, $0 < \sigma_0 < 1$, and

$$R_0(x, t) = r_0(x) e^{-\beta(t)x} + \sum_{k=1}^{\infty} c_k \alpha^{\sigma_0 k} r_0(\alpha^k x) e^{-\beta(t)\alpha^k x}.$$

Now,

$$|R(x, t)| \leq \rho_0 \left(1 + \sum_{k=1}^{\infty} |c_k| \alpha^{\sigma_0 k} \right),$$

and since the above series converges there is thus a number κ_0 such that $|R(x, t)| \leq \kappa_0$. Hence, for any $t > 0$,

$$\left| \frac{m(x, t)}{x} \right| \leq \frac{\Upsilon_0}{x} D(x, \beta(t)) + \frac{\kappa_0}{x^{1-\sigma_0}}.$$

We know from Lemma 3.4.1 that $D(x, \beta(t)) \rightarrow 0$ as $x \rightarrow \infty$ and since $\sigma_0 < 1$, the above inequality indicates that

$$\lim_{x \rightarrow \infty} \frac{m(x, t)}{x} = 0,$$

for any $t > 0$.

Equation (3.31) shows that, for $t > 0$,

$$m(x, t) = \Phi_0(x, t)D(x, \beta(t)) + \frac{xe^{-gt}}{-\beta(t)}\Phi_1(x, t)D_x(x, \beta(t)) + x^{\sigma_1}e^{-\sigma_1gt}R_1(x, t), \quad (3.44)$$

for any $1 < \sigma_1 < 2$, and

$$R_1(x, t) = r_1(x)e^{-\beta(t)x} + \sum_{k=1}^{\infty} c_k \alpha^{\sigma_0 k} r_1(\alpha^k x) e^{-\beta(t)\alpha^k x}.$$

A bound for the term $|R_1|$ can be obtained in a manner similar to that for $|R_0|$, so that there is a number κ_1 such that $|R_1(x, t)| \leq \kappa_1$. Hence,

$$\left| \frac{m(x, t)}{x} \right| \leq \frac{\Upsilon_0}{x} D(x, \beta(t)) + \frac{\Upsilon_1}{\beta(t)} |D_x(x, \beta(t))| + x^{\sigma_1-1} \kappa_1. \quad (3.45)$$

Lemma 3.4.1 shows that $D_x(x, \beta) \rightarrow 0$ as $x \rightarrow 0^+$; consequently, $D(x, \beta(t))/x \rightarrow 0$ (L'Hôpital's rule) and $|D_x(x, \beta(t))| \rightarrow 0$ as $x \rightarrow 0^+$. Since $\sigma_1 > 1$, x^{σ_1-1} also vanishes in this limit and thus for any $t > 0$

$$\lim_{x \rightarrow 0^+} \frac{m(x, t)}{x} = 0.$$

□

We now consider the behaviour of m for large time. The main result is the following theorem.

Theorem 3.5.2. *Under the conditions of Theorem 3.5.1,*

$$\int_0^\infty |m(x, t) - \Phi_0(x, t)D(x, \gamma)| dx \rightarrow 0 \quad (3.46)$$

as $t \rightarrow \infty$.

Proof. Using equation (3.43), we have

$$m(x, t) - \Phi_0(x, t)D(x, \gamma) = \Phi_0(x, t)(D(x, \beta(t)) - D(x, \gamma)) + x^{\sigma_0}e^{-\sigma_0gt}R_0(x, t);$$

consequently,

$$|m(x, t) - \Phi_0(x, t)D(x, \gamma)| \leq \Upsilon_0 |D(x, \beta(t)) - D(x, \gamma)| + x^{\sigma_0}e^{-\sigma_0gt} |R_0(x, t)|. \quad (3.47)$$

Now $\beta(t) = \gamma(1 - e^{-gt}) < \gamma$; therefore,

$$\begin{aligned} |D(x, \beta(t)) - D(x, \gamma)| &= \left| \left(e^{-\beta(t)x} - e^{-\gamma x} \right) + \sum_{k=1}^{\infty} c_k \left(e^{-\beta(t)\alpha^k x} - e^{-\gamma\alpha^k x} \right) \right| \\ &\leq \left(e^{-\beta(t)x} - e^{-\gamma x} \right) + \sum_{k=1}^{\infty} |c_k| \left(e^{-\beta(t)\alpha^k x} - e^{-\gamma\alpha^k x} \right), \end{aligned}$$

so that integrating we get

$$\begin{aligned} \int_0^\infty |D(x, \beta(t)) - D(x, \gamma)| dx &\leq \Upsilon_0 \left(\frac{e^{-gt}}{\beta(t)} + \sum_{k=1}^{\infty} |c_k| \frac{e^{-gt}}{\alpha^k \beta(t)} \right) \\ &\leq \frac{\Upsilon_0 e^{-gt}}{\beta(t)} \left(1 + \sum_{k=1}^{\infty} |c_k| \right). \end{aligned}$$

We know that $\beta(t) \rightarrow 1$ as $t \rightarrow \infty$, so that for (say) $t > (\log 2)/g$, $\beta(t) > 1/2$.

The series in the last inequality converges so that, for $t > (\log 2)/g$,

$$\int_0^\infty |\Phi_0(x, t)| |D(x, \beta(t)) - D(x, \gamma)| dx \leq \tilde{\Upsilon}_0 e^{-gt}, \quad (3.48)$$

where

$$\tilde{\Upsilon}_0 = 2\Upsilon_0 \left(1 + \sum_{k=1}^{\infty} |c_k| \right).$$

We also have, for $t > (\log 2)/g$,

$$\begin{aligned} |R_0(x, t)| &\leq |r_0(xe^{-gt})|e^{-\beta(t)x} + \sum_{k=1}^{\infty} |c_k|\alpha^{\sigma_0 k} |r_0(\alpha^k x e^{-gt})|e^{-\beta(t)\alpha^k x} \\ &\leq \rho_0 e^{-\frac{\gamma x}{2}} \left(1 + \sum_{k=1}^{\infty} |c_k|\alpha^{\sigma_0 k}\right). \end{aligned}$$

The series in the last inequality converges and $x^{\sigma_0} e^{-\gamma x/2} \in L^1[0, \infty)$; hence, there is a number $\tilde{\rho}_0$ such that

$$\int_0^{\infty} x^{\sigma_0} |R_0(x, t)| dx \leq \tilde{\rho}_0. \quad (3.49)$$

Equations (3.47)-(3.49) imply that

$$\int_0^{\infty} |m(x, t) - \Phi_0(x, t)D(x, \gamma)| dx \sim O(e^{-\sigma_0 g t}), \quad (3.50)$$

as $t \rightarrow \infty$.

□

3.6 Discussion

In this chapter we developed a method for solving an IBVP that involves a PDE with a functional term. The problem was originally presented as a model for cell division by Hall and Wake [33], who studied the separable solution. Although the results were tailored to Problem A, it is clear from the transformations leading to equation (3.6) that the method can be used on the differential equation (3.1) provided $r > 0$. The results can be refined for a broader class of initial data; however, it is not clear that the approach used in Section 3.2 can be adapted to division rates that are not monomials. A key step in deriving the solution form (3.22) is the identification of a “partition function”, P , that yields a Mellin transform equation corresponding to a PDE without a functional term (equation

(3.16)). A number of pantograph type ODEs have this structure. For example, the basic model with constant growth and division rates leads to the same partition function P (cf. [71]), but the general solution for the PDE reflects this structure only in the long time asymptotic behaviour of solutions ([76]).

Theorem 3.5.2 shows that the solution m converges (exponentially) in the L^1 norm to the function $\Phi_0 D$ as $t \rightarrow \infty$. What is remarkable is that Φ_0 depends on t and the initial condition $m_0(x)$. For constant growth rates, the limiting solution is purely a function of x and depends weakly on the initial data through a normalisation constant (cf. [55] and [56]). Another feature of Φ_0 is that it is periodic in the time variable, *i.e.*,

$$\Phi_0(x, t) = \Phi_0(x, t + g^{-1} \log \alpha),$$

and this gives the limiting solution its oscillatory character. The amplitude of the oscillations depends on the initial data through the Mellin transform and the value of D . It was shown in [12] that exponential growth gives rise to oscillating solutions for a class of coagulation-fragmentation equations that includes the present cell division equation. The extra structure of this cell division model, however, allows one to not only solve the general problem explicitly, but also determine the limiting solution in detail.

A solution $m(x)$ can be plotted directly from equations (3.22) and (3.26) for a given initial condition $m_0(x)$. We provide three examples that illustrate the influence of the initial data and the oscillatory character of the limiting solution. In all these examples we use $\alpha = 2$, $\gamma = 1$ and $g = 1$. For the first example, let $m_0(x) = x^2 e^{-(x-4)^2/2}$. Figure 3.4 depicts a graph of the solution, which clearly shows the oscillatory nature of the solution. If we change the initial data to $m_0(x) = x^2 e^{-x^2/2}$, then the character of the solution changes noticeably for larger time (Figure 3.5). The oscillations are still there, but the effect of the term Φ_0 is less striking. As an “extreme” case, let $m_0(x) = H(x - 1) - H(x - 2)$, where H

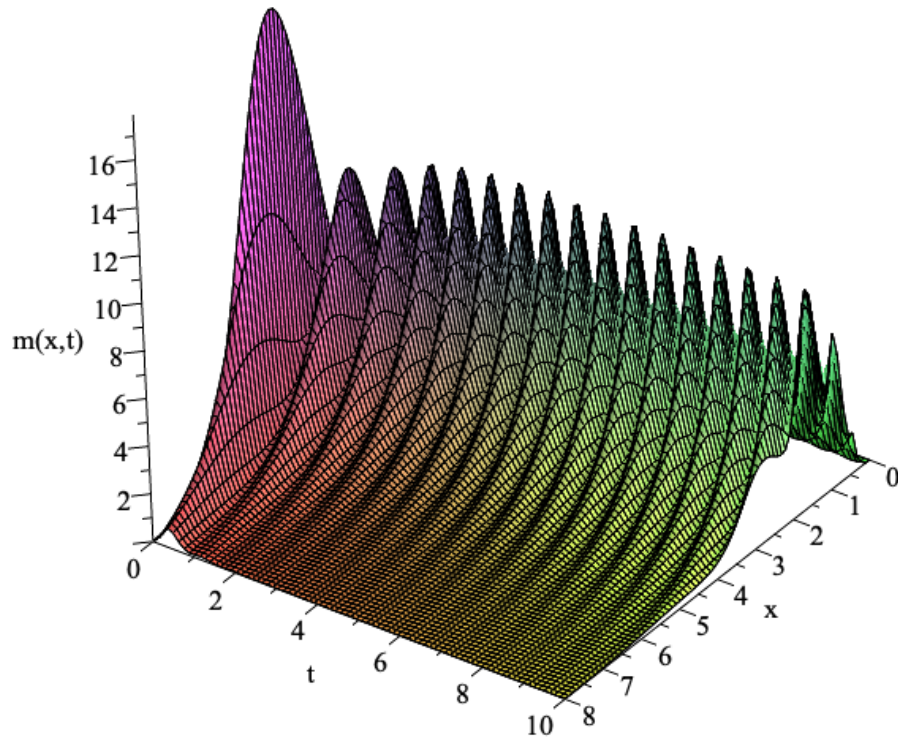


FIGURE 3.4: Illustration of the solution (3.22) with initial distribution $m_0(x) = x^2 e^{-(x-4)^2/2}$, $G(x) = x$, $B(x) = x$ and $\alpha = 2$.

denotes the Heaviside function. In this case

$$M_0(s) = \frac{2^s - 1}{s},$$

so that the zeros of M_0 coincide with those of $P(s)$, leaving the simple pole at $s = 0$. Although m_0 does not satisfy the differentiability conditions, we have that $M(i\tau_j) = 0$ for all $j = \pm 1, \pm 2, \dots$ so there is no question about the series defining Φ_0 converging. As predicted by the analysis, the solution does not have any oscillations (Figure 3.6).

In terms of the original number density n , with $r = 1$, equation (3.46) translates to

$$\int_0^\infty x^2 |e^{-gt} n(x,t) - \Phi_0(x,t) D(x,\gamma)| dx \rightarrow 0, \quad (3.51)$$

so that convergence to the limiting solution is in a weighted L^1 norm. For general

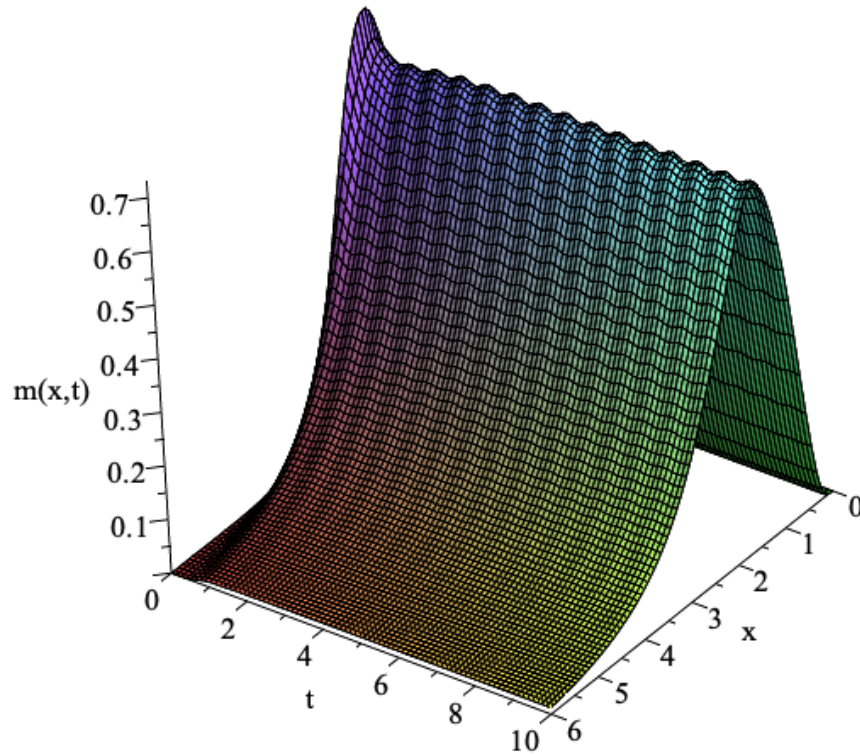


FIGURE 3.5: Illustration of the solution (3.22) with initial distribution $m_0(x) = x^2 e^{-\frac{x^2}{2}}$, $G(x) = x$, $B(x) = x$ and $\alpha = 2$.

$r > 0$, the solution to (3.1) can be recovered by calculating m as before, and then substituting $z(x) = x^r/r$ for x , α^r for α and gr for g in m . This gives a solution of the form

$$n(x, t) = \frac{e^{gt} m(z(x), t)}{x^2}.$$

Making the same substitutions in the limiting function $\Phi_0 D$ we get

$$\int_0^\infty x^{r+1} \left| e^{-gt} n(x, t) - \Phi_0(z(x), t) D(z(x), \gamma) \right| dx \rightarrow 0. \quad (3.52)$$

The parameter r thus determines the weighting of the norm. Note that it does not change the period of Φ_0 .

The transformations used to construct the solution rely crucially on $r > 0$. If $r \leq 0$, then the construction breaks down. Of special interest is the “critical case” when $r = 0$. The large time asymptotic behaviour for this case has been

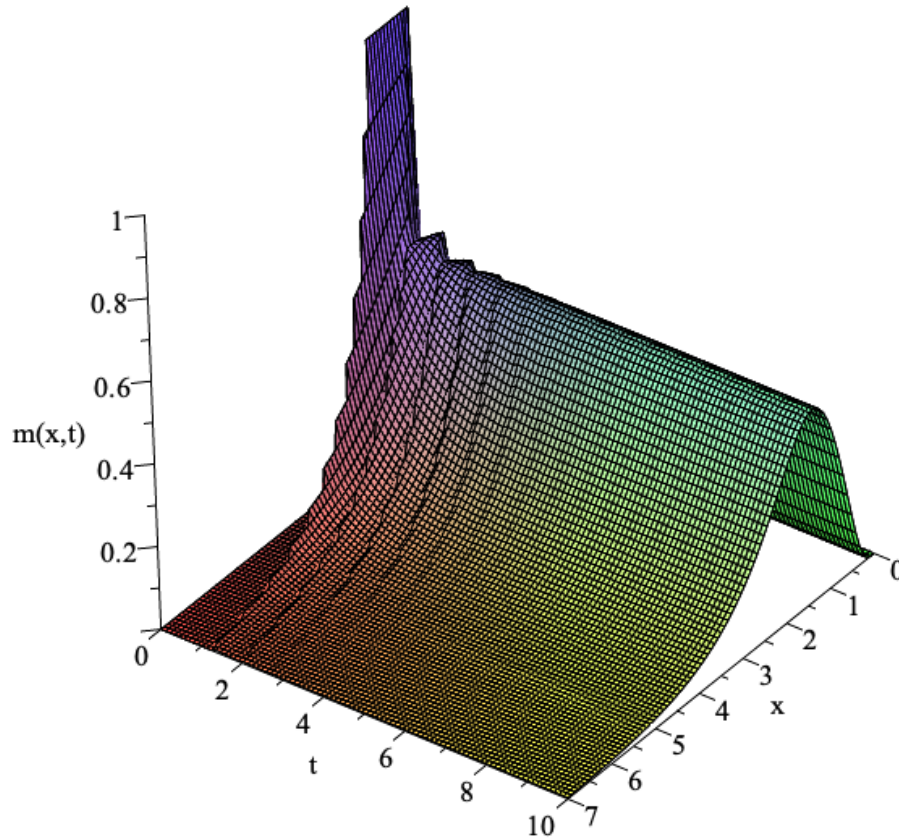


FIGURE 3.6: Illustration of the solution (3.22) with initial distribution $m_0(x) = H(x - 1) - H(x - 2)$, $G(x) = x$, $B(x) = x$ and $\alpha = 2$.

studied by Doumic and Escobedo [25], who showed that the long time dynamics of solutions for this case are very different.

The first signs of trouble occur when one looks for a solution of the form $n(x, t) = A(t)y(x)$, where y is a PDF. Substituting this solution form into equation (3.1) with $r = 0$ leads to the equation

$$g(xy(x))' + (b + \lambda)y(x) = b\alpha^2y(\alpha x), \tag{3.53}$$

where λ is a constant of separation. The problem is that there are two ways to find λ . Integrating both sides of equation (3.53) from 0 to ∞ gives $\lambda = b(\alpha - 1)$. On the other hand, assuming y has a first moment, then multiplying both sides of equation (3.53) by x and integrating from 0 to ∞ yields $\lambda = g$. Thus for any

solution y that decays fast enough to have a first moment, we must have

$$g = b(\alpha - 1), \tag{3.54}$$

which, in general, is not true.

Doumic and Escobedo (*op. cit.*) show, more generally, that there are no solutions of the form $A(t)y(xf(t))$, where A and f are continuously differentiable functions on $[0, \infty)$. They also derive an explicit solution form in terms of an inverse Mellin transform. We will show in Chapter 4 that there is no PDF solution to (3.53) along with the associated boundary conditions and, in fact, a general time dependent solution to this problem, as well as the stochastic growth version with constant dispersion term, can be gleaned directly if the initial condition n_0 is smooth and bounded.

Finally, it is of central interest whether adding a dispersion term to this chapter's case would affect the oscillatory character we have seen. However, using the same techniques to obtain an analytical solution does not work with the dispersive equation, which remains to be explored. We study the influence of the dispersion term in the following chapter for the critical case when $r = 0$.

Chapter 4

Degenerate cases

In this chapter, we consider a class of equations that is qualitatively different. The general form arises from the fragmentation equation (1.4) with Δ given by (2.7) at the critical case when the splitting rate $B(x)$ is constant (*i.e.*, $B(x) = bx^0$), and the growth rate is given by $G(x) = gx$, with a constant dispersion term $D(x) = D$ resulting from an added stochastic growth process. The model describes cell division that reproduces $\alpha > 1$ daughter cells of symmetrical size, where the variables g and b are positive constants, as throughout this thesis, and $D \geq 0$. We thus study equation (2.8) with these parameters and $\mu(x) = 0$. The equation is

$$n_t(x, t) - Dn_{xx}(x, t) + g\left(xn(x, t)\right)_x + bn(x, t) = \alpha^2bn(\alpha x, t), \quad (4.1)$$

and the initial-boundary data are

$$n(x, 0) = n_0(x), \quad (4.2)$$

$$\begin{aligned} \lim_{x \rightarrow 0^+} \left[-Dn_x(x, t) + gxn(x, t) \right] &= 0, \\ \lim_{x \rightarrow \infty} \left[-Dn_x(x, t) + gxn(x, t) \right] &= 0. \end{aligned} \quad (4.3)$$

As noted earlier, there are no general solution techniques for equations of (4.1) type, owing to the functional term $n(\alpha x, t)$, even in the simpler first order case (no dispersion). Analytical solutions to this problem, with and without dispersion, are unknown. Research contributions to the above equation, as noted in Chapter 2, have been mostly limited to the more general formula “the deterministic growth fragmentation equation” (2.6) with a probabilistic approach. More recently, solutions to this case were tailored to equation (2.6) in a weak sense through the Mellin transform and its inverse (cf. [25]). A review by Doumic and van Brunt [24] studied solutions to the first order problem and their long time asymptotic behaviour using the explicit solution devised in [66].

4.1 Deterministic growth model

In the absence of dispersion, the equation (4.1) reduces to

$$n_t(x, t) + g\left(xn(x, t)\right)_x + bn(x, t) = \alpha^2bn(\alpha x, t), \quad (4.4)$$

subject to the initial condition (4.2) and boundary data of the form

$$\begin{aligned} \lim_{x \rightarrow 0^+} xn(x, t) &= 0, \\ \lim_{x \rightarrow \infty} xn(x, t) &= 0. \end{aligned} \quad (4.5)$$

In this section, we show that this problem has no PDF eigenfunction solution. In fact, we construct a general solution by using a sequence of functions defined by a sequence of PDEs that can be solved by elementary means.

It has been observed that there is no long time attracting solution to this problem for L^1 functions (see [24] for the highlights, or [25] for a detailed account). In other words, the eigenvalue problem posed by

$$g(xy(x))' + (b + \lambda)y(x) = \alpha^2 by(\alpha x), \quad (4.6)$$

through the trial solution

$$n(x, t) = N(t)y(x),$$

for some eigenvalue λ with a corresponding eigenfunction $y(x)$, does not satisfy the relation

$$e^{-\lambda t}n(x, t) \rightarrow y(x), \quad (4.7)$$

as $t \rightarrow \infty$ (in the L^1 norm). We show next that if $y(x) \in L^1[0, \infty)$, there is no PDF type solution to equation (4.6) that satisfies the boundary conditions.

As discussed in Chapter 2, the value of λ is limited by the conditions placed on $y(x)$. Although there are two ways to get λ , the equation $\lambda = g$ assumes that $xy(x) \in L^1[0, \infty)$. It may be that $y(x)$ is a PDF with no first moment. We thus consider $y(x) \in L^1[0, \infty)$ that satisfies the associated boundary conditions (4.5), which translate to

$$\begin{aligned} \lim_{x \rightarrow 0^+} xy(x) &= 0, \\ \lim_{x \rightarrow \infty} xy(x) &= 0. \end{aligned} \quad (4.8)$$

We also have

$$\int_0^\infty y(x) = 1. \quad (4.9)$$

The value λ can simply be found by integrating (4.6) with respect to x from 0 to ∞ , which yields

$$\lambda = b(\alpha - 1), \quad (4.10)$$

and equation (4.6) reduces to

$$g(xy(x))' + \alpha by(x) = \alpha^2 by(\alpha x). \quad (4.11)$$

Notice that C/x is a solution to (4.11) for any constant C , though it does not

satisfy (4.9) unless $C = 0$, and for this case (4.9) is not satisfied.

Suppose $y(x)$ satisfies conditions (4.8) and (4.9) and is a solution to equation (4.11). Let

$$\varphi(x) = gxy(x).$$

Conditions (4.8) imply that

$$\begin{aligned} \lim_{x \rightarrow 0^+} \varphi(x) &= 0, \\ \lim_{x \rightarrow \infty} \varphi(x) &= 0. \end{aligned} \tag{4.12}$$

Since y is a PDF solution, we know that φ is non negative and nontrivial. Conditions (4.12) indicate that φ must have a positive global maximum in $(0, \infty)$, and that there must be a largest value of x at which this maximum is achieved, since $\varphi(x) \rightarrow 0$ as $x \rightarrow \infty$. Let x_m denote this largest value. Since y is a solution to (4.11), we have

$$\varphi'(x) + \alpha b \frac{\varphi(x)}{x} = \alpha b \frac{\varphi(\alpha x)}{x}.$$

At x_m we have $\varphi'(x_m) = 0$, and the above equation yields

$$\varphi(x_m) = \varphi(\alpha x_m),$$

so that the maximum must be achieved at $x_m > \alpha x_m$, which contradicts the definition of x_m .

In fact, a general solution to the PDE (4.4) can be found directly if the initial condition n_0 is smooth and bounded. Let

$$n(x, t) = e^{-(g+b)t} m(x, t).$$

Then, equation (4.4) reduces to

$$m_t(x, t) + gxm_x(x, t) = \alpha^2bm(\alpha x, t). \quad (4.13)$$

Now, we construct a solution $m(x, t)$ to equation (4.13) by a sequence of functions

$$m(x, t) = \sum_{k=0}^{\infty} w_k(x, t),$$

where the w_k are defined by a sequence

$$w_0(x, t) = m_0(xe^{-gt}),$$

and for all $k \geq 1$,

$$\frac{\partial}{\partial t}w_k(x, t) + gx\frac{\partial}{\partial x}w_k(x, t) = \alpha^2bw_{k-1}(\alpha x, t), \quad (4.14)$$

with

$$w_k(x, 0) = 0.$$

The choice of the argument for w_0 is motivated by the characteristic projections to (4.14) given by

$$\begin{aligned} x &= \eta e^{g\xi}, \\ t &= \xi. \end{aligned}$$

In terms of the characteristic projections,

$$w_k(x, t) = w_k(\eta e^{g\xi}, \xi) = \tilde{w}(\eta, \xi),$$

$$w_k(\alpha x, t) = w_k(\alpha\eta e^{g\xi}, \xi) = \bar{w}(\eta, \xi).$$

We will drop the tilde for simplification unless there is scope for confusion. Equation (4.14) is thus

$$\frac{\partial}{\partial \xi}w_k(\eta, \xi) = \alpha^2b\bar{w}_{k-1}(\eta, \xi), \quad (4.15)$$

the solution of which is

$$w_k(\eta, \xi) = \alpha^2 b \int_0^\xi \bar{w}_{k-1}(\eta, \tau) d\tau.$$

We find that

$$w_k(\eta, \xi) = \frac{(\alpha^2 b \xi)^k}{k!} m_0(\alpha^k \eta).$$

The general solution, therefore, can be written as

$$n(x, t) = e^{-(b+g)t} \sum_{k=0}^{\infty} n_0(\alpha^k x e^{-gt}) \frac{(b\alpha^2 t)^k}{k!}. \quad (4.16)$$

Note that the uniqueness and non negativity results of Section 3.1 can be adapted for this case.

The long time asymptotic behaviour of n is not obvious from the solution (4.16). We can, however, provide an example for a given initial condition n_0

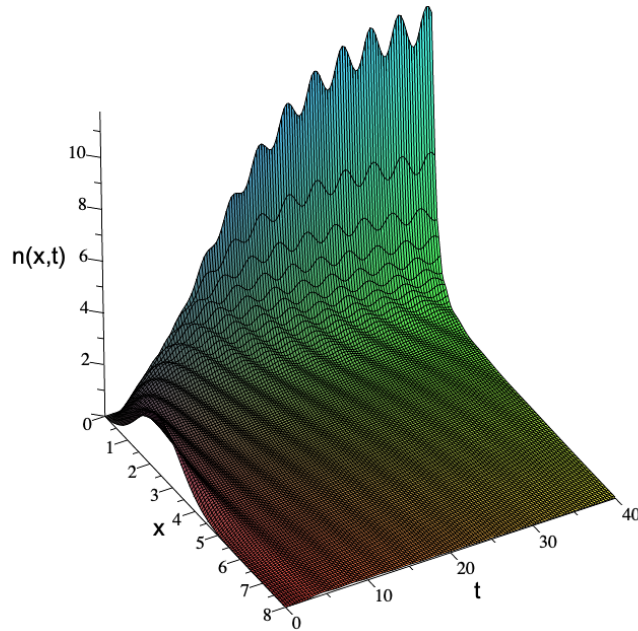


FIGURE 4.1: Illustration for the long time asymptotic behaviour of the solution (4.16) with $G(x) = 0.2x$, $B(x) = 0.2$ and initial distribution $n_0(x) = xe^{-\frac{(x-2)^2}{2}}$.

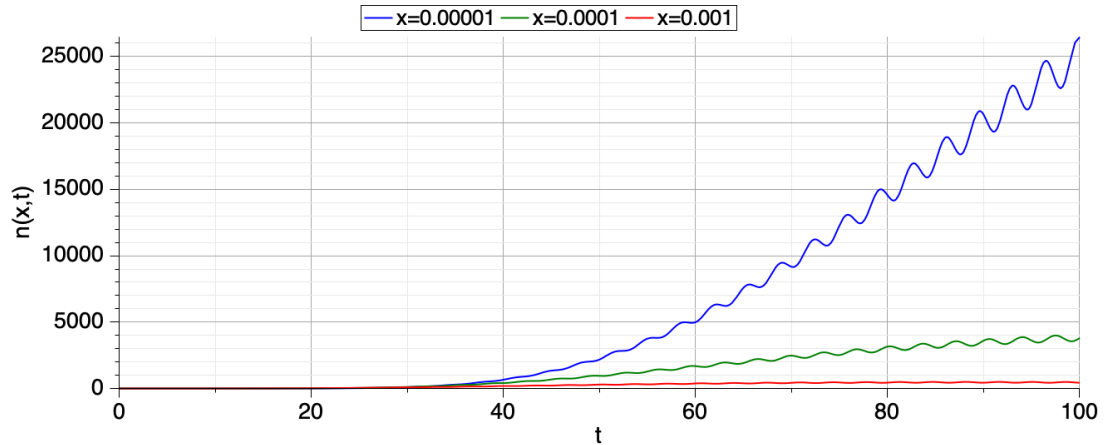


FIGURE 4.2: Spatial snapshots (close to the origin) from Figure 4.1.

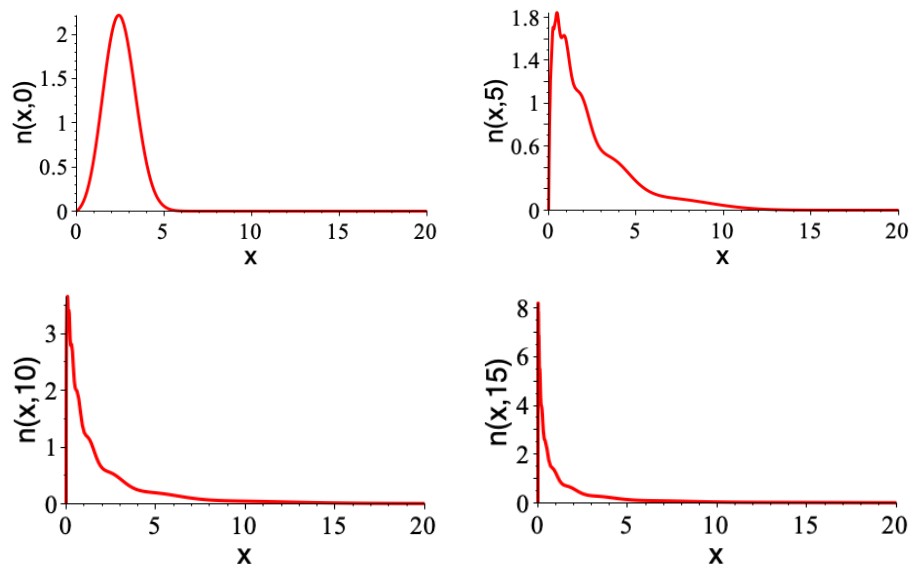


FIGURE 4.3: Temporal snapshots from Figure 4.1.

to examine the influence of the initial data and the oscillatory behaviour of the limiting solution. We consider the initial distribution $n_0(x) = xe^{-\frac{(x-2)^2}{2}}$ with $g = 0.2$, $b = 0.2$ and $\alpha = 2$. We observe that the limiting solution exhibits periodic oscillations but different in character from the model in Chapter 3 (see Figure 4.1). Here, the number of cells is concentrated closer and closer to the origin with an increasing amplitude as time evolves. One can take sectional snapshots along the x axis close to zero to see that as time increases, the limiting solution shape grows toward the origin (cf. Figure 4.2). If we take snapshots

along the t axis, we can observe that the time attracting solution tends to a shape close to a Dirac delta type solution (see Figure 4.3). Actually, it can be shown that a generalised solution of the form

$$n(x, t) = e^{b(\alpha-1)t} \delta(x),$$

satisfies equation (4.4). It is worth noting that this generalised solution also satisfies (4.1) when the dispersion term depends on x .

Doumic and van Brunt (*op. cit.*) also noted the oscillatory character to this problem using the Mellin transform and studied its connection with the explicit solution (4.16). In the next section, we explore the stochastic growth version of the above problem with a constant dispersion term. The central question here is whether the addition of a dispersion term damps the oscillatory solution and perhaps even leads to a PDE that admits a separable PDF solution.

4.2 Incorporating stochastic growth process

In this section, the model incorporates stochastic growth process that gives rise to a dispersion term (as discussed in Section 1.4). In the previous section, the hyperbolic character of equation facilitated the problem solving, but the method cannot be adapted for this case.

Although this section is primarily concerned with linear growth rate and constant dispersion and division rate, we first review the solution techniques and results for the case of constant parameters, since they can be extended, in some sense, to the linear growth rate case.

4.2.1 Constant parameters

The simplest choices for the modelling parameters of the growth equation (4.1) can be constants. Analytical solutions to the IBVP have not been known until recently, when Zaidi [75] developed techniques to solve such a problem for general initial data. In brief, the problem is transformed and simplified into a formula in the form of cumulative function and then recast into an integral form in the Laplace space, where the kernel is an *a priori* Green's function. The Laplace transform method has been found to be a useful tool for growth equations in many cases, as discussed in Chapter 2, including this example. However, the inverse problem remains a challenge, although it was overcome using a Paley-Wiener theorem to ascertain solution existence in a suitable Hardy space. Efendiev *et al.* [27] lately proved that such a problem can be avoided and showed the solution exists in the time domain in a more elegant fashion.

Equation (4.1) for positive constants D , g and b is simplified by a transformation of the form

$$n(x, t) = e^{-bt} \tilde{n}(x, t),$$

and further simplified by setting $\tilde{n}(x, t) = \hat{n}(\hat{x}, t)$ with $\hat{x} = \frac{x}{g}$ and $\hat{D} = \frac{D}{g^2}$. Dropping the tildes and circumflexes, these transformations lead to

$$-Dn_{xx}(x, t) + n_t(x, t) + n_x(x, t) = b\alpha^2 n(\alpha x, t), \quad (4.17)$$

subject to the initial condition (4.2) and the boundary conditions

$$\lim_{x \rightarrow 0^+} \left[-Dn_x(x, t) + n(x, t) \right] = 0, \quad (4.18)$$

$$\lim_{x \rightarrow \infty} \left[-Dn_x(x, t) + n(x, t) \right] = 0. \quad (4.19)$$

Following Zaidi (*op. cit.*), let

$$m(x, t) = \int_x^\infty n(\xi, t) d\xi. \quad (4.20)$$

Then equation (4.17) becomes

$$- Dm_{xx}(x, t) + m_t(x, t) + m_x(x, t) = b\alpha m(\alpha x, t). \quad (4.21)$$

Following up the transformation and applying the conditions (4.18) and (4.19), the boundary condition at zero for equation (4.21) converts to

$$m(0, t) = ke^{b\alpha t},$$

where it is assumed that $m \rightarrow 0$ as $x \rightarrow \infty$ for any $t \geq 0$, and $k = \frac{1}{g}$. The initial condition for m is

$$\begin{aligned} m(x, 0) &= \int_x^\infty n_0(\xi) d\xi \\ &= m_0(x), \end{aligned}$$

where m_0 is non negative because n_0 is a PDF. The solution technique is to apply the Laplace transform with respect to time,

$$\begin{aligned} \mathcal{L}\{m(x, t)\}(s) &= \int_0^\infty e^{-st} m(x, t) dt \\ &= \mathcal{L}(x, s), \end{aligned} \quad (4.22)$$

to equation (4.21), and then find an appropriate Green's function. The implementation of the Laplace transform (4.22) in (4.21) yields

$$- D\mathcal{L}_{xx}(x, s) + \mathcal{L}_x(x, s) + s\mathcal{L}(x, s) = b\alpha\mathcal{L}(\alpha x, t) + m_0(x), \quad (4.23)$$

with boundary conditions of the form

$$\mathcal{L}(0, s) = \frac{k}{s - \alpha b}, \quad (4.24)$$

$$\lim_{x \rightarrow \infty} \mathcal{L}(x, s) = 0. \quad (4.25)$$

The Green's function is found by converting the problem into an IBVP with homogenous boundary conditions. Let

$$\mathcal{L}(x, s) = \frac{F(x)}{s - \alpha b} - V(x, s), \quad (4.26)$$

such that

$$\lim_{x \rightarrow \infty} F(x) = 0, \quad (4.27)$$

and

$$F(0) = k. \quad (4.28)$$

This transforms equation (4.23) into

$$\begin{aligned} -DV_{xx}(x, s) + V_x(x, s) + sV(x, s) - b\alpha V(\alpha x, s) + m_0(x) - F(x) \\ = \frac{1}{s - \alpha b} \{-DF''(x) + F'(x) + sF(x) + \alpha bF(\alpha x)\}, \end{aligned} \quad (4.29)$$

where ' indicates to the derivative with respect to the argument. Zaidi noted that the RHS of equation (4.29) can be reformulated into the well-known second order PE by choosing an $F(x)$ that satisfies

$$-DF''(x) + F'(x) + sF(x) = \alpha bF(\alpha x). \quad (4.30)$$

This equation was proved by Wake *et al.* [73] to have a unique solution of the Dirichlet series form:

$$F(x) = \sum_{j=0}^{\infty} a_n e^{-\alpha^j r x}, \quad (4.31)$$

with a first derivative that can be scaled to a PDF, since $F'(x) < 0$ for all $x > 0$.

The coefficients are

$$a_n = \prod_{k=1}^j \frac{(-1)^j (\alpha b)^j a_0}{(Dr^2 \alpha^{2k} + r\alpha^k - \alpha b)},$$

where $a_0 > 0$ is a number to be determined from (4.28), and the variable r is the positive root of the indicial equation

$$Dr^2 + r - \alpha r = 0.$$

This reformulation leads to

$$-DV_{xx}(x, s) + V_x(x, s) + sV(x, s) = \alpha bV(\alpha x, s) + v_0(x), \quad (4.32)$$

with

$$v_0(x) = F(x) - m_0(x), \quad (4.33)$$

$$V(x, 0) = \lim_{x \rightarrow \infty} V(x, s) = 0. \quad (4.34)$$

The problem consisting of equations (4.32), (4.33) and (4.34) can be recast as an integral equation of the following form

$$V(x, s) = \alpha b \int_0^\infty G(x, \xi, s)V(\alpha \xi, s)d\xi + f(x, s), \quad (4.35)$$

where

$$f(x, s) = \int_0^\infty G(x, \xi, s)v_0(\xi)d\xi,$$

and $G(x, \xi, s)$ is the Green's function associated with the boundary value problem, which satisfies

$$-DG'' + G' + sG = \delta(x - \xi). \quad (4.36)$$

The Green function is

$$G(x, \xi, s) = \begin{cases} G_1(x, \xi, s) = \frac{e^{-m_1\xi}}{D(m_1 - m_2)}(e^{-m_1x} - e^{m_2x}), & 0 < x < \xi, \\ G_2(x, \xi, s) = \frac{e^{m_2x}}{D(m_1 - m_2)}(e^{-m_2\xi} - e^{-m_1\xi}), & \xi < x < \infty, \end{cases}$$

where m_1 and m_2 are given by

$$\begin{aligned} m_1 &= \frac{1 + \sqrt{1 + 4sD}}{2D}, \\ m_2 &= \frac{1 - \sqrt{1 - 4sD}}{2D}. \end{aligned} \tag{4.37}$$

The equation (4.35) can be put in the form of a singular Fredholm equation of the second kind:

$$V(x, s) = b \int_0^\infty G(x, \frac{\xi}{\alpha}, s) V(\alpha\xi, s) d\xi + f(x, s).$$

The solution thus is the Neumann series

$$V(x, s) = f + Kf + K^2f + \dots,$$

where

$$Kf = \alpha b \int_0^\infty G(x, \xi, s) f(\alpha\xi, s) d\xi,$$

and for $j \geq 1$

$$K^{j+1}f = K(K^j f).$$

It can be shown that a unique solution exists. Zaidi (*op. cit.*) used a contraction mapping in the Banach space $(L_s^\infty[0, \infty), \|\cdot\|_\infty)$ of functions $V : [0, \infty) \times \mathbb{C} \rightarrow \mathbb{C}$, such that for $s \in \mathbb{C}$, V is bounded in $[0, \infty)$ if $\Re(s) > \alpha b$. The inverse of the above series directly is formidable; however, Zaidi (*op. cit.*) showed that an inverse exists in the Hardy space $H^2(\Omega)$ with the aid of a Paley-Weiner theorem. Further, it can be shown that

$$|m(x, t)| \sim o(e^{qt}),$$

for some $q > \alpha b$. The reader is directed to [75] for details.

It is not straightforward to glean the long time asymptotic behaviour from the Neumann series. Efendiev *et al.* (*op. cit.*) realised that the Neumann series can be bypassed and the solution constructed in the time domain directly

through the fundamental solution to the Cauchy problem associated with the inverse of the equations (4.32) and (4.33), and that this fundamental solution can be found using the inverse transform of the Green's function in the Laplace space. They noticed that the product of the Green's function in the Neumann series is a Laplace convolution which is a lot easier to invert. That is, to consider the inverse of (4.26)

$$m(x, t) = e^{\alpha bt} F(x) - v(x, t), \quad (4.38)$$

where $F(x)$ is given by (4.31) and $v(x, t)$ is the inverse transform of $V(x, s)$, by which the IBVP (4.32)-(4.34) is inverted back to the time domain; *viz.*,

$$-Dv_{xx}(x, t) + v_t(x, t) + v_x(x, t) = \alpha bv(\alpha x, t), \quad (4.39)$$

$$v(0, t) = 0, \quad (4.40)$$

$\forall t > 0$, and

$$\begin{aligned} v(x, 0) &= F(x) - m_0 \\ &= w_0(x). \end{aligned} \quad (4.41)$$

The solution to the Cauchy problem,

$$\begin{aligned} -Du_{xx}(x, t) + u_t(x, t) + u_x(x, t) &= 0, \\ u(x, 0) &= u_0(x), \end{aligned} \quad (4.42)$$

can be found using the inverse transform for the Green's function $G(x, \xi, s)$. This leads to

$$u(x, t) = \int_0^\infty \Psi(x, \xi, t) u_0(\xi) d\xi, \quad (4.43)$$

where

$$\Psi(x, \xi, t) = \frac{e^{-\frac{(\xi-x+t)^2}{4Dt}}}{2\sqrt{D\pi t}} \left(1 - e^{-\frac{\xi x}{Dt}} \right) \quad (4.44)$$

is the fundamental solution to (4.42). In fact, this solution is a relic from the original Green's function.

Now, the first term in the Neumann series is

$$V_0(x, s) = \int_0^\infty G(x, \xi, s)w_0(\xi)d\xi$$

and this corresponds to

$$v_0(x, t) = \int_0^\infty \Psi(x, \xi, s)w_0(\xi)d\xi.$$

The next term in the Neumann series is

$$\begin{aligned} V_1(x, s) &= \alpha b \int_0^\infty G(x, \xi_1, s) \int_0^\infty G(\alpha\xi_1, \xi_2, s)w_0(\xi_2)d\xi_2d\xi_1 \\ &= \alpha b \int_0^\infty \left\{ \int_0^\infty G(\alpha\xi_1, \xi_2, s)G(x, \xi_1, s)d\xi_1 \right\} w_0(\xi_2)d\xi_2. \end{aligned} \quad (4.45)$$

The product of the Green's functions indicates a Laplace convolution. The $V_1(x, s)$ term thus has an inverse transform

$$v_1(x, t) = \alpha b \int_0^\infty w_0(\xi_2) \int_0^\infty \int_0^t \Psi(x, \xi_1, t - \tau)\Psi(\alpha\xi_1, \xi_2, \tau)d\tau d\xi_1 d\xi_2.$$

It can be verified directly that

$$-D\partial_{xx}v_1(x, t) + \partial_tv_1(x, t) + \partial_xv_1(x, t) = \alpha bv_0(\alpha x, t),$$

in which the term $\Psi(x, \xi, 0)$, arising from the time derivative, acts as a Dirac delta function. The next term in the Neumann series is

$$\begin{aligned} V_2(x, s) &= (\alpha b)^2 \int_0^\infty G(x, \xi_0, s) \int_0^\infty \int_0^\infty G(\alpha\xi_0, \xi_1, s)G(\alpha\xi_1, \xi_2, s)d\xi_1w_0(\xi_2)d\xi_2d\xi_0 \\ &= (\alpha b)^2 \int_0^\infty \int_0^\infty \int_0^\infty G(x, \xi_0, s)G(\alpha\xi_0, \xi_1, s)G(\alpha\xi_1, \xi_2, s)d\xi_0d\xi_1w_0(\xi_2)d\xi_2, \end{aligned}$$

and this suggests a representation as a sequence of convolutions. Let

$$\begin{aligned}\Psi_0(x, \xi_0, t) &= \Psi(x, \xi_0, t), \\ \Psi_1(x, \xi_0, \xi_1, t) &= \int_0^t \Psi_0(x, \xi_0, t - \tau) \Psi_0(\alpha \xi_0, \xi_1, \tau) d\tau, \\ \Psi_2(x, \xi_0, \xi_1, \xi_2, t) &= \int_0^t \Psi_0(x, \xi_0, t - \tau) \Psi_1(\alpha \xi_0, \xi_1, \xi_2, \tau) d\tau, \\ &\vdots \\ \Psi_n(x, \xi_0, \xi_1, \dots, \xi_n, t) &= \int_0^t \Psi_0(x, \xi_0, t - \tau) \Psi_{n-1}(\alpha \xi_0, \xi_1, \dots, \xi_n, \tau) d\tau,\end{aligned}$$

then the formal solution can be written as

$$v(x, t) = \sum_{k=0}^{\infty} v_k(x, t), \quad (4.46)$$

where

$$v_k(x, t) = \int_0^{\infty} \underbrace{\dots}_{k\text{-times}} \int_0^{\infty} \Psi_k(x, \xi_0, \dots, \xi_k, t) w_0(\xi_k) d\xi_1 \dots d\xi_k.$$

The authors put the above formulation in a more conducive form for analysis.

Now,

$$\begin{aligned}v_1(x, t) &= \alpha b \int_0^{\infty} w_0(\xi_2) \int_0^{\infty} \int_0^t \Psi(x, \xi_1, t - \tau) \Psi(\alpha \xi_1, \xi_2, \tau) d\tau d\xi_1 d\xi_2 \\ &= \alpha b \int_0^t \int_0^{\infty} \Psi(x, \xi_1, t - \tau) \int_0^{\infty} w_0(\xi_2) \Psi(\alpha \xi_1, \xi_2, \tau) d\xi_2 d\xi_1 d\tau \\ &= \alpha b \int_0^t \int_0^{\infty} \Psi(x, \xi_1, t - \tau) v_0(\alpha \xi_1, \tau) d\xi_1 d\tau,\end{aligned}$$

where

$$v_0(\alpha \xi_1, \tau) = \int_0^{\infty} w_0(\xi_2) \Psi(\alpha \xi_1, \xi_2, \tau) d\xi_2.$$

Similarly, for $k \geq 0$,

$$v_{k+1}(x, t) = \alpha b \int_0^t \int_0^{\infty} \Psi(x, \xi, t - \tau) v_k(\alpha \xi_1, \tau) d\xi_1 d\tau, \quad (4.47)$$

and so the equation

$$-D\partial_{xx}v_{k+1}(x, t) + \partial_t v_{k+1}(x, t) + \partial_x v_{k+1}(x, t) = \alpha b v_k(\alpha x, t),$$

is satisfied. Now the above reformulation makes the payoff – the series (4.47) can be shown easily to converge uniformly in any set of the form $\Omega_T = \{(x, t) : x \geq 0, 0 \leq t \leq T\}$; moreover,

$$\lim_{t \rightarrow 0} \int_0^\infty |m(x, t)e^{-\alpha bt} - F(x)| dx = 0,$$

where $F(x)$ is defined by (4.31).

4.2.2 Linear growth rate

In Section 4.1, we managed to find a general solution to the deterministic growth case. Also, we showed that there is no PDF solution to the associated boundary value problem. In this section, we show that this property persists, *i.e.*, there is no PDF solution to the associated boundary value problem if the coefficients g and b satisfy a certain inequality. We will exploit the techniques and results in Section 4.2.1 to show that there is a general solution to this case. For uniqueness and positivity of solution, one can adapt the uniqueness proof in Chapter 3, and so the positivity proof would be achieved in principle.

4.2.2.1 The separable solution

We have seen that the separable solution plays a pivotal rôle in the study of long time asymptotic behaviour of solutions. We now look at the separable solution for the second order case. Let

$$n(x, t) = N(t)y(x).$$

Substituting this solution into equation (4.1) with the conditions (4.3) yields

$$-Dy''(x) + (gxy(x))' + (b + \lambda)y(x) = \alpha^2 by(\alpha x), \quad (4.48)$$

$$\lim_{x \rightarrow 0^+} [-Dy'(x) + gxy(x)] = 0, \quad (4.49)$$

and

$$\lim_{x \rightarrow \infty} [-Dy'(x) + gxy(x)] = 0, \quad (4.50)$$

where λ is a separation constant to be determined. Solutions to this kind of problem have been found for the case of constant coefficients (a Dirichlet series type solution [73], eigenfunction expansion type solutions stem from the reformulation of the problem as a singular Sturm-Liouville one [70]), and a case with variable dispersion term and constant coefficients (a modified Bessel function type solution [71]). More solutions to non symmetrical cell division problems and other non cell growth models are also observed, as was discussed in Chapter 2. We show that if the coefficients g and b of the above problem satisfy the inequality

$$g > \alpha b \ln(\alpha), \quad (4.51)$$

then there is no PDF solution in this case.

Suppose that $y(x) \in L^1[0, \infty)$ is a PDF, so that

$$\int_0^\infty y(x) dx = 1, \quad (4.52)$$

and $y(x) \geq 0$ for $x \geq 0$. Then the constant λ is found by integrating (4.48) from zero to infinity with respect to x , and this yields

$$\lambda = b(\alpha - 1),$$

so that (4.48) becomes

$$-Dy''(x) + gxy'(x) + (g + \alpha b)y(x) = \alpha^2 by(\alpha x). \quad (4.53)$$

The zero flux condition (4.49) indicates that

$$y'(0) = 0, \quad (4.54)$$

and

$$Dy''(0) = [g - \alpha b(\alpha - 1)]K, \quad (4.55)$$

where

$$K = \lim_{x \rightarrow 0^+} y(x).$$

We can deduce that $K > 0$ by first recasting (4.53) as

$$\left(e^{-\frac{gx^2}{2}} y(x)\right)' = -e^{-\frac{gx^2}{2}} \phi(x), \quad (4.56)$$

where

$$\phi(x) = \alpha b \int_x^{\alpha x} y(\xi) d\xi.$$

Now, we integrate equation (4.56) over the interval x to ∞ , which gives

$$y(x) = e^{\frac{gx^2}{2}} \int_x^{\infty} e^{-\frac{g\xi^2}{2}} \phi(\xi) d\xi.$$

Since $0 \leq \int_x^{\alpha x} y(\xi) d\xi \leq 1$ and y is a PDF, we have

$$\begin{aligned} \lim_{x \rightarrow 0^+} y(x) &= \int_0^{\infty} e^{-\frac{g\xi^2}{2}} \phi(\xi) d\xi \\ &= K > 0. \end{aligned}$$

We can verify that

$$\lim_{x \rightarrow \infty} xy(x) = 0.$$

Indeed, by using L'Hôpital's rule, we have

$$\lim_{x \rightarrow \infty} xy(x) = \lim_{x \rightarrow \infty} \frac{\int_x^{\infty} e^{-\frac{g\xi^2}{2}} \phi(\xi) d\xi}{\frac{e^{-\frac{gx^2}{2}}}{x}}$$

$$= \lim_{x \rightarrow \infty} \frac{-e^{-\frac{gx^2}{2}} \phi(x)}{-e^{-\frac{gx^2}{2}} \left(g + \frac{1}{x^2}\right)} = 0,$$

where $\phi(x) \rightarrow 0$ as $x \rightarrow \infty$. Similarly, it is straightforward to show that

$$\lim_{x \rightarrow \infty} y'(x) = 0.$$

Suppose that

$$g > \alpha b(\alpha - 1). \quad (4.57)$$

Then equation (4.55) implies that $y''(0) > 0$, so that there is an interval $(0, A)$ in which $y'(x) > 0$. Since y has to decay to zero eventually as $x \rightarrow \infty$, a global maximum must be achieved in $(0, \infty)$; moreover, since $y(x) \rightarrow 0$ as $x \rightarrow \infty$, there must be a largest value x_m at which y achieves this maximum. At such a point, we have $y(x_m) > 0$, $y'(x_m) = 0$, $y''(x_m) \leq 0$ and

$$y(x_m) > y(\alpha x_m).$$

Thus,

$$-Dy''(x_m) + (g + \alpha b)y(x_m) = \alpha^2 by(\alpha x_m),$$

so that

$$(g + \alpha b)y(x_m) \leq \alpha^2 by(\alpha x_m) < \alpha^2 by(x_m),$$

and consequently

$$g < \alpha b(\alpha - 1),$$

which contradicts inequality (4.57). We can sharpen this result. Suppose that

$$g < \alpha b(\alpha - 1).$$

Then $y''(0) < 0$, $y'(x) < 0$ and $y'(x) \in C^0[0, A)$ for x in the interval $(0, A)$. Equation (4.53) can be recast to

$$-Dy'(x) + gxy(x) = \alpha b \int_x^{\alpha x} y(\xi) d\xi.$$

Choose an x which satisfies $y'(x) < 0$ for all $0 < x < \frac{A}{\alpha}$. Since $y(\xi) \leq \frac{\alpha b}{g\xi}$ for $\xi \in (0, A)$, we find

$$\begin{aligned} y(x) &< \frac{\alpha b}{gx} \int_x^{\alpha x} y(\xi) d\xi \\ &\leq \frac{\alpha b}{gx}. \end{aligned}$$

We can reiterate to get

$$\begin{aligned} y(x) &< \frac{\alpha b}{gx} \int_x^{\alpha x} \frac{\alpha b}{g\xi} d\xi, \\ &= \left(\frac{\alpha b}{g}\right)^2 \frac{1}{x} \left(\ln(\alpha x) - \ln(x)\right) \\ &= \left(\frac{\alpha b}{g}\right)^2 \frac{\ln(\alpha)}{x} \\ &< \frac{\alpha b}{gx} \int_x^{\alpha x} \left(\frac{\alpha b}{g}\right)^2 \frac{\ln(\alpha)}{\xi} d\xi, \\ &= \frac{\alpha b}{g} \left(\frac{\alpha b \ln(\alpha)}{g}\right)^2 \frac{1}{x} \\ &\vdots \\ &< \frac{\alpha b}{g} \left(\frac{\alpha b \ln(\alpha)}{g}\right)^k \frac{1}{x}. \end{aligned}$$

If

$$g > \alpha b \ln(\alpha),$$

then $y(x) \equiv 0$ in $(x, \alpha x)$ for $x \in (0, A)$. Since $y(0) = K > 0$ and $y(x) \in C^0[0, A)$, it is a contradiction, and there is no solution for $g > \alpha b \ln(\alpha)$ other than the trivial one.

Finally, suppose that

$$g = \alpha b(\alpha - 1).$$

Then $y''(0) = y'(0) = 0$ with $y(0) = K > 0$. Either y has a global maximum in

$(0, \infty)$ or y is monotonically decreasing in $[0, \infty)$. The argument used to exclude $g > \alpha b(\alpha - 1)$ can be used to eliminate the former case; the argument used to refine the bound $g < \alpha b(\alpha - 1)$ can be applied to the latter case. In any event, we have the condition

$$g \leq \alpha b \ln(\alpha) < \alpha b(\alpha - 1), \quad (4.58)$$

for any PDF solution.

It may be that there is a PDF solution to this problem for g small, but inequality (4.58) shows that for general g , b , α there will not be such a solution. We note that if $g = 0$, it is a special case of the second order PE which is known to admit Dirichlet series solutions of the form

$$y(x) = \sum_{k=0}^{\infty} c_k e^{-a\alpha^k x},$$

where $a = \sqrt{\frac{\alpha b}{D}}$, and

$$c_k = \frac{(-1)^k \alpha^k}{\prod_{n=1}^k (\alpha^{2^n} - 1)} c_0,$$

for $k \in \mathbb{Z}^+$. Moreover, the parameters g , b and α are independent parameters from biology and, unlike the constant coefficient case, the inequality (4.58) places restrictions on these parameters.

4.2.2.2 The general solution

Motivated by the solution techniques and results in Section 4.2.1, we construct a solution to the problem consisting of the equations (4.1)-(4.3) by converting the problem into integral equations through a sequence of functions $\{v_k(x, t)\}$, defined by a sequence of PDEs, at which the integral kernel is an *a priori* function.

Let

$$n(x, t) = e^{-bt} \hat{n}(x, t),$$

then equation (4.1) becomes

$$n_t(x, t) - Dn_{xx}(x, t) + g\left(xn(x, t)\right)_x = \alpha^2bn(\alpha x, t), \quad (4.59)$$

where the hat is dropped for simplification unless there is a danger of confusion.

Now, let

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

be a solution to equation (4.59) that satisfies the conditions (4.2)-(4.3). Then, we define the following sequence for all $k > 0$,

$$\left[\partial_t + \mathcal{L}\right]v_{k+1}(x, t) = \alpha^2bv_k(\alpha x, t), \quad (4.60)$$

where

$$\begin{aligned} v_k(x, 0) &= 0, \\ \lim_{x \rightarrow 0^+} \partial_x v_k(x, t) &= 0, \\ \lim_{x \rightarrow \infty} \left[-D\partial_x v_k(x, t) + gxv_x(x, t) \right] &= 0, \end{aligned} \quad (4.61)$$

and

$$\mathcal{L} = -D\partial_{xx} + gx\partial_x + g.$$

For $k = 0$, the system satisfies the homogenous linear FPE

$$\left[\partial_t + \mathcal{L}\right]v_0(x, t) = 0, \quad (4.62)$$

with

$$v_0(x, 0) = n_0(x), \quad (4.63)$$

$$\lim_{x \rightarrow 0^+} \partial_x v_0(x, t) = 0, \quad (4.64)$$

$$\lim_{x \rightarrow \infty} \left[-D\partial_x v_0(x, t) + gxv_0(x, t) \right] = 0. \quad (4.65)$$

The solution to this problem can be expressed in the form

$$v_0(x, t) = \int_0^\infty \psi(x, \xi, t) n_0(\xi) d\xi, \quad (4.66)$$

in which $\psi(x, \xi, t)$ is the fundamental solution that obeys the following:

- I. $\left[\partial_t + \mathcal{L} \right] \psi(x, \xi, t) = 0, \quad \forall x, t > 0;$
- II. $\lim_{t \rightarrow 0} \psi(x, \xi, t) = \delta(x - \xi), \quad \text{for } 0 < x < \infty;$ and
- III. for any large enough fixed $t > 0,$

$$\begin{cases} \lim_{x \rightarrow 0^+} \left[-D\partial_x \psi(x, \xi, t) + gx\psi(x, \xi, t) \right] = 0, & 0 < \xi < x, \\ \lim_{x \rightarrow \infty} \left[-D\partial_x \psi(x, \xi, t) + gx\psi(x, \xi, t) \right] = 0, & \xi < x < \infty. \end{cases}$$

One can show using the Fourier transform (see [57], Chapter 5) that for all $t > 0$ there is a solution

$$\psi(x, \xi, t) = \frac{K(t)}{\sqrt{\pi}} \left(e^{-K^2(t)(x-\xi e^{gt})^2} - e^{-K^2(t)(x+\xi e^{gt})^2} \right), \quad (4.67)$$

which satisfies I, where

$$K(t) = \sqrt{\frac{g}{2D(e^{2gt} - 1)}}.$$

Notice that we made an odd extension of $G(x, \xi, t)$ from $\delta(x - \xi)$ with respect to the space variable x in order to satisfy the boundary condition at $x \rightarrow 0^+$. Also, notice that $\psi(x, \xi, t)$ is a Gaussian distribution, *i.e.*, $\psi(x, \xi, t) \in C^\infty([0, \infty) \times (0, \infty))$. It is easy to confirm that condition II is satisfied and so is condition (4.63). Namely,

$$\begin{aligned} \int_0^\infty \psi(x, \xi, t) d\xi &= \frac{K(t)}{\sqrt{\pi}} \int_0^\infty e^{-K^2(t)(x-\xi e^{gt})^2} \left(1 - e^{-4x\xi e^{gt}} \right) d\xi \\ &\leq \frac{K(t)}{\sqrt{\pi}} \int_0^\infty e^{-K^2(t)(x-\xi e^{gt})^2} d\xi, \\ &= \frac{e^{-gt}}{\sqrt{\pi}} \int_{-K(t)x}^\infty e^{-u^2} du \end{aligned}$$

$$\leq 1,$$

wherein we set

$$u = K(t)(\xi e^{gt} - x),$$

and use the identity

$$\frac{1}{\sqrt{\pi}} \int_{-\infty}^{\infty} e^{-u^2} du = 1.$$

For the condition III, we first express the spatial derivative:

$$\begin{aligned} \partial_x \psi(x, \xi, t) &= \frac{K(t)}{\sqrt{\pi}} \left[-2K^2(t)(x - \xi e^{gt})e^{-K^2(t)(x - \xi e^{gt})^2} \right] \\ &\quad - \frac{K(t)}{\sqrt{\pi}} \left[-2K^2(t)(x + \xi e^{gt})e^{-K^2(t)(x + \xi e^{gt})^2} \right] \\ &= \frac{2K^3(t)}{\sqrt{\pi}} \xi e^{gt} \left[e^{-K^2(t)(x - \xi e^{gt})^2} + e^{-K^2(t)(x + \xi e^{gt})^2} \right] \\ &\quad - \frac{2K^3(t)}{\sqrt{\pi}} x \left[e^{-K^2(t)(x - \xi e^{gt})^2} - e^{-K^2(t)(x + \xi e^{gt})^2} \right] \\ &= \frac{2K^3(t)}{\sqrt{\pi}} \xi e^{gt} \left[e^{-K^2(t)(x - \xi e^{gt})^2} + e^{-K^2(t)(x + \xi e^{gt})^2} \right] - 2K^2(t)x\psi(x, \xi, t). \end{aligned}$$

As $x \rightarrow 0^+$,

$$\begin{aligned} \lim_{x \rightarrow 0^+} \partial_x \psi(x, \xi, t) &= \frac{2K^3(t)}{\sqrt{\pi}} \xi e^{gt} \left[e^{-K^2(t)(-\xi e^{gt})^2} + e^{-K^2(t)(\xi e^{gt})^2} \right] \\ &= \frac{4K^3(t)}{\sqrt{\pi}} \xi e^{gt} e^{-K^2(t)\xi^2 e^{2gt}} \tag{4.68} \\ &= 0, \end{aligned}$$

for any fixed ξ and sufficiently large t . As $x \rightarrow \infty$, we can see for any fixed ξ that

$$\lim_{x \rightarrow \infty} gx\psi(x, \xi, t) = 0, \tag{4.69}$$

and

$$\begin{aligned} \lim_{x \rightarrow \infty} \partial_x \psi(x, \xi, t) &= \frac{2K^3(t)}{\sqrt{\pi}} \xi e^{gt} \lim_{x \rightarrow \infty} \left[e^{-K^2(t)(x-\xi e^{gt})^2} + e^{-K^2(t)(x+\xi e^{gt})^2} \right] \\ &\quad - 2K^2(t) \lim_{x \rightarrow \infty} x \psi(x, \xi, t) \quad (4.70) \\ &= 0, \end{aligned}$$

since $\psi(x, \xi, t)$ decays exponentially. It is obvious that $v_0(x)$ satisfies condition (4.64), and it is straightforward to verify the same for condition (4.65). We take the first part in (4.65);

$$\begin{aligned} \lim_{x \rightarrow \infty} \partial_x v_0(x, t) &= \lim_{x \rightarrow \infty} \int_0^\infty \partial_x \psi(x, \xi, t) n_0(\xi) d\xi \\ &= \frac{2K^3(t)e^{gt}}{\sqrt{\pi}} \lim_{x \rightarrow \infty} \int_0^\infty \left[e^{-K^2(t)(x-\xi e^{gt})^2} + e^{-K^2(t)(x+\xi e^{gt})^2} \right] \xi n_0(\xi) d\xi \\ &\quad - 2K^2(t) \lim_{x \rightarrow \infty} \int_0^\infty x \psi(x, \xi, t) n_0(\xi) d\xi. \end{aligned}$$

The second part of (4.65) yields

$$\begin{aligned} \lim_{x \rightarrow \infty} x v_0(x, t) &= \lim_{x \rightarrow \infty} \int_0^\infty x \psi(x, \xi, t) n_0(\xi) d\xi \\ &= \frac{K(t)}{\sqrt{\pi}} \lim_{x \rightarrow \infty} \int_0^\infty x \left[e^{-K^2(t)(x-\xi e^{gt})^2} - e^{-K^2(t)(x+\xi e^{gt})^2} \right] n_0(\xi) d\xi. \end{aligned}$$

Since v_0 is differentiable, (4.65) is fulfilled by (4.68), (4.69) and (4.70). The next sequence of solution is

$$v_1(x, t) = \alpha^2 b \int_0^t \int_0^\infty \psi(x, \xi, t - \tau) v_0(\alpha \xi, \tau) d\xi d\tau.$$

One can verify that this solution also satisfies

$$\begin{aligned} \left[\partial_t + \mathcal{L} \right] v_1(x, t) &= \alpha^2 b v_0(\alpha x, t), \\ \lim_{x \rightarrow 0^+} \partial_x v_1(x, t) &= 0, \\ \lim_{x \rightarrow \infty} \left[-D \partial_x v_1(x, t) + g x v_1(x, t) \right] &= 0. \end{aligned}$$

And we can continue in this pattern to generally write

$$v_{k+1}(x, t) = \alpha^2 b \int_0^t \int_0^\infty \psi(x, \xi, t - \tau) v_k(\alpha \xi, \tau) d\xi d\tau.$$

Therefore, the general solution can be written formally as

$$n(x, t) = \sum_{k=0}^{\infty} v_k(x, t). \quad (4.71)$$

This solution satisfies the initial condition (4.2) by construction and can be verified to satisfy the PDE (4.1) for all $t > 0$. Evidently,

$$\begin{aligned} n_t(x, t) &= \int_0^\infty \psi_t(x, \xi, t) n_0(\xi) d\xi + \alpha^2 b \int_0^t \int_0^\infty \psi_t(x, \xi, t - \tau) \sum_{k=0}^{\infty} v_k(\alpha \xi, \tau) d\xi d\tau \\ &\quad + \alpha^2 b \sum_{k=0}^{\infty} v_k(\alpha x, t), \end{aligned}$$

$$n_x(x, t) = \int_0^\infty \psi_x(x, \xi, t) n_0(\xi) d\xi + \alpha^2 b \int_0^t \int_0^\infty \psi_x(x, \xi, t - \tau) \sum_{k=0}^{\infty} v_k(\alpha \xi, \tau) d\xi d\tau,$$

$$\begin{aligned} n_{xx}(x, t) &= \int_0^\infty \psi_{xx}(x, \xi, t) n_0(\xi) d\xi \\ &\quad + \alpha^2 b \int_0^t \int_0^\infty \psi_{xx}(x, \xi, t - \tau) \sum_{k=0}^{\infty} v_k(\alpha \xi, \tau) d\xi d\tau. \end{aligned}$$

Substituting these derivatives into (4.1), we have

$$\begin{aligned} \int_0^\infty \left[\partial_t + \mathcal{L} \right] \psi(x, \xi, t) n_0(\xi) d\xi + \alpha^2 b \int_0^t \int_0^\infty \left[\partial_t + \mathcal{L} \right] \psi(x, \xi, t - \tau) \sum_{k=0}^{\infty} v_k(\alpha \xi, \tau) d\xi d\tau \\ + \alpha^2 b \sum_{k=0}^{\infty} v_k(\alpha x, t) = \alpha^2 B(\alpha x) n(\alpha x, t). \end{aligned}$$

By condition I, the solution satisfies (4.1). The properties of the solution depend on that of n_0 . If n_0 is smooth and bounded, then the solution converges uniformly.

Lemma 4.2.1. *Let $n_0 \geq 0$ be a PDF that is bounded on $[0, \infty)$. Then for any $T > 0$, the series defined by (4.71) converges uniformly in $\Omega_T = \{(x, t) : x \geq$*

$0, 0 \leq t \leq T\}$.

Proof. Since n_0 is bounded, $\|n_0\| = \sup_{x \geq 0} |n_0(x)| < \infty$. The first term in the series (at $k = 0$) shows,

$$\begin{aligned} |v_0(x, t)| &= \left| \int_0^\infty \psi(x, \xi, t) n_0(\xi) d\xi \right| \\ &\leq q \|n_0\|, \end{aligned}$$

where

$$q = \int_0^\infty \psi(x, \xi, t) d\xi.$$

For $k = 1$, we find that

$$\begin{aligned} |v_1(x, t)| &\leq \alpha^2 b \left| \int_0^t \int_0^\infty \psi(x, \xi, t - \tau) v_0(\alpha\xi, \tau) d\xi d\tau \right| \\ &\leq \alpha^2 b q \|n_0\| \int_0^t \int_0^\infty |\psi(x, \xi, t - \tau)| d\xi d\tau \\ &\leq \alpha^2 b q \|n_0\| \int_0^t q d\tau \\ &\leq \alpha^2 b q^2 t \|n_0\|. \end{aligned}$$

Clearly, the same argument on $\psi(x, \xi, t)$ applies to the temporal shift $\psi(\xi_1, \xi_2, t - \tau)$, and any bound for $v_k(x, t)$ is also a bound for $v_k(\alpha x, t)$. So that, at $k = 2$ we have

$$\begin{aligned} |v_2(x, t)| &\leq \alpha^2 b \int_0^t \int_0^\infty |\psi(x, \xi, t - \tau)| |v_1(\alpha\xi, \tau)| d\xi d\tau \\ &\leq \alpha^2 b^2 q^3 \|n_0\| \int_0^t \tau d\tau \\ &\leq (\alpha^2)^2 b^2 q^3 \frac{t^2}{2} \|n_0\|. \end{aligned}$$

For general k we have

$$|v_k(x)| \leq \frac{q \|n_0\| (q \alpha^2 b t)^k}{k!};$$

hence,

$$\begin{aligned}
|n(x, t)| &\leq \sum_{k=0}^{\infty} |v_k(x, t)| \\
&\leq q \|n_0\| \sum_{k=0}^{\infty} C^k \frac{t^k}{k!} \\
&= q \|n_0\| e^{Ct} \\
&\leq q \|n_0\| e^{CT},
\end{aligned}$$

where $C = q\alpha^2 b$. We thus conclude that the series converges uniformly in Ω_T .

□

4.3 Conclusions

In this chapter we constructed general solutions to the cell growth equation with linear growth rate (corresponding to exponential growth) and a constant division rate with and without dispersion. We showed that, in general, there are no PDF type separable solutions in the $L^1[0, \infty)$ norm for this kind of problem, *i.e.*, linear growth and constant division rates. The uniqueness and positivity proofs of solutions for both cases are not shown in this chapter, but one can adapt the techniques from the case in Chapter 3.

In the first order degenerate case, the hyperbolic character of the equation led to the choice of w_0 and simplified the solving for a general solution. We provided an illustration with a Gaussian initial distribution for the long time asymptotic behaviour for this case, as studying this behaviour from the solution (4.16) is not obvious. This showed the oscillatory character of solution in the time domain as predicted for exponential growth, but different in character from the case in Chapter 3. The illustration led to the observation that a Dirac delta type solution is also a generalised solution to (4.4).

For the second order degenerate case, the solution method in Section 4.2.1 led to the solution formulation, which depends on identifying a fundamental solution to the local problem (4.62)-(4.65). We showed that the solution converges uniformly in the domain of definition. It remains elusive to study the long time solution dynamics in the stochastic growth equation. We showed that if the parameters g , b and α satisfy the inequality (4.57), there are no PDF separable solutions. It is not clear that a PDF separable solution exists for the case (4.58).

Finally, it has been noted for related models with a density dependent dispersion term (cf. [27]) that there is a notable effect on the dynamics, but it is unclear in the exponential growth case with constant or variable dispersion term. In the next chapter, we use numerical methods to study possible behaviours and the influence of the dispersion term as a constant.

Chapter 5

Numerical simulation

5.1 Introduction

In this chapter, we apply numerical methods to find approximate solutions to the continuous second order degenerate case introduced in the preceding chapter and study related qualitative properties. In general, this chapter by no means aims to do an extensive numerical analysis but to provide a simple numerical method to further study equation (4.1) and use some established results in order to validate the numerical method. The discretised model involves a truncated function Δ .

In this chapter we consider the equation

$$n_t(x, t) - Dn_{xx}(x, t) + \left(G(x)n(x, t)\right)_x + B(x)n(x, t) = \alpha^2 B(\alpha x)n(\alpha x, t), \quad (5.1)$$

subject to the initial condition

$$n(x, 0) = n_0(x), \quad (5.2)$$

and, for all $t \geq 0$, the boundary data

$$\begin{aligned} \lim_{x \rightarrow 0^+} \left[-Dn_x(x, t) + G(x)n(x, t) \right] &= 0, \\ \lim_{x \rightarrow \infty} \left[-Dn_x(x, t) + G(x)n(x, t) \right] &= 0, \end{aligned} \tag{5.3}$$

where $D \geq 0$. Here, $\alpha > 1$ and $n_0(x)$ is assumed to be a PDF. As an IBVP of one space dimension involving time, the finite difference approximation method can be used (among several methods). This method has been utilised to solve parabolic equations such as the heat equation (see, e.g., [2], [19], [39]), hyperbolic equations such as the advection equation (cf. [60], [77]) and the wave equation ([28]). Here, we implement the forward-time centred-space (FTCS) method with uniform step sizes. The derivatives are approximated with a first order derivative temporally and a second order derivative spatially. The method provides a formula $n(x, t + \Delta t)$ which depends on the values of $n(x, t)$ at time t based on information from the initial and boundary data. We seek numerical solutions to particular cases of equation (5.1) for both the parabolic case and the hyperbolic case ($D = 0$). The numerical application of the hyperbolic case in this chapter serves mainly as a validation exercise, as there are examples at which we know the limiting solutions' properties. It is convenient to develop the aforesaid method to the parabolic case first, and then adapt it to the special case when $D = 0$ (the first order hyperbolic PDE).

5.2 The finite difference method

In principle, the finite difference method replaces the defined domain of independent variables with a finite mesh (grid) of nodes/points and uses difference formulas to approximate the continuous derivatives at each node on the mesh using Taylor's theorem. This leads to a system of algebraic equations. For any approximation method, there are errors, stability and convergence analysis that

warrant further study; however, our goal is to simply design and implement a method in order to produce graphs that suggest possible solution behaviour. We do, however, consider these problems, but not in depth, and the reader is directed to various references for more detailed analysis.

Let n_i^j be the approximated value of the exact solution $n(x, t)$ of equation (5.1) at $(x, t) = (x_i, t_j)$. Suppose that we discretise the x space $0 \leq x \leq x_{max}$ into N equidistant finite nodes and similarly discretise the time space into M suitable uniform steps. Let

$$x_i = (i - 1)\Delta x,$$

and

$$t_j = (j - 1)\Delta t,$$

where $i = 1, 2, \dots, N$ and $j = 1, 2, \dots, M$, as shown in Figure 5.1. The step sizes

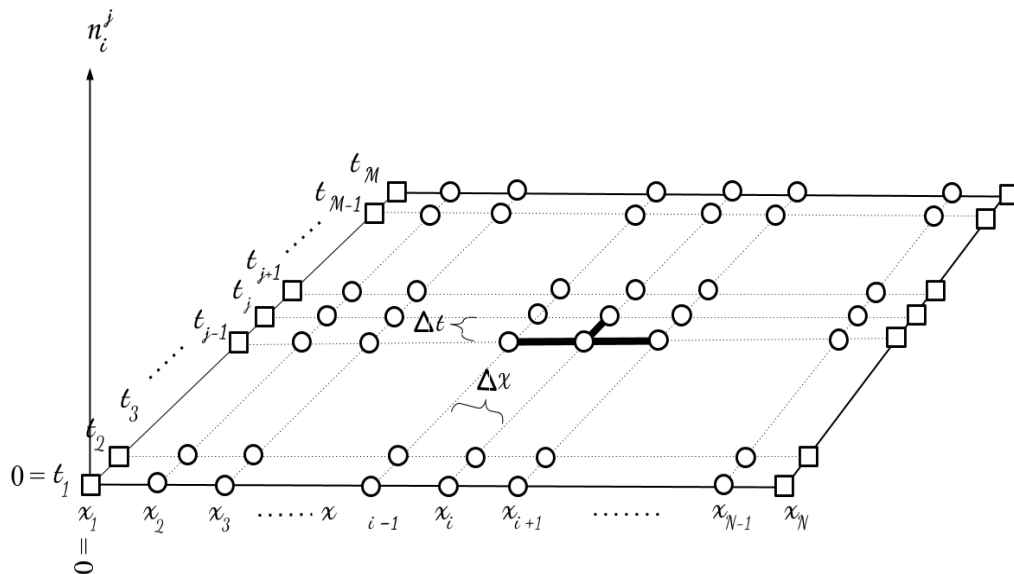


FIGURE 5.1: The discretised space.

Δx and Δt are crucial parameters for stability and convergence of the numerical scheme. Assuming stability generally is a formidable problem, particularly, for non linear systems. For this problem, however, von Neumann analysis (cf. [39]) is sufficient to give guidance on the size of these steps. In brief, it states that for a

chosen Δx , the step size Δt must be small enough to satisfy a certain amplification factor that stems from decomposing the errors using Fourier analysis. In short, we need to choose N and M such that $\Delta t \ll (\Delta x)^2$ for the parabolic equation in order to gain stability, with

$$\Delta x = \frac{x_{max}}{(N-1)},$$

and

$$\Delta t = \frac{t_{max}}{M},$$

at which x_{max} and t_{max} indicate the maximum values for x and t , respectively. This can be relaxed to $\Delta t < \Delta x$ for the hyperbolic equation. The Courant-Friedrichs-Lewy (CFL) condition (cf. [60]) can be used to analyse the stability for hyperbolic equations as well.

The FTCS scheme approximates the continuous derivatives in the x - t space using Taylor series expansion about the points t_j and x_i . This gives

$$\begin{aligned} n_t(x_i, t_j) &= \frac{n(x_i, t_j + \Delta t) - n(x_i, t_j)}{\Delta t} - \frac{\Delta t}{2} n_{tt}(x_i, \tau_j) \\ &\approx \frac{n_i^{j+1} - n_i^j}{\Delta t}, \end{aligned} \quad (5.4)$$

for some $\tau_j \in (t_j, t_{j+1})$, and

$$\begin{aligned} n_x(x, t) &= \frac{n(x + \Delta x, t) - n(x - \Delta x, t)}{2\Delta x} - \frac{\Delta x^2}{6} n_{xxx}(\zeta_i, t_j) \\ &\approx \frac{n_{i+1}^j - n_{i-1}^j}{2\Delta x}, \end{aligned} \quad (5.5)$$

$$\begin{aligned} n_{xx}(x, t) &= \frac{n(x + \Delta x, t) - 2n(x, t) + n(x - \Delta x, t)}{(\Delta x)^2} - \frac{\Delta x^4}{12} n_{xxxx}(\zeta_i, t_j) \\ &\approx \frac{n_{i+1}^j - 2n_i^j + n_{i-1}^j}{(\Delta x)^2}, \end{aligned} \quad (5.6)$$

for $\zeta \in (x_{i-1}, x_{i+1})$, provided n is sufficiently smooth. The functional term $n(x, t)$ is evaluated at any point (x_i, t_j) on the finite mesh by a linear interpolation of $n(x_{h(i)}, t)$ and $n(x_{h(i)+1}, t)$ such that for any unique index $h(i)$,

$x_{h(i)} \leq \alpha x_i < x_{h(i)+1}$. Hence,

$$\begin{aligned} n(\alpha x_i, t_j) &= n(x_{h(i)}, t) + s_i \left(n(x_{h(i)+1}, t) - n(x_{h(i)}, t_j) \right) \\ &= n_{h(i)}^j + s_i \left(n_{h(i)+1}^j - n_{h(i)}^j \right) \\ &= (1 - s_i) n_{h(i)}^j + s_i n_{h(i)+1}^j, \end{aligned} \quad (5.7)$$

where

$$\begin{aligned} s_i &= \left(\frac{\alpha x_i - x_{h(i)}}{x_{h(i)+1} - \alpha x_i} \right) \\ &= \left(\frac{\alpha x_i - x_{h(i)}}{\Delta x} \right). \end{aligned}$$

We set

$$n(\alpha x_i, t_j) = 0, \quad (5.8)$$

for any $\alpha x_i > x_{max}$.

5.2.1 The parabolic case

The finite difference approximation of equation (5.1) using (5.4)-(5.6) yields

$$\begin{aligned} n_i^{j+1} &= \left(1 - \Delta t (B(x_i) + G'(x_i)) \right) n_i^j + \frac{\Delta t}{(\Delta x)^2} D [n_{i+1}^j - 2n_i^j + n_{i-1}^j] \\ &\quad - \frac{\Delta t}{2\Delta x} G(x_i) [n_{i+1}^j - n_{i-1}^j] + \alpha^2 \Delta t B(\alpha x_i) n(\alpha x_i, t_j) \\ &= \xi_i n_i^j + \nu_i n_{i+1}^j + \epsilon_i n_{i-1}^j + P_i^j, \end{aligned} \quad (5.9)$$

where “ ’ ” indicates the derivative with respect to the argument, and

$$\xi_i = 1 - 2 \frac{\Delta t}{(\Delta x)^2} D - \Delta t (B(x_i) + G'(x_i)), \quad (5.10)$$

$$\nu_i = \frac{\Delta t}{(\Delta x)^2} D - \frac{\Delta t}{2\Delta x} G(x_i), \quad (5.11)$$

$$\epsilon_i = \frac{\Delta t}{(\Delta x)^2} D + \frac{\Delta t}{2\Delta x} G(x_i), \quad (5.12)$$

and

$$P_i^j = \Delta t \alpha^2 B(\alpha x_i) \left[(1 - s_i) n_{h(i)}^j + s_i n_{h(i)+1}^j \right]. \quad (5.13)$$

Note that we do not differentiate $G(x)$ numerically, but we use an expression for the derivative ($G'(x)$). The von Neumann stability analysis indicates that

$$\frac{D\Delta t}{(\Delta x)^2} < \frac{1}{2}.$$

The truncation error for this case is

$$E_{ij} = \frac{\Delta t}{2} n_{tt}(x_i, \tau_j) - D \frac{\Delta x^4}{12} n_{xxxx}(\zeta_i, t_j) + G(\zeta_i) \frac{\Delta x^2}{6} n_{xxx}(\zeta_i, t_j).$$

The boundary conditions (5.3) are discretised using central difference along the boundaries, in this situation, at $i = 2$ and $i = N + 2$ (indicated by squares in Figure 5.2) corresponding to $x = 0$ and x_{max} , respectively; hence,

$$n_1^j = n_3^j - \frac{2\Delta x}{D} G(x_2) n_2^j, \quad (5.14)$$

$$n_{N+3}^j = n_{N+1}^j + \frac{2\Delta x}{D} G(x_{N+2}) n_{N+2}^j. \quad (5.15)$$

In this scenario,

$$x_i = (i - 2)\Delta x.$$

The finite difference for the initial condition (5.2) is given by

$$n_i^1 = n_0(x_i), \quad (5.16)$$

which prescribes n_i^1 , for all $2 \leq i \leq N + 1$, by a given function n_0 . One recurring problem in numerical computing is the emergence of the ghost/artificial points x_1 and x_{N+3} (indicated by solid circles in Figure 5.2) in the boundary conditions. Here, the left boundary condition at x_2 is satisfied by (5.16). In order to ensure

$$P_i^1 = \Delta t \alpha^2 B(\alpha x_i) \left[(1 - s_i) n_0(x_{h(i)}) + s_i n_0(x_{h(i)+1}) \right].$$

We have

$$\begin{aligned} n_2^2 &= \xi_2 n_2^1 + \nu_2 n_3^1 + \epsilon_1 n_1^1 + P_2^1 \\ &= \left(\xi_2 - \epsilon_2 \frac{2\Delta x}{D} G(x_2) \right) n_0(x_2) + (\nu_2 + \epsilon_2) n_0(x_3) + P_2^1, \\ n_3^2 &= \xi_3 n_3^1 + \nu_3 n_4^1 + \epsilon_3 n_2^1 + P_3^1 \\ &= \xi_3 n_0(x_3) + \nu_3 n_0(x_4) + \epsilon_3 n_0(x_2) + P_3^1, \\ n_4^2 &= \xi_4 n_4^1 + \nu_4 n_5^1 + \epsilon_4 n_3^1 + P_4^1 \\ &= \xi_4 n_0(x_4) + \nu_4 n_0(x_5) + \epsilon_4 n_0(x_3) + P_4^1, \\ &\vdots \\ n_{N+1}^2 &= \xi_{N+1} n_{N+1}^1 + \nu_{N+1} n_{N+2}^1 + \epsilon_{N+1} n_N^1 + P_{N+1}^1 \\ &= \xi_{N+1} n_0(x_{N+1}) + \nu_{N+1} n_0(x_{N+2}) + \epsilon_{N+1} n_0(x_N) + P_{N+1}^1. \end{aligned}$$

We can now use n_i^2 to evaluate the following time step n_i^3 , *i.e.*,

$$n_i^3 = \xi_i n_i^2 + \nu_i n_{i+1}^2 + \epsilon_i n_{i-1}^2 + P_i^2.$$

We can continue in this manner up to the $t_j = t_M$ step. Accordingly, the problem can be reduced to the linear equation

$$\begin{bmatrix} n_2^{j+1} \\ n_3^{j+1} \\ \vdots \\ \vdots \\ n_{N-1}^{j+1} \\ n_N^{j+1} \\ n_{N+1}^{j+1} \end{bmatrix} = \begin{bmatrix} \xi_2 & \nu_2 & 0 & 0 & 0 & \dots & 0 \\ \epsilon_3 & \xi_3 & \nu_3 & 0 & 0 & \dots & 0 \\ 0 & \ddots & \ddots & \ddots & 0 & \dots & \vdots \\ 0 & 0 & \ddots & \ddots & \ddots & \dots & \vdots \\ \vdots & \vdots & \vdots & \ddots & \ddots & \ddots & 0 \\ 0 & 0 & \dots & 0 & \epsilon_N & \xi_N & \nu_N \\ 0 & 0 & \dots & 0 & 0 & \epsilon_{N+1} & \xi_{N+1} \end{bmatrix} \cdot \begin{bmatrix} n_2^j \\ n_3^j \\ \vdots \\ \vdots \\ n_{N-1}^j \\ n_N^j \\ n_{N+1}^j \end{bmatrix} + \begin{bmatrix} P_2^j + \epsilon_2 n_1^j \\ P_3^j \\ \vdots \\ \vdots \\ P_{N-1}^j \\ P_N^j \\ P_{N+1}^j \end{bmatrix}.$$

5.2.2 The hyperbolic case

If $D = 0$, the IBVP involves a first order hyperbolic equation with boundary data of a Dirichlet type. This means we have no ghost nodes, and the numerical equation reduces to

$$\begin{aligned} n_i^{j+1} &= \left(1 - \Delta t(B(x_i) + G'(x_i))\right)n_i^j - \frac{\Delta t}{2\Delta x}G(x_i)[n_{i+1}^j - n_{i-1}^j] \\ &\quad + \alpha^2 \Delta t B(\alpha x_i) n(\alpha x_i, t_j) \quad (5.17) \\ &= \xi_i n_i^j + \nu_i^0 n_{i+1}^j + \epsilon_i^0 n_{i-1}^j + P_i^j, \end{aligned}$$

where the initial condition is as given by (5.16) with $2 \leq i \leq N - 1$, and the boundary data are

$$G(x_1)n_1^j = 0, \quad (5.18)$$

$$G(x_N)n_N^j = 0, \quad (5.19)$$

with ξ_i and P_i^j as given by (5.10) and (5.13), and ν_i^0 and ϵ_i^0 indicate the value of (5.11) and (5.12), respectively, with $D = 0$. Besides von Neumann stability analysis, the Courant-Friedrichs-Lewy (CFL) condition can be used in this case to provide stability criteria. The CFL condition indicates that if

$$\frac{G(x)\Delta t}{\Delta x} < 1,$$

then numerical stability can be acquired. The truncation error is

$$E_{ij} = \frac{\Delta t}{2} n_{tt}(x_i, \tau_j) + G(\zeta_i) \frac{\Delta x^2}{6} n_{xxx}(\zeta_i, t_j).$$

The numerical solution, hence, is evaluated within the grid points $2 \leq i \leq N - 1$ for all $j \geq 1$, and the matrix form for this system reduces to

$$\begin{bmatrix} n_2^{j+1} \\ n_3^{j+1} \\ \vdots \\ n_{N-2}^{j+1} \\ n_{N-1}^{j+1} \end{bmatrix} = \begin{bmatrix} \xi_2 & \nu_2^0 & 0 & 0 & \dots & 0 \\ \epsilon_3^0 & \xi_3 & \nu_3^0 & 0 & \dots & 0 \\ 0 & \ddots & \ddots & \ddots & \dots & \vdots \\ \vdots & \dots & \ddots & \ddots & \ddots & 0 \\ 0 & \dots & 0 & \epsilon_{N-1}^0 & \xi_{N-1} & \nu_{N-1}^0 \end{bmatrix} \cdot \begin{bmatrix} n_2^j \\ n_3^j \\ \vdots \\ n_{N-2}^j \\ n_{N-1}^j \end{bmatrix} + \begin{bmatrix} P_2^j \\ P_3^j \\ \vdots \\ P_{N-2}^j \\ P_{N-1}^j \end{bmatrix}.$$

We employ the MATLAB software environment to implement both systems. For a better evaluation, we define the approximated solution n_i^j by a vector

$$n^j = \begin{bmatrix} n_2^j \\ n_3^j \\ \vdots \\ n_{N-2}^j \\ n_{N-1}^j \end{bmatrix},$$

for all $j \geq 1$. In this way, the software program works out the numerical evaluation through this vector looping over time steps. In general, we consider the initial condition $n_0(x)$ to be given by a Gaussian type distribution at particular choices of interest for the parameters D , $G(x)$, and $B(x)$ where $\alpha = 2$ and the step size Δx , and Δt are chosen consistently to ensure stability.

5.3 Validating the method

In this section, we use four examples to validate the accuracy of the FTCS scheme for the discretised parabolic and hyperbolic equations stated above. The examples are chosen because the long time asymptotic behaviour of solutions is known. In the following section, we apply the FTCS scheme to the degenerate second order problem discussed in Section 4.2.2.

Example 1

In the first example we consider the case of zero dispersion, and constant growth and division rates. For this example, an analytical solution has been obtained by Zaidi *et al.* [76], where it was also shown that solutions converged to the SSD solution derived by Hall and Wake in [32]. Perthame and Ryzhik [55] also proved that solutions tend towards this SSD.

Let $G(x) = 1$ and $B(x) = 1$, $x \in [0, 30]$ and $t \in [0, 20]$ with step size $\Delta x = 0.02$, $\Delta t = 0.0001$. Using the initial distribution $n_0(x) = e^{-0.5(x-10)^2}$, Figure 5.3

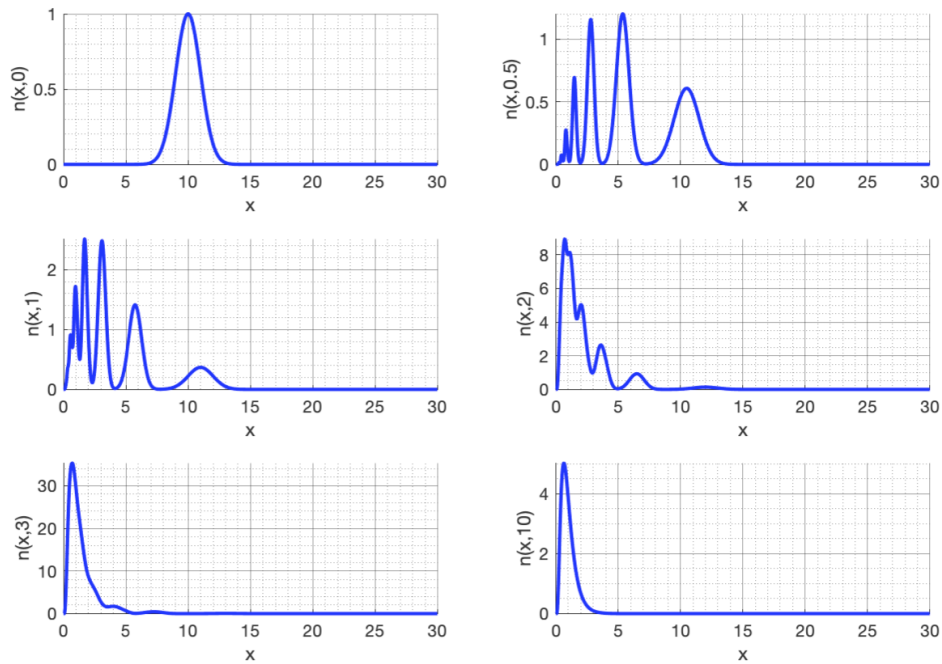


FIGURE 5.3: Example 1. Numerical solutions with $D = 0$, $G(x) = 1$, $B(x) = 1$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-10)^2}$.

depicts the numerical solution for fixed values of time. As expected, the graph of the solution approaches a steady shape as t increases. The graph of $n(x, 10)$ in Figure 5.3 is virtually the same as that for the SSD solution given by Hall and Wake. The analysis of Zaidi *et al.* (*op. cit.*) and Perthame and Ryzhik indicate that solutions converge exponentially fast to the SSD. Figure 5.4 shows the solution for fixed values of x . Here, it can be seen that for a fixed x , $n(x, t)$

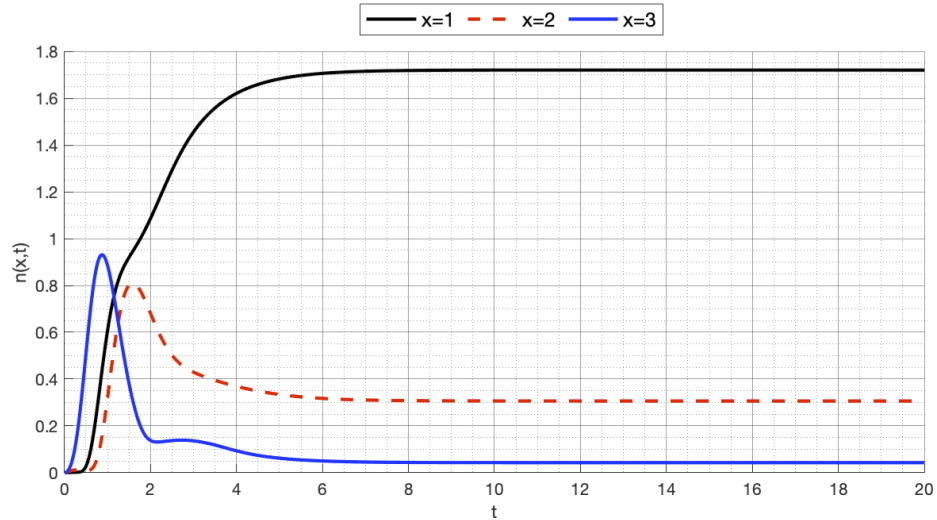


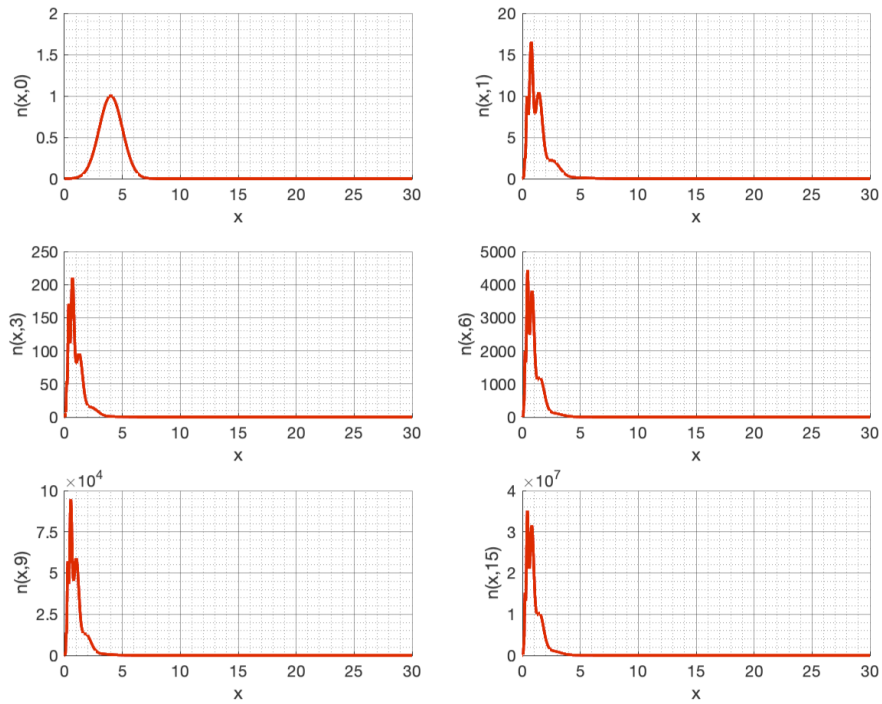
FIGURE 5.4: Example 1. Numerical evaluation of $e^{-\lambda t}n(x,t)$ with $D = 0$, $\lambda = b(\alpha - 1)$, $G(x) = 1$, $B(x) = 1$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-10)^2}$.

becomes nearly a constant after $t = 5$, *i.e.*, this figure suggests that the solution is “nearly the same” as the SSD solution for $t \geq 5$.

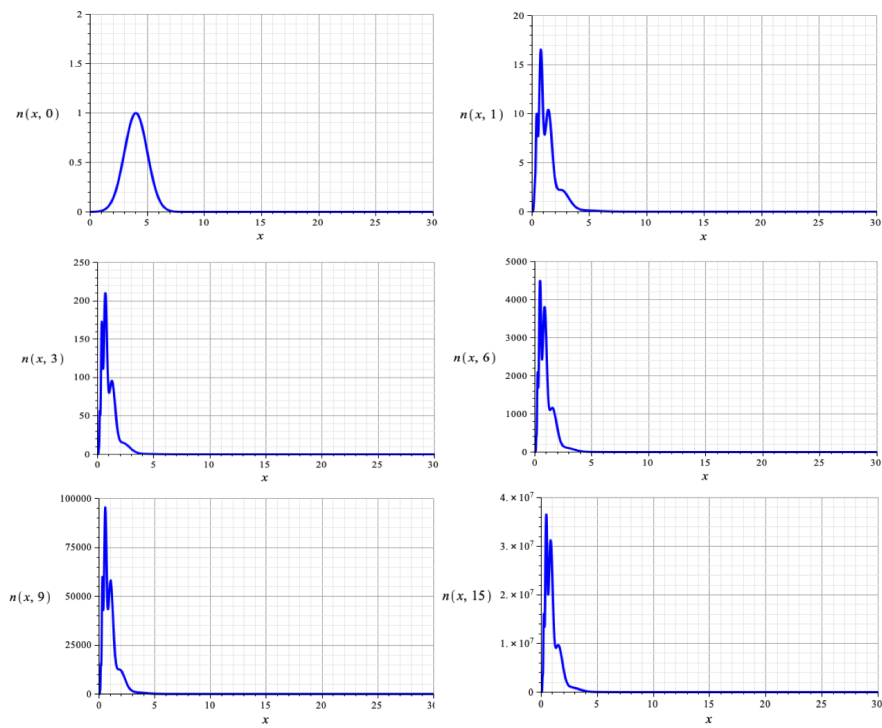
Example 2

For the next example we consider the equation studied in Chapter 3. For this example the growth and division rates are given by linear and monomial functions, respectively. In this case, we know the general solution explicitly (cf. equation (3.22)) and can compare the numerical result directly with the graph produced by the analytical solution. We also know the long time asymptotic behaviour of solutions, and in particular we expect time dependent periodic oscillations with $\ln(2)/g$ period.

Let $G(x) = x$, $B(x) = x$ and $n_0(x) = e^{-\frac{(x-4)^2}{2}}$ over the space $x \in [0, 30]$ and $t \in [0, 15]$ with step size $\Delta x = 0.01$ and $\Delta t = 0.000005$. Figure 5.5 shows the similarities between the numerical solution and the analytical solution. Figure



(a) Numerical solution with step size $\Delta x = 0.01$, $\Delta t = 0.000005$.



(b) Analytical solution.

FIGURE 5.5: Example 2. Numerical solution vs analytical solution with $G(x) = x$, $B(x) = x$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-4)^2}$.

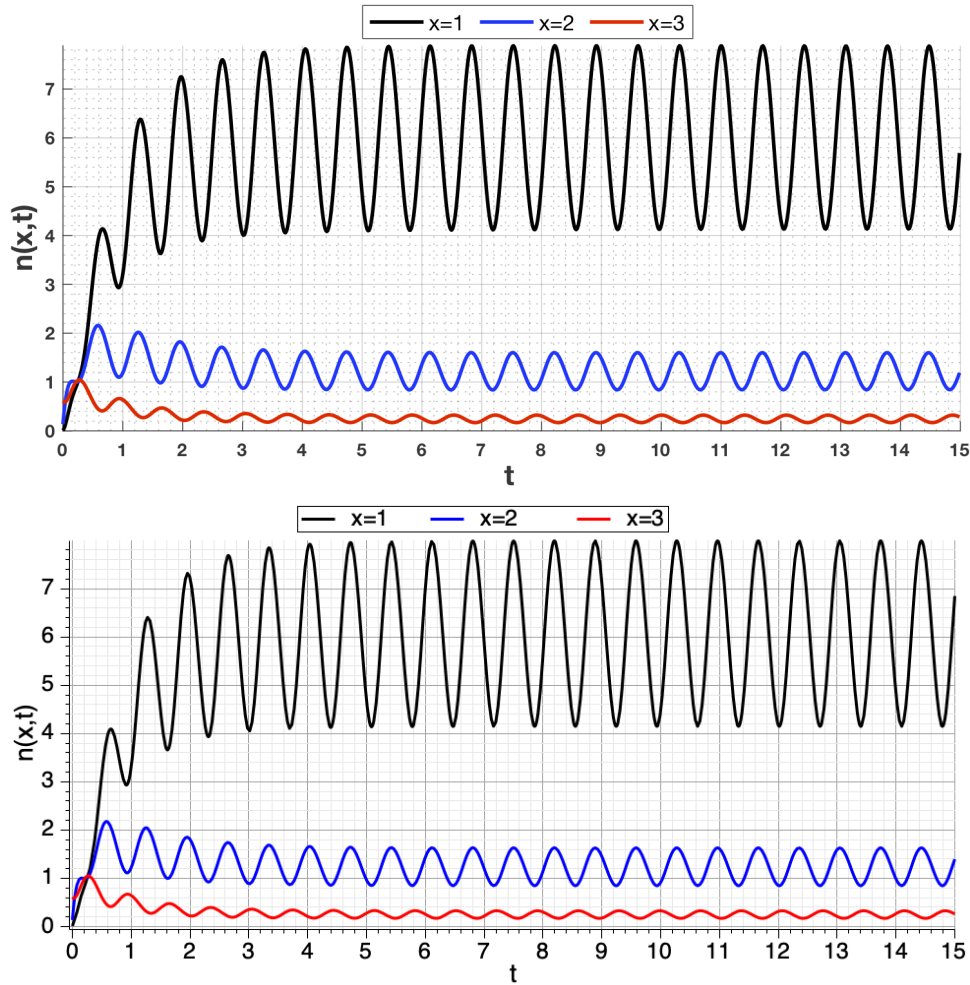
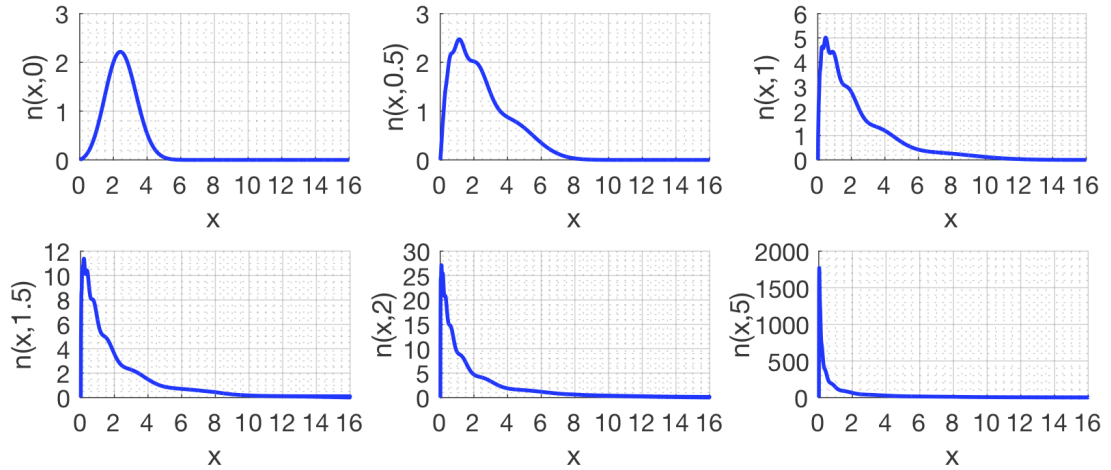
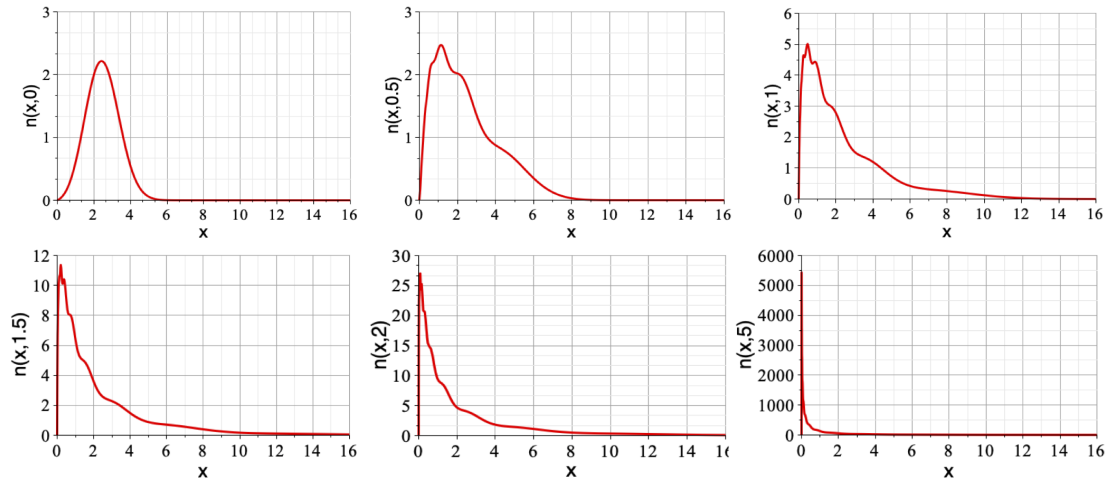


FIGURE 5.6: Example 2. Plots of $e^{-\lambda t}n(x, t)$ for the numerical solution (top) vs the analytic solution (bottom) with $\lambda = g$, $G(x) = x$, $B(x) = x$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-4)^2}$.

5.6 shows the periodic oscillatory behaviour in the time domain that we proved analytically in Chapter 3.

Example 3

We now consider the degenerate first order case from Chapter 4. For this example we also have an explicit solution (equation (4.16)) that can be used for comparison. As an exponential growth example, we know that solutions oscillate time wise.

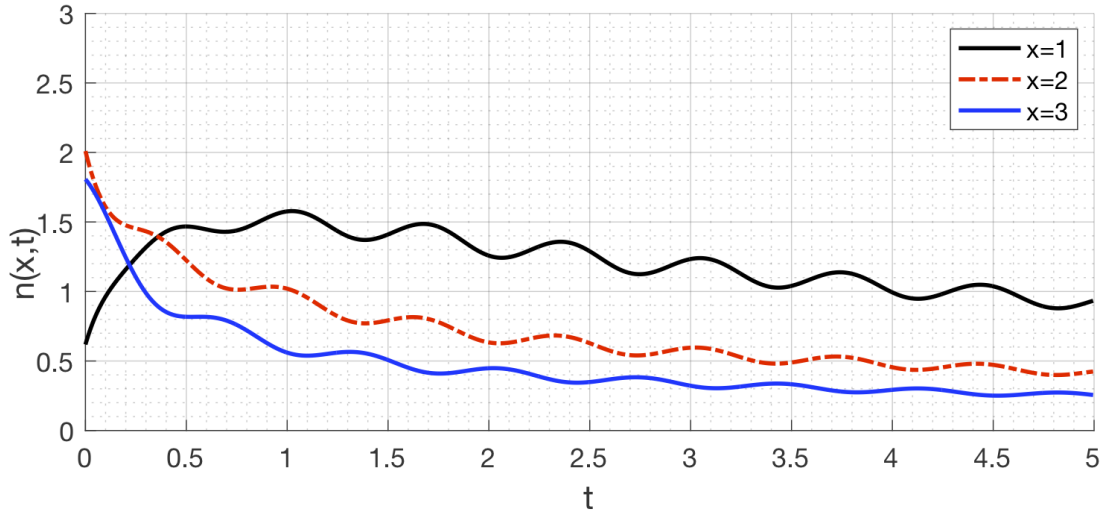
(a) Numerical solution with step size $\Delta x = 0.01$ and $\Delta t = 0.000005$.

(b) Analytical solution

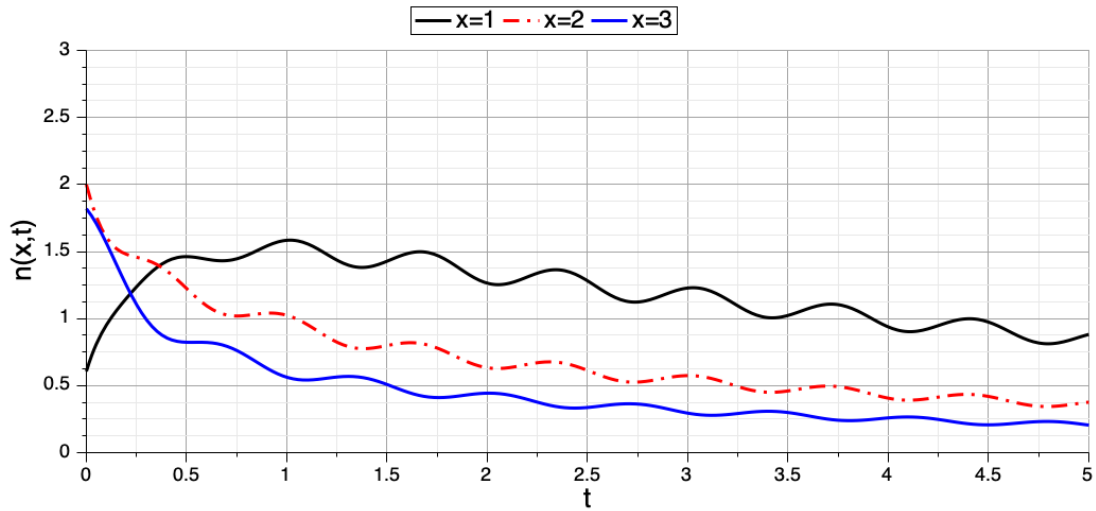
FIGURE 5.7: Example 3. The numerical solution vs the analytical solution with $G(x) = x$, $B(x) = 1$, $\alpha = 2$ and initial distribution $n_0(x) = xe^{-0.5(x-2)^2}$.

Let $G(x) = x$, $B(x) = 1$ and $n_0(x) = xe^{-0.5(x-2)^2}$ over the space $x \in [0, 20]$, $t \in [0, 5]$ with step size $\Delta x = 0.01$ and $\Delta t = 0.000005$. We observed in this case that there are notable numerical errors for large values of x as t increases, and for that reason the discretised space is minimised spatially and time wise to get an acceptable view of the numerical solution. Not surprisingly, one can observe from comparing the numerical solution (Figure 5.7.a) with the analytical one (Figure 5.7.b) that the approximation is less accurate as n approaches $t = 5$. The approximation, however, still captures some of the main solution properties.

For example, as time increases, the non zero values of n tend towards the t axis. We can also capture the long time asymptotic behaviour of solution as shown in



(a) Numerical evaluation with $\Delta t = 0.000005$ and $\Delta x = 0.01$.



(b) Analytical evaluation.

FIGURE 5.8: Example 3. Plots for $e^{-(\lambda t)}n(x, t)$ of the numerical solution vs the analytical solution with $\lambda = b(\alpha - 1)$, $G(x) = x$, $B(x) = 1$, $\alpha = 2$ and initial distribution $n_0(x) = xe^{-0.5(x-2)^2}$.

Figure 5.8.a. The numerical evaluation shows no sign of a long time attracting PDF solution in agreement with the analytical solution in Figure 5.8.b.

Example 4

We now consider the second order case. For this example, Efendiev *et al.* [27] obtained an analytical solution and showed that solutions converge to the SSD solution derived by Wake *et al.* [73] with an exponential rate of convergence.

Let $D = 1$, $G(x) = 1$ and $B(x) = 1$ over $x \in [0, 30]$ and $t \in [0, 25]$ with step size $\Delta x = 0.02$, $\Delta t = 0.0001$ and an initial distribution $n_0(x) = e^{-0.5(x-5)^2}$. The analysis in [27] indicates that the long time solution dynamics for this case is affected by the dispersion term. Indeed, we observe the influence of the dispersion term on the solution behaviour for this case in comparison with Example 1 (the dispersion free case). We see that the solutions approach an SSD after $n(x, 3)$ (Figure 5.3) in the first order case, while in the second order case, this occurs faster, just after $n(x, 1)$ (Figure 5.9). We also see that the long time asymptotic behaviour of solution for fixed x tends to a steady state in the second order case faster than that of Example 1 (cf. Figure 5.4 with Figure 5.10).

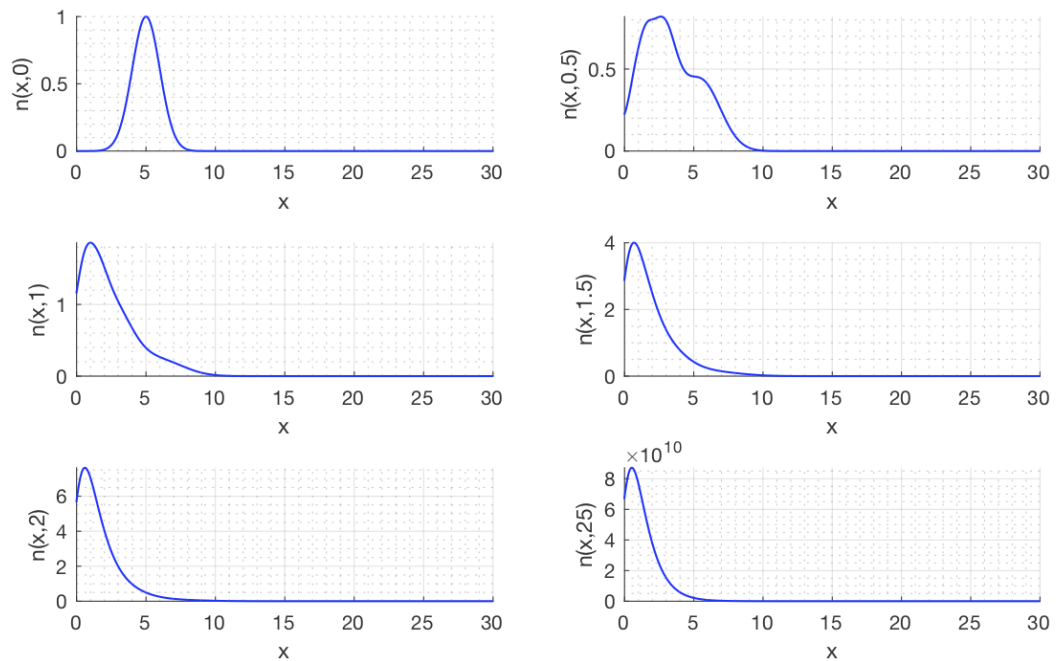


FIGURE 5.9: Example 4. Numerical solution with $D = 1$, $G(x) = 1$, $B(x) = 1$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-5)^2}$.

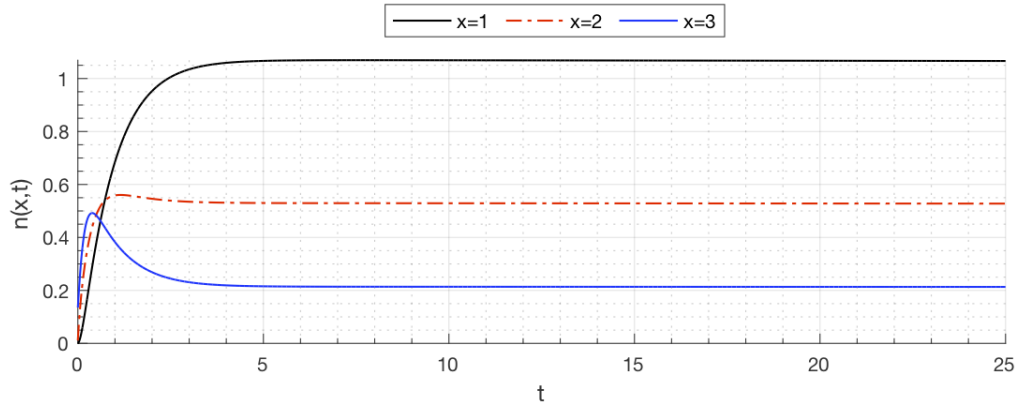


FIGURE 5.10: Example 4. Numerical evaluation for $e^{\lambda t}n(x, t)$ with $\lambda = b(\alpha - 1)$, $D = 1$, $G(x) = 1$, $B(x) = 1$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-5)^2}$.

5.4 The second order degenerate case (SODC)

In this section, we consider the second order degenerate case (SODC) from Chapter 4 with constants D and $B(x)$, and linear $G(x)$. Here, the initial condition is given by $n_0(x) = e^{-(x-5)^2}$, and the space is discretised over $x \in [0, 150]$ and $t \in [0, 35]$ with step size $\Delta x = 0.05$ and $\Delta t = 0.00001$. Note that there will be occasions where the solution space may be truncated spatially or temporally when relatively sufficient information is captured for the solution behaviour. For this case, we do not have detailed analytical results for the long time solution dynamics, but we can use some of the analytical results to study solution properties.

We know from Section 4.2.2.1 that there is no separable PDF solution to equation (4.48) that meets the boundary conditions (4.49) and (4.50) if

$$g > \alpha b \ln(\alpha), \quad (5.20)$$

is satisfied. Let $g = 0.3$, $b = 0.2$ and $\alpha = 2$. Then the inequality (5.20) is satisfied. We look at the effect of the dispersion on the solution.

Let $D = 0.08$. The numerical approximation is depicted in Figure 5.11. The

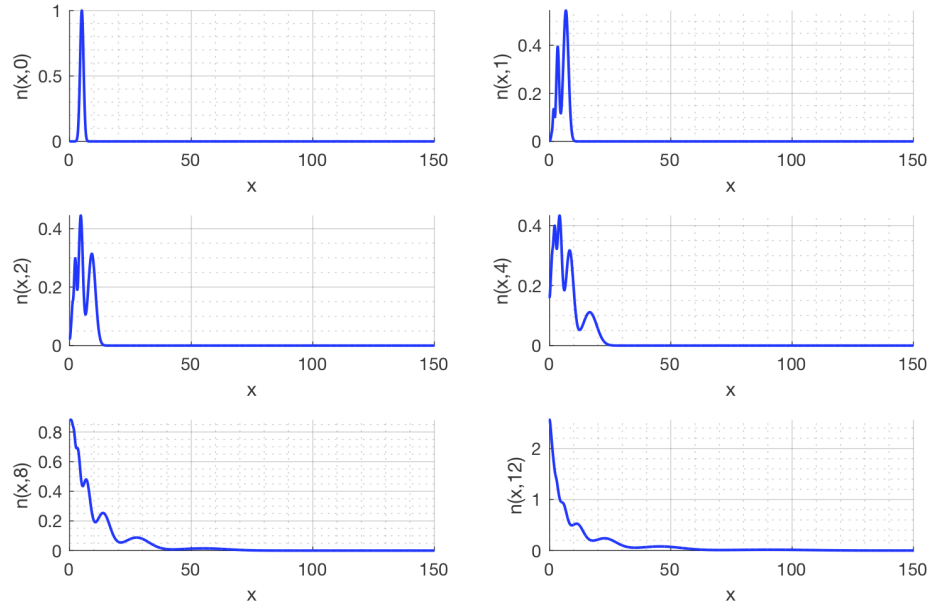


FIGURE 5.11: The SODC. Numerical solution with $D = 0.08$, $G(x) = 0.3x$, $B(x) = 0.2$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

approximation suggests that there is no (at least rapid) convergence towards an SSD, which agrees with the argument in Section 4.2.2.1. We observe in this case that the long time asymptotic behaviour of solution (Figure 5.12) decays towards zero (no steady state) for fixed values of x . Moreover, we observe the influence of

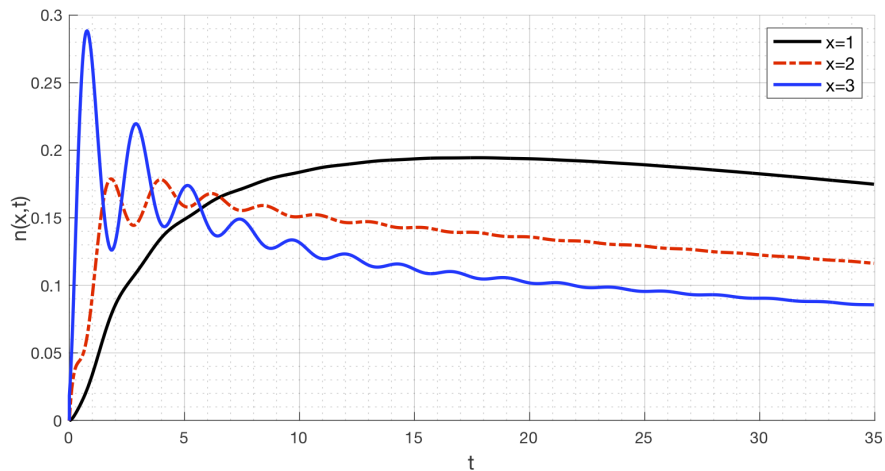


FIGURE 5.12: The SODC. Numerical evaluation for $e^{-\lambda t}n(x,t)$ with $\lambda = b(\alpha - 1)$, $D = 0.08$, $G(x) = 0.3x$, $B(x) = 0.2$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

D in that the local maxima compressed towards zero seen in Figure 5.7 Example 3 (for the first order case) notably stretch out spatially in this case as time evolves.

Now let $D = 0.5$. The numerical evaluation is shown in Figure 5.13. In

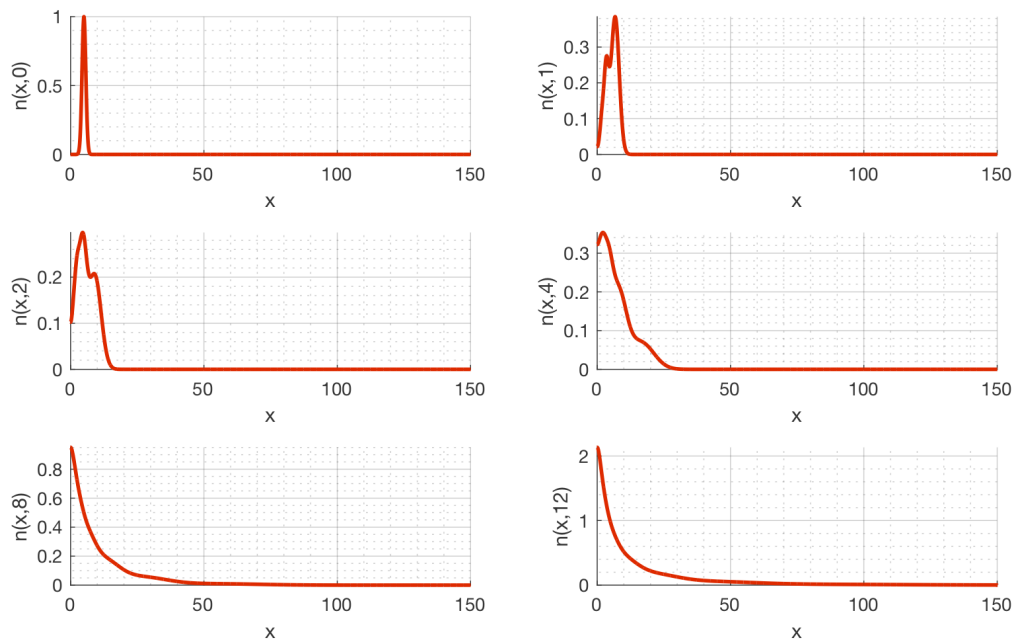


FIGURE 5.13: The SODC. Numerical solution with $D = 0.5$, $G(x) = 0.3x$, $B(x) = 0.2$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

this case, the approximation suggests that there is a PDF separable solution, in disagreement with the analysis in Section 4.2.2.1. This is seen, in particular, at about $n(x,8)$, at which point the oscillatory character of solution begins to smooth out, and the solution thereafter tends to a nearly steady shape. However, Figure 5.14 suggests that the long time attracting solution does not gravitate towards an SSD. We observe in this case that the dispersion term notably damps the oscillations, spatially (Figure 5.13) and time wise (Figure 5.14), seen in the previous case with D small.

Now, we consider, for example, the coefficients $g = 0.2$ and $b = 0.3$ with $\alpha = 2$ such that the inequality

$$g < ab \ln(\alpha) \quad (5.21)$$

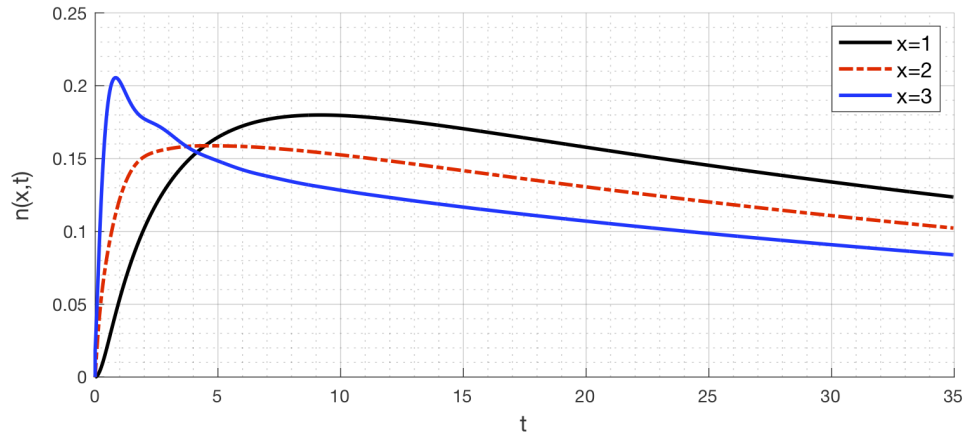


FIGURE 5.14: The SODC. Numerical evaluation for $e^{-\lambda t}n(x, t)$ with $\lambda = b(\alpha - 1)$, $D = 0.5$, $G(x) = 0.3x$, $B(x) = 0.2$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

is satisfied.

Let $D = 0.08$. In this scenario, the numerical solution depicted by Figure 5.15, on one hand, suggests that there are no classical PDF solutions. In fact, the approximation appears to converge to a shape close to a Dirac delta type

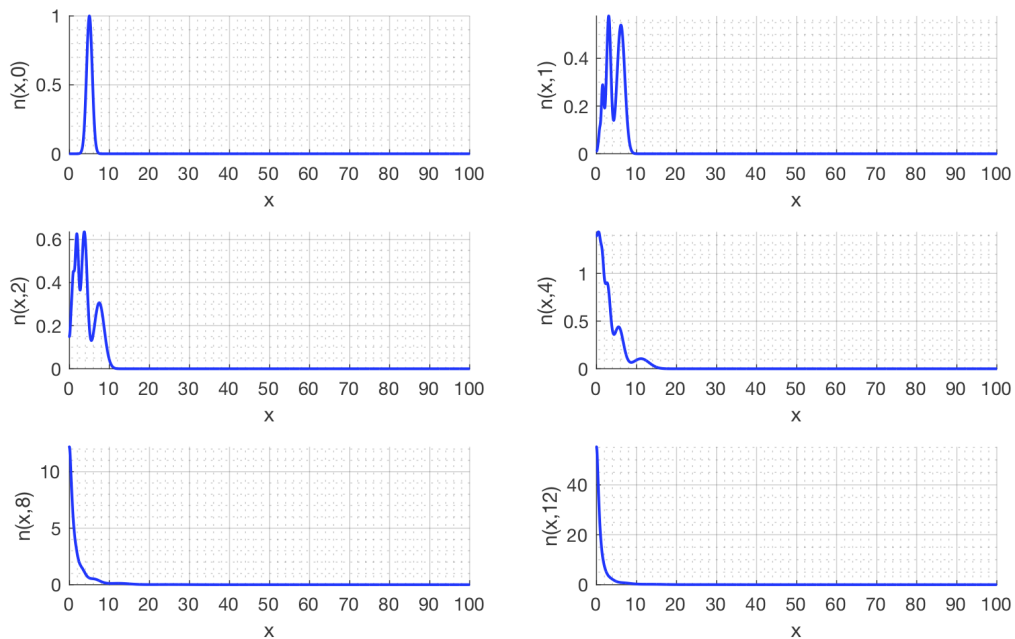


FIGURE 5.15: The SODC. Numerical solution with $D = 0.08$, $G(x) = 0.2x$, $B(x) = 0.3$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

solution as time evolves. On the other hand, the long time asymptotic behaviour

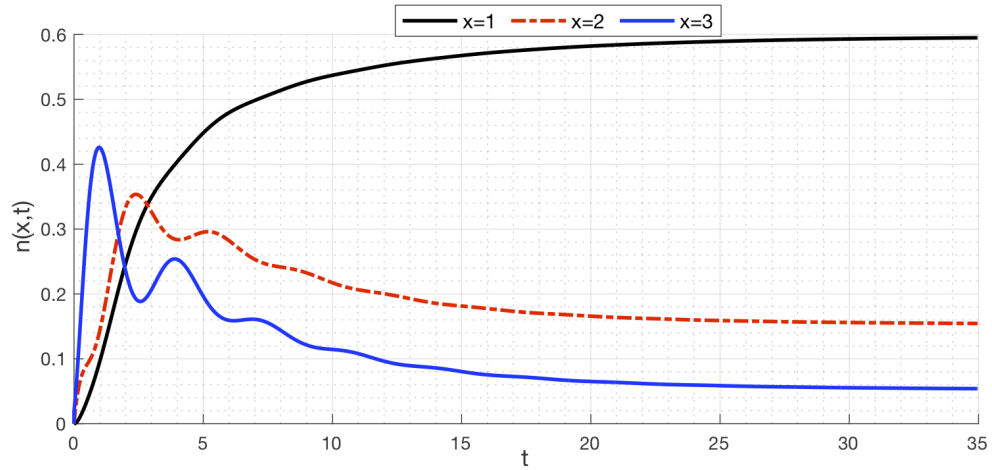


FIGURE 5.16: The SODC. Numerical evaluation for $e^{-\lambda t}n(x, t)$ with $\lambda = b(\alpha - 1)$, $D = 0.08$, $G(x) = 0.2x$, $B(x) = 0.3$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

of solution (Figure 5.16) appears to approach a steady state near $t = 30$ for fixed values of x .

Let $D = 0.5$. In contrast, the numerical solution depicted in Figure 5.17 suggests that there is a solution rapidly approaching an SSD. In addition, the

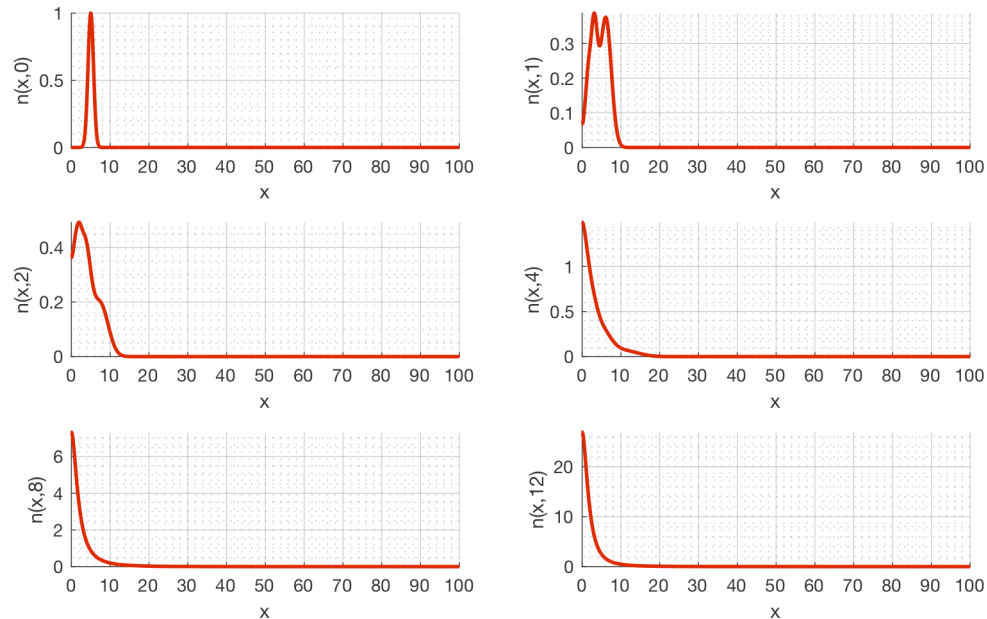


FIGURE 5.17: The SODC. Numerical solution with $D = 0.5$, $G(x) = 0.2x$, $B(x) = 0.3$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

numerical evaluation for the long time solution dynamics for fixed values of x (Figure 5.18) indicates that solutions tend to a steady state (before $t = 26$) more rapidly and with much fewer oscillations than the previous case with D small.

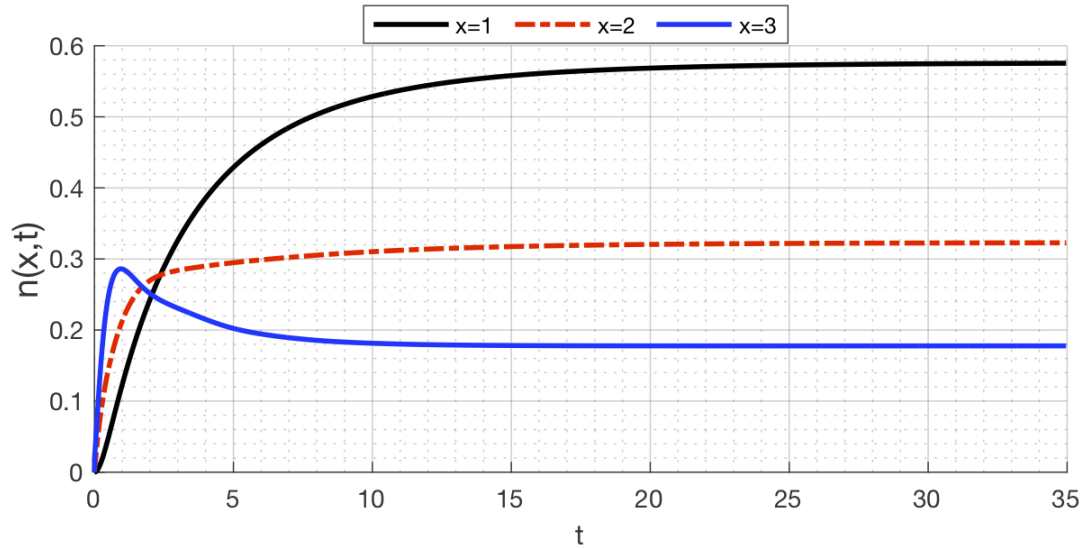


FIGURE 5.18: The SODC. Numerical evaluation for $e^{-\lambda t}n(x,t)$ with $\lambda = b(\alpha - 1)$, $D = 0.5$, $G(x) = 0.2x$, $B(x) = 0.3$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-(x-5)^2}$.

5.5 Discussion

We used the forward-time (of a first order derivative) centred-space (of a second order derivative) finite difference approximation method to find numerical solutions for special cases of equation (4.1). We utilised results from former studies to validate the method.

Here, we looked at a limited sample of the first order and second order equations. Although results for most of these cases were known analytically, the final degenerate case is still open. Our numerical experiments are in agreement with the analysis when inequality (5.20) is satisfied and the dispersion term is small. For D large, it is less clear and a PDF type solution may be available, though not

of the separable type. Regardless whether we have D large or small, the numerical solution with (5.20) is satisfied, suggests that there is no long time attracting solution. If inequality (5.21) is satisfied, the numerical approximation suggests that there is a tendency towards an SSD for D , and that there are long time attracting solutions. One common and remarkable feature is that the dispersion term appears to affect the oscillatory character of solutions and in some cases damps them completely.

We can also observe this damping behaviour when we add a dispersion term to the equation in Chapter 3. Let $D = 0.01$, $G(x) = x$, $B = x$ and $n_0(x) = e^{-\frac{(x-4)^2}{2}}$ over the space $x \in [0, 15]$ and $t \in [0, 15]$ with $\Delta x = 0.01$ and $\Delta t = 0.000005$. The numerical solution in Figure 5.19 suggests a rapid convergence to PDF solutions after $n(x, 3)$. The analytical study of the long time asymptotic behaviour for this case is still open.

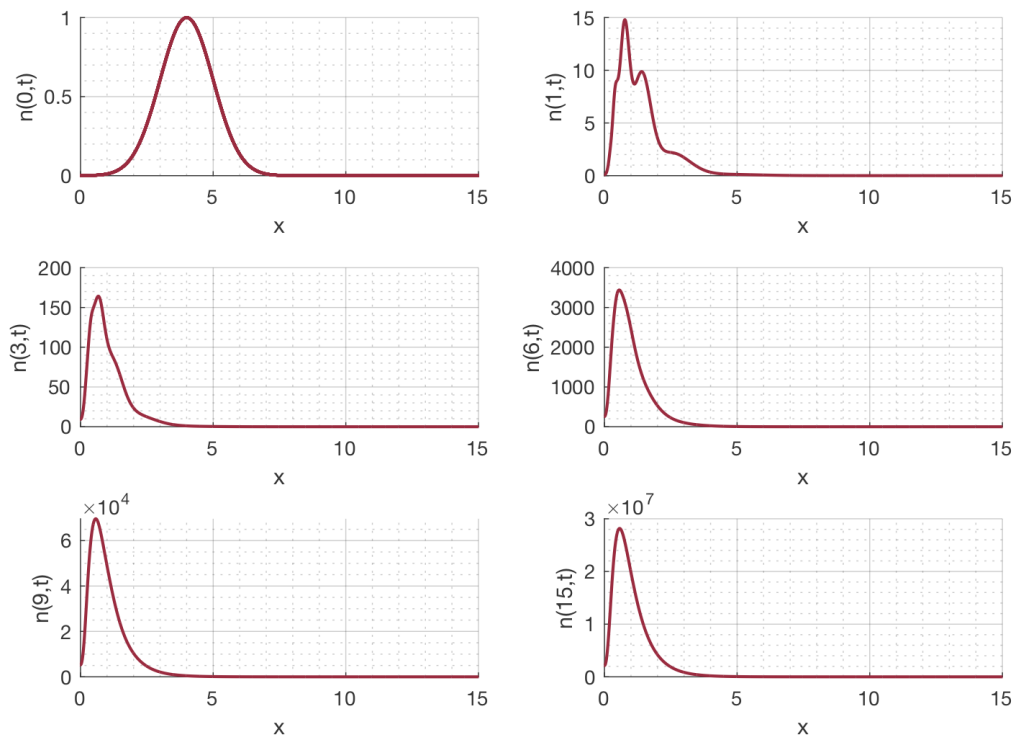


FIGURE 5.19: Numerical solution with $D = 0.01$, $G(x) = x$, $B(x) = x$, $\Delta x = 0.01$, $\Delta t = 0.000005$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-4)^2}$.

The numerical method can be exploited to look at further cases, for instance, the deterministic growth model studied by van Brunt *et al.* [67], in which the growth rate is constant but the division rate models cells which divide only after they reach a minimum size where there is no upper bound on the size. In their model, the growth and division rates are modelled by $G(x) = g$ and $B(x) = bH(x - c)$, respectively, where H is the Heaviside function, c stands for the minimum size at which a cell will divide, and g and b (as before) are positive constants. They show in this case that a class of PDF separable solutions $y(x)$ of Dirichlet type ($D(x, \lambda)$) satisfies the problem within a limited spectrum given by $b < \lambda < \alpha b$ under rapid a decay condition as $x \rightarrow \infty$. Here,

$$y(x) = \begin{cases} 0, & x \in [0, c/\alpha), \\ kb\alpha^2 e^{-(\lambda-b)x} \int_{c/\alpha}^x e^{(\lambda-b)\xi} D(\alpha\xi, \lambda) d\xi, & x \in [c/\alpha, c), \\ kD(x, \lambda), & x \in (c, \infty), \end{cases} \quad (5.22)$$

in which λ is regarded as an eigenvalue, k is some constant used to normalise $y(x)$ and

$$D(x, \lambda) = e^{-\lambda x} + \sum_{k=1}^{\infty} \frac{(-1)^k (\alpha^2 b)^k}{\lambda^k \prod_{m=1}^k (\alpha^m - 1)} e^{-\lambda \alpha^k x}.$$

General solutions to the IBVP in this case remain to be explored.

Let $G(x) = 1$, $B(x) = 1$, $c = 4$, $\alpha = 2$ and $n_0(x) = e^{-0.5(x-8)^2}$ for $x \in [0, 16]$ and $t \in [0, 18]$. The numerical solution is given in Figure 5.20. The sequence of graphs indicates that the numerical solution is converging almost to a steady shape after about $t = 12$, which has similar characteristics to the separable solution derived in [67]. In particular, the solution is not smooth at the points c/α and c , as soon as the solution transients approach $t = 6$. At these points, Figure 5.20 indicates that a non trivial, non PDF general solution may exist within $[c/\alpha, c)$ and in the interval (c, ∞) a general PDF solution may be available. The long time asymptotic behaviour relies on knowing the eigenvalue(s). (The uniqueness of an eigenvalue has yet to be established.)

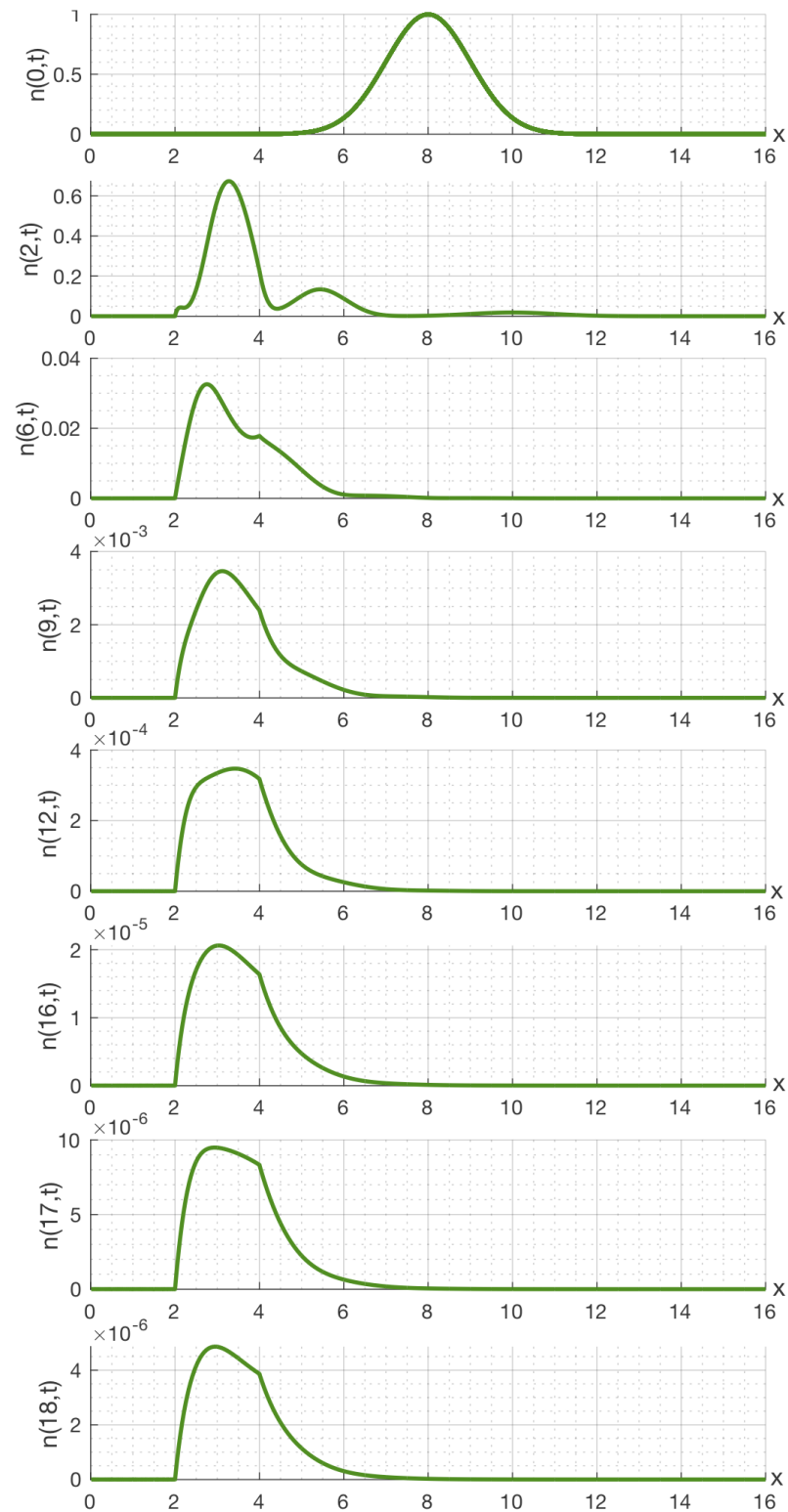


FIGURE 5.20: Numerical solution with $D = 0$, $G(x) = 1$, $B(x) = H(x - 4)$, $\Delta x = 0.01$, $\Delta t = 0.000001$, $\alpha = 2$ and initial distribution $n_0(x) = e^{-0.5(x-8)^2}$.

Other cases to look at, for instance, if the population is restricted and/or what happens if the variance is proportional to the size, modelling uncertainty in growth rate. Finally, one can improve the numerical accuracy using higher order finite difference approximations, or employ more advanced numerical methods. It remains to use these numerical results as guidance to develop analytical methods for studying those problems in the future.

Chapter 6

Conclusions

In this thesis we developed solution techniques to a class of cell division problems with growth and splitting rates given by $G(x) = gx$ and $B(x) = bx^r$, respectively, where g and b are positive constants, and $r \geq 0$. We used these methods to study certain properties of solutions, most notably their long time asymptotic behaviour. The problems are of an initial-boundary value type involving either a first order non local PDE (deterministic growth) or a second order PDE (stochastic growth).

In Chapter 3, we constructed a general solution to the IBVP with zero dispersion and exponential growth when $r > 0$, using the Mellin transform, and showed that this solution is unique and positive. We used the explicit solution to study the long time asymptotic behaviour in detail, and show the oscillatory character, associated to this type of problem (cf. [12]). We showed that the source of the oscillatory terms in the long time asymptotic behaviour comes from the absence of a dominant eigenvalue to Problem A. We proved that the long time attracting solution to Problem A converges to a product of the separable solution in [33] and a function that is periodic in time and depends on the initial condition. We showed that this solution converges exponentially in a weighted L^1 norm as

$t \rightarrow \infty$. We provided some illustrations to examine the influence of the initial data.

In Chapter 4, we derived solutions for the critical case when $r = 0$ with and without a dispersion term. The separable solution to the PDE plays a central rôle for SSDs. In the case of linear growth, solutions approach the separable solution as $t \rightarrow \infty$. For exponential growth, solutions oscillate in time around the separable solution. For the degenerate cases, we have shown that no (classical) separable PDF solution exists. This is in contrast with exponential growth when $r > 0$. In this case, a PDF separable solution always exists. The absence of a PDF separable solution for the first order degenerate case, along with the analytical solution, indicates that solutions do not approach a (classical) SSD.

We have also shown for the second order case that there are no PDF separable solutions when

$$g > ab \ln(\alpha).$$

This result, along with the numerical evidence of the previous chapter, suggests that solutions do not approach an SSD when the above inequality is satisfied. If

$$g < ab \ln(\alpha),$$

then the numerical evidence is less clear. Here, it may be that for a suitable range of D , there are attracting solutions. This is a potential direction for future work.

For exponential growth, when $D > 0$ and $r > 0$, the numerical evidence suggests that the dispersion damps the oscillations so it may be that, with dispersion added, the long time asymptotic behaviour of solutions loses its oscillatory character. This is also a direction for future work.

Bibliography

- [1] Almalki, A. “An Initial-Boundary Value Problem Arising in a Cell population Growth Modelling.” MSc thesis, University of Massey, 2012.
- [2] Ames, W. F. *Numerical Methods in Partial Differential Equations*. 3rd Ed., Academic Press, 1992.
- [3] Anderson, E. C., et al. “Cell Growth and Division. IV. Determination of Volume Growth Rate and Division Probability.” *Biophysical Journal*, vol. 9, no. 2, 1969, pp. 246–263. doi:10.1016/S0006-3495(69)86383-6.
- [4] Anderson, E. C., and D. F. Petersen. “Cell Growth and Division. II. Experimental Studies in Mammalian Suspension Cultures.” *Biophysical Journal*, vol. 7, no. 4, 1967, pp. 353–364. doi:10.1016/S0006-3495(67)86593-7.
- [5] Andrews, G. E. *The Theory of Partitions*. Cambridge University Press, 1998.
- [6] Basse, B., et al. “On a Cell-Growth Model for Plankton.” *Mathematical Medicine and Biology: A Journal of the IMA*, vol. 21, no. 1, 2004, pp. 49–6. doi:10.1093/imammb/21.1.49.
- [7] Begg, R. “Cell-Population Growth Modelling and Nonlocal Differential Equations.” PhD Thesis, University of Canterbury, 2007.
- [8] Begg, R., et al. “On the Stability of Steady Size-Distributions for a Cell-Growth Process with Dispersion.” *Differential and Integral Equations*, vol. 21, 2008, pp. 1–24. url:<https://projecteuclid.org/443/euclid.die/1356039056>.
- [9] Bell, G. I., and E. C. Anderson. “Cell Growth and Division. I. A Mathematical Model with Applications to Cell Volume Distributions in Mammalian

- Suspension Cultures.” *Biophysical Journal*, vol. 7, no. 4, 1967, pp. 329–351. doi:10.1016/S0006-3495(67)86592-5.
- [10] Bell, G. I. “Cell Growth and Division: III. Conditions for Balanced Exponential Growth in a Mathematical Model.” *Biophysical Journal*, vol. 8, no. 4, 1968, pp. 431–444. doi:10.1016/S0006-3495(68)86498-7.
- [11] Bellman, R., and K. L. Cooke. *Differential-Difference Equations*. Academic Press, 1963.
- [12] Bernard, É., et al. “Cyclic Asymptotic Behaviour of a Population Reproducing by Fission into Two Equal Parts.” *Kinetic and Related Models*, vol. 12, no. 3, 2019, pp. 551–571. doi:10.3934/krm.2019022.
- [13] Beysens, D., et al. *Fragmentation Phenomena: Proceedings of the Workshop, Les Houches 12-17 April 1993*. World Scientific, 1995.
- [14] Borok, V., and J. Zitomirskii. “The Cauchy Problem for Linear Partial Differential Equations with Linear Transformed Arguments”. *Soviet Mathematics Doklady*, vol. 12, 1971, pp. 1412–1416.
- [15] Bujorianu, L. M. *Stochastic Reachability Analysis of Hybrid Systems*. Springer, 2012.
- [16] Collins, J. F., and M. H. Richmond. “Rate of Growth of *Bacillus Cereus* Between Divisions.” *Journal of general microbiology*, vol. 28, 1962, pp. 15–33. doi:10.1099/00221287-28-1-15.
- [17] Conlon, I., and M. Raff. “Differences in the Way a Mammalian Cell and Yeast Cells Coordinate Cell Growth and Cell-Cycle Progression.” *Journal of Biology*, vol. 2, no. 1, 2003. doi:10.1186/1475-4924-2-7.
- [18] Cooper, G. M. *The Cell: A Molecular Approach*. ASM Press, 2000.
- [19] Cooper, J. M. *Introduction to Partial Differential Equations with MATLAB*. Birkhäuser Boston, 2012.
- [20] Da Costa, F. P., et al. “Unimodality of Steady Size Distributions of Growing Cell Populations.” *Journal of Evolution Equations*, vol. 1, no. 4, 2001, pp. 405–409. doi:10.1007/pl00001379.

- [21] Derfel, G., and J. Zitomirskii. “Behaviour at Zero of the Solutions of Functional Differential Equations.” *Theory Funct. Funct. Anal. Appl.* [*Teor. Funktsii, Funktsional Anal. i Prilozhen*, published in Russian], N31, 1979, pp. 44–49.
- [22] Diekmann, O. “The Dynamics of Structured Populations: Some Examples.” *Mathematics in Biology and Medicine. Lecture Notes in Biomathematics, Bari, Italy, July 18-22, 1983*: Proceedings, edited by Capasso V., Grosso E. & Paveri-Fontana, S. L., Springer, 1985. doi:10.1007/978-3-642-93287-8_2.
- [23] Diekmann, O., et al. “On the Stability of the Cell Size Distribution.” *Journal of Mathematical Biology*, vol. 19, no. 2, 1984, pp. 227–248. doi:10.1007/bf00277748.
- [24] Doumic, M., and B. van Brunt. “Explicit Solution and Fine Asymptotics for a Critical Growth-Fragmentation Equation.” *ESAIM: Proceedings and Surveys*, vol. 62, 2018, pp. 30–42. doi:10.1051/proc/201862030.
- [25] Doumic, M., and M. Escobedo. “Time Asymptotics for a Critical Case in Fragmentation and Growth-Fragmentation Equations.” *Kinetic and Related Models*, vol. 9, no. 2, 2016, pp. 251–297. doi:10.3934/krm.2016.9.251.
- [26] Doumic, M., and P. Gabriel. “Eigenelements of a General Aggregation-Fragmentation Model.” *Mathematical Models and Methods in Applied Sciences*, vol. 20, no. 5, 2010, pp. 757–783. doi:10.1142/S021820251000443X.
- [27] Efendiev, M., et al. “A Functional Partial Differential Equation Arising in a Cell Growth Model with Dispersion.” *Mathematical Methods in the Applied Sciences*, vol. 41, no. 4, 2018, pp. 1541–1553. doi:10.1002/mma.4684.
- [28] Faires, J. D., and R. L. Burden. *Numerical Methods*. 4th Ed., Cengage Learning, 2012.
- [29] Flajolet, P., et al. “Mellin Transforms and Asymptotics: Harmonic Sums.” *Theoretical Computer Science*, vol. 144, no. 1-2, 1995, pp. 3–58. doi:10.1016/0304-3975(95)00002-e.

- [30] Fredrickson, A. G., et al. “Statistics and Dynamics of Prokaryotic Cell Populations.” *Mathematical Biosciences*, vol. 1, no. 3, 1967, pp. 327–374. doi:10.1016/0025-5564(67)90008-9.
- [31] Hall, B. K. *Evolutionary Developmental Biology*. 2nd Ed., Kluwer Academic Publishers, 1999.
- [32] Hall, A. J., and G. C. Wake. “A Functional Differential Equation Arising in Modelling of Cell Growth.” *The Journal of the Australian Mathematical Society. Series B. Applied Mathematics*, vol. 30, no. 4, 1989, pp. 424–435. doi:10.1017/s0334270000006366.
- [33] Hall, A. J., and G. C. Wake. “Functional Differential Equations Determining Steady Size Distributions for Populations of Cells Growing Exponentially.” *The Journal of the Australian Mathematical Society. Series B. Applied Mathematics*, vol. 31, no. 4, 1990, pp. 434–453. doi:10.1017/s0334270000006779.
- [34] Hall, A. J., et al. “Steady Size Distributions for Cells in One-Dimensional Plant Tissues.” *Journal of Mathematical Biology*, vol. 30, no. 2, 1991, pp. 101–123. doi:10.1007/bf00160330.
- [35] Hall, A. J. “Steady Size Distributions in Cell Populations.” PhD thesis, University of Massey, 1991.
- [36] Heijmans, H. J. A. M. “On the Stable Size Distribution of Populations Reproducing by Fission into Two Unequal Parts.” *Mathematical Biosciences*, vol. 72, no. 1, 1984, pp. 19–50. doi:10.1016/0025-5564(84)90059-2.
- [37] Heijmans, H. J. A. M. “An Eigenvalue Problem Related to Cell Growth.” *Journal of Mathematical Analysis and Applications*, vol. 111, no. 1, 1985, pp. 253–280. doi:10.1016/0022-247x(85)90215-x.
- [38] Hritonenko, N., and Y. Yatsenko. *Mathematical Modeling in Economics, Ecology and the Environment*. Springer US, 2013.
- [39] Isaacson, E., and H. B. Keller. *Analysis of Numerical Methods*. Dover Publications, New York, 1994.

- [40] Iserles, A. “On the Generalized Pantograph Functional-Differential Equation”. *European Journal of Applied Mathematics*, vol. 4, no. 1, 1993, pp. 1–38. doi:10.1017/s0956792500000966.
- [41] Kato, T., and J. B. McLeod. “The Functional-Differential Equation $y'(x) = ay(\lambda x) + by(x)$.” *Bulletin of the American Mathematical Society*, vol. 77, no. 6, 1971, pp. 891–937. doi:10.1090/s0002-9904-1971-12805-7.
- [42] Kim, H. K. “Advanced Second Order Functional Differential Equations.” PhD thesis, University of Massey, 1998.
- [43] Koch, A. L., and M. Schaechter. “A Model for Statistics of the Cell Division Process.” *Journal of General Microbiology*, vol. 29, no. 3, 1962, pp. 435–454. doi:10.1099/00221287-29-3-435.
- [44] Malthus, T. R. *An Essay on the Principle of Population*. St. Paul’s London, 1798.
- [45] McKendrick, A. G. “Applications of Mathematics to Medical Problems.” *Proceedings of the Edinburgh Mathematical Society*, vol. 44, 1926, pp. 98–130., doi:10.1017/S0013091500034428.
- [46] Metz, J. A. J., and O. Diekmann. *The Dynamics of Physiologically Structured Populations*. Springer-Verlag, Berlin, 1986.
- [47] Michel, P. “Existence of a Solution to the Cell Division Eigenproblem.” *Mathematical Models and Methods in Applied Sciences*, vol. 16, no. supp01, 2006, pp. 1125–1153. doi:10.1142/s0218202506001480.
- [48] Michel, P. et al. “General Relative Entropy Inequality: an Illustration on Growth Models.” *Journal de Mathématiques Pures et Appliquées*, vol. 84, no. 9, 2005, pp. 1235–1260. doi:10.1016/j.matpur.2005.04.001.
- [49] Mitchison, S. M. *The Biology of the Cell Cycle*. Cambridge University Press, 1971.
- [50] Morgan, D. O. *The Cell Cycle: Principle of Control*. New Science Press, 2007.

- [51] Morgan, D. R. “A Remarkable Sequence Derived from Euler Products.” *Journal of Mathematical Physics*, vol. 41, no. 10, 2000, pp. 7109–7212. doi:10.1063/1.1290380.
- [52] Murray, A., and T. Hunt. *The Cell Cycle: An Introduction*. Oxford University Press, 1993.
- [53] Øksendal, B. *Stochastic Differential Equations: An Introduction with Applications*. 5th Ed., Springer, 2000.
- [54] Oster, G., and Y. Takahashi. “Models for Age-Specific Interactions in a Periodic Environment.” *Ecological Monographs*, vol. 44, no. 4, 1974, pp. 483–501. doi:10.2307/1942451.
- [55] Perthame, B., and L. Ryzhik. “Exponential Decay for the Fragmentation or Cell-Division Equation.” *Journal of Differential Equations*, vol. 210, no. 1, 2005, pp. 155–177. doi:10.1016/j.jde.2004.10.018.
- [56] Perthame B. *Transport Equations in Biology*. Birkhäuser, 2007.
- [57] Risken, H. *The Fokker-Planck Equation: Method of Solution and Applications*. 2nd Ed., Springer-Verlag, 1996.
- [58] Scherbaum, O., and G. Rasch. “Cell Size Distribution and Single Cell Growth in *Tetrahymena Pyriformis* Gl.” *Acta Pathologica Microbiologica Scandinavica*, vol. 41, no. 2, 1957, pp. 161–182. doi:10.1111/j.1699-0463.1957.tb01014.x.
- [59] Sharpe, F. R., and A. J. Lotka. “L. A Problem in Age-Distribution.” *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science*, vol. 21 no. 124, 1911, pp. 435–438. doi:10.1080/14786440408637050
- [60] Smith, G. D. *Numerical Solution of Partial Differential Equations*. 3rd Ed., Clarendon Press, 1985. ISBN: 9780198596509
- [61] Sinko, J., and W. Streifer. “A New Model for Age-Size Structure of a Population.” *Ecology*, vol. 48, no. 6, 1967, pp. 910–918. doi:10.2307/1934533.
- [62] Sinko, J., and W. Streifer. “A Model for Population Reproducing by Fission.” *Ecology*, vol. 52, no. 2, 1971, pp. 330–335. doi:10.2307/1934592.

- [63] Thieme, H. R. *Mathematics in Population Biology*. Princeton University Press, 2003.
- [64] Tucker, S. L., and S. O. Zimmerman. “A Nonlinear Model of Population Dynamics Containing an Arbitrary Number of Continuous Structure Variables.” *SIAM Journal on Applied Mathematics*, vol. 48, no. 3, 1988, pp. 549–591. doi:10.1137/0148032.
- [65] Turner, J. J., et al. “Cell Size Control in Yeast.” *Current Biology*, vol. 22, no. 9, 2012, pp. R350–R359. doi:10.1016/j.cub.2012.02.041.
- [66] Van Brunt, B., et al. “On a Cell Division Equation with a Linear Growth Rate.” *The ANZIAM Journal*, vol. 59, no. 3, 2018, pp. 293–312. doi:10.1017/s1446181117000591.
- [67] Van Brunt, B., et al. “A Cell Growth Model Adapted for The Minimum Cell Size Division.” *The ANZIAM Journal*, vol. 57, no. 2, 2015, pp. 138–149. doi:10.1017/s1446181115000218.
- [68] Van Brunt, B., and M. Vlieg-Hulstman. “An Eigenvalue Problem Involving a Functional Differential Equation Arising in a Cell Growth Model.” *The ANZIAM Journal*, vol. 51, no. 4, 2010, pp. 383–393. doi:10.1017/s1446181110000866.
- [69] Van Brunt, B., and M. Vlieg-Hulstman. “Eigenfunctions Arising From a First-Order Functional Differential Equation in a Cell Growth Model.” *The ANZIAM Journal*, vol. 52, no. 1, 2010, pp. 46–58. doi:10.1017/s1446181110000575.
- [70] Van Brunt, B., et al. “On a Singular Sturm-Liouville Problem Involving an Advanced Functional Differential Equation.” *European Journal of Applied Mathematics*, vol. 12, no. 6, 2001, pp. 625–644. doi:10.1017/s0956792501004624.
- [71] Van Brunt, B., and G. C. Wake. “A Mellin Transform Solution to a Second-Order Pantograph Equation with Linear Dispersion Arising in a Cell Growth Model.” *European Journal of Applied Mathematics*, vol. 22, no. 2, 2011, pp. 151–168. doi:10.1017/s0956792510000367.

- [72] Von Foerster, H. “Some Remarks on Changing Populations.” *The Kinetics of Cellular Proliferation*, edited by Stohlman, J. F., Grune and Stratton, New York, 1959, pp. 382–407.
- [73] Wake, G. C., et al. “Functional Differential Equations for Cell-growth Models with Dispersion.” *Communications in Applied Analysis*, vol. 4, 2000, pp. 561–574.
- [74] Webb, G. F. “Population Models Structured by Age, Size, and Spatial Position.” *Population Models in Biology and Epidemiology. Lecture Notes in Mathematics*, edited by Magal P., Ruan S., vol. 1936, 2008, Springer-Berlin, pp. 1–49. doi:10.1007/978-3-540-78273-5_1.
- [75] Zaidi, A. “Mathematics of Cell Growth.” PhD Thesis, University of Massey, 2014.
- [76] Zaidi, A. et al. “Solutions to an Advanced Functional Partial Differential Equation of the Pantograph Type.” *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences*, vol. 471, no. 2179, 2015, p. 20140947. doi:10.1098/rspa.2014.0947.
- [77] Zikanov, O. *Essential Computational Fluid Dynamics*. Wiley, 2011.



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STATEMENT OF CONTRIBUTION DOCTORATE WITH PUBLICATIONS/MANUSCRIPTS

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