A theoretical analysis of certain types of nonlinear evolution equations with applications

R Guiem

orcid.org 0000-0001-6086-1353

Thesis submitted in fulfilment of the requirements for the degree

Doctor of Philosophy in Applied Mathematics

at the North-West University

Promoter: Prof SC Oukouomi Noutchie

Co-promoter: Dr RY M'pika Massoukou

Graduation: April 2019

Student number: 26561980

PREFACE

The work described in this thesis was carried out in the School of Mathematical and Statistical Sciences, North-West University, Mafikeng Campus, from February 2015 to August 2018, under the supervision of Professor Suares Clovis Oukouomi Noutchie and the co-supervision of Doctor Rodrigue Yves M'pika Massoukou.

This study is an original work of the author and has not previously been submitted in any form for any degree or diploma to any other tertiary institution. Where use has been made of the works of other authors, they duly have been acknowledged.

ABSTRACT

The aim of this study was to examine and analyse the existence results of a class of nonlinear evolution equations that describe various phenomena from different areas such as Biology, Physics and Chemistry.

First, the global dynamics of a coupled system of partial differential equations with ordinary differential equations modelling an SVEIR epidemic model with age-dependent vaccination was examined by constructing a Lyapunov functionals and application of Lasalle's invariance principle.

Next, the solvability of a nonlinear non-autonomous integro-differential equation describing coagulation-fragmentation processes with growth was investigated using a modified monotone method. Existence and uniqueness of results were obtained thanks to Gronwall inequality. In particular, a new concept of upper-lower solution was introduced and a comparison principle established.

Finally, the global existence of weak solutions of a nonlinear system, consisting of a differential equation, coupled with a non-autonomous integro-differential equation describing the dynamic of prion proliferation was established by employing a weak compactness method. It is assumed that polymers can split into two or more pieces at a certain rate that not only depends on the sizes of the polymers involved but also on time. The degradation and splitting rates were also considered to be unbounded.

DECLARATION 1 - PLAGIARISM

I, Richard GUIEM declare that:

1. The research reported in this thesis, except where otherwise indicated, is my original research:
2. This thesis has not been submitted for any degree or examination at any other university.
3. This thesis does not contain data, pictures, graphs or information from other authors, unless specifically acknowledged as being sourced from other persons.
4. This thesis does not contain the writing of other authors, unless specifically acknowledged as being sourced from other researchers. Where other written sources have been quoted,
   - Their words have been re-written but the general information attributed to them and acknowledged.
   - Where their exact words have been used, they have been italicised and placed in quotation marks, and acknowledged.
5. This thesis does not contain text, graphics or tables copied and pasted from the internet, unless specifically acknowledged, and the sources acknowledged in the thesis.

Signed: ....

DECLARATION 2 - PUBLICATIONS

Published papers:

—— A new method for solving coagulation-fragmentation equations;

—— A novel method for solving a coagulation-fragmentation model with growth; and

—— Global dynamics of an SVEIR model with age-dependent vaccination, infection and latency.

Manuscript in progress:

—— A non-autonomous prion model

Signed: ....

DEDICATION

I dedicate this thesis to my lovely wife,
Eugénie GUIEM,

my beloved mother,
Honorée MATALÉ KADÉ

and my dear father,
Jean Pierre KADÉ.

ACKNOWLEDGEMENTS

I am grateful to God Almighty, for the courage, strength and health received during my studies in the Republic of South Africa.

My profound gratitude goes to my promoter, Prof. S.C. Oukouomi Noutchie, for accepting me as his student and for introducing me to this research area. I appreciate his commitment, encouragement and the valuable advice received throughout my PhD studies.

I am deeply grateful to my co-promoter, Dr R.Y. M'pika Massoukou, for his valuable discussions and suggestions pertaining to this study.

I am thankful to the lecturers in the Department of Mathematics and the members of staff of the North-West University, for the support and for providing me with a conducive environment to carry out this research successfully. I take this opportunity to also thank the North-West University for the financial assistance received during my studies.

I would like to acknowledge the Rector of the University of Maroua, for allowing me to pursue this programme, not forgetting the financial assistance I received during my studies.

I also wish to thank Prof. Kolyang (UMa), Prof. D.E. Houpa Danga (UN), Dr O. Videme Bossou (UY1) and Dr Y. Kouakep Tchaptchie for their advice.

I am sincerely grateful to my colleagues in the Department of Computer Science and Telecommunications of the National Advanced School of Engineering, Maroua as well as the members of staff of the school for their encouragement.

To my wonderful family, thank you for your support, especially during the tough days. Special thanks go to my wife, Eugenie Guiem, my daughter, Eliora, my son, Elie, my father, Jean Pierre Kade, my mothers Matale and Madouli, my step-mother, Aminatou Baba, my brothers, sisters, step-brothers and step-sisters.

To all my brothers and sisters in the Lord Jesus Christ in Maroua and everyone who supported me in prayers, God bless you all.

Finally, I wish to thank my friends, relatives and acquaintances, who, in one way or another, contributed to the success of this study.

Contents

1 Introduction **1**

1.1 Epidemiological models of age-structured population 1

1.2 Coagulation fragmentation processes with growth 3

1.3 Outline of the study 5

2 Preliminary and auxiliary results **7**

2.1 Functional analysis 7

2.1.1 Gronwall's and Bellman's inequalities 7

2.1.2 Compactness results 8

2.2 Non-autonomous evolution equations 13

2.2.1 Linear evolution equations 14

3 Age-dependent SVEIR model **17**

3.1 Introduction 17

3.2 Preliminaries and existence of equilibria 22
3.2.1 Basic results 22
3.2.2 Equilibria and the basic reproduction number 30
3.3 Uniform persistence 33
3.4 Stability of equilibria 39
3.4.1 Local stability of equilibria 39
3.4.2 Global stability of equilibria 45

4 Monotone method 57

4.1 Introduction 57
4.2 Coagulation-fragmentation model 58
4.2.1 Description of the model 58
4.2.2 Comparison principle 60
4.2.3 Analysis of the problem 67
4.3 Coagulation-fragmentation model with growth 73
4.3.1 Preliminaries 73
4.3.2 Existence and uniqueness of the solution 83

5 Non-autonomous prion model 90

5.1 Introduction 90

5.2 Preliminaries 90

5.2.1 Description of the model 91

5.2.2 Previous results 93

5.2.3 Assumptions 95

5.3 Global existence of a weak solution 96

6 Conclusion 105

Bibliography 107

Chapter 1

Introduction

The aim of this study was to explore existence results in some Banach spaces, of some classes of first order differential equations such as a coupled system of partial differential equations and ordinary differential equations, a scalar integro-differential and a coupled system of integro-differential equations which remain a subject of discussion and investigation in the literature. The main concerns were equations arising in epidemiology (SVEIR epidemic, prion replication) and in non-autonomous transport-coagulation-fragmentation theory. To achieve this goal, epidemiological models of age-structured population and coagulation-fragmentation were introduced.

1.1 Epidemiological models of age-structured population

Epidemiological models for the transmission of diseases generally divide the population into subclasses of diseases such as susceptible, vaccinated, exposed, infective, removed or immune. In addition, for the purpose of accuracy, several epidemic models add some structure to the model such as size, spatial location or age. Age is one of the key factors in the study of infectious diseases population models since individuals from different age groups may differ from one another with regard to size, survival capacities, behaviour, reproduction or exposition. Furthermore, according to different age groups, some infectious diseases may also have different infections and mortality rates [11]. For example, chicken pox is spread mainly by interaction between children of the same age group while most cases of HIV-AIDS occur among adults or teenagers. In this regard, in a population structured by age, it is crucial to specify the contact rates between members of the population, which will depend on the age of individuals.

One of the most important considerations in formulating an age-structured population model is to find a suitable mathematical setting for the model. In this study, the Banach space L^1 was chosen, since the physical interpretation of the density function requires that it should be integrable, and the mathematical treatment of the model requires that the density functions belong to a complete normed vector space. In addition, the L^1 norm of the density is a natural measure of the size of the population.

In other to formulate this approach, we denote by $u(t,a) = (u_1(t,a), \cdots u_n(t,a))^{\mathrm{T}}$ where $u_i(t,a)$ is the density function with regard to age at time t of the i^{th} subclass of a population divided into n subclasses, with age $a \in [0, A)$, $A \leq \infty$ and time $t \in \mathbb{R}_+$ and T denotes the transpose. The density $u(t,a)$ is given by an equation that can be a discrete-time model (when time is regarded as a discrete variable) or a continuous time model (when time is regarded as a continuous variable). Such models are called evolution equations and are constructed by balancing the change of the system in time against its age (generally spatial) behaviour. Thus, in the continuous case, $\int_{a_1}^{a_2} u(t,a)\,da$ accounts for the number of individuals according to their ages, between a_1 and a_2 at time t. The total population of the system at time t is given by the formula $N(t) = \int_0^\infty u(t,a)\,da$. The average rate of change in the total size of the population in the time interval $(t, t+h)$ is given by:

$$\frac{N(t+h)-N(t)}{h} = \frac{1}{h}\int_0^h u(t+h,a)\,da + \frac{1}{h}\int_0^\infty [u(t+h,a+h) - u(t,a)]\,da. \tag{1.1}$$

As $h \to 0$, the term on the left-hand side converges to the instantaneous rate of change of the total size of the population at time t, the first term on the right converges to the instantaneous birth rate at time t, and the last term on the right-hand side converges to the instantaneous rate of change of the total population at time t due to causes other than births.

This leads to the following general formulation of age-structured population model (see [72]):

$$\frac{dN(t)}{dt} = F(u(t,\cdot)) + \int_0^\infty G(u(t,a))\,da, \tag{1.2}$$

where $F(u(t,\cdot))$ accounts for the birth rate at time t and $\int_0^\infty G(u(t,a))\,da$ denotes the rate of change of total population $N(t)$ at time t due to causes other than births.

Depending on the considered subclasses, one can easily identify from (1.2), the form of F and G for the proposed SVEIR epidemic model (3.1) in Chapter 3.

The asymptotic behaviour of the equilibria (disease-free equilibrium and endemic equilibrium) of the population's dynamic is one of the fundamental properties in the study of epidemics in a population. Lyapunov functions play a very important role in carrying out the global stability of the equilibria. The basic reproduction number, as a threshold parameter, plays a fundamental role in mathematical modelling for infectious diseases and allows one to predict whether an infectious disease spreads in a given susceptible population when introduced into the host population.

1.2 Coagulation fragmentation processes with growth

Coagulation-fragmentation processes with growth describe the dynamics of enlarging particles under the combined effect of aggregation and breakage. Multiple fragmentation, in this case, is observed in the situation where each particle can grow and divide into many pieces (generally more than two). The particles can be, for instance, stellar fragment, polymer chains and are represented by a variable $x > 0$, which may refer to mass, size and concentration. These phenomena occur in applied sciences such as in rock fracture, droplet break-up, evolution of phytoplankton aggregate, polymerization and depolymerization. In 1957, Melzak derived the first (autonomous) coagulation-fragmentation equation without growth [47]. The equation was formulated as follows:

$$\begin{aligned}\partial_t w(t,x) = -w(t,x)\int_0^x \frac{y}{x}\beta(x,y)\,dy + \int_x^\infty \beta(y,x)w(t,y)dy \\ +\frac{1}{2}\int_0^x \kappa(x-y,y)w(t,x-y)w(t,y)dy \\ -w(t,x)\int_0^\infty \kappa(x,y)w(t,y)dy,\end{aligned} \tag{1.3}$$

where $w(t,x)$ accounted for the distribution of particles of size x at time t. The fragmentation rate, $\beta(x,y)$, corresponds to the rate at which each particle of size y is obtained from the splitting of particle of size x. The function $\kappa(x,y)$, represents the rate at which particles of size x coalesce with particles of size y.

Under some assumptions on model parameters, Melzak established the global existence of a unique solution to (1.3), which is continuous, nonnegative and bounded. Later on, he also obtained existence results of the non-autonomous model derived from (1.3), where β and k were considered as time-dependent parameters. In recent years, the solvability of the problem described in (1.3) has been widely investigated in the literature (see [6, 12, 16, 39, 44, 45, 46, 52] and references herein) using various methods such as semigroup theory, methods of characteristic, numerical analysis method and, recently, the monotone method [33, 34]. Unless the autonomous case, where several results are found on the well-posedness of the coagulation-fragmentation model, there are only few authors who have investigated the well-posedness of the following general non-autonomous equation (see [14, 46] and references herein):

$$\begin{aligned}\partial_t u(t,x) + \partial_x(\tau(t,x)u(t,x)) + \mu(t,x)u(t,x) = -\alpha(t,x)u(t,x) \\ +\int_{x+x_0}^\infty \alpha(t,y)\beta(x|y)u(t,y)\,dy \\ +\frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)u(t,x-y)u(t,y)\,dy \\ -u(t,x)\int_{x_0}^\infty \kappa(x,y)u(t,y)\,dy, \quad (t,x)\in(0,T)\times(x_0,\infty)\end{aligned} \tag{1.4}$$

subject to the boundary condition

$$\tau(t,x_0)u(t,x_0) = \int_{x_0}^{\infty} \gamma(t,y)u(t,y)\,dy, \quad t \in [0,T). \tag{1.5}$$

The problem is considered in the Banach space L^1 for the same reasons mentioned in Section 1.1. The monotone method for non-autonomous evolution equation is one of the powerful tools for the investigation of well-posedness of (1.4)-(1.5). It consists of the construction of two sequences, that are nonnegative and monotone, known as lower and upper solutions. Thereafter, Gronwall's inequality and the comparison principle were used to establish the convergence of the above-mentioned sequences to a unique flow of the model.

1.3 Outline of the study

This study focuses on a certain class of first-order nonlinear evolution equations. The aim was to investigate the dynamics of such equations. In order to achieved the desired results, some methods based on stability theory in epidemiology and functional analysis were applied in the study. Although these methods are somewhat well-known, this study often required particular results. Hence, a summary of these accessory results is given in Chapter 2.

In Chapter 3, motivated by [71, 69], the researchers propose a new SVEIR epidemic model, with age-dependent vaccination, latency and infection originated from an existing SVEIR formulated in [75]. The proposed model consists of a coupled system of nonlinear ordinary and partial differential equations of the form (3.1)-(3.3), as given in Section 3.2. In this model, the waning vaccine-induced immunity depends on vaccination age and the vaccinated individuals can lose their immunity and, therefore, become susceptible again. In addition to the assumption based on age-dependence vaccination and vaccine-age-dependence waning vaccine-induced immunity as in [75], continuous age-structure in latency and infection and particular form of the incidence rate were considered. The aim was to construct Lyapunov functionals and apply Lasalle's invariance principle to investigate the global dynamic of the model. More precisely, the intention was to determine the basic reproduction number, $\Re_0$, which is an important threshold parameter from which one can obtain the global stability of disease-free equilibrium and endemic equilibrium.

In Chapter 4, the monotone method was used to investigate a non-autonomous transport-coagulation-fragmentation equation, with bounded model parameters. In the first part of this Chapter, we were concerned with the model without growth (4.1)-(4.2) while the last part deals with the transport model (4.21)-(4.23). In both cases, the method consists in constructing two nonnegative monotone sequences $(\underline{u}^k)$ and $(\overline{u}^k)$ defined as upper and lower solutions, respectively. By making use of the comparison principle and Gronwall's inequality, the convergence of $(\underline{u}^k)$ and $(\overline{u}^k)$ to a unique solution $u(t,x)$ of the model was established.

In Chapter 5, a Prion model with multiple fragmentations was considered. The model consists of an ordinary differential equation (5.1), coupled with a nonlinear non-autonomous integro-differential equation (5.2) subject to an initial condition (5.3) and a boundary condition (5.4). The degradation rate $\mu(t,x)$ and the fragmentation rate $\beta(t,x)$ are considered to be unbounded under the additional assumption $\mu(t,x)+\beta(t,x) \leq \rho(t,x)x^{\alpha}$. A weak compactness method was used, from functional analysis, to show the global existence of a weak solution of the model, generalising the works done in [62, 68] for autonomous prion model with binary splitting.

Chapter 2

Preliminary and auxiliary results

The purpose of this chapter is to provide some basic results on compact operators and non-autonomous evolution equations on Banach spaces, mostly without proof, for the convenience of later reference in subsequent chapters.

2.1 Functional analysis

2.1.1 Gronwall's and Bellman's inequalities

Gronwall's and Bellman's inequalities play a crucial role in the study of differential equations. Gronwall's inequality was first used to establish boundedness and stability of differential equations after the study by R. Bellman [19]. Gronwall's inequality led to a very important inequality named after Bellman.

It should be noted that these two important inequalities are used later in the study.

Theorem 2.1.1. (**Gronwall's ineguality**)

Let f, g and h be given functions from $[x_0, M)$ into $\mathbb{R}$, where $x_0 \in \mathbb{R}$ and $M \leq \infty$. If f is continuous, $g \in L^{\infty}_{loc}([x_0, M))$, $h \in L^{1}_{loc}([x_0, M); \mathbb{R}_+)$ and

$$f(x) \leq g(x) + \int_{x_0}^{x} f(y)h(y)\,dy$$

for each $x \in [x_0, M)$*, then* $f(x) \leq g(x) + \int_{x_0}^{x} g(y)h(y) \exp\left(\int_y^x h(v)\,dv\right) dy$*, for each* $x \in [x_0, M)$*.*

Proof. See [32]. □

The spaces $L^{\infty}_{loc}([x_0, M))$ and $L^1_{loc}([x_0, M); \mathbb{R}_+)$ denote the space of locally measurable functions and essentially bounded $g : [x_0, M) \to \mathbb{R}$ and the space of locally integrable functions $h : [x_0, M) \to \mathbb{R}_+$, respectively.

In the particular case where $g(x) = c_0$, for $c_0 \geq 0$, Gronwall's inequality is reduced to the following Bellman's inequality:

Theorem 2.1.2. (**Bellman's inequality**)

Let f*, and* h *be given functions from* $[x_0, M)$ *into* $\mathbb{R}$*, where* $x_0 \in \mathbb{R}$ *and* $M \leq \infty$*. If* f *is continuous,* $h \in L^1_{loc}([x_0, M); \mathbb{R}_+)$*,* $c_0 \in \mathbb{R}_+$ *and*

$$f(x) \leq c_0 + \int_{x_0}^{x} f(y)h(y)\,dy$$

for each $x \in [x_0, M)$*, then*

$$f(x) \leq c_0 \exp\left(\int_{x_0}^{x} h(y)\,dy\right)$$

for each $x \in [x_0, M)$*.*

Proof. See [19, Lemma 1]. □

Next, some compactness results are given in some function spaces.

2.1.2 Compactness results

Some basic definitions are provided before stating the compactness results. In the following, we denote by X, a real Banach space and by $C(I, X)$, the space of all continuous functions from I into X, where I is a compact subset of $\mathbb{R}$. We also denote by $L^p(I, X)$, $1 \leq p < \infty$, the space of measurable functions $f : I \to X$ such that

$$\int_I \|f(t)\|_X^p\,dt < \infty.$$

Definition 2.1.3.

A subset K in a topological space is called:

(i) compact, if every generalised sequence in K has, at least, one generalised subsequence, which converges to some element of K;

(ii) sequentially compact, if every generalised sequence in K has, at least, one subsequence, which converges to some element of K;

(iii) relatively compact, if its closure $\bar{K}$ is compact;

(iv) relatively sequentially compact, if its closure $\bar{K}$ is sequentially compact.

Definition 2.1.4.

A subset K in a real Banach space X is called precompact (or totally bounded), if for all $\epsilon > 0$, there exists a finite subset $K_\epsilon \subset X$, such that K is included in the union of all closed balls, with radii ϵ and whose centres belong to K_ϵ.

Theorem 2.1.5.

Let X be a real Banach space.

(i) A subset K in X is relatively compact if and only if it is precompact.

(ii) A subset K in X is strongly relatively compact if and only if it is strongly relatively sequentially compact.

Proof. See [77, p.13].
(i) By using contrapositive, suppose K is not precompact (i.e. not totally bounded). Then there exist a positive real number ϵ and an infinite sequence $\{x_n\}$ of points belonging to K such that $d(x_i, x_j) \geq \epsilon$ for $i \neq j$. Then, if one cover the compact set $\bar{K}$ by a system of open spheres of radii $< \epsilon$, no finite subsystem of this system can cover $\bar{K}$. For, this subsystem cannot cover the infinite subset $\{x_i\} \subseteq K \subseteq \bar{K}$. Thus a relatively compact subset of X must be precompact.
Suppose, conversely, that K is precompact as a subset of the Banach space X. Then the

closure $\bar{K}$ is complete and is totally bounded with K. one has to show that $\bar{K}$ is compact. To this purpose, one shall first show that any infinite sequence $\{y_n\}$ of $\bar{K}$ contains a subsequence $\{y_{(n)'}\}$ which converges to a point of $\bar{K}$. Because of the total boundedness of K, there exist, for any $\epsilon > 0$, a point $z_\epsilon \in \bar{K}$ and a subsequence $\{y_{n'}\}$ of $\{y_n\}$ such that $d(y_{n'}, y_n) < \dfrac{\epsilon}{2}$ for $n = 1, 2, ...$; consequently, $d(y_{n'}, y_{m'}) \leq d(y_{n'}, z_\epsilon) + d(z_\epsilon, y_{m'}) < \epsilon$ for $n, m = 1, 2, ...$ one set $\epsilon = 1$ and obtain the sequence $\{y_{i'}\}$, and then apply the same reasoning as above with $\epsilon = 2^{-1}$ to this sequence $\{y_{i'}\}$. one thus obtains a subsequence $\{y_{n''}\}$ of $\{y_{n'}\}$ such that

$$d(y_{n'}, y_{m'}) < 1, \quad d(y_{n''}, y_{m''}) < \frac{1}{2} \quad (n, m = 1, 2, ...). \tag{2.1}$$

By repeating the process, one obtains a subsequence $\{y_{n^{(k+1)}}\}$ of the sequence $\{y_{n^{(k)}}\}$ such that

$$d(y_{n^{(k+1)}}, y_{m^{(k+1)}}) < \frac{1}{2^k}, \quad (n, m = 1, 2, ...). \tag{2.2}$$

Then the subsequence $\{y_{(n)'}\}$ of the original sequence $\{y_n\}$, defined by the diagonal method:

$$y_{(n)'} = y_{n^{(n)}}, \tag{2.3}$$

surely satisfies $\lim\limits_{n,m\to\infty} d(y_{n'}, y_{m'}) = 0$. Hence, by the completeness of $\bar{K}$, there must exist a point $y \in \bar{K}$ such that $\lim\limits_{n\to\infty} d(y_{(n)'}, y) = 0$.

Next, one shows that the set $\bar{K}$ is compact. One remark that there exists a countable family $\{F\}$ of open sets F of X such that, if U is any open set of X and $x \in U \cap \bar{K}$, there is a set $F \in \{F\}$ for which $x \in F \subseteq U$. This may be proved as follows. $\bar{K}$ being totally bounded, it can be covered, for any $\epsilon > 0$, by a finite system of open spheres of radii ϵ and centres belonging to $\bar{K}$. Letting $\epsilon = 1, 1/2, 1/3, ...$ and collecting the countable family of the corresponding finite systems of open spheres, one obtain the desired family $\{F\}$ of open sets.

Let now $\{U\}$ be any open covering of $\bar{K}$. Let $\{F^*\}$ be the subfamily of the family $\{F\}$ defined as follows: $F \subseteq \{F^*\}$ if and only if $F \subseteq \{F\}$ and there is some $U \in \{U\}$ with $F \subseteq U$. By the property of $\{F\}$ and the fact that $\{U\}$ covers $\bar{K}$, one sees that this countable family $\{F^*\}$ of open sets covers $\bar{K}$. Now let $\{U^*\}$ be a subfamily of $\{U\}$ obtained by selecting just one $U \in \{U\}$ such that $F \subseteq U$, for each $F \in \{F^*\}$. Then $\{U^*\}$ is a countable family of open sets which covers $\bar{K}$. One has to show that some finite subfamily of $\{U^*\}$ covers $\bar{K}$. Let the sets in $\{U^*\}$ be indexed as $U_1, U_2, ...$ Suppose that, for each n, the finite union $\bigcup_{j=1}^{n} U_j$ fails to cover $\bar{K}$. Then there is some point $x_n \in \left(K - \bigcup_{k=1}^{n} U_k\right)$. By what was proved above, the sequence $\{x_n\}$ contains a subsequence $\{x_{(n)'}\}$ which converges to a point, say x_∞, in $\bar{K}$. Then $x_\infty \in U_N$ for some index N, and so $x_n \in U_N$ for infinitely many values of n, in particular for an $n > N$. This contradicts the fact that x_n was chosen so that $x_n \in \left(K - \bigcup_{k=1}^{n} U_k\right)$. Hence one has proved that $\bar{K}$ is compact.

(ii) The proof of (ii) follows the same lines as those in (i). □

The compactness criterion of sets in the Banach space $X = L^P(\mathbb{R}_+)$, are obtained from the Fréchet-Kolmogorov theorem for the compactness of sets in $L^P(\mathbb{R})$ (see [77, X.1]).

Theorem 2.1.6.

Let K be a subset of $X = L^P(\mathbb{R}_+)$, $1 \le p \le \infty$. Then, K has a compact closure if and only if:

(i) $\sup_{g\in K} \int_0^\infty |g(s)|^p \, ds < \infty$;

(ii) $\lim_{r\to\infty} \int_r^\infty |g(s)|^p \, ds \to 0$ *uniformly for* $g \in K$;

(iii) $\lim_{h\searrow 0} \int_0^\infty |g(s+h) - g(s)|^p \, ds \to 0$ *uniformly for* $g \in K$;

(iv) $\lim_{h\searrow 0} \int_0^h |g(s)|^p \, ds \to 0$ *uniformly for* $g \in K$.

Proof. The proof is the same as in [77, Theorem (Fréchet-Kolmogorov)] by identifying $L^P(\mathbb{R}_+)$ with the space of functions in $L^P(\mathbb{R})$, which are 0 on the negative half-line. □

Definition 2.1.7.

A subset $\{u_n(\tau)\}_{n\ge1,\tau\in I}$ in X is called:

(i) equibounded on I, if

$$\sup_{n\ge1,\tau\in I} \|u_n(\tau)\| < \infty;$$

(ii) equicontinuous on I, if

$$\lim_{\delta \searrow 0} \sup_{n\geq 1,\, |\tau-\tau'|\leq \delta} \|u_n(\tau) - u_n(\tau')\| = 0.$$

Theorem 2.1.8. (**Arzelâ-Ascoli**)

A subset $\{u_n(\tau)\}_{n\geq 1, \tau\in I}$ in X is relatively compact in X if the following two conditions are satisfied:

(i) $u_n(\tau)$ is equibounded for each $n \geq 1$;

(ii) $u_n(\tau)$ is equicontinuous for each $n \geq 1$.

Proof. See [77, Theorem (Ascoli-Arzelà)].
From the Bolzano-Weierstrass theorem, a bounded sequence of real (or complex) numbers contains a convergent subsequence. Hence, for fixed $\tau \in I$, the sequence $\{u_n(\tau)\}_{n\geq 1}$ contains a convergent subsequence. On the other hand, since the space X is compact, there exists a countable dense subset $\{\tau_n\} \subseteq X$ such that, for every $\epsilon > 0$, there exists a finite subset $\{\tau_n : 1 \leq n \leq k(\epsilon)\}$ of $\{\tau_n\}$ satisfying the condition

$$\sup_{\tau_j \in X} \inf_{1\leq j\leq k(\epsilon)} d(\tau, \tau_j) \leq \epsilon.$$

The proof of this fact is obtained as follows. Since X is compact, it is totally bounded (i.e. precompact). Thus there exists, for any $\delta > 0$, a finite system of points belonging to X such that any point of X has a distance $\leq \delta$ from some point of the system. Letting $\delta = 1, 2^{-1}, 3^{-1}, ...$ and collecting the corresponding finite systems of points, one obtains a sequence $\{\tau_n\}$ with the stated properties. One then applies the diagonal process of choice to the sequence $\{u_n(\tau)\}$ so that one obtains a subsequence $\{u_{n'}\}$ of $\{u_n\}$ which converges for $\tau = \tau_1, \tau_2, ..., \tau_k, ...$ simultaneously. By the equicontinuity of $\{u_n(\tau)\}$, there exists, for every $\epsilon > 0$, a $\delta = \delta(\epsilon) > 0$ such that $d(\tau', \tau'') \leq \delta$ implies $|u_n(\tau') - u_n(\tau'')| \leq \epsilon$ for $n = 1, 2, ...$ Hence, for every $\tau \in X$, there exits a j with $j \leq k(\epsilon)$ such that

$$\begin{aligned} |u_{n'}(\tau) - u_{m'}(\tau)| &\leq |u_{n'}(\tau) - u_{n'}(\tau_j)| + |u_{n'}(\tau_j) - u_{m'}(\tau_j)| + |u_{m'}(\tau_j) - u_{m'}(\tau)| \\ &\leq 2\epsilon + |u_{n'}(\tau_j) - u_{m'}(\tau_j)| \end{aligned}$$

Thus $\lim\limits_{n,m\to+\infty} \max\limits_{\tau} |u_{n'}(\tau) - u_{m'}(\tau)| \leq 2\epsilon$, and so $\lim\limits_{n,m\to+\infty} \|u_{n'} - u_{m'}\| = 0.$ □

In the following, a variant of Arzelà-Ascoli's theorem is given.

Theorem 2.1.9. (**Arzelà-Ascoli**)

A subset K in $C(I, X)$ is relatively sequentially compact if and only if K is equicontinuous on I and there is a dense subset D in I such that for each $\tau \in D$, the set

$$K(\tau) := \{u(\tau); u \in K\}$$

is relatively compact in X.

Proof. See [67, Theorem 1.3.2]. □

Next, the following definition on uniformly integrability is given.

Definition 2.1.10. *A subset K in $L^p(I, X)$, with $1 \leq p \leq \infty$, is said to be uniformly integrable if K is bounded in $L^p(I, X)$.*

Theorem 2.1.11. (**Dunford-Pettis**)

A subset $(u_n)_{n\geq 1}$ in $L^1(I, X)$ is weakly relatively compact if and only if it is uniformly integrable.

Proof. See [24, p. 101]. □

In the next section, some important results on non-autonomous evolution equations are given.

2.2 Non-autonomous evolution equations

In this section, we review a natural generalisation of the following linear autonomous abstract Cauchy problem (ACP)

$$\begin{cases} \dfrac{du(t)}{dt} = Au(t), \quad t > 0, \\ \lim\limits_{t\to 0^+} u(t) = u_0, \end{cases} \tag{2.4}$$

where the fixed operator A is replaced by the time-dependent operator $A(t)$, for $t \in \mathbb{R}_+$.

2.2.1 Linear evolution equations

The following definition is stated.

Definition 2.2.1. (Non-autonomous Abstract Cauchy Problem)

Let X be a Banach space and $(A(t))_{t\geq 0}$ a family of bounded linear operators with domain $D(A(t))$ contained in X and also given an element $x \in X$. Then, the abstract problem

$$\begin{cases} \dfrac{du(t)}{dt} = A(t)u(t), \quad \text{for} \quad s, t \in \mathbb{R}, \quad t \geq s, \\ u(s) = x, \end{cases} \tag{2.5}$$

is called a non-autonomous Abstract Cauchy problem (nACP).

The classical solution of the nACP (2.5) can be defined as follows.

Definition 2.2.2.

Let $(A(t), D(A(t))$, for $t \in \mathbb{R}$, be linear operators on the Banach space X. A function u is said to be a classical solution to the nACP (2.5) *if:*

1. *for $s \in \mathbb{R}$ and $x \in D(A(s))$, $u = u(\cdot, s, x)$ is continuously differentiable on $[s, \infty)$ such that $u(t) \in D(A(t))$; and*
2. *u satisfies* (2.5) *for $t \geq s$.*

It should be recalled that the solutions of the linear autonomous ACP (2.4) are given by a strongly continuous semigroup $(S(t))_{t\geq 0}$ on X which satisfies the strongly continuity condition

$$\lim_{t \to 0^+} S(t)x = x \quad \text{for any } x \in X, \tag{2.6}$$

and the semigroup properties

$$\begin{cases} S(t+s) = S(t)S(s) \quad \text{for all } t, s \geq 0, \\ S(0) = I. \end{cases} \tag{2.7}$$

In the non-autonomous case, an evolution system $(U(t,s))_{t\geq s\in\mathbb{R}}$ is considered.

Remark 2.1. *The strongly continuous semigroup* $(S(t))_{t\geq 0}$ *on* X *is called a semigroup of contraction on* X *if*

$$\|S(t)\|_X \leq 1, \quad t \geq 0.$$

Definition 2.2.3. (**Evolution system**)

A system $(U(t,s))_{t\geq s\in\mathbb{R}}$ *of bounded linear operators on a Banach space* X *is said to be an evolution system (or evolution family or propagator) if:*

(i) for each $u \in X$*, the function* $(t,s) \mapsto U(t,s)u$ *is continuous for* $t \geq s \in \mathbb{R}$*;*

(ii) $U(t,s) = U(t,r)U(r,s)$*,* $U(t,t) = I$*, for* $t \geq r \geq s \in \mathbb{R}$*; and*

(iii) $\|U(t,s)\| \leq Ce^{\beta(t-s)}$*,* $t \geq s$ *for some constants* $C, \beta > 0$*.*

The evolution family is strongly continuous if:

(iv) $(t,s) \to U(t,s)$ *is strongly continuous for* $t \geq r \geq s \in \mathbb{R}$*, and is uniformly continuous whenever.*

It should be noted that a strongly continuous evolution family $(U(t,s))_{t\geq s\in\mathbb{R}}$ can be defined from a strongly continuous semigroup $(S(t))_{t\geq 0}$ as follows:

$$U(t,s) := S(t-s).$$

Proposition 2.2.4. *Let* X *be a Banach space and* Y_t *a subspace of* X*. The nACP* (2.5) *is well-posed on* Y_t *if and only if there is an evolution family solving* (2.5) *on* Y_t*.*

Proof. See [50, Section 3.2]. □

Remark 2.2. *By well-posedness of* (2.5)*, we mean existence, uniqueness and continuous dependence on the initial data.*

To every evolution family, one can associate strongly continuous semigroups on X-valued function spaces called evolution semigroups. Evolution semigroups completely characterise the behaviour of the evolution family and are given by:

Definition 2.2.5. (**Evolution semigroup**)

For every strongly continuous evolution family $(U(t,s))_{t\geq s\geq 0}$*, one defines the corresponding evolution semigroup* $(\mathscr{U}(t))_{t\geq 0}$ *on the space* $L^1(\mathbb{R},X)$ *by*

$$[\mathscr{U}(t)\psi](\theta) := U(\theta,\theta-t)\psi(\theta-t) \tag{2.8}$$

for $\psi \in L^1(\mathbb{R},X)$*,* $\theta \in \mathbb{R}$ *and* $t \geq 0$*. Its generator is denoted by* $(\mathscr{A}, D(\mathscr{A}))$*.*

Proposition 2.2.6. *The evolution semigroup* $(\mathscr{U}(t))_{t\geq 0}$ *defined on the space* $L^1(\mathbb{R},X)$ *by* (2.8) *is a strongly continuous semigroup on* $L^1(\mathbb{R},X)$*.*

Proof. See [28, Lemma 9.10].
It is easy to see that $(\mathscr{U}(t))_{t\geq 0}$ is a semigroup of bounded operators on $L^1(\mathbb{R},X)$ with $\|\mathscr{U}(t)\| \leq Me^{wt}$. For $f \in C_c(\mathbb{R},X)$, the space of continuous functions with compact support in $\mathbb{R}$, it is easy to see that $\mathscr{U}(t)f \to f$ in $L^1(\mathbb{R},X)$ as $t \to 0$. Since $C_c(\mathbb{R},X)$ is dense in $L^1(\mathbb{R},X)$, it implies strong continuity of $(\mathscr{U}(t))_{t\geq 0}$. □

Chapter 3

Global dynamics of an SVEIR model with age-dependent vaccination, infection and latency

3.1 Introduction

Protection induced by vaccines plays a significant role in preventing and reducing the transmission of infectious diseases. One of the greatest successes of vaccination is illustrated through the eradication of small-pox. It is reported in [75] that the case of small-pox was last recorded in 1977. Immunity conveyed by vaccination depends on different vaccines and vaccination policies – lifelong immunity occurs for certain vaccines while immunisation period is induced by some vaccines. However, waning vaccine-induced immunity takes place (naturally) after the immunisation process. It is reported in [53] that a significant decay in the proportion of chicken pox took place in the United States of America in 1995 after conducting a universal vaccination campaign. Surprisingly, new cases of chicken pox appeared mainly in highly vaccinated school communities in US. Some studies have been conducted and revealed waning vaccine-induced immunity in children under protection induced by vaccines. Moreover, this was also investigated in [22, 54, 55] and it was proved that such waning of immunity is attached to the time since vaccination and the age at vaccination. In this regard, it was published in [56, 73] that the time of vaccine-induced immunity depends on individual features and the age of the vaccine.

From the above-mentioned statements and citations, it is necessary to associate waning vaccine-induced immunity to vaccination in infectious disease models and interesting to investigate the impact of waning vaccine-induced immunity on the dynamics of infectious diseases. Many mathematical models on vaccination have already been investigated (see [20, 25, 41, 53, 60, 65, 70, 71, 74, 76]). Some of the models cited above considered either age-dependent vaccination, while some did not.

Despite vaccination age structure being the main and appropriate feature required in the dynamics of infectious diseases, with waning induced-vaccine immunity, most epidemiological models with vaccination, including waning induced-vaccine immunity, were studied after assuming a constant rate of immunity loss (see [41, 74, 25]). Age-dependent vaccination was considered in some epidemiological models studied recently in [26, 38, 40, 53, 69, 75]. However, some of these works considered either waning vaccine-induced immunity or not, either vaccine-age-dependent waning vaccine-induced immunity or not, either age-dependent latency or not, either age-dependent relapse or not, either age-dependent infection or not. In [26], an SVIR epidemic model with continuous age-dependent vaccination was formulated to establish the global stability of equilibria. In [38], an SVIJS epidemic model with age-dependent vaccination was considered to study the asymptotical behaviour of the equilibria, after assuming that age-dependent vaccine-induced immunity decays with time after vaccination. In [40], an SVIS epidemic model with age-dependent vaccination, vaccine-age-dependent waning vaccine-induced immunity and treatment was formulated to investigate backward bifurcations. In [53], an SVIR epidemic model with age of vaccination was considered to establish global stability of equilibria, after assuming that vaccine-induced immunity decays with time after vaccination. In [69], an SVEIR epidemic model with age-dependence vaccination, latency and relapse was formulated to established the global stability of the equilibria. In [75], a multi-group SVEIR epidemic model with latent class and age of vaccination was formulated to study global stability of equilibria, after assuming that vaccine-induced immunity decays with time after vaccination. Likewise, in [26, 38, 40].

Recently, in [71], an SVEIR epidemic model with continuous age-structure in the latent and infectious classes and without continuous age-structure in the vaccinated class was formulated to prove the global stability of equilibria; while in [69], an SVEIR epidemic model with continuous age-structure in the latent, infectious and recovered classes, and with vaccine-age-dependent waning vaccine-induced immunity was formulated. Moreover, in [71], the latency and infection ages are denoted by the same variable a. Similarly, in [69], the latency, relapse and vaccination ages are denoted by the same variable a. In spite of this, to the best of our knowledge, the global dynamics of an SVEIR epidemic model with continuous age-structure in latency, infection, vaccination and vaccine-age-dependence waning vaccine-induced immunity has not yet been neither considered nor investigated using the approach of Lyapunov fonctionals. The aim of this study is to fill this gap by investigating the global dynamics of an SVEIR epidemic model as defined above. Motivated by [69, 71], a new SVEIR epidemic model originated from an existing SVEIR formulated in [75] is proposed, by considering continuous age-structure in latency and infection in addition to age-dependence vaccination and vaccine-age-dependence waning vaccine-induced immunity [48] (which the authors took into account in [75]). However, the latency, infection and ages of vaccination are all denoted by a, as in [69, 71]. Moreover, in this chapter, a more significant incidence rate (taking into account tranmission by both age rate-mates infective individuals and infective individuals of any age) of the form

$$S(t)\int_0^\infty \left(K_0(a)i(a,t) + \int_0^\infty K(a,a^{'})i(a^{'},t)\,da^{'} \right) da$$

is also considered, where $K_0(a)$ and $K(a,a^{'})$ are defined below, instead of the classical incidence rate of the form

$$S(t)\int_0^\infty \beta(a)i(a,t)\,da,$$

where $\beta(a)$ denotes the coefficient of transmission of diseases from infective individuals, with age of infection a, to susceptible individuals. The latter is considered in the references herein where continuous age-structure in infection is taken into account.

The model splits the total population into five epidemiological groups as follows: the susceptible group; the vaccinated group; the latent group; the infected group; and the removed group. Let $R(t)$ and $S(t)$ be the number of individuals in the removed and susceptible groups at time t, respectively. Let $v(a,t)$, $e(a,t)$ and $i(a,t)$ be the density of vaccinated, (latently) infected and (actively) infected individuals with vaccination, latency and infection age a at time t, respectively. It follows that $V(t)$, $E(t)$ and $I(t)$ defined by

$$V(t) = \int_0^\infty v(a,t)\,da, \quad E(t) = \int_0^\infty e(a,t)\,da, \quad I(t) = \int_0^\infty i(a,t)\,da,$$

are the number of individuals in the vaccinated, latent and infected compartments, respectively.

The model investigated consists of a coupled system of nonlinear ordinary and partial differential equations of the form

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}S(t) &= \Lambda - (\nu + \mu^0)S(t) + \int_0^\infty \alpha(a)v(a,t)\,da \\
&\quad - S(t)\int_0^\infty \left(K_0(a)i(a,t) + \int_0^\infty K(a,a^{'})i(a^{'},t)\,da^{'} \right) da \\
\frac{\partial}{\partial t}v(a,t) &= -\frac{\partial}{\partial a}v(a,t) - \eta(a)v(a,t) \\
\frac{\partial}{\partial t}e(a,t) &= -\frac{\partial}{\partial a}e(a,t) - \varrho(a)e(a,t) \\
\frac{\partial}{\partial t}i(a,t) &= -\frac{\partial}{\partial a}i(a,t) - \sigma(a)i(a,t) \\
\frac{\mathrm{d}}{\mathrm{d}t}R(t) &= \int_0^\infty \gamma(a)i(a,t)\,da - \mu^0 R(t),
\end{aligned} \tag{3.1}$$

where $\eta(a) = \alpha(a) + \mu(a)$, $\varrho(a) = \varepsilon(a) + \mu(a)$, $\sigma(a) = \gamma(a) + \mu(a)$, with boundary conditions

$$\begin{aligned}
v(0,t) &= \nu S(t) \\
e(0,t) &= S(t)\int_0^\infty \left(K_0(a)i(a,t) + \int_0^\infty K(a,a^{'})i(a^{'},t)\,da^{'} \right) da \\
i(0,t) &= \int_0^\infty e(a,t)\varepsilon(a)\,da.
\end{aligned} \tag{3.2}$$

and initial conditions

$$
\begin{aligned}
&S(0) = S_0 > 0,\; v(a,0) = v_0(a) > 0,\; e(a,0) = e_0(a) > 0, \\
&i(a,0) = i_0(a) > 0,\; R(0) = R_0 > 0,
\end{aligned}
\tag{3.3}
$$

where S_0 and R_0 are initial size of susceptible and removed individuals, respectively, and $v_0(a)$, $e_0(a)$ and $i_0(a)$ are initial age-density of vaccinated, latent and infective individuals, respectively. Moreover, v_0, e_0 and i_0 are Lebesgue integrable functions, and it is assumed that the recruitment of newly vaccinated individuals in the vaccinated compartment is done at age zero.

The meaning of parameters in (3.1)-(3.2) is given below:

Λ	–	constant recruitment rate of susceptible individuals;
ν	–	rate of vaccination of susceptible individuals;
μ^0	–	natural mortality rate of individuals;
$\alpha(a)$	–	age-specific rate of waning vaccine-induced immunity;
$\mu(a)$	–	age-specific natural mortality rate;
$\gamma(a)$	–	age-specific removal rate;
$\varepsilon(a)$	–	age-specific rate moving from latent to infective;
$K_0(a)$	–	age-specific infection rate of susceptible individuals by infective individuals (of the same age – intracohort contagion); and
$K(a,a^{'})$	–	probability that an infective individual of age $a^{'}$ will successfully infect a susceptible individual of age a, after contact.

In the sequel, the following assumptions are made on parameters in (3.1)-(3.2)

A0 (i) $\Lambda, \nu, \mu^0 > 0$, with $\nu < \mu^0$.

(ii) $\alpha, \eta, \varrho, \sigma, \gamma, \varepsilon, K_0 \in \mathrm{L}^\infty_+(0,\infty)$ and $K \in \mathrm{L}^1\big((0,\infty), \mathrm{L}^\infty_+(0,\infty)\big)$ with essential upper bounds $\bar{\alpha}, \bar{\eta}, \bar{\varrho}, \bar{\sigma}, \bar{\gamma}, \bar{\varepsilon}, \bar{K}_0$ and $\bar{K}(a,\cdot)$, respectively.

(iii) $K_0(a), K(\cdot,a^{'}), \alpha(a), \gamma(a), \varepsilon(a)$ are Lipschitz continuous on $\mathbb{R}_+$ with coefficients $M_{K_0}, M_K, M_\alpha, M_\gamma, M_\varepsilon$, respectively.

(iv) There exists $\tilde{\mu} \in (0,\mu^0]$ such that $\eta(a) - \alpha(a), \varrho(a) - \varepsilon(a), \sigma(a) - \gamma(a) > \tilde{\mu}$.

A1: $\nu < \mu^0$;

A2: $R(\cdot)$ is a decreasing function of t for any constant removal rate γ^0 such that $\gamma^0 \geq \bar{\gamma}$;

A3: $\eta(a)\Lambda < (\eta(a) - \alpha(a)) \left(1 - \int_0^\infty \alpha(a) e^{-\int_0^a \eta(s)\, ds} da \right)$, for every a.

This chapter consists of five additional sections, including the introduction, structured as follows: In Section 3.2, some preliminary results on compactness property of the semi-flow generated by (3.1)-(3.2) are presented and its asymptotic smoothness property discussed. This section also deals with the existence of equilibria and the formulation of the threshold parameter $\Re_0$ (the basic reproduction number). The uniform persistence property of (3.1)-(3.2) is addressed in Section 3.3. Local and global stability of the steady states for (3.1) are examined in Section 3.4.

3.2 Preliminaries and existence of equilibria

3.2.1 Basic results

We consider the Banach space

$$\mathbb{X} = \mathbb{R} \times \mathrm{L}^1(0, \infty) \times \mathrm{L}^1(0, \infty) \times \mathrm{L}^1(0, \infty) \times \mathbb{R}$$

endowed with the norm

$$\|(x, \varphi, \psi, \phi, y)\|_{\mathbb{X}} = |x| + \|\varphi\|_1 + \|\psi\|_1 + \|\phi\|_1 + |y|,$$

where $\|\cdot\|_1 = \|\cdot\|_{\mathrm{L}^1}$, for any $(x, \varphi, \psi, \phi, y) \in \mathbb{X}$. Let us denote by $\mathbb{X}_+$, the positive cone of the Banach space $\mathbb{X}$ such that

$$\mathbb{X}_+ = \mathbb{R}_+ \times \mathrm{L}^1_+(0, \infty) \times \mathrm{L}^1_+(0, \infty) \times \mathrm{L}^1_+(0, \infty) \times \mathbb{R}_+.$$

For any initial value $\mathbf{X}_0 = (S_0, v_0(\cdot), e_0(\cdot), i_0(\cdot), R_0) \in \mathbb{X}_+$ satisfying the following conditions

$$v_0(0) = \nu S_0$$

$$e_0(0) = S_0 \int_0^\infty \left(K_0(a) i_0(a) + \int_0^\infty K(a,a^{'}) i_0(a^{'})\, da^{'} \right) da$$
$$i_0(0) = \int_0^\infty \varepsilon(a) e_0(a)\, da$$

the system (3.1) is well-posed, under assumption **A1**, due to [37]. Thus, a continuous semi-flow $\Phi : \mathbb{R}_+ \times \mathbb{X}_+ \to \mathbb{X}_+$ is obtained and defined by the (3.1) such that

$$\Phi(t, \mathbf{X}_0) = \Phi_t(\mathbf{X}_0) = (S(t), v(\cdot,t), e(\cdot,t), i(\cdot,t), R(t)), \quad t \in \mathbb{R}_+, \quad \mathbf{X}_0 \in \mathbb{X}_+. \tag{3.4}$$

Now, we introduce the functions

$$\chi(\alpha) = e^{-\int_0^a \eta(\tau)\, d\tau}, \quad \vartheta(\alpha) = e^{-\int_0^a \varrho(\tau)\, d\tau}, \quad \zeta(\alpha) = e^{-\int_0^a \sigma(\tau)\, d\tau}, \text{ for } \alpha \geq 0.$$

By integrating the second, third and fourth equations of (3.1) along the characteristic $t - a =$ constant, one obtains

$$v(a,t) = \begin{cases} v(0, t-a)\chi(a), & 0 \leq a \leq t, \\ v_0(a-t)\frac{\chi(a)}{\chi(a-t)}, & 0 \leq t \leq a, \end{cases} \quad , \qquad e(a,t) = \begin{cases} e(0, t-a)\vartheta(a), & 0 \leq a \leq t, \\ e_0(a-t)\frac{\vartheta(a)}{\vartheta(a-t)} & 0 \leq t \leq a, \end{cases}$$
$$i(a,t) = \begin{cases} i(0, t-a)\zeta(a), & 0 \leq a \leq t, \\ i_0(a-t)\frac{\zeta(a)}{\zeta(a-t)} & 0 \leq t \leq a, \end{cases} \tag{3.5}$$

where

$$\begin{aligned} v(0, t-a) &= \nu S(t-a) \\ e(0, t-a) &= S(t-a) \int_0^\infty \left(K_0(a) i(a, t-a) + \int_0^\infty K(a,a^{'}) i(a^{'}, t-a)\, da^{'} \right) da \\ i(0, t-a) &= \int_0^\infty \varepsilon(a) e(a, t-a)\, da. \end{aligned} \tag{3.6}$$

Taking the norm of $\Phi_t(\mathbf{X}_0)$ and using the positiveness of the components of $\Phi_t(\mathbf{X}_0)$, one obtains

$$\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}} = S(t) + \|v(\cdot,t)\|_1 + \|e(\cdot,t)\|_1 + \|i(\cdot,t)\|_1 + R(t). \tag{3.7}$$

Differentiating (3.7) with respect to t leads to

$$\frac{\mathrm{d}}{\mathrm{d}t}\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}} = \frac{\mathrm{d}S(t)}{\mathrm{d}t} + \frac{\mathrm{d}}{\mathrm{d}t}\|v(\cdot,t)\|_1 + \frac{\mathrm{d}}{\mathrm{d}t}\|e(\cdot,t)\|_1 + \frac{\mathrm{d}}{\mathrm{d}t}\|i(\cdot,t)\|_1 + \frac{\mathrm{d}R(t)}{\mathrm{d}t}. \tag{3.8}$$

Next, we seek for the estimates of each time-derivative on the right hand side (3.8). First, we have

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\|v(\cdot,t)\|_1 &= \frac{\mathrm{d}}{\mathrm{d}t}\left(\int_0^t v(0,t-a)\chi(a)\,da + \int_t^\infty v_0(a-t)\frac{\chi(a)}{\chi(a-t)}\,da\right)\\ &= \frac{\mathrm{d}}{\mathrm{d}t}\int_0^t v(0,s)\chi(t-s)\,ds + \int_0^\infty \frac{v_0(\varsigma)}{\chi(\varsigma)}\frac{\mathrm{d}}{\mathrm{d}t}\chi(t+\varsigma)\,d\varsigma.\end{aligned} \tag{3.9}$$

Applying the Leibniz Integral Rule to the first integral in (3.9) yields

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\|v(\cdot,t)\|_1 &= \chi(0)v(0,t) + \int_0^t v(0,s)\frac{\mathrm{d}}{\mathrm{d}t}\chi(t-s)\,ds + \int_0^\infty \frac{v_0(\varsigma)}{\chi(\varsigma)}\frac{\mathrm{d}}{\mathrm{d}t}\chi(t+\varsigma)\,d\varsigma\\ &= v(0,t) - \int_0^t v(0,s)\eta(t-s)\chi(t-s)\,ds\\ &\quad - \int_0^\infty v_0(\varsigma)\eta(t+\varsigma)\frac{\chi(t+\varsigma)}{\chi(\varsigma)}\,d\varsigma\\ &= \nu S(t) - \int_0^\infty \eta(a)v(a,t)\,da.\end{aligned} \tag{3.10}$$

Likewise, we also have

$$\frac{\mathrm{d}}{\mathrm{d}t}\|e(\cdot,t)\|_1 = e(0,t) - \int_0^\infty \varrho(a)e(a,t)\,da \tag{3.11}$$

and

$$\frac{\mathrm{d}}{\mathrm{d}t}\|i(\cdot,t)\|_1 = \int_0^\infty \varepsilon(a)e(a,t)\,da - \int_0^\infty \sigma(a)i(a,t)\,da. \tag{3.12}$$

Therefore, one obtains

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}&\left(S(t)+\|v(\cdot,t)\|_1+\|e(\cdot,t)\|_1+\|i(\cdot,t)\|_1+R(t)\right)\\&=\Lambda-\mu^0(S(t)+R(t))-\int_0^\infty(\eta(a)-\alpha(a))v(a,t)\,da\\&-\int_0^\infty(\varrho(a)-\varepsilon(a))v(a,t)\,da-\int_0^\infty(\sigma(a)-\gamma(a))i(a,t)\,da.\end{aligned}\tag{3.13}$$

Using (iv) of **A1**, (3.13) yields

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}&\left(S(t)+\|v(\cdot,t)\|_1+\|e(\cdot,t)\|_1+\|i(\cdot,t)\|_1+R(t)\right)\\&\leq\Lambda-\tilde{\mu}\left(S(t)+\|v(\cdot,t)\|_1+\|e(\cdot,t)\|_1+\|i(\cdot,t)\|_1+R(t)\right),\end{aligned}\tag{3.14}$$

that is,

$$\frac{\mathrm{d}}{\mathrm{d}t}\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}}\leq\Lambda-\tilde{\mu}\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}}.$$

Thus, we obtain

$$\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}}\leq\frac{\Lambda}{\tilde{\mu}}-e^{-\tilde{\mu}t}\left(\frac{\Lambda}{\tilde{\mu}}-\|\mathbf{X}_0\|_{\mathbb{X}}\right),$$

where $\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}}=\|\mathbf{X}_0\|_{\mathbb{X}}$.

If we consider the state space Γ of (3.1), defined by

$$\Gamma=\left\{(x,\varphi,\psi,\phi,y)\in\mathbb{X}_+:\ \|(x,\varphi,\psi,\phi,y)\|_{\mathbb{X}}\leq\frac{\Lambda}{\tilde{\mu}}\right\},\tag{3.15}$$

one obtains

$$\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}}\leq\frac{\Lambda}{\tilde{\mu}},$$

for any $t\geq 0$, whenever $\mathbf{X}_0\in\Gamma$. Moreover

$$\limsup_{t\to\infty}\|\Phi_t(\mathbf{X}_0)\|_{\mathbb{X}}\leq\frac{\Lambda}{\tilde{\mu}},$$

for any $\mathbf{X}_0\in\mathbb{X}_+$.

Then, the following results are stated:

Lemma 3.2.1. *The set Γ is positively invariant for Φ; that is,*

$$\Phi_t(\boldsymbol{X}_0)\subset\Gamma,\quad\forall t\geq 0,\quad \boldsymbol{X}_0\in\Gamma.$$

Moreover, $\Phi_t(\boldsymbol{X}_0)$ is point dissipative and the set Γ is an attractor in $\mathbb{X}_+$.

Since the aim is to use the Lasalle's Invariance Principle, we are required to establish the relative compactness of the orbit $\{\Phi_t(\mathbf{X}_0) : t \geq 0\}$ in $\mathbb{X}_+$ due to the infinite dimensional Banach space $\mathbb{X}$. For this, we consider the mappings Θ and Ψ, $(\Theta, \Psi : \mathbb{R}_+ \times \mathbb{X}_+ \to \mathbb{X}_+)$, such that

$$\begin{aligned} \Theta(t, \mathbf{X}_0) &= \Theta_t(\mathbf{X}_0) = (0, \tilde{\theta}_v(\cdot, a), \tilde{\theta}_e(\cdot, a), \tilde{\theta}_i(\cdot, a), 0) \\ \Psi(t, \mathbf{X}_0) &= \Psi_t(\mathbf{X}_0) = (S(t), \tilde{v}(\cdot, a), \tilde{e}(\cdot, a), \tilde{i}(\cdot, a), R(t)), \end{aligned} \tag{3.16}$$

where

$$\begin{aligned} \tilde{\theta}_v(a,t) &= \begin{cases} 0, & 0 \leq a \leq t, \\ \\ v(a,t), & 0 \leq t \leq a, \end{cases} \quad , \quad \tilde{v}(a,t) = \begin{cases} v(a,t), & 0 \leq a \leq t, \\ \\ 0 & 0 \leq t \leq a, \end{cases} \\ \tilde{\theta}_e(a,t) &= \begin{cases} 0, & 0 \leq a \leq t, \\ \\ e(a,t) & 0 \leq t \leq a, \end{cases} \quad , \quad \tilde{e}(a,t) = \begin{cases} e(a,t), & 0 \leq a \leq t, \\ \\ 0 & 0 \leq t \leq a, \end{cases} \\ \tilde{\theta}_i(a,t) &= \begin{cases} 0, & 0 \leq a \leq t, \\ \\ i(a,t) & 0 \leq t \leq a, \end{cases} \quad , \quad \tilde{i}(a,t) = \begin{cases} i(a,t), & 0 \leq a \leq t, \\ \\ 0 & 0 \leq t \leq a. \end{cases} \end{aligned} \tag{3.17}$$

Thus, $\Phi_t(\mathbf{X}_0) = \Theta_t(\mathbf{X}_0) + \Psi_t(\mathbf{X}_0)$, for any $t \geq 0$; and from the proof of [72, Proposition 3.13] and Lemma 3.2.1, we obtain to the following result.

Theorem 3.2.2. *For $\boldsymbol{X}_0 \in \Gamma$, the orbit $\{\Phi_t(\boldsymbol{X}_0) : t \geq 0\}$ has a compact closure in $\mathbb{X}_+$ if the following conditions are satisfied:*

(i) There exists a map $\Delta : \mathbb{R}_+ \times \mathbb{R}_+ \to \mathbb{R}_+$ such that for any $r > 0$, $\lim_{t\to\infty} \Delta(t, r) = 0$, and if $\boldsymbol{X}_0 \in \Gamma$ with $\|\boldsymbol{X}_0\|_{\mathbb{X}} \leq r$, then $\|\Theta_t(\boldsymbol{X}_0)\|_{\mathbb{X}} \leq \Delta(t, r)$ for any $t \geq 0$.

(ii) For any $t \geq 0$, $\Psi_t(\cdot)$ maps any bounded sets of Γ into a set with compact closure in $\mathbb{X}_+$.

For verifying (i) and (ii) of Theorem 3.2.2, the following two lemmas are needed:

Lemma 3.2.3. *For $r > 0$, let $\Delta(t, r) = e^{-\tilde{\mu}t} r$. Then, $\lim_{t\to\infty} \Delta(t, r) = 0$. Then, (i) of Theorem 3.2.2 holds.*

Proof. Clearly, it is observed that $\lim_{t\to\infty} \Delta(t,r) = 0$. Making use of some equations in (3.5), we obtain

$$\tilde{\theta}_v(a,t) = \begin{cases} 0, & 0 \le a \le t, \\ \\ v_0(a-t)\frac{\chi(a)}{\chi(a-t)}, & 0 \le t \le a, \end{cases}, \qquad \tilde{\theta}_e(a,t) = \begin{cases} 0, & 0 \le a \le t, \\ \\ e_0(a-t)\frac{\vartheta(a)}{\vartheta(a-t)} & 0 \le t \le a, \end{cases}$$

$$\tilde{\theta}_i(a,t) = \begin{cases} 0, & 0 \le a \le t, \\ \\ i_0(a-t)\frac{\zeta(a)}{\zeta(a-t)} & 0 \le t \le a. \end{cases} \tag{3.18}$$

Taking the initial condition $\mathbf{X}_0 \in \Gamma$ such that $\|\mathbf{X}_0\|_{\mathbb{X}} \le r$ and $t \ge 0$, we obtain

$$\begin{aligned} \|\Theta_t(\mathbf{X}_0)\|_{\mathbb{X}} &= |0| + \|\tilde{\theta}_v(\cdot,t)\|_1 + \|\tilde{\theta}_e(\cdot,t)\|_1 + \|\tilde{\theta}_i(\cdot,t)\|_1 + |0| \\ &= \int_t^\infty \left| v_0(a-t)\frac{\chi(a)}{\chi(a-t)} \right| da + \int_t^\infty \left| e_0(a-t)\frac{\vartheta(a)}{\vartheta(a-t)} \right| da \\ &+ \int_t^\infty \left| i_0(a-t)\frac{\zeta(a)}{\zeta(a-t)} \right| da \\ &= \int_0^\infty \left| v_0(s)\frac{\chi(s+t)}{\chi(s)} \right| ds + \int_0^\infty \left| e_0(s)\frac{\vartheta(s+t)}{\vartheta(s)} \right| ds \\ &+ \int_0^\infty \left| i_0(s)\frac{\zeta(s+t)}{\zeta(s)} \right| ds \\ &= \int_0^\infty \left| v_0(s)e^{-\int_s^{s+t} \eta(\tau)\,d\tau} \right| ds + \int_0^\infty \left| e_0(s)e^{-\int_s^{s+t} \varrho(\tau)\,d\tau} \right| ds \\ &+ \int_0^\infty \left| i_0(s)e^{-\int_s^{s+t} \sigma(\tau)\,d\tau} \right| ds \\ &\le e^{-\tilde{\mu}t}\left(\|v_0\|_1 + \|e_0\|_1 + \|i_0\|_1\right) \\ &\le e^{-\tilde{\mu}t}\|\mathbf{X}_0\|_{\mathbb{X}} \\ &\le e^{-\tilde{\mu}t}r = \Lambda(t,r). \end{aligned} \tag{3.19}$$

□

Lemma 3.2.4. *For $t \geq 0$, $\Psi_t(\cdot)$ maps any bounded sets of Γ into a set with a compact closure in $\mathbb{X}_+$.*

Proof. Since $R(t)$ and $S(t)$ remain in the compact set $[0, \Lambda/\tilde{\mu}]$ by Lemma 3.2.1, it is sufficient to show that $\tilde{v}(a,t)$, $\tilde{e}(a,t)$ and $\tilde{i}(a,t)$ remain in a precompact subset of $\mathrm{L}^1_+(0,\infty)$, which does not depend on the initial data $\mathbf{X}_0 \in \Gamma$. To achieve this, the following conditions (see [63, Theorem B.2]) must be satisfied for $\tilde{v}(a,t)$, $\tilde{e}(a,t)$ and $\tilde{i}(a,t)$.

(i) The supremum of $\|\tilde{z}(\cdot,t)\|_1$ with respect to $\mathbf{X}_0 \in \Gamma$ is finite;

(ii) $\lim\limits_{h\to\infty} \int_h^\infty \tilde{z}(a,t)\, da = 0$ uniformly with respect to $\mathbf{X}_0 \in \Gamma$;

(iii) $\lim\limits_{h\to 0^+} \int_h^\infty |\tilde{z}(a+h,t) - \tilde{z}(a,t)|\, da = 0$ uniformly with respect to $\mathbf{X}_0 \in \Gamma$;

(iv) $\lim\limits_{h\to 0^+} \int_0^h \tilde{z}(\alpha,t)\, d\alpha = 0$ uniformly with respect to $\mathbf{X}_0 \in \Gamma$;

where $\tilde{z} \in \{\tilde{v}, \tilde{e}, \tilde{i}\}$. It follows from (3.5) and (3.17) that

$$\tilde{e}(a,t) = \begin{cases} e_0(t-a)\vartheta(a), & 0 \leq a \leq t, \\ \\ 0, & 0 \leq t \leq a, \end{cases} \quad , \tag{3.20}$$

and hence, using Lemma 3.2.1, we obtain

$$0 \leq \tilde{v}(a,t) \leq \nu \frac{\Lambda}{\tilde{\mu}} e^{-\tilde{\mu}a}, \tag{3.21}$$

and hence, (i), (ii) and (iv) follow. To establish (iii), we take a sufficiently small h such that $h \in (0,t)$ and show that

$$\int_0^\infty |\tilde{v}(a+h,t) - \tilde{v}(a,t)|\, da = \int_{t-h}^t |0 - \nu S(t-a)\chi(a)|\, da$$
$$+ \nu \int_0^{t-h} |S(t-a-h)\chi(a+h) - S(a,t)\chi(a)|\, da$$

$$
\begin{aligned}
&\leq \nu\frac{\Lambda}{\tilde{\mu}}h + \nu\int_0^{t-h} S(t-a-h)\left(\chi(a)-\chi(a+h)\right)\,da \\
&+ \nu\int_0^{t-h} \chi(a)\left|S(t-a-h)-S(a,t)\right|\,da \qquad (3.22)\\
&\leq \nu\frac{\Lambda}{\tilde{\mu}}h + \nu\frac{\Lambda}{\tilde{\mu}}\left(\int_0^{t-h}\chi(a)\,da - \int_0^{t-h}\chi(a+h)\,da\right) \\
&+ \nu\int_0^{t-h} \chi(a)\left|S(t-a-h)-S(a,t)\right|\,da \\
&\leq \nu\frac{\Lambda}{\tilde{\mu}}h + \nu\frac{\Lambda}{\tilde{\mu}}\left(\int_0^{t}\chi(a)\,da + \int_t^{h}\chi(a)\,da\right) \\
&+ \nu\int_0^{t-h} \chi(a)\left|S(t-a-h)-S(a,t)\right|\,da \\
&\leq \nu\left(2\Lambda + l_S\right)\frac{h}{\tilde{\mu}}.
\end{aligned}
$$

Indeed, $\chi(a)$ is a non-decreasing function of a such that $0 \leq \chi(a) \leq 1$ and satisfying

$$
\begin{aligned}
\int_0^{t-h} |\chi(a+h)-\chi(a)|\,da &= \int_0^{t-h}\left(\chi(a)-\chi(a+h)\right)\,da \\
&= \int_0^{t-h}\chi(a)\,da - \int_0^{t-h}\chi(a+h)\,da \\
&= \int_0^{t-h}\chi(a)\,da - \int_h^{t}\chi(a)\,da \\
&= \int_0^{t-h}\chi(a)\,da - \int_h^{t-h}\chi(a)\,da - \int_{t-h}^{t}\chi(a)\,da \\
&= \int_0^{h}\chi(a)\,da - \int_{t-h}^{t}\chi(a)\,da \\
&\leq \int_0^{h}\chi(a)\,da \leq h.
\end{aligned}
$$

On the other hand, the Lipschitz continuity of $S(\cdot)$ is obtained from the first equation of (3.1), using the boundedness of the solution of (3.1) (see Lemma 3.2.1); that is, there exists $l_S > 0$ such that $|S(t_1) - S(t_2)| \leq l_S|t_1 - t_2|$ for any $t_1, t_2 \geq 0$.

Since $\nu(2\Lambda + l_S)h/\tilde{\mu}$ does not depend on the initial data $\mathbf{X}_0 \in \Gamma$ and $\nu(2\Lambda + l_S)h/\tilde{\mu} \to 0$ as $h \to 0^+$, it follows from (3.22) that (iii) is satisfied. □

Therefore, from Lemma 3.2.1 and Theorem 3.2.2, the existence result of global attractors (see [35]) follows.

Theorem 3.2.5. *The semi-flow $\{\Phi_t(\boldsymbol{X}_0) : t \geq 0\}$ has a global attractor in $\mathbb{X}_+$, which attracts any bounded subset of $\mathbb{X}_+$.*

3.2.2 Equilibria and the basic reproduction number

The system (3.1) has a unique disease-free equilibrium $E^0 = (S^0, v^0(a), e^0(a), i^0, R^0)$, where

$$\begin{aligned} S^0 &= \frac{\Lambda}{\mu^0 + \nu\left(1 - \int\limits_0^\infty \alpha(a) e^{-\int\limits_0^a \eta(s)\,ds}\, da\right)}, \\ v^0(a) &= \nu S^0 e^{-\int\limits_0^a \eta(s)\,ds},\ e^0(a) = i^0(a) = 0,\ R^0 = 0. \end{aligned} \tag{3.23}$$

Apart from E^0, the system (3.1) could also have an endemic equilibrium. We suppose that there exists an endemic equilibrium for the system (3.1) denoted by $E^* = (S^*, v^*, e^*, i^*, R^*)$. Therefore, the following equations:

$$\begin{aligned} 0 &= \Lambda - (\nu + \mu^0)S^* + \int\limits_0^\infty \alpha(a) v^*(a)\, da \\ &\quad - S^* \int\limits_0^\infty \left(K_0(a) i^*(a) + \int\limits_0^\infty K(a, a') i^*(a')\, da' \right) da \\ 0 &= -\frac{\mathrm{d}}{\mathrm{d}a} v^*(a) - \eta(a) v^*(a) \\ 0 &= -\frac{\mathrm{d}}{\mathrm{d}a} e^*(a) - \varrho(a) e^*(a) \\ 0 &= -\frac{\mathrm{d}}{\mathrm{d}a} i^*(a) - \sigma(a) i^*(a) \end{aligned} \tag{3.24}$$

$$0 = \int_0^\infty \gamma(a) i^*(a)\, da - \mu^0 R^*.$$

are satisfied. In addition, E^* also satisfies the equations (3.2) i.e.,

$$\begin{aligned} v^*(0) &= \nu S^* \\ e^*(0) &= S^* \int_0^\infty \left(K_0(a) i^*(a) + \int_0^\infty K(a,a^{'}) i^*(a^{'})\, da^{'} \right) da \\ i^*(0) &= \int_0^\infty \varepsilon(a) e^*(a)\, da. \end{aligned} \tag{3.25}$$

The second equation of (3.24) and the first equation of (3.25) give

$$v^*(a) = \nu S^* e^{-\int_0^a \eta(s)\, ds}. \tag{3.26}$$

It follows from the third equation of (3.24) that

$$e^*(a) = e^*(0) e^{-\int_0^a \varrho(s)\, ds}. \tag{3.27}$$

Equations (3.2) and (3.27), together with the fourth equation of (3.24), yield

$$i^*(a) = e^*(0) \left(e^{-\int_0^a \sigma(s)\, ds} \int_0^\infty \varepsilon(a) e^{-\int_0^a \varrho(s)\, ds}\, da \right). \tag{3.28}$$

We introduce parameter $\Re_0$, L, J and P such that

$$\begin{aligned} \Re_0 &= S^0 L \int_0^\infty \left(K_0(a) e^{-\int_0^a \sigma(s)\, ds} + \int_0^\infty K(a,a^{'}) e^{-\int_0^{a^{'}} \sigma(s)\, ds}\, da^{'} \right) da \\ L &= \int_0^\infty \varepsilon(a) e^{-\int_0^a \varrho(s)\, ds}\, da \\ J &= \int_0^\infty \gamma(a) e^{-\int_0^a \sigma(s)\, ds}\, da \\ P &= \int_0^\infty \alpha(a) e^{-\int_0^a \eta(s)\, ds}\, da. \end{aligned} \tag{3.29}$$

By substituting (3.28) into the second equation of (3.25), we have

$$S^* = \frac{S^0}{\Re_0} \tag{3.30}$$

and hence,

$$v^*(a) = \frac{v^0(a)}{\Re_0}. \tag{3.31}$$

Then, substituting (3.26), (3.28) and (3.30) into the first equation of (3.24) yields

$$e^*(0) = \Lambda\left(1 - \frac{1}{\Re_0}\right). \tag{3.32}$$

Therefore, it easily follows that

$$\begin{aligned} e^*(a) &= \Lambda\left(1 - \frac{1}{\Re_0}\right)\vartheta(a) \\ i^*(a) &= \Lambda\left(1 - \frac{1}{\Re_0}\right)L\zeta(a) \\ R^* &= \frac{\Lambda}{\mu^0}\left(1 - \frac{1}{\Re_0}\right)LJ. \end{aligned} \tag{3.33}$$

A threshold condition is derived from the existence condition for the endemic equilibrium E^* such that $\Re_0 > 1$. Thus, the parameter $\Re_0$, given by the first equation of (3.29), can be called the basic reproduction number of the system (3.1). Moreover, $\Re_0$ can also be expressed as

$$\Re_0 = \Re_{\text{intra}} + \Re_{\text{inter}}, \tag{3.34}$$

where

$$\begin{aligned} \Re_{\text{intra}} &= \frac{\Lambda L}{\mu^0 + \nu(1-P)} \int_0^\infty K_0(a)\zeta(a)\,da, \\ \Re_{\text{inter}} &= \frac{\Lambda L}{\mu^0 + \nu(1-P)} \int_0^\infty \left(\int_0^\infty K(a,a')\zeta(a')\,da'\right) da. \end{aligned} \tag{3.35}$$

$\Re_{\text{intra}}$ and $\Re_{\text{inter}}$ can be understood, respectively, as the basic reproduction numbers for the corresponding model with purely intracohort infection mechanism (i.e. a situation in which individuals can only be infected by their age-mates) and for the corresponding model with purely intercohort infection mechanism (i.e. a situation in which individuals can be infected by those of any age).

Therefore, it is stated that

Theorem 3.2.6. *If $\Re_0 \leq 1$, then the system* (3.1) *has only a disease-free equilibrium E^0; while if $\Re_0 > 1$, then the system* (3.1) *also has an endemic equilibrium E^* in addition to the disease-free equilibrium E^0.*

3.3 Uniform persistence

This section is devoted to the uniform persistence of the system (3.1) under the condition $\Re_0 > 1$. For this, we introduce a function $\rho : \mathbb{X}_+ \to \mathbb{R}_+$ defined by

$$\rho(x, \varsigma, \varpi, \upsilon, y) = x \int_0^\infty \left(K_0(a)\upsilon(a) + \int_0^\infty K(a, a^{'})\upsilon(a^{'})\, da^{'} \right) da,$$

where $(x, \varsigma, \varpi, \upsilon, y) \in \mathbb{X}_+$. Furthermore, we consider the set $\mathbb{X}_0$ defined by

$$\mathbb{X}_0 = \{\mathbf{X}_0 \in \mathbb{X}_+ : \rho\left(\Phi_{t_0}\left(\mathbf{X}_0\right)\right) > 0 \,\text{for some}\, t_0 \in \mathbb{R}_+\}$$

such that $\Phi_t\left(\mathbf{X}_0\right) \to E^0$ as $t \to \infty$ whenever $\mathbf{X}_0 \in \mathbb{X}_+ \backslash \mathbb{X}_0$.

Definition 3.3.1. *[63, p. 61]. The system* (3.1) *is uniformly weakly ρ-persistent (respectively, uniformly strongly ρ-persistent) if there exists a positive ϵ^*, independent of initial conditions, such that*

$$\limsup_{t\to\infty} \rho\left(\Phi_t(\boldsymbol{X}_0)\right) > \epsilon^* \,(\textit{respectively}, \quad \liminf_{t\to\infty} \rho\left(\Phi_t(\boldsymbol{X}_0)\right) > \epsilon^*)$$

for $\boldsymbol{X}_0 \in \mathbb{X}_+$.

Theorem 3.3.2. *If $\Re_0 > 1$, then the system* (3.1) *is uniformly weakly ρ-persistent.*

Proof. It is assumed that for any $\epsilon^* > 0$, one can find $\mathbf{X}_0^{\epsilon^*} \in \mathbb{X}_+$ such that

$$\limsup_{t\to\infty} \rho\left(\Phi_t(\mathbf{X}_0^{\epsilon^*})\right) \leq \epsilon^*.$$

Since $\Re_0 > 1$, then one can find a small enough $\epsilon_0^* > 0$ such that

$$\begin{aligned} 1 < &\left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^*\right) \left(\int_0^\infty \varepsilon(t)\vartheta(t)\, dt\right) \\ &\int_0^\infty \left(K_0(a)\zeta(a) + \int_0^\infty K(a, a^{'})\zeta(a^{'})\, da^{'} \right) da. \end{aligned} \tag{3.36}$$

In particular, one can find $\mathbf{X}_0^{\frac{\epsilon_0^*}{2}} \in \mathbb{X}_+$ such that

$$\limsup_{t\to\infty} \rho\left(\Phi_t(\mathbf{X}_0^{\frac{\epsilon_0^*}{2}})\right) \le \frac{\epsilon_0^*}{2}.$$

One can assume that, for any $t \ge 0$, $\rho\left(\Phi_t(\mathbf{X}_0^{\frac{\epsilon_0^*}{2}})\right) \le \epsilon_0^*$. It follows from Equation $(3.1)_1$ that

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}S(t) &\ge \Lambda - \epsilon_0^* - (\nu+\mu^0)S(t) + \int_0^t \alpha(a)v(a,t)\,da \\
&= \Lambda - \epsilon_0^* - (\nu+\mu^0)S(t) + \int_0^t \alpha(a)\zeta(a)v(0,t-a)\,da \\
&\ge \Lambda - \epsilon_0^* - (\nu+\mu^0)S(t) + \nu\int_0^t \alpha(a)\chi(a)S(t-a)\,da.
\end{aligned}$$

If one applies the Laplace transform $\mathcal{L}$ to the above inequality, one obtains

$$\lambda\mathcal{L}\left\{S(t)\right\} - S_0 \ge \frac{\Lambda-\epsilon_0^*}{\lambda} - (\nu+\mu^0)\mathcal{L}\left\{S(t)\right\} + \nu\mathcal{L}\left\{\alpha(t)\chi(t)\right\}\mathcal{L}\left\{S(t)\right\}.$$

It follows that

$$\begin{aligned}
\mathcal{L}\left\{S(t)\right\} &\ge \frac{S_0\lambda + \Lambda - \epsilon_0^*}{\lambda\left(\lambda+\mu^0+\nu\left(1-\mathcal{L}\left\{\alpha(t)\chi(t)\right\}\right)\right)} \\
&\ge \frac{S_0\lambda + \Lambda - \epsilon_0^*}{\lambda\left(\lambda+\mu^0+\nu\right)} \\
&= \frac{\Lambda-\epsilon_0^*}{\nu+\mu^0}\cdot\frac{1}{\lambda} + \left(S_0 - \frac{\Lambda-\epsilon_0^*}{\nu+\mu^0}\right)\frac{1}{\lambda+\nu+\mu^0}
\end{aligned}$$

and hence,

$$\begin{aligned}
S(t) &\ge \frac{\Lambda-\epsilon_0^*}{\nu+\mu^0}\mathcal{L}^{-1}\left\{\frac{1}{\lambda}\right\} + \left(S_0 - \frac{\Lambda-\epsilon_0^*}{\nu+\mu^0}\right)\mathcal{L}^{-1}\left\{\frac{1}{\lambda+\nu+\mu^0}\right\} \\
&= \frac{\Lambda-\epsilon_0^*}{\nu+\mu^0} + e^{-(\nu+\mu^0)t}\left(S_0 - \frac{\Lambda-\epsilon_0^*}{\nu+\mu^0}\right), \quad \text{for any } t \ge 0.
\end{aligned}$$

This yields $\limsup_{t\to\infty} S(t) \ge \frac{\Lambda-\epsilon_0}{\nu+\mu^0}$. It can be assumed that for any $t \ge 0$,

$$S(t) \ge \frac{\Lambda-\epsilon_0^*}{\nu+\mu^0} - \epsilon_0^*.$$

Now, we consider the boundary condition defined by the second equation of (3.2) and obtain

$$
\begin{aligned}
e(0,t) &\geq S(t) \int_0^t \left(K_0(a)i(a,t) + \int_0^t K(a,a^{'})i(a^{'},t)\,da^{'} \right) da \\
&\geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^* \right) \left(\int_0^t K_0(a)i(a,t)\,da + \int_0^t K(a,a^{'})i(a^{'},t)\,da^{'}\,da \right) \\
&\geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^* \right) \left(\int_0^t K_0(a)i(0,t-a)\zeta(a)\,da + \int_0^t K(a,a^{'})i(0,t-a^{'})\zeta(a^{'})\,da^{'}\,da \right) \\
&\geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^* \right) \left(\int_0^t K_0(a)\zeta(a) \left(\int_0^{t-a} \varepsilon(b)\vartheta(b)e(0,t-a-b)\,db \right) da \right. \\
&\quad \left. + \int_0^t \int_0^t K(a,a^{'})\zeta(a^{'}) \left(\int_0^{t-a^{'}} \varepsilon(b^{'})\vartheta(b^{'})e(0,t-a^{'}-b^{'})\,db^{'} \right) da^{'}\,da \right).
\end{aligned}
$$

If one applies the Laplace Transform $\mathcal{L}$ to the above inequality so that

$$
\begin{aligned}
\mathcal{L}\{e(0,t)\} \geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^* \right) &\left(\mathcal{L}\{K_0(t)\zeta(t)\} + \frac{1}{\lambda}\mathcal{L}\{K(\cdot,t)\zeta(t)\} \right) \\
&\mathcal{L}\{\varepsilon(t)\vartheta(t)\}\,\mathcal{L}\{e(0,t)\},
\end{aligned}
$$

dividing the above inequality by $\mathcal{L}\{e(0,t)\}$ yields

$$
\begin{aligned}
1 &\geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^* \right) \left(\mathcal{L}\{K_0(t)\zeta(t)\} + \frac{1}{\lambda}\mathcal{L}\{K(\cdot,t)\zeta(t)\} \right) \mathcal{L}\{\varepsilon(t)\vartheta(t)\} \\
&\geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^* \right) \left(\int_0^\infty e^{-\lambda t}\varepsilon(t)\vartheta(t)\,dt \right) \\
&\qquad \times \left(\int_0^\infty e^{-\lambda t}K_0(t)\zeta(t)\,dt + \int_0^\infty e^{-\lambda t} \left(\int_0^t K(t,s)\zeta(s)\,ds \right) dt \right) \\
&= \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^* \right) \left(\int_0^\infty e^{-\lambda t}\varepsilon(t)\vartheta(t)\,dt \right) \\
&\qquad \times \left(\int_0^\infty e^{-\lambda t}K_0(t)\zeta(t)\,dt + \int_0^\infty \int_0^t e^{-\lambda t}K(t,s)\zeta(s)\,ds\,dt \right)
\end{aligned}
$$

$$= \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^*\right) \left(\int_0^\infty e^{-\lambda t} \varepsilon(t)\vartheta(t)\, dt\right)$$
$$\times \int_0^\infty \left(e^{-\lambda t} K_0(t)\zeta(t) + \int_0^t e^{-\lambda t} K(t,s)\zeta(s)\, ds\right) dt.$$

First, if one takes the limit inferior as $t \to \infty$ on both sides of the above inequality, one obtains

$$1 \geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^*\right) \left(\int_0^\infty e^{-\lambda t} \varepsilon(t)\vartheta(t)\, dt\right)$$
$$\times \int_0^\infty \left(e^{-\lambda t} K_0(t)\zeta(t) + \liminf_{t\to\infty} \int_0^t e^{-\lambda t} K(t,s)\zeta(s)\, ds\right) dt$$
$$= \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^*\right) \left(\int_0^\infty e^{-\lambda t} \varepsilon(t)\vartheta(t)\, dt\right)$$
$$\times \int_0^\infty \left(e^{-\lambda t} K_0(t)\zeta(t) + \int_0^\infty e^{-\lambda t} K(t,s)\zeta(s)\, ds\right) dt.$$

Next, we take the limit as $\lambda \to 0$ of both sides of the above inequality, to obtain

$$1 \geq \left(\frac{\Lambda - \epsilon_0^*}{\nu + \mu^0} - \epsilon_0^*\right) \left(\int_0^\infty \varepsilon(t)\vartheta(t)\, dt\right)$$
$$\times \int_0^\infty \left(K_0(t)\zeta(t) + \int_0^\infty K(t,s)\zeta(s)\, ds\right) dt,$$

which contradicts the inequality given in (3.36). □

Combining the results from Theorems 3.2.5 and 3.3.2 with [66, Theorem 3.2] lead to the uniform (strong) ρ-persistence such that

Theorem 3.3.3. *If $\Re_0 > 1$, then the semi-flow Φ is uniformly (strongly) ρ-persistent.*

Definition 3.3.4. *A total trajectory of a continuous semi-flow Φ, defined by (3.4), is a function $\boldsymbol{X} : \mathbb{R} \to \mathbb{X}_+$ such that $\Phi_t(\boldsymbol{X}(r)) = \boldsymbol{X}(t + r)$ for any $(t, r) \in \mathbb{R}_+ \times \mathbb{R}$.*

It should be noted that a global attractor will only contain points with total trajectories through them as it needs to be invariant. So, the α-limit point of a total trajectory $\mathbf{X}$, passing through $\mathbf{X}(0) = \mathbf{X}_0$, is given by

$$\alpha(\mathbf{X}_0) = \bigcap_{t\geq 0} \overline{\bigcup_{s\geq t} \mathbf{X}(s)}.$$

A total trajectory $\mathbf{X}(t) = (S(t), v(\cdot,t), e(\cdot,t), i(\cdot,t), R(t))$ satisfies

$$\begin{aligned} v(a,r) &= \nu S(r-a)\chi(a), \quad (a,r) \in \mathbb{R}_+ \times \mathbb{R}, \\ e(a,r) &= e(0,r-a)\vartheta(a), \quad (a,r) \in \mathbb{R}_+ \times \mathbb{R}, \\ i(a,r) &= i(0,r-a)\zeta(a), \quad (a,r) \in \mathbb{R}_+ \times \mathbb{R}. \end{aligned}$$

Corollary 3.3.5. *Let $\mathcal{A}$ and $\boldsymbol{X}(t)$ be, respectively, a global attractor of Φ in $\mathbb{X}_+$ and a total trajectory of Φ in $\mathcal{A} \cap \mathbb{X}_+$. If $\Re_0 > 1$, then there exists $\epsilon > 0$ such that*

$$S(t), v(0,t), e(0,t), i(0,t), R(t) \geq \epsilon, \qquad for\ any\ t \geq 0. \tag{3.37}$$

Proof. We consider the boundary condition given by the second equation of (3.2). Using (3.15) and (ii) of **A1**, we obtain

$$\begin{aligned} e(0,t) &\leq 4\|i(t)\|_1 S(t) \max\left\{\bar{K}_0, \|\bar{K}\|_1\right\} \\ &\leq 4\frac{\Lambda^2}{\tilde{\mu}^2} \max\left\{\bar{K}_0, \|\bar{K}\|_1\right\} =: \bar{\mathcal{K}}. \end{aligned} \tag{3.38}$$

Using the first equality of (3.1), we have

$$\begin{aligned} S'(t) &\geq \Lambda - (\nu - \mu^0)S(t) \\ &\quad - S(t)\int_0^\infty \left(K_0(a)\zeta(a)i(0,t-a) + \int_0^\infty K(a,a')\zeta(a)i(0,t-a')\,da' \right) da \\ &\geq \Lambda - (\nu - \mu^0)S(t) - L\bar{\mathcal{K}}S(t)\int_0^\infty \left(K_0(a)\zeta(a) + \int_0^\infty K(a,a')\zeta(a)\,da' \right) da \\ &\geq \Lambda - \left(\nu + \mu^0 + \frac{\bar{\mathcal{K}}}{S^0}\Re_0\right) S(t); \end{aligned}$$

that is,

$$S'(t) \geq \Lambda - \left(\nu + \mu^0 + \frac{\bar{\mathcal{K}}}{S^0}\Re_0\right) S(t).$$

This yields

$$S(t) \geq \frac{\Lambda S^0}{(\nu+\mu^0)S^0+\bar{\mathcal{K}}} + e^{-\left(\nu+\mu^0+\frac{\bar{\mathcal{K}}}{S^0}\Re_0\right)t}\left(S_0 - \frac{\Lambda S^0}{(\nu+\mu^0)S^0+\bar{\mathcal{K}}}\right). \tag{3.39}$$

Taking $\liminf\limits_{t\to\infty}$ in (3.39) leads to

$$\liminf_{t\to\infty} S(t) \geq \frac{\Lambda S^0}{(\nu+\mu^0)S^0+\bar{\mathcal{K}}} =: \epsilon_1.$$

Therefore, $S(t) \geq \epsilon_1$. It follows that $v(0,t) \geq \epsilon_1\nu =: \epsilon_2$.

Now, we consider again the boundary condition given by the second equation of (3.2). It is easy to see that

$$e(0,t) = \rho\left(\Phi_t(\mathbf{X}_0)\right) = \rho\left(\mathbf{X}(t)\right)$$

and hence,

$$e(0,t) \geq \liminf_{t\to\infty} \rho\left(\mathbf{X}(t)\right).$$

It follows from Theorem 3.3.3 and Definition 3.3.1, that $e(0,t) \geq \epsilon^* =: \epsilon_3$.

Furthermore, if the boundary condition given by the third equation of (3.2) is considered, one obtains

$$i(0,t) = \int_0^\infty \vartheta(\alpha)\varepsilon(\alpha)e(0,t-\alpha)\,d\alpha \geq \epsilon_3 \int_0^\infty \vartheta(\alpha)\varepsilon(\alpha)\,d\alpha =: \epsilon_4.$$

Finally, the fifth equation of (3.1) leads to

$$\frac{\mathrm{d}}{\mathrm{d}t}R(t) \geq \epsilon_4 \int_0^\infty \gamma(a)\zeta(a)\,da - \mu^0 R(t)$$

and hence,

$$R(t) \geq \frac{\epsilon_4}{\mu^0} + e^{-\mu^0 t}\left(R_0 - \frac{\epsilon_4}{\mu^0}\int_0^\infty \gamma(a)\zeta(a)\,da\right). \tag{3.40}$$

By taking the limit inferior as $t \to \infty$ in (3.40), we obtain

$$\liminf_{t\to\infty} R(t) \geq \frac{\epsilon_4}{\mu^0}\int_0^\infty \gamma(a)\zeta(a)\,da =: \epsilon_5,$$

and, therefore, $R(t) \geq \epsilon_5$. By choosing ϵ such that $\epsilon = \min\limits_i \{\epsilon_i\}$, for $i \in \{1,2,3,4,5\}$, we obtain

$$S(t), v(0,t), e(0,t), i(0,t), R \geq \epsilon.$$

□

3.4 Stability of equilibria

3.4.1 Local stability of equilibria

The conditions of stability for each equilibrium are derived through linearisation technique around the equilibrium.

The conditions of stability for the disease-free equilibrium E^0 can be investigated through the following result:

Theorem 3.4.1. *If $\Re_0 < 1$, then E^0 is locally asymptotically stable; if $\Re_0 > 1$, then E^0 is unstable.*

Proof. To investigate the stability of the disease-free equilibrium E^0, we denote by $\tilde{S}(t)$, $\tilde{v}(a,t)$, $\tilde{e}(a,t)$, $\tilde{i}(a,t)$, $\tilde{R}(t)$ the perturbations of $S(t)$, $v(a,t)$, $e(a,t)$, $i(a,t)$, $R(t)$, respectively, such that

$$\begin{aligned} \tilde{S}(t) = S(t) - S^0, \quad \tilde{v}(a,t) = v(a,t) - v^0(a) \\ \tilde{e}(a,t) = e(a,t), \quad \tilde{i}(a,t) = i(a,t), \quad \tilde{R}(t) = R(t). \end{aligned} \tag{3.41}$$

The perturbations satisfy the following equations:

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t}\tilde{S}(t) &= -(\nu+\mu^0)\tilde{S}(t) + \int_0^\infty \alpha(a)\tilde{v}(a,t)\,da \\ &\quad - S^0 \int_0^\infty \left(K_0(a)\tilde{i}(a,t) + \int_0^\infty K(a,a^{'})\tilde{i}(a^{'},t)\,da^{'} \right) da \\ \frac{\partial}{\partial t}\tilde{v}(a,t) &= -\frac{\partial}{\partial a}\tilde{v}(a,t) - \eta(a)\tilde{v}(a,t) \\ \frac{\partial}{\partial t}\tilde{e}(a,t) &= -\frac{\partial}{\partial a}\tilde{e}(a,t) - \varrho(a)\tilde{v}(a,t) \\ \frac{\partial}{\partial t}\tilde{i}(a,t) &= -\frac{\partial}{\partial a}\tilde{i}(a,t) - \sigma(a)\tilde{v}(a,t) \\ \frac{\mathrm{d}}{\mathrm{d}t}\tilde{R} &= \int_0^\infty \gamma(a)\tilde{i}(a,t)\,da - \mu^0\tilde{R}, \end{aligned} \tag{3.42}$$

after substituting (3.41) into (3.1) and neglecting the terms of order higher or equal to two, with boundary conditions

$$\begin{aligned}\tilde{v}(0,t) &= \nu\tilde{S}(t)\\ \tilde{e}(0,t) &= S^0\int_0^\infty\left(K_0(a)\tilde{i}(a,t)+\int_0^\infty K(a,a^{'})\tilde{i}(a^{'},t)\,da^{'}\right)\,da\\ \tilde{i}(0,t) &= \int_0^\infty \varepsilon(a)\tilde{e}(a,t)\,da,\end{aligned} \tag{3.43}$$

after substituting (3.41) into (3.2) and neglecting the terms of order higher or equal to two.

Now, we consider the exponential solutions of system (3.42)-(3.43) of the form

$$\tilde{S}(t)=\bar{S}e^{\lambda t},\quad \tilde{v}(a,t)=\bar{v}(a)e^{\lambda t},\quad \tilde{e}(a,t)=\bar{e}(a)e^{\lambda t},\quad \tilde{i}(a,t)=\bar{i}(a)e^{\lambda t},\quad \tilde{R}(t)=\bar{R}e^{\lambda t}, \tag{3.44}$$

where $\bar{S}$, $\bar{v}(a)$, $\bar{e}(a)$, $\bar{i}(a)$, and λ (real or complex number) satisfy the following system of equations:

$$\begin{aligned}\lambda\bar{S} &= -(\nu+\mu^0)\bar{S}+\int_0^\infty \alpha(a)\bar{v}(a)\,da\\ &\quad - S^0\int_0^\infty\left(K_0(a)\bar{i}(a)+\int_0^\infty K(a,a^{'})\bar{i}(a^{'})\,da^{'}\right)\,da\\ \lambda\bar{v}(a) &= -\frac{d}{da}\bar{v}(a)-\eta(a)\bar{v}(a)\\ \lambda\bar{e}(a) &= -\frac{d}{da}\bar{e}(a)-\varrho(a)\bar{v}(a)\\ \lambda\bar{i}(a) &= -\frac{d}{da}\bar{i}(a)-\sigma(a)\bar{v}(a)\\ \lambda\bar{R} &= \int_0^\infty \gamma(a)\bar{i}(a)\,da-\mu^0\bar{R},\end{aligned} \tag{3.45}$$

with boundary conditions

$$\begin{aligned}\bar{v}(0) &= \nu\bar{S}\\ \bar{e}(0) &= S^0\int_0^\infty\left(K_0(a)\bar{i}(a)+\int_0^\infty K(a,a^{'})\bar{i}(a^{'})\,da^{'}\right)\,da\end{aligned} \tag{3.46}$$

$$\tilde{i}(0) = \int_0^\infty \varepsilon(a)\bar{e}(a)\,da.$$

From the second, third and fourth equation of (3.45), we obtain

$$\bar{v}(a) = \bar{v}(0)e^{-\lambda a - \int_0^a \eta(s)\,ds}, \quad \bar{e}(a) = \bar{e}(0)e^{-\lambda a - \int_0^a \varrho(s)\,ds}, \quad \bar{i}(a) = \bar{i}(0)e^{-\lambda a - \int_0^a \sigma(s)\,ds}, \tag{3.47}$$

respectively; where $\bar{v}(0)$, $\bar{e}(0)$, and $\bar{i}(0)$ are given by (3.46).

Substituting the last equation of (3.47) into the boundary condition given by the second equation of (3.46) yields the characteristic equation

$$\mathfrak{C}^0(\lambda) = 1, \tag{3.48}$$

where

$$\mathfrak{C}^0(\lambda) = S^0 \left(\int_0^\infty \varepsilon(a) e^{-\lambda a - \int_0^a \varrho(s)\,ds} da \right) \times \int_0^\infty \left(K_0(a) e^{-\lambda a - \int_0^a \sigma(s)\,ds} + \int_0^\infty K(a, a^{'}) e^{-\lambda a^{'} - \int_0^{a^{'}} \varrho(s)\,ds} da^{'} \right) da,$$

and such that $\mathfrak{C}^0(0) = \Re_0$. It is not difficult to see that $\frac{d}{d\lambda}\mathfrak{C}^0(\lambda) = -\mathfrak{C}^0(\lambda) < 0$. Thus, $\mathfrak{C}^0(\lambda)$ is a decreasing continuous function of λ which approaches ∞ as $\lambda \to -\infty$ and 0 as $\lambda \to \infty$. Hence, the characteristic equation (3.48) admits a real solution λ^* such that $\lambda^* < 0$ whenever $\mathfrak{C}^0(0) < 1$, and $\lambda^* > 0$ whenever $\mathfrak{C}^0(0) > 1$.

On the other hand, by assuming a complex solution $\lambda = \alpha + i\beta$ of the characteristic equation $\mathfrak{C}^0(\lambda) = 1$, it can be noted that $\Re\left(e^\lambda\right) \leq e^{\Re(\lambda)}$ is always true. Thus, we clearly obtain $\Re\mathfrak{C}^0(\lambda) \leq \mathfrak{C}^0(\Re\lambda)$. It follows from the characteristic equation $\mathfrak{C}^0(\lambda) = 1$ that $\Re\mathfrak{C}^0(\lambda) = 1$ and $\Im\mathfrak{C}^0(\lambda) = 0$. Therefore, we obtain $1 \leq \mathfrak{C}^0(\Re\lambda)$, i.e. $\mathfrak{C}^0(\lambda^*) \leq \mathfrak{C}^0(\Re\lambda)$. Hence, $\Re\lambda \leq \lambda^*$, since $\mathfrak{C}^0(\lambda)$ is a decreasing function.

It results from the above statements that all eigenvalues of the characteristic equation $\mathfrak{C}^0(\lambda) = 1$ have a negative real part whenever $\mathfrak{C}^0(0) < 1$, i.e. $\Re_0 < 1$. Thus, the disease-free equilibrium E^0 is locally asymptotically stable if $\Re_0 < 1$. Otherwise, $\mathfrak{C}^0(0) \geq 1$, i.e. the unique real solution of the characteristic equation $\mathfrak{C}^0(\lambda) = 1$ is positive, and hence, the disease-free equilibrium E^0 is unstable. □

Theorem 3.4.2. *If $\Re_0 > 1$ then, E^* is locally asymptotically stable.*

Proof. Likewise for the disease-free equilibrium, the disease-endemic equilibrium is perturbed by letting

$$\begin{aligned}&\tilde{S}(t) = S(t) - S^*, \quad \tilde{v}(a,t) = v(a,t) - v^*(a), \quad \tilde{e}(a,t) = e(a,t) - e^*(a),\\ &\tilde{i}(a,t) = i(a,t) - i^*(a), \quad \tilde{R}(t) = R(t) - R^*.\end{aligned} \tag{3.49}$$

Substituting $S(t) = \tilde{S}(t) + S^*$, $v(a,t) = \tilde{v}(a,t) + v^*(a)$, $e(a,t) = \tilde{e}(a,t) + e^*(a)$, $i(a,t) = \tilde{i}(a,t) + i^*(a)$, $R(t) = \tilde{R}(t) + R^*$ into (3.1) and neglecting the terms of second order and above, the perturbations satisfy the following linear system:

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\tilde{S}(t) &= -(\nu + \mu^0)\tilde{S}(t) + \int_0^\infty \alpha(a)\tilde{v}(a,t)\,da\\
&\quad - S^* \int_0^\infty \left(K_0(a)\tilde{i}(a,t) + \int_0^\infty K(a,a^{'})\tilde{i}(a^{'},t)\,da^{'} \right) da\\
&\quad - \tilde{S}(t) \int_0^\infty \left(K_0(a)i^*(a) + \int_0^\infty K(a,a^{'})i^*(a^{'})\,da^{'} \right) da\\
\frac{\partial}{\partial t}\tilde{v}(a,t) &= -\frac{\partial}{\partial a}\tilde{v}(a,t) - \eta(a)\tilde{v}(a,t)\\
\frac{\partial}{\partial t}\tilde{e}(a,t) &= -\frac{\partial}{\partial a}\tilde{e}(a,t) - \varrho(a)\tilde{v}(a,t)\\
\frac{\partial}{\partial t}\tilde{i}(a,t) &= -\frac{\partial}{\partial a}\tilde{i}(a,t) - \sigma(a)\tilde{v}(a,t)\\
\frac{\mathrm{d}}{\mathrm{d}t}\tilde{R} &= \int_0^\infty \gamma(a)\tilde{i}(a,t)\,da - \mu^0\tilde{R},
\end{aligned} \tag{3.50}$$

with boundary conditions

$$\begin{aligned}
\tilde{v}(0,t) &= \nu\tilde{S}(t)\\
\tilde{e}(0,t) &= S^* \int_0^\infty \left(K_0(\alpha)\tilde{i}(\alpha,t) + \int_0^\infty K(\alpha,\alpha^{'})\tilde{i}(\alpha^{'},t)\,d\alpha^{'} \right) d\alpha\\
&\quad + \tilde{S}(t) \int_0^\infty \left(K_0(\alpha)i^*(\alpha) + \int_0^\infty K(\alpha,\alpha^{'})i^*(\alpha^{'})\,d\alpha^{'} \right) d\alpha
\end{aligned} \tag{3.51}$$

$$\tilde{i}(0,t) = \int_0^\infty \varepsilon(\alpha)\tilde{e}(v,t)\,d\alpha,$$

after substituting $S(t) = \tilde{S}(t) + S^*$, $v(a,t) = \tilde{v}(a,t) + v^*(a)$, $e(a,t) = \tilde{e}(a,t) + e^*(a)$, $i(a,t) = \tilde{i}(a,t) + i^*(a)$, $R(t) = \tilde{R}(t) + R^*$ into (3.2) and neglecting the terms of second order and above.

Now, the exponential solutions of system (3.50)-(3.51) of the form

$$\tilde{S}(t) = \bar{S}e^{\lambda t}, \quad \tilde{v}(a,t) = \bar{v}(a)e^{\lambda t}, \quad \tilde{e}(a,t) = \bar{e}(a)e^{\lambda t}, \quad \tilde{i}(a,t) = \bar{i}(a)e^{\lambda t}, \quad \tilde{R}(t) = \bar{R}e^{\lambda t}, \tag{3.52}$$

are considered, where $\bar{S}$, $\bar{v}(a)$, $\bar{e}(a)$, $\bar{i}(a)$, and λ (real or complex number) satisfy the following system of equations:

$$\begin{aligned}
\lambda\bar{S} &= -(\nu+\mu^0)\bar{S} + \int_0^\infty \alpha(a)\bar{v}(a)\,da \\
&\quad - S^*\int_0^\infty \left(K_0(a)\bar{i}(a) + \int_0^\infty K(a,a^{'})\bar{i}(a^{'})\,da^{'} \right) da \\
&\quad - \bar{S}\int_0^\infty \left(K_0(a)i^*(a) + \int_0^\infty K(a,a^{'})i^*(a^{'})\,da^{'} \right) da \\
\lambda\bar{v}(a) &= -\frac{\mathrm{d}}{\mathrm{d}a}\bar{v}(a) - \eta(a)\bar{v}(a) \\
\lambda\bar{e}(a) &= -\frac{\mathrm{d}}{\mathrm{d}a}\bar{e}(a) - \varrho(a)\bar{v}(a) \\
\lambda\bar{i}(a) &= -\frac{\mathrm{d}}{\mathrm{d}a}\bar{i}(a) - \sigma(a)\bar{v}(a) \\
\lambda\bar{R} &= \int_0^\infty \gamma(a)\bar{i}(a)\,da - \mu^0\bar{R},
\end{aligned} \tag{3.53}$$

with boundary conditions

$$\begin{aligned}
\bar{v}(0) &= \nu\bar{S} \\
\bar{e}(0) &= S^*\int_0^\infty \left(K_0(a)\bar{i}(a) + \int_0^\infty K(a,a^{'})\bar{i}(a^{'})\,da^{'} \right) da \\
&\quad + \bar{S}\int_0^\infty \left(K_0(a)i^*(a) + \int_0^\infty K(a,a^{'})i^*(a^{'})\,da^{'} \right) da
\end{aligned} \tag{3.54}$$

$$\tilde{i}(0) = \int_0^\infty \varepsilon(a)\bar{e}(a)\,da.$$

Similar to the process leading to the characteristic equation (3.48), the characteristic equation at the disease-endemic equilibrium E^* is given by:

$$(\lambda + \mu^0 + \nu A_\lambda)\mathfrak{C}^*(\lambda) - B - (\lambda + \mu^0 + \nu A_\lambda) = 0, \tag{3.55}$$

where

$$\mathfrak{C}^*(\lambda) = \frac{\mathfrak{C}^0(\lambda)}{\mathfrak{R}_0} > 0$$
$$A_\lambda = 1 - \int_0^\infty \alpha(a) e^{-\lambda a - \int_0^a \eta(s)\,ds}\,da > 0$$
$$B = \int_0^\infty \left(K_0(a)i^*(a) + \int_0^\infty K(a,a^{'})i^*(a^{'})\,da^{'} \right) da > 0.$$

It is sufficient to prove that (3.55) has no root with nonnegative real part. Thus, it is assumed that (3.55) has a complex root with a nonnegative real part denoted by

$$\lambda = \alpha + i\beta,$$

where $\alpha \geq 0$ and $\beta \neq 0$. It follows from (3.55) that

$$(\alpha + i\beta + \mu^0 + \nu A_{\alpha+i\beta})\mathfrak{C}^*(\alpha + i\beta) - B - (\alpha + i\beta + \mu^0 + \nu A_{\alpha+i\beta}) = 0,$$

where

$$\mathfrak{C}^*(\alpha + i\beta) = \frac{\mathfrak{C}^0(\alpha + i\beta)}{\mathfrak{R}_0} > 0$$
$$A_{\alpha+i\beta} = 1 - \int_0^\infty \alpha(a) e^{-\alpha a - \int_0^a \eta(s)\,ds} e^{-i\beta a}\,da > 0$$
$$B = \int_0^\infty \left(K_0(\alpha)i^*(\alpha) + \int_0^\infty K(\alpha,\alpha^{'})i^*(\alpha^{'})\,d\alpha^{'} \right) d\alpha > 0,$$

and, hence,

$$\mathfrak{C}^*(\alpha + i\beta) = \Re\mathfrak{C}^*(\alpha + i\beta) + \Im\mathfrak{C}^*(\alpha + i\beta),$$

where

$$\Re\mathfrak{C}^*(\alpha+i\beta) = 1 + \frac{B}{K_{\alpha\beta}}\left(\alpha+\mu^0+\nu-\nu\int_0^\infty \alpha(a)e^{-\alpha a-\int_0^a \eta(s)\,ds}\cos\beta a\,da\right) > 1 \tag{3.56}$$

and

$$\Im\mathfrak{C}^*(\alpha+i\beta) = -\frac{B}{K_{\alpha\beta}}\left(\beta-\nu\int_0^\infty \alpha(a)e^{-\alpha a-\int_0^a \eta(s)\,ds}\sin\beta a\,da\right) < 0,$$

with

$$K_{\alpha\beta} = \left(\alpha+\mu^0+\nu-\nu\int_0^\infty \alpha(a)e^{-\alpha a-\int_0^a \eta(s)\,ds}\cos\beta a\,da\right)^2 + \left(\beta-\nu\int_0^\infty \alpha(a)e^{-\alpha a-\int_0^a \eta(s)\,ds}\sin\beta a\,da\right)^2 > 0.$$

Since $\Re\mathfrak{C}^*(\alpha+i\beta) \leq \mathfrak{C}^*(\alpha)$ is always true and $\mathfrak{C}^*(\alpha) \leq \mathfrak{C}^*(0) = 1$ ($\mathfrak{C}^*$ is a decreasing function of λ), thus $\Re\mathfrak{C}^*(\alpha+i\beta) \leq 1$.

Therefore, the latter statement contradicts (3.56). □

3.4.2 Global stability of equilibria

To investigate the global asymptotic stability of equilibria of system (3.1), the suitable Volterra-type Lyapunov functions of the form

$$G(X) = X - 1 - \ln X, \quad X > 0, \tag{3.57}$$

is used.

The following results are stated:

Theorem 3.4.3. *The disease-free equilibrium E^0 of* (3.1) *is globally asymptotically stable if $\Re_0 \leq 1$.*

Proof. A Lyapunov function L^0 of the form

$$L^0(t) = L_1^0(t) + L_2^0(t) + L_2^0(t) + L_4^0(t) + L_5^0(t)$$

is considered, where

$$L_1^0(t) = S^0 G\left(\frac{S(t)}{S^0}\right), \quad L_2^0(t) = \int_0^\infty v^0(a) G\left(\frac{v(a,t)}{v^0(a)}\right) da$$

$$L_3^0(t) = \int_0^\infty \varphi(a) e(a,t)\, da, \quad L_4^0(t) = \int_0^\infty \omega(a) i(a,t)\, da, \quad L_5^0(t) = C^0 R(t).$$

The functions φ and ω are nonnegative and should be chosen suitably and carefully. $\dot{L}_i^0$, $i = 1, \ldots, 5$, denote the derivatives of L_i^0 with respect to t along the solution to (3.1) and are given by

$$\begin{aligned}
\dot{L}_1^0(\cdot) &= (\nu + \mu^0) S^0 \left(2 - \frac{S^0}{S} - \frac{S}{S^0}\right) + \left(1 - \frac{S^0}{S}\right) \int_0^\infty \alpha(a) v(a,\cdot) \left(1 - \frac{v^0(a)}{v(a,\cdot)}\right) da, \\
&\quad + S^0 \int_0^\infty \left(K_0(a) i(a,\cdot) + \int_0^\infty K(a,a') i(a',\cdot)\, da'\right) da - e(0,\cdot) \\
\dot{L}_2^0(\cdot) &= -\lim_{a\to\infty} v(a,\cdot) + \nu\left(S - S^0 \ln S\right) + \nu S^0 (1 - \ln\nu) \\
&\quad - \int_0^\infty \eta(a)\left(v(a,\cdot) - v^0(a) \ln v(a,\cdot)\right) da \qquad (3.58) \\
\dot{L}_3^0(\cdot) &= -\lim_{a\to\infty} \varphi(a) e(a,\cdot) + \varphi(0) e(0,\cdot) + \int_0^\infty \left(\dot{\varphi}(a) - \varrho(a)\varphi(a)\right) e(a,\cdot)\, da, \\
\dot{L}_4^0(\cdot) &= -\lim_{a\to\infty} \omega(a) i(a,\cdot) + \omega(0) i(0,\cdot) + \int_0^\infty \left(\dot{\omega}(a) - \sigma(a)\omega(a)\right) i(a,\cdot)\, da, \\
\dot{L}_5^0(\cdot) &= C^0 \int_0^\infty \gamma(a) i(a,\cdot)\, da - C^0 \mu^0 R.
\end{aligned}$$

Therefore,

$$\begin{aligned}
\dot{L}^0(\cdot) &= (\nu + \mu^0) S^0 \left(2 - \frac{S^0}{S} - \frac{S}{S^0}\right) + \left(\varphi(0) - 1\right) e(0,\cdot) + \nu(S - S^0 \ln S) \\
&\quad + \nu S^0 (1 - \ln\nu) - \left(1 - \frac{S^0}{S}\right) \int_0^\infty \alpha(a) v^0(a)\, da - C^0 \left(\mu^0 R + \int_0^\infty \gamma(a) i(a,\cdot)\, da\right), \\
&\quad - \frac{S^0}{S} \int_0^\infty \alpha(a) v(a,\cdot)\, da + \int_0^\infty \alpha(a) v(a,\cdot)\, da - \int_0^\infty \eta(a)\left(v(a,\cdot) - v^0(a) \ln v(a,\cdot)\right) da
\end{aligned}$$

$$+\int_0^\infty \left(\omega'(a) - \omega(a)\sigma(a) + S^0 K_0(a) + S^0 \int_0^\infty \frac{K(a,a')i(a',\cdot)}{i(a,\cdot)}\right) i(a,\cdot)\,da$$
$$+\int_0^\infty \left(\varphi'(a) - \varrho(a)\varphi(a) + \omega(0)\varepsilon(a)\right) e(a,\cdot)\,da,$$

i.e.,

$$\begin{aligned}\dot{L}^0(\cdot) =&(\nu+\mu^0)S^0\left(2-\frac{S^0}{S}-\frac{S}{S^0}\right) + (\varphi(0)-1)\,e(0,\cdot) + \nu(S - S^0\ln S)\\ &+\nu S^0(1-\ln\nu) - \left(1-\frac{S^0}{S}\right)\int_0^\infty \alpha(a)v^0(a)\,da\\ &- C^0\left(\mu^0 R - \int_0^\infty \gamma(a)i(a,\cdot)\,da\right) - \frac{S^0}{S}\int_0^\infty \alpha(a)v(a,\cdot)\,da\\ &+\int_0^\infty \alpha(a)v(a,\cdot)\,da - \int_0^\infty \eta(a)\left(v(a,\cdot) - v^0(a)\ln v(a,\cdot)\right)\,da\\ &+\int_0^\infty \left(\omega'(a) - \sigma(a)\omega(a) + S^0K_0(a) + S^0\int_0^\infty K(a,a')e^{-\int_a^{a'}\sigma(s)\,ds}\,da'\right) i(a,\cdot)\,da\\ &+\int_0^\infty \left(\varphi'(a) - \varrho(a)\varphi(a) + \omega(0)\varepsilon(a)\right) e(a,\cdot)\,da,\end{aligned} \tag{3.59}$$

after choosing a and a' such that

$$\frac{i(a',t)}{\zeta(a')} = \frac{i(a,t)}{\zeta(a)}.$$

It should be noted that

$$\nu(S - S^0\ln S) + \nu S^0(1-\ln\nu) - \left(1-\frac{S^0}{S}\right)\int_0^\infty \alpha(a)v^0(a)\,da = -\nu S^0(1+\ln\nu S)$$
$$+\frac{1}{S}\left[\nu S^2 + \left(2\nu S^0 + (\Lambda - (\nu+\mu^0)S^0)\right)S - (\Lambda - (\nu+\mu^0)S^0)S^0\right],$$

after using $\int_0^\infty \alpha(a)v^0(a)\,da = -\Lambda + (\nu+\mu^0)S^0$. Thus, Equation (3.59) becomes

$$\dot{L}^0(\cdot) = (\nu+\mu^0)S^0\left(2-\frac{S^0}{S}-\frac{S}{S^0}\right) + (\varphi(0)-1)\,e(0,\cdot)$$

$$
\begin{aligned}
&- C^0 \left(\mu^0 R - \int_0^\infty \gamma(a) i(a,\cdot)\, da \right) - \nu S^0 (1 + \ln \nu S) \\
&+ \frac{1}{S} \left[\nu S^2 + \left(2\nu S^0 + (\Lambda - (\nu + \mu^0) S^0) \right) S - (\Lambda - (\nu + \mu^0) S^0) S^0 \right] \\
&- \frac{S^0}{S} \int_0^\infty \alpha(a) v(a,\cdot)\, da - \int_0^\infty \left((\eta(a) - \alpha(a)) v(a,\cdot) - \eta(a) v^0(a) \ln v(a,\cdot) \right) da \qquad (3.60) \\
&+ \int_0^\infty \left(\omega^{'}(a) - \sigma(a)\omega(a) + S^0 K_0(a) + S^0 \int_0^\infty K(a,a^{'}) e^{-\int_a^{a^{'}} \sigma(s)\, ds} da^{'} \right) i(a,\cdot)\, da \\
&+ \int_0^\infty \left(\varphi^{'}(a) - \varrho(a)\varphi(a) + \omega(0)\varepsilon(a) \right) e(a,\cdot)\, da.
\end{aligned}
$$

Using assumption **A2**, we demonstrate that

$$
\mu^0 R(t) - \int_0^\infty \gamma(a) i(a,t)\, da \geq \mu^0 R(t) - \bar{\gamma} \int_0^\infty i(a,t)\, da \geq \mu^0 R(t) - \gamma^0 I(t) > 0, \qquad (3.61)
$$

where

$$
I(t) = \int_0^\infty i(a,\cdot)\, da.
$$

Using assumption **A3**, we obtain

$$
\begin{aligned}
&\int_0^\infty \left((\eta(a) - \alpha(a)) v(a,\cdot) - \eta(a) v^0(a) \ln v(a,\cdot) \right) da \\
&\quad > \int_0^\infty \left(\eta(a)(1 - v^0(a)) - \alpha(a) \right) v(a,\cdot)\, da \\
&\quad > \int_0^\infty \left(\eta(a)(1 - \nu S^0) - \alpha(a) \right) v(a,\cdot)\, da \qquad (3.62) \\
&\quad > \int_0^\infty \left(\eta(a) \left(1 - \Lambda \left(1 - \int_0^\infty \alpha(a) e^{-\int_0^a \eta(s)\, ds} da \right)^{-1} \right) - \alpha(a) \right) v(a,\cdot)\, da > 0.
\end{aligned}
$$

Next, functions ω and φ are chosen such that

$$
\omega(a) = S^0 \int_0^\infty \left(K_0(u) + \int_0^\infty K(u,a^{'}) e^{-\int_u^{a^{'}} \sigma(s)\, ds} da^{'} \right) e^{-\int_a^u \sigma(s)\, ds} du \qquad (3.63)
$$

and

$$\varphi(a) = \omega(0) \int_0^\infty \varepsilon(u) e^{-\int_a^u \varrho(s)\,ds} \, du. \tag{3.64}$$

It follows from (3.63) and (3.64) that $\varphi(0) = \Re_0$ and

$$\omega(0) = S^0 \int_0^\infty \left(K_0(u) e^{-\int_0^u \sigma(s)\,ds} + \int_0^\infty K(u,a') e^{-\int_0^{a'} \sigma(s)\,ds} \, da' \right) du.$$

Moreover, by differentiation of (3.63) and (3.64) with respect to age a, we obtain

$$\omega'(a) - \sigma(a)\omega(a) + S^0 K_0(a) + S^0 \int_0^\infty K(a,a') e^{-\int_a^{a'} \sigma(s)\,ds} \, da' = 0$$

and

$$\varphi'(a) - \varrho(a)\varphi(a) + \omega(0)\varepsilon(a),$$

respectively. Therefore, (3.60) is reduced to

$$\begin{aligned} \dot{L}^0(\cdot) = & -\frac{(\nu+\mu^0)}{S}\left(S - S^0\right)^2 + (\Re_0 - 1)\, e(0,\cdot) \\ & - C^0 \left(\mu^0 R - \int_0^\infty \gamma(a) i(a,\cdot)\, da \right) - \nu S^0 (1 + \ln \nu S) \\ & + \frac{1}{S}\left[\nu S^2 + \left(2\nu S^0 + (\Lambda - (\nu+\mu^0)S^0)\right) S - (\Lambda - (\nu+\mu^0)S^0)S^0 \right] \\ & - \frac{S^0}{S} \int_0^\infty \alpha(a) v(a,\cdot)\, da - \int_0^\infty \left((\eta(a) - \alpha(a)) v(a,\cdot) - \eta(a) v^0(a) \ln v(a,\cdot) \right) da. \end{aligned} \tag{3.65}$$

We denote

$$F(S) = \nu S^2 + \left(2\nu S^0 + (\Lambda - (\nu+\mu^0)S^0)\right) S - (\Lambda - (\nu+\mu^0)S^0)S^0. \tag{3.66}$$

Since

$$\frac{\Lambda}{\mu^0 + \nu} < S^0 < \frac{\Lambda}{\mu^0 - \nu},$$

it is easy to check that $F(S)$ has two negative (real) roots. Moreover, $F(S) > 0$ for every $S \geq 0$. Therefore, the sign of $\dot{L}^0(\cdot)$ will be determined by the sign of

$$F(0) - (\nu+\mu^0)(S(t) - S^0)^2 = -\Lambda S^0 - (\nu+\mu^0) S(t)(S(t) - 2S^0).$$

Thus, three cases occur as follows:

Case 1: $S(t) > 2S^0$. It is easy to see that $F(0) - (\nu + \mu^0)(S(t) - S^0)^2 < 0$ and, therefore, $\dot{L}^0(t) \leq 0$ if $\Re_0 \leq 1$.

Case 2: $S(t) = 2S^0$. For this value of $S(t)$, we have $F(0) - (\nu + \mu^0)(S(t) - S^0)^2 = -\Lambda S^0 < 0$ and, therefore, $\dot{L}^0(t) \leq 0$ if $\Re_0 \leq 1$.

Case 3: $0 < S(t) < 2S^0$. For such values of $S(t)$ we have $F(0) - (\nu + \mu^0)(S(t) - S^0)^2 = -(\Lambda - 2(\nu + \mu^0)S(t))S^0 - (\nu + \mu^0)S^2$. Since $2^{-1}(\nu + \mu^0)^{-1}\Lambda < 2S^0$, it follows that $F(0) - (\nu + \mu^0)(S(t) - S^0)^2 < 0$ for any $0 < S(t) < 2^{-1}(\nu + \mu^0)^{-1}\Lambda$. Therefore, $\dot{L}^0(t) \leq 0$ if $\Re_0 \leq 1$.

It results from the above that the derivative of $L^0(t)$ along the solutions of Equation (3.1) is $\dot{L}^0(t) \leq 0$. If $S(t) = S^0$, $v(a,t) = v^0(a)$, and $e(a,t) = i(a,t) = R(t) = 0$ are simultaneously satisfied with $\Re_0 = 1$, then $\dot{L}^0(t) = 0$ holds. Moreover, it can be verified $\left\{(S, v, e, i, R) : \dot{L}^0(t) = 0\right\} = \{E^0\}$. Therefore, it results from Lasalle's Invariance Theorem [13, p. 200] that E^0 is globally asymptotically stable, if $\Re_0 \leq 1$. □

Theorem 3.4.4. *The endemic equilibrium E^* of* (3.1) *is globally asymptotically stable on the set, if $\Re_0 > 1$.*

Proof. To prove the above result, a Lyapunov function of the form given below is considered:

$$L^*(t) = L_1^*(t) + L_2^*(t) + L_3^*(t) + L_4^*(t) + L_5^*(t),$$

where

$$L_1^*(t) = S^* G\left(\frac{S(t)}{S^*}\right), \quad L_2^*(t) = \int_0^\infty v^*(a) G\left(\frac{v(a,t)}{v^*(a)}\right) da, \quad L_3^*(t) = \int_0^\infty e^*(a) G\left(\frac{e(a,t)}{e^*(a)}\right) da$$

$$L_4^*(t) = \int_0^\infty i^*(a) G\left(\frac{i(a,t)}{i^*(a)}\right) da, \quad L_5^*(t) = R^* G\left(\frac{R(t)}{R^*}\right),$$

with $G(X) = X - \ln X - 1$, for X positive.

Thus, we have

$$\dot{L}_1^*(\cdot) = \left(1 - \frac{S^*}{S}\right)\left[\Lambda - (\nu + \mu^0)S + \int_0^\infty \alpha(a)v(a,\cdot)\,da - S\int_0^\infty \left(K_0(a)i(a,\cdot) + \int_0^\infty K(a^{'},a)i(a^{'},\cdot)\,da^{'}\right)\,da\right]$$

Using Equations (3.23), (3.30) and (3.31) together with the first equation of (3.24), we obtain

$$\begin{aligned}\dot{L}_1^*(\cdot) = {} & \frac{\Lambda}{\Re_0}\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) + \left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right)\int_0^\infty \alpha(a)v^*(a)\,da \\ & + \left(1 - \frac{S^*}{S}\right)\left[-\int_0^\infty \alpha(a)v^*(a)\,da + \int_0^\infty \alpha(a)v(a,\cdot)\,da\right. \\ & -S\int_0^\infty \left(K_0(a)i(a,\cdot) + \int_0^\infty K(a^{'},a)i(a^{'},\cdot)\,da^{'}\right)\,da \\ & \left. -S^*\int_0^\infty \left(K_0(a)i^*(a) + \int_0^\infty K(a^{'},a)i^*(a^{'})\,da^{'}\right)\,da\right].\end{aligned}$$

Some terms are carefully added and subtracted to the above expression, and the group of terms identified in the form given by $G(X) = X - 1 - \ln X$. We obtain

$$\begin{aligned}\dot{L}_1^*(\cdot) = {} & \frac{\Lambda}{\Re_0}\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right) - \int_0^\infty \alpha(a)v^*(a)\left[G\left(\frac{S^*v(a,\cdot)}{Sv^*(a)}\right)\right. \\ & \left. -G\left(\frac{S^*}{S}\right) - G\left(\frac{v(a,\cdot)}{v^*(a)}\right)\right]\,da - 2G\left(\frac{S^*}{S}\right)\int_0^\infty \alpha(a)v^*(a)\,da \\ & - S^*\int_0^\infty K_0(a)i^*(a)\left[G\left(\frac{Si(a,\cdot)}{S^*i^*(a)}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right]\,da \\ & - S^*\int_0^\infty\int_0^\infty K(a^{'},a)i^*(a^{'})\left[G\left(\frac{Si(a^{'},\cdot)}{S^*i^*(a^{'})}\right) - G\left(\frac{i(a^{'},\cdot)}{i^*(a^{'}}\right)\right]\,da^{'}\,da.\end{aligned} \tag{3.67}$$

By differentiating L_2^* with respect to t, we obtain

$$\dot{L}_2^*(\cdot) = -\int_0^\infty \left(1 - \frac{v^*(a)}{v(a,\cdot)}\right)\left(\frac{\partial}{\partial t}v(a,\cdot) + \eta(a)v(a,\cdot)\right)\,da. \tag{3.68}$$

Since

$$v^*(a)\frac{\partial}{\partial t}G\left(\frac{v(a,\cdot)}{v^*(a)}\right) = \left(1-\frac{v^*(a)}{v(a,\cdot)}\right)\left(\frac{\partial}{\partial t}v(a,\cdot)+\eta(a)v(a,\cdot)\right)$$

thus, Equation (3.68) yields

$$\dot{L}_2^*(\cdot) = -\int_0^\infty v^*(a)\frac{\partial}{\partial t}G\left(\frac{v(a,\cdot)}{v^*(a)}\right)\,da. \tag{3.69}$$

Using the second equation of (3.24) after integrating by part, we obtain

$$\dot{L}_2^*(\cdot) = v^*(0)G\left(\frac{S}{S^*}\right) - \int_0^\infty \eta(a)v^*(a)G\left(\frac{v(a,\cdot)}{v^*(a)}\right)\,da. \tag{3.70}$$

Moreover, the following equation

$$v^*(0)G\left(\frac{S}{S^*}\right) = v^*(0)\int_0^\infty \eta(a)e^{-\int_0^\infty \eta(s)\,ds}G\left(\frac{S}{S^*}\right)\,da = \int_0^\infty \eta(a)v^*(a)G\left(\frac{S}{S^*}\right)\,da, \tag{3.71}$$

yields

$$\dot{L}_2^*(\cdot) = -\int_0^\infty \eta(a)v^*(a)\left[G\left(\frac{v(a,\cdot)}{v^*(a)}\right) - G\left(\frac{S}{S^*}\right)\right]\,da. \tag{3.72}$$

Similar to L_2^*, from L_3^* and L_4^* we obtain

$$\dot{L}_3^*(\cdot) = -\int_0^\infty \varrho(a)e^*(a)\left[G\left(\frac{e(a,\cdot)}{e^*(a)}\right) - G\left(\frac{e(0,\cdot)}{e^*(0)}\right)\right]\,da \tag{3.73}$$

and

$$\dot{L}_4^*(\cdot) = -\int_0^\infty \sigma(a)i^*(a)\left[G\left(\frac{i(a,\cdot)}{i^*(a)}\right) - G\left(\frac{i(0,\cdot)}{i^*(0)}\right)\right]\,da, \tag{3.74}$$

respectively, using the fifth equation of (3.24), L_5^* leads to

$$\begin{aligned}\dot{L}_5^*(\cdot) =& \mu^0R^*\left(2-\frac{R}{R^*}-\frac{R^*}{R}\right)\\ &-\int_0^\infty \gamma(a)i^*(a)\left[G\left(\frac{R^*i(a,\cdot)}{Ri^*(a)}\right) - G\left(\frac{R^*}{R}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right]\,da.\end{aligned} \tag{3.75}$$

By combining (3.67), (3.72), (3.73), (3.74), and (3.75), we obtain

$$\dot{L}^*(\cdot) = \frac{\Lambda}{\Re_0}\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right) - \int_0^\infty \alpha(a)v^*(a)\left[G\left(\frac{S^*v(a,\cdot)}{Sv^*(a)}\right) - G\left(\frac{S^*}{S}\right)\right.$$

$$-G\left(\frac{v(a,\cdot)}{v^*(a)}\right)\Bigg] \, da - 2G\left(\frac{S^*}{S}\right)\int_0^\infty \alpha(a)v^*(a)\,da$$

$$- S^*\int_0^\infty K_0(a)i^*(a)\left[G\left(\frac{Si(a,\cdot)}{S^*i^*(a)}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right] da$$

$$- S^*\int_0^\infty\int_0^\infty K(a^{'},a)i^*(a^{'})\left[G\left(\frac{Si(a^{'},\cdot)}{S^*i^*(a^{'})}\right) - G\left(\frac{i(a^{'},\cdot)}{i^*(a^{'}}\right)\right] da^{'}\,da$$

$$+ G\left(\frac{S}{S^*}\right)\int_0^\infty \eta(a)v^*(a)\,da - \int_0^\infty \eta(a)v^*(a)G\left(\frac{v(a,\cdot)}{v^*(a)}\right) da$$

$$- \int_0^\infty \varrho(a)e^*(a)\left[G\left(\frac{e(a,\cdot)}{e^*(a)}\right) - G\left(\frac{e(0,\cdot)}{e^*(0)}\right)\right] da$$

$$- \int_0^\infty \sigma(a)i^*(a)\left[G\left(\frac{i(a,\cdot)}{i^*(a)}\right) - G\left(\frac{i(0,\cdot)}{i^*(0)}\right)\right] da\mu^0 R^*\left(2 - \frac{R}{R^*} - \frac{R^*}{R}\right)$$

$$- \int_0^\infty \gamma(a)i^*(a)\left[G\left(\frac{R^*i(a,\cdot)}{Ri^*(a)}\right) - G\left(\frac{R^*}{R}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right] da.$$

This yields

$$\dot{L}^*(\cdot) = \frac{\Lambda}{\Re_0}\left(2 - \frac{S^*}{S} - \frac{S}{S^*}\right)$$

$$- \int_0^\infty \alpha(a)v^*(a)\left[G\left(\frac{S^*v(a,\cdot)}{Sv^*(a)}\right) - G\left(\frac{S^*}{S}\right) - G\left(\frac{v(a,\cdot)}{v^*(a)}\right)\right] da$$

$$- S^*\int_0^\infty K_0(a)i^*(a)\left[G\left(\frac{Si(a,\cdot)}{S^*i^*(a)}\right) - G\left(\frac{S}{S^*}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right] da$$

$$- S^*\int_0^\infty\int_0^\infty K(a^{'},a)i^*(a^{'})\left[G\left(\frac{Si(a^{'},\cdot)}{S^*i^*(a^{'})}\right) - G\left(\frac{S}{S^*}\right) - G\left(\frac{i(a^{'},\cdot)}{i^*(a^{'}}\right)\right] da^{'}\,da$$

$$- 2G\left(\frac{S^*}{S}\right)\int_0^\infty \alpha(a)v^*(a)\,da - \int_0^\infty \eta(a)v^*(a)G\left(\frac{v(a,\cdot)}{v^*(a)}\right) da$$

$$- \left[S^*\int_0^\infty\left(K_0(a)i^*(a) + \int_0^\infty K(a^{'},a)i^*(a^{'})\,da^{'}\right) da - \int_0^\infty \eta(a)v^*(a)\,da\right] G\left(\frac{S}{S^*}\right)$$

$$
\begin{aligned}
&-\int_0^\infty \varrho(a)e^*(a)G\left(\frac{e^*(0)e(a,\cdot)}{e(0,t)e^*(a)}\right)da-\int_0^\infty \sigma(a)i^*(a)G\left(\frac{i^*(0)i(a,\cdot)}{i(0,t)i^*(a)}\right)da\\
&-\int_0^\infty \varrho(a)e^*(a)\left(1-\frac{e^*(0)}{e(0,\cdot)}\right)\left(\frac{e(a,\cdot)}{e^*(a)}-\frac{e(0,\cdot)}{e^*(0)}\right)da\\
&-\int_0^\infty \sigma(a)i^*(a)\left(1-\frac{i^*(0)}{i(0,\cdot)}\right)\left(\frac{i(a,\cdot)}{i^*(a)}-\frac{i(0,\cdot)}{i^*(0)}\right)da+\mu^0R^*\left(2-\frac{R}{R^*}-\frac{R^*}{R}\right)\\
&-\int_0^\infty \gamma(a)i^*(a)\left[G\left(\frac{R^*i(a,\cdot)}{Ri^*(a)}\right)-G\left(\frac{R^*}{R}\right)-G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right]da.
\end{aligned}
$$

Since

$$
S^*\int_0^\infty\left(K_0(a)i^*(a)+\int_0^\infty K(a',a)i^*(a')\,da'\right)da=1,\quad \int_0^\infty \eta(a)e^{-\int_0^\infty \eta(s)\,ds}\,da=1,
$$

thus,

$$
\begin{aligned}
\dot{L}^*(\cdot)=&\frac{\Lambda}{\Re_0}\left(2-\frac{S^*}{S}-\frac{S}{S^*}\right)\\
&-\int_0^\infty \alpha(a)v^*(a)\left[G\left(\frac{S^*v(a,\cdot)}{Sv^*(a)}\right)-G\left(\frac{S^*}{S}\right)-G\left(\frac{v(a,\cdot)}{v^*(a)}\right)\right]da\\
&-S^*\int_0^\infty K_0(a)i^*(a)\left[G\left(\frac{Si(a,\cdot)}{S^*i^*(a)}\right)-G\left(\frac{S}{S^*}\right)-G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right]da\\
&-S^*\int_0^\infty\int_0^\infty K(a',a)i^*(a')\left[G\left(\frac{Si(a',\cdot)}{S^*i^*(a')}\right)-G\left(\frac{S}{S^*}\right)-G\left(\frac{i(a',\cdot)}{i^*(a'}\right)\right]da'\,da\\
&-2G\left(\frac{S^*}{S}\right)\int_0^\infty \alpha(a)v^*(a)\,da-\int_0^\infty \eta(a)v^*(a)G\left(\frac{v(a,\cdot)}{v^*(a)}\right)da \qquad (3.76)\\
&-(1-\nu S^*)\,G\left(\frac{S}{S^*}\right)-\int_0^\infty \varrho(a)e^*(a)G\left(\frac{e^*(0)e(a,\cdot)}{e(0,t)e^*(a)}\right)da\\
&-\int_0^\infty \varrho(a)e^*(a)\left(1-\frac{e^*(0)}{e(0,\cdot)}\right)\left(\frac{e(a,\cdot)}{e^*(a)}-\frac{e(0,\cdot)}{e^*(0)}\right)da
\end{aligned}
$$

$$- \int_0^\infty \sigma(a) i^*(a) G\left(\frac{i^*(0) i(a,\cdot)}{i(0,t) i^*(a)}\right) da + \mu^0 R^* \left(2 - \frac{R}{R^*} - \frac{R^*}{R}\right)$$
$$- \int_0^\infty \sigma(a) i^*(a) \left(1 - \frac{i^*(0)}{i(0,\cdot)}\right)\left(\frac{i(a,\cdot)}{i^*(a)} - \frac{i(0,\cdot)}{i^*(0)}\right) da$$
$$- \int_0^\infty \gamma(a) i^*(a) \left[G\left(\frac{R^* i(a,\cdot)}{R i^*(a)}\right) - G\left(\frac{R^*}{R}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right)\right] da.$$

Using assumption **A3**, it is easy to see that $\Lambda < 1 - \int_0^\infty \alpha(a) e^{-\int_0^a \eta(s)\,ds} da$. Hence, $\frac{S^0}{\Re_0} < \frac{1}{\nu}$ for $\Re_0 > 1$; i.e., $1 - \nu S^* > 0$ for $\Re_0 > 1$. Moreover,

- $G\left(\frac{S^* v(a,\cdot)}{S v^*(a)}\right) - G\left(\frac{S^*}{S}\right) - G\left(\frac{v(a,\cdot)}{v^*(a)}\right) = \left(1 - \frac{S^*}{S}\right)\left(1 - \frac{v(a,\cdot)}{v^*(a)}\right) > 0$
$\Leftrightarrow \left(\frac{S}{S^*} < 1 \quad \text{and} \quad \frac{v(a,\cdot)}{v^*(a)} > 1\right) \text{ or } \left(\frac{S}{S^*} > 1 \quad \text{and} \quad \frac{v(a,\cdot)}{v^*(a)} < 1\right)$;
- $G\left(\frac{S i(a,\cdot)}{S^* i^*(a)}\right) - G\left(\frac{S}{S^*}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right) = \left(1 - \frac{S}{S^*}\right)\left(1 - \frac{i(a,\cdot)}{i^*(a)}\right) > 0$
$\Leftrightarrow \left(\frac{S}{S^*} > 1 \quad \text{and} \quad \frac{i(a,\cdot)}{i^*(a)} > 1\right) \text{ or } \left(\frac{S}{S^*} < 1 \quad \text{and} \quad \frac{i(a,\cdot)}{i^*(a)} < 1\right)$;
- $\left(1 - \frac{e^*(a)}{e(0,\cdot)}\right)\left(\frac{e(a,\cdot)}{e^*(a)} - \frac{e(0,\cdot)}{e^*(0)}\right) > 0$
$\Leftrightarrow \left(\frac{e(a,\cdot)}{e^*(a)} < \frac{e(0,\cdot)}{e^*(0)} < 1\right) \text{ or } \left(\frac{e(a,\cdot)}{e^*(a)} > \frac{e(0,\cdot)}{e^*(0)} > 1\right)$;
- $\left(1 - \frac{i^*(a)}{i(0,\cdot)}\right)\left(\frac{i(a,\cdot)}{i^*(a)} - \frac{i(0,\cdot)}{i^*(0)}\right) > 0$
$\Leftrightarrow \left(\frac{i(a,\cdot)}{i^*(a)} < \frac{i(0,\cdot)}{i^*(0)} < 1\right) \text{ or } \left(\frac{i(a,\cdot)}{i^*(a)} > \frac{i(0,\cdot)}{i^*(0)} > 1\right)$;
- $G\left(\frac{R^* i(a,\cdot)}{R i^*(a)}\right) - G\left(\frac{R^*}{R}\right) - G\left(\frac{i(a,\cdot)}{i^*(a)}\right) = \left(1 - \frac{R^*}{R}\right)\left(1 - \frac{i(a,\cdot)}{i^*(a)}\right) > 0$
$\Leftrightarrow \left(\frac{R}{R^*} < 1 \quad \text{and} \quad \frac{i(a,\cdot)}{i^*(a)} > 1\right) \text{ or } \left(\frac{R}{R^*} > 1 \quad \text{and} \quad \frac{i(a,\cdot)}{i^*(a)} < 1\right)$.

Therefore, we obtain

$$\dot{L}^*(t) < 0, \tag{3.77}$$

in the following cases:

(i) $\frac{S}{S^*} < 1$, $\frac{v(a,\cdot)}{v^*(a)} > 1$, $\frac{e(a,\cdot)}{e^*(a)} > \frac{e(0,\cdot)}{e^*(0)} > 1$, $\frac{i(a,\cdot)}{i^*(a)} < \frac{i(0,\cdot)}{i^*(0)} < 1$, and $\frac{R}{R^*} > 1$;

(ii) $\frac{S}{S^*} < 1$, $\frac{v(a,\cdot)}{v^*(a)} > 1$, $\frac{e(a,\cdot)}{e^*(a)} < \frac{e(0,\cdot)}{e^*(0)} < 1$, $\frac{i(a,\cdot)}{i^*(a)} < \frac{i(0,\cdot)}{i^*(0)} < 1$, and $\frac{R}{R^*} > 1$;

(iii) $\frac{S}{S^*} > 1$, $\frac{v(a,\cdot)}{v^*(a)} < 1$, $\frac{e(a,\cdot)}{e^*(a)} > \frac{e(0,\cdot)}{e^*(0)} > 1$, $\frac{i(a,\cdot)}{i^*(a)} > \frac{i(0,\cdot)}{i^*(0)} > 1$, and $\frac{R}{R^*} < 1$;

(iv) $\frac{S}{S^*} > 1$, $\frac{v(a,\cdot)}{v^*(a)} < 1$, $\frac{e(a,\cdot)}{e^*(a)} < \frac{e(0,\cdot)}{e^*(0)} < 1$, $\frac{i(a,\cdot)}{i^*(a)} > \frac{i(0,\cdot)}{i^*(0)} > 1$, and $\frac{R}{R^*} < 1$.

From (3.77), we say that the derivative of $L^*(t)$ along the solutions of Equation (3.1) is $\dot{L}^*(t) < 0$. If $S(t) = S^*$, $v(a,t) = v^*(a)$, $e(a,t) = e^*(a)$, $i(a,t) = i^*(a)$, $R(t) = R^*$ are simultaneously satisfied, then we obtain $\dot{L}^*(t) = 0$ from (3.76). Moreover, it can be verified $\left\{(S,v,e,i,R) : \dot{L}^*(t) = 0\right\} = \{E^*\}$. Therefore, it results from Lasalle's Invariance Theorem [13, p. 200] that E^* is globally asymptotically stable, if $\Re_0 > 1$. $\square$

The results from Theorems 3.4.3 and 3.4.4 show that there is a threshold parameter, referred to as the basic reproduction number and denoted by $\Re_0$, that is essential in the stability analysis of the global behaviour of the system defined by (3.1). Moreover, such a parameter can play a crucial role in the implementation of human vaccination policies. As seen in the following equation:

$$\frac{\partial \Re_0}{\partial \nu} = -\frac{\Lambda(1-P)}{\left(\mu^0 + \nu(1-P)\right)^2} \int_0^\infty \left(K_0(a)\zeta(a) + \int_0^\infty K(a,a^{'})\zeta(a^{'})\, da^{'} \right) da < 0,$$

the rise in rate of vaccination of (infant) susceptible individuals against an SEIR infection can reduce the spread of the infection and assist in the elaboration of policies to reduce and prevent the spread of the infection.

Chapter 4

Coagulation-fragmentation models using the monotone method

4.1 Introduction

Coagulation-fragmentation equations describe the dynamics of particles enlargement under the combined effect of aggregation and breakage. These phenomena occur in chemical engineering and natural sciences such as in rock fracture, droplet break-up, evolution of phytoplankton aggregate, polymerization and depolymerization. During the last decades, many investigations have been conducted on coagulation, fragmentation and both coagulation-fragmentation processes with growth (see for example [4, 6, 8, 14, 15, 16, 17, 39, 52, 64, 78] and the references therein). Many of these investigations dealt with the well-posedness of the dynamical system governing the evolution of the system of particles (see for example [5, 6, 17, 18, 39, 52]). In the literature, three common methods are generally employed to established the well-posedness of the model. The first method is based on the semigroup theory. It is elegant and one of the most used in applied sciences (see for example [14, 15, 16, 17, 18, 39, 44, 45, 52]). The second method is the well-known characteristics method, which has also been used extensively to determine the existence and uniqueness of solutions (see [21] and references therein). The third approach is the finite difference approximation technique. This technique is useful in the context of classical conservation laws (see [23]) and is very effective in the investigation of the physical properties and asymptotic behaviour of solutions.

Ackleh in [1, 2, 3, 4, 5, 7, 8, 9] used the monotone method to investigate coagulation equations with growth without fragmentation. In this approach, monotone sequences of upper-lower solutions are constructed to prove the existence and uniqueness of the solution using the comparison principle. To the best of our knowledge, the monotone method has not been developed for coagulation-fragmentation equations. The main purpose of this study is to undertake such a task in order to establish the well-posedness of this evolution problem.

In Section 4.2, a non-autonomous coagulation-fragmentation model was analysed in the Banach space $X_1 = L^1((0,T) \times (x_0,\infty), x\,dx)$. Subsequently, in Section 4.3, a non-autonomous coagulation-fragmentation with growth was considered in the Banach space $X_0 = L^1((0,T) \times (x_0,\infty),\, dx)$.

4.2 Coagulation-fragmentation model

In this section, coagulation-fragmentation processes are first described and assumptions considered. Next, upper and lower solutions are defined and the comparison principle proved. Finally, the local existence and uniqueness of the solution of the model is established and show that this solution is also global.

4.2.1 Description of the model

Denoting the particle mass distribution x at time t by $u(t,x)$, the coagulation- fragmentation process is derived by the following nonlinear non-autonomous integro-differential equation:

$$\begin{aligned}\partial_t u(t,x) + \alpha(t,x)u(t,x) = &+ \int_{x+x_0}^{\infty} \beta(x|y)\alpha(t,y)u(t,y)dy \\ &+ \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)u(t,y)u(t,x-y)dy \end{aligned} \tag{4.1}$$

$$- u(t,x)\int_{x_0}^{\infty}\kappa(x,y)u(t,y)dy,$$

for $(t,x)\in(0,T)\times(x_0,\infty)$, subject to the initial condition

$$u(0,x)=u_0(x),\ \text{for}\quad x\in[x_0,\infty), \tag{4.2}$$

where the characteristic function χ_I ($I=[2x_0,\infty)$) guarantees no particle of mass less than $2x_0$ ($x_0>0$) can emerge as a result of coagulation. In equation (4.1), the coefficient $\alpha(t,x)$, denotes the fragmentation rate of particle masses x at time t, and $\beta(x|y)$ represents the mass distribution of daughter particles of mass x after fragmentation of an aggregate of size y. The function $\kappa(x,y)$ is said to be the rate at which an aggregate of size x fuses with the one of size y.

In equation (4.1), the meaning the terms are given as, from left to the right, the diminution of amount of particles in the size range $(x;x+dx)$ as a result of splitting, the augmentation of amount of particles of size x as the result of splitting of larger ones, the increase in the amount of particles of size $x\ge 2x_0$ caused by coalescence of aggregates of size $x-y$ and y ($x_0\le y\le x-x_0$), where the factor $1/2$ means that either an aggregate of size y sticks to the one of size $x-y$ or vice versa. The last term represents loss of particles of size x due to fusion with particles of size y, ($y\ge x_0$).

We base our analysis on the following hypotheses:

(A1) $\beta(x|y)\ge 0$ is a continuous function on $(x_0,\infty)\times(x_0,\infty)$ with $\|\beta\|_\infty<\infty$; $\beta(x|y)=0$ for $x+x_0>y$ and $\int_{x_0}^{y-x_0}\beta(x|y)dx=y$ for every $y>2x_0$;

(A2) $\alpha(t,x)\in L^\infty([0,T]\times(x_0,\infty))$. Particle sizes below $2x_0$ do not split since the least possible particle size is x_0. Hence, we suppose that $0=\alpha(t,x)$ for $2x_0>x$;

(A3) $\kappa(x,y)\ge 0$ in $L^\infty((x_0,\infty)\times(x_0,\infty))$, where $\|\kappa\|_\infty:=\operatorname{ess\,sup}\{\kappa(x,y);(x,y)\in(x_0,\infty)\times(x_0,\infty)\}$;

(A4) $u_0(x)\ge 0$ on $[x_0,\infty)$ and $u_0(x)\in L^1((x_0,\infty))\cap L^\infty((x_0,\infty))$.

For simplicity, let $D_T=(0,T)\times(x_0,\infty)$ and $C^1_{0,r}(D_T)=\{\psi\in C^1(D_T):\exists x_\psi\in(x_0,\infty)$ such that $\psi\equiv 0$ for $x\ge x_\psi\}$.

4.2.2 Comparison principle

The definition of the solution of (4.1)-(4.2) is given as follows:

Definition 4.2.1. *$u(t,x)$ is called a solution of (4.1)-(4.2) on D_T if all the following hold:*

1. *$u \in X_1 = L^1(D_T, x\,dx)$.*
2. *$u(x,0) = u_0(x)$ a.e. in (x_0, ∞).*
3. *For each $t \in (0,T)$ and every nonnegative $\xi(t,x) \in C^1_{0,r}(D_T)$,*

$$\begin{aligned}
\int_{x_0}^{\infty} xu(t,x)\xi(t,x)\,dx &= \int_{x_0}^{\infty} xu(0,x)\xi(0,x)dx \\
&+ \int_{x_0}^{\infty}\int_0^t xu(s,x)\xi_s(s,x)\,ds\,dx \\
&+ \int_0^t\int_{2x_0}^{\infty} u(s,y)\alpha(s,y)\int_{x_0}^{y-x_0} x\beta(x|y)\xi(s,x)\,dx\,dy\,ds \\
&+ \int_{x_0}^{\infty}\int_0^t x\xi(s,x)(\mathcal{F}u)(s,x)\,ds\,dx \\
&- \int_{x_0}^{\infty}\int_0^t x\xi(s,x)u(s,x)\int_{x_0}^{\infty}\kappa(x,y)u(s,y)\,dy\,ds\,dx \\
&- \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\alpha(s,x)u(s,x)\,ds\,dx
\end{aligned} \tag{4.3}$$

where

$$(\mathcal{F}u)(t,x) = \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)u(t,x-y)u(t,y)\,dy. \tag{4.4}$$

Let a pair of lower and upper solutions of the model (4.1)-(4.2) be defined as follows.

Definition 4.2.2. *Given a pair $(\underline{u}, \overline{u})$, the functions $\underline{u}(t,x)$ and $\overline{u}(t,x)$ are said to be a lower and an upper solution to (4.1)-(4.2) on D_T, respectively, if:*

1. *$\underline{u}, \overline{u} \in X_1 = L^1(D_T, xdx)$.*

2. $\overline{u}(0,x) \geq u_0(x) \geq \underline{u}(0,x)$ *a.e. in* (x_0,∞).

3. *For each* $t \in (0,T)$ *and every nonnegative* $\xi(t,x) \in C^1_{0,r}(D_T)$,

$$\begin{aligned}\int_{x_0}^{\infty} x\underline{u}(t,x)\xi(t,x)\,dx \leq & \int_{x_0}^{\infty} x\underline{u}(0,x)\xi(0,x)dx \\ & + \int_{x_0}^{\infty}\int_0^t x\underline{u}(s,x)\xi_s(s,x)\,ds\,dx \\ & + \int_0^t\int_{2x_0}^{\infty} \underline{u}(s,y)\alpha(s,y)\int_{x_0}^{y-x_0} x\beta(x|y)\xi(s,x)\,dx\,dy\,ds \\ & + \int_{x_0}^{\infty}\int_0^t x\xi(s,x)(\mathcal{F}\underline{u})(s,x)\,ds\,dx \\ & - \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\underline{u}(s,x)\int_{x_0}^{\infty}\kappa(x,y)\overline{u}(s,y)\,dy\,ds\,dx \\ & - \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\alpha(s,x)\underline{u}(s,x)\,ds\,dx.\end{aligned} \tag{4.5}$$

$$\begin{aligned}\int_{x_0}^{\infty} x\overline{u}(t,x)\xi(t,x)\,dx \geq & \int_{x_0}^{\infty} x\overline{u}(0,x)\xi(0,x)dx \\ & + \int_{x_0}^{\infty}\int_0^t x\overline{u}(s,x)\xi_s(s,x)\,ds\,dx \\ & + \int_0^t\int_{2x_0}^{\infty} \overline{u}(s,y)\alpha(s,y)\int_{x_0}^{y-x_0} x\beta(x|y)\xi(s,x)\,dx\,dy\,ds \\ & + \int_{x_0}^{\infty}\int_0^t x\xi(s,x)(\mathcal{F}\overline{u})(s,x)\,ds\,dx \\ & - \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\overline{u}(s,x)\int_{x_0}^{\infty}\kappa(x,y)\underline{u}(s,y)\,dy\,ds\,dx \\ & - \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\alpha(s,x)\overline{u}(s,x)\,ds\,dx\end{aligned} \tag{4.6}$$

Based on Definition 4.2.2, the comparison principle is stated and proved as follows:

Theorem 4.2.3. *Let assumptions* $(A1)-(A4)$ *hold. If* $\underline{u}$ *and* $\overline{u}$ *are nonnegative lower and upper solutions of the model* (4.1)-(4.2)*, respectively; then,* $\underline{u} \leq \overline{u}$ *a.e. in* D_T.

Proof. A negative function v is considered such that $v = \underline{u} - \overline{u}$ and ξ is chosen so that $\xi \in C^1_{0,r}((0,T)\times(x_0,n))$, $n \in \mathbb{N}^*$, with $C^1_{0,r}((0,T)\times(x_0,n)) = \{\psi \in C^1((0,T)\times(x_0,n)) :$

$\exists x_\psi \in (x_0, n)$ so that $0 \equiv \psi$ for $x_\psi \le x\}$. Thus, v satisfies

$$0 \ge v(0,x) = -(\overline{u}(0,x) - \underline{u}(0,x)) \quad \text{a.e. in } [x_0,\infty) \tag{4.7}$$

and

$$\begin{aligned}\int_{x_0}^{\infty} xv(t,x)\xi(t,x)\,dx &\le \int_{x_0}^{\infty} xv(0,x)\xi(0,x)dx \\ &+ \int_{x_0}^{\infty}\int_0^t xv(s,x)\xi_s(s,x)\,ds\,dx \\ &+ \int_0^t\int_{2x_0}^{\infty}\alpha(s,y)v(s,y)\int_{x_0}^{y-x_0} x\xi(s,x)\beta(x|y)\,dx\,dy\,ds \\ &+ \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\left[(\mathcal{F}\underline{u})(s,x) - (\mathcal{F}\overline{u})(s,x)\right]\,ds\,dx \\ &+ \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\overline{u}(s,x)\int_{x_0}^{\infty}\kappa(x,y)v(s,y)\,dy\,ds\,dx \\ &- \int_{x_0}^{\infty}\int_0^t x\xi(s,x)v(s,x)\int_{x_0}^{\infty}\kappa(x,y)\overline{u}(s,y)\,dy\,ds\,dx \\ &- \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\alpha(s,x)v(s,x)\,ds\,dx.\end{aligned} \tag{4.8}$$

Upon manipulation,

$$\begin{aligned}&\int_{x_0}^{\infty}\int_0^t x\xi(s,x)\left[(\mathcal{F}\underline{u})(s,x) - (\mathcal{F}\overline{u})(s,x)\right]\,ds\,dx \\ &= \frac{1}{2}\int_{x_0}^{\infty}\int_0^t x\xi(s,x)\chi_{I}(x)\int_{x_0}^{x-x_0}\kappa(x-y,y)\left[\underline{u}(s,x-y)v(s,y)\right. \\ &\left.+v(s,x-y)\overline{u}(s,y)\right]\,dy\,ds\,dx\end{aligned} \tag{4.9}$$

is obtained.

It follows that

$$\begin{aligned}&\int_{x_0}^{\infty}\int_0^t x\xi(s,x)\left[(\mathcal{F}\underline{u})(s,x) - (\mathcal{F}\overline{u})(s,x)\right]\,ds\,dx \\ &= \frac{1}{2}\int_0^t\int_{x_0}^{\infty} v(s,y)\int_{y+x_0}^{\infty} x\xi(s,x)\chi_{I}(x)\kappa(x-y,y)\underline{u}(s,x-y)\,dx\,dy\,ds\end{aligned}$$

$$+\frac{1}{2}\int_0^t\int_{x_0}^\infty \overline{u}(s,y)\int_{y+x_0}^\infty x\xi(s,x)\chi_{_I}(x)\kappa(x-y,y)v(s,x-y)\,dx\,dy\,ds \tag{4.10}$$
$$=\int_0^t\int_{x_0}^\infty \frac{1}{2}v(s,y)\int_{x_0}^\infty (y+z)\xi(s,y+z)\chi_{_I}(y+z)\kappa(z,y)\underline{u}(s,z)\,dz\,dy\,ds$$
$$+\frac{1}{2}\int_0^t\int_{x_0}^\infty \overline{u}(s,y)\int_{x_0}^\infty (y+z)\xi(s,y+z)\chi_{_I}(y+z)\kappa(z,y)v(s,z)\,dz\,dy\,ds.$$

Let $\xi(t,x)=e^{\lambda t}\zeta(t,x)$, where $\zeta\in C^1_{0,r}((0,T)\times(x_0,n))$ and a positive λ is picked such that $\lambda-\alpha(t,x)-\displaystyle\int_{x_0}^\infty \overline{u}(s,y)\kappa(x,y)\,dy\geq 0$ on D_T. Then,

$$e^{\lambda t}\int_{x_0}^\infty xv(t,x)\zeta(t,x)\,dx$$
$$\leq \int_{x_0}^\infty xv(0,x)\zeta(0,x)dx+\int_{x_0}^\infty\int_0^t xv(s,x)e^{\lambda s}\zeta_s(s,x)\,ds\,dx$$
$$+\int_0^t\int_{2x_0}^\infty \alpha(s,y)v(s,y)\int_{x_0}^{y-x_0} xe^{\lambda s}\zeta(s,x)\beta(x|y)\,dx\,dy\,ds$$
$$+\int_{x_0}^\infty\int_0^t xv(s,x)e^{\lambda s}\zeta(s,x)\left(\lambda-\alpha(s,x)-\int_{x_0}^\infty\kappa(x,y)\overline{u}(s,y)\,dy\right)ds\,dx \tag{4.11}$$
$$+\frac{1}{2}\int_0^t\int_{x_0}^\infty v(s,y)\int_{x_0}^\infty (y+z)e^{\lambda s}\zeta(s,y+z)\chi_{_I}(y+z)\kappa(z,y)\underline{u}(s,z)\,dz\,dy\,ds$$
$$+\frac{1}{2}\int_0^t\int_{x_0}^\infty \overline{u}(s,y)\int_{x_0}^\infty (y+z)e^{\lambda s}\zeta(s,y+z)\chi_{_I}(y+z)\kappa(z,y)v(s,z)\,dz\,dy\,ds$$
$$+\int_{x_0}^\infty\int_0^t xe^{\lambda s}\zeta(s,x)\overline{u}(s,x)\int_{x_0}^\infty \kappa(x,y)v(s,y)\,dy\,ds\,dx$$

is obtained.

A backward problem is formulated as follows:

$$\begin{aligned}
0&=\zeta_s(s,x), && 0<s<t, \quad x_0<x<n\\
0&=\zeta(s,n), && 0<s<t\\
\chi^1(x)&=\zeta(t,x), && x_0\leq x\leq n.
\end{aligned}\tag{4.12}$$

Here, $\chi^1\in C_0^\infty((x_0,n))$, $0\leq\chi^1\leq 1$.

The existence of $\zeta\in C^1_{0,r}((0,T)\times(x_0,n))$ follows from the fact that by the variable change $\iota = t - s$, the above problem (4.12) can be written into

$$\begin{aligned} \zeta_\iota(\iota, x) =& 0, \qquad 0 < s < t, \quad x_0 < x < n \\ \zeta(\iota, n) =& 0, \qquad 0 < s < t \\ \zeta(0, x) =& \chi^1(x), \qquad n \geq x \geq x_0. \end{aligned} \tag{4.13}$$

From (4.13), $0 \leq \zeta \leq 1$ on $(0, T) \times (x_0, n)$ is obtained.

Thereafter, ζ is substituted into (4.11) to obtain

$$\begin{aligned} \int_0^n xv(t,x)\chi^1(x)dx \leq & \int_{x_0}^\infty xv(0,x)^+ \, dx \\ & + \int_0^t \int_{2x_0}^\infty x\alpha(s,x)v(s,x)^+ \, dx \, ds \\ & + \nu \int_0^t \int_{x_0}^\infty xv(s,x)^+ \, dx \, ds \end{aligned} \tag{4.14}$$

where

$$\begin{aligned} \nu =& \sup_{\overline{D_T}} \Bigg[\left(\lambda - \alpha(s,x) - \int_{x_0}^\infty \kappa(x,y)\overline{u}(t,y) \, dy \right) \\ & + \frac{1}{2} \int_{x_0}^\infty \chi_{_I}(x+z)\kappa(z,x)\underline{u}(t,z) \, dz \\ & + \frac{3}{2} \|\kappa\|_\infty \int_{x_0}^\infty (1 + \chi_{_I}(x+y))\overline{u}(t,y) \, dy \Bigg] \end{aligned}$$

and

$$v(s,x)^+ = \sup_{\overline{D_T}} \{v(s,x), 0\}.$$

From the initial data for v in (4.7),

$$\int_{x_0}^n xv(t,x)\chi^1(x)dx \leq \int_0^t \int_{2x_0}^\infty x\alpha(s,x)v(s,x)^+ \, dx \, ds + \nu \int_0^t \int_{x_0}^\infty xv(s,x)^+ \, dx \, ds,$$

is thus, found.

From the assumption $(A2)$, $\alpha(t,x) = 0$ for $x < 2x_0$ is obtained, and then

$$\int_{x_0}^{n} xv(t,x)\chi^1(x)dx \leq \int_0^t \int_{x_0}^{\infty} (\alpha(s,x) + \nu)xv(s,x)^+ \, dx \, ds.$$

Since this inequality holds for every χ^1, a sequence $\{\chi^1_\kappa\}$ can be chosen on $(0,n)$ converging to

$$\chi^1 = \begin{cases} 1 & \text{if} \quad v(t,x) > 0 \\ 0 & \text{otherwise.} \end{cases}$$

Therefore,

$$\int_{x_0}^{n} xv(t,x)^+ dx \leq \int_0^t \int_{x_0}^{\infty} (\alpha(s,x) + \nu)xv(s,x)^+ \, dx \, ds$$

is obtained, where ν does not depend on n. As $n \to \infty$, one obtains

$$\int_{x_0}^{\infty} xv(t,x)^+ dx \leq \int_0^t \int_{x_0}^{\infty} (\alpha(s,x) + \nu)xv(s,x)^+ \, dx \, ds.$$

From assumption $(A2)$, there is a positive constant η so that

$$\int_{x_0}^{\infty} xv(t,x)^+ dx \leq (\nu + \eta) \int_0^t \int_{x_0}^{\infty} xv(s,x)^+ \, dx \, ds. \tag{4.15}$$

From Theorem 2.1.1, one obtains

$$\int_{x_0}^{\infty} xv(t,x)^+ dx = 0.$$

It then follows that $v \leq 0$ a.e. in D_T. Thus, the proof is completed. □

Remark 4.1. *From the proof of Theorem 4.2.3, it follows that for any* $v \in L^1(D_T, xdx)$*, if* $v(0,x) \leq 0$ *a.e. in* (x_0, ∞)*, and the following inequality holds for every nonnegative*

$\xi \in C^1_{0,r}(D_T)$:

$$\begin{aligned}\int_{x_0}^{\infty} xv(t,x)\xi(t,x)\,dx &\le \int_{x_0}^{\infty} xv(0,x)\xi(0,x)dx \\ &+ \int_{x_0}^{\infty}\int_0^t xv(s,x)\xi_s(s,x)\,ds\,dx \\ &+ \int_0^t\int_{2x_0}^{\infty}\alpha(s,y)v(s,y)\int_{x_0}^{y-x_0} x\xi(s,x)\beta(x|y)\,dx\,dy\,ds \\ &+ \int_{x_0}^{\infty}\int_0^t x\xi(s,x)A(s,x)v(s,x)\,ds\,dx \\ &+ \int_{x_0}^{\infty}\int_0^t xv(s,x)\int_{x_0}^{\infty}\xi(s,x+y)B(s,x,y)\,dy\,ds\,dx\end{aligned} \tag{4.16}$$

where $B \ge 0$, $A \in L^\infty(D_T)$ and $\int_{x_0}^\infty B(t,x,y)\,dy \in L^\infty(D_T)$, then $v(t,x) \le 0$ a.e. in D_T. This result is used later in Section 4.3.

Corollary 4.2.4. *Let the assumption $(A1)-(A4)$ hold and $\underline{u}$ and $\overline{u}$ be nonnegative lower and upper solutions to (4.1)-(4.2), respectively. If u is the solution to (4.1)-(4.2), then*

$$\overline{u} \ge u \ge \underline{u} \qquad a.e.\ in\ D_T.$$

Proof. It is first claimed that $u \ge 0$, since if $v = -u$, v satisfies (4.16) with $A(t,x) = -\alpha(t,x) - \int_{x_0}^\infty \kappa(x,y)\overline{u}(t,y)\,dy$, and $B(t,x,y) = \frac{1}{2}\chi_I(x+y)\kappa(x,y)\ u(t,y)$. Then, let $v = u - \overline{u}$. Since $-u(t,x)\displaystyle\int_{x_0}^{\infty}\kappa(x,y)u(t,y)\,dy \le 0$ and $\overline{u}$ satisfies

$$\begin{aligned}\int_{x_0}^{\infty} x\overline{u}(t,x)\xi(t,x)\,dx &\ge \int_{x_0}^{\infty} x\overline{u}(0,x)\xi(0,x)dx \\ &+ \int_{x_0}^{\infty}\int_0^t x\overline{u}(s,x)\xi_s(s,x)\,ds\,dx \\ &+ \int_0^t\int_{2x_0}^{\infty}\alpha(s,y)\overline{u}(s,y)\int_{x_0}^{y-x_0} x\xi(s,x)\beta(x|y)\,dx\,dy\,ds \\ &+ \int_{x_0}^{\infty}\int_0^t x\xi(s,x)(\mathcal{F}\overline{u})(s,x)\,ds\,dx \\ &- \int_{x_0}^{\infty}\int_0^t x\xi(s,x)\alpha(s,x)\overline{u}(s,x)\,ds\,dx\end{aligned}$$

one can see that v satisfies (4.16) with $A(t,x) = -\alpha(t,x)$, and

$$B(t,x,y) = \frac{1}{2}\chi_{_I}(x+y)[\kappa(x,y)u(t,y) + \kappa(x,y)\overline{u}(t,y)],$$

which shows $u \leq \overline{u}$. Now, let $v = \underline{u} - u$. Since

$$\int_{x_0}^{\infty} \kappa(x,y)u(t,y)u(t,x)dy \leq \int_{x_0}^{\infty} \kappa(x,y)\overline{u}(t,y)u(t,x)dy,$$

v satisfies (4.16) with

$$A(t,x) = -\alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}(t,y)\,dy,$$

and

$$B(t,x,y) = \frac{1}{2}\chi_{_I}(x+y)[\kappa(x,y)\underline{u}(t,y) + \kappa(x,y)u(t,y)],$$

hence, $\underline{u} \leq u$. Thus, the proof is completed. □

4.2.3 Analysis of the problem

In this section, two monotone sequences of upper and lower solutions are constructed to show their convergence to the unique global solution.

Suppose that $\underline{u}^0(t,x)$ and $\overline{u}^0(t,x)$ are a pair of lower and upper solutions of (4.1)-(4.2) and are continuously differentiable in t. Under the hypothesis $(A2)$, a positive constant M can be chosen such that

$$M - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}(t,y)\,dy \geq 0 \quad \text{ for } (t,x) \in \overline{D}_T$$

and $\underline{u}^0(t,x) \leq u(t,x) \leq \overline{u}^0(t,x)$. Thus, two sequences $\{\underline{u}^k\}_{k=0}^{\infty}$ and $\{\overline{u}^k\}_{k=0}^{\infty}$ can be set up as follows:

For $k = 1,2,...$, let $\underline{u}^k$ and $\overline{u}^k$ satisfy the equation

$$\begin{aligned}\underline{u}^k_t &= -\alpha(t,x)\underline{u}^{k-1} + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\underline{u}^{k-1}(t,y)dy - M(\underline{u}^k - \underline{u}^{k-1}) \\ &\quad + \mathcal{F}\underline{u}^{k-1} - \underline{u}^{k-1}\int_{x_0}^{\infty} \kappa(x,y)\overline{u}^{k-1}(t,y)\,dy \quad \text{ on } D_T \\ \underline{u}(0,x) &= u_0(x) \quad \text{ in } [0,\infty)\end{aligned} \tag{4.17}$$

and

$$\begin{aligned}\overline{u}^k_t &= -\alpha(t,x)\overline{u}^{k-1} + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\overline{u}^{k-1}(t,y)dy - M(\overline{u}^k - \overline{u}^{k-1}) \\ &\quad + \mathcal{F}\overline{u}^{k-1} - \overline{u}^{k-1}\int_{x_0}^{\infty} \kappa(x,y)\underline{u}^{k-1}(t,y)\,dy \quad \text{ on } D_T \\ \overline{u}(0,x) &= u_0(x) \quad \text{ in } [0,\infty).\end{aligned} \tag{4.18}$$

The existence of solutions to problems (4.17) and (4.18) follows from the fact that (4.17) and (4.18) are both linear problems with initial conditions. It is first shown that $\underline{u}^0 \le \underline{u}^1 \le \overline{u}^1 \le \overline{u}^0$. Let $v(t,x) = \underline{u}^0 - \underline{u}^1$. Then, v satisfies (4.16) with $A(t,x) = -M$, and $B(t,x,y) = 0$. Thus, from Remark 4.1 $v \le 0$, $\underline{u}^0 \le \underline{u}^1$ is obtained. Similarly, $\overline{u}^1 \le \overline{u}^0$ is obtained.

Then, let $v(t,x) = \underline{u}^1 - \overline{u}^0$. Since $\underline{u}^0 \le \underline{u}^1$ and $\overline{u}^1 \le \overline{u}^0$, v satisfies (4.16) with

$$A(t,x) = -\alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^0(t,y)\,dy,$$

and

$$B(t,x,y) = \frac{1}{2}\chi_I(x+y)\kappa(x,y)[\underline{u}^1(t,y) + \overline{u}^0(t,y)].$$

Hence, $\underline{u}^1 \le \overline{u}^0$. Likewise, it is clearly seen that $\overline{u}^1 \ge \underline{u}^0$.

Thus, $\underline{u}^1$ and $\overline{u}^1$ are claimed as lower and upper solutions to (4.1)-(4.2), respectively. Since $\underline{u}^0 \le \underline{u}^1$ and $\overline{u}^1 \le \overline{u}^0$, on the one hand, the right-hand side of the equation in (4.17) satisfies

$$
\begin{aligned}
&-\alpha(t,x)\underline{u}^0 + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\underline{u}^0(t,y)dy - M(\underline{u}^1 - \underline{u}^0) \\
&\quad + \mathcal{F}\underline{u}^0 - \underline{u}^0 \int_{x_0}^{\infty} \kappa(x,y)\overline{u}^0(t,y)\,dy \\
&= \int_{x+x_0}^{\infty} \alpha(t,y)\underline{u}^0(t,y)\beta(x|y)dy - M\underline{u}^1 \\
&\quad + \left(M - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}^0(t,y)\,dy\right)\underline{u}^0 \\
&\quad + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\underline{u}^0(t,x-y)\underline{u}^0(t,y)dy \\
&\le \int_{x+x_0}^{\infty} \alpha(t,y)\underline{u}^1(t,y)\beta(x|y)dy - M\underline{u}^1 \\
&\quad + \left(M - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}^1(t,y)\,dy\right)\underline{u}^1 \\
&\quad + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\underline{u}^1(t,x-y)\underline{u}^1(t,y)dy \\
&= -\alpha(t,x)\underline{u}^1 + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\underline{u}^1(t,y)dy \\
&\quad + \mathcal{F}\underline{u}^1 - \underline{u}^1 \int_{x_0}^{\infty} \kappa(x,y)\overline{u}^1(t,y)\,dy.
\end{aligned}
$$

In (4.18), the right-hand side satisfies

$$
\begin{aligned}
&-\alpha(t,x)\overline{u}^0 + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\overline{u}^0(t,y)dy - M(\overline{u}^1 - \overline{u}^0) \\
&\quad + \mathcal{F}\overline{u}^0 - \overline{u}^0 \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^0(t,y)\,dy \\
&= \int_{x+x_0}^{\infty} \alpha(t,y)\overline{u}^0(t,y)\beta(x|y)dy - M\overline{u}^1 \\
&\quad + \left(M - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^0(t,y)\,dy\right)\overline{u}^0 \\
&\quad + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\overline{u}^0(t,x-y)\overline{u}^0(t,y)dy \\
&\ge \int_{x+x_0}^{\infty} \alpha(t,y)\overline{u}^1(t,y)\beta(x|y)dy - M\overline{u}^1 \\
&\quad + \left(M - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^1(t,y)\,dy\right)\overline{u}^1 \\
&\quad + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\overline{u}^1(t,x-y)\overline{u}^1(t,y)dy
\end{aligned}
$$

$$= -\alpha(t,x)\overline{u}^1 + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\overline{u}^1(t,y)dy$$
$$+ \mathcal{F}\overline{u}^1 - \overline{u}^1 \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^1(t,y)\, dy.$$

It is then assumed that for some $k > 1$, $\underline{u}^k$ and $\overline{u}^k$ are a lower solution and an upper solution of (4.1)-(4.2), respectively. Proceeding analogously, it can be shown that $\underline{u}^k \leq \underline{u}^{k+1} \leq \overline{u}^{k+1} \leq \overline{u}^k$ and that $\underline{u}^{k+1}$ and $\overline{u}^{k+1}$ are also a lower solution and an upper solution of (4.1)-(4.2), respectively. Hence, by induction, two monotone sequences are obtained that satisfy

$$\underline{u}^0 \leq \underline{u}^1 \leq \cdots \leq \underline{u}^k \leq \overline{u}^k \leq \cdots \leq \overline{u}^1 \leq \overline{u}^0 \quad \text{a.e. in } \overline{D}_T$$

for each $k = 0, 1, 2, \cdots$. The monotonicity of the sequences $\{\underline{u}^k\}_k$ and $\{\overline{u}^k\}_k$ yields the existence of $\underline{u}$ and $\overline{u}$ so that $\underline{u}^k$ and $\overline{u}^k$ converge pointwise to $\underline{u}$ and $\overline{u}$ in D_T, respectively. Furthermore, $\underline{u} \leq \overline{u}$ a.e. in D_T.

Next, we want to prove that $\underline{u} = \overline{u}$. For this, a function v is considered such that $v = \overline{u} - \underline{u}$. As proven earlier, $\underline{u} \leq \overline{u}$, thus, $v(t,x) \geq 0$ and $v(0,x) = 0$. In (4.8), let $\xi(t,x) = \xi(x)$, where $\xi(x) \equiv 1$ for $x_0 \leq x \leq n$, $\xi(x) \equiv 0$ for $n+2 \leq x < \infty$, and $-1 \leq \xi' \leq 0$ for $n \leq x \leq n+2$, one obtains

$$\begin{aligned}
\int_{x_0}^{n} xv(t,x)\, dx &\leq \int_0^t \int_{x_0}^{\infty} x\left[(\mathcal{F}\overline{u})(s,x) - (\mathcal{F}\underline{u})(s,x)\right]\, dx\, ds \\
&\quad + \int_0^t \int_{x_0}^{\infty} x\overline{u}(s,x) \int_{x_0}^{\infty} \kappa(x,y)v(s,y)\, dy\, dx\, ds \\
&\leq \tilde{\nu} \int_0^t \int_{x_0}^{\infty} xv(s,x)\, dx\, ds
\end{aligned} \tag{4.19}$$

where

$$\begin{aligned}
\tilde{\nu} = &\sup_{\overline{D_T}} \left[\frac{1}{2}\int_{x_0}^{\infty} \chi_{{}_I}(x+z)\kappa(z,x)\underline{u}(t,z)\, dz \right.\\
&\left. + \frac{3}{2}\|\kappa\|_\infty \int_{x_0}^{\infty} (1+\chi_{{}_I}(x+y))\overline{u}(t,y)\, dy\right],
\end{aligned}$$

$\tilde{\nu}$ does not depend on n. As $n \to \infty$, one obtains

$$\int_{x_0}^{\infty} xv(t,x)\,dx \leq \int_0^t \int_{x_0}^{\infty} \tilde{\nu} xv(s,x)\,dx\,ds.$$

Hence, from the Theorem 2.1.1, one obtains $v(t,x) = 0$, that is, $\overline{u} = \underline{u}$. Let $u = \overline{u} = \underline{u}$, it follows that u is a solution to (4.1)-(4.2).

To establish the uniqueness of u, it is assumed that w is another solution of (4.1)-(4.2). Since for each k, $\underline{u}^k$ and $\overline{u}^k$ are lower and upper solutions to (4.1)-(4.2), respectively, by Corollary 4.2.4, $\underline{u}^k \leq w \leq \overline{u}^k$, implies $u \equiv w$, after taking the limit as $k \to \infty$.

From the above, the following result is stated:

Theorem 4.2.5. *Let assumptions* $(A1) - (A4)$ *hold. If* $\underline{u}^0(t,x)$ *and* $\overline{u}^0(t,x)$ *are non-negative lower and upper solutions to* (4.1)-(4.2)*, respectively, then there are convergent and monotone sequences* $\{\underline{u}^k(t,x)\}$ *and* $\{\overline{u}^k(t,x)\}$ *such that* $\lim_{k\to\infty} \underline{u}^k(t,x) = u(t,x) = \lim_{k\to\infty} \overline{u}^k(t,x)$*, where* u *is the unique solution to* (4.1)-(4.2).

Next, we want to show that the function u as defined in Theorem 4.2.5, has the following property:

Theorem 4.2.6. *Let assumptions* $(A1) - (A4)$ *hold. Then,* $P(t) = \int_{x_0}^{\infty} xu(t,x)dx$ *is continuous in the existence interval, where* $u(t,x)$ *is the solution to* (4.1)-(4.2).

Proof. From assumptions $(A1) - (A4)$, to establish that $P(t)$ is continuous over $[0,T]$, one only needs to show that the following equation is satisfied:

$$\begin{aligned}\int_{x_0}^{\infty} xu(t,x)\,dx = &\int_{x_0}^{\infty} xu(0,x)dx + \int_{x_0}^{\infty}\int_0^t x(\mathcal{F}u)(s,x)\,ds\,dx \\ &- \int_{x_0}^{\infty}\int_0^t xu(s,x)\int_{x_0}^{\infty} \kappa(x,y)u(s,y)\,dy\,ds\,dx.\end{aligned} \tag{4.20}$$

For this purpose, we pick $\xi(t,x) = \xi(x)$, where $1 \equiv \xi(x)$ for $n \geq x \geq x_0$, $0 \equiv \xi(x)$ for $n+2 \leq x < \infty$, and $0 \geq \xi' \geq -1$ for $n+2 \geq x \geq n$. From Definition 4.2.1, one obtains

$$\Bigg| \int_{x_0}^{\infty} xu(t,x)\,dx - \int_{x_0}^{\infty} xu(0,x)dx - \int_{x_0}^{\infty}\int_0^t x(\mathcal{F}u)(s,x)\,ds\,dx$$

$$
\begin{aligned}
&+\int_{x_0}^{\infty}\int_0^t xu(s,x)\int_{x_0}^{\infty}\kappa(x,y)u(s,y)\,dy\,ds\,dx\Bigg| \\
&= \Bigg|\int_n^{\infty} x[u(t,x)-u(0,x)][1-\xi(x)]\,dx \\
&\quad -\int_n^{\infty}\int_0^t x(\mathcal{F}u)(s,x)[1-\xi(x)]\,ds\,dx \\
&\quad +\int_n^{\infty}\int_0^t xu(s,x)[1-\xi(x)]\int_{x_0}^{\infty}\kappa(x,y)u(s,y)\,dy\,ds\,dx\Bigg| \\
&\le \left(2+\frac{3}{2}\|\kappa\|_\infty \sup_{[0,T]}\| u(t,\cdot)\|_1\right)\sup_{[0,T]}\int_n^{\infty} xu(t,x)\,dx.
\end{aligned}
$$

Since $u\in L^1(D_T, x\,dx)$, $\sup_{[0,T]}\int_n^{\infty} xu(t,x)\,dx \to 0$ as $n\to\infty$, thus, leading to (4.20). □

The previous result yields the following on global existence:

Theorem 4.2.7. *Let assumptions* $(A1)-(A4)$ *hold. Then, the solution* $u(t,x)$ *of* (4.1)-(4.2) *exists, for* $t\ge 0$, *and is unique.*

Proof. From Definition 4.2.1, it suffices to prove that $P(t)$ is global with respect to time t. To this end, we consider (4.20) and find

$$
\begin{aligned}
P(t) &= P(0)-\frac{1}{2}\int_{x_0}^{\infty}\int_0^t xu(s,x)\int_{x_0}^{\infty}\kappa(x,y)u(s,y)\,dy\,ds\,dx \\
&\le \delta\int_0^t P(r)dr + P(0),
\end{aligned}
$$

where $\delta = 0$. One then obtains

$$P(t)\le P(0).$$

Thus, the proof is completed. □

The convergence of the constructed sequences to the unique global solutions of (4.1)-(4.2) has been shown. The next section focuses on the scenario where the growth term is involved in the current model.

4.3 Coagulation-fragmentation model with growth

In this section, the same method as in Section 4.2 is followed in order to establish the well-posedness of a nonlinear non-autonomous coagulation-fragmentation equation with growth in the space $X_0 = L^1(D_T, dx)$.

4.3.1 Preliminaries

The following coagulation-fragmentation model with growth is considered:

$$\begin{aligned}
&\partial_t u(t,x) + \partial_x(u(t,x)\tau(t,x)) + \mu(t,x)u(t,x) = -\alpha(t,x)u(t,x)\\
&\quad + \int_{x+x_0}^{\infty} \alpha(t,y)u(t,y)\beta(x|y)\,dy\\
&\quad + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)u(t,x-y)u(t,y)\,dy\\
&\quad - u(t,x)\int_{x_0}^{\infty} \kappa(x,y)u(t,y)\,dy, \quad (t,x) \in (0,T)\times(x_0,\infty)
\end{aligned} \tag{4.21}$$

subject to the boundary condition

$$\tau(t,x_0)u(t,x_0) = \int_{x_0}^{\infty} \gamma(t,y)u(t,y)\,dy, \quad t \in [0,T), \tag{4.22}$$

and the initial condition

$$u(0,x) = u_0(x), \quad x \in [x_0,\infty). \tag{4.23}$$

The function $\tau(t,x)$, in equation (4.21), denotes the growth rate of a particle of size x at time t as a result of splitting within it, and the coefficient $\mu(t,x)$ is the sinking rate of the clusters of size x at time t. In equation (4.22), the function $\gamma(t,x)$ accounts for the amount of particles that separate an aggregate of size x and integrate the single cell population.

The remaining parameters and terms have the same meaning as in Section 4.2.1.

The same assumptions $(A2)-(A4)$ as in Section 4.2.1 are considered and make further assumptions on the current parameters.

(A5) $\mu(t,x) \in C([0,T] \times [x_0, +\infty))$ where $\|\mu\|_\infty < \infty$.

(A6) $0 \le \beta(x|y) \in C((x_0,\infty) \times (x_0,\infty))$ with $\|\beta\|_\infty < \infty$; $\beta(x|y) = 0$ for $y < x + x_0$. Furthermore, the number of daughter particles are considered to be bounded i.e. $\sup_{2x_0<y} n(y) = M < \infty$, $M \in \mathbb{R}_+$ where $n(y) = \sup_{2x_0<y} \int_{x_0}^{y-x_0} \beta(x|y)\, dx$.

(A7) $\tau(t,x) \in C^1((0,T) \times (x_0,\infty))$ where $\|\tau_x\|_\infty < \infty$. In addition, $\tau(t,x) > 0$ for $(t,x) \in [0,T] \times [x_0,\infty]$ and $\lim_{x\to\infty} \tau(t,x) = 0$ for $t \in [0,T]$.

(A8) $0 \le \gamma(t,y) \in C([0,T] \times (x_0,\infty))$ where $\|\gamma\|_\infty < \infty$.

A similar notation for D_T and $C^1_{0,r}(D_T)$ as in Section 4.2.1 is used. The definition of the solution of problem (4.21)-(4.23) is introduced as follows:

Definition 4.3.1. *$u(t,x)$ is called a solution of (4.21)-(4.23) on D_T if all the following hold:*

1. *$u \in X_0 = L^1(D_T, dx)$.*
2. *$u(x,0) = u_0(x)$ a.e. in (x_0,∞).*
3. *For every $t \in (0,T)$ and every nonnegative $\xi(t,x) \in C^1_{0,r}(D_T)$,*

$$
\begin{aligned}
\int_{x_0}^{\infty} \xi(t,x)u(t,x)\,dx &= \int_{x_0}^{\infty} \xi(0,x)u(0,x)\,dx \\
&+ \int_0^t \xi(s,x_0) \int_{x_0}^{\infty} \gamma(s,x)u(s,x)\,dx \\
&+ \int_{x_0}^{\infty} \int_0^t [\xi_s(s,x) + \tau(s,x)\xi_x(s,x)]u(s,x)\,ds\,dx \\
&+ \int_0^t \int_{2x_0}^{\infty} u(s,y)\alpha(s,y) \int_{x_0}^{y-x_0} \beta(x|y)\xi(s,x)\,dx\,dy\,ds \\
&+ \int_{x_0}^{\infty} \int_0^t \xi(s,x)(\mathcal{F}u)(s,x)\,ds\,dx \\
&- \int_{x_0}^{\infty} \int_0^t \xi(s,x)u(s,x) \int_{x_0}^{\infty} \kappa(x,y)u(s,y)\,dy\,ds\,dx \\
&- \int_{x_0}^{\infty} \int_0^t \xi(s,x)\mu(s,x)u(s,x)\,ds\,dx \\
&- \int_{x_0}^{\infty} \int_0^t \xi(s,x)\alpha(s,x)u(s,x)\,ds\,dx
\end{aligned}
\tag{4.24}
$$

where

$$(\mathcal{F}v)(t,x) = \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)v(t,x-y)v(t,y)\,dy. \tag{4.25}$$

The following definition is required to establish the comparison principle:

Definition 4.3.2. *Given a pair* $(\underline{u},\overline{u})$*, the functions* $\underline{u}(t,x)$ *and* $\overline{u}(t,x)$ *are said to be lower and upper solutions to* (4.21)-(4.23) *on* D_T*, respectively, if:*

1. $\overline{u},\underline{u} \in X_0 = L^1(D_T,dx)$.
2. $\underline{u}(0,x) \le u_0(x) \le \overline{u}(0,x)$ *a.e. in* (x_0,∞).
3. *For any* $t \in (0,T)$ *and any nonnegative* $\xi(t,x) \in C^1_{0,r}(D_T)$,

$$\begin{aligned}
\int_{x_0}^{\infty} \xi(t,x)\underline{u}(t,x)\,dx \le{}& \int_{x_0}^{\infty} \xi(0,x)\underline{u}(0,x)\,dx \\
&+ \int_0^t \xi(s,x_0)\int_{x_0}^{\infty}\gamma(s,x)\underline{u}(s,x)\,dx \\
&+ \int_{x_0}^{\infty}\int_0^t [\xi_s(s,x)+\tau(s,x)\xi_x(s,x)]\underline{u}(s,x)\,ds\,dx \\
&+ \int_0^t\int_{2x_0}^{\infty}\alpha(s,y)\underline{u}(s,y)\int_{x_0}^{y-x_0}\xi(s,x)\beta(x|y)\,dx\,dy\,ds \\
&+ \int_{x_0}^{\infty}\int_0^t \xi(s,x)(\mathcal{F}\underline{u})(s,x)\,ds\,dx \\
&- \int_{x_0}^{\infty}\int_0^t \xi(s,x)\underline{u}(s,x)\int_{x_0}^{\infty}\kappa(x,y)\overline{u}(s,y)\,dy\,ds\,dx \\
&- \int_{x_0}^{\infty}\int_0^t \xi(s,x)\mu(s,x)\underline{u}(s,x)\,ds\,dx \\
&- \int_{x_0}^{\infty}\int_0^t \xi(s,x)\alpha(s,x)\underline{u}(s,x)\,ds\,dx.
\end{aligned} \tag{4.26}$$

$$
\begin{aligned}
\int_{x_0}^{\infty} \xi(t,x)\overline{u}(t,x)\,dx \geq & \int_{x_0}^{\infty} \xi(0,x)\overline{u}(0,x)\,dx \\
& + \int_0^t \xi(s,x_0) \int_{x_0}^{\infty} \gamma(s,x)\overline{u}(s,x)\,dx \\
& + \int_{x_0}^{\infty} \int_0^t [\xi_s(s,x) + \tau(s,x)\xi_x(s,x)]\overline{u}(s,x)\,ds\,dx \\
& + \int_0^t \int_{2x_0}^{\infty} \alpha(s,y)\overline{u}(s,y) \int_{x_0}^{y-x_0} \xi(s,x)\beta(x|y)\,dx\,dy\,ds \\
& + \int_{x_0}^{\infty} \int_0^t \xi(s,x)(\mathcal{F}\overline{u})(s,x)\,ds\,dx \\
& - \int_{x_0}^{\infty} \int_0^t \xi(s,x)\overline{u}(s,x) \int_{x_0}^{\infty} \kappa(x,y)\underline{u}(s,y)\,dy\,ds\,dx \\
& - \int_{x_0}^{\infty} \int_0^t \xi(s,x)\mu(s,x)\overline{u}(s,x)\,ds\,dx \\
& - \int_{x_0}^{\infty} \int_0^t \xi(s,x)\alpha(s,x)\overline{u}(s,x)\,ds\,dx
\end{aligned}
\tag{4.27}
$$

Based on Definition 4.3.2, the following result referred to as comparison principle is stated and proved.

Theorem 4.3.3. *Let assumptions* (*A*2) − (*A*8) *hold. If* $\underline{u}$ *and* $\overline{u}$ *are lower and upper solutions to* (4.21)-(4.23)*, respectively, then,* $\underline{u} \leq \overline{u}$ *in* D_T*.*

Proof. A negative function v is considered such that $v = \underline{u} - \overline{u}$ and ξ chosen so that $\xi \in C^1_{0,r}((0,T)\times(x_0,n))$, $n \in \mathbb{N}^*$, where $C^1_{0,r}((0,T)\times(x_0,n)) = \{\psi \in C^1((0,T)\times(x_0,n)) : \exists x_\psi \in (x_0,n) \text{ so that } 0 \equiv \psi \text{ for } x_\psi \leq x\}$. Thus, v satisfies

$$
0 \geq v(0,x) = -(\overline{u}(0,x) - \underline{u}(0,x)) \quad \text{a.e. in } [x_0,\infty) \tag{4.28}
$$

and

$$
\begin{aligned}
\int_{x_0}^{\infty} v(t,x)\xi(t,x)\,dx \leq & \int_{x_0}^{\infty} v(0,x)\xi(0,x)\,dx \\
& + \int_0^t \xi(s,x_0) \int_{x_0}^{\infty} \gamma(s,x)v(s,x)\,dx
\end{aligned}
$$

$$
\begin{aligned}
&+\int_{x_0}^{\infty}\int_0^t [\xi_s(s,x)+\tau(s,x)\xi_x(s,x)]v(s,x)\,ds\,dx \\
&+\int_0^t\int_{2x_0}^{\infty}\alpha(s,y)v(s,y)\int_{x_0}^{y-x_0}\xi(s,x)\beta(x|y)\,dx\,dy\,ds \\
&+\int_{x_0}^{\infty}\int_0^t \xi(s,x)\left[(\mathcal{F}\underline{u})(s,x)-(\mathcal{F}\overline{u})(s,x)\right]\,ds\,dx \qquad (4.29)\\
&-\int_{x_0}^{\infty}\int_0^t \xi(s,x)v(s,x)\int_{x_0}^{\infty}\kappa(x,y)\overline{u}(s,y)\,dy\,ds\,dx \\
&+\int_{x_0}^{\infty}\int_0^t \xi(s,x)\overline{u}(s,x)\int_{x_0}^{\infty}\kappa(x,y)v(s,y)\,dy\,ds\,dx \\
&-\int_{x_0}^{\infty}\int_0^t \xi(s,x)\mu(s,x)v(s,x)\,ds\,dx \\
&-\int_{x_0}^{\infty}\int_0^t \xi(s,x)\alpha(s,x)v(s,x)\,ds\,dx.
\end{aligned}
$$

Upon manipulation, one obtains

$$
\begin{aligned}
&\int_{x_0}^{\infty}\int_0^t \xi(s,x)\left[(\mathcal{F}\underline{u})(s,x)-(\mathcal{F}\overline{u})(s,x)\right]\,ds\,dx \\
&=\frac{1}{2}\int_{x_0}^{\infty}\int_0^t \xi(s,x)\chi_{_I}(x)\int_{x_0}^{x-x_0}\kappa(x-y,y)\left[\underline{u}(s,x-y)v(s,y)\right. \\
&\left.+v(s,x-y)\overline{u}(s,y)\right]\,dy\,ds\,dx \\
&=\frac{1}{2}\int_0^t\int_{x_0}^{\infty}v(s,y)\int_{y+x_0}^{\infty}\xi(s,x)\chi_{_I}(x)\kappa(x-y,y)\underline{u}(s,x-y)\,dx\,dy\,ds \qquad (4.30)\\
&+\frac{1}{2}\int_0^t\int_{x_0}^{\infty}\overline{u}(s,y)\int_{y+x_0}^{\infty}\xi(s,x)\chi_{_I}(x)\kappa(x-y,y)v(s,x-y)\,dx\,dy\,ds \\
&=\frac{1}{2}\int_0^t\int_{x_0}^{\infty}v(s,y)\int_{x_0}^{\infty}\xi(s,y+z)\chi_{_I}(y+z)\kappa(z,y)\underline{u}(s,z)\,dz\,dy\,ds \\
&+\frac{1}{2}\int_0^t\int_{x_0}^{\infty}\overline{u}(s,y)\int_{x_0}^{\infty}\xi(s,y+z)\chi_{_I}(y+z)\kappa(z,y)v(s,z)\,dz\,dy\,ds.
\end{aligned}
$$

Let $\xi(t,x)=e^{\lambda t}\zeta(t,x)$, where $\zeta\in C^1_{0,r}((0,T)\times(x_0,n))$ and a positive λ is picked such that

$$\lambda-\mu(t,x)-\alpha(t,x)-\int_{x_0}^{\infty}\overline{u}(s,y)\kappa(x,y)\,dy\geq 0 \text{ on } D_T.$$

Then, one finds

$$
\begin{aligned}
& e^{\lambda t}\int_{x_0}^{\infty}\zeta(t,x)v(t,x)\,dx \\
& \leq \int_{x_0}^{\infty}\zeta(0,x)v(0,x)dx + \int_0^t e^{\lambda s}\zeta(s,x_0)\int_{x_0}^{\infty}\gamma(s,x)v(s,x)\,dx \\
& + \int_{x_0}^{\infty}\int_0^t e^{\lambda s}[\zeta_s(s,x)+\tau(s,x)\zeta_x(s,x)]v(s,x)\,ds\,dx \\
& + \int_0^t\int_{2x_0}^{\infty}\alpha(s,y)v(s,y)\int_{x_0}^{y-x_0}e^{\lambda s}\zeta(s,x)\beta(x|y)\,dx\,dy\,ds \\
& + \int_{x_0}^{\infty}\int_0^t v(s,x)e^{\lambda s}\zeta(s,x)\times \\
& \left(\lambda-\mu(s,x)-\alpha(s,x)-\int_{x_0}^{\infty}\kappa(x,y)\overline{u}(s,y)\,dy\right)ds\,dx \\
& + \frac{1}{2}\int_0^t\int_{x_0}^{\infty}v(s,y)\int_{x_0}^{\infty}e^{\lambda s}\zeta(s,y+z)\chi_{_I}(y+z)\kappa(z,y)\underline{u}(s,z)\,dz\,dy\,ds \\
& + \frac{1}{2}\int_0^t\int_{x_0}^{\infty}\overline{u}(s,y)\int_{x_0}^{\infty}e^{\lambda s}\zeta(s,y+z)\chi_{_I}(z+y)v(s,z)\kappa(z,y)\,dz\,dy\,ds \\
& + \int_{x_0}^{\infty}\int_0^t e^{\lambda s}\zeta(s,x)\overline{u}(s,x)\int_{x_0}^{\infty}\kappa(x,y)v(s,y)\,dy\,ds\,dx.
\end{aligned} \tag{4.31}
$$

A backward problem is formulated as follows:

$$
\begin{aligned}
0 &= \zeta_s+\tau\zeta_s, \qquad 0<s<t, \qquad 0<x<n \\
0 &= \zeta(s,n), \qquad 0<s<t \\
\chi_1(x) &= \zeta(t,x), \qquad\qquad 0\leq x\leq n,
\end{aligned} \tag{4.32}
$$

where $\chi_1 \in C_1^{\infty}(\overline{D_T})$ and $0 \leq \chi_1 \leq 1$.

The existence of ζ such that $\zeta \in C^1_{0,r}((0,T)\times(x_0,n))$ follows from the fact that by the change of variable $\iota = t-s$, the above system (4.32) can be rewritten as:

$$
\begin{aligned}
0 &= \zeta_\iota-\tau\zeta_s, \qquad 0<\iota<t, \qquad 0<x<n \\
0 &= \zeta(\iota,n), \qquad 0<\iota<t \\
\chi_1(x) &= \zeta(\iota,x), \qquad\qquad 0\leq x\leq n.
\end{aligned} \tag{4.33}
$$

From (4.33), one has $0 \leq \zeta \leq 1$ on $(0,T)\times(0,n)$.

Thereafter, such a ζ is substituted in (4.31) to obtain

$$\begin{aligned}
&\int_0^n \chi_1(x)v(t,x)dx \\
&\quad \leq \nu \int_0^t \int_{x_0}^\infty v(s,x)^+ \, dx \, ds + \int_{x_0}^\infty v(0,x)^+ \, dx \\
&\qquad + \int_0^t \int_{2x_0}^\infty \alpha(s,y)v(s,y) \int_{x_0}^{y-x_0} e^{-\lambda(t-s)}\zeta(s,x)\beta(x|y) \, dx \, dy \, ds
\end{aligned} \tag{4.34}$$

where

$$\begin{aligned}
\nu = \sup_{\overline{D_T}} \Bigg[&\gamma(s,x) + \left(\lambda - \mu(t,x) - \alpha(t,x) - \int_{x_0}^\infty \kappa(x,y)\overline{u}(s,y) \, dy \right) \\
&+ \frac{1}{2} \int_{x_0}^\infty \chi_{_I}(x+z)\kappa(z,x)\underline{u}(t,z) \, dz \\
&+ \frac{3}{2}\|\kappa\|_\infty \int_{x_0}^\infty (1+\chi_{_I}(x+y))\overline{u}(t,y) \, dy \Bigg]
\end{aligned}$$

and

$$v(s,x)^+ = \sup_{\overline{D_T}} \{v(s,x), 0\} .$$

From (4.25), one obtains

$$\begin{aligned}
\int_{x_0}^n \chi_1(x)v(t,x) \, dx \leq &\int_0^t \int_{2x_0}^\infty \alpha(s,y)v(s,y)^+ \int_{x_0}^{y-x_0} \beta(x|y) \, dx \, dy \, ds \\
&+ \nu \int_0^t \int_{x_0}^\infty v(s,x)^+ \, dx \, ds.
\end{aligned}$$

From assumption $(A6)$, one has

$$\sup_{2x_0<y} n(y) = M < \infty$$

and then,

$$\begin{aligned}
\int_{x_0}^n v(t,x)\chi_1(x)dx \leq &\int_0^t \int_{2x_0}^\infty M\alpha(s,x)v(s,x)^+ \, dx \, ds \\
&+ \nu \int_0^t \int_{x_0}^\infty v(s,x)^+ \, dx \, ds.
\end{aligned}$$

From assumption $(A2)$, $\alpha(t,x) = 0$ for $x < 2x_0$ and there is a positive constant η such that $\|\alpha\|_\infty \leq \eta$. Thus,

$$\int_{x_0}^{n} v(t,x)\chi_1(x)dx \leq (\nu + M\eta)\int_0^t \int_{x_0}^{\infty} v(s,x)^+ \, dx\, ds.$$

Since this inequality holds for every χ_1, one can choose a sequence $\{\chi_{1k}\}$ on $(0,n)$ converging to

$$\chi_1 = \begin{cases} 1 & \text{if} \quad v(t,x) > 0 \\ 0 & \text{otherwise.} \end{cases}$$

Therefore, one finds

$$\int_{x_0}^{n} v(t,x)^+ dx \leq (\nu + M\eta)\int_0^t \int_{x_0}^{\infty} v(s,x)^+ \, dx\, ds,$$

where ν does not depend on n. As $n \to \infty$, one obtains

$$\int_{x_0}^{\infty} v(t,x)^+ dx \leq (\nu + M\eta)\int_0^t \int_{x_0}^{\infty} v(s,x)^+ \, dx\, ds.$$

From Theorem 2.1.1, implies

$$\int_{x_0}^{\infty} v(t,x)^+ dx = 0.$$

□

Remark 4.2. *It follows from the proof of Theorem 4.3.3 that, for every* $v \in L^1(D_T, dx)$, *if* $v(0,x) \leq 0$ *a.e. in* (x_0, ∞), *and the following inequality holds for any nonnegative* $\xi \in C^1_{0,r}(D_T)$*:*

$$\int_{x_0}^{\infty} v(t,x)\xi(t,x)\, dx \leq \int_{x_0}^{\infty} v(0,x)\xi(0,x)dx$$
$$+ \int_0^t \xi(s,x_0)\int_{x_0}^{\infty} A(s,x)v(s,x)\, dx\, ds$$

$$
\begin{aligned}
&+ \int_{x_0}^{\infty}\int_0^t [\xi_s(s,x) + \tau(s,x)\xi_x(s,x)]v(s,x)\,ds\,dx \\
&+ \int_0^t \int_{2x_0}^{\infty} \alpha(s,y)v(s,y) \int_{x_0}^{y-x_0} \xi(s,x)\beta(x|y)\,dx\,dy\,ds \\
&+ \int_{x_0}^{\infty}\int_0^t \xi(s,x)B(s,x)v(s,x)\,ds\,dx \\
&+ \int_{x_0}^{\infty}\int_0^t v(s,x) \int_{x_0}^{\infty} \xi(s,x+y)C(s,x,y)\,dy\,ds\,dx
\end{aligned} \tag{4.35}
$$

where $0 \leq A, C,\ A, B \in L^\infty(D_T)$ *and* $\int_{x_0}^{\infty} C(t,x,y)\,dy \in L^\infty(D_T)$, *thus* $v(t,x) \leq 0$ *a.e. in* D_T. *This result is used later in Section 4.3.2.*

Corollary 4.3.4. *Let assumptions* $(A2) - (A8)$ *hold and* $\overline{u}$ *and* $\underline{u}$ *be, respectively, non-negative upper and lower solutions to* (4.21)-(4.23). *If* u *is the solution to* (4.21)-(4.23), *then,*

$$
\overline{u} \geq u \geq \underline{u} \quad \text{a.e. in } D_T.
$$

Proof. First, it is assumed that $0 \leq u$, as if $v = -u$, then, v satisfies (4.35) with

$$
A(t,x) = \gamma(t,x),
$$

$$
B(t,x,y) = -\mu(t,x) - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}(t,y)\,dy
$$

and

$$
C(t,x,y) = \frac{1}{2}\chi_I(x+y)\kappa(x,y)u(t,y).
$$

Then, let $v = u - \overline{u}$. Since

$$
-u(t,x)\int_{x_0}^{\infty} \kappa(x,y)u(t,y)\,dy \leq 0
$$

and $\overline{u}$ satisfies

$$
\begin{aligned}
\int_{x_0}^{\infty} x\overline{u}(t,x)\xi(t,x)\,dx \geq & \int_{x_0}^{\infty} x\overline{u}(0,x)\xi(0,x)dx \\
& + \int_0^t \xi(s,x_0)\int_{x_0}^{\infty}\gamma(s,x)\overline{u}(s,x)\,dx\,ds \\
& + \int_{x_0}^{\infty}\int_0^t [\xi_s(s,x)+\tau(s,x)\xi_x(s,x)]\overline{u}(s,x)\,ds\,dx \\
& + \int_0^t\int_{2x_0}^{\infty}\alpha(s,y)\overline{u}(s,y)\int_{x_0}^{y-x_0}\xi(s,x)\beta(x|y)\,dx\,dy\,ds \\
& + \int_{x_0}^{\infty}\int_0^t \xi(s,x)(\mathcal{F}\overline{u})(s,x)\,ds\,dx \\
& - \int_{x_0}^{\infty}\int_0^t \xi(s,x)\mu(s,x)\overline{u}(s,x)\,ds\,dx \\
& - \int_{x_0}^{\infty}\int_0^t \xi(s,x)\alpha(s,x)\overline{u}(s,x)\,ds\,dx.
\end{aligned}
$$

One can see that v satisfies (4.35) with

$$A(t,x) = \gamma(t,x),$$

$$B(t,x) = -\mu(t,x) - \alpha(t,x),$$

and

$$C(t,x,y) = \frac{1}{2}\chi_I(x+y)[\kappa(x,y)u(t,y) + \kappa(x,y)\overline{u}(t,y)],$$

which shows $u \leq \overline{u}$. Now let $v = \underline{u} - u$.

Since

$$\int_{x_0}^{\infty}\kappa(x,y)u(t,y)u(t,x)dy \leq \int_{x_0}^{\infty}\kappa(x,y)\overline{u}(t,yu(t,x))dy,$$

v satisfies (4.35) with

$$A(t,x) = \gamma(t,x),$$

$$B(t,x,y) = -\mu(t,x) - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}(t,y)\,dy,$$

and

$$C(t,x,y) = \frac{1}{2}\chi_I(x+y)[\kappa(x,y)\underline{u}(t,y) + \kappa(x,y)u(t,y)],$$

hence, $\underline{u} \leq u$. Thus, the proof is completed. □

4.3.2 Existence and uniqueness of the solution

Suppose that $\overline{u}^0(t,x)$ and $\underline{u}^0(t,x)$ are a pair of upper and lower solutions to (4.21)-(4.23), respectively, under hypotheses $(A5)$ and $(A6)$, one can select $M > 0$ so that

$$M - \alpha(t,x) - \mu(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}(t,y)\,dy \geq 0 \quad \text{for } (t,x) \in \overline{D}_T$$

and

$$\underline{u}^0(t,x) \leq u(t,x) \leq \overline{u}^0(t,x).$$

Two sequences $\{\underline{u}^k\}_{k=0}^{\infty}$ and $\{\overline{u}^k\}_{k=0}^{\infty}$ are then set up as follows:

For $k = 1, 2, ...$, let $\underline{u}^k$ and $\overline{u}^k$ satisfy the system

$$\begin{aligned}
&\underline{u}_t^k + (\tau\underline{u}^k)_x = -\mu(t,x)\underline{u}^{k-1} - \alpha(t,x)\underline{u}^{k-1} \\
&\quad + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\underline{u}^{k-1}(t,y)dy - M(\underline{u}^k - \underline{u}^{k-1}) \\
&\quad + \mathcal{F}\underline{u}^{k-1} - \underline{u}^{k-1}\int_{x_0}^{\infty} \kappa(x,y)\overline{u}^{k-1}(t,y)\,dy \quad \text{on } D_T \\
&\tau(t,x_0)\underline{u}^k(t,x_0) = \int_{x_0}^{\infty} \underline{u}^{k-1}(t,y)\gamma(t,y)\,dy \quad \text{on } (0,T) \\
&\underline{u}(0,x) = u_0(x), \quad x \geq 0
\end{aligned} \tag{4.36}$$

and

$$\overline{u}_t^k + (\tau\overline{u}^k)_x = -\mu(t,x)\overline{u}^{k-1} - \alpha(t,x)\overline{u}^{k-1}$$

$$
\begin{aligned}
&+\int_{x+x_0}^{\infty}\alpha(t,y)\beta(x|y)\overline{u}^{k-1}(t,y)dy - M(\overline{u}^k-\overline{u}^{k-1})\\
&+\mathcal{F}\overline{u}^{k-1}-\overline{u}^{k-1}\int_{x_0}^{\infty}\kappa(x,y)\underline{u}^{k-1}(t,y)\,dy \quad \text{on } D_T \qquad (4.37)\\
\tau(t,x_0)\overline{u}^k(t,x_0) &= \int_{x_0}^{\infty}\overline{u}^{k-1}(t,y)\gamma(t,y)\,dy \quad \text{on } (0,T)\\
\overline{u}(0,x) &= u_0(x), \quad x\geq 0.
\end{aligned}
$$

The existence of solutions to problems (4.36) and (4.37) follows from the fact that (4.36) and (4.37) are both linear problems with local boundary conditions. It is first shown that

$$\underline{u}^0 \leq \underline{u}^1 \leq \overline{u}^1 \leq \overline{u}^0.$$

Let $v(t,x) = \underline{u}^0 - \underline{u}^1$. Then, v satisfies (4.35) with $A(t,x) = 0$, $B(t,x) = -M$, and $C(t,x,y) = 0$.

Thus, from Remark 4.2 $v \leq 0$, $\underline{u}^0 \leq \underline{u}^1$ is obtained. Similarly, it can be proved that $\overline{u}^1 \leq \overline{u}^0$.

Then, let $v(t,x) = \underline{u}^1 - \overline{u}^0$. Since $\underline{u}^0 \leq \underline{u}^1$ and $\overline{u}^1 \leq \overline{u}^0$, v satisfies (4.35) with

$$A(t,x) = 0,$$

$$B(t,x) = -\mu(t,x) - \alpha(t,x) - \int_{x_0}^{\infty}\kappa(x,y)\underline{u}^0(t,y)\,dy,$$

and

$$C(t,x,y) = \frac{1}{2}\chi_I(x+y)[\kappa(x,y)\underline{u}^1(t,y) + \kappa(x,y)\overline{u}^0(t,y)].$$

Hence, $\underline{u}^1 \leq \overline{u}^0$. Likewise, it is easily seen that $\underline{u}^0 \leq \overline{u}^1$.

Next, it is claimed that $\overline{u}^1$ and $\underline{u}^1$ are upper and lower solutions to (4.21)-(4.23), respectively. Since $\underline{u}^0 \leq \underline{u}^1$ and $\overline{u}^1 \leq \overline{u}^0$, on the one hand, the right-hand side of the equation in (4.36) satisfies

$$
\begin{aligned}
&- \mu(t,x)\underline{u}^0 - \underline{u}^0\alpha(t,x) + \int_{x+x_0}^{\infty} \beta(x|y)\alpha(t,y)\underline{u}^0(t,y)dy \\
&\quad - M(\underline{u}^1 - \underline{u}^0) + \mathcal{F}\underline{u}^0 - \underline{u}^0 \int_{x_0}^{\infty} \kappa(x,y)\overline{u}^0(t,y)\,dy \\
&= \int_{x+x_0}^{\infty} \alpha(t,y)\underline{u}^0(t,y)\beta(x|y)dy \\
&\quad + \left(M - \mu(t,x) - \alpha(t,x) - \int_{x_0}^{\infty} \overline{u}^0(t,y)\kappa(x,y)\,dy\right)\underline{u}^0 \\
&\quad - M\underline{u}^1 + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\underline{u}^0(t,y)\underline{u}^0(t,x-y)dy \\
&\le \int_{x+x_0}^{\infty} \alpha(t,y)\underline{u}^1(t,y)\beta(x|y)dy \\
&\quad + \left(M - \mu(t,x) - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\overline{u}^1(t,y)\,dy\right)\underline{u}^1 \\
&\quad - M\underline{u}^1 + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\underline{u}^1(t,x-y)\underline{u}^1(t,y)dy \\
&= -\mu(t,x)\underline{u}^1 - \alpha(t,x)\underline{u}^1 + \int_{x+x_0}^{\infty} \alpha(t,y)\underline{u}^1(t,y)\beta(x|y)dy \\
&\quad + \mathcal{F}\underline{u}^1 - \underline{u}^1 \int_{x_0}^{\infty} \overline{u}^1(t,y)\kappa(x,y)\,dy.
\end{aligned}
$$

In (4.37), the right hand side satisfies

$$
\begin{aligned}
&- \mu(t,x)\overline{u}^0 - \alpha(t,x)\overline{u}^0 + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\overline{u}^0(t,y)dy \\
&\quad - M(\overline{u}^1 - \overline{u}^0) + \mathcal{F}\overline{u}^0 - \overline{u}^0 \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^0(t,y)\,dy \\
&= \int_{x+x_0}^{\infty} \alpha(t,y)\overline{u}^0(t,y)\beta(x|y)dy \\
&\quad + \left(M - \mu(t,x) - \alpha(t,x) - \int_{x_0}^{\infty} \underline{u}^0(t,y)\kappa(x,y)\,dy\right)\overline{u}^0 \\
&\quad - M\overline{u}^1 + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\overline{u}^0(t,y)\overline{u}^0(t,x-y)dy \\
&\ge \int_{x+x_0}^{\infty} \beta(x|y)\alpha(t,y)\overline{u}^1(t,y)dy \\
&\quad + \left(M - \mu(t,x) - \alpha(t,x) - \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^1(t,y)\,dy\right)\overline{u}^1
\end{aligned}
$$

$$
\begin{aligned}
& - M\overline{u}^1 + \frac{\chi_I(x)}{2}\int_{x_0}^{x-x_0} \kappa(x-y,y)\overline{u}^1(t,x-y)\overline{u}^1(t,y)dy \\
&= -\mu(t,x)\overline{u}^1 - \alpha(t,x)\overline{u}^1 + \int_{x+x_0}^{\infty} \alpha(t,y)\beta(x|y)\overline{u}^1(t,y)dy \\
& + \mathcal{F}\overline{u}^1 - \overline{u}^1 \int_{x_0}^{\infty} \kappa(x,y)\underline{u}^1(t,y)\,dy.
\end{aligned}
$$

Assuming that for some $k > 1$, $\overline{u}^k$ and $\underline{u}^k$ are upper and lower solutions of (4.21)-(4.23), respectively and proceeding analogously, it can be shown that

$$u^k \leq \underline{u}^{k+1} \leq \overline{u}^{k+1} \leq \overline{u}^k$$

and that $\underline{u}^{k+1}$ and $\overline{u}^{k+1}$ are also lower an upper solutions of (4.21)-(4.23), respectively. Hence, by induction, two monotone sequences are obtained that satisfy

$$\underline{u}^0 \leq \underline{u}^1 \leq \cdots \leq \underline{u}^k \leq \overline{u}^k \leq \cdots \leq \overline{u}^1 \leq \overline{u}^0 \quad \text{a.e. in } \overline{D}_T$$

for each $k = 0, 1, 2, \cdots$. Since the sequences $\{\overline{u}^k\}_k$ and $\{\underline{u}^k\}_k$ are monotone, thus one can find functions $\overline{u}$ and $\underline{u}$ such that $\overline{u}^k \to \overline{u}$ and $\underline{u}^k \to \underline{u}$ pointwise in the set D_T. It is clear that $\underline{u} \leq \overline{u}$ almost everywhere in D_T.

Next, one wants to prove that $\overline{u} = \underline{u}$. For this, a function v is considered such that $v = \overline{u} - \underline{u}$. As proven earlier $\overline{u} \geq \underline{u}$, thus $v(t,x) \geq 0$ and $v(0,x) = 0$. In (4.29), let $\xi(t,x) = \xi(x)$, where $\xi(x) \equiv 1$ for $x_0 \leq x \leq n$, $\xi(x) \equiv 0$ for $n+2 \leq x < \infty$, and $-1 \leq \xi' \leq 0$ for $n \leq x \leq n+2$, one obtains

$$
\begin{aligned}
\int_{x_0}^{n} v(t,x)\,dx &\leq \int_0^t \int_{x_0}^{\infty} \gamma(s,x)v(s,x)\,dx\,ds \\
&+ \int_0^t \int_{x_0}^{\infty} \left[(\mathcal{F}\overline{u})(s,x) - (\mathcal{F}\underline{u})(s,x)\right]\,dx\,ds \\
&+ \int_0^t \int_{x_0}^{\infty} \overline{u}(s,x) \int_{x_0}^{\infty} \kappa(x,y)v(s,y)\,dy\,dx\,ds \\
&\leq \tilde{\nu} \int_0^t \int_{x_0}^{\infty} v(s,x)\,dx\,ds
\end{aligned}
\tag{4.38}
$$

where

$$
\begin{aligned}
\tilde{\nu} = \sup_{\overline{D_T}} \Bigg[& \gamma(t,x) + \frac{1}{2}\int_{x_0}^{\infty} \chi_{_I}(x+z)\kappa(z,x)\underline{u}(t,z)\,dz \\
& + \frac{3}{2}\|\kappa\|_\infty \int_{x_0}^{\infty} (1+\chi_{_I}(x+y))\overline{u}(t,y)\,dy \Bigg],
\end{aligned}
$$

$\tilde{\nu}$ does not depend on n. Since $n \to \infty$, one obtains

$$
\int_{x_0}^{\infty} v(t,x)\,dx \le \int_0^t \int_{x_0}^{\infty} \tilde{\nu} v(s,x)\,dx\,ds.
$$

Hence, from the Theorem 2.1.1, it follows $v(t,x) = 0$, that is, $\underline{u} = \overline{u}$. Let $u = \underline{u} = \overline{u}$, it follows that u is a solution to (4.21)-(4.23).

To establish the uniqueness of u, it is assumed that w is another solution of (4.21)-(4.23). Since for each k, $\overline{u}^k$ and $\underline{u}^k$ are upper and lower solutions to (4.21)-(4.23), respectively, by Corollary 4.3.4, $\underline{u}^k \le w \le \overline{u}^k$, it shows $u \equiv w$, after taking the limit as $k \to \infty$.

From the above, the following important result is formulated:

Theorem 4.3.5. *Let assumptions* $(A2)-(A8)$ *hold. If* $\underline{u}^0(t,x)$ *and* $\overline{u}^0(t,x)$ *are nonnegative lower and upper solutions to* (4.21)-(4.23)*, respectively, then, there are convergent and monotone sequences* $\{\overline{u}^k(t,x)\}_k$ *and* $\{\underline{u}^k(t,x)\}_k$ *such that* $\lim_{k\to\infty} \underline{u}^k(t,x) = u(t,x) = \lim_{k\to\infty} \overline{u}^k(t,x)$*, where* u *is the unique solution to* (4.21)-(4.23).

One can now show that the solution of (4.21)-(4.23) verifies the following theorem:

Theorem 4.3.6. *Let assumptions* $(A2)-(A8)$ *hold. Then,* $P(t) = \int_{x_0}^{\infty} u(t,x)dx$ *is a continuous function in* $[0,T]$*, where* $u(t,x)$ *is the solution to* (4.21)-(4.23).

Proof. From assumptions $(A2)-(A8)$, to prove $P(t)$ is continuous over $[0,T]$, one only needs to show that the following equation is fulfilled:

$$
\begin{aligned}
\int_{x_0}^{\infty} u(t,x)\,dx = & \int_{x_0}^{\infty}\int_0^t (\mathcal{F}u)(s,x)\,ds\,dx + \int_{x_0}^{\infty} u(0,x)dx \\
& - \int_{x_0}^{\infty}\int_0^t u(s,x)\int_{x_0}^{\infty} \kappa(x,y)u(s,y)\,dy\,ds\,dx \\
& - \int_{x_0}^{\infty}\int_0^t \mu(s,x)u(s,x)\,ds\,dx.
\end{aligned} \tag{4.39}
$$

To achieve this, one considers $\xi(t,x) \equiv \xi(x)$, with $1 \equiv \xi(x)$ for $x_0 \le x \le n$, $0 = \xi(x)$ for $n+2 \le x < \infty$, and $-1 \le \xi' \le 0$ for $n \le x \le n+2$. Using Definition 4.3.1, one finds

$$\begin{aligned}
&\Big|\int_{x_0}^{\infty}\int_0^t u(s,x)\gamma(s,x)\,ds\,dx - \int_{x_0}^{\infty} u(0,x)dx + \int_{x_0}^{\infty} u(t,x)\,dx \\
&\quad + \int_{x_0}^{\infty}\int_0^t \mu(s,x)u(s,x)\,ds\,dx - \int_{x_0}^{\infty}\int_0^t (\mathcal{F}u)(s,x)\,ds\,dx \\
&\quad + \int_{x_0}^{\infty}\int_0^t u(s,x)\int_{x_0}^{\infty} \kappa(x,y)u(s,y)\,dy\,ds\,dx\Big| \\
&= \Big|\int_n^{\infty} [u(t,x)-u(0,x)][-\xi(x)+1]\,dx \\
&\quad + \int_n^{\infty}\int_0^t \tau(s,x)\xi'(x)u(s,x)\,ds\,dx \\
&\quad + \int_{x_0}^{\infty}\int_0^t \mu(s,x)u(s,x)[-\xi(x)+1]\,ds\,dx \\
&\quad - \int_n^{\infty}\int_0^t (\mathcal{F}u)(s,x)[-\xi(x)+1]\,ds\,dx \\
&\quad + \int_n^{\infty}\int_0^t u(s,x)[-\xi(x)+1]\int_{x_0}^{\infty} \kappa(x,y)u(s,y)\,dy\,ds\,dx\Big| \\
&\le \left(2 + \|\gamma\|_\infty T + \|\tau\|_\infty + \|\mu\|_\infty + \frac{3}{2}\|\kappa\|_\infty \sup_{[0,T]} \| \, u(t,\cdot) \, \|_1\right) \times \\
&\quad \sup_{[0,T]} \int_n^{\infty} u(t,x)\,dx.
\end{aligned}$$

Since $u \in L^1(D_T)$, $\sup_{[0,T]} \int_n^{\infty} u(t,x)\,dx \to 0$ as $n \to \infty$, it leads to (4.39). □

The global existence of solution is, therefore, obtained.

Theorem 4.3.7. *Assuming* $(A2)-(A8)$ *hold. Then, the solution* u *of* (4.21)-(4.23) *exists in* $[0,\infty[$.

Proof. From Definition 4.3.1, it suffices to prove that $P(t)$ does not blow up in finite time. To achieve this, (4.39) is used to obtain

$$
\begin{aligned}
P(t) &= P(0) + \int_{x_0}^{\infty} \int_0^t \gamma(s,x)u(s,x)\,ds\,dx - \int_{x_0}^{\infty} \int_0^t \mu(s,x)u(s,x)\,ds\,dx \\
&\quad - \frac{1}{2} \int_{x_0}^{\infty} \int_0^t u(s,x) \int_{x_0}^{\infty} \kappa(x,y)u(s,y)\,dy\,ds\,dx \\
&\le P(0) + \delta \int_0^t P(s)ds
\end{aligned}
$$

with $\delta = \|\gamma\|_{\infty}$. From Lemma 2.1.2, one then obtains

$$
P(t) \le P(0)e^{\delta t}.
$$

Thus, the proof is completed. □

Chapter 5

Non-autonomous prion model

5.1 Introduction

In this chapter, is investigated the solvability of a nonlinear system consisting of a differential equation, coupled with a non-autonomous integro-differential equation describing the dynamic of prion proliferation , where PrP^{SC} polymers can split into two or more pieces at a rate, β, that not only depends on the sizes of the polymers involved but also on time. The degradation and splitting rates are assumed to be unbounded, and the global existence of a weak solution is established thanks to a weak compactness method.

In Section 5.2, the model is described, previous results summarised and assumptions given that are considered throughout the chapter. Section 5.3 focuses on the global existence of a weak solution.

5.2 Preliminaries

Prion diseases are a group of uncommon and fatal degenerative cerebrum disorders that affect both humans and animals and, are sometimes, transmitted to humans through the consumption of infected meat. The most typical form of prion disease that affects humans is CJD (Creutzfeldt-Jakob disease) [10]. Prions are commonly regarded as a polymeric form of a normal protein monomer PrP^{C} (prion protein cellular) normally produced in the body and its mechanism is not yet well-understood. The polymeric infectious prion PrP^{Sc} (prion protein scrapies) grows by attaching units of normal prion PrP^{C} and transforming the latter into the form corresponding to the infectious state. Above a minimum size $x_0 > 0$, the PrP^{Sc} polymers become stable and can grow to chains containing several monomers units. PrP^{Sc} polymers have the ability to split into smaller polymers, thus resulting in infectious polymers capable of elongating and splitting again. If after splitting, a smaller polymer falls below the minimum length x_0, it degrades immediately into normal PrP^{C} monomers. The leading theory of prion replication is nucleated polymerization (see for example [27, 31, 43, 51, 57, 58] and the references herein).

The spitting of PrP^{Sc} polymers is one of the most important key phases in the replication process. Unfortunately, its precise mechanism is not yet determined. According to Masel, Jansen and Nowak [43], the fragmentation rate of PrP^{Sc} is a linear function of the size of aggregates. The authors assumed that all the kinetic coefficients of the model are constant. Recent studies have shown the limit of such hypotheses (see for example [49, 61]). In fact, the fragmentation of PrP^{Sc} polymers, according to their size, shows that the infectious capability of polymers may depend on their size [61]. In vivo aggregates with small sizes produced by PMCA (Protein Misfolding Cyclic Amplification), are less infectious than aggregates with important sizes. The reverse effect is observed after stabilising aggregates on the nitrocellulose particle. Several other mechanisms of fragmentation have been considered in the literature (see for example [36, 42]). In this chapter, the focus is on a more general model for prion replication, with multiple fragmentation.

5.2.1 Description of the model

One denotes by $v(t)$, the population of PrP^{C} monomers at time t and by $u = u(t,x)$, the population density of PrP^{Sc} polymers of size $x \geq x_0$ at time $t \geq 0$, where $x_0 > 0$ is the minimum length. The interaction between the PrP^{C} monomers and the PrP^{Sc}

polymers can be described as follows:

$$\dot{v} = \lambda - \gamma v - v \int_{x_0}^{\infty} \tau(x)u(t,x)dx + \int_{x_0}^{\infty} u(t,x)\beta(t,x) \int_0^{x_0} yk(t,y,x)\,dy\,dx \tag{5.1}$$

$$\partial_t u = -v(t)\partial_x(\tau(x)u) - (\mu(t,x) + \beta(t,x))u + \int_x^{\infty} \beta(t,y)k(t,x,y)u(t,y)\,dy \tag{5.2}$$

for $x \in (x_0, \infty)$ subject to the initial conditions

$$v(0) = v_0, \quad u(0,x) = u_0(x), \quad x \in (x_0, \infty), \tag{5.3}$$

and the boundary condition

$$u(t, x_0) = 0, \quad t > 0. \tag{5.4}$$

The constants λ and γ in (5.1) represent the background source of monomers and the degradation rate of monomers, respectively. The functions $\tau(x) > 0$ and $\beta(t,x) \geq 0$ represent the polymerisation rate of polymers of size x and the fragmentation rates of polymers of size x at time t, respectively. The coefficient $k(t,y,x) \geq 0$ denotes the formation rate of polymers of size $y < x$ after fragmentation. In (5.2), the term $\mu(t,x) \geq 0$ accounts for the degradation rate of polymers of size x at time t.

In Equation (5.1), the integral terms are described, from left to the right by the diminution of the amount of monomers due to polymerisation mechanism and the increase of the number of monomers due to fragmentation of polymers into polymers of sizes below the minimum length x_0. The transport term $v(t)\partial_x(\tau(x)u)$, in (5.2), represents the reduction in the amount of polymers of size x due to polymerisation. Finally, the last two terms containing β on the right hand side in (5.2), account for the loss and gain of polymers due to fragmentation, respectively.

In the following sections, previous results are summarised and the main contribution of the chapter provided.

5.2.2 Previous results

A discrete model, proposed by Masel and colleagues, in 1999, was used for the first time to study the replication of prion [43]. Latter, Greer and colleagues introduced, in 2006, the continuous version of the above-mentioned-model. In [31], the asymptotic behaviour of the system of ordinary differential equations was investigated with parameters of the form

$$\tau \equiv \text{const}, \quad \mu \equiv \text{const}, \quad \beta(x) = \beta x, \quad k(y,x) = \frac{1}{x}. \tag{5.5}$$

Then, the following functions were introduced:

$$P(t) = \int_{x_0}^{\infty} u(t,x)x\,dx \quad \text{and} \quad U(t) = \int_{x_0}^{\infty} u(t,x)\,dx \tag{5.6}$$

representing the total number of monomers in polymers at time t, and the total number of polymers at time t, respectively. The system (5.1)-(5.4) was transformed into a system of ordinary differential equations

$$\begin{aligned} \dot{U} &= \beta P - \mu U - 2\beta x_0 U \\ \dot{V} &= \lambda - \gamma V - \tau UV + \beta x_0^2 U \\ \dot{P} &= \tau UV - \mu P - \beta x_0^2 U \end{aligned} \tag{5.7}$$

subjects to the initial conditions

$$U(0) = U_0 \geq 0, \quad V(0) = V_0 \geq 0, \quad P(0) = P_0 \geq x_0 U_0. \tag{5.8}$$

The local stability of the disease steady state as well as the global stability of the disease-free steady state were proved. Indeed, the global stability of the unique steady state; namely, the disease-free equilibrium $(U, V, P) = (0, \lambda/\gamma, 0)$, for the system (5.7), was established under the condition

$$\mu + x_0\beta \geq \sqrt{\lambda\beta\tau/\gamma} \tag{5.9}$$

and the instability of the disease-free equilibrium, for the system (5.7), was obtained for the condition

$$\mu + x_0\beta < \sqrt{\lambda\beta\tau/\gamma}.$$

In this latter case, in addition to the disease-free equilibrium, there is the disease equilibrium, which is locally stable.

Several investigations were carried out based on Greer's model. Most of these studies focused on global stability analysis, while very few used the semigroup approach. Some of them are ([30],[59] and the references herein), where the authors studied global stability. The semigroups approach, combined with the characteristics method, was used in [29] to perform the well-posedness analysis of the model in the space

$$Z_+ := \mathbb{R}_+ \times L^1_+((0,\infty), x\,dx)$$

with parameters described as in (5.5). Moreover, depending on whether or not (5.9) holds, the convergence of the solution to a steady state was proved.

These results were extended in [62] to model parameters different from (5.5) using Kato's theory for hyperbolic evolution equations. Indeed, for a constant polymerisation rate τ, an unbounded degradation rate $\mu(x)$ and an unbounded fragmentation rate $\beta(x)$, result for well-posedness was established under the following assumptions, upon the formation rate of polymers:

$$k(y,x) = k(x-y,x), \quad x > x_0, \quad 0 < y < x; \tag{5.10}$$

that is, binary splitting of polymers, and

$$\int_0^x k(y,x)\,dx = 1, \quad x > x_0, \quad 0 < y < x. \tag{5.11}$$

Conditions (5.10) and (5.11) imply

$$2\int_0^x xk(y,x)\,dx = x, \quad x > x_0, \quad 0 < y < x \tag{5.12}$$

(that there is conservation of the number of monomers after fragmentation). Furthermore, for unbounded parameters $\mu(x)$ and $\beta(x)$, the existence of the global weak solutions was proved. In both cases, under some extra growth hypotheses, the infection-free equilibrium $(\lambda/\gamma, 0) = (V, U)$ was shown to be globally asymptotically stable.

Assuming (5.10) and (5.11), the global existence of weak solutions of the model with unbounded size-dependent polymerisation and degradation rates was established in [68], improving results obtained in [62] for constant rate of polymerisation.

The case of multiple fragmentation has not been considered so far in prion models. The aim was to establish the well-posedness of the model (5.1)-(5.4), regardless of assumptions (5.10) and (5.11), where model parameters are not only size-dependent, but also time-dependent. $\beta(t, x)$ and $\mu(t, x)$ were considered to be unbounded. The weak compactness method was used to obtain the result.

The following section focuses on assumptions used in the remaining sections of the chapter.

5.2.3 Assumptions

The problem (5.1)-(5.4) is considered in the state X_1 (Banach space) defined by

$$X_1 := L^1([x_0, \infty), x\,dx) = \{u; \|\psi\|_1 := \int_{x_0}^{\infty} x|\psi(x)|\,dx\}.$$

where $\|\cdot\|$, is the natural norm in the Lebesgue space L^1. X_{1+} denotes the positive cone in X_1.

It is then assumed that:

(H1) $\lambda > 0$ and $\gamma > 0$;

(H2) $\mu(t, x)$ and $\beta(t, x)$ are nonnegative unbounded parameters on $[0, \infty) \times [x_0, \infty)$;

(H3) $\tau(x)$ is a nonnegative continuously differentiable function on $[x_0, \infty)$ with τ_x bounded; and

$$\tau(x) \leq \tau^* x, \quad x \geq x_0, \tag{5.13}$$

where $0 < \tau^* < \infty$;

(H4) $k(t, y, x) \geq 0$ is a measurable function such that $k(t, y, x) = 0$ for almost any $x < y$ and any $t \in [0, T]$ i.e. PrP^{Sc} polymers of size less than x_0 do not fragment since the minimum size of a particle is x_0; and the number of monomer units is supposed to be preserved during splitting, that is,

$$\int_0^x yk(t, y, x)\, dy = x \text{ for any } y > x_0 \text{ and almost any } t \in [0, \infty) \tag{5.14}$$

which means multiple fragmentation conserves the number of monomers.

The assumption of varying polymerisation rate, $\tau(x)$, according to size for globular aggregates seems to be more appropriate compared to linear polymerisation since the geometry of the polymers may differ on the levels [43]. The assumption of an unbounded splitting rate $\beta(t, x)$ and an unbounded degradation rate $\mu(t, x)$ also appears to be biologically significant.

5.3 Global existence of a weak solution

In this section, one denotes by X_{1w}, the space X_1, as defined in Section 5.2.3, equipped with its weak topology and by A, the linear part of (5.2) that is,

$$[A(t)u](x) = -(\mu(t, x) + \beta(t, x))u(x) + \int_x^\infty \beta(t, y)k(t, x, y)u(y)\, dy, \text{ a.e. } t \geq 0,\ x \geq x_0.$$

The following definition, of a global weak solution to (5.1)-(5.4), was introduced in [68] for autonomous prion model. It is adapted to the problem in hand (non-autonomous).

Definition 5.3.1. *Given v_0, $u_0 \in X_{1+}$, the pair (v, u) is called a global weak flow to* (5.1)-(5.4) *if:*

(i) the function $v \in C^1(\mathbb{R}_+)$ is a nonnegative flow to (5.1)*;*

(ii) the function $u \in L^\infty_{loc}(\mathbb{R}_+, X_{1+}) \cap C(\mathbb{R}_+, X_{1w})$;

(iii) for every $0 < t$ *and for* $\phi \in W^1_\infty([x_0,\infty))$, $A[u] \in L((0,\infty)\times[x_0,\infty))$*; and*

$$\begin{aligned}&\int_{x_0}^{\infty}\phi(x)u(t,x)\,dx - \int_0^t v(s)\int_{x_0}^{\infty}\phi'(x)\tau(x)u(s,x)\,dx\,ds\\&=\int_{x_0}^{\infty}\phi(x)u_0(x)\,dx + \int_0^t\int_{x_0}^{\infty}\phi(x)A[u(s)](x)\,dx\,ds.\end{aligned} \tag{5.15}$$

To establish the global existence of a weak flow as stated in Definition 5.3.1, the following additional assumptions are considered:

(H2') There exists $\alpha \geq 1$ and $\rho \in L^\infty_+([0,\infty)\times[x_0,\infty))$ such that

$$\mu(t,x)+\beta(t,x) \leq \rho(t,x)x^\alpha, \ \text{ a.e. } \ t\geq 0 \ \text{ and } \ x\in[x_0,\infty), \tag{5.16}$$

where for all $t \geq 0$, $\rho(t,x) \to 0$ as $x \to \infty$;

(H3') In the case $\alpha = 1$,

$$\tau(x) \leq \rho(t,x)x, \ \text{ a.e. } \ t \geq 0 \text{ and } x \in [x_0,\infty); \tag{5.17}$$

(H4') Given $R > x_0$ and $\epsilon > 0$, a positive δ can be found such that

$$\sup_{\Sigma\subset(x_0,R),|\Sigma|\leq\delta}\left(\operatorname*{ess\,sup}_{t\geq0,x\in[x_0\infty)}\frac{\beta(t,x)}{x^\alpha}\int_{x_0}^{x}\mathbf{1}_\Sigma(y)k(t,y,x)\,dy\right)\leq\epsilon. \tag{5.18}$$

where $\mathbf{1}_\Sigma$ is the indicator function, $\Sigma \subset [x_0,\infty)$ a measurable set and $|\Sigma|$ its Lebesgue measure.

In the following, one denotes by B, the linear operator defined by

$$[Bu](x) = \partial_x(\tau(x)u(x)), \ \text{ a.e. } \ x \geq x_0,$$

with domain $D(B)$ given by

$$D(B) = \{f \in X_1; \partial_x(\tau f) \in X_1, \ f(x_0) = 0\}.$$

One denotes by $B_v(t)$, the non-linear part of (5.2), containing B, defined by

$$-B_v(t) := -v(t)B, \quad 0 \le t \le T < \infty. \tag{5.19}$$

Before stating the main result of this chapter, the following lemmas needed for the proof of the main result are given as follows:

Lemma 5.3.2. *Let $u_n \to u$ in X_{1w+}. Assuming f_n and f are measurable functions on $[x_0,\infty)$ such that $f_n \to f$ a.e.*

(i) If $\|f_n\|_\infty \le c$, with $c > 0$, then $f_n u_n \to fu$ in X_{1w}.

(ii) If ρ and α satisfy conditions as in (5.16) and if $|f_n(x)| \to \rho(t,x)x^\alpha$ for a.e. $x \in [x_0,\infty)$, $t \ge 0$ and

$$\int_{x_0}^{\infty} x^\alpha u_n(x)\, dx \le c, \quad n \in \mathbb{N},$$

then $f_n u_n \to fu$ in X_{1w}.

Proof. See [62, Lemma 4.2]. □

Lemma 5.3.3. *Assume τ satisfies (5.13) and consider $v \in C([0,T],\mathbb{R}_+)$. Denote by $(U_{B_v}(t,s))_{0\le s\le t\le T}$, the unique propagator in X_1 for $(-B_v(t))_{0\le t\le T}$, as defined in (5.19). For $M > x_0$ and $\delta > 0$, we set*

$$\lambda_M(\delta) := \tau^* M \sup_{\Sigma\subset(x_0,M),|\Sigma|\le\delta} \int_\Sigma \frac{dy}{\tau(y)}.$$

Then, for any $f \in X_{1+}$ and $0 \le s \le t \le T$, the following holds:

$$\sup_{\Sigma\subset(x_0,M),|\Sigma|\le\delta} \int_\Sigma U_{B_v}(t,s) f\, dx \le \sup_{\mathcal{F}\subset(x_0,M),|\mathcal{F}|\le\lambda_M(\delta)} \int_{\mathcal{F}} f\, dx.$$

Proof. We define

$$\left(W(t)f\right)(x) := \mathbf{1}_{[t,\infty)}(\Phi(x)) \frac{f(\Phi^{-1}(\Phi(x)-t))}{\tau(x)} \tau(\Phi^{-1}(\Phi(x)-t))$$

for any $x > x_0$, $t \ge 0$ and $f \in X_{1+}$, with

$$\Phi(x) = \int_{x_0}^{x} \frac{dy}{\tau(y)}, \quad x \in [x_0,\infty). \tag{5.20}$$

It can easily be proved that the family $(W(t))_{t\geq 0}$ is a C_0 positive semigroup on X_1, which satisfies $\|W(t)\|_{\mathcal{L}(L^1)} \leq e^{\tau^* t}$. For any given measurable subset $\Sigma \subset (x_0, M)$ and any $f \in X_{1+}$, one has

$$\int_\Sigma (W(t)f)(x)\,dx = \int_\Sigma \mathbf{1}_{[t,\infty)}(\Phi(x)) \frac{f(\Phi^{-1}(\Phi(x)-t))}{\tau(x)} \tau(\Phi^{-1}(\Phi(x)-t))\,dx.$$

Considering the fact that the function $\Phi'(x) = \dfrac{1}{\tau(x)} > 0$, that is, Φ is increasing on $[x_0, \infty)$ and the definition of the indicator function, one obtains

$$\begin{aligned}
\mathbf{1}_{[t,\infty)}(\Phi(x)) &= \begin{cases} 1 & \text{if } \Phi(x) \in [t, \infty) \\ 0 & \text{if } \Phi(x) \notin [t, \infty) \end{cases} \\
&= \begin{cases} 1 & \text{if } x \in [\Phi^{-1}(t), \infty) \\ 0 & \text{if } x \notin [\Phi^{-1}(t), \infty) \end{cases} \\
&= \mathbf{1}_{[\Phi^{-1}(t),\infty)}(x)
\end{aligned}$$

hence,

$$\int_\Sigma (W(t)f)(x)\,dx = \int_{\Phi^{-1}(t)}^{\infty} \mathbf{1}_\Sigma(x) \frac{\tau(\Phi^{-1}(\Phi(x)-t))}{\tau(x)} f(\Phi^{-1}(\Phi(x)-t))\,dx.$$

By letting $x = \Phi^{-1}(\Phi(x)-t)$, one obtains

$$\int_\Sigma (W(t)f)(x)\,dx = \int_{x_0}^{\infty} \mathbf{1}_{\Phi^{-1}((\Phi(\Sigma)-t)\cap(0,\infty))}(x) f(x)\,dx. \tag{5.21}$$

Under assumption (5.13), and using the invariance of the Lebesgue measure with respect translations and that $\Phi^{-1}((\Phi(\Sigma)-t)\cap(0,\infty)) \subset (x_0, M)$, one obtains

$$\begin{aligned}
|\Phi^{-1}((0,\infty)) \cap (\Phi(\Sigma)-t)| &\leq |\Sigma| \\
&\leq \tau^* \int_\Sigma y \frac{dy}{\tau(y)} \\
&\leq \tau^* M \int_\Sigma \frac{dy}{\tau(y)} \\
&\leq \lambda_M(\delta).
\end{aligned} \tag{5.22}$$

The unique evolution family to $(-B_v(t))_{0\leq t\leq T}$ is given by

$$U_{B_v}(t,s) = W\left(\int_s^t v(p)\,dp\right), \qquad 0 \leq s \leq t \leq T.$$

By integrating on Σ and making use of (5.21), one obtains for any $f \in X_{1+}$ and $0 \leq s \leq t \leq T$,

$$\int_{\Sigma} U_{B_v}(t,s) f \, dx = \int_{x_0}^{\infty} \mathbf{1}_{\Phi^{-1}((\Phi(\Sigma) - \int_s^t v(p)\, dp) \cap (0,\infty))}(x) f(x) \, dx.$$

One deduces, from the definition of the indicator function and from (5.22), the inequality,

$$\sup_{\Sigma \subset (x_0, M), |\Sigma| \leq \delta} \int_{\Sigma} U_{B_v}(t,s) f \, dx \leq \sup_{\mathcal{F} \subset (x_0, M), |\mathcal{F}| \leq \lambda_M(\delta)} \int_{\mathcal{F}} f \, dx.$$

Thus, the proof is completed. □

Next, the main result of this chapter is given.

$$X_1^{\alpha} = L^1([x_0, \infty), x^{\alpha} \, dx), \qquad \alpha \geq 1,$$

is considered.

Theorem 5.3.4. *Assuming* (5.16)-(5.18) *holds. Given any* $v_0 > 0$ *and* $u_0 \in X_{1+}^{\alpha}$*, there exists, at least, a global weak flow* (v, u) *to the system* (5.1)-(5.4)*. Furthermore,* $u \in L^{\infty}_{loc}(\mathbb{R}_+, X_1^{\alpha})$*. In addition, if* $\operatorname{supp}(u_0) \subset [x_0, S_0]$ *for some* $S_0 > x_0$*, then,* $\operatorname{supp}(u(t)) \subset [x_0, S(t)]$*, for* $t \geq 0$ *where* S *is the global solution to the ordinary differential equation*

$$\begin{aligned} \dot{S}(t) &= (v\tau) S(t), \quad t > 0, \\ S(0) &= S_0. \end{aligned} \tag{5.23}$$

Proof. One denotes by $\mathcal{D}([x_0, \infty))$, the space of all test functions on $[x_0, \infty)$, and $\mathcal{D}_+[x_0, \infty)$ its positive cone. Let $u_n^0 \in \mathcal{D}_+([x_0, \infty))$ be such that $u_n^0 \to u^0$ in X_1^{α}. We set $\mu_n := \min\{\mu, n\}$ and $\beta_n := \min\{\beta, n\}$. It is easy to verify that μ_n and β_n also satisfy assumptions (5.16) and (5.18). One denotes by

$$(v_n, u_n) \in C^1(\mathbb{R}_+, \mathbb{R} \times X_1) \cap C(\mathbb{R}_+, \mathbb{R}_+ \times D(B))$$

the classical flow to (5.1)-(5.4) for bounded μ and β bounded, where (u^0, β, μ) is replaced by (u_n^0, β_n, μ_n) (see [68, Theorem 2.1]). There exists $R > 1$ satisfying $R \geq \|v\|_{C^1(\mathbb{R}_+)} \geq v(t) \geq R^{-1}$, for any $t \geq 0$, thanks to the identity

$$\dot{v}(t) + \frac{d}{dt}\int_{x_0}^{\infty} xu(t,x)\,dx = \lambda - \gamma v(t) - \int_{x_0}^{\infty} x\mu(t,x)u(t,x)\,dx$$

that is,

$$\dot{v}(t) + \gamma v(t) = \lambda - \frac{d}{dt}\int_{x_0}^{\infty} xu(t,x)\,dx - \int_{x_0}^{\infty} x\mu(t,x)u(t,x)\,dx.$$

By multiplying each side of the equality by $e^{\gamma t}$, one obtains

$$\frac{d}{dt}(e^{\gamma t}v(t)) = e^{\gamma t}\lambda - e^{\gamma t}\frac{d}{dt}\int_{x_0}^{\infty} xu(t,x)\,dx - e^{\gamma t}\int_{x_0}^{\infty} x\mu(t,x)u(t,x)\,dx$$

After integrating the latter equation with respect to t, it follows that

$$e^{\gamma t}v(t) - v_0 = \lambda\int_0^t e^{\gamma s}\,ds - \int_0^t e^{\gamma s}\frac{d}{dt}\int_{x_0}^{\infty} xu(s,x)\,dx - \int_0^t e^{\gamma s}\int_{x_0}^{\infty} x\mu(t,x)u(t,x)\,dx$$

$$v(t) + \|u(t)\|_{X_1} \leq \lambda/\gamma.$$

Hence,

$$v_n(t) + \|u_n(t)\|_{X_1} \leq \lambda/\gamma. \tag{5.24}$$

After integrating by part and making use of (5.14), one obtains

$$\int_{x_0}^{x} y^{\alpha}k(t,y,x)\,dy \leq x^{\alpha}, \quad x > x_0. \tag{5.25}$$

Since u_n is the solution of (5.2), by making use of (5.13), (5.24) and (5.25), one obtains

$$\begin{aligned}
\frac{d}{dt}\int_{x_0}^{\infty} x^{\alpha}u_n(t,x)\,dx = &-\int_{x_0}^{\infty} x^{\alpha}v_n(t)\partial_x\left(\tau(x)u_n(t,x)\right)\,dx \\
&-\int_{x_0}^{\infty} x^{\alpha}\left(\mu_n(t,x)+\beta_n(t,x)\right)u_n(t,x)\,dx \\
&+\int_{x_0}^{\infty}\int_{x_0}^{x} y^{\alpha}\beta_n(t,x)k(t,y,x)u_n(t,x)\,dy\,dx \\
\leq\ &\alpha v_n(t)\int_{x_0}^{\infty} x^{\alpha-1}\tau(x)u_n(t,x)\,dx \\
&-\int_{x_0}^{\infty} x^{\alpha}\left(\mu_n(t,x)+\beta_n(t,x)\right)u_n(t,x)\,dx
\end{aligned}$$

$$
\begin{aligned}
&+\int_{x_0}^{\infty} x^{\alpha}\beta_n(t,x)u_n(t,x)\,dx\\
&\leq \alpha v_n(t)\int_{x_0}^{\infty} x^{\alpha-1}\tau(x)u_n(t,x)\,dx\\
&\leq \tau^*\alpha v_n(t)\int_{x_0}^{\infty} x^{\alpha}u_n(t,x)\,dx\\
&\leq \tau^*\alpha\frac{\lambda}{\gamma}\int_{x_0}^{\infty} x^{\alpha}u_n(t,x)\,dx
\end{aligned}
$$

from which

$$\|u_n(t)\|_{X_1^\alpha} \leq C(T), \quad n\geq 1, \quad 0\leq t\leq T \tag{5.26}$$

where $C(T) = \|u(0)\|e^{\tau^*\alpha T\lambda/\gamma}$. From (5.1) and by making use of (5.16), (5.24) and (5.26), one obtains

$$\max_{t\in[0,T]} |\dot{v}_n| \leq \lambda/\gamma.$$

Thus,

$$|v_n(t) - v_n(t')| \leq \frac{\lambda}{\gamma}|t-t'|.$$

There exists $\delta > 0$, such that for all $t, t' \in [0,T]$, $|t-t'| \leq \delta$ implies

$$|v_n(t) - v_n(t')| \leq \delta\lambda/\gamma.$$

and then,

$$\lim_{\delta\searrow 0}\sup_{n\geq 1, |t-t'|\leq\delta} |v_n(t) - v_n(t')| = 0.$$

Hence, the sequence $(v_n)_{n\geq 1}$ is equicontinuous in $C([0,T])$. One derives from (5.24), the inequality $\sup_{n\geq 1, t\in[0,T]} |v_n(t)| < \infty$, which shows that $(v_n)_{n\geq 1}$ is equibounded in $C([0,T])$. Therefore, according to Theorem 2.1.8, the sequence $(v_n)_{n\geq 1}$ is indeed, relatively compact in $C([0,T])$.

Next, we show that the sequence $(u_n(t))_{n\geq 1, t\in[0,T]}$ is also relatively compact in X_{1w}. From (5.24), one obtains

$$\lim_{R\to\infty}\sup_{n\geq 1, t\in[0,T]}\int_R^{\infty} u_n(t,x)\,dx = 0. \tag{5.27}$$

The family $(U_{B_v}(t,s))_{0\le s\le t\le T}$ being the unique evolution family in X_1 for $(-B_v(t))_{0\le t\le T}$ as denoted in 5.3.3, one writes u_n as

$$u_n(t) = U_{B_{v_n}}(t,0)u_n^0 + \int_0^t U_{B_{v_n}}(t,s)A_n[u_n(s)]\,ds, \quad t \in [0,T], \tag{5.28}$$

and deduce from Lemma (5.3.3), the inequalities

$$\begin{aligned}\int_\Sigma u_n(t,x)\,dx &\le \int_{\Sigma\cap(x_0,R)} u_n(t,x)\,dx + \int_R^\infty u_n(t,x)\,dx\\ &\le \sup_{\Sigma\subset(x_0,R),|\mathcal{F}|\le\lambda_R(\delta)} \int_{\mathcal{F}} u_n^0(x)\,dx\\ &\quad + \int_0^t \sup_{\Sigma\subset(x_0,R),|\mathcal{F}|\le\lambda_R(\delta)} \int_{x_0}^\infty u_n(s,x)\beta_n(t,x)\\ &\quad \times \int_{x_0}^x \mathbf{1}_{\mathcal{F}}(y)k(t,y,x)\,dy\,dx\,ds + \frac{1}{R}\|u_n(t)\|_{X_1},\end{aligned} \tag{5.29}$$

for $\delta > 0$ and $R > x_0$, where Σ is any arbitrary measurable subset of $[x_0,\infty)$ such that $|\Sigma| \le \delta$. By making use of assumptions (5.16), (5.18), (5.26), and $\lambda_R(\delta) \to 0$ when $\delta \to 0^+$, one obtains

$$\lim_{|\Sigma|\to 0} \sup_{n\ge 1,t\in[0,T]} \int_\Sigma u_n(t,x)\,dx = 0. \tag{5.30}$$

Since the equicontinuity of $(u_n(t))_{n\ge1,t\in[0,T]}$ in X_{1w} is guaranteed by (5.24)-(5.27), it follows from Theorem 2.1.11 that the sequence $(u_n(t))_{n\ge1,t\in[0,T]}$ is relatively compact in X_{1w}.

From Theorem 2.1.9, there exists a subsequence $((v_{n_k},u_{n_k}))_{n_k\in\mathbb{N}}$ and a function $(v,u) \in C(\mathbb{R}_+,\mathbb{R}\times X_1)$ such that

$$(v_{n_k},u_{n_k}) \to (v,u) \in C(\mathbb{R}_+,\mathbb{R}\times X_1).$$

Relabelling the latter, one obtains

$$(v_n,u_n) \to (v,u) \in C(\mathbb{R}_+,\mathbb{R}\times X_1) \tag{5.31}$$

which establishes the existence of $(v,u) \in C(\mathbb{R}_+,\mathbb{R}\times X_1)$.

Next, it is proved that (v, u) is, indeed, a weak flow to (5.1)-(5.4). By making use of assumptions (5.16), (5.26), (5.13) and (5.17), and applying Lemma 5.3.2, it is concluded that (v, u) satisfies (iii) of Definition 5.3.1. From Lemma 5.3.2, it is deduced that $v \in C^1(\mathbb{R}_+)$ and is a nonnegative solution to 5.1, thus verifies (i) of Definition 5.3.1.

Assuming $\mathrm{supp}(u_0) \subset [x_0, S_0]$ for some $S_0 > x_0$ and (5.13), (5.14), (5.16)-(5.18) it is finally shown that the weak solution (u, v) satisfies $[x_0, S(t)] \supset \mathrm{supp}(u(t))$, for any $t \geq 0$, where S is the flow of the ordinary differential equation (5.23). The sequence $(u_n^0) \subset \mathcal{D}^+([x_0, \infty))$ is chosen such that $\mathrm{supp}(u_n^0) \subset [x_0, S_0]$. The sequence $((v_n, u_n))_{n\geq 1}$ satisfies $\mathrm{supp}(u_n(t)) \subset [x_0, S_n(t)]$ where

$$S_n(t) = S_0 + \tau \int_0^t v_n(r)\, dr, \quad t \geq 0,\, n \geq 1.$$

Since $\lim_{n\to\infty} S_n(t) = S(t)$ and

$$\int_{S(t)}^{\infty} u(t,x)\, dx = \lim_{n\to\infty} \int_{S_n(t)}^{\infty} u_n(t,x)\, dx = 0,$$

by (5.31) and Lemma 5.3.2, it follows that $\mathrm{supp}(u(t)) \subset [x_0, S(t)]$, for any $t \geq 0$.

Thus, the proof is completed.

$\square$

Chapter 6

Conclusion

The main aim of this study was to establish the well-posedness of certain nonlinear time dependent evolution equations.

In Chapter 3, a new SVEIR epidemiological model with age-dependent vaccination, infection and latency was proposed, where the waning vaccine-induced immunity depends on age of vaccination and the vaccinated individuals can lose their immunity and, therefore, fall back to the susceptible class. Our main input was the consideration of continuous age-structure in latency and infection as well as the incidence rate of the form $S(t)\int_0^\infty \left(K_0(a)i(a,t) + \int_0^\infty K(a,a^{'})i(a^{'},t)\,da^{'}\right)\,da$. An appropriate Lyapunov functionals was constructed and Lasalle's invariance principle applied to investigate the global dynamic of the model. As a result, the global stability of the disease-free equilibrium and endemic equilibrium was obtained and fully determined by the basic reproduction number $\Re_0$. More precisely, it was shown that, if $\Re_0 > 1$, then the disease free equilibrium is globally asymptotically stable and, if $\Re_0 \leq 1$, the endemic equilibrium is globally asymptotically stable.

In Chapter 4, a non-autonomous transport coagulation-fragmentation equation with bounded model parameters was examined. Our main concern was to propose a new method consisting of construction of nonnegative monotone upper and lower solutions ($\overline{u}^k(t,x)$ and $\underline{u}^k(t,x)$ respectively), and establish their convergence to a unique solution $u(t,x)$ of the model, for $t \in \mathbb{R}_+$. This was done by making use of the comparison principle and Gronwall's inequality.

Finally, in Chapter 5, a Prion model with multiple fragmentations was studied. Here, the degradation and splitting rates were considered to be unbounded under some additional assumptions that were purposely adapted to obtain the current results. A weak compactness method, based on Arzelà-Ascoli and Dunford-Pettis theorems and which consists of construction of sequences $(v_n,u_n) \to (u,v)$ was used to investigate the global existence of a weak solution of the model.

Although various techniques were employed to investigate certain class of nonlinear evolution equations, there are still different angles through which further investigations could be considered. For instance, it would be interesting to investigate the analysis of a coagulation and multiple fragmentation model with time dependent coefficients. One can consider the fragmentation rate $a(t, x)$ to be only locally integrable with respect to time t and locally bounded with respect to mass x. Similar investigations could also be done for non-autonomous coagulation and multiple fragmentation models with growth where the growth rate assumption is in fact more relaxed.

It would also be interesting to follow-up the analysis of global stability of the disease-free equilibrium as well as the existence of a classical solution for non-autonomous prion model, with unbounded time and size dependent velocity $\tau(t, x)$. The investigation of the existence of a classical solution of such problem could be done using, for instance, the theory of nonlinear semigroup for non-autonomous abstract Cauchy problems.

Bibliography

[1] A. S. Ackleh, K. Deng, *A monotone method for first order nonlocal hyperbolic initial-boundary value problems*, Appl. Anal., **67** (1997), 173–183.

[2] A. S. Ackleh, K. Deng, *A monotone approximation for a nonlinear non-autonomous size-structured population model*, Appl. Math. Comp., **108** (2000), 103–113.

[3] A. S. Ackleh, K. Deng, *Existence-uniqueness of solutions for a nonlinear non-autonomous size-structured population model: an upper-lower solution approach*, Canadian Appl. Math. Quart., **8** (2000), 1–15.

[4] A. S. Ackleh, K. Deng, *Monotone scheme for nonlinear first order hyperbolic initial-boundary value problems*, Appl. Math. Lett., **13** (2000), 111–119.

[5] A. S. Ackleh, K. Deng, *On a first-order hyperbolic coagulation model*, Math. Meth. Appl. Sci., **26** (2003), 703–715.

[6] A. S. Ackleh, *Parameter estimation in size-structured coagulation-fragmentation phytoplankton population model*, Nonlinear Anal., **28** (1997), 837–854.

[7] A. S. Ackleh, H. T. Banks, K. Deng, *A difference approximation for a coupled system of nonlinear size-structured populations*, Nonlinear Anal., **50** (2002), 727–748.

[8] A. S. Ackleh, B. G. Fitzpatrick, *Modeling aggregation and growth processes in an algal population model: analysis and computation*, J. Math. Biol., **35** (1997), 480–502.

[9] A. S. Ackleh, K. Ito, *An implicit finite difference scheme for the nonlinear size-structured population model*, Num. Funct. Anal. Optim., **18** (1997), 865–884.

[10] A. Aguzzi, *Prion diseases of humans and farm animals: epidemiology, genetics, and pathogenesis*, J. Neurochem., **97** (2006), 17–26.

[11] R. M. Anderson, R. M. May, *Infectious Diseases of Humans*, Dynamics and Control, Oxford University Press, Oxford, 1991.

[12] R. Arlotti, J. Banasiak, *Non-autonomous fragmentation equation via evolution semigroups*, Math. Meth. Appl. Sci., **33** (2010), 1201–1210.

[13] P. Auger, R. Bravo de la Parra, J.-C. Poggiale, E. Sánchez, T. Nguyen-Huu, *Aggregation of Variables and Applications to Population Dynamics*. In: P. Magal, S. Ruan, (eds.) Structured Population Models in Biology and Epidemiology, Lecture Notes in Mathematics 1936, Springer-Verlag, Berlin Heidelberg, (2008) 209–263.

[14] J. Banasiak, L. Arlotti, *Perturbations of Positive Semigroups with Applications*, Springer, London, 2006.

[15] J. Banasiak, A. Bobrowski, M. Lachowicz, *Semigroups of Operators-Theory and Applications*, Springer Proceedings in Mathematics & Statistics, Będlewo, 2013.

[16] J. Banasiak, W. Lamb, *Coagulation, Fragmentation and Growth Processes in a Size Structured Population*, Discrete and Continuous Dynamical Systems, **11** (2009), 1–23.

[17] J. Banasiak, S. C. Oukouomi Noutchie, R. Rudnicki, *Global solvability of a fragmentation-coagulation equation with growth and restricted coagulation*, Journal of Nonlinear Mathematical Physics, **16** (2009), 13–26.

[18] H. T. Banks, F. Kappel, C. Wang, *Weak solutions and differentiability for size structured population models*, Internat. Ser. Numer. Math., **100** (1991), 35–50.

[19] R. Bellman, *Stability Theory of Differential Equations*, McGraw Hill, New York, 1953.

[20] S. M. Blower, A. R. McLean, *Prophylactic vaccines, risk behavior change, and the probability of eradicating HIV in San Francisco*, Sci., **265** (1994), 1451–1454.

[21] A. Calsina, J. Saldana, *A model of physiologically structured population dynamics with a nonlinear individual growth rate*, J. Math. Biol., **33** (1995), 335–364.

[22] S. S. Chaves, P. Gargiullo, J. X. Zhang et al., *Loss of vaccine-induced immunity to varicella over time*, N. Engl. J. Med., **356** (2007), 1121–1129.

[23] M. G. Crandall, A. Majda, *Monotone difference approximations for scalar conservation laws*, Math. Comp., **34** (1980), 1–21.

[24] J. Diestel, J. J. Uhl, *Vector Measures*, American Mathematical Society, Providence 1977.

[25] D. Q. Ding, X. H. Ding, *Global stability of multi-group vaccination epidemic models with delays*, Nonlinear Anal.: Real World Appl., **12** (2011), 1991–1997.

[26] X. Duan, S. Yuan, X. Li, *Global stability of an SVIR model with age of vaccination*, Appl. Math. Comput., **226** (2014), 528–540.

[27] M. Eigen, *Prionics or the kinetic basis of prion diseases*, Biophys. Chem., **63** (1996), 11–18.

[28] K. J. Engel, R. Nagel, *One-Parameter Semigroups for Linear Evolution Equations*, Graduate Texts in Mathematics, Springer, 2000.

[29] H. Engler, J. Prüss, G. Webb, *Analysis of a model for the dynamics of prions II*, J. Math. Anal. Appl., **324** (2006), 98–117.

[30] M. L. Greer, L. V. D. Driessche, L. Wang, G. F. Webb, *Effets of general incidence and polymer joining on nucleated polymerization in a model of prion proliferation*, J. Appl. Math., **68** (2007), 154–170.

[31] M. L. Greer, L. Pujo-Menjouet, G.F. Webb, *A mathematical analysis of the dynamics of prion proliferation*, J. Theoret. Biol., **242** (2006), 598–606.

[32] T. H. Gronwall, *Note on the derivatives with respect to a parameter of the solutions of a system of differential equations*, Ann. Math., **20** (1919), 292–296.

[33] R. Guiem, S. C. Oukouomi Noutchie, *A novel method for solving a coagulation-fragmentation model with growth*, Journal of Algebra and Applied Mathematics, **14** (2016), 79–100.

[34] R. Guiem, S. C. Oukouomi Noutchie, *A new method for solving a coagulation-fragmentation equation*, Journal of Analysis and Applications, **14** (2016), 87–105.

[35] J. K. Hale, *Asymptotic Behavior of Dissipative Systems*, Amer. Math. Soc., Providence, 1988.

[36] D. Hall, H. Edskes, *Silent prions lying in wait: a two-hit model of prion/amyloid formation and infection*, J. Mol. Biol., **336** (2004), 775–786.

[37] M. Iannelli, *Mathematical Theory of Age-Structured Population dynamics*, Applied Mathematics Monographs, 7, Consiglio Nazionale delle Ricerche, Giardini, Pisa, 1995.

[38] M. Iannelli, M. Martcheva, X. Z. Li, *Strain replacement in an epidemic model with super- infection and perfect vaccination*, Math. Biosci., **195** (2005), 23–46.

[39] W. Lamb, *Existence and uniqueness results for the continuous coagulation and fragmentation equation*, Math. Meth. Appl. Sci., **27** (2004), 703–721.

[40] X.-Z. Li, J. Wang, M. Ghosh, *stability and bifurcation of an SIVS epidemic model with treatment and age vaccination*, Appl. Math. Model., **34** (2010), 437–450.

[41] J. Q. Li, Y. L. Yang, Y. C. Zhou, *Global stability of an epidemic model with latent stage and vaccination*, Nonlinear Anal.: Real World Appl., **12** (2011), 2163–2173.

[42] J. Masel, V. A. Jansen, *The kinetics of proteinase K digestion of linear prion polymers*, Proc. Biol. Sci., **266** (1999), 1927–1931.

[43] J. Masel, V. Jansen, M. Nowak, *Quantifying the kinetic parameters of prion replication*, Bio. Chem., **77** (1999), 139–152.

[44] D. J. McLaughlin , W. Lamb, A. C. McBride, *A semigroup approach to fragmentation models*, SIAM Journal of Mathematical Analysis, **28** (1997), 1158–1172.

[45] D. J. McLaughlin , W. Lamb, A. C. McBride, *Existence and uniqueness results for the non-autonomous coagulation and multiple-fragmentation equation*, Mathematical Methods in Applied Sciences, **21** (1998), 1067–1084.

[46] D. J. McLaughlin, W. Lamb, A. C. McBride, *Existence Results for Non-autonomous Multiple-fragmentation Models*, Math. Meth. Appl. Sci., **20** (1997), 1313–1323.

[47] Z. A. Melzak, *A Scalar Transport Equation*, Trans. Amer. Math. Soc., **85** (1957) 547–560.

[48] R. Y. M'pika Massoukou, S. C. Oukouomi Noutchie, R. Guiem, *Global Dynamics of an SVEIR Model with Age-Dependent Vaccination, Infection, and Latency*, Abstr. Appl. Anal., **2018** (2018) 21p.

[49] D. E. Moustaine, V. Perrier, L. Smeller, R. Lange, J. Torrent, *Full-length prion protein aggregates to amyloid fibrils and spherical particles by distinct pathways*, FEBS J., **275** (2008), 2021–2031.

[50] G. Nickel, *On Evolution Semigroups and Wellposedness of Nonautonomous Cauchy Problems*, Ph.D. thesis, Universität Tübingen, 1996.

[51] M. A. Nowak, D. C. Krakauer, A. Klug, R. M. May, *Prion infection dynamics*, Integrative Biology, **1** (1998), 3–15.

[52] S. C. Oukouomi Noutchie, *Coagulation-fragmentation dynamics in size and position structured population models*, Ph.D Dissertation, UKZN, 2009.

[53] R. Peralta, C. Vargas-De-León, P. Miramontes, *Global stability results in SVIR epidemic model with immunity loss depending on vaccine-age*, Abstr. Appl. Anal., **2015** (2015), 1–8.

[54] S. A. Plotkin, *Correlates of protection induced by vaccination*, Clin. vacc. Immunol., **17** (2010), 1055–1065.

[55] S. A. Plotkin, *Complex correlates of protection after vaccination*, Clin. Infect. Dis., **56** (2013), 1458–1465.

[56] M. Prelog, *Differential approaches for vaccination from childhood to old age*, J. Gerontol., **59** (2013), 230–239.

[57] S. B. Prusiner, *Novel proteinaceous invectious particles cause scrapie*, Science, **216** (1986), 136–144.

[58] S. B. Prusiner, *Prions*, Sci. Amer., **4** (1986), 50–59.

[59] J. Prüss, L. Pujo-Menjouet, G. Webb, R. Zacher, *Analysis of a model for the dynamics of prions*, Discrete Contin. Dyn. Syst. Ser., **6** (2006), 225–235.

[60] G. P. Sahu, J. Dhar, *Analysis of an SVEIS epidemic model with partial temporary immunity and saturation incidence rate*, Appl. Math. Model., **36** (2012), 908–923.

[61] J. R. Silveira, G. J. Raymond, A. G. Hughson, R. E. Race, V. L. Sim, S. F. Hayes, B. Caughey, *The most infectious prion protein particles*, Nature, **437** (2005), 257–261.

[62] G. Simonett, C. Walker, *On the solvability of a mathematical model for prion proliferation*, J. Math. Anal. Appl., **324** (2006), 580–603.

[63] H. L. Smith, H. R. Thieme, *Dynamical Systems and Population Persistence*, Amer. Math. Soc., Providence, 2011.

[64] M. V. Smoluchowski, *Versuch einer Mathematischen Theorie der Koagulationskinetic Kolloider Lösunger*, Z. Phys. Chem., **92** (1917), 129–168.

[65] X. Y. Song, Y. Jiang, H. M. Wei, *Analysis of a saturation incidence SVEIRS epidemic model with partial temporary immunity and pulse and two time delays*, Appl. Math. Comput., **214** (2009), 381–390.

[66] H. R. Thieme, *Uniform persistence and permanence for non-autonomous semiflows in population biology*, Math. Biosci., **166** (2000), 173–201.

[67] I.I. Vrabie, *Compactness Methods for Nonlinear Evolutions*, Pitman Monographs Surveys Pure Appl. Math.,32, Longman Scientific and Technical, Harlow, 1987.

[68] C. Walker, *Prion proliferation with unbounded polymerization rates*, Electronic Journal of Differential Equations, Conference, **15** (2007), 387–397.

[69] J. Wang, X. Dong, H. Sun, *Analysis of an SVEIR model with age-dependence vaccination, latency and relapse*, J. Nonlinear Sci. Appl., **10** (2017), 3755–3776.

[70] J. Wang, J. Lang, W. Chen, *Global threshold dynamics of an SVIR model with age-dependent infection and relapse*, J. Biol. Dyn., **11** (2016), 427–454.

[71] J. Wang, R. Zhang, T. Kuniya, *The stability analysis of an SVEIR model with continuous age-structure in the exposed and infectious classes*, J. Biol. Dyn., **9** (2015), 73–101.

[72] G. F. Webb, *Theory of Non-linear Age Dependent Population Dynamics*, Marcel Dekker, New York, 1985.

[73] N. Wood, C. -A. Siegrist, *Neonatal immunization: where do we stand?*, Curr. Opin. Infect. Dis., **24** (2011), 190–195.

[74] Y. Xiao, S. Tang, *Dynamics of infection with nonlinear incidence in a simple vaccination model*, Nonlinear Anal.: Real World Appl., **11** (2010), 4154–4163.

[75] J. Xu, Y. Zhou, *Global stability of a multi-group model with generalized nonlinear incidence and vaccination age*, Disc. Cont. Dyn. Syst. B, **21** (2016), 977–996.

[76] J. Yang, S. Tang, *Global stability and optimal control for tuberculosis model with vaccination and treatment*, Disc. Cont. Dyn. Syst. B, **21** (2016), 1009–1022.

[77] K. Yosida, *Functional Analysis*, second ed., Springer, 1968.

[78] R. M. Ziff, E. D. McGrady, *The kinetics of cluster fragmentation and depolymerization*, J. Phys. A. Math. Gen., **18** (1985), 3027–3037.