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Asymptotic behaviour of integro-differential equations describing clonal evolution of leukemia

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To my best friend and wife Anna

Abstract

This thesis is devoted to the analysis of a system of integro-differential equations describing leukemia, a type of blood cancer. Existence and uniqueness for arbitrary times are shown and the long-term behaviour of the solution is characterised. In order to achieve the asymptotic behaviour of the solution it is proved that a normalized (with respect to total mass) solution forms a Dirac sequence, thus the solution converges for time tending to infinity to a Dirac measure. Moreover the total mass converges, too, which is shown by combining an asymptotic stability result via a Lyapunov function with a perturbation argument. Additionally, the convergence result is generalised to a suitable measure space.

Furthermore, the model is extended by an additional integral term with a small multiplicative coefficient in order to capture the idea of mutation. For this newly obtained system it is shown existence and uniqueness of both a solution for arbitrary times and a positive steady state. The latter is achieved by interpreting the steady state equations as an eigenvalue problem and by using the Krein-Rutman theorem. The local asymptotic stability of the steady state is proven by using linearised stability. The spectrum, which is crucial for linearised stability, is investigated with the method of the Weinstein-Aronszajn formula. Moreover, it is proven that the stable steady state of the extended model converges weakly* to the stable steady state of the original model if the coefficient of the newly introduced integral term tends to zero.

Lastly, a numerical scheme, which has been used to simulate the original model, is illustrated and its convergence to the analytical solution is proven.

Zusammenfassung

Diese Doktorarbeit ist der Analyse eines Systems von Integro-Differentialgleichungen gewidmet, die eine häufige Form des Blutkrebs (Leukämie) beschreiben. Es wird gezeigt, dass eine eindeutige Lösung für beliebig große Zeiten existiert, sowie das Langzeitverhalten dieser Lösung untersucht. Das asymptotische Verhalten der Lösung resultiert aus der Erkenntnis, dass eine geeignet normalisierte Lösung (normalisiert bzgl. der Gesamtmasse) eine Diracfolge bildet, was die Konvergenz der Lösung zu einem Diracmaß zur Folge hat. Außerdem wird die Konvergenz der Gesamtmasse bewiesen indem die asymptotische Stabilität durch die Konstruktion einer Lyapunovfunktion eines bereits bekannten Systems mit einem Störungsargument kombiniert wird. Diese Resultate werden dann auf Maßräume weiter verallgemeinert.

Desweiteren wird das eingeführte System aus Integro-Differentialgleichungen durch einen zusätzlichen Integralterm mit einem betragsmäßig kleinem Koeffizienten erweitert um dem Konzept der Mutation Rechnung zu tragen. Es werden die Existenz und Eindeutigkeit einer Lösung und eines Gleichgewichtpunkts bewiesen. Letzteres geschieht durch Uminterpretation der Gleichgewichtsgleichung zu einem Eigenwertproblem, welches mit dem Krein-Rutman Theorem gelöst werden kann. Die lokale asymptotische Stabilität wird durch linearisierte Stabilität erzielt. Die dazu notwendige Untersuchung des Spektrums erfolgt durch die erste Weinstein-Aronszajn Formel. Darüber hinaus wird gezeigt, dass das Gleichgewicht des neuen Systems gegen das Gleichgewicht des ursprünglichen Systems schwach* konvergiert, wenn der eingeführte Koeffizient gegen null geht.

Als letzter Punkt wird ein numerisches Verfahren erläutert, mit dem auch das ursprüngliche Model simuliert wurde, und die Konvergenz der numerischen gegen die analytische Lösung bewiesen.

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Related Publications

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Notation

$\frac{\mathrm{d}}{\mathrm{d}t}$	Total derivative with respect to t
$\frac{\partial}{\partial t}, \frac{\partial}{\partial \rho}$	Partial derivative with respect to t and ρ
$\langle \cdot, \cdot \rangle$	Dual pairing
$\mathcal{L}(X)$	The set of all linear functionals on the space X
$\mathbb{R}_+$	The set of non-negative real numbers
$\Re(z)$	Real part of the complex number z
$\rho(A)$	Resolvent set of a linear operator A
$\sigma(A)$	Spectrum of a linear operator A
E'	Dual space of the Banach space E
$R(\lambda, A)$	Resolvent mapping of the linear operator A and the complex number λ
$r(A)$	Spectral radius of the linear operator A
$rg(f)$	Range of the function f

Contents

Chapter 1

Introduction

Mathematical models describing evolutionary processes are often formulated as systems of differential equations. The solution of such systems in a biological context is usually interpreted as the density or total amount of members of a population. In a variety of applications it is insufficient to investigate the density of a population alone, instead it is necessary to specify the dynamic behaviour of an individual more accurately according to differences among the members of a population. In such applications the model has to be extended by an additional variable, often referred to as structure variable, to describe the heterogeneity. Mathematical models equipped with a structural variable to account for a heterogeneous population are referred to as structured population models.

The earliest works of these models are written by Sharpe and Lotka in the year 1911, [57] and McKendricks in 1925, [50]. Therein the dynamics of biological agents (a population of cells or individuals) are modelled and the structural variable describes the age of each individual. Models which characterise the heterogeneity of a population by age are called age-structured population models.. The papers above already show how the introduction of an age-structure can lead to a model formulated as a partial differential equation. Yet, age is not the only trait which can be addressed by structured population models. Later on the applications of structured population models were extended to sizes of individuals, [28, 48], sex, [65] or spatial disparities, [42, 49].

Structured population models often consist of integro-differential equations, that is, additionally to derivatives the equations contain integral terms. For instance, an age-structured population model describing the dynamics of cells can include an integral term because the reproduction rate of an individual may depend on the total amount of cells, see [64, Chapter 1]. In general, integral terms appear if a non-local feedback, a dependence on the whole population, or a heterogeneous subpopulation

is modelled.
The references given above share a common purpose: understanding the influence of individual differences on the dynamics of a population. When proceeding from a biological setting, introducing a structural variable leads to interesting questions, for instance "How does the biological heterogeneity impact on the overall population in the long term?" or "Is it possible to single out a specific advantageous trait which makes the individual with this trait more successful in their course of action?". These biological questions can be translated via structured population models into a mathematical objective, namely, the analysis of the long-term behaviour of the solution to the given structured population model. The analysis of the long-term behaviour is comprised of finding steady states and their stability or instability properties.

The aim of this dissertation is to propose a structured population model comprised of two integro-differential equations describing a specific cell population and to determine the long-term behaviour of the solution of the model. Moreover, the model is extended structurally to incorporate the concept of mutation. This thesis attempts to give an answer to the question whether the extended model admits stable steady states and how these steady states are related to the original model.

The long-term behaviour of integro-differential equations has been studied in various different settings. In [4], Ackleh et al. consider a scalar equation in a measure space, i.e.

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\mu(t,q)(A) = \int\limits_A \left(q_1 f_1(\mu(t,q)(Q) - q_2 f_2(\mu(t,q)(Q))\right)\mu(t,q)(\mathrm{d}q) \\ \mu(0,q)(A) = \mu^0(q)(A) > 0, \end{cases}$$

where $Q \subset (0,\infty)\times(0,\infty)$ is compact, $A \subset Q$, $q_1, q_2 \in Q$ and f_1, f_2 are locally Lipschitz continuous, non-negative and decreasing and increasing respectively. μ is the unknown and shall belong to a suitable measure space. For this equation the author showed that the solution converges weakly* to a Dirac measure which is concentrated at the maximum value of the ratio $\frac{f_1}{f_2}$. This convergence could be achieved by proving that the total mass is strictly positive for all times and that the solution converges to zero on all sets, which do not contain the maximum point of the ratio of $\frac{f_1}{f_2}$. This technique was also applied in [2].
A similar approach is taken in [27]. In this paper the following problem is investi-

gated

$$\frac{\partial f}{\partial t} = s[f]f,$$

where

$$s[f](y) := a(y) - \int_Y b(y, y')f(y')\,\mathrm{d}y'$$

and $Y \subset \mathbb{R}$ is a compact interval, $a \in W^{1,\infty}(Y), a > 0$ a.e., $b \in W^{1,\infty}(Y \times Y)$, $\inf_{y,y' \in Y} b(y, y') > 0$. After rescaling time by $t' = \frac{t}{\varepsilon}, \varepsilon > 0$ Desvillettes et al. show that the solution of the rescaled problem converges for $\varepsilon \to 0$ to a limit function which support is contained in the set of zeroes of the function

$$R_\varepsilon(t, y) := \int_0^t s[f_\varepsilon(\sigma, \cdot)](y)\,\mathrm{d}\sigma.$$

The convergence is obtained by showing boundedness of $f_\varepsilon, R_\varepsilon, \frac{\partial R_\varepsilon}{\partial t}$ and $\frac{\partial R_\varepsilon}{\partial y}$ to extract a weakly* convergent subsequence of f_ε. Due to the compact embedding of $W^{1,\infty}((0, T \times Y))$ into $C([0, T] \times Y)$ uniform convergence of R_ε can be achieved. Having established convergence of the solution, the key idea is like in [2, 4], namely that the solution converges everywhere to zero outside a set determined by the right-hand side $s[f]$.

Rescaling can be a useful tool to prove convergence to a Dirac measure for parabolic equations as well. In [53] Perthame and Barles consider the problem

$$\frac{\partial}{\partial t} n_\varepsilon(t, x) + \varepsilon \Delta n_\varepsilon(t, x) = \frac{n_\varepsilon(t, x)}{\varepsilon} R(x, I_\varepsilon(t)),\ x \in \mathbb{R}^d, t \geq 0,$$

with

$$I_\varepsilon(t) := \int_{\mathbb{R}^d} \psi(x) n_\varepsilon(t, x)\,\mathrm{d}x,$$

$\psi \in W^{2,\infty}(\mathbb{R}^d), 0 < \psi_m \leq \psi \leq \psi_M < \infty$ and R is essentially a Lipschitz-continuous function with respect to I and a $W^{2,\infty}$-function with respect to x. The authors prove convergence of the solution to a Dirac measure by showing that the solution converges to a function, which is a viscosity solution of a Hamilton-Jacobi equation. So the concept of the vanishing viscosity is exploited to obtain the convergence to a Dirac measure. More involved equations have been considered with the same ansatz in [8, 44].

The Hamilton-Jacobi approach can also be used in the case of a system of integro-differential equations instead of a scalar setting. The idea of obtaining the convergence to a Dirac measure is essentially the same as in the scalar case but with one more difficulty: viscosity solutions are a strictly scalar concept, because it is necessary to have an ordering in the underlying range space of the viscosity solution. Hence, it is necessary to transform the multidimensional case to the scalar case, which is not feasible for arbitrary systems. In [43, 49] it is shown how a system can be treated with the Hamilton-Jacobi ansatz.
A different approach to the long-term behaviour of integro-differential equations is done by interpreting the steady state equation for a given structured population model as an eigenvalue problem associated with the eigenvalue zero. In [16, 17, 18, 24] it is proposed under which conditions it is possible to interpret a steady state problem as eigenvalue problem. However, strong assumptions on the operators involved are needed to guarantee a solution for the eigenvalue problem. This technique is the most influential for this thesis, hence it will be discussed in more detail in the chapters to come.

The dissertation is organised as follows. In **Chapter 2** a system of integro-differential equations is introduced with initial data in the space of continuous and integrable functions. Existence and uniqueness for arbitrary times is established and the existence and stability of a steady state is proven and characterised explicitly. Additionally, the result is generalised to initial data in a suitable measure space. The difficulties in this part lie in the non-linearly incorporated integral term and in the specification of the sense of convergence to the steady state.
In **Chapter 3** the model of Chapter 2 is extended by adding an integral operator with a small coefficient. Apart from existence and uniqueness of a solution for arbitrary times, the existence and local asymptotic stability of a non-trivial steady state is proven. Furthermore, the convergence of the steady state in the extended system converges to the steady state of the original system. The challenge in this chapter lies in the treatment of an eigenvalue problem and in the determination of the spectrum of the operators involved.
Chapter 4 elucidates a numerical scheme to do simulation for the models proposed in this thesis. Additionally, a rigorous proof of the qualitative convergence of the scheme is given.

Chapter 2

A system of non-linear integro-differential equations

2.1 Origin of the model

2.1.1 Biology of Leukemia

The model discussed in this dissertation describes a cancer of the blood production system, i.e. leukemia. This type of cancer conquers the blood production system and causes the production of malignant, non-functional cells. The cancerous cells sustain their population by cell division (proliferation). After division either cells become more complex and gain more functionality, which is called differentiation or they produce duplicates of themselves, which is called self-renewal. Undifferentiated cells with the ability to self-renew are called stem cells, [5, Chapter 20].
Recent experimental evidence indicates that cancer cell populations of leukemic cells are composed of multiple clones consisting of genetically identical cells [29] and maintained by cells with stem-like properties [12, 34]. However, leukemic stem cells are heterogeneous, see [29, 41, 45]. Despite this heterogeneity only few cells contribute to the growth of the total mass of cancer cells. In the case of acute myeloid leukemia (AML) at most 4 clones and in the case of acute lymphoblastic leukemia (ALL) at most 10 clones are responsible for the growth of the total mass, see [29, 45]. The knowledge about the driving forces behind cancer cell growth is important to develop better counter strategies for this cancer type. In most cases of ALL the cells responsible for a relapse have been present at the initial diagnosis, but were undetectable by routine methods, [21, 46, 66]. Additionally, these cells are rather resistant to chemotherapy due to quiescence, a very slow cell cycle or other intrinsic mechanisms, see [21, 46]. Similar difficulties are described in AML, [29, 36].

It is unknown whether relapses in patients are due to mutation of the cancer cells or a selection process induced by the therapy. A mathematical model can help to explain whether a selection process alone is sufficient to explain a relapse or if mutation is a necessary impact factor for relapses.

2.1.2 Compartment model

A discrete model to describe leukemia was proposed in [62] and a multi compartment version in [61]. Therein, the multi-compartment model describes the dynamics of healthy cells denoted by $c_j, j = 1, 2$, and n clonal types of leukemic cells, denoted by $l_j^i, j = 1, 2, i = 1, \ldots, n$. The index j indicates that there are two types of healthy cells and likewise of cancerous cells, which shall describe proliferating and non-proliferating cells, respectively. The parameters are denoted by $p^c > 0$ and $p^{l_i} > 0$ for the proliferation rate of healthy cells and leukemic cells, respectively. Additionally, there are self-renewal fractions $0 < a^c < 1$ and $0 < a^{l_i} < 1$, again for healthy and cancerous cells, respectively, which are fractions of the progeny cells which remain in the compartment of proliferating cells. Consequently, $(1 - a^c)$ and $(1 - a^{l_i})$ are fractions of cells that differentiate and lose their ability to proliferate. Lastly, $d_2^c, d_2^{l_i} > 0$ are the death rates of the non-proliferating healthy and leukemic cells, respectively. The idea of a structured population comes into play in the proliferation and self-renewal rates, which can differ for each leukemic cell. Bringing all this together, the system from [61] assumes the following form

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}c_1(t) &= (2a^c s(t) - 1)p^c c_1(t), \\ \frac{\mathrm{d}}{\mathrm{d}t}c_2(t) &= 2(1 - a^c s(t))p^c c_1(t) - d_2^c c_2(t), \\ \frac{\mathrm{d}}{\mathrm{d}t}l_1^1(t) &= (2a^{l_1} s(t) - 1)p^{l_1} l_1^1(t), \\ \frac{\mathrm{d}}{\mathrm{d}t}l_2^1(t) &= 2(1 - a^{l_1} s(t))p^{l_1} l_1^1(t) - d_2^{l_1} l_2^1(t), \\ & \vdots \\ \frac{\mathrm{d}}{\mathrm{d}t}l_1^n(t) &= (2a^{l_n} s(t) - 1)p^{l_n} l_1^n(t), \\ \frac{\mathrm{d}}{\mathrm{d}t}l_2^n(t) &= 2(1 - a^{l_n} s(t))p^{l_n} l_1^n(t) - d_2^{l_n} l_2^n(t), \end{cases} \tag{2.1}$$

where the function $s(t)$ is given by

$$s(t) = \frac{1}{1 + K^c c_2(t) + K^l \sum_{i=1}^{n} l_2^i(t)},$$

for $K^c, K^l > 0$. The system is equipped with non-negative initial data. The feedback loop $s(t)$ decreases if the total population of non-proliferating cells increase. The ansatz to incorporate such a feedback loop is justified by clinical evidence found in [40] or [58]. A non-linear feedback signal $s(t)$ was proposed in [47] and is based on a Tikhonov-type quasi steady state approximation. With System (2.1) it was possible to see, that different self-renewal rates can influence the prognosis of the progression of acute leukemia. Furthermore, for system (2.1) it is known, that the clonal evolution of the cancerous cells is determined by the self-renewal rate. In fact, the model implies that all cell types die out except those, which are equipped with the highest self-renewal rate, [62].

In this dissertation we consider a model with a continuum of possible self-renewal states. So in contrast to the compartment model (2.1), we introduce a continuous function a for measuring the self-renewal rate for different cell types x, where x belongs to a subset of $\mathbb{R}^n$. The finite sum contained in $s(t)$ is replaced by an integral term. This way we obtain an integro-differential equation (IDE), which for the sake of simplicity consists of two equations. That means that we distinguish only between undifferentiated and differentiated cell types. The biological aim is to learn if selection alone suffices to explain a relapse. Mathematically this translates to the question if there exists solution to the proposed model and what kind of steady state the model admits.

2.2 Model description and assumptions

The system of equations we want to analyse is given by

$$\begin{cases} \frac{\partial}{\partial t}u(t,x) &= \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) pu(t,x), \\ \frac{\partial}{\partial t}v(t,x) &= 2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right) pu(t,x) - dv(t,x), \\ u(0,x) &= u^0(x), \\ v(0,x) &= v^0(x). \end{cases} \tag{2.2}$$

Here we write $\rho_1(t) = \int_\Omega u(t,x)\,\mathrm{d}x$ and $\rho_2(t) = \int_\Omega v(t,x)\,\mathrm{d}x$.

In (2.2) u plays the role of the density of non-dividing cells and v is the density of mature, differentiated or non-dividing cells. The two densities are dependent on

time t and trait x. The stem cells u can proliferate with rate p. If a cell is proliferating, it gives birth to two daughter cells. Either the daughter cells are also stem cells or they are differentiated cells. The trait-dependent self-renewal rate a is the fraction of daughter cells which belong to the population of non-dividing cells u. This ratio is further influenced by ρ_2, which is the total mass of differentiated cells. The strength of this feedback is measured by the constant k. The differentiated cells' growth is given by the density of proliferating cells u which mature and the density of dying cells of v. The death rate is denoted by the constant d.

In the forthcoming analysis we will use the following

Assumption 1.

1. $\Omega \subset \mathbb{R}^n$ *is an open and bounded set.*
2. $u^0, v^0 \in C(\Omega) \cap L^1(\Omega)$ *with* $u^0, v^0 > 0$
3. $a \in C(\overline{\Omega})$ *with* $0 < a(x) < 1$ *for all* $x \in \overline{\Omega}$. *Furthermore, let* $\frac{1}{2} < \bar{a} < 1$ *be the maximum of* a.
4. $k, p, d \in \mathbb{R}_+$ *are constants.*

Remark 2.1. *The reason we assume the maximum of* a *to be bigger than* $\frac{1}{2}$ *is that otherwise*

$$\left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) < \left(\frac{2\bar{a}}{1+k\rho_2(t)} - 1\right) < 0.$$

If the right-hand side of (2.2) *is negative for all values of* a *the steady state is given by* $(0, 0)$.

2.3 Motivation for using metric spaces

IDE's long-term behaviour have been studied extensively, see for instance [2, 4, 6, 15, 19], for a first overview of different aspects of IDEs. All these results have in common, that IDEs are regularity preserving, i.e. the regularity given by the initial data is neither increased nor decreased by the dynamics of an IDE. The model (2.2) is endowed with initial data in $L^1(\Omega)$, see Assumption 1. Hence, it is expected to obtain a solution, which is contained in $L^1(\Omega)$. The compartment model (2.1) describes a selection process, which leads to a decay to zero of all cell types, except those equipped with the highest self-renewal rate. The analogy of the maximal value

in the discrete case is the maximum point of the function a. In the continuous setting the description of the corresponding behaviour translates into the convergence of the solution to a Dirac measure, which is located at the maximizer of the function a. This rises an important question: If the solution converges to a Dirac measure, in which sense does the convergence hold? There are several possibilities:
Let us assume that the solution of the IDE (2.2) is given by $u \in C^1(\mathbb{R}_+, L^1(\Omega))$, $\Omega \subset \mathbb{R}^n$ open and bounded. The canonical norm of this space is

$$\begin{aligned} \|\cdot\|_{C^1(\mathbb{R}_+,L^1(\Omega))} &: C^1(\mathbb{R}_+, L^1(\Omega)) \to \mathbb{R}_+, \\ u \mapsto \|u\|_{C^1(\mathbb{R}_+,L^1(\Omega))} &:= \max_{t\in\mathbb{R}_+} \left(\|u(t,\cdot)\|_{L^1(\Omega)} + \left\| \tfrac{\partial}{\partial t} u(t,\cdot) \right\|_{L^1(\Omega)} \right). \end{aligned}$$

Measures do not belong to the space $C^1(\mathbb{R}_+, L^1(\Omega))$, hence it is impossible to show convergence to a measure with respect to this norm.

This leads to the necessity to change the norm in order to be applicable to measures. Dirac measures belong in particular to the space of positive Radon measures, which we denote by $\mathcal{M}^+(\Omega)$. This space is canonically endowed with the total variation norm, i.e. $(\mathcal{M}^+(\Omega), \|\cdot\|_{TV})$,

$$\begin{aligned} \|\cdot\|_{TV} &: \mathcal{M}^+(\Omega) \to \mathbb{R}_+, \\ \mu \mapsto \|\mu\|_{TV} &:= \mu_+(\Omega) + \mu_-(\Omega). \end{aligned}$$

Here μ_+, μ_- are the two components defined in the Hahn-Jordan decomposition, see for instance [10]. This norm is only applicable to measures, so we have to interpret $L^1(\Omega)$ as a subspace of $\mathcal{M}^+(\Omega)$. This can be done in the following way. Let $f \in L^1(\Omega)$, $f \geq 0$ almost everywhere, then we can define a measure $\mu \in \mathcal{M}^+(\Omega)$ by setting $\mu := f\mathrm{d}x$, where $\mathrm{d}x$ stands for the Lebesgue measure. Although it is possible to interpret L^1-functions as measures, thus the total variation norm applies to these functions, it is not suitable for proving convergence to a Dirac measure. The reason is that for a Dirac delta concentrated in x_1, denoted by δ_{x_1}, and $u(t,x)\,\mathrm{d}x$, it holds for all $t \in \mathbb{R}_+$

$$\begin{aligned} \|\delta_{x_1} - u(t,x)\,\mathrm{d}x\|_{TV} = &\sup_{A\subset\Omega} \{(\delta_{x_1}(A) - u(t,x)\mathrm{d}x(A))_+\} \\ &+ \sup_{A\subset\Omega} \{(\delta_{x_1}(A) - u(t,x)\,\mathrm{d}x(A))_-\} \geq 2. \end{aligned}$$

To see the lower bound choose as $A = \{x_1\}$ and the Dirac measure equals 1, whereas the measure $u(t,x)\,\mathrm{d}x$ is continuous with respect to the Lebesgue measure and consequently equals 0 for a single point. Therefore, we cannot expect norm convergence. We need to weaken the notion of convergence so that it is possible for the solution to converge to a Dirac measure. The difficulties with the norms illustrated above lead to the necessity to weaken the notion of convergence. Instead of convergence in the canonical norms of the respective spaces, a suitable metric is considered.
The metric we want to utilize is the so called bounded Lipschitz distance or, alternatively, flat metric [33, 67].

2.4 Preliminary results and definitions

Definition 2.2. *Let $\mu, \nu \in \mathcal{M}^+(\Omega)$. The distance function $\rho_F : \mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega) \to [0,\infty]$ is defined by*

$$\rho_F(\mu,\nu) := \sup\left\{ \int_\Omega \psi \mathrm{d}(\mu-\nu) \Big|\ \psi \in C^1(\Omega), \|\psi\|_{W^{1,\infty}} \leq 1 \right\}, \tag{2.3}$$

where

$$\|\psi\|_{W^{1,\infty}} := \max\{\|\psi\|_{L^\infty(\Omega)}, \|\partial_x \psi\|_{L^\infty(\Omega)}\}.$$

The flat metric ρ_F is particularly advantageous, since it metrizes the weak* topology on each tight subset of Radon measures with uniformly bounded total variation, see [7, 33, 56]. We present here basic results related to the space of positive Radon measures equipped with flat metric ρ_F, compare to [52].

Lemma 2.3. *The flat metric is scale invariant, i.e. for $\theta \in \mathbb{R}$ and $\mu, \nu \in \mathcal{M}^+(\Omega)$ it holds*

$$\rho_F(\theta \cdot \mu, \theta \cdot \nu) = \theta \rho_F(\mu,\nu).$$

The 1-Wasserstein metric also metrizes weak* convergence, but is only defined for probability measures. We will not give the general definition of the 1-Wasserstein metric, because there exists a representation formula, which allows for a convenient computation of the metric. This representation formula for the $1-$Wasserstein metric is sometimes referred to as Kantorovich-Rubinstein distance, see [67, Remark 6.5].

Definition 2.4. *For two probability measures μ_1, μ_2 we define the 1-Wasserstein metric as*

$$W_1(\mu_1, \mu_2) = \sup \left\{ \int_\Omega \psi \, \mathrm{d}(\mu_1 - \mu_2) \middle| \psi \in W^{1,\infty}(\Omega), \|\partial_x \psi\|_\infty \leq 1 \right\}.$$

Although the 1-Wasserstein metric is only valid for probability measures it is closely related to the flat metric, which is depicted in the following

Proposition 2.5. *Let $\mu_1, \mu_2 \in \mathcal{M}^+(\Omega)$ with ρ_1, ρ_2 denoting the mass of the measures, respectively. Then the following estimate holds*

$$\rho_F(\mu_1, \mu_2) \leq \min\{\rho_1, \rho_2\} W_1\left(\frac{\mu_1}{\rho_1}, \frac{\mu_2}{\rho_2}\right) + |\rho_1 - \rho_2|.$$

The proof can be found in [65] and is given here, because this inequality plays a crucial role in the rest of this chapter.

Proof. Applying Lemma 2.3 together with the triangle inequality yields

$$\rho_F(\mu_1, \mu_2) = \rho_1 \rho_F\left(\frac{\mu_1}{\rho_1}, \frac{\mu_2}{\rho_1}\right) \leq \rho_1 \rho_F\left(\frac{\mu_1}{\rho_1}, \frac{\mu_2}{\rho_2}\right) + \rho_1 \rho_F\left(\frac{\mu_2}{\rho_2}, \frac{\mu_2}{\rho_1}\right) =: I + II.$$

Now due to more admissable test functions for the 1-Wasserstein metric than the flat metric, we can infer

$$I \leq \rho_1 W_1\left(\frac{\mu_1}{\rho_1}, \frac{\mu_2}{\rho_2}\right).$$

Estimating the second term II is a straight forward consequence of the definition of the flat metric

$$\rho_1 \rho_F\left(\frac{\mu_2}{\rho_2}, \frac{\mu_2}{\rho_1}\right) \leq \rho_1 \sup \|\psi\|_{W^{1,\infty}} \left|1 - \frac{\rho_2}{\rho_1}\right| = |\rho_1 - \rho_2|.$$

The same estimate could be done with ρ_2 instead of ρ_1 and so we can conclude. □

2.5 Existence and uniqueness

Due to the fact that no space derivatives are involved in equation (2.2), the system can be seen as an ordinary differential equation (ODE) with values in a Banach space, namely in $L^1(\Omega)$. Interpreted as an ODE, existence and uniqueness of a solution of system (2.2) follows from the Picard-Lindelöf theorem. The classical

Picard-Lindelöf theorem is formulated for finite dimensional spaces, most often $\mathbb{R}^n$, see for example [68]. But the theorem can be extended to Banach spaces, see [54, Satz 1.17]. Thus it is necessary to prove Lipschitz-continuity with respect to the norm of the Banach space involved.

2.5.1 Local-in-time existence and uniqueness

Proposition 2.6. *Let Assumption 1 hold. Then for some $T > 0$ there exists a unique non-negative solution $(u, v)^T \in C^1([0, T), (C(\Omega) \cap L^1(\Omega))^2)$.*

Proof. Firstly, rewrite (2.2) into

$$\xi' = \begin{pmatrix} u \\ v \end{pmatrix}' = \begin{pmatrix} \left(\frac{2a}{1+k\rho_2} - 1\right) pu \\ 2\left(1 - \frac{a}{1+k\rho_2}\right) pu - dv \end{pmatrix} =: f(\xi),$$

with $\xi = (u, v)^T$ and $\xi' = \frac{\mathrm{d}}{\mathrm{d}t}\xi$. For the sake of readability the arguments are omitted in this proof. Note that we consider $C(\Omega) \cap L^1(\Omega) \subset L^1(\Omega)$. Now we need to prove that $f : (L^1(\Omega))^2 \to (L^1(\Omega))^2$ is locally Lipschitz-continuous. To do so choose $\xi_1 = (u_1, v_1)^T, \xi_2 = (u_2, v_2)^T \in (L^1(\Omega))^2$, write $\rho_2^1 = \int_\Omega v_1 \,\mathrm{d}x$, $\rho_2^2 = \int_\Omega v_2 \,\mathrm{d}x$ and consider

$$\begin{aligned} \|f(\xi_1) - f(\xi_2)\|_{L^1(\Omega)} &= \left\| \left(\frac{2a}{1+k\rho_2^1} - 1\right) pu_1 - \left(\frac{2a}{1+k\rho_2^2} - 1\right) pu_2 \right\|_{L^1(\Omega)} \\ &\quad + \left\| 2\left(1 - \frac{a}{1+k\rho_2^1}\right) pu_1 - dv_1 \right. \\ &\quad \left. -2\left(1 - \frac{a}{1+k\rho_2^2}\right) pu_2 + dv_2 \right\|_{L^1(\Omega)} =: I + II. \end{aligned}$$

We can estimate as follows

$$\begin{aligned} I &\leq p\|u_1 - u_2\|_{L^1(\Omega)} + 2p\bar{a} \left\| \frac{u_1}{1+k\rho_2^1} - \frac{u_2}{1+k\rho_2^2} \right\|_{L^1(\Omega)} \\ &= p\|u_1 - u_2\|_{L^1(\Omega)} + 2p\bar{a} \left\| \frac{u_1}{1+k\rho_2^1} - \frac{u_1}{1+k\rho_2^2} + \frac{u_1}{1+k\rho_2^2} - \frac{u_2}{1+k\rho_2^2} \right\|_{L^1(\Omega)} \\ &\leq p\|u_1 - u_2\|_{L^1(\Omega)} + 2p\bar{a} \left(\left\| \frac{u_1}{1+k\rho_2^1} - \frac{u_1}{1+\rho_2^2} \right\|_{L^1(\Omega)} + \left\| \frac{u_1}{1+\rho_2^2} - \frac{u_2}{1+k\rho_2^2} \right\|_{L^1(\Omega)} \right) \\ &\leq p\|u_1 - u_2\|_{L^1(\Omega)} + 2p\bar{a} \left(\|u_1\|_{L^1(\Omega)} k \left|\rho_2^1 - \rho_2^2\right| + \|u_1 - u_2\|_{L^1(\Omega)} \right) \\ &\leq p\|u_1 - u_2\|_{L^1(\Omega)} + 2p\bar{a} \left(\|u_1\|_{L^1(\Omega)} k \|v_1 - v_2\|_{L^1(\Omega)} + \|u_1 - u_2\|_{L^1(\Omega)} \right). \end{aligned}$$

Here we used in the fourth step that the function $h : \mathbb{R}_+ \to \mathbb{R}, x \mapsto \frac{1}{1+kx}$ is Lipschitz-continuous because of its bounded derivative. Eventually, we obtain

$$I \leq p(1+2\bar{a}) \left\|u_1 - u_2\right\|_{L^1(\Omega)} + 2p\bar{a} \left\|u_1\right\|_{L^1(\Omega)} \left\|v_1 - v_2\right\|_{L^1(\Omega)}. \tag{2.4}$$

For term II we can estimate

$$II \quad \leq \quad d \left\|v_1 - v_2\right\|_{L^1(\Omega)} + 2p \left\|u_1 - u_2\right\|_{L^1(\Omega)} + 2p\bar{a} \left\| \frac{u_1}{1+k\rho_2^1(t)} - \frac{u_2}{1+k\rho_2^2(t)} \right\|_{L^1(\Omega)}.$$

Using again the triangle inequality as we have done for I, we obtain

$$II \leq 2p(\bar{a}+1) \left\|u_1 - u_2\right\|_{L^1(\Omega)} + \left(d + 2p\bar{a} \left\|u_1\right\|_{L^1(\Omega)}\right) \left\|v_1 - v_2\right\|_{L^1(\Omega)}. \tag{2.5}$$

Adding inequality (2.4) and (2.5), we achieve

$$\begin{aligned} \left\|f(\xi_1) - f(\xi_2)\right\|_{(L^1(\Omega))^2} &\leq C(u_1) \left(\left\|u_1 - u_2\right\|_{L^1(\Omega)} + \left\|v_1 - v_2\right\|_{L^1(\Omega)}\right) \\ &= C(u_1) \left\|\xi_1 - \xi_2\right\|_{(L^1(\Omega))^2}, \end{aligned}$$

where $C(u_1) = \max\left\{4p\bar{a} + 3p, 4p\bar{a} \left\|u_1\right\|_{L^1(\Omega)} + d\right\}$. This concludes the local existence and uniqueness according to [54, Satz 1.17].
Let $(u,v)^T \in C^1([0,T), (C(\Omega) \cap L^1(\Omega))^2)$ be such a local-in-time solution. For the non-negativity, we observe first that v can be implicitly represented as

$$v(t,x) = e^{-dt} \left(v^0(x) + \int_0^t 2 \left(1 - \frac{a(x)}{1+k\rho_2(s)}\right) pu(s,x) e^{ds} \, \mathrm{d}s \right).$$

Thus it suffices to prove that $u(t,x) \geq 0$ and $v(t,x) \geq 0$ follows. Let

$$t^* := \inf \left\{ t \in \mathbb{R}_+ \,|u(t,x) = 0, x \in \Omega \right\}.$$

Then both $(0, v(t^*,x)e^{-d(t-t^*)})$ and $(u(t,x), v(t,x))$ are solutions of (2.2) which coincide at $(0, v(t^*,x))$. This contradicts the local uniqueness and hence a t^* as above cannot exist. Consequently, $u(t,x) > 0$ for all $t \in [0,T]$. A similar proof can be found in [23, Section 3.2]. □

2.5.2 Global-in-time existence and uniqueness

Since we are interested in the long-term behaviour of the solution it does not suffice to consider a local-in-time solution, but we need to show global-in-time existence and uniqueness. Essentially, the problem why we do not have global existence in Proposition 2.6 is the constant C which depends on the L^1-norm of u, or equivalently, on $\rho_1(t)$. Thus, if we show that $\rho_1(t)$ is uniformly bounded, we obtain global existence and uniqueness. Therefore, as a first step, we look at

Lemma 2.7. *Let Assumption 1 hold and let $(u,v)^T$ be the solution of Proposition 2.6 then $\rho_1, \rho_2 \in C^1([0,T))$ and there exists a constant $M_1 > 0$ such that*

$$\rho_1(t) \leq M_1 \rho_2(t) \tag{2.6}$$

for all $t \geq 0$.

Proof. ρ_1, ρ_2 are continuously differentiable, because u and v are continuously differentiable with respect to t. Let $U(t,x) = \frac{u(t,x)}{v(t,x)}$ for $t \geq 0$. Differentiating with respect to time yields

$$\begin{aligned}
\frac{\partial}{\partial t}U(t,x) &= \frac{\partial}{\partial t}\frac{u(t,x)}{v(t,x)} = \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p\frac{u(t,x)}{v(t,x)} \\
&\quad -\frac{u(t,x)}{v(t,x)}\left(2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right)p\frac{u(t,x)}{v(t,x)} - d\right) \\
&= U(t,x)\left(\left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right)p + d \right. \\
&\quad \left. -2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right)pU(t,x)\right).
\end{aligned} \tag{2.7}$$

Using the non-negativity ρ_2 and the boundedness of $a(x)$, we deduce

$$\left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right)p + d \leq 2p\bar{a} + d$$

and

$$1 - \frac{a(x)}{1+k\rho_2(t)} > 1 - \bar{a}.$$

We observe that

$$\frac{\partial}{\partial t}U(t,x) \leq U(t,x)\left(2p\bar{a} + d - 2(1-\bar{a})U(t,x)\right).$$

The right-hand side becomes negative if and only if

$$U(t,x) > \frac{2p\bar{a}+d}{2(1-\bar{a})}.$$

So we see that if $U(t,x)$ exceeds this threshold it decays. The only way for U to exceed this bound is to be bigger than this threshold in the beginning. Hence we can conclude that

$$\forall\ (t,x) \in [0,T) \times \Omega : \quad U(t,x) \leq \max\left\{ \max_{x\in\overline{\Omega}} U(0,x), \frac{2p\bar{a}+d}{2p(1-\bar{a})} \right\} =: M_1.$$

By definition of U we can infer that

$$\forall\ (t,x) \in [0,T) \times \Omega : \quad u(t,x) \leq M_1 v(t,x).$$

Integrating both sides with respect to x over Ω yields the proposition. □

Remark 2.8. *In this proof the argument for boundedness in logistic type equations has been used, see for example [63, p.20]. It will appear repeatedly in other proofs, as well. We will refer to this kind of argument as logistic argument.*

Now we have all results needed to prove boundedness of total mass, which can be summarized in

Lemma 2.9. *Let Assumption 1 hold, then there exist constants $M_2 > 0$ and $M_3 > 0$ such that for all $t \in [0,T)$*

$$\rho_1(t) \leq M_2 \quad \textit{and} \quad \rho_2(t) \leq M_3.$$

Proof. To show boundedness of ρ_1, we apply inequality (2.6) to the first equation of (2.2) in combination with boundedness of $a(x)$

$$\begin{aligned}\frac{\partial}{\partial t}u(t,x) &= \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) pu(t,x) \leq \left(\frac{2a(x)}{1+\frac{k}{M_1}\rho_1(t)} - 1\right) pu(t,x) \\ &\leq \left(\frac{2\bar{a}}{1+\frac{k}{M_1}\rho_1(t)} - 1\right) pu(t,x).\end{aligned}$$

Integrating this inequality with respect to x over Ω yields

$$\frac{\mathrm{d}}{\mathrm{d}t}\rho_1(t) \leq \left(\frac{2\bar{a}}{1+\frac{k}{M_1}\rho_1(t)} - 1\right) p\rho_1(t).$$

Changing the integral and the derivative is legit because of Leibniz' rule.
Similarly as in the proof of Lemma 2.7, we apply the logistic argument. Then we can deduce that the right-hand side of this inequality becomes negative if and only if

$$\rho_1(t) > \frac{(2\bar{a}-1)M_1}{k}.$$

Subsequently, we conclude that

$$\rho_1(t) \leq \max\left\{\rho_1(0), \frac{(2\bar{a}-1)M_1}{k}\right\} =: M_2. \tag{2.8}$$

Boundedness of ρ_2 results from the second equation of (2.2), non-negativity of ρ_2 and the assumptions on a. It holds

$$\frac{\partial}{\partial t}v(t,x) = 2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right)pu(t,x) - dv(t,x) \leq 2pu(t,x) - dv(t,x).$$

Integrating with respect to x over Ω and using (2.8), we obtain

$$\frac{\mathrm{d}}{\mathrm{d}t}\rho_2(t) \leq 2p\rho_1(t) - d\rho_2(t) \leq 2pM_2 - d\rho_2(t).$$

Solving this inequality yields,

$$\rho_2(t) \leq \max\left\{\rho_2(0), \frac{2pM_2}{d}\right\} =: M_3. \tag{2.9}$$

□

Summarizing these results lead to

Theorem 2.10. *Under Assumption 1 there exists a global unique solution* $(u,v)^T \in C^1([0,\infty),(C(\Omega)\cap L^1(\Omega))^2)$ *of system* (2.2).

Proof. We have seen in the proof of Proposition 2.6 that the right-hand side of equation (2.2) is locally Lipschitz continuous. In the notation of this proof, we have

$$\|f(\xi_1) - f(\xi_2)\|_{L^1(\Omega)} \leq C(u_1)\|\xi_1 - \xi_2\|_{(L^1(\Omega))^2},$$

with the Lipschitz constant $C(u_1) = \max\left\{4p\bar{a} + 3p, 4p\bar{a}\,\|u_1\|_{L^1(\Omega)} + d\right\}$. Lemma 2.9 provides an upper bound for the constant $C(u_1)$, namely,

$$C(u_1) = \max\left\{4p\bar{a} + 3p, 4p\bar{a}\,\|u_1\|_{L^1(\Omega)} + d\right\} \leq \max\left\{4p\bar{a} + 3p, 4p\bar{a}M_2 + d\right\}.$$

Hence the function f is globally Lipschitz continuous for all $t \geq 0$. □

2.6 Main result

For solutions in IDEs it is possible to observe concentration effects, that is, the solution of an IDE converges to a Dirac measure for time tending to infinity. In the scalar case, there are already several results, which address this limiting behaviour, see [27], or for an IDE considered in measure spaces see [2, 4].
Considering systems of IDEs is more intricate, but still, there are already some results regarding the system case, see for instance [8, 16, 17, 20].
The techniques developed and applied for systems of IDEs are either dependent on the linearity (with respect to the non-local term) of the system or make strong use of a particular structure of the investigated equations.The same holds true for system (2.2). Although the methods provided by the works above are not directly applicable for the system considered in this thesis, the idea to exploit the specific structure of the model allows showing that the solution $(u, v)^T$ converges to a tuple of Dirac measures, both concentrated in the same point, but weighted with different total masses. This is summarized in

Theorem 2.11. *Let Assumptions 1 hold and let $(u, v)^T$ be a solution of (2.2). Let*

$$\Omega_{max} := \left\{x \in \overline{\Omega}\,\middle|\, x = \operatorname{argmax}_{y\in\Omega} a(y)\right\},$$

then, the following assertions are true.

i) Let $\Omega_{max} = \{\bar{x}\}$, i.e. Ω consists of a single point. Then both u and v converge weakly in $\mathcal{M}^+(\Omega)$ to a Dirac measure δ concentrated in $\bar{x}$ with some weight $\bar{\rho}_i \in \mathbb{R}, i = 1, 2$. That is*

$$u(t, x) \overset{t\to\infty}{\rightharpoonup^*} \bar{\rho}_1\delta_{\bar{x}}, \quad v(t, x) \overset{t\to\infty}{\rightharpoonup^*} \bar{\rho}_2\delta_{\bar{x}} \quad \text{in } \mathcal{M}^+(\Omega),$$

with $\bar{\rho}_1 = \frac{2\bar{a}-1}{k}$ and $\bar{\rho}_2 = \frac{p}{d}\frac{2\bar{a}-1}{k}$.

ii) Let Ω_{max} be a connected set. Then there exist $f, g \in L^1(\Omega)$, determined by the initial data, such that

$$\|u(t,\cdot) - f\|_{L^1(\Omega)} \xrightarrow{t\to\infty} 0, \quad \|v(t,\cdot) - g\|_{L^1(\Omega)} \xrightarrow{t\to\infty} 0.$$

iii) Let $\Omega_{max} = \{\bar{x}_1, \bar{x}_2\}$. Then there exist constants $\rho_1^1, \rho_1^2, \rho_2^1, \rho_2^2 > 0$ such that

$$u(t,x) \overset{t\to\infty}{\rightharpoonup}{}^* \rho_1^1 \delta_{\bar{x}_1} + \rho_1^2 \delta_{\bar{x}_2}, \quad v(t,x) \overset{t\to\infty}{\rightharpoonup}{}^* \rho_2^1 \delta_{\bar{x}_1} + \rho_2^2 \delta_{\bar{x}_2}.$$

Before we begin to prove Theorem 2.11 it might be useful to understand how the points of concentration emerge. Let us look at the first equation of (2.2) to illustrate the concept. Any steady state $(\bar{u}, \bar{v})$ has to fulfil the equation

$$0 = \left(\frac{2a(x)}{1 + k\bar{\rho}_2} - 1 \right) p\bar{u},$$

where $\bar{\rho}_2 = \int_\Omega \bar{v} \, \mathrm{d}x$. Since we only look for non-trivial steady states, the equation can only be true, if and only if $\bar{\rho}_2$ is given by

$$\bar{\rho}_2 = \frac{2a(x) - 1}{k}.$$

Now, $a(x)$ can have different values, so we have to exclude the cases, where the possible concentration point is not equal to $\bar{x}$. Figure 2.1 shows an example of $\frac{2a(x)-1}{k}$ and three possible choices of $\bar{\rho}_2$ for the first component of system (2.2).
The first case is when $\bar{\rho}_2$ takes the value 0.3. In this case, we can see in Figure 2.1 that it holds

$$\frac{2a(x)}{1 + k\bar{\rho}_2} - 1 > 0, \quad \text{for } x \in [0.4, 0.6].$$

Then the right-hand side of (2.2) is strictly positive in $[0.4, 0.6]$. This would lead to an infinite growth of the total mass $\rho_1(t)$, which is excluded by Lemma 2.9.
The second case is when $\bar{\rho}_2$ takes the value 0.7. Then the right-hand side of (2.2) is strictly negative, hence the solution would converge to 0 for all $x \in \Omega$, which excludes a concentration in a single point.
In conclusion, the only possible outcome is that $\bar{\rho}_2$ takes exactly the maximal value of $a(x)$, here 0.6, and the solution decays everywhere, except in the point $\bar{x}$, where the function a attains its maximum.

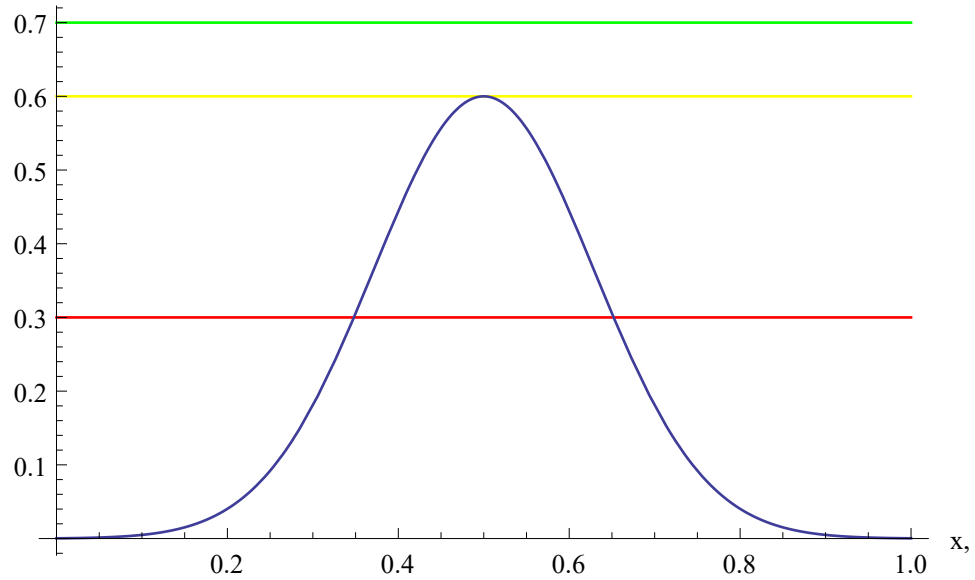

Figure 2.1: The blue line depicts $\frac{2a(x)-1}{k}$ and three possible steady states $\bar{\rho}_2$ are given in green, yellow and red.

The idea of the proof of Theorem 2.11 is based on the inequality introduced in Proposition 2.5, namely,

$$\rho_F(\mu_1, \mu_2) \leq \min\{\rho_1, \rho_2\} W_1\left(\frac{\mu_1}{\rho_1}, \frac{\mu_2}{\rho_2}\right) + |\rho_1 - \rho_2|.$$

As mentioned in the preliminaries convergence in the flat metric implies weak* convergence. By the inequality above it is necessary to show three results: strict positivity of total mass, mass convergence and that the normalised solution converges to a Dirac measure with respect to the 1-Wasserstein metric.
The first step to achieve these objectives will be to show strict positivity of total mass. The second step is to show pointwise convergence to zero for all $x \in \Omega \setminus \Omega_{max}$. This pointwise convergence in combination with the strict positivity of total mass allows proving the convergence to a Dirac measure with respect to the 1-Wasserstein metric. This result can then be used to prove convergence of total mass.

2.6.1 Strict positivity of total mass

Before we prove strict positivity of total masses, we need the following technical result.

Lemma 2.12. *Let Assumption 1 hold. Then there exist a constant $M_4 > 0$ and a sufficiently small number $\gamma > 0$ such that for all $t \geq 0$*

$$\rho_2(t) \leq M_4 \rho_1^\gamma(t). \tag{2.10}$$

Proof. Calculating the derivative of the quotient of these two quantities, we obtain using again the notation $\rho_i'(t) = \frac{\mathrm{d}}{\mathrm{d}t}\rho_i(t), i = 1, 2,$

$$\begin{aligned}
\frac{d}{dt}\frac{\rho_2(t)}{\rho_1^\gamma(t)} &= \frac{\rho_2'(t)\rho_1^\gamma(t) - \rho_2(t)\gamma\rho_1^{\gamma-1}(t)\rho_1'(t)}{\rho_1^{2\gamma}(t)} \\
&= \frac{\int_\Omega 2(1 - \frac{a(x)}{1+k\rho_2(t)})pu(t,x) - dv(t,x)\,\mathrm{d}x}{\rho_1^\gamma(t)} \\
&\quad - \frac{\rho_2(t)}{\rho_1^\gamma(t)} \frac{\gamma \int_\Omega \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) pu(t,x)\,\mathrm{d}x}{\rho_1} \\
&\leq \frac{\int_\Omega 2(1 - \frac{a(x)}{1+k\rho_2(t)})pu(t,x) - dv(t,x)\,\mathrm{d}x}{\rho_1^\gamma(t)} + \frac{\rho_2(t)}{\rho_1^\gamma(t)}\gamma p \\
&\leq 2p\rho_1^{1-\gamma}(t) + \frac{\rho_2(t)}{\rho_1^\gamma(t)}(\gamma p - d) \leq 2pM_2^{1-\gamma} + \frac{\rho_2(t)}{\rho_1^\gamma(t)}(\gamma p - d).
\end{aligned}$$

This estimate holds for arbitrary γ, so in particular for those satisfying $\gamma p - d < 0$. Solving the inequality, we deduce that for all $t \geq 0$

$$\frac{\rho_2}{\rho_1^\gamma}(t) \leq \max\left\{\frac{\rho_2(0)}{\rho_1^\gamma(0)}, \frac{2pM_2^{1-\gamma}}{d - \gamma p}\right\} =: M_4.$$

□

Corollary 2.13. *Let $\Omega = \Omega_{>\varepsilon} \cup \Omega_{<\varepsilon}$ with $0 < \varepsilon \ll 1$ and*

$$\Omega_{>\varepsilon} := \left\{x \in \Omega \,\middle|\, a(x) > \frac{1}{2} + \varepsilon\right\}, \quad \Omega_{<\varepsilon} := \left\{x \in \Omega \,\middle|\, a(x) \leq \frac{1}{2} + \varepsilon\right\}.$$

Let $\rho_>(t) = \int\limits_{\Omega_{>\varepsilon}} u(t,x)\,\mathrm{d}x$, then we can find a constant $M_5 > 0$ such that for all $t \geq 0$

$$\rho_2(t) \leq M_5 \left(\rho_>(t)\right)^\gamma.$$

Proof. Let $\rho_<(t) = \int\limits_{\Omega_{<\varepsilon}} u(t,x)\,\mathrm{d}x$. Then we can use the implicit formula for the solution $u(t,x)$, i.e.

$$u(t,x) = u^0(x)\exp\left(\int\limits_0^t \left(\frac{2a(x)}{1+k\rho_2(\tau)} - 1\right) p\,\mathrm{d}\tau\right)$$

to deduce that

$$\begin{aligned}
\frac{\rho_>(t)}{\rho_<(t)} &= \frac{\int\limits_{\Omega_{>\varepsilon}} u^0(x)\exp\left(\int\limits_0^t \left(\frac{2a(x)}{1+k\rho_2(\tau)} - 1\right) p\,\mathrm{d}\tau\right)\,\mathrm{d}x}{\int\limits_{\Omega_{<\varepsilon}} u^0(x)\exp\left(\int\limits_0^t \left(\frac{2a(x)}{1+k\rho_2(\tau)} - 1\right) p\,\mathrm{d}\tau\right)\,\mathrm{d}x} \\
&\geq \frac{\inf\limits_{x\in\Omega_{\varepsilon>}} \exp\left(\int\limits_0^t \left(\frac{2a(x)}{1+k\rho_2(\tau)} - 1\right) p\,\mathrm{d}\tau\right) \int\limits_{\Omega_{>\varepsilon}} u^0(x)\,\mathrm{d}x}{\sup\limits_{x\in\Omega_{<\varepsilon}} \exp\left(\int\limits_0^t \left(\frac{2a(x)}{1+k\rho_2(\tau)} - 1\right) p\,\mathrm{d}\tau\right) \int\limits_{\Omega_{<\varepsilon}} u^0(x)\,\mathrm{d}x} \\
&= \frac{\rho_>(0)}{\rho_<(0)}.
\end{aligned}$$

Combining this inequality with the inequality (2.10) yields

$$\begin{aligned}
\rho_2(t) &\leq M_4\left(\rho_1(t)\right)^\gamma = M_4\left(\rho_>(t) + \rho_<(t)\right)^\gamma \leq M_4(\rho_>(t))^\gamma \left(1 + \frac{\rho_>(0)}{\rho_<(0)}\right)^\gamma \\
&= M_5\left(\rho_>(t)\right)^\gamma,
\end{aligned}$$

where $M_5 := M_4\left(1 + \frac{\rho_>(0)}{\rho_<(0)}\right)^\gamma$. □

Lemma 2.14. *Let Assumption 1 hold and let $(u,v)^T$ be a solution of (2.2), then both ρ_1 and ρ_2 are strictly positive.*

Proof. Let $\Omega_{<\varepsilon}, \Omega_{>\varepsilon}, \rho_>(t)$ and $\rho_<(t)$ as in Corollary 2.13 and its proof. Then we have

$$\rho_1(t) = \int\limits_{\Omega_{>\varepsilon}} u(t,x)\,\mathrm{d}x + \int\limits_{\Omega_{<\varepsilon}} u(t,x)\,\mathrm{d}x.$$

Again due to the non-negativity of $u(t,x)$ both terms are also non-negative. Hence it suffices to show that one of the two terms is strictly bigger than zero to prove the assertion. Thus integrating the first equation of (2.2) with respect to x over $\Omega_{>\varepsilon}$

yields, using Corollary 2.13 and $\underline{a} := \inf_{x\in\Omega_{>\varepsilon}} a(x)$

$$\frac{\mathrm{d}}{\mathrm{d}t}\rho_>(t) = \int\limits_{\Omega_{>\varepsilon}} \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) pu(t,x)\,\mathrm{d}x \geq \left(\frac{2\underline{a}}{1+kM_5\rho_>^\gamma(t)} - 1\right) p\rho_>(t).$$

By the logistic argument we can deduce that for each small $\varepsilon > 0$

$$\rho_>(t) \geq \min\left\{\rho_>(0), \left(\frac{(2\underline{a}-1)}{kM_5}\right)^{\frac{1}{\gamma}}\right\} =: M_6 > 0. \tag{2.11}$$

So we obtain

$$\forall\, t \in \mathbb{R}_+ : \quad \rho_1(t) = \int\limits_{\Omega_{>\varepsilon}} u(t,x)\,\mathrm{d}x + \int\limits_{\Omega_{<\varepsilon}} u(t,x)\,\mathrm{d}x \geq M_6 > 0.$$

Note that the necessity to split the integral into two parts, $\Omega_{>\varepsilon}$ and $\Omega< \varepsilon$, arises from the fact that we need to guarantee that the constant M_6, as it is defined in (2.11), is positive. This can only be assured by the right choice of the domain of the infimum of a.

Once equipped with inequality (2.11), we can achieve strict positivity of $\rho_2(t)$. Integrate the second equation of (2.2) with respect to x over Ω and estimate by using non-negativity of v

$$\frac{\mathrm{d}}{\mathrm{d}t}\rho_2(t) \;=\; \int\limits_{\Omega} 2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right) pu(t,x)\,\mathrm{d}x - d\rho_2(t) \geq 2(1-\bar{a})pM_6 - d\rho_2(t).$$

Solving the inequality yields

$$\rho_2(t) \geq \min\left\{\rho_2(0), \frac{2(1-\bar{a})pM_6}{d}\right\} =: M_7. \tag{2.12}$$

□

Lemma 2.14 and Lemma 2.9 guarantee that neither does the total mass tend to infinity, nor does it vanish. Hence the total mass is preserved in the sense that although it might change with time, it is confined in a hose with maximal diameter $|M_2 - M_6|$ for ρ_1 and $|M_3 - M_7|$ for ρ_2.

2.6.2 Pointwise convergence to zero

The aim stated in the main result Theorem 2.11 is to prove that the solution converges to a Dirac measure. Achieving this goal means now to show that the solution converges in all $x \in \Omega$ to zero except those, where the self-renewal rate a attains its maximum. This is stated in

Lemma 2.15. *Let $x_1, x_2 \in \Omega$ such that $a(x_1) - a(x_2) < 0$. Then*

$$\frac{u(t,x_1)}{u(t,x_2)} \to 0 \quad \textit{for} \quad t \to \infty.$$

Proof. We estimate the derivative of the quotient

$$\begin{aligned}\frac{\partial}{\partial t}\frac{u(t,x_1)}{u(t,x_2)} &= \left(\frac{2a(x_1)}{1+k\rho_2(t)} - 1\right) p\frac{u(t,x_1)}{u(t,x_2)} - \left(\frac{2a(x_2)}{1+k\rho_2(t)} - 1\right) p\frac{u(t,x_1)}{u(t,x_2)} \\ &= \frac{u(t,x_1)}{u(t,x_2)}\left(\frac{2(a(x_1)-a(x_2))p}{1+k\rho_2(t)}\right) \\ &\leq \frac{u(t,x_1)}{u(t,x_2)}\frac{2(a(x_1)-a(x_2))p}{1+kM_3}.\end{aligned}$$

Solving the inequality leads to

$$\frac{u(t,x_1)}{u(t,x_2)} \leq \frac{u^0(x_1)}{u^0(x_2)} \exp\left(\frac{2(a(x_1)-a(x_2))pt}{1+kM_3}\right). \tag{2.13}$$

Since $x_1, x_2 \in \Omega$ were chosen such that $a(x_1) - a(x_2) < 0$, the right-hand side of (2.13) tends to zero as t tends to infinity. □

Corollary 2.16. *Let $x_1, x_2 \in \Omega$ such that $a(x_1) = a(x_2)$. Then, $\frac{u(t,x_1)}{u(t,x_2)}$ is constant in time.*

Proof. This corollary is an immediate consequence of the proof of Lemma 2.15, because of the equality

$$\frac{\partial}{\partial t}\frac{u(t,x_1)}{u(t,x_2)} = \frac{u(t,x_1)}{u(t,x_2)}\left(\frac{2(a(x_1)-a(x_2))p}{1+k\rho_2(t)}\right).$$

If $a(x_1) = a(x_2)$, then the time derivative is zero for all $t \in \mathbb{R}_+$. □

Another important consequence of Lemma 2.15 is

Corollary 2.17. *Suppose that Assumption 1 holds. Then for all $x \in \Omega \setminus \Omega_{max}$ the solution $u(t,x) \to 0$ and $v(t,x) \to 0$ as $t \to \infty$.*

Proof. Lemma 2.15 provides a decay to zero of the quotient $\frac{u(t,x_1)}{u(t,x_2)}$ for two points $x_1, x_2 \in \overline{\Omega}$, such that $a(x_1) - a(x_2) < 0$ and $t \to \infty$. If this quotient tends to zero, either $u(t, x_1) \to 0$ or $u(t, x_2) \to \infty$, or both. If $u(t, x_1)$ tends to zero, we are done. So let us assume instead that $u(t, x_1)$ does not tend to zero but $u(t, x_2) \to \infty$. Then, due to the continuity of the function a, if the quotient tends to zero in a point x_2, it does so for a ball $B_\delta(x_2)$ with some suitably small $\delta > 0$. Hence,

$$\exists\, \delta > 0 \,\forall\, y \in B_\delta(x_2): \quad \frac{u(t,x_1)}{u(t,y)} \xrightarrow{t\to\infty} 0.$$

Since $u(t, x_1)$ does not converge to zero, it must be valid that $u(t, y) \to \infty$ for all $y \in B_\delta(x_2)$. Since a ball has positive Lebesgue measure, it would mean that the function u tends to infinity on a set of positive measure, which would result in an unbounded total mass. This is excluded by Lemma 2.9. Hence $u(t, x_2)$ cannot tend to infinity and, subsequently, $u(t, x_1)$ tends to zero for all $x_1 \notin \Omega_{max}$.
The convergence of the second component v can be achieved by looking at the second equation of (2.2). Using the positivity of u yields

$$\frac{\partial}{\partial t} v(t,x) = 2\left(1 - \frac{a(x)}{1 + k\rho_2(t)}\right) pu(t,x) - dv(t,x) \leq 2pu(t,x) - dv(t,x).$$

Solving the inequality gives an implicit estimate for v, namely,

$$v(t,x) \leq e^{-dt}\left(v^0(x) + \int_0^t e^{ds} u(s,x)\,\mathrm{d}s\right).$$

The first term on the right-hand side converges to zero, because v^0 is independent of t and the exponential converges to zero for t tending to infinity. For the second term, either the integral is finite for t tending to infinity, then the product of the integral and the exponential converges to zero, or the integral tends to infinity. If the latter is true, then l'Hopital's theorem can be applied, because both e^{dt} and $\int_0^t e^{ds} u(s,x)\,\mathrm{d}s$ are differentiable functions which tend to infinity for t tending to infinity. Hence it holds true

$$\lim_{t\to\infty} \frac{\int_0^t e^{ds} u(s,x)\,\mathrm{d}s}{e^{dt}} = \lim_{t\to\infty} \frac{e^{dt} u(t,x)}{d e^{dt}} = \lim_{t\to\infty} \frac{u(t,x)}{d}.$$

Since $u(t,x) \to 0$ for $t \to 0$ and all $x \in \Omega \setminus \Omega_{max}$, we can infer that $v(t,x) \to 0$ for $t \to 0$ and all $x \in \Omega \setminus \Omega_{max}$. □

Combining Corollary 2.16 and Corollary 2.17 suffices to prove Theorem 2.11, *ii*).

Proof of Theorem 2.11, ii). Let Ω_{max} be a connected set. According to Corollary 2.17, we have

$$\forall\, x \in \Omega \setminus \Omega_{max}: \quad u(t,x) \xrightarrow{t\to\infty} 0.$$

On the other hand, Corollary 2.16 provides that

$$\forall\, x_1, x_2 \in \Omega_{max}\, \forall\, t \in \mathbb{R}_+: \quad \frac{u(t,x_1)}{u(t,x_2)} = \frac{u^0(x_1)}{u^0(x_2)}.$$

So due to the dominated convergence theorem, we obtain the convergence of $u(t,x)$ to an L^1-function, which is identically zero on $\Omega \setminus \Omega_{max}$ and its values in Ω_{max} is determined by the initial datum $u^0(x)$.
Since v converges to zero if and only if u does so (combine Lemma 2.7 and Lemma 2.15), $v > 0$ on Ω_{max}. Because of Lemma 2.9 the assertion holds true. □

We have seen that the solution $(u,v)^T$ converges to zero everywhere except in Ω_{max} but at the same time the total mass stays strictly positive. So heuristically, the total mass has to concentrate exactly in the points, where the solution does not converge to zero. As we will see, these two properties are indeed enough to prove convergence to a Dirac measure, if Ω_{max} consists of a single point.

2.6.3 Weak* convergence to a Dirac measure with respect to 1-Wasserstein metric

The 1-Wasserstein metric is defined on the space of probability measures and, therefore, we need to interpret the solution $(u,v)^T \in C^1([0,\infty), (C(\Omega) \cap L^1(\Omega))^2)$ of equation (2.2) as measures. This can be done by interpreting $L^1(\Omega)$ as a subspace of $\mathcal{M}^+(\Omega)$. Thus $u(t,\cdot) \in L^1(\Omega) \subset \mathcal{M}^+(\Omega)$ is then the density function of a weighted Lebesgue measure, i.e. there exists a measure $\mu \in C^1(\mathbb{R}_+, \mathcal{M}^+(\Omega))$ such that for the Lebesgue measure $\mathrm{d}x$ it holds $\mu(t) = u(t,x)\,\mathrm{d}x$.

Lemma 2.18. *Let $(u,v)^T$ be the solution of (2.2) and $\Omega_{max} = \{\bar{x}\}$, then*

$$\frac{u(t,x)}{\rho_1(t)} \overset{t\to\infty}{\rightharpoonup^*} \delta_{\bar{x}}, \quad \frac{v(t,x)}{\rho_2(t)} \overset{t\to\infty}{\rightharpoonup^*} \delta_{\bar{x}}, \quad \text{in } \mathcal{M}^+(\Omega).$$

Proof. We show that $\delta_t := \frac{u(t,x)\,\mathrm{d}x}{\rho_1(t)}$ is a Dirac sequence. The non-negativity of $u(t,x)$ and strict positivity of $\rho_1(t)$ imply

$$\forall\, t \in \mathbb{R}_+ : \quad \delta_t \geq 0.$$

By definition it holds

$$\forall\, t \in \mathbb{R}_+ : \quad \int_\Omega \delta_t = \frac{1}{\rho_1(t)} \int_\Omega u(t,x)\,\mathrm{d}x = 1.$$

Using the decay estimate provided by Lemma 2.15 we obtain with $\tilde{x} = \operatorname{argmax}_{\overline{\Omega}\setminus B_{\frac{r}{2}}(\bar{x})} a(x)$.

$$\begin{aligned}\int_{\Omega\setminus B_r(\bar{x})} \delta_t &= \int_{\Omega\setminus B_r(\bar{x})} \frac{u(t,x)}{\rho_1(t)}\,\mathrm{d}x = \int_{\Omega\setminus B_r(\bar{x})} \frac{u(t,x)}{u(t,\tilde{x})}\frac{u(t,\tilde{x})}{\rho_1(t)}\,\mathrm{d}x \\ &\leq \int_{\Omega\setminus B_r(\bar{x})} \frac{u^0(x)}{u^0(\tilde{x})} \exp\left(\frac{2(a(x)-a(\tilde{x}))pt}{1+kM_3}\right)\frac{u(t,\tilde{x})}{\rho_1(t)}\,\mathrm{d}x.\end{aligned}$$

Taking the limit t tends to infinity, on both sides we see by the dominated convergence theorem that

$$\lim_{t\to\infty} \int_{\Omega\setminus B_r(\bar{x})} \delta_t = 0,$$

for all $r > 0$. This proves that δ_t is a Dirac sequence.
We can argue analogously for $\frac{v(t,x)}{\rho_2(t)}$. □

Corollary 2.19. *The measure δ_t, defined in the proof of Lemma 2.18, converges with respect to the 1-Wasserstein metric to a Dirac measure concentrated in $\bar{x}$, i.e.*

$$W_1(\delta_t, \delta_{\bar{x}}) \xrightarrow{t\to\infty} 0.$$

Proof. The proof is immediate with Lemma 2.18.

$$\begin{aligned}W_1\left(\frac{u(t,x)\,\mathrm{d}x}{\rho_1(t)}, \delta_{\bar{x}}\right) &= \sup\left\{\int_\Omega \psi(x)\frac{u(t,x)}{\rho_1(t)}\,\mathrm{d}x - \int_\Omega \psi(x)\,\mathrm{d}\delta_{\bar{x}} \,\middle|\, \psi \in W^{1,\infty}(\Omega), \|\partial_x\psi\|_\infty \leq 1\right\} \\ &= \sup\left\{\int_\Omega \psi(x)\frac{u(t,x)}{\rho_1(t)}\,\mathrm{d}x - \psi(\bar{x}) \,\middle|\, \psi \in W^{1,\infty}(\Omega), \|\partial_x\psi\|_\infty \leq 1\right\}.\end{aligned}$$

We can infer that

$$W_1\left(\frac{u(t,x)\,\mathrm{d}x}{\rho_1(t)},\delta_{\bar{x}}\right)\xrightarrow{t\to\infty}\sup\left\{\psi(\bar{x})-\psi(\bar{x})\,\middle|\,\psi\in W^{1,\infty}(\Omega),\|\partial_x\psi\|_\infty\leq 1\right\}=0.$$

□

2.6.4 Convergence of total masses

Although we have seen that a suitably normalised solution of (2.2) converges to a Dirac measure, it remains unclear up to this point how exactly the total masses behave. A priori it could be possible that the integrals $\rho_i(t), i=1,2$, oscillate for all times and the rescaled solution could still converge to a Dirac measure, whose peak "jumps". To exclude this possibility, the convergence of total masses has to be proven separately.

Proposition 2.20. *Suppose that Assumption 1 holds and*

$$(\rho_1,\rho_2)=\left(\int_\Omega u(\cdot,x)\mathrm{d}x,\int_\Omega v(\cdot,x)\mathrm{d}x\right)$$

be the total masses of the solution of (2.2)*. It holds*

$$|\rho_1(t)-\bar{\rho}_1|\xrightarrow{t\to\infty}0,\quad |\rho_2(t)-\bar{\rho}_2|\xrightarrow{t\to\infty}0,$$

where $(\bar{\rho}_1,\bar{\rho}_2)$ *are stationary solutions of the corresponding ODE model with the maximal value of the self-renewal parameter* $\bar{a}$*, i.e.*

$$\begin{aligned}0&=\left(\frac{2\bar{a}}{1+k\bar{\rho}_2}-1\right)p\bar{\rho}_1,\\ 0&=2\left(1-\frac{\bar{a}}{1+k\bar{\rho}_2}\right)p\bar{\rho}_1-d\bar{\rho}_2.\end{aligned}\tag{2.14}$$

The proof is mainly based on a perturbation argument. Roughly speaking, we make use of the fact that perturbations which vanish at infinity do not change the steady states if the former system admits a Lyapunov function. Intuitively, this is not surprising, because the perturbation impacts less and less as time approaches infinity. The exact formulation is technical, though, as we will see in the proof of

Lemma 2.21. *Let $F : \mathbb{R}^2 \to \mathbb{R}^2$ be Lipschitz-continuous and let u be the unique non-negative solution of*

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}u(t) = F(u(t)), \\ u(0) = u^0. \end{cases}$$

Let $V \in C^1((\mathbb{R}_+)^2)$ be a strict Lyapunov function for this equation with compact level sets and minimum $\delta > 0$. Let $\bar{u}$ be the unique globally stable positive stationary solution of the above equation. If $f \in C^1(\mathbb{R}_+)$ with $\lim_{t\to\infty} |f(t)| = 0$ and $\tilde{u}$ is a solution of

$$\frac{\mathrm{d}}{\mathrm{d}t}\tilde{u}(t) = F(\tilde{u}(t)) + f(t),$$

which is strictly positive, i.e.

$$\exists c > 0 \; \forall t > 0 : \quad \tilde{u}(t) \geq c > 0$$

and

$$\forall u^0 \; \exists\, c(u^0) > 0 : \quad |\nabla_{\tilde{u}} V(\tilde{u})| < c(u^0),$$

then $\tilde{u}(t) \to \bar{u}$ for $t \to \infty$.

Proof. Let $\bar{u}$ be the unique globally stable stationary solution of

$$\begin{cases} \frac{\mathrm{d}u(t)}{\mathrm{d}t} = F(u(t)), \\ u(0) = u^0. \end{cases}$$

Furthermore, let $V \in C^1((\mathbb{R}_+)^2)$ be the strict Lyapunov function for this equation, i.e.

$$\frac{\mathrm{d}V(u)}{\mathrm{d}t} < 0, \; \frac{\mathrm{d}V(u)}{\mathrm{d}t} = 0 \Leftrightarrow u = \bar{u}, \; V(\bar{u}) = \delta$$

and V shall have compact level sets. Let $\tilde{u}$ be the strictly positive solution of

$$\begin{cases} \frac{\mathrm{d}\tilde{u}(t)}{\mathrm{d}t} = F(\tilde{u}(t)) + f(t), \\ \tilde{u}(0) = u^0, \end{cases}$$

where $f \in C^1(\mathbb{R}^+)$ tends to zero for t tending to infinity. For arbitrary $a > \delta$, we define a cutting function

$$V_a(u) := \begin{cases} V(u) - a, & V(u) > a, \\ 0, & V(u) \leq a. \end{cases}$$

Since $V \in C^1(\mathbb{R}^2_+)$ we can infer that $V_a \in W^{1,\infty}(U)$, where $U \subset (\mathbb{R}^+)^2$, $rg\,(\tilde{u}) \in U$. Then we can define the time derivative of $V_a(\tilde{u}(t))$ based on the chain rule. $\nabla_{\tilde{u}} V_a(\tilde{u})$ is defined in classical sense only outside the curve $V(\tilde{u}(t)) = a$, but it has Clarke derivative (generalised subdifferential for a locally Lipschitz function, [22]) on the curve $V = a$. In the following, in notion of $\nabla_{\tilde{u}} V_a(\tilde{u})$ we extend the classical definition with the maximal element of the Clarke derivative on the set where the classical derivative is not defined. Since $\frac{\mathrm{d}}{\mathrm{d}t} V(u(t)) < 0$ we can infer that

$$0 \leq V(u(t)) \leq V(u^0).$$

The same holds true for $V_a(u(t))$, because it is a downwards shift of $V(u(t))$. Thus applying an arbitrary positive function to $V_a(u(t))$ means that the positive function is defined on a compact set. A strictly positive, continuous function on a compact set attains its minimum. Let β_a be such a function and let this minimal value be δ'. Then choose a constant $\tilde{\beta}_a \in \mathbb{R}_+$ such that $\tilde{\beta}_a V_a(u^0) < \frac{\delta'}{2}$ and so we obtain that $\beta_a(V_a(\tilde{u}(t)) \geq \tilde{\beta}_a V_a(\tilde{u}(t))$. Then we can estimate

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t} V_a(\tilde{u}(t)) &= \nabla_{\tilde{u}} V_a(\tilde{u}(t)) \frac{\mathrm{d}}{\mathrm{d}t} \tilde{u}(t) \\
&= \nabla_{\tilde{u}} V_a(\tilde{u}(t)) \cdot F(\tilde{u}(t)) + \nabla_{\tilde{u}} V_a(\tilde{u}(t)) \cdot f(t) \\
&\leq -\tilde{\beta}_a V_a(\tilde{u}(t)) + |\nabla_{\tilde{u}} V_a(\tilde{u}(t))|\,|f(t)|\,.
\end{aligned}$$

At this point we use the assumption that

$$\forall u^0\, \exists\, c = c(u^0) > 0 : |\nabla_u V_a(u(t))| \leq c(u^0) = c$$

and estimate

$$\frac{\mathrm{d}}{\mathrm{d}t} V_a(\tilde{u}(t)) \leq -\tilde{\beta}_a V_a(\tilde{u}(t)) + c\,|f(t)|\,.$$

By the comparison principle we obtain

$$V_a(\tilde{u}(t)) \leq V_a(u^0) e^{-\tilde{\beta}_a t} + c \int_0^t |f(s)|\, e^{-\tilde{\beta}_a (t-s)}\, \mathrm{d}s.$$

Since we consider this inequality first on the compact set $[0, t]$, the integral is well defined. We want to show that the right-hand side tends to zero as t tends to infinity. The first term is converging to 0. The second term, however, does not need to converge to zero necessarily, because $f \in L^1_{loc}(\Omega)$, which might cause a diverging

integral. If the integral is finite, we are done. So let us assume that the integral tends to infinity for t tending to infinity. Since both the exponential function as well as $|f(s)|$ are continuous functions the integral is a continuously differentiable function with respect to t. Rewriting the integral

$$\int_0^t |f(s)|\, e^{-\tilde{\beta}_a(t-s)}\, \mathrm{d}s = \frac{\int_0^t |f(s)|\, e^{\tilde{\beta}_a s}\, \mathrm{d}s}{e^{\tilde{\beta}_a t}}$$

we can apply l'Hospital's Theorem.

$$\lim_{t\to\infty} \frac{\int_0^t |f(s)|\, e^{\tilde{\beta}_a s}\, \mathrm{d}s}{e^{\tilde{\beta}_a t}} = \lim_{t\to\infty} \frac{|f(t)|}{\tilde{\beta}_a} = 0.$$

Thus we obtain for all $a > \delta$ that $V_a(\tilde{u}(t))$ tends to zero as t tends to infinity. Hence

$$V(\tilde{u}(t)) \to a, \quad \text{as } t \to \infty.$$

V has compact level sets and $V(u) = \delta$ if and only if $u = \bar{u}$, thus we can conclude that $\tilde{u}(t)$ converges to $\bar{u}$. □

The idea of the proof of Proposition 2.20 is to make use of knowledge about ODE system (2.14) for which a Lyapunov functional is known. This way we get the asymptotically stable steady state without further effort and are left to prove that system (2.2) is a perturbation of the ODE system (2.14) in the sense of Lemma 2.21.

Proof of Proposition 2.20. To show convergence of the total mass of a solution of (2.2) to a global equilibrium, we integrate the equations of (2.2) with respect to x over Ω and obtain

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\rho_1(t) &= \int_\Omega \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) pu(t,x)\mathrm{d}x, \\ \frac{d}{dt}\rho_2(t) &= 2\int_\Omega \left(1 - \frac{a(x)}{1+k\rho_2(t)}\right) pu(t,x)\mathrm{d}x - d\int_\Omega v(t,x)\mathrm{d}x, \\ \rho_1(0) &= \int_\Omega u^0(x)\mathrm{d}x, \\ \rho_2(0) &= \int_\Omega v^0(x)\mathrm{d}x. \end{cases} \tag{2.15}$$

This can be rewritten by adding a zero as

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\rho_1(t) &= \left(\frac{2\bar{a}}{1+k\rho_2(t)} - 1\right) p\rho_1(t) + \frac{2p}{1+k\rho_2(t)} \int_\Omega (a(x) - \bar{a})\, u(t,x)\mathrm{d}x, \\ \frac{\mathrm{d}}{\mathrm{d}t}\rho_2(t) &= 2\left(1 - \frac{\bar{a}}{1+k\rho_2(t)}\right) p\rho_1(t) \\ &\quad + \frac{2p}{1+k\rho_2(t)} \int_\Omega (\bar{a} - a(x))\, u(t,x)\mathrm{d}x - d\rho_2(t), \\ \rho_1(0) &= \int_\Omega u^0(x)\mathrm{d}x, \\ \rho_2(0) &= \int_\Omega v^0(x)\mathrm{d}x. \end{cases} \tag{2.16}$$

System (2.16) can be seen as a perturbation of a finite dimensional model, which is obtained by setting the function a to a constant value $\bar{x}$, that is

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\eta_1 &= \left(\frac{2\bar{a}}{1+k\eta_2} - 1\right) p\eta_1, \\ \frac{\mathrm{d}}{\mathrm{d}t}\eta_2 &= 2\left(1 - \frac{\bar{a}}{1+k\eta_2}\right) p\eta_1 - d\eta_2, \\ \eta_1(0) &= \eta_1^0 > 0, \\ \eta_2(0) &= \eta_2^0 > 0. \end{cases} \tag{2.17}$$

According to Lemma 2.21, it is necessary to prove for the finite dimensional system asymptotic stability of the positive steady state via a Lyapunov function. A Lyapunov function for this system has been constructed in [31]. It takes the form

$$V(\eta_1, \eta_2) := \frac{1}{pG(\bar{\eta}_2)} V_1(\eta_1, \eta_2) + \frac{1}{d} V_2(\eta_1, \eta_2), \tag{2.18}$$

where

$$\begin{aligned} V_1(\eta_1, \eta_2) &:= \frac{\eta_1}{\bar{\eta}_1} - 1 - \ln \frac{\eta_1}{\bar{\eta}_1}, \\ V_2(\eta_1, \eta_2) &:= \frac{\eta_2}{\bar{\eta}_2} - 1 - \frac{1}{\bar{\eta}_2} \int_{\bar{\eta}_2}^{\eta_2} \frac{G(\bar{\eta}_2)}{G(\xi)} d\xi, \end{aligned}$$

$(\bar{\eta}_1, \bar{\eta}_2)$ is the positive stationary solution of (2.17) and

$$G(\eta_2) := 2\left(1 - \frac{\bar{a}}{1 + k\eta_2}\right) \text{ for } \eta_2 \geq 0. \tag{2.19}$$

Compactness of level sets of V follows from uniform boundedness of the solutions of the model. Direct calculations, presented in [31, p. 6], allow to check that

$$\frac{\mathrm{d}}{\mathrm{d}t} V(\eta_1(t), \eta_2(t)) \leq 0. \tag{2.20}$$

We define

$$\Sigma := \left\{(\eta_1, \eta_2) \in \mathbb{R}^2 | \eta_1 > 0, \eta_2 > 0\right\},$$

$$E := \left\{(\eta_1(t), \eta_2(t)) \in \overline{\Sigma} \,\middle|\, V(\eta_1(t), \eta_2(t)) < +\infty, \tfrac{\mathrm{d}}{\mathrm{d}t} V(\eta_1(t), \eta_2(t)) = 0 \right\}$$

where $\overline{\Sigma}$ is the closure of Σ. Let M be the maximum invariant set in E. Then M consists of the positive equilibrium. By La Salle's invariance principle, we conclude that every solution in Σ tends to M. Thus, the positive equilibrium of (2.17) is globally attractive in E.

It is left to prove the assumptions on the perturbation. Using the fact that $\rho_1(t) \leq M_1\rho_2(t)$ for all $t \geq 0$, that $\rho_1(t) \geq M_6 > 0$ for all $t \geq 0$ and with $C = \frac{2pM_1}{k}$ we look at the perturbation and deduce that

$$\begin{aligned}
\left| \frac{2p}{1 + k\rho_2(t)} \int_\Omega (a(x) - \bar{a}) u(t,x) \,\mathrm{d}x \right| &\leq \frac{C}{\rho_1(t)} \int_\Omega |a(x) - \bar{a}| \, u(t,x) \,\mathrm{d}x \\
&= C \int_\Omega |a(x) - \bar{a}| \, \frac{u(t,x)}{\rho_1(t)} \,\mathrm{d}x \\
&\xrightarrow{t\to\infty} C \, |\bar{a} - \bar{a}| = 0.
\end{aligned}$$

The convergence is due to Lemma 2.18. The continuity of the perturbation is provided by the differentiability of the solution $(u(t,x), v(t,x))^T$.
Since the perturbed problem (2.16) is in fact the ODE of total masses we already know that the total masses are strictly positive. Lastly we need to show that the Lyapunov function used admits the estimate for the gradient.

$$|\nabla_\eta V(\eta(t))| = \frac{1}{\bar{\eta}_1} - \frac{1}{\eta_1} + \frac{1}{\bar{\eta}_2} + \frac{G(\bar{\eta}_2)}{\bar{\eta}_2 G(\eta_2)}.$$

In terms of system (2.16) we have $G(\bar{\eta}_2) = 1, \bar{\eta}_1 = \bar{\rho}_1, \bar{\eta}_2 = \bar{\rho}_2, \eta_i(t) = \rho_i(t), i = 1, 2$. Thus we estimate

$$|\nabla_\rho V(\rho_1, \rho_2)| \leq \frac{1}{\bar{\rho}_1} - \frac{1}{M_2} + \frac{1}{\bar{\rho}_2} + \frac{1}{2\bar{\rho}_2} = C(\rho_1^0).$$

Now Lemma 2.21 applies and we obtain that

$$\rho_i(t) \to \bar{\rho}_i, \ i = 1, 2, \quad \text{as } t \to \infty.$$

□

See Figure 2.3 for an illustration of the convergence of the total masses.

Proof of Theorem 2.11, i). According to Proposition 2.5, we have

$$\rho_F(u(t,x)\,\mathrm{d}x, \bar{\rho}_1\delta_{\bar{x}}) \leq \min\{\rho_1(t), \bar{\rho}_1\}\, W_1\left(\frac{u(t,x)\,\mathrm{d}x}{\rho_1(t)}, \delta_{\bar{x}}\right) + |\rho_1(t) - \bar{\rho}_1|\,.$$

Corollary 2.19 provides the convergence of the first and Proposition 2.20 gives the convergence of the second term to zero. Changing u, resp. ρ_1 by v, resp. ρ_2, we obtain the same result for the second component of the solution.
Since convergence with respect to the flat metric implies weak* convergence, the result follows. □

An illustration of the result Theorem 2.11, *i*), see Figure 2.2.

2.6.5 Convergence result for discrete Ω_{max}

The last assertion we have to prove is Theorem 2.11, *iii*). We know that the total mass stays strictly positive for all times (Lemma 2.14) and that the solution cannot decay in the maximum of the function a (Lemma 2.16). Hence it is obvious, that the solution converges to a sum of Dirac measures if Ω_{max} is a discrete set. Nevertheless, it is interesting to investigate how the total mass is distributed between two Dirac deltas. If the shape of the function a at its maximum points is in a certain sense "similar" it is possible to characterise the relation between the masses concentrated in each Dirac delta.

Proposition 2.22. *Let Assumption 1 hold. Let the set Ω_{max} consist of two points $\bar{x}_1, \bar{x}_2$. Let U be an open neighbourhood of $\bar{x}_1$. If there exists a diffeomorphism $\Phi \in C^1(U)$ such that*

$$\begin{aligned} \Phi(\bar{x}_1) &= \bar{x}_2, \\ a(x) &= a(\Phi(x)) \quad \textit{for all} \quad x \in U, \end{aligned}$$

then the solution $(u,v)^T$ of system (2.2) converge to stationary measures, which are linear combinations of Dirac measures concentrated in $\bar{x}_1$ and $\bar{x}_2$, multiplied by strictly positive constants $\rho_1^1, \rho_1^2, \rho_2^1, \rho_2^2$, namely

$$u(t,x) \overset{t\to\infty}{\rightharpoonup^*} \rho_1^1\delta_{\bar{x}_1} + \rho_1^2\delta_{\bar{x}_2},$$

$$v(t,x) \overset{t\to\infty}{\rightharpoonup^*} \rho_2^1 \delta_{\bar{x}_1} + \rho_2^2 \delta_{\bar{x}_2}.$$

Proof. The proof makes use of a comparison between the total masses at the two distinct maxima of a. For this purpose choose the diffeomorphism Φ as in the assumptions. Using the first equation of (2.2), we derive an implicit formula for u, namely

$$u(t,x) = u^0(x) \exp\left(\int_0^t \left(\frac{2a(x)}{1+k\rho_2(\tau)} - 1 \right) p \, \mathrm{d}\tau \right).$$

Then we can deduce by changing variables that

$$\begin{aligned}
\int_U u(t,x)\,\mathrm{d}x &= \int_U u^0(x) \exp\left(\int_0^t \left(\frac{2a(x)}{1+k\rho_2(\tau)} - 1 \right) p \, \mathrm{d}\tau \right) \mathrm{d}x \\
&= \int_U u^0(x) \exp\left(\int_0^t \left(\frac{2a(\Phi(x))}{1+k\rho_2(\tau)} - 1 \right) p \, \mathrm{d}\tau \right) \mathrm{d}x \\
&= \int_U \frac{u^0(x)}{u^0(\Phi(x))} u(t,\Phi(x))\,\mathrm{d}x \\
&= \int_{\Phi(U)} \frac{u^0(\Phi^{-1}(y))}{u^0(y)} \left|\det J\Phi(y)\right| u(t,y)\,\mathrm{d}y \\
&= \frac{u^0(\Phi^{-1}(y^*))}{u^0(y^*)} \left|\det J\Phi(y^*)\right| \int_{\Phi(U)} u(t,x)\,\mathrm{d}x.
\end{aligned}$$

In the last equation we used the mean value formula for integrals with some $y^* \in \Phi(U)$. By Corollary 2.17 $u(\cdot, y)$ converges to zero for all $y \in \Phi(U) \setminus B_r(x_2)$ for every $r > 0$. Hence, for t large enough $y^* \in B_r(x_2)$. Hence we obtain

$$\lim_{t\to 0} \int_U u(t,x)\,\mathrm{d}x = \frac{u^0(\Phi^{-1}(y^*))}{u^0(y^*)} \left|\det J\Phi(y^*)\right| \lim_{t\to\infty} \int_{\Phi(U)} u(t,y)\,\mathrm{d}y.$$

Note that y^* still depends on the radius of the ball around x_2. Letting r tend to zero in combination with the continuity of u^0 and Φ yields

$$\lim_{t\to\infty} \int_U u(t,x)\,\mathrm{d}x = \frac{u^0(x_1)}{u^0(x_2)} \left|\det J\Phi(x_2)\right| \lim_{t\to\infty} \int_{\Phi(U)} u(t,y)\,\mathrm{d}y. \tag{2.21}$$

Since Φ is a diffeomorphism $|\det J\Phi(x_2)| \neq 0$ and the initial data is also chosen such that it is positive, see Assumption 1. Accordingly,

$$\lim_{t\to\infty} \int_U u(t,x)\,\mathrm{d}x = 0 \quad \Leftrightarrow \quad \lim_{t\to\infty} \int_{\Phi(U)} u(t,x)\,\mathrm{d}x = 0.$$

By the strict positivity of the total mass, Lemma 2.14, the integrals cannot be both zero, so they both have to be positive.
Denoting

$$\rho_1^1 = \lim_{t\to\infty} \int_U u(t,x)\,\mathrm{d}x \quad \text{and} \quad \rho_1^2 = \lim_{t\to\infty} \int_{\Phi(U)} u(t,y)\,\mathrm{d}y$$

it holds $\rho_1^1 + \rho_1^2 = \bar{\rho}_1$ and $u(t,x) \rightharpoonup^* \rho_1^1\delta_{\bar{x}_1} + \rho_1^2\delta_{\bar{x}_2}$.
The result for $v(t,x)$ follows from the fact that we already know that if $u(t,x)$ vanishes, so does $v(t,x)$, see Corollary 2.17, and that for some arbitrary set $U \subset \Omega$,

$$\int_U u(t,x)\,\mathrm{d}x \leq M_1 \int_U v(t,x)\,\mathrm{d}x,$$

see Lemma 2.7. Choose

$$\rho_2^1 := \lim_{t\to\infty} \int_U v(t,x)\,\mathrm{d}x \quad \text{and} \quad \rho_2^2 = \lim_{t\to\infty} \int_{\Phi(U)} v(t,x)\,\mathrm{d}x.$$

□

An illustration of the coexistence of two different species is given by Figure 2.4.

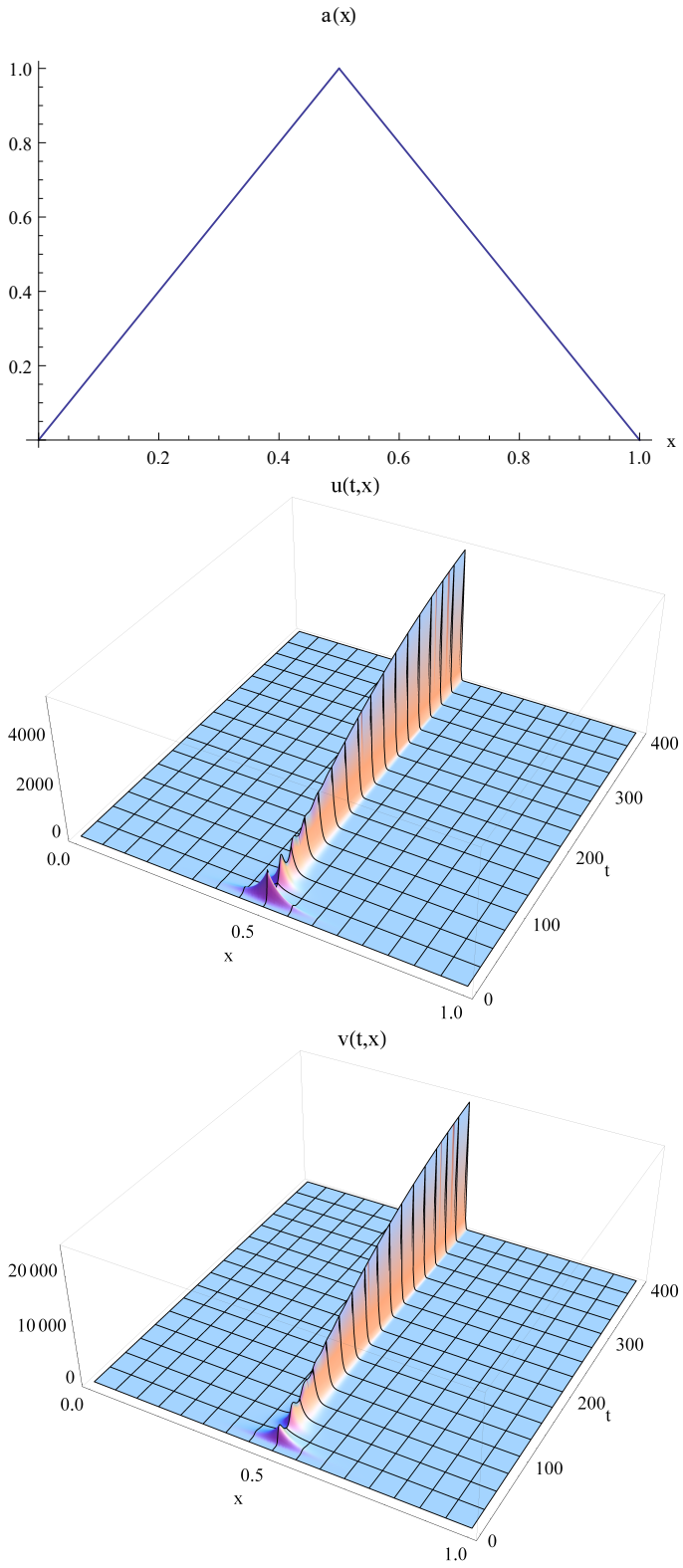

Figure 2.2: Self-renewal rate a and the corresponding concentration effect of the solution $(u, v)^T$. The simulation used the parameters $k = 0.01, p = 0.9, d = 0.2, a(x) = 2x$ for $0 \leq x < 0.5$ and $2 - 2x$ for $0.5 \leq x \leq 1, u^0(x) = 1, v^0(x) = 1$.

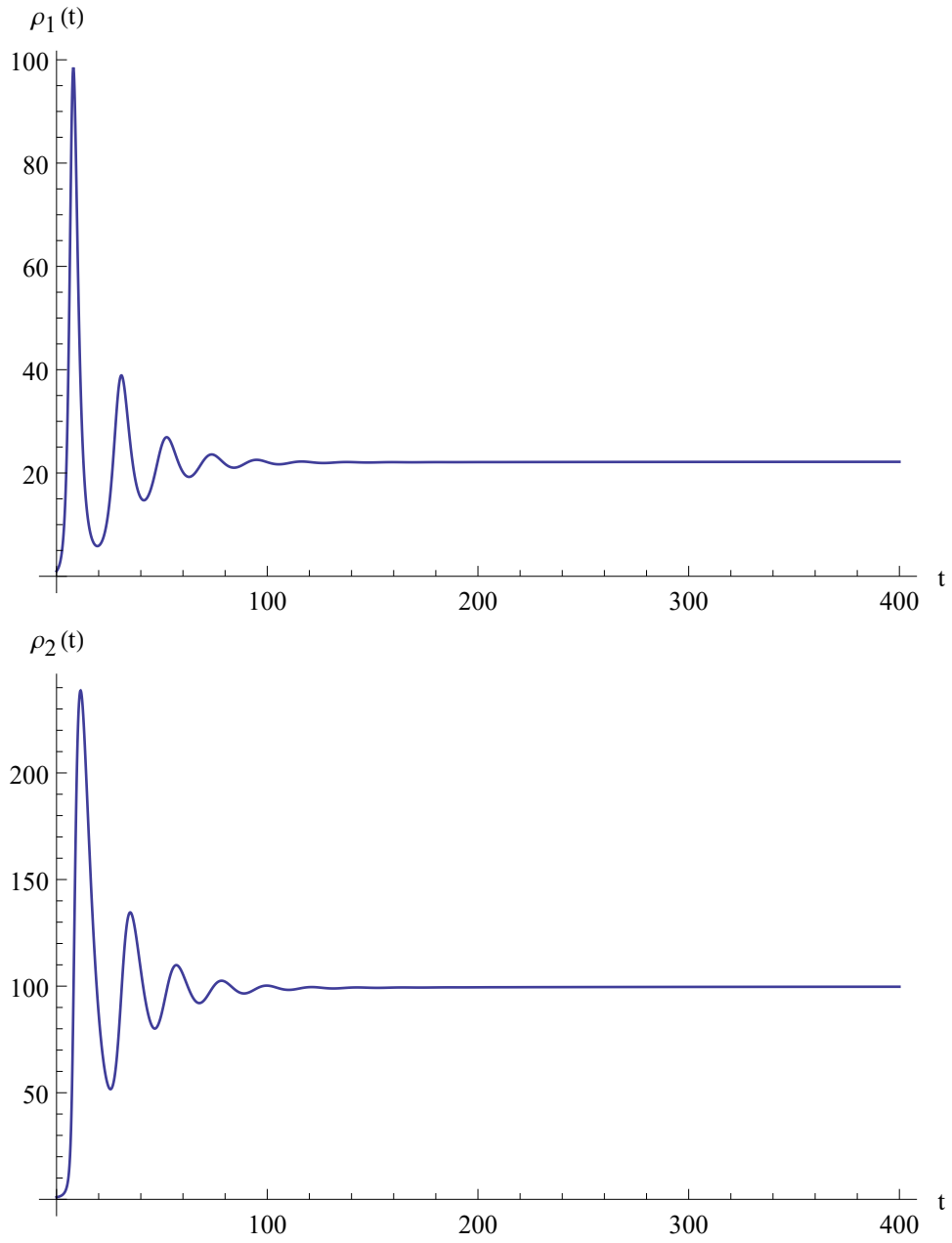

Figure 2.3: Simulation of total masses with parameters $k = 0.01, p = 0.9, d = 0.2, a(x) = 2x$ for $0 \leq x < 0.5$ and $2 - 2x$ for $0.5 \leq x \leq 1, u^0(x) = 1, v^0(x) = 1$.

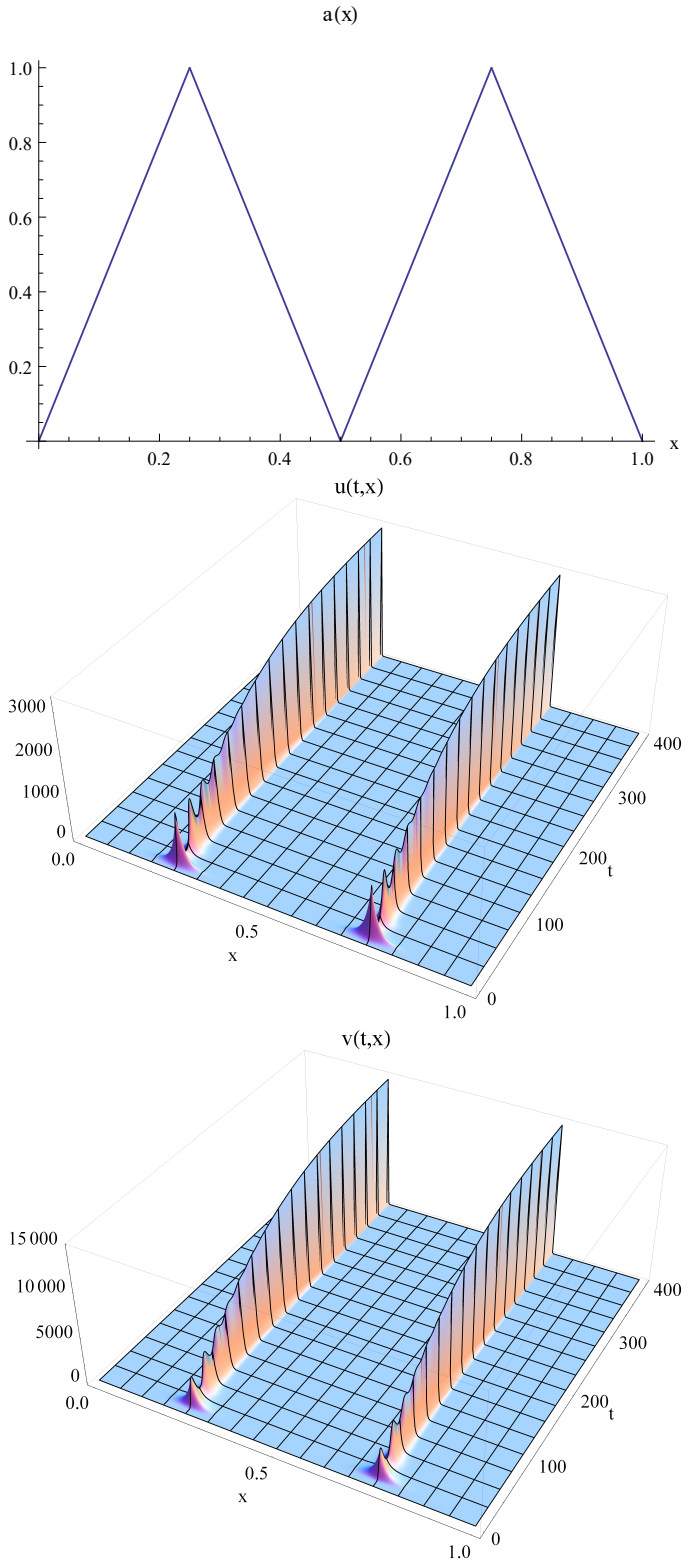

Figure 2.4: Simulation depicting coexistence with parameters $k = 0.01, p = 0.9, d = 0.2, a(x) = 4x$ for $0 \leq x < 0.25$, $2 - 4x$ for $0.25 \leq x \leq 0.5$, $4(x - 0.5)$ for $0.5 < x < 0.75$ and $4(1 - x)$ for $0.75 \leq x \leq 1, u^0(x) = 1, v^0(x) = 1$.

2.7 Generalization to measure spaces

In the previous section we have seen that if we start with a function in $L^1(\Omega) \cap C(\Omega)$ the solution of equation (2.2) will be continuous for all finite times but will converge to a Dirac measure eventually. Since this convergence is strongly dependent on pointwise estimates it is not possible to lessen the assumption on the initial data without changing the proofs profoundly.
This section is intended to address this issue. In other words, is it possible to choose the initial datum in $\mathcal{M}^+(\Omega)$ and achieve a convergence of the obtained solution to a Dirac measure if time tends to infinity? For scalar IDEs there already exist results showing this behaviour, see [2, 4]. The novelty of this section lies in the proposal how to treat a system of IDEs formulated in measure spaces instead of a scalar model.

We investigate the following initial value problem

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\mu(t) &= \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p\mu(t), \\ \frac{\mathrm{d}}{\mathrm{d}t}\nu(t) &= 2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right) p\mu(t) - d\nu(t), \\ \mu(0) &= \mu^0, \\ \nu(0) &= \nu^0, \end{cases} \tag{2.22}$$

where $\rho_2(t) = \int\limits_\Omega \mathrm{d}\nu(t)$.
The aim is to find a solution $(\mu, \nu)^T$ of (2.22) which belongs to the space $C^1([0,T), (\mathcal{M}^+(\Omega))^2)$. To do so, we will need the following assumptions

Assumption 2.

1. $\Omega \subset \mathbb{R}^n$ *is open and bounded*
2. $a \in C(\Omega)$ *with* $0 < a(x) < 1$ *for all* $x \in \Omega$, *let* $\bar{a} := \max_{x\in\Omega} a(x) > \frac{1}{2}$ *with* $\bar{x} = \mathrm{argmax}_{x\in\Omega} a(x)$ *and* $a \neq const$
3. $\mu^0, \nu^0 \in \mathcal{M}^+(\Omega)$ *and for all* $\delta > 0$ *it holds* $\mu^0(B_\delta(\bar{x})) > 0$, $\nu^0(B_\delta(\bar{x})) > 0$
4. $k, p, d \in \mathbb{R}_+$ *are constants*

System (2.22) is an abbreviated description of the equation we need to analyse, because it omits the argument concerning the sets on which the measures act. Hence we need to clarify what we mean by a differential equation in measure spaces and also what we call a solution. Since in system (2.2) no space derivative is involved the generalisation of the notion of a solution in measure spaces is straight forward.

Definition 2.23. *Let $\mathcal{B}(\Omega)$ be the Borelian σ-algebra and let $B \in \mathcal{B}(\Omega)$. Let us consider the differential equation*

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\mu(t)(B) &= \int\limits_B \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p \,\mathrm{d}\mu(t), \\ \frac{\mathrm{d}}{\mathrm{d}t}\nu(t)(B) &= \int\limits_B 2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right) p \,\mathrm{d}\mu(t) - d\nu(t)(B), \\ \mu(0)(B) &= \mu^0(B), \\ \nu(0)(B) &= \nu^0(B). \end{cases} \tag{2.23}$$

We call the tuple $(\mu,\nu)^T$ a solution, if $(\mu,\nu)^T \in C^1(\mathbb{R}_+, (\mathcal{M}^+(\Omega))^2)$, i.e. $\mu(t)(\cdot), \nu(t)(\cdot)$ are continuously differentiable functions and $\mu(\cdot)(B), \nu(\cdot)(B)$ are positive Radon measures, and $(\mu,\nu)^T$ solves equation (2.23) for all $t \in \mathbb{R}_+$ and all $B \in \mathcal{B}(\Omega)$.

2.7.1 Existence and uniqueness

Proposition 2.24. *Let Assumption 2 hold, then there exists a unique local-in-time solution $(\mu,\nu)^T \in C^1([0,T), (\mathcal{M}^+(\Omega))^2)$.*

The proof is almost exactly like the proof of Proposition 2.6. It is given here, because it needs minor adjustments to fit the measure setting.

Proof. We want to apply the Banach space version of Picard-Lindelöf to equation (2.22). Therefore, we rewrite (2.22) in a more abstract form by setting $\xi(t) := (\mu(t), \nu(t))$ and defining a function $f : \mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega) \to \mathcal{M}^+(\Omega) \times \mathcal{M}^+(\Omega)$ by

$$f(\xi(t)) := \left(\left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p\mu(t), 2\left(1 - \frac{a(x)}{1+k\rho_2(t)}\right) p\mu(t) - d\nu(t)\right)^T.$$

Equipped with this definition, we can write (2.22) as

$$\frac{\mathrm{d}}{\mathrm{d}t}\xi(t) = f(\xi(t)). \tag{2.24}$$

Hence we have to show that the right-hand side of (2.24) is Lipschitz-continuous with respect to ξ. Then we calculate with $\xi^1 = (\mu^1,\nu^1)^T$, $\xi^2 = (\mu^2,\nu^2)^T$, $\rho_2^1 = \int_\Omega \mathrm{d}\nu^1(t)$ and $\rho_2^2(t) = \int_\Omega \mathrm{d}\nu^2(t)$

$$\begin{aligned} \left\|f(\xi^1(t)) - f(\xi^2(t))\right\|_{TV} &= \left\|\left(\frac{2a(x)}{1+k\rho_2^1(t)} - 1\right) p\mu^1(t) - \left(\frac{2a(x)}{1+k\rho_2^2(t)} - 1\right) p\mu^2(t)\right\|_{TV} \\ &\quad + \left\|2\left(1 - \frac{a(x)}{1+k\rho_2^1(t)}\right) p\mu^1(t) - d\nu^1(t)\right. \end{aligned}$$

$$
\begin{aligned}
& -2\left(1-\frac{a(x)}{1+k\rho_2^2(t)}\right)p\mu^2(t)+d\nu^2(t)\Big\|_{TV} \\
\leq\ & p\left\|\mu^1(t)-\mu^2(t)\right\|_{TV} \\
& +\left\|\frac{2a(x)p}{1+k\rho_2^1(t)}\mu^1(t)-\frac{2a(x)p}{1+k\rho_2^2(t)}\mu^2(t)\right\|_{TV} \\
& +d\left\|\nu^1(t)-\nu^2(t)\right\|_{TV}+2p\left\|\mu^1(t)-\mu^2(t)\right\|_{TV} \\
& +\left\|\frac{2a(x)p}{1+k\rho_2^1(t)}\mu^1(t)-\frac{2a(x)p}{1+k\rho_2^2(t)}\mu^2(t)\right\|_{TV} \\
\leq\ & 3p\left\|\mu^1(t)-\mu^2(t)\right\|_{TV}+d\left\|\nu^1(t)-\nu^2(t)\right\|_{TV} \\
& +4\bar{a}p\left\|\frac{\mu^2}{1+k\rho_2^2(t)}-\frac{\mu^1(t)}{1+k\rho_2^1(t)}\right\|_{TV}.
\end{aligned}
$$

Having a look at the last term on the right-hand side we can estimate it by

$$
\begin{aligned}
\left\|\frac{\mu^2(t)}{1+k\rho_2^2(t)}-\frac{\mu^1(t)}{1+k\rho_2^1(t)}\right\|_{TV} &= \left\|\frac{\mu^2(t)}{1+k\rho_2^2(t)}-\frac{\mu^2(t)}{1+k\rho_2^1(t)}+\frac{\mu^2(t)}{1+k\rho_2^1(t)}\right. \\
&\quad \left.-\frac{\mu^1(t)}{1+k\rho_2^1(t)}\right\|_{TV} \\
&\leq \left\|\mu^2(t)\right\|_{TV}\left|\rho_2^1(t)-\rho_2^2(t)\right|+\left\|\mu^2(t)-\mu^1(t)\right\|_{TV} \\
&\leq \left\|\mu^2(t)\right\|_{TV}\left\|\nu^1(t)-\nu^2(t)\right\|_{TV} \\
&\quad +\left\|\mu^1(t)-\mu^2(t)\right\|_{TV}.
\end{aligned}
$$

Combining this inequality with the one above we end up with

$$
\begin{aligned}
\left\|f(\xi^1(t))-f(\xi^2(t))\right\|_{TV} &\leq p(3+4\bar{a})\left\|\mu^1(t)-\mu^2(t)\right\|_{TV} \\
&\quad +\left(d+4\bar{a}p\left\|\mu^2(t)\right\|_{TV}\right)\left\|\nu^1(t)-\nu^2(t)\right\|_{TV} \\
&\leq C\left(\left\|\mu^1(t)-\mu^2(t)\right\|_{TV}+\left\|\nu^1(t)-\nu^2(t)\right\|_{TV}\right) \\
&= C\left\|\xi^1(t)-\xi^2(t)\right\|_{TV}
\end{aligned}
$$

with $C = \max\{p(3+4\bar{a}), d+4\bar{a}p\left\|\mu^2(t)\right\|_{TV}\}$. By Picard-Lindelöf, we obtain a local-in-time solution. □

Since the computations for the total masses in Section 2.5.2 were independent of the domain of integration, these results transfer directly to the measures μ and ν. Thus we obtain

Lemma 2.25. *Under Assumption 2 there exists a constant $M_1 > 0$ such that for all $t \geq 0$ and all $A \in \mathcal{B}(\Omega)$ with $\nu^0(A) > 0$*

$$\mu(t)(A) \leq M_1 \nu(t)(A).$$

Lemma 2.26. *Under Assumption 2 there exist constants $M_2 > 0$ and $M_3 > 0$ such that for all $t \geq 0$*

$$\rho_1(t) \leq M_2, \quad \rho_2(t) \leq M_3.$$

Lemma 2.27. *Under Assumption 2 there exists $\gamma > 0$ and a constant $M_4 > 0$ such that for all $t \geq 0$ and all $A \in \mathcal{B}(\Omega)$ such that $\mu^0(A) > 0$*

$$\nu(t)(A) \leq M_4(\mu(t)(A))^\gamma$$

for γ small enough.

Lemma 2.28. *Under Assumption 2 there exist constants $M_5 > 0$ and $M_6 > 0$ such that for all $t \geq 0$*

$$\rho_1(t) \geq M_5, \quad \rho_2(t) \geq M_6.$$

The proofs are exactly the same as for Lemma 2.7, Lemma 2.9, Lemma 2.12 and Lemma 2.14, respectively. This is also the reason why the resulting constants in Lemma 2.25 to 2.28 are identical with the constants defined in the proofs of Lemma 2.7 to 2.14.

Theorem 2.29. *There exists a global-in-time unique solution of system* (2.23) $(\mu, \nu) \in C^1([0, \infty), (\mathcal{M}^+(\Omega))^2)$

Proof. Combining Proposition 2.24 with Lemma 2.26 yields the result for global existence in $\mathcal{M}(\Omega)$. The strict positivity and, therefore, a solution in $\mathcal{M}^+(\Omega)$ is due to Lemma 2.28. □

2.7.2 Weak* convergence to a Dirac measure

For the convergence to a Dirac measure the general concept of the proof of Section 2.6.3 can be maintained and only needs adjustment to suit the measure setting. That is, it is necessary to show that the normalised solution of (2.23) defines a Dirac sequence. First we show, that the solution converges to zero for all sets which do not contain the maximum point of a. This can then be utilized to show that the normalised measure converges weakly* to a Dirac measure concentrated in $\bar{x}$.

Lemma 2.30. *Let Assumption 2 hold, then there exists $\delta^* > 0$ such that for all $\delta < \delta^*$ holds*

$$\mu(t)(\Omega \setminus B_\delta(\bar{x})) \to 0,\ \nu(t)(\Omega \setminus B_\delta(\bar{x})) \to 0 \quad \text{as } t \to \infty$$

Proof.

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\frac{\mu(t)(\Omega \setminus B_\delta(\bar{x}))}{\mu(t)(B_\delta(\bar{x}))} &= \int\limits_{\Omega\setminus B_\delta(\bar{x})} \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p \,\mathrm{d}\mu(t) \cdot (\mu(t)(B_\delta(\bar{x})))^{-1} \\
&\quad - \frac{\mu(t)(\Omega \setminus B_\delta(\bar{x}))}{\mu(t)(B_\delta(\bar{x}))} \int\limits_{B_\delta(\bar{x})} \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p \,\mathrm{d}\mu(t) \\
&\quad \cdot (\mu(t)(B_\delta(\bar{x})))^{-1} \\
&= \frac{\mu(t)(\Omega \setminus B_\delta(\bar{x}))}{\mu(t)(B_\delta(\bar{x}))} \cdot \\
&\quad \left[\int\limits_{\Omega\setminus B_\delta(\bar{x})} \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p \,\mathrm{d}\mu(t) \cdot (\mu(t)(\Omega \setminus B_\delta(\bar{x})))^{-1}\right. \\
&\quad \left. - \int\limits_{B_\delta(\bar{x})} \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p \,\mathrm{d}\mu(t) \cdot (\mu(t)(B_\delta(\bar{x})))^{-1}\right] \\
&= \frac{\mu(t)(\Omega \setminus B_\delta(\bar{x}))}{\mu(t)(B_\delta(\bar{x}))} \frac{2p}{1+k\rho_2(t)} \cdot \\
&\quad \left[\fint_{\Omega\setminus B_\delta(\bar{x})} a(x) \,\mathrm{d}\mu(t) - \fint_{B_\delta(\bar{x})} a(x) \,\mathrm{d}\mu(t)\right].
\end{aligned}$$

Here

$$\fint_A g(x) \,\mathrm{d}\mu = \frac{1}{\mu(A)} \int_A g(x) \,\mathrm{d}\mu,$$

for a function $g \in C(\Omega)$ and some $A \in \mathcal{B}(\Omega)$ with $\mu(A) > 0$. Let $\bar{a} = a(\bar{x})$, then

$$\fint_\Omega a(x) \,\mathrm{d}\mu(t) < \bar{a}, \tag{2.25}$$

since we chose the function a not to be constant. We want to show

$$\exists\, \delta^* > 0\ \forall\, \delta < \delta^*\ \forall\, t \geq 0: \quad \fint_{\Omega\setminus B_\delta(\bar{x})} a(x) \,\mathrm{d}\mu(t) - \fint_{B_\delta(\bar{x})} a(x) \,\mathrm{d}\mu(t) < 0.$$

Let us assume instead

$$\forall\, \delta^* > 0\ \exists \delta < \delta^*\ \exists\, t^* \geq 0: \quad \fint_{\Omega\setminus B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t^*) - \fint_{B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t^*) \geq 0.$$

Then it holds

$$\fint_{\Omega\setminus B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t^*) \geq \fint_{B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t^*).$$

Taking the limit $\delta^* \to 0$, hence $\delta \to 0$, we obtain

$$\fint_{\Omega} a(x)\,\mathrm{d}\mu(t^*) = \lim_{\delta\to 0} \fint_{\Omega\setminus B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t^*) \geq \lim_{\delta\to 0} \fint_{B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t^*) = \bar{a},$$

which contradicts inequality (2.25). Denoting now with $\delta < \delta^*$

$$h(t) = \fint_{\Omega\setminus B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t) - \fint_{B_\delta(\bar{x})} a(x)\,\mathrm{d}\mu(t),$$

we have $h(t) < 0$ for all $t \in \mathbb{R}_+$ and we can estimate using Lemma 2.26

$$\frac{\mathrm{d}}{\mathrm{d}t}\frac{\mu(t)(\Omega\setminus B_\delta(\bar{x}))}{\mu(t)(B_\delta(\bar{x}))} \leq \frac{1}{1+kM_3} h(t) \frac{\mu(t)(\Omega\setminus B_\delta(\bar{x}))}{\mu(t)(B_\delta(\bar{x}))}.$$

Solving this inequality yields

$$\frac{\mu(t)(\Omega\setminus B_\delta(\bar{x}))}{\mu(t)(B_\delta(\bar{x}))} \leq \frac{\mu^0(\Omega\setminus B_\delta(\bar{x}))}{\mu^0(B_\delta(\bar{x}))} e^{\frac{1}{1+kM_3}\int_0^t h(s)\,\mathrm{d}s} \xrightarrow{t\to\infty} 0.$$

Because of the boundedness of $\mu(t)(\Omega) = \rho_1(t)$, see Lemma 2.26, it has to hold $\mu(t)(\Omega\setminus B_\delta(\bar{x})) \to 0$ for $t \to \infty$.
This convergence to zero in combination with Lemma 2.27 yields convergence to zero for the second component of the solution, i.e. $\nu(t)(\Omega\setminus B_r(\bar{x})) \to 0$ for $t \to \infty$. □

At this point we know that the measure μ is strictly positive for all times and additionally, that it converges to zero for all sets which do not contain the point $\bar{x}$. As in Section 2.6.3, these two properties suffice to prove that the normalised measure μ converges weakly* to a Dirac measure which is located in $\bar{x}$. The Portmanteau theorem, [9, Kapitel *IV*, §30, Satz 30.10] provides a useful criterion to prove the convergence. For the sake of convenience it is stated here again with adjusted notation.

Lemma 2.31. *For all sequences* $(\mu_n)_{n\in\mathbb{N}} \subset \mathcal{M}_1^+(X) := \{\mu \in \mathcal{M}^+(\Omega) \,|\mu(\Omega) = 1\}$ *the following two assertions are equivalent:*

i) μ_n *converges weakly* to* $\mu \in \mathcal{M}_1^+(X)$

ii) For all closed sets $A \subset X$

$$\limsup_{n\to\infty} \mu_n(A) \leq \mu(A).$$

Equipped with this tool we can prove

Lemma 2.32. *The measure* $\frac{\mu(t)(A)}{\mu(t)(\Omega)}$ *converges weakly* to a Dirac measure, which is concentrated in the maximum of a, that is*

$$\frac{\mu(t)}{\mu(t)(\Omega)} \rightharpoonup^* \delta_{\bar{x}} \quad \text{in } \mathcal{M}^+(\Omega)$$

as t tends to infinity.

Proof. First of all, we have to see that $\frac{\mu(t)}{\mu(t)(\Omega)}$ is a probability measure. This is immediate since $\mu(t)$ is a positive Radon measure and $\frac{\mu(t)(\Omega)}{\mu(t)(\Omega)} = 1$ for all $t \geq 0$. Let us denote $\delta_t(A) = \frac{\mu(t)(A)}{\mu(t)(\Omega)}$. According to Lemma 2.31 it suffices to show that

$$\limsup_{t\to\infty} \delta_t(A) \leq \delta_{\bar{x}}(A)$$

for all closed subsets A of X. Since we are interested in the convergence to a Dirac measure it is enough to consider two cases.

Case 1: $\bar{x} \notin A$
In this case we can assume that A can be written as $A = \Omega \setminus B_\delta(\bar{x})$ and we have

$$\delta_{\bar{x}}(A) = 0 = \limsup_{t\to\infty} \delta_t(A)$$

according to Lemma 2.30.

Case 2: $\bar{x} \in A$
Here we can assume that $A = \overline{B_\delta(\bar{x})}$ and we obtain

$$\limsup_{t\to\infty} \delta_t(A) \leq 1 = \delta_{\bar{x}}(A)$$

by construction of δ_t. Thus we can conclude that $\delta_t \rightharpoonup^* \delta_{\bar{x}}$ for $t \to \infty$. □

Lemma 2.33. *The total masses $\rho_1(t) = \mu(t)(\Omega)$, $\rho_2(t) = \nu(t)(\Omega)$ converge to $\bar{\rho}_1$, $\bar{\rho}_2$ from Proposition 2.20, respectively, namely,*

$$\lim_{t\to\infty} |\rho_1(t) - \bar{\rho}_1| = 0, \quad \lim_{t\to\infty} |\rho_2(t) - \bar{\rho}_2| = 0.$$

Proof. We want to apply Lemma 2.21 to equation (2.23). We can rewrite the equation in the same way as in the proof of Proposition 2.20, i.e.

$$\begin{aligned} \frac{\mathrm{d}}{\mathrm{d}t}\rho_1(t) &= \int_\Omega \left(\frac{2a(x)}{1+k\rho_2(t)} - 1\right) p \,\mathrm{d}\mu(t) \\ &= \left(\frac{2\bar{a}}{1+k\rho_2(t)} - 1\right) p\rho_1(t) + \underbrace{\frac{2p}{1+k\rho_2(t)} \int_\Omega (a(x) - \bar{a}) \,\mathrm{d}\mu(t)}_{=:f(t)}. \end{aligned}$$

According to Lemma 2.21, we need to prove that $f \in C^1(\mathbb{R}_+)$, $\lim_{t\to\infty} |f(t)| = 0$ and that the solution obtained by the perturbation is still positive. By Theorem 2.29 we obtain that $f \in C^1(\mathbb{R}_+)$. Lemma 2.28 guarantees that the perturbed solution is still positive. The only thing left to show is the convergence to zero. Using Lemma 2.26, Lemma 2.25 and Lemma 2.32 yields

$$\begin{aligned} \lim_{t\to\infty} \left| \frac{2p}{1+k\rho_2(t)} \int_\Omega (a(x) - \bar{a}) \,\mathrm{d}\mu(t) \right| &\leq \lim_{t\to\infty} \frac{2pM_1}{k\rho_1(t)} \int_\Omega |a(x) - \bar{a}| \,\mathrm{d}\mu(t) \\ &= \frac{2pM_1}{k} |\bar{a} - \bar{a}| = 0. \end{aligned}$$

Analogously, the result can be obtained for ρ_2. □

These results lead to the following

Theorem 2.34. *The solution $(\mu(t), \nu(t))^T$ converges with respect to the flat metric to a Dirac measure concentrated in $\bar{x}$ as t tends to infinity.*

Proof. We use the estimate

$$\rho_F(\mu(t), \bar{\rho}_1\delta_{\{\bar{x}\}}) \leq \min\{\rho_1(t), \bar{\rho}_1\} W_1\left(\frac{\mu(t)}{\rho_1(t)}, \delta_{\{\bar{x}\}}\right) + |\rho_1(t) - \bar{\rho}_1|.$$

Now according to Lemma 2.33, $|\rho_1(t) - \bar{\rho}_1| \to 0$. Hence it remains to show that the 1-Wasserstein-metric converges to zero.

$$\begin{aligned} W_1\left(\frac{\mu(t)}{\rho_1(t)}, \delta_{\bar{x}}\right) &= \sup\left\{ \int_\Omega \psi(x) \frac{1}{\rho_1(t)} \,\mathrm{d}\mu(t) - \int_\Omega \psi(x)\,\mathrm{d}\delta_{\bar{x}} \,\middle|\, \psi \in W^{1,\infty}(\Omega), \|\partial_x \psi\|_\infty \leq 1 \right\} \\ &= \sup\left\{ \int_\Omega \psi(x) \frac{1}{\rho_1(t)} \,\mathrm{d}\mu(t) - \psi(\bar{x}) \,\middle|\, \psi \in W^{1,\infty}(\Omega), \|\partial_x \psi\|_\infty \leq 1 \right\} \\ &\overset{t\to\infty}{\longrightarrow} \sup\left\{ \psi(\bar{x}) - \psi(\bar{x}) \,\middle|\, \|\partial_x \psi\|_\infty \leq 1 \right\} = 0. \end{aligned}$$

The argument works analogously for ν. □

Biological implications

We have seen that regardless of the chosen initial data we obtain under suitable assumptions that the solutions of (2.2) and (2.23) converge to a Dirac measure for time tending to infinity. Biologically, this result can be interpreted as extinction of all cell types, which do not have the highest self-renewal fraction. Thus the self-renewal potential governs the selection process. More precisely, Theorem 2.11 shows that, in a well-mixed cell production system, a negative non-linear feedback such as that proposed in [38, 39, 47] leads to the selection of the subpopulation with the highest self-renewal potential. The assumption that the cell population is well-mixed leads to the non-local effect and is modelled using the integral term. This assumption reflects well the structure of the blood system, see for instance [51].

Consequently, our results suggest that the greater clonal heterogeneity observed in solid cancers compared to blood cancers may be due to spatial effects in cell-cell interactions. Furthermore, the results stress the importance of self-renewal in cancer dynamics and allow concluding that slowly proliferating cancer cells are able to explain clinical dynamics and observations such as treatment resistance. The importance of this observation in the context of leukemia evolution, response to chemotherapy and dynamics of the disease relapses is discussed in [61]. The results obtained allow explaining recent experimental results on clonal selection in AML (acute myeloid leukemia) during disease development and relapse after chemotherapy [29].

Chapter 3

Extended system of non-linear integro-differential equations

We have seen in Chapter 2 how the solution of system (2.2) behaves for infinite times. Although it is known that pure selection can lead to a mass concentration, see [2, 4] for a measure setting, it is not so evident in the system case. More often a different setting is considered in the context of concentration effects. It includes the idea of mutation. There is still no agreement on how to model mutation, though. Essentially, there are two ways to do that.

Firstly, it is done by adding a diffusive term, most often given by the Laplacian, see [43, 44, 49, 53]. If mutation is modelled by diffusion, mutation can occur at all times within a cell's life cycle. The most important implication of that is that via diffusion cells can mutate although they are not proliferating. Consequently, mutation does not change the overall amount of individuals and just their genetic expression, total mass should be unaffected by mutation. Due to Green's formula a conservation of masses is guaranteed. The disadvantages are that the modelling aspect of the Laplacian as mutation is debatable. Diffusion allows only mutation to occur from one trait to neighbouring traits without the possibility to "jump" over some traits to reach a specific trait directly. In this sense mutation modelled by diffusion displays "small mutations". From a mathematical point of view the diffusive ansatz provides nice properties of the obtained solution and a huge library of results concerning semi-linear parabolic equations. Nevertheless, as the references above show, the difficulty lies in the characterisation of the long-term behaviour.

Secondly, mutation can be modelled by adding an integral operator, see for instance [16, 17, 18, 27]. If this approach is taken, mutations can solely occur during proliferation and excludes the ability to mutate without cell division. This is justifiable because the majority of mutations do occur during proliferation, see [32, Kapitel 10],

[5, Chapter 9]. This inaccuracy regarding the amount of mutations is compensated by the more accurate description of the actual change in genetic expressions. In contrast to the diffusive ansatz it is possible, due to the integral kernel, to characterise the aforementioned jumps in the traits. In this sense, mutation modelled by integral operators displays "rare mutation". The mathematical advantage of integral operators is that they admit convenient properties, like compactness. The disadvantage is the non-local structure which has to be dealt with and which makes the analysis more complicated.
Both approaches have still one aspect in common: They flatten out the sharp spikes, which occur in system (2.2), compare Figure 2.2 and Figure 3.1. This effect prevents the solution to exhibit a concentration phenomenon. Still, it is possible to investigate, whether the obtained steady states converge, if the diffusion or integral coefficient tends to zero.
Although it is known that convergence of steady states to Dirac measures can occur in both models with diffusion or integral operators as mutation, see the references above, the methods to obtain these convergences are completely different. In the regime of a reaction-diffusion equation (RDE), the most common ansatz is to transform the RDE into a Hamilton-Jacobi equation, for which the viscosity solution provides the desired convergence result. For scalar equations the WKB-method is the usual ansatz, which does this transformation. In the case of a system, it strongly depends on the structure, because it is necessary to transform a system into a scalar Hamilton-Jacobi equation.
In contrast if mutation is modelled by an integral term, the mathematical tools are given by an infinite dimensional version of the Perron-Frobenius theorem, which restricts the method to positive operators.
For model (2.2) we take the second approach.

3.1 Preliminary results and definitions

For the purpose of studying the steady states of the extended system we want to use the theoretical framework of Banach spaces, which are endowed with an order. This is reasonable because we are only interested in steady state solutions which are non-negative. Naturally, an order in Banach spaces cannot be complete in general but only be a partial order. This means, that it is necessary to define how the ordering is working and what kind of Banach space we obtain after the introduction of the order. Before we can define the appropriate Banach space we need, we have

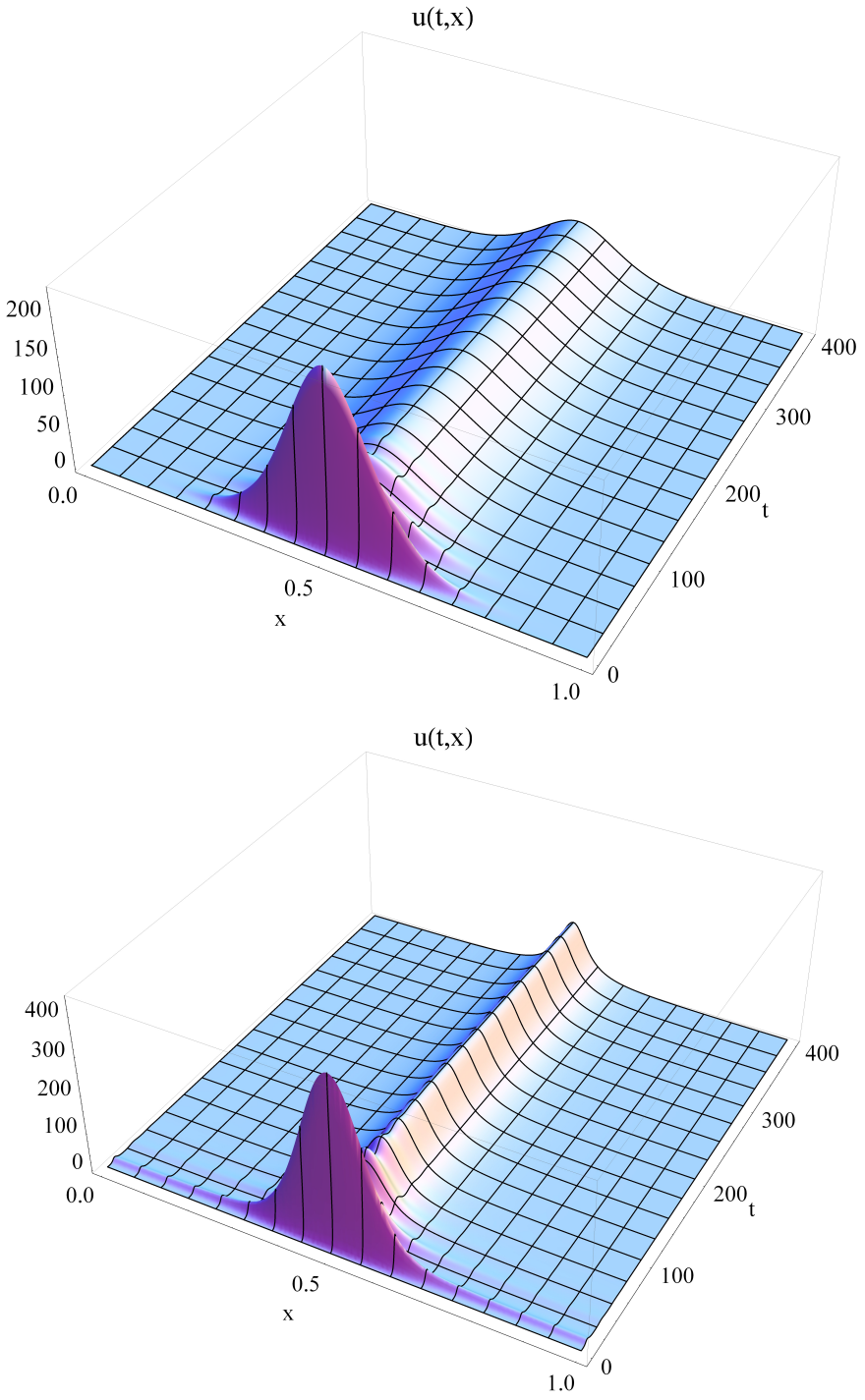

Figure 3.1: The upper simulation depicts the solution for system (2.2) with diffusion (coefficient $\varepsilon = 0.01$) and the lower with an integral operator (coefficient $\varepsilon = \frac{3}{4}$)

to introduce several other concepts. These definitions can be found in [55, Chapter I, §1], and are summarized in

Definition 3.1. *A vector space E over $\mathbb{R}$, endowed with an order relation $\leq$, is called an ordered vector space if and only if for all $x, y, z \in E$ and all $\lambda \in \mathbb{R}_+$*

$$\begin{aligned} x \leq y &\Rightarrow x + z \leq y + z, \\ x \leq y &\Rightarrow \lambda x \leq \lambda y. \end{aligned}$$

We call an ordered vector space a vector lattice if for all $x, y \in E$ holds
$x \vee y := \sup\{x, y\}, x \wedge y := \inf\{x, y\} \in E$.
We define

$$|x| := x \vee (-x) = x^+ - x^-,$$

where $x^+ = x \vee 0$, $x^- = (-x) \vee 0$.

So far we only needed a vector space to define an order. Since a vector space has little structure we were completely free how to choose an order. However, introducing a norm in a vector space raises a fundamental question for the order: Is the order contradictory to the norm? In the best case the ordering should be reflected in the norm and should not produce counter intuitive relations. This explains the following definition coming from [55, Chapter I, §5, Definition 5.1].

Definition 3.2. *Let E be a vector lattice. A semi-norm (norm) p on E is called a lattice semi-norm (norm) if for all $x, y \in E$*

$$|x| \leq |y| \Rightarrow p(x) \leq p(y).$$

If p is a lattice norm on E, the pair (E, p) is called a normed (vector) lattice; if in addition (E, p) is complete, it is called a Banach lattice.

The example of a Banach lattice which is most important for our framework is $\left(L^1(\Omega), \|.\|_{L^1(\Omega)}\right)$ endowed with the order

$$f \leq g :\Leftrightarrow f(x) \leq g(x), \quad \text{for almost every } x \in \Omega.$$

Note that

$$f \geq g :\Leftrightarrow g \leq f.$$

By the monotonicity of the integral it is immediate that $L^1(\Omega)$ in combination with the order above is a Banach lattice. The space $L^1(\Omega)$ is also a good counterexample

for an ordered vector space which does not satisfy the compatibility condition of order and norm in Definition 3.2. If we define the order the other way around, namely

$$f \leq g \Leftrightarrow f(x) \geq g(x), \quad \text{for almost every } x \in \Omega,$$

then this order still satisfies the requirement of Definition 3.1, hence $L^1(\Omega)$ endowed with this order is a vector lattice. But it is not a Banach lattice since the order is contradicting the norm relations.

Now that we know how to compare elements of a Banach space with one another, we are able to define positivity. An element f of a Banach space E is called positive if $f \geq 0$. The next step will be to look at operators defined on a Banach lattice, which are order preserving. Namely, let E, F be Banach lattices, then we are interested in linear operators $A : E \to F$ such that the following order preserving property is valid

$$\forall\, f \in E :\ f \geq 0 \Rightarrow Af \geq 0. \tag{3.1}$$

This leads to the definition with its origin in [55, Chapter II, §2, Definition 2.4].

Definition 3.3. *Let E, F be ordered vector spaces and $A : E \to F$ be a linear operator. Then we call A a positive operator if property* (3.1) *holds true.*

The following definition generalises the concept of irreducibility of matrices for linear operators.

Definition 3.4. *Let E be a Banach lattice of dimension bigger than* 1 *and let $L \subset \mathcal{L}(E)$ be a semi-group. Then we say that L is irreducible if and only if*

$$\forall\, x \in E, x > 0\, \forall\, x' \in E', x' > 0\, \exists\, T \in L : \quad \langle Tx, x' \rangle > 0.$$

Note that according to [55, Chapter 3, §8], Definition 3.4 is not the the most general way of defining irreducibility. Since the more general version of the definition does not give us any advantage in the analysis to come, we are content with this more functional analytic definition. The most intuitive example for an irreducible operator is the Laplace operator in the context of the heat equation

$$\begin{cases} \frac{\partial}{\partial t} u(t,x) & = \Delta u(t,x), \quad \text{in } \mathbb{R}_+ \times \mathbb{R}^n \\ u(0,x) & = g(x), \quad \text{for } x \in \mathbb{R}^n. \end{cases}$$

The Laplace operator generates a strongly continuous semi-group $T(t) \subset \mathcal{L}(\mathbb{R}^n)$ on $L^p(\mathbb{R}^n)$, see for instance [30, Chapter II, Section 2]. The semi-group can be computed explicitly for $g \in L^p(\mathbb{R}^n)$

$$T(t)g(x) = \frac{1}{(4\pi t)^{\frac{n}{2}}} \int_{\mathbb{R}^n} e^{-\frac{|x-y|^2}{4t}} g(y)\,\mathrm{d}y.$$

Let us denote the semi-group in light of Definition 3.4 L, i.e. $L = \{T(t)\,|t \in \mathbb{R}_+\}$. So as long as the initial temperature g is not identically zero and positive otherwise, the temperature at any other positive time $t > 0$ is strictly positive. Going back to Definition 3.4 this means, we choose $E = L^p(\mathbb{R}^n)$ and accordingly $E' = L^q(\mathbb{R}^n)$, with conjugated exponent q. Then for an arbitrary $f \in L^q(\mathbb{R}^n), f > 0$, there exists $T \in L$ (equivalently, there exists a time $t^* > 0$ such that $T = T(t^*)$) such that

$$\langle Tg, f\rangle = \int_{\mathbb{R}^n} T(t^*)g(x)f(x)\,\mathrm{d}x > 0.$$

An important corollary of this definition describes how irreducibility can be computed rather simply in the case of an integral kernel operator. It can be found in [55, Chapter V, §6, Example 4].

Corollary 3.5. *Let (X, Σ, μ) be a σ-finite measure space and let $E := L^p(\mu)$ with $1 \leq p < \infty$. Assume that $T \in \mathcal{L}(X)$ is given by the $(\Sigma \times \Sigma)$- measurable kernel $\kappa \geq 0$ on $X \times X$, such that*

$$Tf(t) = \int_X \kappa(s,t)f(s)\,\mathrm{d}\mu(s),\ \textit{a.e. on } [0,\infty),$$

for each $f \in E$. Then T is irreducible if and only if

$$\int_{X\setminus S}\int_S \kappa(s,t)\,\mathrm{d}\mu(s)\,\mathrm{d}\mu(t) > 0$$

for each $S \in \Sigma$ such that $\mu(S) > 0$ and $\mu(X \setminus S) > 0$.
In particular, if $\kappa(t,s) > 0$ for all $(t,s) \in (X \times X)$ then T is irreducible.

Analogously to the finite dimensional case it is possible to specify the dominant eigenvalue of an operator, which is positive and irreducible. In finite dimensions this result is known as the Perron-Frobenius theorem [35, Kapitel 4, §1]. In infinite

dimensions it is possible to prove a similar result which is referred to as the Krein-Rutman theorem. The version presented here is from [25, Theorem 12.3]. For the sake of convenience the theorem here is shortened and slightly adjusted to display better what is important for our purpose.

Theorem 3.6 (Krein-Rutman)**.** *Let E be a Banach lattice and $T \in \mathcal{L}(E)$ a positive, irreducible, compact operator, then the following assertions are true*

i) $r(T) > 0$ is a pole of the resolvent of T of order 1.

ii) $r(T)$ is an algebraically simple eigenvalue of T. The eigenspace is spanned by a quasi-interior eigenvector, i.e. it is spanned by $x \in E$ for which holds

$$\forall\, x' \in E' : \quad \langle x, x' \rangle > 0.$$

iii) $r(T)$ is the only eigenvalue of T having a positive eigenfunction.

As a next step we need to define the determinant of a linear operator. The determinant in finite dimensional spaces is a mapping from the space of matrices to its underlying field. So a good ansatz would be to find a matrix representation of an operator for which we can then define the determinant easily.
According to [37, Chapter 1, §3], this can be done for linear operators with finite dimensional range, namely, let X, Y be real vector spaces and $T : X \to Y$, with $\dim(rg(T)) = M < \infty$ and $\dim X = N < \infty$. Let $x_1, \ldots, x_N$ be a basis of X and let $y_1, \ldots, y_M$ be a basis of $rg(T)$. Then we can write with $\xi_1, \ldots, \xi_N \in \mathbb{R}$

$$Tu = \sum_{k=1}^{N} \xi_i T x_i. \tag{3.2}$$

Each Tx_i, $i = 1, \ldots, N$, can then be represented by the basis in $rg(T)$, i.e.

$$Tx_i = \sum_{j=1}^{M} \tau_{ji} y_j. \tag{3.3}$$

Inserting equation (3.3) into (3.2) yields

$$Tu = \sum_{k=1}^{N} \xi_k \sum_{j=1}^{M} \tau_{jk} y_j = \sum_{j=1}^{M} \sum_{k=1}^{N} \xi_k \tau_{jk} y_j.$$

The $M \times N$ matrix $(\tau_{jk})_{\substack{j=1,\dots,M \\ k=1,\dots,N}}$ is then a matrix representation of the linear operator T. Although this representation is virtually the well known fact, that in finite dimensional spaces all linear mappings are given by a matrix, it is still the key aspect to define the determinant for linear and degenerate operators. The following definition comes from [37, Chapter III, §4.3].

Definition 3.7. *Let X, Y be Banach spaces. A linear operator $T : X \to Y$ is called degenerate if and only if* $\dim(rg(T)) < \infty$.

Knowing how to define the matrix of an operator mapping a finite dimensional space into a finite dimensional space allows now to define the determinant of $Id + T$, if T is a linear, degenerate operator, by restricting the operator to the finite dimensional range.

Definition 3.8. *Let T be a linear, degenerate operator then we define the determinant of $Id + T$ by*

$$\det(Id + T) := \det(Id_{|rg(T)} + T_{|rg(T)}).$$

Another useful property of an operator is the notion of boundedness with respect to different operator. The following definition comes from [37, Chapter IV, §1, p. 190].

Definition 3.9. *Let X be a Banach space, T and A shall be operators with the same domain space X and $D(T) \subset D(A)$. Additionally, let for constants $a, b \in \mathbb{R}_+$ hold*

$$\|Au\| \leq a \|u\| + b \|T\|, \quad u \in D(T),$$

then we call A a T-bounded operator.

Note that bounded, linear operators A are T-bounded for arbitrary T, such that $D(T) \subset D(A)$.
These definition allows for considering the so called Weinstein-Aronszajn determinant. The definition is taken from [37, Chapter IV, §6.1].

Definition 3.10. *Let T be a linear operator and let A be a relatively degenerate operator with respect to T, i.e. A is T-bounded and degenerate. Then for $\zeta \in \rho(T)$ the Weinstein-Aronszajn determinant is given by*

$$\omega(\zeta) := \omega(\zeta; T, A) = \det\left(Id + AR(\zeta, T)\right). \tag{3.4}$$

This determinant is interesting because it allows for deducing the interplay of the spectrum of an operator of the form $T + A$ in terms of the spectrum of T plus the zeroes and poles of the Weinstein-Aronszajn determinant. Before we state the exact result, we need to define two functions which are necessary for the precise formulation.
Let ϕ be some arbitrary meromorphic function defined in a domain Γ of the complex plane. Then we define the multiplicity function $\nu(\zeta, \phi)$ of ϕ by

$$\nu(\zeta,\phi) = \begin{cases} k, & \text{if } \zeta \text{ is a zero of } \phi \text{ of order } k, \\ -k, & \text{if } \zeta \text{ is a pole of order } \phi \text{ of order } k, \\ 0, & \text{for other } \zeta \in \Gamma. \end{cases} \tag{3.5}$$

In a similar manner we define a multiplicity function $\tilde{\nu}(\zeta, T)$ for a closed operator T by

$$\tilde{\nu}(\zeta,T) = \begin{cases} 0, & \text{if } \zeta \in \rho(T), \\ \dim(P), & \text{if } \zeta \text{ is an isolated point of } \sigma(T), \\ +\infty, & \text{else.} \end{cases}, \tag{3.6}$$

where P is the projection corresponding to the isolated eigenvalue. Now we can state the following from [37, Theorem 6.2, p. 247].

Theorem 3.11 (Weinstein-Aronszajn formula)**.** *Let T be a closed operator defined on a Banach space X, let A be a T-degenerate operator in X and let $\omega(\zeta)$ be defined as in* (3.4)*. If $\Gamma \subset \mathbb{C}$ consists only of isolated eigenvalues of T with finite multiplicities, then $\omega(\zeta)$ is meromorphic in Γ and we have for $S = T + A$*

$$\tilde{\nu}(\zeta, S) = \tilde{\nu}(\zeta, T) + \nu(\zeta, \omega), \quad \zeta \in \Gamma. \tag{3.7}$$

The usefulness of the Weinstein-Aronszajn formula lies in the fact that equation (3.7) describes how an eigenvalue of an operator changes if it is perturbed. Let us assume the operator A and B fulfil the assumptions of Theorem 3.11. Furthermore, let $0 \in \rho(A)$. Then, by definition (3.6), it holds $\tilde{\nu}(0, A) = 0$. Subsequently, the Weinstein-Aronszajn formula provides the equation

$$\tilde{\nu}(0, A + B) = \nu(0, \omega).$$

Thus, whether 0 is an eigenvalue of $A + B$ is solely determined by the Weinstein-Aronszajn determinant. For instance, let 0 be a zero of order 1 of the determinant, then Theorem 3.11 implies that 0 is an eigenvalue of $A + B$, although 0 is not contained in the spectrum of A. Conversely, if 0 is neither a zero nor a pole of any order of the determinant, 0 lies in the resolvent of $A + B$.

These important results portrayed in this section enable us to analyse the behaviour of the solution of the following model.

3.2 Model and Assumptions

The purpose of this chapter is to generalise system (2.2) by incorporating the idea of mutation via an integral kernel operator. The new system is given by

$$\begin{cases} \frac{\partial}{\partial t}v_\varepsilon(t,x) &= 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon(t)}\right)pu_\varepsilon(t,x) - dv_\varepsilon(t,x), \\ \frac{\partial}{\partial t}u_\varepsilon(t,x) &= \left(\frac{2a(x)}{1+k\rho_\varepsilon(t)} - (1+\varepsilon\hat{\kappa})\right)pu_\varepsilon(t,x) + \varepsilon\int\limits_\Omega \kappa(x,y)u_\varepsilon(t,y)\,\mathrm{d}y, \\ u_\varepsilon(0,x) &= u^0(x), v_\varepsilon(0,x) = v^0(x), \end{cases} \tag{3.8}$$

where for notational reasons the equations are switched in comparison to (2.2) and

$$\rho_\varepsilon(t) = \int\limits_\Omega v_\varepsilon(t,x)\,\mathrm{d}x.$$

Note that ρ_ε plays the same role as ρ_2 in Chapter 2, but in order to keep the notation simple, we neglect the index number.
We will use the following assumptions throughout the whole chapter.

Assumption 3.

1. $\Omega \subset \mathbb{R}^n$ *is an open and bounded set with* $|\Omega| = 1$.
2. $a \in C^1(\overline{\Omega})$ *with* $0 < a(x) < 1$ *for all* $x \in \Omega$ *and there exists* $x_0 \in \Omega$ *such that* $a(x_0) > \frac{1}{2}$, $\bar{x} = \mathrm{argmax}_{x\in\overline{\Omega}} a(x)$, $\bar{a} = a(\bar{x})$.
3. $u^0, v^0 \in C(\Omega) \cap L^1(\Omega)$ *with* $u^0, v^0 > 0$
4. $\kappa \in C(\overline{\Omega}\times\overline{\Omega})$ *with* $\sup_{x\in\Omega}\int_\Omega \kappa(x,y)\,\mathrm{d}y = 1$ *and* $0 < \kappa(x,y) \leq 1$ *for all* $(x,y) \in \overline{\Omega}\times\overline{\Omega}$.
5. $\hat{\kappa}, k, p, d \in \mathbb{R}_+$ *and* $\varepsilon > 0$.

Remark 3.12. *Mutation is modelled in* (3.8) *by the influx of mutated cells coming from trait* y *to trait* x *(the integral operator scaled by* ε*) and the outflux of cells which mutate away from trait* x *(the term proportional to the amount of cells of trait* x*, namely* $-\varepsilon\hat{\kappa}pu_\varepsilon(t,x)$*). Due to the conservative nature of mutation for the total population, the following relation holds true for all* $t \in \mathbb{R}_+$

$$\int\limits_\Omega\int\limits_\Omega \kappa(x,y)u_\varepsilon(t,y)\,\mathrm{d}y\,\mathrm{d}x = \hat{\kappa}p\int\limits_\Omega u_\varepsilon(t,x)\,\mathrm{d}x.$$

3.3 Global-in-time Existence and Uniqueness

The following theorem provides the existence and uniqueness of the solution.

Theorem 3.13. *Let Assumption 3 hold, then for all $\varepsilon > 0$ there exists a unique, non-negative solution $(u_\varepsilon, v_\varepsilon) \in C^1(\mathbb{R}_+, (L^1(\Omega))^2)$.*

Proof. As we have seen in Chapter 2 Picard-Lindelöf solves the local existence problem for equation (2.2). Since

$$\left| \int_\Omega \kappa(x,y) \left(u_\varepsilon^1(t,y) - u_\varepsilon^2(t,y) \right) \mathrm{d}y \right| \leq \left\| u_\varepsilon^1(t,\cdot) - u_\varepsilon^2(t,\cdot) \right\|_{L^1(\Omega)},$$

by Assumption 3, local existence follows directly, with local Lipschitz constant $L = L(\|u_\varepsilon(t,\cdot)\|_{L^1(\Omega)})$.
In order to prove global existence, we need to prove a uniform bound for $\|u_\varepsilon(t,\cdot)\|_{L^1(\Omega)}$. We can employ a similar approach as in Chapter 2 by computing the following derivative for $\rho(t) = \int_\Omega u_\varepsilon(t,x)\,\mathrm{d}x$

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\frac{\rho(t)}{\rho_\varepsilon(t)} &= \frac{\int_\Omega \left(\frac{2a(x)}{1+k\rho_\varepsilon(t)} - (1+\varepsilon\hat{\kappa}) \right) p u_\varepsilon(t,x)\,\mathrm{d}x + \varepsilon \int_\Omega \kappa(x,y) u_\varepsilon(t,y)\,\mathrm{d}y}{\rho_\varepsilon(t)} \\
&\quad - \frac{\rho(t)}{\rho_\varepsilon(t)} \left(\frac{\int_\Omega 2\left(1 - \frac{a(x)}{1+k\rho_\varepsilon(t)}\right) p u_\varepsilon(t,x)\,\mathrm{d}x}{\rho_\varepsilon(t)} - d \right) \\
&\leq \frac{\rho(t)}{\rho_\varepsilon(t)} \left((2\bar{a} - (1+\varepsilon\hat{\kappa}))p + d + \varepsilon - 2(1-\bar{a})p\frac{\rho(t)}{\rho_\varepsilon(t)} \right).
\end{aligned}$$

The right-hand side becomes negative if and only if the term in brackets becomes negative which is true if and only if

$$\frac{\rho(t)}{\rho_\varepsilon(t)} > \frac{(2\bar{a} - (1+\varepsilon\hat{\kappa}))p + d + \varepsilon}{2(1-\bar{a})p}.$$

By the logistic argument we can infer

$$\rho(t) \leq \max\left\{ \frac{\rho(0)}{\rho_\varepsilon(0)}, \frac{(2\bar{a} - (1+\varepsilon\hat{\kappa}))p + d + \varepsilon}{2(1-\bar{a})p} \right\} =: C_\varepsilon \rho_\varepsilon(t).$$

Now we can use this inequality in the second equation of (3.8), which is integrated with respect to x over Ω and denote $C = \frac{k}{C_\varepsilon}$

$$\begin{aligned}
\frac{\mathrm{d}}{\mathrm{d}t}\rho(t) &= \int_\Omega \left(\frac{2a(x)}{1+k\rho_\varepsilon(t)} - (1+\varepsilon\hat{\kappa})\right) p u_\varepsilon(t,x)\,\mathrm{d}x + \varepsilon \int_\Omega \int_\Omega \kappa(x,y) u_\varepsilon(t,y)\,\mathrm{d}y\,\mathrm{d}x \\
&\leq \int_\Omega \left(\frac{2a(x)}{1+C\rho(t)} - (1+\varepsilon\hat{\kappa})\right) p u_\varepsilon(t,x)\,\mathrm{d}x + \varepsilon\rho(t) \\
&\leq \rho(t)\left(\left(\frac{2\bar{a}}{1+C\rho(t)} - 1 + \varepsilon\hat{\kappa})\right) p + \varepsilon\right).
\end{aligned}$$

Using the logistic argument we obtain

$$\rho(t) \leq \max\left\{\rho(0), \frac{(2\bar{a} - (1+\varepsilon\hat{\kappa}))p + \varepsilon}{C(p-\varepsilon)}\right\}.$$

Proving positivity can be done exactly as in the proof of Proposition 2.6. □

3.4 Existence and uniqueness of non trivial steady states

We are interested in the existence of non-trivial steady states. We will follow for the existence of steady states the idea given in [23]. The framework in this paper is also a two dimensional system of differential equations, but in contrast to equation (3.8), the author discusses an ODE coupled to an IDE, instead of a system of IDEs. The structure of the ODE is a logistic type equation. This ODE structure allows for a steady state, which is given by a constant. The IDE's steady state is then dependent on this constant, hence, the constant can be interpreted as a parameter. Additionally, the steady state problem is thought of as an eigenvalue problem, associated to the eigenvalue 0, for which a positive eigenfunction is sought, still dependent on the parameter given by the steady state of the ODE. Then it is necessary to choose the parameter in such a way, that the eigenvalue problem and the steady state problem for the ODE is solved simultaneously.

3.4.1 Existence of strictly positive eigenfunction

For this purpose, it is convenient to adjust equation (3.8) by integrating the first equation. This yields an ordinary differential equation for ρ_ε and so we only need to deal with a constant as a steady state instead of a function $\bar{v}_\varepsilon(\cdot)$. Going back to the function is done by inserting the steady state $(u_\varepsilon, \rho_\varepsilon)$ into the first equation of (3.8) and solve for v_ε. Hence we obtain

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}\rho_\varepsilon(t) &= \int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon(t)}\right) p u_\varepsilon(t,x)\,\mathrm{d}x - d\rho_\varepsilon(t), \\ \frac{\partial}{\partial t}u_\varepsilon(t,x) &= \left(\frac{2a(x)}{1+k\rho_\varepsilon(t)} - (1+\varepsilon\hat{\kappa})\right) p u_\varepsilon(t,x) + \varepsilon \int\limits_\Omega \kappa(x,y) u_\varepsilon(t,y)\,\mathrm{d}y, \\ u_\varepsilon(0,x) &= u^0(x), \\ \rho_\varepsilon(0) &= \rho^0 := \int\limits_\Omega v^0(x)\,\mathrm{d}x. \end{cases} \tag{3.9}$$

The corresponding steady state equation is given by

$$\begin{cases} 0 = \int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right) p u_\varepsilon(x)\,\mathrm{d}x - d\rho_\varepsilon, \\ 0 = \left(\frac{2a(x)}{1+k\rho_\varepsilon} - (1+\varepsilon\hat{\kappa})\right) p u_\varepsilon(x) + \varepsilon \int\limits_\Omega \kappa(x,y) u_\varepsilon(y)\,\mathrm{d}y. \end{cases} \tag{3.10}$$

Let us define for $\rho_\varepsilon > 0$

$$\begin{aligned} B_{\rho_\varepsilon,\varepsilon} : L^1(\Omega) \to L^1(\Omega), \qquad & B_{\rho_\varepsilon,\varepsilon} u_\varepsilon(x) := \left(\frac{2a(x)}{1+k\rho_\varepsilon} - (1+\varepsilon\hat{\kappa}) \right) p u_\varepsilon(x), \\ K_\varepsilon : L^1(\Omega) \to L^1(\Omega), \qquad & K_\varepsilon u_\varepsilon(x) := \varepsilon \int_\Omega \kappa(x,y) u_\varepsilon(y)\,\mathrm{d}y, \\ C_{\varepsilon,\rho_\varepsilon} : L^1(\Omega) \to L^1(\Omega), \qquad & C_{\varepsilon,\rho_\varepsilon} u_\varepsilon := B_{\rho_\varepsilon} u_\varepsilon + K_\varepsilon u_\varepsilon. \end{aligned}$$

If a non-trivial steady exists, the first equation of (3.10) provides a constant $\rho \in (0,\infty)$ as a solution. The second equation of (3.10) is then interpreted as an eigenvalue problem for $C_{\varepsilon,\rho}$, which is still dependent on the parameter ρ, namely, we are looking for a function $\varphi_{\varepsilon,\rho}$ and a constant $\lambda_\varepsilon(\rho)$ such that

$$C_{\varepsilon,\rho}\varphi_{\varepsilon,\rho} = \lambda_\varepsilon(\rho)\varphi_{\varepsilon,\rho}. \tag{3.11}$$

We obtain the steady state equation, which we are actually interested in, if ρ can be chosen such that $\lambda_\varepsilon(\rho) = 0$. Of course we need to ensure that the first steady state equation is still true. Since for an arbitrary eigenfunction $\varphi_{\varepsilon,\rho}$ the scalar multiple $u_\varepsilon := c_\varepsilon \varphi_{\varepsilon,\rho}$ for some $c_\varepsilon \in (0,\infty)$ is also an eigenfunction, we can choose

$$c_\varepsilon := \frac{d\rho}{\int_\Omega 2\left(1 - \frac{a(x)}{1+k\rho}\right) p\varphi_{\varepsilon,\rho}(x)\,\mathrm{d}x}.$$

The zero of $\lambda_\varepsilon(\rho)$ and the function u_ε solve equation (3.10).
So instead of tackling the steady state problem directly, we have a look at the eigenvalue problem (3.11) and observe, that 0 is an eigenvalue to the corresponding eigenfunction $\varphi_{\varepsilon,\rho}$ of $C_{\varepsilon,\rho}$ if and only if

$$\begin{aligned} & B_{\rho,\varepsilon}\varphi_{\varepsilon,\rho} + K_\varepsilon\varphi_{\varepsilon,\rho} = 0, \\ \Leftrightarrow \quad & K_\varepsilon\varphi_{\varepsilon,\rho} = -B_{\rho,\varepsilon}\varphi_{\varepsilon,\rho}, \\ \Leftrightarrow \quad & K_\varepsilon\left(-B_{\rho,\varepsilon}^{-1}\psi_{\varepsilon,\rho}\right) = \psi_{\varepsilon,\rho} \end{aligned}$$

with $\psi_{\varepsilon,\rho} := -B_{\rho,\varepsilon}\varphi_{\varepsilon,\rho}$, meaning that $\psi_{\varepsilon,\rho}$ is an eigenfunction corresponding to 1 as an eigenvalue of the operator

$$\begin{aligned} T_{\varepsilon,\rho} &: L^1(\Omega) \to L^1(\Omega), \\ (T_{\varepsilon,\rho}u)(x) &:= \varepsilon \int_\Omega \kappa(x,y) \frac{1+k\rho}{((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y))p} u(y)\,\mathrm{d}y \\ &= K_\varepsilon \circ (-B_{\rho,\varepsilon}^{-1})u(x). \end{aligned} \tag{3.12}$$

This operator is only well defined for certain values of ρ because otherwise the denominator in the integrand can become 0. Accordingly we restrict ρ to exclude the denominator from becoming zero by choosing only $\rho \in (\bar{\rho} - \frac{\varepsilon\hat{\kappa}}{1+\varepsilon\hat{\kappa}}, \infty)$. Here $\bar{\rho}$ coincides with $\bar{\rho}_2$ from Proposition 2.20. This is also the reason why the inverse of $B_{\rho,\varepsilon}$ exists, because $B_{\rho,\varepsilon}$, as a multiplication operator, is invertible if it does not have a zero. The exploitation of this equivalence of the eigenvalues 1 and $\lambda_\varepsilon(\rho)$ is illustrated in [23], but goes back to [14, Proposition 2.1].
We need to investigate the eigenvalue problem for the operator $T_{\varepsilon,\rho}$ and guarantee, that there exist a non-negative eigenfunction.

Proposition 3.14. *Let $T_{\varepsilon,\rho}$ be as in equation (3.12) for $\rho \in (\bar{\rho} - \frac{\varepsilon\hat{\kappa}}{1+\varepsilon\hat{\kappa}}, \infty)$, then the spectral radius $r(T_{\varepsilon,\rho})$ is an algebraically simple eigenvalue of $T_{\varepsilon,\rho}$ with a strictly positive eigenfunction. Moreover, $r(T_{\varepsilon,\rho})$ is the only eigenvalue of $T_{\varepsilon,\rho}$ having a positive eigenfunction.*

Proof. $T_{\varepsilon,\rho}$ is by definition and the choice of ρ a positive operator. It is also evident that $T_{\varepsilon,\rho}$ is a bounded operator. If we define

$$\tilde{\kappa}(x,y) := \kappa(x,y) \frac{1+k\rho}{((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y))p},$$

then $\tilde{\kappa} > 0$ and $\tilde{\kappa}$ is continuous on $\overline{\Omega}^2$, hence $T_{\varepsilon,\rho} : L^1(\Omega) \to L^1(\Omega)$ is irreducible due to Corollary 3.5. Additionally, according to [1, Corollary 5.1], $T_{\varepsilon,\rho} : L^1(\Omega) \to L^1(\Omega)$ is compact if and only if for all $\iota > 0$ there exists $\delta > 0, R > 0$ such that for almost all $x \in \Omega$ and for every $h \in \mathbb{R}^n$ with $|h| < \delta$ holds

$$\int_{\mathbb{R}^n \setminus B_R(0)} |\bar{\kappa}(x,y)|\,\mathrm{d}y < \iota, \quad \int_{\mathbb{R}^n} |\bar{\kappa}(x,y+h) - \bar{\kappa}(x,y)|\,\mathrm{d}y < \iota.$$

Accordingly, let $\iota > 0$ be arbitrary but fixed. Then define

$$\bar{\kappa}(x,y) := \begin{cases} \tilde{\kappa}(x,y), & y \in \Omega \\ 0, & y \notin \Omega \end{cases}.$$

As Ω is bounded, choose $R > 0$ such that $|\Omega \setminus B_R(0)| < \frac{\iota}{\max\limits_{(x,y)\in\overline{\Omega}^2} \tilde{\kappa}(x,y)}$ and obtain

$$\int\limits_{\mathbb{R}^n \setminus B_R(0)} |\bar{\kappa}(x,y)| \, \mathrm{d}y = \int\limits_{\Omega \setminus B_R(0)} |\tilde{\kappa}(x,y)| \, \mathrm{d}y \leq \max_{(x,y)\in\overline{\Omega}^2} \tilde{\kappa}(x,y) \, |\Omega \setminus B_R(0)| < \iota.$$

Due to the dominated convergence theorem and the continuity of $\tilde{\kappa}$ it also holds

$$\int\limits_{\mathbb{R}^n} |\bar{\kappa}(x,y+h) - \bar{\kappa}(x,y)| \, \mathrm{d}y = \int\limits_{\Omega} |\tilde{\kappa}(x,y+h) - \tilde{\kappa}(x,y)| \, \mathrm{d}y < \iota,$$

for $|h|$ small enough.
The Krein-Rutman theorem for Banach lattices, see Theorem 3.6, gives the result. □

We know now that the operator $T_{\varepsilon,\rho}$ admits a strictly positive solution to the eigenvalue problem with eigenvalue $r(T_{\varepsilon,\rho})$. It is left to show, that it is possible to choose ρ in such a way, that $r(T_{\varepsilon,\rho}) = 1$ and that this choice of ρ is unique. Remember that showing $r(T_{\varepsilon,\rho}) = 1$ is equivalent to showing $\lambda_\varepsilon(\rho) = 0$.
The idea is to prove, that $r(T_{\varepsilon,\rho})$ is continuous with respect to ρ and strictly monotone. This ansatz goes back to [14].

Lemma 3.15. *Let $r(T_{\varepsilon,\rho})$ be the strictly positive eigenvalue of the operator $T_{\varepsilon,\rho}$, then for ε small enough $r(T_{\varepsilon,\rho})$ is a strictly decreasing function and continuous in $\rho \in (\bar{\rho}, \infty)$.*

Remark 3.16. *In general the spectrum of an operator does not need to be continuously dependent on the operator itself. It is possible to show that for a linear operator T the spectrum $\sigma(T)$ depends upper semi-continuously on T, compare [37, Theorem* 3.1*, p. 208]. The upper semi-continuity prevents the spectrum to expand arbitrarily fast, but it cannot prevent it from decaying, see for instance [37, Example* 3.8*]. If it is sufficient to have a look at a finite system of isolated eigenvalues, continuity can be achieved if the investigated operator T is closed, see [37, Chapter IV*, §3.5*, p. 213].*

Proof of Lemma 3.15. The operator $T_{\varepsilon,\rho}$ is continuous, so in particular closed and it depends continuously on ρ. Furthermore, the eigenvalue $r(T_{\varepsilon,\rho})$ is simple and strictly dominant, thus $r(T_{\varepsilon,\rho})$ depends continuously on ρ, compare to Remark 3.16. For the monotonicity we utilize the following relation for some arbitrary linear operator A

$$r(A) = \lim_{n\to\infty} \|A^n\|_\infty^{\frac{1}{n}},$$

where $\|.\|_\infty$ is the operator norm. We have to show that

$$\left\|T^n_{\varepsilon,\rho_1}\right\|_\infty^{\frac{1}{n}} > \left\|T^n_{\varepsilon,\rho_2}\right\|_\infty^{\frac{1}{n}} \text{ for } \rho_1 < \rho_2.$$

A straight forward proof by induction shows that

$$T^n_{\varepsilon,\rho}u(x) = \int_{\Omega^n} \kappa(x,y_n)\prod_{i=1}^{n-1}\kappa(y_i,y_{i+1})\frac{(1+k\rho)^n}{\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p}u(y_n)\,\mathrm{d}y_1\cdots\mathrm{d}y_n.$$

In order to obtain monotonicity, we compute the derivative of $T^n_{\varepsilon,\rho}$ with respect to ρ. The differential operator and the integral can be interchanged, because of Leibniz' integral rule. This implies denoting with $\mathrm{d}\vec{y} = \mathrm{d}y_1\cdots\mathrm{d}y_n$

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}\rho}(T^n_{\varepsilon,\rho}u)(x) &= \frac{\mathrm{d}}{\mathrm{d}\rho}\int_{\Omega^n} \kappa(x,y_n)\prod_{i=1}^{n-1}\kappa(y_i,y_{i+1})\frac{(1+k\rho)^n}{\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p}u(y_n)\,\mathrm{d}\vec{y}\\ &= \int_{\Omega^n} \kappa(x,y_n)\prod_{i=1}^{n-1}\kappa(y_i,y_{i+1})\frac{\mathrm{d}}{\mathrm{d}\rho}\frac{(1+k\rho)^n}{\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p}u(y_n)\,\mathrm{d}\vec{y}.\end{aligned}$$

Both κ and u are positive functions, so the sign of the derivative is solely determined by the derivative of the fraction. Performing the derivative yields

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}\rho}\frac{(1+k\rho)^n}{\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p} &= \frac{kn(1+k\rho)^{n-1}\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p}{\left(\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\right)^2}\\ &\quad - \frac{(1+k\rho)^n\frac{\mathrm{d}}{\mathrm{d}\rho}\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p}{\left(\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\right)^2}.\end{aligned}$$

Again we see that it is sufficient to look only at a small part of this derivative to determine the sign, namely the numerator. The claim is

$$kn\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p-(1+k\rho)\frac{\mathrm{d}}{\mathrm{d}\rho}\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p<0$$

and can be shown by induction over $n\in\mathbb{N}$.
Let $n=1$, then

$$k((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_1))p-(1+k\rho)(1+\varepsilon\hat{\kappa})kp=-2kpa(y_1)<0,$$

by Assumption 3.
Let the statement be true for $n\in\mathbb{N}$. Then have a look at the derivative for $n+1$

$$\begin{aligned}
& k(n+1)\prod_{i=1}^{n+1}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\\
& -(1+k\rho)\frac{\mathrm{d}}{\mathrm{d}\rho}\prod_{i=1}^{n+1}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\\
= \;& kn\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\cdot((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_{n+1}))p\\
& +k\prod_{i=1}^{n+1}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\\
& -(1+k\rho)\left[\frac{\mathrm{d}}{\mathrm{d}\rho}\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\cdot((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_{n+1}))p\right.\\
& \left.+kp\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\right]\\
= \;& ((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_{n+1}))p\left[kn\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\right.\\
& \left.-(1+k\rho)\frac{\mathrm{d}}{\mathrm{d}\rho}\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\right]\\
& +k\left[\prod_{i=1}^{n+1}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\right.\\
& \left.-(1+k\rho)p\prod_{i=1}^{n}((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y_i))p\right]<0,
\end{aligned}$$

because the first term is negative due to the induction assumption and the second term is negative because $1 + k\rho > (1 + k\rho)(1 + \varepsilon\hat{\kappa}) - 2a(y_{n+1})$ for ε small enough. Thus $T^n_{\varepsilon,\rho_1} u > T^n_{\varepsilon,\rho_2} u$ for all $u \in L^1(\Omega), u \geq 0$ and $\rho_1 < \rho_2$. Then, taking the operator norm on both sides and using that the function $x \mapsto x^{\frac{1}{n}}$ is strictly monotone, we obtain

$$\left\|T^n_{\varepsilon,\rho_1}\right\|^{\frac{1}{n}}_\infty \geq \left\|T^n_{\varepsilon,\rho_2}\right\|^{\frac{1}{n}}_\infty \text{ for all } n \in \mathbb{N} \Rightarrow r(T_{\varepsilon,\rho_1}) \geq r(T_{\varepsilon,\rho_2}) \quad \text{for } \rho_1 < \rho_2.$$

It is left to show that the spectral radius is not only monotone but strictly monotone. For this purpose let us assume that there exists $\rho_1 < \rho_2$ such that $r(T_{\varepsilon,\rho_1}) = r(T_{\varepsilon,\rho_2})$. Since $r(T_{\varepsilon,\rho})$ is monotone this implies that $r(T_{\varepsilon,\rho_1}) = r(T_{\varepsilon,\rho}) = c$ for all $\rho \in [\rho_1, \rho_2]$. As c is a eigenvalue of $T_{\varepsilon,\rho}$, it holds that 1 is an eigenvalue of $\frac{1}{c}T_{\varepsilon,\rho}$ for all $\rho \in [\rho_1, \rho_2]$. Let $D := \{z \in \mathbb{C} | \Re(z) > 0\}$, then $\rho \mapsto \frac{1}{c}T_{\varepsilon,\rho}$ is an analytic function, because $T_{\varepsilon,\rho}$ is a rational function in ρ without poles. Additionally, $\frac{1}{c}T_{\varepsilon,\rho}$ is compact, because $T_{\varepsilon,\rho}$ is. Furthermore, $(1 - \frac{1}{c}T_{\varepsilon,\rho})^{-1}$ exists for some $\rho \in D$, that is, choose in accordance with the monotonicity $\rho > \rho_2$ to achieve the existence of the inverse. Due to [59, Corollary 1], we can deduce that the function $\rho \mapsto \frac{1}{c}T_{\varepsilon,\rho}$ is a meromorphic function on D. Meromorphic functions are analytic except on a set of measure zero. Since 1 is an eigenvalue of $\frac{1}{c}T_{\varepsilon,\rho}$ on the interval $[\rho_1, \rho_2]$, it cannot be analytic on this interval. □

Up to this point we showed that the spectral radius $r(T_{\varepsilon,\rho})$ is continuous and strictly decreasing in ρ. Hence it is necessary to prove that there exists some $\rho \in (\bar{\rho} - \frac{\varepsilon\hat{\kappa}}{1+\varepsilon\hat{\kappa}}, \infty)$ such that $r(T_{\varepsilon,\rho}) = 1$. This is provided by

Lemma 3.17. *For all $\varepsilon < \varepsilon_0$ there exists a unique $\rho \in (\bar{\rho}, \infty)$ such that $r(T_{\varepsilon,\rho}) = 1$.*

Proof. Due to Lemma 3.15 and the mean value theorem it suffices to show that there exists some $\rho_1, \rho_2 \in (\bar{\rho}, \infty)$ such that $r(T_{\varepsilon,\rho_1}) < 1$ and $r(T_{\varepsilon,\rho_2}) > 1$. We can observe that

$$\lim_{\rho\to\infty} T_{\varepsilon,\rho} = T_\varepsilon = \frac{\varepsilon}{1 + \varepsilon\hat{\kappa}} \int_\Omega \kappa(x, y) u_\varepsilon(y) \, \mathrm{d}y.$$

T_ε is a compact operator, hence the spectrum is bounded. Thus, there exists a $\varepsilon_0 > 0$ such that for all $\varepsilon < \varepsilon_0$, $\|T_\varepsilon\|_\infty < 1$. Since $r(T_\varepsilon) \leq \|T_\varepsilon\|_\infty$ we obtain $r(T_\varepsilon) < 1$ for $\varepsilon < \varepsilon_0$. As $r(T_{\varepsilon,\rho})$ is continuous with respect to ρ, we can find $\rho_1 \in (\bar{\rho}, \infty)$ such that

$r(T_{\varepsilon,\rho_1}) < 1$. Fixing $\varepsilon < \varepsilon_0$ with $r(T_{\varepsilon,\rho_1}) < 1$, we can then choose ρ such that

$$\begin{aligned}\|T_{\varepsilon,\rho}\|_\infty &= \sup_{\substack{u\in L^1(\Omega)\\ \|u\|_{L^1(\Omega)}=1}} \left| \varepsilon \int_\Omega \kappa(x,y) \frac{1+k\rho}{((1+k\rho)(1+\varepsilon\hat{\kappa})-2a(y))p} u(y)\,\mathrm{d}y \right| \\ &\geq \frac{1+k\rho}{|(1+k\rho)(1+\varepsilon\hat{\kappa})-2\bar{a}|}\varepsilon \sup_{\substack{u\in L^1(\Omega)\\ \|u\|_{L^1(\Omega)}=1}} \int_\Omega \kappa(x,y)u(y)\,\mathrm{d}y.\end{aligned}$$

Choose ρ_2 close enough to $\frac{2\bar{a}-1}{k} = \bar{\rho}$ and obtain that $\|T_{\varepsilon,\rho}\|_\infty > 1$. □

Theorem 3.18. *There exists some $\varepsilon_0 > 0$ such that for all $\varepsilon < \varepsilon_0$ there exists a unique, non-trivial steady state $(\rho_\varepsilon, u_\varepsilon)$ of system* (3.11).

Proof. Combination of Proposition 3.14 and Lemma 3.17 yields the result. □

3.5 Convergence of the steady states

In the previous section we have seen that we obtain non-trivial steady states by achieving non-negative eigenfunctions for the operator $T_{\varepsilon,\rho}$ and by solving uniquely the equation $\lambda_\varepsilon(\rho) = 0$. The next step is to prove that these steady states converge as ε tends to zero. This will be done in two steps. First we will show that $\lambda_\varepsilon(\rho) \to \lambda(\rho)$ pointwisely and this yields secondly the convergence of the corresponding eigenfunctions $\varphi_{\varepsilon,\rho}$. Additionally, the convergence of the eigenvalues $\lambda_\varepsilon(\rho)$ allows for deducing the convergence of the zeros of the eigenvalues, namely the convergence of the steady state component ρ_ε.

3.5.1 Existence of eigenvalues

Similarly as in the beginning of the previous section we can compute

$$\begin{aligned} B_{\rho,\varepsilon}\varphi_{\varepsilon,\rho} + K_\varepsilon\varphi_{\varepsilon,\rho} &= \lambda_\varepsilon(\rho)\varphi_{\varepsilon,\rho} \\ \Leftrightarrow K_\varepsilon(\lambda_\varepsilon(\rho)Id - B_{\rho,\varepsilon})^{-1}\psi_{\varepsilon,\rho} &= \psi_{\varepsilon,\rho}, \end{aligned}$$

for $\psi_{\varepsilon,\rho} = (\lambda_\varepsilon(\rho)Id - B_{\rho,\varepsilon})\varphi_{\varepsilon,\rho}$. Analogously to the previous section, the equivalence above is the equivalence between searching for the eigenvalue $\lambda_\varepsilon(\rho)$ for $C_{\varepsilon,\rho}$ and searching for the eigenvalue 1 for $K_\varepsilon(\lambda_\varepsilon(\rho)Id - B_{\rho,\varepsilon})^{-1}$. Naturally, we have to show first that we can obtain eigenvalues and corresponding eigenfuntions to the operator at all. According to [14, Theorem 2.2], it is enough to check, whether it is possible to choose some λ_1 such that $r(K_\varepsilon(\lambda_1 Id - B_{\rho,\varepsilon})^{-1}) > 1$.

Proposition 3.19. *There exists $\lambda_1 > r(B_{\rho,\varepsilon})$ such that $r(K_\varepsilon(\lambda_1 Id - B_{\rho,\varepsilon})^{-1}) > 1$.*

Proof. The spectral radius of $B_{\rho,\varepsilon} : L^1(\Omega) \to L^1(\Omega)$ is given by

$$r(B_{\rho,\varepsilon}) = \max_{x\in\overline{\Omega}} \left(\frac{2a(x)}{1+k\rho} - (1+\varepsilon\hat{\kappa}) \right) p.$$

Then let us define the function $q : \mathbb{R} \times \Omega \to \mathbb{R}$ by

$$q(\lambda, y) := \lambda - \left(\frac{2a(y)}{1+k\rho} - (1+\varepsilon\hat{\kappa}) \right) p.$$

Then we need to prove that

$$\exists \lambda_1 > r(B_{\rho,\varepsilon})\ \exists g \in L^1(\Omega), g > 0\ \forall x \in \Omega : \quad \varepsilon \int_\Omega \kappa(x,y) q(\lambda_1, y)^{-1} g(y)\,\mathrm{d}y > g(x).$$

Observe that $\operatorname{argmin}_{x\in\Omega} q(r(B_{\rho,\varepsilon}),x) = \operatorname{argmax}_{x\in\Omega}\left(\frac{2a(x)}{1+k\rho} - (1+\varepsilon\hat{\kappa})\right)p = \bar{x}$. Due to the definition of q we obtain

$$\begin{cases} q(r(B_{\rho,\varepsilon}),\bar{x}) & = 0, \\ \frac{\partial}{\partial y} q(r(B_{\rho,\varepsilon}),y)_{|y=\bar{x}} & = 0. \end{cases} \tag{3.13}$$

Choose for some small $\delta > 0$, $g = \chi_{B_\delta(\bar{x})}$. Hence we can estimate

$$\begin{aligned} \varepsilon \int_\Omega \kappa(x,y) q(\lambda_1,y)^{-1} g(y)\,\mathrm{d}y &= \varepsilon \int_{B_\delta(\bar{x})} \kappa(x,y) q(\lambda_1,y)^{-1}\,\mathrm{d}y \\ &\geq \varepsilon \min_{x,y\in\overline{\Omega}} \kappa(x,y) \int_{B_\delta(\bar{x})} q(\lambda_1,y)^{-1}\,\mathrm{d}y. \end{aligned} \tag{3.14}$$

Expanding the function q by the Taylor formula up to the 0th order around $\bar{x}$ yields

$$q(\lambda_1,y) = q(\lambda_1,\bar{x}) + o\left(\|y-\bar{x}\|\right). \tag{3.15}$$

Inserting equation (3.15) into inequality (3.14) allows deducing

$$\varepsilon \int_\Omega \kappa(x,y) q(\lambda_1,y)^{-1} g(y)\,\mathrm{d}y \geq \varepsilon \min_{x,y\in\overline{\Omega}} \kappa(x,y) \int_{B_\delta(\bar{x})} \frac{1}{q(\lambda_1,\bar{x}) + o\left(\|y-\bar{x}\|\right)}\,\mathrm{d}y > 1,$$

by using the first equation of (3.13), choosing δ small enough and λ_1 close enough to $r(B_{\rho,\varepsilon})$. □

3.5.2 Convergence of the eigenvalues

Now that we know that there exists always an eigenvalue $\lambda_\varepsilon(\rho)$ to the operator $C_{\varepsilon,\rho}$, we can deduce its limiting behaviour. It is characterised by

Lemma 3.20. *Let $\lambda_\varepsilon(\rho)$ be the strictly dominant eigenvalue of the operator $C_{\varepsilon,\rho}$, then for all $\rho \in (\bar{\rho},\infty)$*

$$\lambda_\varepsilon(\rho) \xrightarrow{\varepsilon\to 0} \max_{x\in\overline{\Omega}} \left(\frac{2a(x)}{1+k\rho} - 1\right) p.$$

Proof. Let us denote for notational simplicity $\mu(x) := \left(\frac{2a(x)}{1+k\rho} - 1\right)p$, $\mu_\varepsilon(x) := \left(\frac{2a(x)}{1+k\rho} - (1+\varepsilon\hat{\kappa})\right)p$. We have to show that for all $\delta > 0$ there exists ε_0

such that for all $\varepsilon < \varepsilon_0$ it holds

$$\lambda_\varepsilon(\rho) \in B_\delta(\mu(\bar{x})).$$

Due to [16, p. 140], we know that

$$r(A) \geq \sup\{\mu \in \mathbb{R} \,|Af \geq \mu f, \text{ for some } 0 < f \in D(A)\}. \tag{3.16}$$

Because of this inequality it suffices to construct two functions $f_1, f_2 > 0$ such that $(\lambda_\varepsilon - \delta)f_1 \leq B_{\rho,\varepsilon} f_1$ and $C_{\varepsilon,\rho} f_2 \geq (\mu(\bar{x}) - \delta)f_2$.
In order to construct the function f_1 we have to see that

$$\forall u \in L^1(\Omega),\ u \geq 0 \exists \Omega' \subset \Omega\, \forall x \in \Omega' : \quad \int_\Omega \kappa(x,y)u(y)\,\mathrm{d}y \leq u(x). \tag{3.17}$$

If $\operatorname{esssup}_\Omega u = \infty$ the statement is obvious. It is left to show the statement is true for $\operatorname{esssup}_\Omega u < \infty$. Since $u \neq const$ and $\sup_{x\in\Omega} \int_\Omega \kappa(x,y)\,\mathrm{d}y = 1$ it holds

$$\int_\Omega \kappa(x,y)u(y)\,\mathrm{d}y < \operatorname{esssup}_{x\in\Omega} u(x).$$

Because of the strict inequality and the fact that u is not constant we can choose some $\delta > 0$ such that

$$\int_\Omega \kappa(x,y)u(y)\,\mathrm{d}y \leq \operatorname{esssup}_{x\in\Omega} u(x) - \delta.$$

Set $\Omega' := \left\{x \in \Omega \,\middle|\, u(x) \geq \operatorname{esssup}_{x\in\Omega} u(x) - \frac{\delta}{2}\right\}$. Then $|\Omega'| > 0$ and

$$\forall x \in \Omega' : \quad \int_\Omega \kappa(x,y)u(y)\,\mathrm{d}y \leq u(x).$$

Using the property of the eigenvalue $\lambda_\varepsilon(\rho)$ with the corresponding eigenfunction φ_ε yields

$$\lambda_\varepsilon(\rho)\varphi_\varepsilon(x) = B_{\rho,\varepsilon}\varphi_\varepsilon(x) + K_\varepsilon\varphi_\varepsilon(x) \leq B_\rho\varphi_\varepsilon(x) + \delta\varphi_\varepsilon(x),$$

for all $x \in \Omega'$ and $\varepsilon_0 > \delta \geq \varepsilon$ and with $B_\rho u = \left(\frac{2a(x)}{1+k\rho} - 1\right) pu$. Rearranging this inequality leads to

$$(\lambda_\varepsilon(\rho) - \delta)\varphi_\varepsilon(x) \leq B_\rho\varphi_\varepsilon(x).$$

Hence we know for $f_1 := \chi_{\Omega'}\varphi_\varepsilon$ that $(\lambda_\varepsilon(\rho)-\delta)f_1 \leq B_\rho f_1$ and eventually $\lambda_\varepsilon(\rho)-\delta \leq r(B_\rho) = \mu(\bar{x})$.
Let v_ε be a non-negative eigenfunction corresponding to $\mu_\varepsilon(x)$ and let $\delta > 0$ be such that $\mu_\varepsilon(x) \geq \mu_\varepsilon(\bar{x}) - \delta$ for all $x \in \Omega''$, where $\Omega'' \subset \Omega$ is a suitably chosen set. Denote $f_2 := v_\varepsilon \chi_{\Omega''}$ Then, due to the positivity of K_ε,

$$C_{\varepsilon,\rho} f_2 = B_{\rho,\varepsilon} f_2 + K_\varepsilon f_2 \geq \mu_\varepsilon(x)\bar{v}_\varepsilon \geq (\mu_\varepsilon(\bar{x}) - \delta) f_2.$$

According to inequality (3.16) we obtain $\lambda_\varepsilon(\rho) \geq \mu_\varepsilon(\bar{x}) - \delta$. Furthermore, we know

$$|\mu(x) - \mu_\varepsilon(x)| \leq \varepsilon \leq \delta.$$

Thus we achieved

$$\forall \delta > 0\ \exists\, \varepsilon_0 > 0\ \forall \varepsilon < \varepsilon_0 : \quad \lambda_\varepsilon(\rho) \in B_{2\delta}(\mu(\bar{x})).$$

□

3.5.3 Convergence of eigenfunction

Now we are able to prove weak* convergence of the steady state component u_ε. This component is given by $u_\varepsilon = c_\varepsilon \varphi_{\varepsilon,\rho_\varepsilon}$, thus it is necessary to prove that both, the constants c_ε and the eigenfunctions $\varphi_{\varepsilon,\rho_\varepsilon}$, converge. As a first step, we show

Proposition 3.21. *Let $\varphi_{\varepsilon,\rho}$ be the the unique positive eigenfunction of $\lambda_\varepsilon(\rho)$ of $C_{\varepsilon,\rho}$, then*

$$\varphi_{\varepsilon,\rho} \rightharpoonup^* \delta_{\bar{x}} \quad \text{in } \mathcal{M}^+(\Omega), \quad \text{as } \varepsilon \to 0.$$

Proof. The ansatz to prove convergence of the steady state is to show that the eigenfunctions form a Dirac sequence.
By Proposition 3.19 the eigenfunction $\varphi_{\varepsilon,\rho}$ of $C_{\varepsilon,\rho}$ is strictly positive, namely $\varphi_{\varepsilon,\rho} > 0$ for all $\varepsilon > 0$ and, because it is an eigenfunction in $L^1(\Omega)$, can be normalized to $\|\varphi_{\varepsilon,\rho}\|_{L^1(\Omega)} = 1$. It is left to show that for $\Omega^c \subset \Omega$ with $\bar{x} \notin \Omega^c$ and $\operatorname{dist}(\bar{x}, \Omega^c) > 0$

$$\int_{\Omega^c} \varphi_{\varepsilon,\rho}(x)\,\mathrm{d}x \xrightarrow{\varepsilon\to 0} 0.$$

According to Lemma 3.20 we have $\lambda_\varepsilon(\rho) \to \max_{x\in\Omega}\left(\frac{2a(x)}{1+k\rho}-1\right)p$ as $\varepsilon \to 0$. Hence for any Ω^c as chosen above it is possible to choose $\varepsilon < \varepsilon_0$ such that

$$\forall x \in \Omega^c: \quad \lambda_\varepsilon(\rho) > \left(\frac{2a(x)}{1+k\rho}-1\right)p. \tag{3.18}$$

Using the steady state equation for $\varphi_{\varepsilon,\rho}$ and $\lambda_\varepsilon(\rho)$ with respect to $C_{\varepsilon,\rho}$ we obtain

$$\begin{aligned} 0 &= \int\limits_{\Omega^c}\left(\frac{2a(x)}{1+k\rho}-(1+\varepsilon\hat{\kappa})\right)p\varphi_{\varepsilon,\rho}(x)-\lambda_\varepsilon(\rho)\varphi_{\varepsilon,\rho}(x)\,\mathrm{d}x+\varepsilon\int\limits_{\Omega^c}\int\limits_{\Omega}\kappa(x,y)\varphi_{\varepsilon,\rho}(y)\,\mathrm{d}y\,\mathrm{d}x \\ &\leq \left(\max_{x\in\Omega^c}\left(\frac{2a(x)}{1+k\rho}-1\right)p-\lambda_\varepsilon(\rho)\right)\int\limits_{\Omega^c}\varphi_{\varepsilon,\rho}(x)\,\mathrm{d}x+\varepsilon\int\limits_{\Omega^c}\int\limits_{\Omega}\kappa(x,y)\varphi_{\varepsilon,\rho}(y)\,\mathrm{d}y\,\mathrm{d}x. \end{aligned}$$

By inequality (3.18) the first term is negative and bounded, hence by rearranging the inequality we get for a constant $C > 0$

$$C\int\limits_{\Omega^c}\varphi_{\varepsilon,\rho}(x)\,\mathrm{d}x \leq \varepsilon\int\limits_{\Omega^c}\int\limits_{\Omega}\kappa(x,y)\varphi_{\varepsilon,\rho}(y)\,\mathrm{d}y\,\mathrm{d}x \leq \varepsilon.$$

Thus $\varphi_{\varepsilon,\rho}$ is a Dirac sequence and converges subsequently to the Dirac measure concentrated in $\bar{x}$. □

Proposition 3.22. *Let ρ_ε be the unique zero of $\lambda_\varepsilon(\rho)$, hence the first component of the steady state and let $\bar{\rho} = \bar{\rho}_2 = \frac{2\bar{a}-1}{k}$. Then*

$$\rho_\varepsilon \xrightarrow{\varepsilon\to 0} \bar{\rho}_2.$$

Proof. Starting with the steady state equation (3.10), which is integrated over Ω, we can estimate using Hölder's inequality and Assumption 3,

$$\begin{aligned} 0 &= \int\limits_{\Omega}\left(\frac{2a(x)}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)pu_\varepsilon(x)\,\mathrm{d}x+\varepsilon\int\limits_{\Omega}\int\limits_{\Omega}\kappa(x,y)u_\varepsilon(y)\,\mathrm{d}y\,\mathrm{d}x \\ &\leq \left(\frac{2\bar{a}}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)p\left\|u_\varepsilon\right\|_{L^1(\Omega)}+\varepsilon\left\|u_\varepsilon\right\|_{L^1(\Omega)} \end{aligned}$$

After division by $\|u_\varepsilon\|_{L^1(\Omega)}$, which is strictly positive for all $\varepsilon > 0$ and rearrangement, this inequality yields

$$0 \leq \left(1+\varepsilon\hat{\kappa}-\frac{2\bar{a}}{1+k\rho_\varepsilon}\right)p \leq \varepsilon.$$

The positivity stems from the fact that ρ_ε is a component of the steady state. Then $\left(1+\varepsilon\hat{\kappa}-\frac{2\bar{a}}{1+k\rho_\varepsilon}\right)p$ is a sequence, which converges to zero. Since $\varepsilon\hat{\kappa}$ goes to zero for ε tending to zero, it has to hold that ρ_ε converges to the value, which makes the term $\left(1-\frac{2\bar{a}}{1+k\rho}\right)$ zero. This value is unique and given by $\bar{\rho}_2$. Subsequently, we obtain the desired result. □

Theorem 3.23. *Let $(u_\varepsilon, \rho_\varepsilon)^T$ be the solution of equation (3.9). Then it holds*

$$u_\varepsilon \rightharpoonup^* \bar{\rho}_1\delta_{\bar{x}} \quad \textit{in } \mathcal{M}^+(\Omega), \quad \rho_\varepsilon \to \bar{\rho}_2 \quad \textit{in } \mathbb{R},$$

where $\bar{\rho}_1, \bar{\rho}_2$ are the same stationary solutions as in Proposition 2.20.

Proof. The convergence of ρ_ε is already proven by Proposition 3.22.
The convergence of u_ε is done in two steps. By construction $u_\varepsilon = c_\varepsilon\varphi_{\varepsilon,\rho_\varepsilon}$. The same argument as in Proposition 3.21 yields the convergence of $\varphi_{\varepsilon,\rho_\varepsilon}$ to the Dirac delta located at $\bar{x}$. Because of this property of $\varphi_{\varepsilon,\rho_\varepsilon}$ and the convergence of ρ_ε, it follows

$$c_\varepsilon = \frac{d\rho_\varepsilon}{\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)p\varphi_{\varepsilon,\rho_\varepsilon}\,\mathrm{d}x} \xrightarrow{\varepsilon\to 0} \frac{d\bar{\rho}}{2p\left(1-\frac{\bar{a}}{1+k\bar{\rho}}\right)} = \bar{\rho}_1,$$

where $\bar{\rho}_1$ is the same as in Proposition 2.20. This concludes the proof. □

For an illustration of the convergence result, see Figure 3.2.

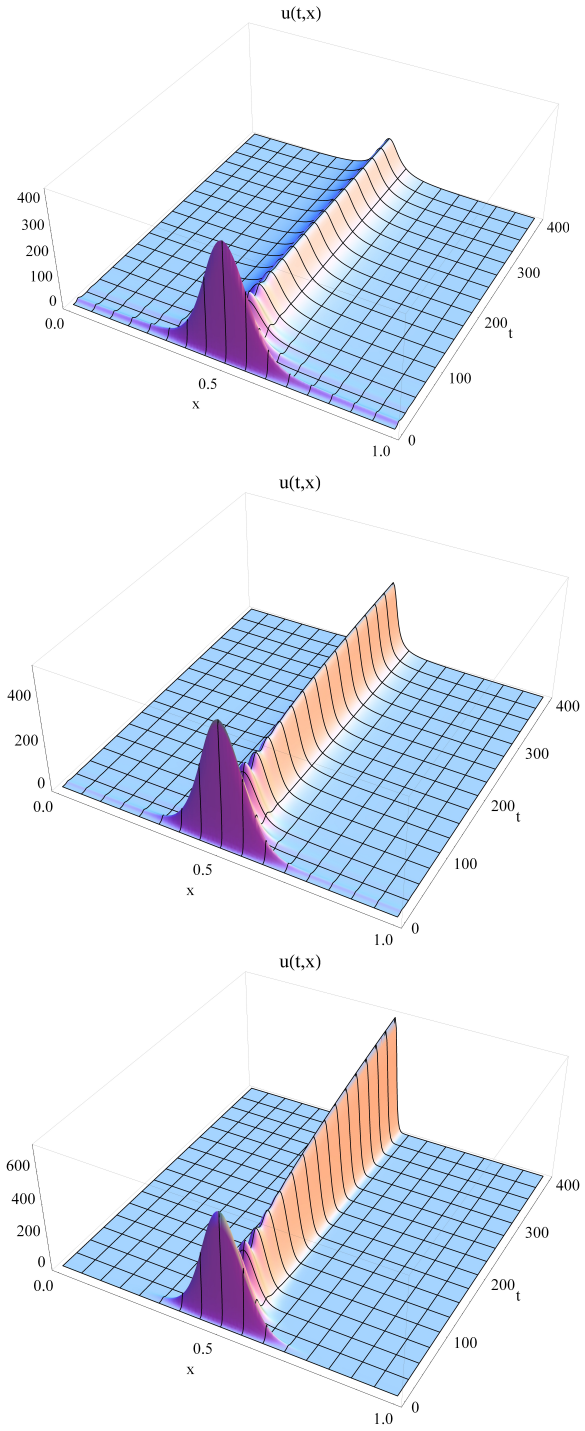

Figure 3.2: The simulations depict the first solution $u_\varepsilon(t, x)$ for different values of ε. Going from top to bottom, the values of ε are $\frac{3}{4}$, $\frac{1}{3}$ and $\frac{1}{100}$.

3.6 Stability of the steady states

In Section 3.4.1 we proved, that system (3.8) admits a non-negative steady state $(\rho_\varepsilon, u_\varepsilon)^T$, compare Theorem 3.18. The next step is to analyse the stability of these steady states. In classical ODE theory, see for instance [68], a useful tool to determine the stability of a non-linear system of ODEs is the method of linearised stability. This well known method can be generalized to Banach spaces and semigroups, see for instance [69, Propositions 4.17 and 4.19]. Analogously to the ODE case it is a necessary condition for asymptotic stability that all eigenvalues of the linearised operator have negative real part.
Although the aforementioned referenced propositions are essentially sufficient to prove stability of the steady states of (3.8), in [18] we can find results more suited for the upcoming analysis. For the sake of convenience, the stability results [18, Theorem 1 and 2] are formulated here. Note that the formulation is summarized into one

Theorem 3.24. *Let z_ε be a non-trivial positive steady state of*

$$\frac{\partial}{\partial t} z(t,x) = A_\varepsilon(F(z))z, \tag{3.19}$$

where $F : (L^1(\Omega))^2 \to \mathbb{R}$ is linear and $A_\varepsilon(E)$, i.e. $A_\varepsilon(\cdot)$ for a fixed value $E = F(z_0)$ with some arbitrary but fixed $z_0 \in \mathbb{R} \times L^1(\Omega)$, be a generator of a C^0-semigroup on $L^1(\Omega)$. Let $\tilde{A}_\varepsilon + S_\varepsilon$ be the linearisation of A_ε at the equilibrium z_ε. Let $\omega_\varepsilon(\lambda), \omega_0(\lambda)$ be the Weinstein-Aronszajn determinants for $\tilde{A}_\varepsilon + S_\varepsilon$ and $\tilde{A}_0 + S_0$ respectively. $D := \{\lambda \in \mathbb{C} \,|\, \Re(\lambda) \geq 0, \lambda \neq 0\}$. Let $\omega_\varepsilon(\lambda), \omega_0(\lambda)$ be holomorphic functions in D, $\omega_0(\lambda)$ shall not vanish in D and

$$\omega_\varepsilon(\lambda) \xrightarrow{\varepsilon \to 0} \omega_0(\lambda) \tag{3.20}$$

uniformly in λ on compact sets in D. Additionally, assume that

$$\exists L > 0 \; \forall \, |\lambda| > L : \quad \left\| S_\varepsilon R(\lambda, \tilde{A}_\varepsilon) \right\|_\infty < \frac{1}{2}. \tag{3.21}$$

If 0 is a strictly dominant eigenvalue of $\tilde{A}_\varepsilon$ with algebraic multiplicity 1, P_ε is the projection onto the eigenspace of the eigenvalue 0 and

$$F\left(P_\varepsilon S_\varepsilon z_\varepsilon\right) \neq 0 \quad \textit{and} \quad \liminf_{(\varepsilon,\lambda)\to(0^+,0)} \lambda F\left((\tilde{A}_\varepsilon - \lambda)^{-1} S_\varepsilon z_\varepsilon\right) \neq 0, \tag{3.22}$$

then for ε small enough the steady state z_ε is locally asymptotically stable.

According to this theorem the first step in proving asymptotic stability of the steady state is to write system (3.9) into the form (3.19). Therefore, we define

$$F : C(\mathbb{R}_+) \times L^1(\Omega) \to C(\mathbb{R}_+), (\rho, u) \mapsto \rho,$$

and

$$A_\varepsilon \left(F \begin{pmatrix} \rho \\ u \end{pmatrix} \right) : C(\mathbb{R}_+) \times L^1(\Omega) \to C(\mathbb{R}_+) \times C(\mathbb{R}_+, L^1(\Omega))$$

$$A_\varepsilon \left(F \begin{pmatrix} \rho \\ u \end{pmatrix} \right) = A_\varepsilon(\rho) = \begin{pmatrix} -d & \int\limits_\Omega 2\left(1 - \frac{a(x)}{1+k\rho}\right) p \cdot \, \mathrm{d}x \\ 0 & \left(\frac{2a(x)}{1+k\rho} - (1+\varepsilon\hat{\kappa})\right) p \cdot + \varepsilon \int\limits_\Omega \kappa(x,y) \cdot \, \mathrm{d}y \end{pmatrix},$$

where we indicate by dots the multiplication and the application of the integral operator, respectively. Note that for fixed ρ, the operator $A_\varepsilon(\rho) : \mathbb{R} \times L^1(\Omega) \to \mathbb{R} \times L^1(\Omega)$ generates a C^0-semigroup, because it can be written like this

$$\begin{aligned} A_\varepsilon(\rho) &= \begin{pmatrix} -d & \int\limits_\Omega 2\left(1 - \frac{a(x)}{1+k\rho}\right) p \cdot \, \mathrm{d}x \\ 0 & \left(\frac{2a(x)}{1+k\rho} - (1+\varepsilon\hat{\kappa})\right) p \cdot + \varepsilon \int\limits_\Omega \kappa(x,y) \cdot \, \mathrm{d}y \end{pmatrix} \\ &= \begin{pmatrix} -d & 0 \\ 0 & \left(\frac{2a(x)}{1+k\rho} - (1+\varepsilon\hat{\kappa})\right) p \cdot \end{pmatrix} + \begin{pmatrix} 0 & \int\limits_\Omega 2\left(1 - \frac{a(x)}{1+k\rho}\right) p \cdot \, \mathrm{d}x \\ 0 & \varepsilon \int\limits_\Omega \kappa(x,y) \cdot \, \mathrm{d}y \end{pmatrix}. \end{aligned}$$

The first term is a multiplication operator, hence it generates a C^0-semigroup on $L^1(\Omega)$, according to [30, Chapter II, Section 2]. The second term is a linear operator, thus the sum still generates a C^0-semigroup, see [30, Chapter III].

3.6.1 Linearisation of the system

For the linearisation we need to compute the Frechét derivative of the operator $A_\varepsilon(\rho)$ at the equilibrium $(\rho_\varepsilon, u_\varepsilon)^T$. Since the linearisation is a local concept, it suffices to derive the Gateaux derivative, [54, Satz 2.5]. System (3.9) admits the steady state $z_\varepsilon = (\rho_\varepsilon, u_\varepsilon)^T$ around which we want to linearise. In an abstract form this means to choose a perturbation $s \in \mathbb{R} \times L^1(\Omega)$ such that $z = z_\varepsilon + s$. Then we obtain by

differentiation, the fact that $\frac{\partial}{\partial t} z_\varepsilon = 0$ and by Taylors formula

$$\frac{\partial}{\partial t} s = A_\varepsilon(F(z_\varepsilon) + F(s))(z_\varepsilon + s) = \left(A_\varepsilon(F(z_\varepsilon)) + DA_\varepsilon(z_\varepsilon)F(s) + \ldots\right)(z_\varepsilon + s).$$

Taking now only the linear terms yields

$$\frac{\partial}{\partial t} s = A_\varepsilon(F(z_\varepsilon))s + DA_\varepsilon(F(z_\varepsilon))F(s)z_\varepsilon. \tag{3.23}$$

Doing the linearisation now for system (3.9) yields with $\varphi \in \mathbb{R}_+, \psi \in L^1(\Omega)$ and some $\delta > 0$

1.

$$\frac{\mathrm{d}}{\mathrm{d}\delta}\left[\int_\Omega 2\left(1 - \frac{a(x)}{1 + k(\rho_\varepsilon + \delta\varphi)}\right) p u_\varepsilon(x)\,\mathrm{d}x - d(\rho_\varepsilon + \delta\varphi)\right]\Big|_{\delta=0} = \int_\Omega \frac{2a(x)kpu_\varepsilon(x)\varphi}{(1 + k\rho_\varepsilon)^2}\,\mathrm{d}x - d\varphi.$$

2.

$$\frac{\mathrm{d}}{\mathrm{d}\delta}\left[\int_\Omega 2\left(1 - \frac{a(x)}{1 + k\rho_\varepsilon}\right) p(u_\varepsilon(x) + \delta\psi(x))\,\mathrm{d}x - d\rho_\varepsilon\right]\Big|_{\delta=0} = \int_\Omega 2\left(1 - \frac{a(x)}{1 + k\rho_\varepsilon}\right) p\psi(x)\,\mathrm{d}x.$$

3.

$$\frac{\mathrm{d}}{\mathrm{d}\delta}\left[\left(\frac{2a(x)}{1 + k(\rho_\varepsilon + \delta\varphi)} - (1 + \varepsilon\hat{\kappa})\right) p u_\varepsilon + \varepsilon \int_\Omega \kappa(x, y) u_\varepsilon(y)\,\mathrm{d}y\right]\Big|_{\delta=0} = -\frac{2a(x)kpu_\varepsilon(x)\varphi}{(1 + k\rho_\varepsilon)^2}.$$

4.

$$\frac{\mathrm{d}}{\mathrm{d}\delta}\left[\left(\frac{2a(x)}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)p(u_\varepsilon(x)+\delta\psi(x))+\varepsilon\int_\Omega\kappa(x,y)(u_\varepsilon(y)+\delta\psi(y))\,\mathrm{d}y\right]\Big|_{\delta=0}$$
$$=\left(\frac{2a(x)}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)p\psi(x)+\varepsilon\int_\Omega\kappa(x,y)\psi(y)\,\mathrm{d}y.$$

This yields that

$$\begin{aligned}DA_\varepsilon(F(z_\varepsilon))&=\begin{pmatrix}\int_\Omega\frac{2a(x)kpu_\varepsilon(x)\cdot}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x-d\cdot & \int_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)p\cdot\,\mathrm{d}x\\ -\frac{2a(x)kpu_\varepsilon(x)\cdot}{(1+k\rho_\varepsilon)^2} & \left(\frac{2a(x)}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)p\cdot+\varepsilon\int_\Omega\kappa(x,y)\cdot\,\mathrm{d}y\end{pmatrix}\\&=\begin{pmatrix}-d & \int_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)p\cdot\,\mathrm{d}x\\ 0 & \left(\frac{2a(x)}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)p\cdot+\varepsilon\int_\Omega\kappa(x,y)\cdot\,\mathrm{d}y\end{pmatrix}+\begin{pmatrix}\int_\Omega\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2} & 0\\ -\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2} & 0\end{pmatrix}\\&=:\tilde{A}_\varepsilon+G_\varepsilon.\end{aligned}$$

Observe, that $\tilde{A}_\varepsilon=A_\varepsilon(F(z_\varepsilon))=A_\varepsilon(\rho_\varepsilon)$. The linearisation (3.23), the fact that F maps into $\mathbb{R}$ and that z_ε is the steady state of $\tilde{A}_\varepsilon$ implies

$$D\tilde{A}_\varepsilon F(s)z_\varepsilon=(\tilde{A}_\varepsilon+G_\varepsilon)F(s)z_\varepsilon=F(s)\tilde{A}_\varepsilon z_\varepsilon+G_\varepsilon F(s)z_\varepsilon=G_\varepsilon F(s)z_\varepsilon=:S_\varepsilon s.$$

We can infer that the linearisation is given by $\tilde{A}_\varepsilon+S_\varepsilon$ with

$$\begin{aligned}&\tilde{A}_\varepsilon:\mathbb{R}_+\times L^1(\Omega)\to\mathbb{R}_+\times L^1(\Omega),\\&\tilde{A}_\varepsilon=A_\varepsilon(\rho_\varepsilon)=\begin{pmatrix}-d & \int_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)p\cdot\,\mathrm{d}x\\ 0 & \left(\frac{2a(x)}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)p\cdot+\varepsilon\int_\Omega\kappa(x,y)\cdot\,\mathrm{d}y\end{pmatrix}\qquad(3.24)\\&S_\varepsilon:\mathbb{R}_+\times L^1(\Omega)\to\mathbb{R}_+\times L^1(\Omega),\\&S_\varepsilon=\begin{pmatrix}\int_\Omega\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2} & 0\\ -\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2} & 0\end{pmatrix}.\qquad(3.25)\end{aligned}$$

Repeating the computations for system (2.2) yields

$$\tilde{A}_0:\mathbb{R}_+\times\mathcal{M}^+(\Omega)\to\mathbb{R}_+\times\mathcal{M}^+(\Omega),$$

$$\tilde{A}_0 = A_0(\bar{\rho}) = \begin{pmatrix} -d & \int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\bar{\rho}}\right)p\cdot \,\mathrm{d}x \\ 0 & \left(\frac{2a(x)}{1+k\bar{\rho}}-1\right)p\cdot \end{pmatrix}$$

$$S_0 : \mathbb{R}_+ \times \mathcal{M}^+(\Omega) \to \mathbb{R}_+ \times \mathcal{M}^+(\Omega),$$

$$S_0 = \begin{pmatrix} \int\limits_\Omega \frac{2a(x)kp\bar{u}\cdot}{(1+k\bar{\rho})^2}\,\mathrm{d}x & 0 \\ -\frac{2a(x)kp\bar{u}}{(1+k\bar{\rho})^2} & 0 \end{pmatrix}.$$

Motivation of Theorem's 3.24 assumptions

Theorem 3.24 contains several technical assumptions to ensure stability. The important concept behind this theorem is the method of linearised stability. For linearised stability to work, it is necessary to guarantee, that the linearised operator does not have eigenvalues with non-negative real part. All assumptions in Theorem 3.24 exclude certain parts of the spectrum. There are mainly three parts, which are ruled out: the set, where the real part is bigger than a specific threshold, i.e. $\left\{\lambda \in \sigma(\tilde{A}_\varepsilon + S_\varepsilon)\,||\lambda| > L_2,\, \Re(\lambda) \geq 0\right\}$, then the set, where the eigenvalue is smaller than some threshold, i.e. $\left\{\lambda \in \sigma(\tilde{A}_\varepsilon + S_\varepsilon)\,||\lambda| < L_1,\, \lambda \neq 0\right\}$ and 0 must also be excluded. In the following a heuristical explanation is given for the assumptions made in Theorem 3.24 to elucidate why exactly the assumptions are needed to guarantee the absence of the said sets in the spectrum.

Set with big real part:
Let us assume that the Weinstein-Aronszajn determinant $\omega_\varepsilon(\lambda)$ does not have a zero. Furthermore, we already know that 0 is the dominant eigenvalue of $\tilde{A}_\varepsilon$, thus there exists no eigenvalue of $\tilde{A}_\varepsilon$ with positive real part. Then, according to the definition of the multiplicity function for operators (3.6), $\tilde{\nu}(\zeta, \tilde{A}_\varepsilon) = 0$ for all $\zeta \in \mathbb{C}$ with $\Re(\zeta) > 0$. If $\omega_\varepsilon(\zeta)$ is analytic for all such ζ (so it has no pole) and has no zero, then the multiplicity function $\nu(\zeta, \omega_\varepsilon) = 0$. By Theorem 3.11 we obtain

$$\forall\, \zeta \in \mathbb{C},\, \Re(\zeta) > 0 : \quad \tilde{\nu}(\zeta, \tilde{A}_\varepsilon + S_\varepsilon) = \tilde{\nu}(\zeta, \tilde{A}_\varepsilon) + \nu(\zeta, \omega_\varepsilon) = 0.$$

Because of the definition of $\tilde{\nu}$, see (3.6), it holds that $\{\zeta \in \mathbb{C}\,|\Re(\zeta) > 0\} \not\subset \sigma(\tilde{A}_\varepsilon + S_\varepsilon)$. This explains why in Theorem 3.24 it is assumed that $\omega_0(\lambda)$ has no zero. This way, for ε small enough ω_ε does not have a zero as well in the set with real part bigger than a threshold, see [18, Theorem 1]. The assumed holomorphicity excludes poles.

Set with small real part:
Following the same argument as above it is sufficient to prove that ω_ε has no zero in the set with small real part. According to [18, Proposition 2] this can be achieved by proving the lim inf-condition in (3.22).

The set containing only 0*:*
The final step in achieving stability is to prove that $\sigma(\tilde{A}_\varepsilon + S_\varepsilon)$ does not contain 0. The answer is given again by the Weinstein-Aronszajn formula. The definition of the multiplicity function for operators, see (3.6) implies that if $\zeta \in \sigma(\tilde{A}_\varepsilon)$ is an isolated eigenvalue of $\tilde{A}_\varepsilon$ then $\tilde{\nu}(\zeta, \tilde{A}_\varepsilon) = \dim(P)$, where P is the spectral projection onto the eigenspace corresponding to the eigenvalue ζ. Proposition 3.14 provides a one dimensional eigenspace for the eigenvalue 0 of $\tilde{A}_\varepsilon$, which implies that $\tilde{\nu}(0, \tilde{A}_\varepsilon) = 1$. So in order to exclude 0 from the spectrum of $\tilde{A}_\varepsilon + S_\varepsilon$, we need to ascertain that $\tilde{\nu}(0, \tilde{A}_\varepsilon + S_\varepsilon) = 0$. This can be only done if $\nu(0, \omega_\varepsilon) = -1$.
The relation $\nu(0, \omega_\varepsilon) = -1$ means, that 0 is a pole of order 1 for the Weinstein-Aronzsajn determinant. So let $\xi_\varepsilon \in rg(S_\varepsilon)$, namely, $\xi_\varepsilon = DA_\varepsilon(F(z_\varepsilon))z_\varepsilon$, where z_ε is the eigenfunction corresponding to the eigenvalue 0. Note, that this is only possible, since F maps into a one dimensional space. Then it has to hold

$$\lim_{\lambda \to 0} \lambda \left((Id + S_\varepsilon R(\lambda, \tilde{A}_\varepsilon))\xi_\varepsilon \right) = S_\varepsilon \lim_{\lambda \to 0} \lambda R(\lambda, \tilde{A}_\varepsilon)\xi_\varepsilon = S_\varepsilon P_\varepsilon \xi_\varepsilon.$$

According to [30, Chapter IV, Section 1], 0 is a pole of $R(\lambda, \tilde{A}_\varepsilon)$ if and only if $S_\varepsilon P_\varepsilon \xi_\varepsilon \neq 0$. Since the eigenspace of 0 is spanned by the vector ξ_ε, we obtain with some $\beta_\varepsilon \in \mathbb{R}$

$$S_\varepsilon P_\varepsilon \xi_\varepsilon = S_\varepsilon \beta_\varepsilon z_\varepsilon = \beta_\varepsilon S_\varepsilon z_\varepsilon = \beta_\varepsilon DA_\varepsilon(F(z_\varepsilon))F(z_\varepsilon)z_\varepsilon = \beta_\varepsilon F(z_\varepsilon)\xi_\varepsilon.$$

So $\omega_\varepsilon(\lambda)$ has a pole of first order if and only if neither β_ε nor $F(z_\varepsilon)z_\varepsilon$ is zero. Since the spectral projection admits a decomposition of the underlying space, we obtain $L^1(\Omega) = \langle z_\varepsilon \rangle \oplus rg(\tilde{A}_\varepsilon)$. This means that $\beta_\varepsilon \neq 0$ is equivalent to $\xi_\varepsilon \notin rg(\tilde{A}_\varepsilon)$. So we need to assume

$$\xi_\varepsilon \notin rg(\tilde{A}_\varepsilon) \quad \text{and} \quad F(z_\varepsilon) \neq 0.$$

This is equivalent to $F(P_\varepsilon DA_\varepsilon(F(z_\varepsilon))z_\varepsilon) \neq 0$, according to [18, Proof of Proposition 1].

Theorem 3.25. *Let Assumption 3 hold and additionally, let κ be separable in its variables, i.e.*

$$\exists \kappa_1, \kappa_2 \in C(\overline{\Omega}) : \ \kappa(x,y) = \kappa_1(x)\kappa_2(y).$$

Let $\tilde{A}_\varepsilon, \tilde{A}_0, S_\varepsilon, S_0$ be as in Section 3.6.1. Then the steady state $(\rho_\varepsilon, u_\varepsilon)^T$ provided by Theorem 3.18 is locally asymptotically stable.

The proof of this theorem is done by the application of Theorem 3.24. Since this theorem has a lot of assumptions, the proof is split into several parts, each dealing with a different assumption.

3.6.2 Convergence of the Weinstein-Aronszajn determinants

To define the Weinstein-Aronszajn determinants $\omega_\varepsilon(\lambda), \omega_0(\lambda)$ we need to prove that S_ε is $\tilde{A}_\varepsilon$-bounded and S_0 is $\tilde{A}_0$-bounded and that $\dim(rg(S_\varepsilon)), \dim(rg(S_0)) < \infty$. Since S_ε and S_0 are identical apart from the considered spaces, it suffices to look at S_ε and the results for S_0 follow immediately.
The operator S_ε acts only on the first component of $(\rho, u)^T$ and for ρ it is a multiplication operator, hence it is linear. Due to the assumptions on the function a and the regularity of the steady state u_ε the operator S_ε is bounded. Thus it is $\tilde{A}_\varepsilon$-bounded.
The next step is to show that S_ε has finite range.

$$S_\varepsilon \begin{pmatrix} \rho \\ u \end{pmatrix} = \begin{pmatrix} \int_\Omega \frac{2a(x)kpu_\varepsilon\rho}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x \\ -\frac{2a(x)kpu_\varepsilon\rho}{(1+k\rho_\varepsilon)^2} \end{pmatrix} = \rho \begin{pmatrix} \int_\Omega \frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x \\ -\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2} \end{pmatrix}, \tag{3.26}$$

which is the basis vector of $rg(S_\varepsilon)$, hence $\dim(rg(S_\varepsilon)) = 1$. The same argument holds for S_0. Now that we know that the Weinstein-Aronszajn determinant is well defined, we can prove condition (3.20).

Lemma 3.26. *Let $\omega_\varepsilon(\lambda), \omega_0(\lambda)$ be the Weinstein- Aronszajn determinants for $\tilde{A}_\varepsilon, \tilde{A}_0$ respectively. Then*

$$\omega_\varepsilon(\lambda) \xrightarrow{\varepsilon \to 0} \omega_0(\lambda)$$

uniformly in $\lambda \in D = \{\lambda \in \mathbb{C} \,|\, \Re(\lambda) \geq 0, \lambda \neq 0\}$. Both $\omega_\varepsilon(\lambda)$ and $\omega_0(\lambda)$ are holomorphic in D.

Proof. In order to prove the convergence we estimate

$$|\omega_\varepsilon(\lambda) - \omega_0(\lambda)| = \left|\det\left(Id + S_\varepsilon R(\tilde{A}_\varepsilon, \lambda)_{|rg(S_\varepsilon)}\right) - \det\left(Id + S_0 R(\tilde{A}_0, \lambda)_{|rg(S_0)}\right)\right|$$

$$\leq \left|\det\left(Id + S_\varepsilon R(\tilde{A}_\varepsilon, \lambda)_{|rg(S_\varepsilon)}\right) - \det\left(Id + S_\varepsilon R(\tilde{A}_0, \lambda)_{|rg(S_\varepsilon)}\right)\right|$$
$$+ \left|\det\left(Id + S_\varepsilon R(\tilde{A}_0, \lambda)_{|rg(S_\varepsilon)}\right) - \det\left(Id + S_0 R(\tilde{A}_0, \lambda)_{|rg(S_0)}\right)\right|.$$

For the first term on the right-hand side we can show even more than convergence of the determinants. We show that

$$\left\|S_\varepsilon(\tilde{A}_\varepsilon - \lambda)^{-1}_{|R(S_\varepsilon)} - S_\varepsilon(\tilde{A}_0 - \lambda)^{-1}_{|R(S_\varepsilon)}\right\|_\infty \xrightarrow{\varepsilon\to 0} 0.$$

Analogously to [24, proof of Proposition 1], denote by $B_\varepsilon := \tilde{A}_\varepsilon - \tilde{A}_0$, then $\|B_\varepsilon\|_\infty \to 0$ as $\varepsilon \to 0$. Additionally, we can compute using the second resolvent identity, see for instance [70, p. 306],

$$\begin{aligned} R(\lambda, \tilde{A}_0 + B_\varepsilon)\left(Id - B_\varepsilon R(\lambda, \tilde{A}_0)\right) &= R(\lambda, \tilde{A}_0 + B_\varepsilon) - R(\lambda, \tilde{A}_0 + B_\varepsilon)B_\varepsilon R(\lambda, \tilde{A}_0) \\ &= R(\lambda, \tilde{A}_0 + B_\varepsilon) + R(\lambda, \tilde{A}_0) - R(\lambda, \tilde{A}_0 + B_\varepsilon) \\ &= R(\lambda, \tilde{A}_0). \end{aligned}$$

This leads to

$$\begin{aligned} (\tilde{A}_\varepsilon - \lambda)^{-1} = R(\lambda, \tilde{A}_\varepsilon) = R(\lambda, \tilde{A}_0 + B_\varepsilon) &= R(\lambda, \tilde{A}_0)\left(Id - B_\varepsilon R(\lambda, \tilde{A}_0)\right)^{-1} \\ &= R(\lambda, \tilde{A}_0)\sum_{n=0}^{\infty}\left(B_\varepsilon R(\lambda, \tilde{A}_0)\right)^n. \end{aligned}$$

The last step could be done due to the fact that B_ε converges to 0 and hence we can use the Neumann series. This equality can now be used in

$$\begin{aligned} \left\|S_\varepsilon(\tilde{A}_\varepsilon - \lambda)^{-1} - S_\varepsilon(\tilde{A}_0 - \lambda)^{-1}\right\|_\infty &= \left\|S_\varepsilon R(\lambda, \tilde{A}_0)\left(\sum_{n=0}^{\infty}(B_\varepsilon R(\lambda, \tilde{A}_0))^n - Id\right)\right\|_\infty \\ &= \left\|S_\varepsilon R(\lambda, \tilde{A}_0)\sum_{n=1}^{\infty}(B_\varepsilon R(\lambda, \tilde{A}_0))^n\right\|_\infty \\ &\leq \|S_\varepsilon\|_\infty \left\|R(\lambda, \tilde{A}_0)\right\|_\infty \frac{\left\|B_\varepsilon R(\lambda, \tilde{A}_0)\right\|_\infty}{1 - \left\|B_\varepsilon R(\lambda, \tilde{A}_0)\right\|_\infty} \\ &\to 0, \end{aligned}$$

because S_ε and $R(\lambda, \tilde{A}_0)$ are bounded operators and B_ε converges to 0 as ε tends to 0. The convergence of the determinant follows from the continuity of the determinant

in combination with the uniform convergence above.
It is left to prove that

$$\left|\det\left(Id + S_\varepsilon R(\tilde{A}_0,\lambda)_{|R(S_\varepsilon)}\right) - \det\left(Id + S_0 R(\tilde{A}_0,\lambda)_{|R(S_0)}\right)\right| \overset{\varepsilon\to 0}{\longrightarrow} 0.$$

For this purpose we compute the determinant explicitly. According to Section 3.1 we need to derive the basis representation of the investigated operator. The basis of $rg(S_\varepsilon)$ is given by equation (3.26). Then we can determine the range of $Id + S_\varepsilon R(\tilde{A}_0,\lambda)_{|rg(S_\varepsilon)}$.

$$\left(Id + S_\varepsilon R(\tilde{A}_0,\lambda)\right)\begin{pmatrix}\int\limits_\Omega \frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x\\ -\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2}\end{pmatrix} = \begin{pmatrix}\int\limits_\Omega \frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x\\ -\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2}\end{pmatrix} + S_\varepsilon R(\tilde{A}_0,\lambda)\begin{pmatrix}\int\limits_\Omega \frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x\\ -\frac{2a(x)kpu_\varepsilon}{(1+k\rho_\varepsilon)^2}\end{pmatrix}.$$

At this point we need to compute the operator $S_\varepsilon R(\tilde{A}_0,\lambda)$ explicitly. It holds

$$R(\tilde{A}_0,\lambda) = \begin{pmatrix} -\frac{1}{d+\lambda} & \frac{1}{d+\lambda}\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\bar{\rho}}\right)p\frac{1}{\left(\frac{2a(x)}{1+k\bar{\rho}}-1\right)p-\lambda}\cdot\,\mathrm{d}x \\ 0 & \frac{1}{(d+\lambda)\left[\left(\frac{2a(x)}{1+k\bar{\rho}}-1\right)p-\lambda\right]}\end{pmatrix}$$

For the sake of simplicity, let us denote by

$$A = \int\limits_\Omega \frac{2a(x)pu_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x, \quad B = -\frac{2a(x)pu_\varepsilon}{(1+k\rho_\varepsilon)^2},$$

then we obtain

$$S_\varepsilon R(\tilde{A}_0,\lambda) = \begin{pmatrix} -\frac{1}{d+\lambda}A & \frac{1}{d+\lambda}A\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\bar{\rho}}\right)p\frac{1}{\left(\frac{2a(x)}{1+k\bar{\rho}}-1\right)p-\lambda}\cdot\,\mathrm{d}x \\ -\frac{1}{d+\lambda}B & -\frac{1}{d+\lambda}\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\bar{\rho}}\right)p\frac{1}{\left(\frac{2a(x)}{1+k\bar{\rho}}-1\right)p-\lambda}B\,\mathrm{d}x\end{pmatrix}.$$

Applying this operator to some vector $(A,B)^T \in rg(S_\varepsilon)$, yields

$$\begin{aligned} S_\varepsilon R(\tilde{A}_0,\lambda)\begin{pmatrix}A\\B\end{pmatrix} &= \begin{pmatrix} A\left[-\frac{1}{d+\lambda}A + \frac{1}{d+\lambda}\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\bar{\rho}}\right)p\frac{1}{\left(\frac{2a(x)}{1+k\bar{\rho}}-1\right)p-\lambda}B\,\mathrm{d}x\right] \\ B\left[-\frac{1}{d+\lambda}A + \frac{1}{d+\lambda}\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\bar{\rho}}\right)p\frac{1}{\left(\frac{2a(x)}{1+k\bar{\rho}}-1\right)p-\lambda}B\,\mathrm{d}x\right]\end{pmatrix} \\ &= \mathrm{tr}(S_\varepsilon R(\tilde{A}_0,\lambda))\begin{pmatrix}A\\B\end{pmatrix}\end{aligned}$$

Eventually, we get

$$\left(Id + S_\varepsilon R(\tilde{A}_0, \lambda)\right) \begin{pmatrix} A \\ B \end{pmatrix} = \left(1 + \operatorname{tr}(S_\varepsilon R(\tilde{A}_0, \lambda))\right) \begin{pmatrix} A \\ B \end{pmatrix}.$$

We see that $Id + S_\varepsilon R(\tilde{A}_0, \lambda)$ leaves $rg(S_\varepsilon)$ invariant and since the range is one dimensional, the matrix representation is given by the number $1 + \operatorname{tr}(S_\varepsilon R(\tilde{A}_0, \lambda))$, and hence, again due to the one dimensionality, this is the value of the determinant. Analogously, we obtain that the determinant of $Id + S_0 R(\tilde{A}_0, \lambda)$ is given by $1 + \operatorname{tr}(S_0 R(\tilde{A}_0, \lambda))$. We are left to prove

$$\left|\operatorname{tr}(S_\varepsilon R(\tilde{A}_0, \lambda)) - \operatorname{tr}(S_0 R(\tilde{A}_0, \lambda))\right| \xrightarrow{\varepsilon \to 0} 0.$$

Direct calculation yields that

$$\begin{aligned} \operatorname{tr}(S_\varepsilon R(\tilde{A}_0, \lambda)) &= -\frac{1}{d+\lambda} \int_\Omega \frac{2a(x)kpu_\varepsilon(x)}{(1+k\rho_\varepsilon)^2} \, \mathrm{d}x \\ &\quad + \frac{1}{d+\lambda} \int_\Omega 2\left(1 - \frac{a(x)}{1+k\bar{\rho}}\right) p \frac{1}{\left(\frac{2a(x)}{1+k\bar{\rho}} - 1\right) p - \lambda} \frac{2a(x)kpu_\varepsilon(x)}{(1+k\rho_\varepsilon)^2} \, \mathrm{d}x. \end{aligned}$$

According to Theorem 3.23 we know that ρ_ε converges strongly to $\bar{\rho}$ in $\mathbb{R}$ and u_ε converges weakly* to $\delta_{\bar{x}}$ in $\mathcal{M}^+(\Omega)$. Hence

$$\begin{aligned} \operatorname{tr}(S_\varepsilon R(\tilde{A}_0, \lambda)) &\xrightarrow{\varepsilon \to 0} -\frac{1}{d+\lambda} \frac{2\bar{a}kp}{(1+k\bar{\rho})^2} - \frac{1}{\lambda(d+\lambda)} 2\left(1 - \frac{\bar{a}}{1+k\bar{\rho}}\right) p \frac{2\bar{a}kp}{(1+k\bar{\rho})^2} \\ &= \operatorname{tr}(S_0 R(\tilde{A}_0, \lambda)). \end{aligned}$$

By definition of the Weinstein-Aronszajn determinant, $\omega_\varepsilon(\lambda)$ and $\omega_0(\lambda)$ are holomorphic in D, see [37, p. 245]. □

3.6.3 Boundedness of $S_\varepsilon R(\lambda, \tilde{A}_\varepsilon)$

Lemma 3.27. *There exists a constant $L > 0$ such that for all $|\lambda| > L$*

$$\left\| S_\varepsilon R(\lambda, \tilde{A}_\varepsilon) \right\|_\infty < \frac{1}{2}.$$

Proof. Since $\sup_{\varepsilon<\varepsilon_0}\left\|\tilde{A}_\varepsilon\right\|_\infty$ and $\sup_{\varepsilon<\varepsilon_0}\|S_\varepsilon\|_\infty$ are bounded, we have for $|\lambda| > 2\left\|\tilde{A}_\varepsilon\right\|_\infty$

$$\left\|S_\varepsilon R(\lambda,\tilde{A}_\varepsilon)\right\|_\infty = \left\|S_\varepsilon\lambda^{-1}\sum_{n=0}^{\infty}\left(\lambda^{-1}\tilde{A}_\varepsilon\right)^n\right\|_\infty \leq \frac{\|S_\varepsilon\|_\infty}{\lambda-\left\|\tilde{A}_\varepsilon\right\|_\infty} \leq \frac{2\|S_\varepsilon\|_\infty}{|\lambda|}.$$

Choose $L > \max\left\{2\left\|\tilde{A}_\varepsilon\right\|_\infty, 4\|S_\varepsilon\|_\infty\right\}$ to conclude. □

3.6.4 Excluding 0 from the spectrum

Lemma 3.28. *For the steady state z_ε it holds*

$$F\left(P_\varepsilon S_\varepsilon z_\varepsilon\right) \neq 0. \tag{3.27}$$

Proof. We have seen that

$$\begin{aligned} A_\varepsilon(\rho_\varepsilon) &= \begin{pmatrix} -d & \int_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)p\cdot\,\mathrm{d}x \\ 0 & \left(\frac{2a(x)}{1+k\rho_\varepsilon}-(1+\varepsilon\hat{\kappa})\right)p\cdot+\varepsilon\int_\Omega\kappa(x,y)\cdot\,\mathrm{d}y \end{pmatrix} \\ &= \begin{pmatrix} -d & \int_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)p\cdot\,\mathrm{d}x \\ 0 & C_{\varepsilon,\rho_\varepsilon} \end{pmatrix}. \end{aligned}$$

Hence the spectrum of $\tilde{A}_\varepsilon$ is given by $\sigma(\tilde{A}_\varepsilon)=\sigma(C_{\varepsilon,\rho_\varepsilon})\cup\{-d\}$. Since the operator's $C_{\varepsilon,\rho_\varepsilon}$ dominant eigenvalue is 0 with multiplicity 1, so it is for $\tilde{A}_\varepsilon$. Since the algebraic multiplicity is 1 and cannot be exceeded by the geometric multiplicity, the dimension of the eigenspace corresponding to the eigenvalue 0 is also 1. This means, that any projection onto the eigenspace has to have the following form up to a multiplicative constant

$$P_\varepsilon\begin{pmatrix}\rho\\u\end{pmatrix} := \begin{cases} Id, & (\rho,u)^T = c(\rho_\varepsilon,u_\varepsilon)^T, c\in\mathbb{R}, \\ (\rho_\varepsilon,u_\varepsilon)^T, & else. \end{cases}. \tag{3.28}$$

The definition of the projection P_ε in combination with (3.22) yields

$$\forall 0<\varepsilon<\varepsilon_0: \quad F\left(P_\varepsilon\begin{pmatrix}\rho\\u\end{pmatrix}\right)=\rho_\varepsilon\neq 0,$$

by Theorem 3.18. □

3.6.5 Excluding values with small positive real part from the spectrum

The last step is to show

Lemma 3.29. *For the steady state z_ε it holds*

$$\liminf_{(\varepsilon,\lambda)\to(0^+,0)} \lambda F\left((\tilde{A}_\varepsilon-\lambda)^{-1}S_\varepsilon z_\varepsilon\right)\neq 0. \tag{3.29}$$

Proof. It is necessary to determine the resolvent operator $R(\lambda,\tilde{A}_\varepsilon)$ first. It reads like the following

$$(\tilde{A}_\varepsilon-\lambda)^{-1}=\begin{pmatrix} \frac{-1}{d+\lambda} & \frac{1}{d+\lambda}\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)pR(\lambda,C_{\varepsilon,\rho_\varepsilon})\cdot\,\mathrm{d}x \\ 0 & R(\lambda,C_{\varepsilon,\rho_\varepsilon})\end{pmatrix},$$

which can be confirmed by left and right multiplication. This yields

$$\begin{aligned}&(\tilde{A}_\varepsilon-\lambda)^{-1}\begin{pmatrix}\int\limits_\Omega \frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x\\ -\frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\end{pmatrix}\\ =\;&\begin{pmatrix}\frac{-1}{d+\lambda}\left(\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)pR(\lambda,C_{\varepsilon,\rho_\varepsilon})\frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x+\int\limits_\Omega\frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x\right)\\ R(\lambda,C_{\varepsilon,\rho_\varepsilon})\frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\end{pmatrix}.\end{aligned}$$

Condition (3.29) reads then

$$\begin{aligned}&\liminf_{(\varepsilon,\lambda)\to(0^+,0)}\lambda F\left((\tilde{A}_\varepsilon-\lambda)^{-1}S_\varepsilon\begin{pmatrix}\rho_\varepsilon\\ u_\varepsilon\end{pmatrix}\right)\\ =\;&\liminf_{(\varepsilon,\lambda)\to(0^+,0)}\frac{-\lambda}{d+\lambda}\left(\int\limits_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)pR(\lambda,C_{\varepsilon,\rho_\varepsilon})\frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x+\int\limits_\Omega\frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x\right)\end{aligned}$$

It is known that lim inf is superadditive, i.e. for two sequences $(a_n)_{n\in\mathbb{N}},(b_n)_{n\in\mathbb{N}}\subset\mathbb{R}$ the following holds true

$$\liminf_{n\to\infty}(a_n+b_n)\geq\liminf_{n\to\infty}a_n+\liminf_{n\to\infty}b_n.$$

Furthermore, let us assume that a_n converges, then the equality holds (likewise if b_n converges). Thus we check that

$$\lim_{(\varepsilon,\lambda)\to(0^+,0)} \frac{\lambda}{d+\lambda} \int_\Omega \frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x = 0 \cdot \frac{2\bar{a}kp\bar{\rho}}{(1+k\bar{\rho})^2} = 0.$$

Subsequently we only need to investigate

$$\liminf_{(\varepsilon,\lambda)\to(0^+,0)} \frac{1}{d+\lambda} \int_\Omega 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right) p\lambda R(\lambda, C_{\varepsilon,\rho_\varepsilon}) \frac{2a(x)kpu_\varepsilon\rho_\varepsilon}{(1+k\rho_\varepsilon)^2}\,\mathrm{d}x.$$

Here arises a problem, which makes the determination of the limit difficult. Since 0 is an eigenvalue of $C_{\varepsilon,\rho_\varepsilon}$ the limiting behaviour of $\lambda R(\lambda, C_{\varepsilon,\rho_\varepsilon})$ for λ tending to zero is not obvious, because the resolvent tends to infinity while λ tends to zero.
The separation of variables of κ allows deriving explicitly the resolvent $R(\lambda, C_{\varepsilon,\rho_\varepsilon})$. Due to this separation we can write

$$C_{\varepsilon,\rho_\varepsilon}u = \left(\frac{2a(x)}{1+k\rho_\varepsilon} - (1+\varepsilon\hat{\kappa})\right) pu + \varepsilon\kappa_1(x) \int_\Omega \kappa_2(y)u(y)\,\mathrm{d}y = -\alpha(x)u + \varepsilon\kappa_1(x)Lu,$$

where $\alpha(x) = \left(1+\varepsilon\hat{\kappa} - \frac{2a(x)}{1+k\rho_\varepsilon}\right) p > 0$, since ρ_ε is the steady state of equation (3.9) and $Lu = \int_\Omega \kappa_2(y)u(y)\,\mathrm{d}y$. Then we can compute

$$\begin{aligned} (C_{\varepsilon,\rho_\varepsilon} - \lambda)v &= g, \\ \Leftrightarrow -\alpha(x)v + \varepsilon\kappa_1(x)Lv - \lambda v &= g, \\ \Leftrightarrow\ \varepsilon\kappa_1(x)Lv - (\alpha(x)+\lambda)v &= g. \end{aligned}$$

Since $\alpha(x) > 0$, the inverse of $(\alpha(x)+\lambda)$ exists and we obtain

$$\varepsilon(\alpha(x)+\lambda)^{-1}\kappa_1(x)Lv - v = (\alpha(x)+\lambda)^{-1}g.$$

Solving this equation for v yields

$$v = -(\alpha(x)+\lambda)^{-1}g + \varepsilon(\alpha(x)+\lambda)^{-1}\kappa_1(x)Lv. \tag{3.30}$$

The aim is to get rid of Lv, because then we would have obtained an explicit formula for v.

Applying the linear operator L to both sides results in

$$Lv = -L\left((\alpha(x)+\lambda)^{-1}g\right) + \varepsilon L\left((\alpha(x)+\lambda)^{-1}\kappa_1(x)\right)Lv. \tag{3.31}$$

Note that this computation is only possible because of the separation of variables of κ, because otherwise it would not be possible to plug $Lv \in \mathbb{R}$ out of L. Rearrangement of the equation leads to

$$-L\left((\alpha(x)+\lambda)^{-1}g\right) = \left(1 - \varepsilon L\left((\alpha(x)+\lambda)^{-1}\kappa_1(x)\right)\right)Lv. \tag{3.32}$$

Now beginning with the steady state equation we have

$$-\alpha(x)u_\varepsilon + \varepsilon\kappa_1(x)Lu_\varepsilon = 0,$$

which is equivalent to

$$u_\varepsilon = \varepsilon\frac{\kappa_1(x)}{\alpha(x)}Lu_\varepsilon. \tag{3.33}$$

Applying to both sides the operator L yields and dividing by $Lu_\varepsilon > 0$

$$Lu_\varepsilon = \varepsilon L\left(\frac{\kappa_1(x)}{\alpha(x)}\right)Lu_\varepsilon \;\Leftrightarrow\; 1 = \varepsilon L\left(\frac{\kappa_1(x)}{\alpha(x)}\right). \tag{3.34}$$

Substituting equation (3.34) into equation (3.32) yields

$$\begin{aligned}\left(1 - \varepsilon L\left((\alpha(x)+\lambda)^{-1}\kappa_1(x)\right)\right)Lv &= \varepsilon\left(L\left(\frac{\kappa_1(x)}{\alpha(x)}\right) - L\left((\alpha(x)+\lambda)^{-1}\kappa_1(x)\right)\right)Lv \\ &= \varepsilon\lambda L\left(\frac{\kappa_1(x)}{\alpha(x)(\alpha(x)+\lambda)}\right)Lv. \end{aligned}\tag{3.35}$$

Inserting equation (3.35) into equation (3.32) gives

$$Lv = \frac{-1}{\varepsilon\lambda}L\left(\frac{\kappa_1(x)}{\alpha(x)(\alpha(x)+\lambda)}\right)^{-1} L\left((\alpha(x)+\lambda)^{-1}g\right).$$

Plugging the term for Lv into equation (3.30) gives us the inverse

$$v = -(\alpha(x)+\lambda)^{-1}g - (\alpha(x)+\lambda)^{-1}\kappa_1(x)\frac{1}{\lambda}L\left(\frac{\kappa_1(x)}{\alpha(x)(\alpha(x)+\lambda)}\right)^{-1} L\left((\alpha(x)+\lambda)^{-1}g\right)$$

$$
\begin{aligned}
&= \frac{1}{\varepsilon\lambda} L\left(\frac{\kappa_1(x)}{\alpha(x)(\alpha(x)+\lambda)}\right)^{-1}\left[-\varepsilon\lambda(\alpha(x)+\lambda)^{-1} g L\left(\frac{\kappa_1(x)}{\alpha(x)(\alpha(x)+\lambda)}\right)\right.\\
&\quad \left.-\varepsilon(\alpha(x)+\lambda)^{-1}\kappa_1(x) L\left((\alpha(x)+\lambda)^{-1} g\right)\right]\\
&= \frac{1}{\varepsilon\lambda} L\left(\frac{\kappa_1(x)}{\alpha(x)(\alpha(x)+\lambda)}\right)^{-1}\left[-(\alpha(x)+\lambda)^{-1} g + \varepsilon(\alpha(x)+\lambda)^{-1} g L\left((\alpha(x)+\lambda)^{-1}\kappa_1(x)\right)\right.\\
&\quad \left.-\varepsilon(\alpha(x)+\lambda)^{-1}\kappa_1(x) L\left((\alpha(x)+\lambda)^{-1} g\right)\right]\\
&=: R(\lambda, C_{\varepsilon,\rho_\varepsilon}). \qquad (3.36)
\end{aligned}
$$

Let us define

$$
\beta_\varepsilon(x) := \frac{2a(x)kp\rho_\varepsilon}{(1+k\rho_\varepsilon)^2},\ H_\varepsilon(x) := 2\left(1-\frac{a(x)}{1+k\rho_\varepsilon}\right)p,
$$

in order to shorten the notational effort. Note that

$$
\lim_{\varepsilon\to 0} H_\varepsilon(x) = 2\left(1-\frac{a(x)}{1+k\bar\rho}\right)p =: H(x), \quad \lim_{\varepsilon\to 0}\beta_\varepsilon(x) = \frac{2a(x)kp\bar\rho}{(1+k\bar\rho)^2} =: \beta(x).
$$

We need to determine the following limiting process

$$
\liminf_{(\varepsilon,\lambda)\to(0^+,0)} \int_\Omega H_\varepsilon(x)\lambda R(\lambda, C_{\varepsilon,\rho_\varepsilon})\beta_\varepsilon(x)u_\varepsilon(x)\,\mathrm{d}x =: \liminf_{(\varepsilon,\lambda)\to(0^+,0)} \Xi(\varepsilon,\lambda).
$$

Inserting into this problem the formula of the resolvent operator derived in (3.36), we obtain

$$
\begin{aligned}
\Xi(\varepsilon,\lambda) &= \int_\Omega H_\varepsilon(x)\frac{1}{\varepsilon} L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1}\cdot\\
&\quad \left[-(\alpha(x)+\lambda)^{-1}\beta_\varepsilon(x)u_\varepsilon(x) + \varepsilon(\alpha(x)+\lambda)^{-1}\beta_\varepsilon(x)u_\varepsilon(x) L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right)\right.\\
&\quad \left.-\varepsilon(\alpha(x)+\lambda)^{-1}\kappa_1(x) L\left(\frac{\beta_\varepsilon(y)u_\varepsilon(y)}{\alpha(y)+\lambda}\right)\right]\mathrm{d}x.
\end{aligned}
$$

For a better distinction between the terms, let us define

$$
I := -\int_\Omega \frac{1}{\varepsilon} H_\varepsilon(x) L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1}(\alpha(x)+\lambda)^{-1}\beta_\varepsilon(x)u_\varepsilon(x)\,\mathrm{d}x,
$$

$$
\begin{aligned}
II &:= \int_\Omega H_\varepsilon(x)(\alpha(x)+\lambda)^{-1}\beta_\varepsilon(x)u_\varepsilon(x)L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1} L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right)\mathrm{d}x,\\
III &:= -\int_\Omega H_\varepsilon(x)(\alpha(x)+\lambda)^{-1}\kappa_1(x)L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1} L\left(\frac{\beta_\varepsilon(y)u_\varepsilon(y)}{\alpha(y)+\lambda}\right)\mathrm{d}x,\\
\Xi(\varepsilon,\lambda) &= I+II+III.
\end{aligned}
$$

We show that term I converges and so we can apply again the rule for the limes inferior

$$\liminf \Xi = \lim I + \liminf(II+III).$$

We observe that using relation (3.33)

$$
\begin{aligned}
I &= -\int_\Omega H_\varepsilon(x)\frac{\beta_\varepsilon(x)\kappa_1(x)Lu_\varepsilon}{\alpha(x)(\alpha(x)+\lambda)}L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1}\mathrm{d}x\\
&= -Lu_\varepsilon\int_\Omega H_\varepsilon(x)\frac{\beta_\varepsilon(x)}{\kappa_2(x)}\frac{\kappa_1(x)\kappa_2(x)}{\alpha(x)(\alpha(x)+\lambda)}L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1}\mathrm{d}x.
\end{aligned}
$$

Denote now

$$g_\varepsilon(x) := \frac{\kappa_1(x)\kappa_2(x)}{\alpha(x)(\alpha(x)+\lambda)}L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1},$$

then g_ε defines a Dirac sequence. Due to the definition

$$\forall\,\varepsilon>0: \quad g_\varepsilon(x)>0 \text{ and } \int_\Omega g_\varepsilon(x)\,\mathrm{d}x = 1.$$

Let $\bar{x}\in\Omega$ be the element, which maximises the function a and let $\Omega^c\subset\Omega$ such that $\bar{x}\notin\Omega^c$ and $\operatorname{dist}(\bar{x},\Omega^c)>0$.
We know by Theorem 3.23 that

$$\alpha(x) = \left(1+\varepsilon\hat{\kappa}-\frac{2a(x)}{1+k\rho_\varepsilon}\right)p \overset{\varepsilon\to 0}{\longrightarrow} \left(1-\frac{2a(x)}{1+k\bar{\rho}}\right)p,$$

and thus we can conclude that $\frac{\kappa_1(x)\kappa_2(x)}{\alpha(x)(\alpha(x)+\lambda)}$ converges and is subsequently bounded on Ω^c.
Then we can estimate utilizing (3.34)

$$\int_\Omega \frac{\kappa_1(x)\kappa_2(x)}{\alpha(x)(\alpha(x)+\lambda)}\,\mathrm{d}x \geq \frac{1}{\max\limits_{x\in\Omega}(\alpha(x)+\lambda)}\int_\Omega \frac{\kappa_1(x)\kappa_2(x)}{\alpha(x)}\,\mathrm{d}x = \frac{1}{\max\limits_{x\in\Omega}(\alpha(x)+\lambda)}L\left(\frac{\kappa_1}{\alpha}\right)$$

$$= \frac{1}{\varepsilon \max\limits_{x\in\Omega}(\alpha(x)+\lambda)} \overset{\varepsilon\to 0}{\longrightarrow} \infty.$$

This implies that

$$\forall\, \Omega^c \subset \Omega, \bar{x} \notin \Omega^c, \operatorname{dist}(\bar{x}, \Omega^c) > 0 : \quad \int\limits_{\Omega^c} g_\varepsilon(x)\,\mathrm{d}x \to 0 \quad \text{for } \varepsilon \to 0.$$

Since we additionally know by Theorem 3.23 that u_ε converges weakly*, we infer

$$Lu_\varepsilon = \int\limits_{\Omega} \kappa_2(y) u_\varepsilon(y)\,\mathrm{d}y \to \bar{\rho}_1 \kappa_2(\bar{x}) \quad \text{for } \varepsilon \to 0.$$

Thus we obtain

$$I \overset{\varepsilon\to 0}{\longrightarrow} -\bar{\rho}_1 H(\bar{x})\beta(\bar{x}) < 0.$$

The only thing left to show is that $\liminf(II+III)$ does not converge to $\bar{\rho}_1 H(\bar{x})\beta(\bar{x})$. We will show even more by proving that $\liminf(II+III) \leq 0$. We use again equation (3.33) and estimate

$$\begin{aligned}
&\liminf_{(\varepsilon,\lambda)\to(0^+,0)} \Bigg[\varepsilon \int\limits_{\Omega} H_\varepsilon(x) \frac{\beta_\varepsilon(x) L u_\varepsilon \kappa_1(x)}{\alpha(x)(\alpha(x)+\lambda)} L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1} \mathrm{d}x L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right) \\
&\quad -\varepsilon \int\limits_{\Omega} H_\varepsilon(x) \frac{\kappa_1(x)}{\alpha(x)+\lambda} L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1} \mathrm{d}x L\left(\frac{\beta_\varepsilon(y)u_\varepsilon(y)}{\alpha(y)(\alpha(y)+\lambda)}\right) \Bigg] \\
= \;& \liminf_{(\varepsilon,\lambda)\to(0^+,0)} \Bigg[\varepsilon \int\limits_{\Omega} H_\varepsilon(x) \frac{L u_\varepsilon \beta_\varepsilon(x)}{\kappa_2(x)} \frac{\kappa_1(x)\kappa_2(x)}{\alpha(x)(\alpha(x)+\lambda)} L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1} \cdot \\
&\quad \left(L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right) - \frac{\alpha(x)}{L u_\varepsilon \beta_\varepsilon(x)} L\left(\frac{\beta_\varepsilon(y)u_\varepsilon(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)\right) \mathrm{d}x \Bigg] \\
\leq \;& \liminf_{(\varepsilon,\lambda)\to(0^+,0)} \Bigg[\int\limits_{\Omega} H_\varepsilon(x) \frac{L u_\varepsilon \beta_\varepsilon(x)}{\kappa_2(x)} \frac{\kappa_1(x)\kappa_2(x)}{\alpha(x)(\alpha(x)+\lambda)} L\left(\frac{\kappa_1(y)}{\alpha(y)(\alpha(y)+\lambda)}\right)^{-1} \mathrm{d}x \cdot \\
&\quad \varepsilon L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right) \Bigg] \\
= \;& \bar{\rho}_1 H(\bar{x})\beta(\bar{x}) \cdot \liminf_{(\varepsilon,\lambda)\to(0^+,0)} \varepsilon L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right)
\end{aligned}$$

Since

$$\lim_{\lambda\to 0}\lim_{\varepsilon\to 0} \varepsilon L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right) = 0.$$

it holds

$$\liminf_{(\varepsilon,\lambda)\to(0^+,0)} \varepsilon L\left(\frac{\kappa_1(y)}{\alpha(y)+\lambda}\right) = 0,$$

which implies directly that

$$\liminf_{(\varepsilon,\lambda)\to(0^+,0)} (II + III) \leq 0,$$

which concludes the proof. □

Remark 3.30. *Note that the separation of variables of κ is needed only, because of the explicit computation of the resolvent $R(\lambda, C_{\varepsilon,\rho_\varepsilon})$. All results up to this point do not need this assumption and work for Assumption 3 alone.*

Chapter 4

Numerical Analysis

This chapter aims at presenting the numerical scheme employed to obtain all simulations done within this thesis. These simulations are based on the Escalator-Boxcar-Train (EBT) method. The first paper proposing the EBT method is written by A.M. de Roos, [26], and goes back to the year 1988. This scheme was developed for a structured population model given by

$$\begin{cases} \frac{\partial}{\partial t}\eta(t,x) + \nabla \cdot [\nu(t,x)\eta(t,x)] &= -d(t,x)\eta(t,x),\ x \in \Omega, t \in (0,T), \\ \psi \cdot [\nu(t,x_0)\eta(t,x_0)] &= B(t,x_0,\eta(t,\cdot)),\ x_0 \in \partial\Omega, t \in (0,T), \end{cases} \tag{4.1}$$

where d, ν are arbitrary functions of t and x only, ψ is the inward pointing normal vector and B is a linear functional in η.
The main idea behind the EBT method is to approximate the solution η by a sum of Dirac measures concentrated at different points $x_1, \ldots, x_n \in \Omega$ and weighting these measures by some suitable functions $m_i(t)$, $i = 1, \ldots, n$. Then, there are two steps to be dealt with. Firstly, due to the transport term, it is necessary to determine where the Dirac deltas are shifted to and whether new Dirac deltas come into existence. Secondly, it is necessary to determine, how the weight functions develop, because they determine the total mass at a certain point x_i.
This method was widely used in theoretical biology. The essential idea of tracking the location of mass and the amount of this mass suited the biological background of moving cells adequately. Although implementation was straight forward and allowed for an accessible biological interpretation, it was not before the year 2013 that it was possible to show the convergence of this method rigorously, see [13].

In this thesis we discussed system (2.2), which does not include partial differential operators like in equation (4.1). Hence the EBT method seems to be too strong a

tool to be used effectively. And indeed, as we will see soon, the EBT scheme leads to a "naive" discretisation of system (2.2). The reason why we still apply this method is that we are able to obtain the numerical convergence also for the formulation in measure spaces, namely for equation (2.22). The advantage lies in the flat metric, which suffices to show convergence of the scheme.

4.1 The numerical scheme

Since there is no transport or other partial differential operator, the location of the Dirac measures can be fixed to a certain amount of points to be chosen at the beginning. Let us say that these locations are denoted by $x_1, \dots, x_n \in \Omega$. Then we can define the following approximating measures

$$\mu^n(t) = \sum_{i=1}^{n} m_i(t)\delta_{x_i}, \quad \nu^n(t) = \sum_{i=1}^{n} n_i(t)\delta_{x_i} \tag{4.2}$$

and, accordingly, an approximation for the initial data

$$\mu^0 = \sum_{i=1}^{n} m_i^0\delta_{x_i}, \quad \nu^0 = \sum_{i=1}^{n} n_i^0\delta_{x_i}.$$

Here $m_i(t),\ i = 1, \dots, n$, is the solution to the the system

$$\begin{cases} \frac{\mathrm{d}}{\mathrm{d}t}m_i(t) &= \left(\frac{2a(x_i)}{1+k\sum\limits_{i=1}^{n} n_i(t)} - 1\right) pm_i(t), \\ \frac{\mathrm{d}}{\mathrm{d}t}n_i(t) &= 2\left(1 - \frac{a(x_i)}{1+k\sum\limits_{i=1}^{n} n_i(t)}\right) pm_i(t) - dn_i(t), \quad i = 1, \dots, n. \\ m_i(0) &= m_i^0, \\ n_i(0) &= n_i^0. \end{cases} \tag{4.3}$$

This system of equations could be solved for example by Euler's method or Runge-Kutta method, both explicitly or implicitly. The simulations done in this thesis used an implicit Runge-Kutta method of fourth order, to avoid any difficulties with stiffnes. As it turned out, using an explicit method did not change the results, so it might be sufficient and cost saving to use explicit methods. However, a rigorous numerical analysis is not presented here to validate the sufficiency of an explicit method.

The convergence of the numerical solution to the analytical solution of system (4.3) is provided by standard literature, it is left to show that the measures defined in (4.2) do converge to the solution of system (2.22).

4.2 Convergence of the numerical scheme

Let us denote by

$$\mu_{ap}^n(t) = \sum_{i=1}^n m_i^{ap}(t)\delta_{x_i}, \quad \nu_{ap}^n(t) = \sum_{i=1}^n n_i^{ap}(t)\delta_{x_i},$$

where (m_i^{ap}, n_i^{ap}), $i = 1, \ldots, n$, is the numerical solution of system (4.3), then we have to prove that $\rho_F(\mu(t), \mu_{ap}^n(t)) \to 0$ as $n \to \infty$. Therefore, by the triangle inequality, we obtain

$$\rho_F(\mu(t), \mu_{ap}^n(t)) \leq \rho_F(\mu(t), \mu^n(t)) + \rho_F(\mu^n(t), \mu_{ap}^n(t)).$$

Here stands the first term on the right-hand side for the approximation in space (trait) and the second term for the approximation in time. The second term can be estimated like

$$\begin{aligned}
\rho_F(\mu^n(t), \mu_{ap}^n(t)) &= \sup\left\{ \int_\Omega \varphi(x)\,\mathrm{d}(\mu^n(t) - \mu_{ap}^n(t)) \,\middle|\, \varphi \in C^1(\Omega), \|\varphi\|_{W^{1,\infty}(\Omega)} \leq 1 \right\} \\
&\leq \sup\left\{ \sum_{i=1}^n |\varphi(x_i)|\,|m_i(t) - m_i^{ap}(t)| \,\middle|\, \varphi \in C^1(\Omega), \|\varphi\|_{W^{1,\infty}(\Omega)} \leq 1 \right\} \\
&\leq C \sum_{i=1}^n \|m_i - m_i^{ap}\|_{L^p((0,T))}.
\end{aligned}$$

The L^p-norm can be chosen arbitrarily (regarding $p \geq 1$) because the Runge-Kutta scheme converges for arbitrary L^p-norms. So it is left to show that for all $\varepsilon > 0$ there exists $n \in \mathbb{N}$ large enough such that

$$\rho_F(\mu(t), \mu^n(t)) < \varepsilon.$$

Since both μ^n and ν^n are sums of Dirac measures confined to a bounded domain Ω, they are tight and bounded. According to the Prohorov Theorem, see for instance [11, Theorem 8.6.2], there exists a weakly* convergent subsequence, which is denoted,

by abuse of notation again μ^n and ν^n, respectively. Let $\tilde{\mu}, \tilde{\nu}$ be the respective limits. For the subsequence it holds for an arbitrary set $A \in \mathcal{B}(\Omega)$

$$\frac{\mathrm{d}}{\mathrm{d}t}\mu^n(t)(A) = \int_A \left(\frac{2a(x)}{1 + k\sum_{i=1}^{n} n_i(t)} - 1 \right) p \, \mathrm{d}\mu^n(t).$$

Since both μ^n and ν^n converge weakly* we obtain

$$\lim_{n\to\infty} \frac{\mathrm{d}}{\mathrm{d}t}\mu^n(t)(A) = \lim_{n\to\infty} \int_A \left(\frac{2a(x)}{1 + k\sum_{i=1}^{n} n_i(t)} - 1 \right) p \, \mathrm{d}\mu^n(t) = \int_A \left(\frac{2a(x)}{1 + k\tilde{\nu}(\Omega)} - 1 \right) p \, \mathrm{d}\tilde{\mu}.$$

It is left to show that the limit and the derivative commute. For fixed set A the function $\mu^n(t)(A)$ is a differentiable function and we need to prove that the time derivative is uniformly convergent, because only then it is possible to interchange the limit and the derivative. Hence we want to apply the Arzela-Ascoli Theorem. Pointwise boundedness comes from boundedness of solutions of system (4.3), see [60]. What is left to show is the equicontinuity of $\mu^n(t)(A)$. With the same arguments as in Lemma 2.14, we obtain a uniform bound from below for $\sum_{i=1}^{n} n_i(t)$, i.e. there exists $C_2 > 0$, independent of n, such that $\sum_{i=1}^{n} n_i(t) \geq C_2 > 0$. A uniform upper bound for m_i and n_i was already proven in [60, Proposition 3.1], hence $m_i(t) \leq C_1$ for all $i = 1, \ldots, n$. Thus we are able to estimate with $a(x_i) = a_i$

$$\begin{aligned}
\left\| \frac{\mathrm{d}}{\mathrm{d}t}\mu^n(\cdot)(A) \right\|_\infty &= \left\| \sum_{i=1}^{n} \left(\frac{2a_i}{1 + k\sum_{i=1}^{n} n_i(\cdot)} - 1 \right) p m_i(\cdot) \right\|_\infty \\
&\leq \left(\frac{2}{1 + knC_2} - 1 \right) p \sum_{i=1}^{n} \|m_i\|_\infty \\
&\leq \left(\frac{2}{1 + knC_2} - 1 \right) pnC_1 \leq \frac{2pC_1}{kC_2}.
\end{aligned}$$

We see that $\mu^n(t)(A)$ is uniformly Lipschitz-continuous and hence, it is equicontinuous. Similarly, we can argue for $\nu^n(t)(A)$, if we remember, that we can obtain analogously as in Lemma 2.9 a uniform bound for $\sum_{i=1}^{n} m_i(t) \leq C_3$, where C_3 is

independent of n.

$$\left\|\frac{\mathrm{d}}{\mathrm{d}t}\nu(\cdot)(A)\right\|_\infty = \left\|\sum_{i=1}^{n} 2\left(1-\frac{a_i}{1+k\sum\limits_{i=1}^{n} n_i}\right)pm_i - d\sum_{i=1}^{n} n_i\right\|_\infty \leq 2pC_3 + dC_4$$

According to the Arzela-Ascoli theorem it is possible to extract a subsequence of $\mu^n(t)(A), \nu^n(t)(A)$, we denote it by $\mu^{n_m}(t)(A)$ and $\nu^{n_m}(t)(A)$ such that

$$\lim_{m\to\infty}\frac{\mathrm{d}}{\mathrm{d}t}\mu^{n_m}(t)(A) = \frac{\mathrm{d}}{\mathrm{d}t}\lim_{m\to\infty}\mu^{n_m}(t)(A) = \frac{\mathrm{d}}{\mathrm{d}t}\tilde{\mu}(t)(A),$$
$$\lim_{m\to\infty}\frac{\mathrm{d}}{\mathrm{d}t}\nu^{n_m}(t)(A) = \frac{\mathrm{d}}{\mathrm{d}t}\lim_{m\to\infty}\nu^{n_m}(t)(A) = \frac{\mathrm{d}}{\mathrm{d}t}\tilde{\nu}(t)(A).$$

That the limit function is indeed $\tilde{\mu}, \tilde{\nu}$ respectively, is due to the uniqueness of the weak* limit. Going back to the equation for the sequence μ^n and considering instead the equation for the subsequence yields

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\tilde{\mu}(t)(A) &= \lim_{m\to\infty}\frac{\mathrm{d}}{\mathrm{d}t}\mu^{n_m}(t)(A) = \lim_{m\to\infty}\int_A\left(\frac{2a(x)}{1+k\sum\limits_{i=1}^{n_m} n_i(t)} - 1\right)p\,\mathrm{d}\mu^{n_m}(t)\\ &= \int_A\left(\frac{2a(x)}{1+k\tilde{\nu}(t)(\Omega)} - 1\right)p\,\mathrm{d}\tilde{\mu}(t)\end{aligned}$$

together with the second equation

$$\begin{aligned}\frac{\mathrm{d}}{\mathrm{d}t}\tilde{\nu}(t)(A) &= \lim_{m\to\infty}\frac{\mathrm{d}}{\mathrm{d}t}\nu^{n_m}(t)(A)\\ &= \lim_{m\to\infty}\int_A 2\left(1-\frac{a(x)}{1+k\sum\limits_{i=1}^{m} n_i(t)}\right)p\,\mathrm{d}\mu^{n_m}(t) - d\nu^{n_m}(t)(A)\\ &= \int_A 2\left(1-\frac{a(x)}{1+k\tilde{\nu}(t)(\Omega))}\right)p\,\mathrm{d}\tilde{\mu}(t) - d\tilde{\nu}(t)(A).\end{aligned}$$

Since the solution of equation (2.23) is unique, we obtain that $(\tilde{\mu}, \tilde{\nu}) = (\mu, \nu)$. These arguments hold for any subsequence of (μ^n, ν^n) and so every subsequence contains a subsequence which converges to the same limit. Subsequently, the whole sequence (μ^n, ν^n) converges weakly* to (μ, ν).

Chapter 5

Conclusion

5.1 Summary

In Chapter 2 we have seen that system (2.2) endowed with initial data in $C(\Omega) \cap L^1(\Omega)$ admits a steady state contained in $\mathcal{M}^+(\Omega)$, the space of positive Radon measures. Since the space of the steady state differs from the space of the solution for finite times, it was necessary to introduce a suitable metric, namely the flat metric, to characterise the convergence of the solution to the steady state. The flat metric metrizes the weak* convergence in $\mathcal{M}^+(\Omega)$ so that we obtain eventually, that the solution of (2.2) converges weakly* to a Dirac measure concentrated at the maximizing value of the function a.

The result was obtained by proving pointwise decay to zero of the solution for all points not contained in Ω_{max}, the set of all points which maximize the function a. In combination with strict positivity of total masses, $\left(\frac{u(t,x)}{\rho_1(t)}, \frac{v(t,x)}{\rho_2(t)}\right)$ formed Dirac sequences with t being the sequence parameter. Although this led to the convergence to a Dirac measure, the associated mass was yet indetermined. In order to specify the mass associated with the Dirac measure we showed the convergence of the total masses ρ_1 and ρ_2. The idea behind this proof was to rearrange the system for the total masses (2.15) such that it was a perturbation of a finite dimensional system, namely system (2.17). Since a Lyapunov function could be constructed for this finite dimensional version of (2.2), the system exhibited an attractive steady state. The perturbation argument implied that the attractive steady state for the finite dimensional system is also the attractive steady state of system (2.15).

Although the convergence results depended strongly on pointwise estimates, it was shown that the results could be generalised to initial data in $\mathcal{M}^+(\Omega)$, because the underlying idea of showing that the rescaled solution forms a Dirac sequence could

be transferred to the more general case.

The novelty in Chapter 2 lies in the new structured population model for describing leukemia that has been proposed. Furthermore, the approach to obtain the long-term behaviour of the solution of the scalar model illustrated in [2, 4] could be generalised to the case of a system of equations, regardless of the space of the initial data, i.e. $L^1(\Omega)$ or $\mathcal{M}^+(\Omega)$. So for the solution of equation (2.2) it was possible to fully characterise the long-term behaviour.

In Chapter 3 model (2.2) was extended by introducing an additional integral term, which was added to the equation of the first component u. Determination of the steady states of the extended system (3.8) was accomplished by interpreting the steady state equations as eigenvalue problem for the eigenvalue 0. The challenge was to find a positive eigenfunction corresponding to the eigenvalue 0. Rearranging the operators allowed proving compactness, positivity and irreducibility. The Krein-Rutman theorem provided a unique positive eigenfunction, hence a unique, positive steady state. In contrast to Chapter 2 the steady state was more regular, that is, it is a L^1-function instead of a measure. This suggests that the incorporated integral operator in this chapter has a regularizing effect on the steady state. Following the idea of linearised stability we could prove that the steady states obtained are locally asymptotically stable. One key aspect in the proof of the stability result was the exploitation of the Weinstein-Aronszajn formula. This formula describes the spectrum of an additively perturbed operator by the sum of the spectrum of the unperturbed operator and the zeroes or poles of the Weinstein-Aronszajn determinant of the perturbation.
As a next step it was shown how the irregular steady state from Chapter 2 is related to the regular steady state in Chapter 3. Letting the coefficient of the additional integral operator in system (3.8) go to zero resulted in the weak* convergence of the regular steady states to the irregular steady states. In this sense system (3.8) is a natural extension of system (2.2).

Chapter 3 showed how the stability theory set forth in [18] can be applied to a system of two structured equations instead of one ODE and one structured equation, [24]. Consequently, this chapter illustrates that the stability theory of [18] is applicable to an even wider range of problems.

In Chapter 4 a numerical scheme was proposed suitable to simulate the solution of the models considered in this thesis. We gave a qualitative convergence result of the numerical solution to the analytical solution in order to justify the discretization.

5.2 Outlook

The results achieved in this dissertation can be the starting point for several new projects. The most immediate is the question whether it is possible to weaken certain assumptions. For example in Theorem 3.25 a particular form of the integral kernel was assumed. This form (separated variables) was needed only in one specific step, namely in computing a resolvent operator explicitly. Consequently, the question arises if it is possible to compute the resolvent explicitly without this assumption or to find a different way of proving assumption (3.22).
Moreover, it was mentioned in Chapter 3, that the Laplacian can be used to model mutation instead of an integral operator. So it would be interesting to see if the results in this thesis can be transferred to a model where the integral term is substituted by the Laplacian. The simulations shown in Chapter 3 suggest that similar results might be feasible.
Lastly, a generalisation of system (3.8) to measure spaces would be a challenging project, because it would be necessary to extend the integral operator to measure spaces. In a recently published paper [3] by Ackleh et al. so called measure kernels are introduced. These kernels generalise integral kernels from $L^1(\Omega)$ to measure spaces. Yet, this generalisation raises the questions about its properties: is an integral operator equipped with a measure kernel still a positive, compact, irreducible operator? Even if the operator itself possesses these properties, for the theory presented in Chapter 3 to apply, the linearisation needs to meet also rather strong assumptions.

References

[1] *Compactness Criteria for Integral Operators in L^∞ and L^1 spaces*, volume 123. American Mathematical Society, Dec. 1995.

[2] A. Ackleh, B. Fitzpatrick, and H. Thieme. Rate distributions and survival of the fittest: a formulation on the space of measures. *Discrete and Continuous Dynamical Systems Series B*, 5(4):917, 2005.

[3] A. S. Ackleh, J. Cleveland, and H. R. Thieme. Population dynamics under selection and mutation: Long-time behavior for differential equations in measure spaces. *Journal of Differential Equations*, 261(2):1472–1505, 2016.

[4] A. S. Ackleh, D. F. Marshall, H. E. Heatherly, and B. G. Fitzpatrick. Survival of the fittest in a generalized logistic model. *Mathematical Models and Methods in Applied Sciences*, 9(09):1379–1391, 1999.

[5] B. Alberts, D. Bray, K. Hopkin, A. Johnson, J. Lewis, M. Raff, K. Roberts, and P. Walter. *Essential cell biology*. Garland Science, 4 edition, 2013.

[6] N. Alibaud. Existence, uniqueness and regularity for nonlinear parabolic equations with nonlocal terms. *Nonlinear Differential Equations and Applications NoDEA*, 14(3-4):259–289, 2007.

[7] L. Ambrosio, N. Fusco, and D. Pallara. Functions of bounded variation and free discontinuity problems. *Oxford Math. Monogr*, 2000.

[8] G. Barles and B. Perthame. Concentrations and constrained hamilton-jacobi equations arising in adaptive dynamics. *Contemporary Mathematics*, 439:57–68, 2007.

[9] H. Bauer. *Maß-und Integrationstheorie*. Walter de Gruyter, 1992.

[10] P. Billingsley. *Probability and measure*. John Wiley & Sons, 2008.

[11] V. Bogačev. *Measure theory. 2 (2007)*. Springer, 2007.

[12] D. Bonnet and J. E. Dick. Human acute myeloid leukemia is organised as a hierarchy that originates from a primitive hematopoietic cell. *Nat Med*, 3:730–7, 1997.

[13] A. Brannstrom, L. Carlsson, and D. Simpson. On the convergence of the escalator boxcar train. *SIAM Journal on Numerical Analysis*, 51(6):3213–3231, 2013.

[14] R. Bürger. Perturbations of positive semigroups and applications to population genetics. *Mathematische Zeitschrift*, 197(2):259–272, 1988.

[15] J. A. Cañizo, J. A. Carrillo, and S. Cuadrado. Measure solutions for some models in population dynamics. *Acta applicandae mathematicae*, 123.1:141–156, 2013.

[16] À. Calsina and S. Cuadrado. Small mutation rate and evolutionarily stable strategies in infinite dimensional adaptive dynamics. *Journal of mathematical biology*, 48(2):135–159, 2004.

[17] À. Calsina and S. Cuadrado. Stationary solutions of a selection mutation model: The pure mutation case. *Mathematical Models and Methods in Applied Sciences*, 15(07):1091–1117, 2005.

[18] À. Calsina and S. Cuadrado. Asymptotic stability of equilibria of selection-mutation equations. *Journal of mathematical biology*, 54(4):489–511, 2007.

[19] J. A. Carrillo, R. M. Colombo, P. Gwiazda, and A. Ulikowska. Structured populations, cell growth and measure valued balance laws. *J. Diff. Eq.*, 252:3245–3277, 2012.

[20] J. A. Carrillo, S. Cuadrado, and B. Perthame. Adaptive dynamics via hamilton–jacobi approach and entropy methods for a juvenile-adult model. *Mathematical Biosciences*, 205(1):137–161, 2007.

[21] S. Choi, M. J. Henderson, E. Kwan, E. H. Beesley, R. Sutton, A. Y. Bahar, J. Giles, N. C. Venn, L. D. Pozza, D. L. Baker, et al. Relapse in children with acute lymphoblastic leukemia involving selection of a preexisting drug-resistant subclone. *Blood*, 110:632–9, 2007.

[22] H. Clarke. *Optimization and Nonsmooth Analysis*. John Wiley & Sons, 1983.

[23] S. Cuadrado. Equilibria of a predator prey model of phenotype evolution. *Journal of Mathematical Analysis and Applications*, 354(1):286–294, 2009.

[24] S. Cuadrado. Stability of equilibria of a predator prey model of phenotype evolution. *Math. Biosci. Eng*, 6:701–718, 2009.

[25] D. Daners and P. K. Medina. *Abstract evolution equations, periodic problems and applications*, volume 279. Chapman & Hall/CRC, 1992.

[26] A. M. De Roos. Numerical methods for structured population models: the escalator boxcar train. *Numerical methods for partial differential equations*, 4(3):173–195, 1988.

[27] L. Desvillettes, P. E. Jabin, S. Mischler, G. Raoul, et al. On selection dynamics for continuous structured populations. *Communications in Mathematical Sciences*, 6(3):729–747, 2008.

[28] O. Diekmann, H. A. Lauwerier, T. Aldenberg, and J. A. J. Metz. Growth, fission and the stable size distribution. *Journal of mathematical biology*, 18(2):135–148, 1983.

[29] L. Ding, T. J. Ley, D. E. Larson, C. A. Miller, D. C. Koboldt, J. S. Welch, and J. F. DiPersio. Clonal evolution in relapsed acute myeloid leukaemia revealed by whole-genome sequencing. *Nature*, 481:506–510, 2012.

[30] K.-J. Engel and R. Nagel. One-parameter semigroups for linear evolution equations. 2000.

[31] P. Getto, A. Marciniak-Czochra, Y. Nakata, et al. Global dynamics of two-compartment models for cell production systems with regulatory mechanisms. *Mathematical biosciences*, 245(2):258–268, 2013.

[32] Jochen Graw. *Genetik*. Springer Spektrum, 6 edition, 2015.

[33] P. Gwiazda, T. Lorenz, and A. Marciniak-Czochra. A nonlinear structured population model: Lipschitz continuity of measure-valued solutions with respect to model ingredients. *Journal of Differential Equations*, 248(11):2703–2735, 2010.

[34] K. J. Hope, L. Jin, and J. E. Dick. Acute myeloid leukemia originates from a hierarchy of leukemic stem cell classes that differ in self-renewal capacity. *Nat Immunology*, 5:738–43, 2004.

[35] B. Huppert. *Angewandte Lineare Algebra*. Walter de Gruyter, 1990.

[36] M. Jan and R. Majeti. Clonal evolution of acute leukemia genomes. *Oncogene*, 32:135–40, 2013.

[37] T. Kato. *Perturbation theory for linear operators*. Springer Science & Business Media, 1984.

[38] A. Lander. The 'stem cell' concept: is it holding us back? *J. Biol.*, 8(8):70, 2009.

[39] A. Lander, K. Gokoffski, F. Wan, Q. Nie, and A. Calof. Cell lineages and the logic of proliferative control. *PLoS Biology*, 7, 2009.

[40] J. E. Layton, H. Hockman, W. P. Sheridan, and G. Morstyn. Evidence for a novel in vivo control mechanism of granulopoiesis: mature cell-related control of a regulatory growth factor. *Blood*, 74(4):1303–1307, 1989.

[41] T. J. Ley, E. R. Mardis, L. Ding, B. Fulton, M. D. McLellan, K. Chen, D. Dooling, B. H. Dunford-Shore, S. McGrath, M. Hickenbotham, et al. Dna sequencing of a cytogenetically normal acute myeloid leukaemia genome. *Nature*, 456:66–72, 2008.

[42] Sébastien Lion and Minus van Baalen. Self-structuring in spatial evolutionary ecology. *Ecology Letters*, 11(3):277–295, 2008.

[43] A. Lorz, T. Lorenzi, M. E. Hochberg, J. Clairambault, and B. Perthame. Populational adaptive evolution, chemotherapeutic resistance and multiple anticancer therapies. *ESAIM: Mathematical Modelling and Numerical Analysis*, 47(2):377–399, 2013.

[44] A. Lorz, S. Mirrahimi, and B. Perthame. Dirac mass dynamics in multidimensional nonlocal parabolic equations. *Communications in Partial Differential Equations*, 36(6):1071–1098, 2011.

[45] C. Lutz, V. T. Hoang, E. Buss, and A. D. Ho. Identifying leukemia stem cells - is it feasible and does it matter? *Cancer Lett*, 338:10–14, 2012.

[46] C. Lutz, P. S. Woll, G. Hall, A. Castor, H. Dreau, G. Cazzaniga, J. Zuna, C. Jensen, S. A. Clark, A. Biondi, et al. Quiescent leukaemic cells account for minimal residual disease in childhood lymphoblastic leukaemia. *Leukemia*, 27:1204–7, 2013.

[47] A. Marciniak-Czochra, T. Stiehl, A. D. Ho, W. Jäger, and W. Wagner. Modeling of asymmetric cell division in hematopoietic stem cells-regulation of self-renewal is essential for efficient repopulation. *Stem cells and development*, 18(3):377–386, 2009.

[48] J. A. Metz and O. Diekmann. *The dynamics of physiologically structured populations*, volume 68. Springer, 2014.

[49] S. Mirrahimi. Adaptation and migration of a population between patches. *Discrete & Continuous Dynamical Systems-Series B*, 18(3), 2013.

[50] A. G. M'Kendrick. Applications of mathematics to medical problems. *Proceedings of the Edinburgh Mathematical Society*, 44:98–130, 1925.

[51] C. E. Muller-Sieburg, H. B. Sieburg, J. M. Bernitz, and G. Cattarossi. Stem cell heterogeneity: implications for aging and regenerative medicine. *Blood*, 119(17):3900–3907, 2012.

[52] H. Neunzert. An introduction to the nonlinear boltzmann-vlasov equation, in kinetic theories and the boltzmann equation. *Springer, Berlin, Lecture Notes in Math.*, 1048:60–110, 1981.

[53] B. Perthame and G. Barles. Dirac concentrations in lotka-volterra parabolic pdes. *Indiana University Mathematics Journal*, 57(7):3275–3301, 2008.

[54] M. Ruzicka. *Nichtlineare Funktionalanalysis: Eine Einführung*. Springer-Verlag, 2006.

[55] H. H. Schaefer and H. H. Schaefer. *Banach lattices*. Springer, 1974.

[56] L. Schwartz. *Radon Measures*. Oxford University Press, 1973.

[57] F. R. Sharpe and A. J. Lotka. A problem in age-distribution. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science*, 21(124):435–438, 1911.

[58] K. Shinjo, A. Takeshita, K. Ohnishi, and R. Ohno. Granulocyte colony-stimulating factor receptor at various differentiation stages of normal and leukemic hematopoietic cells. *Leukemia & lymphoma*, 25(1-2):37–46, 1997.

[59] S. Steinberg. Meromorphic families of compact operators. *Archive for Rational Mechanics and Analysis*, 31(5):372–379, 1968.

[60] T. Stiehl. *Mathematical Modeling of Stem Cell Dynamics in Acute Leukemias*. PhD thesis, Heidelberg University, 2014.

[61] T. Stiehl, N. Baran, A. D. Ho, and A. Marciniak-Czochra. Clonal selection and therapy resistance in acute leukaemias: mathematical modelling explains different proliferation patterns at diagnosis and relapse. *Journal of The Royal Society Interface*, 11(94):20140079, 2014.

[62] T. Stiehl and A. Marciniak-Czochra. Mathematical modeling of leukemogenesis and cancer stem cell dynamics. *Mathematical Modelling of Natural Phenomena*, 7(1):166–202, 2012.

[63] G. Teschl. *Ordinary differential equations and dynamical systems*, volume 140. American Mathematical Society Providence, 2012.

[64] S. Tuljapurkar and H. Caswell. *Structured-population models in marine, terrestrial, and freshwater systems*, volume 18. Springer Science & Business Media, 2012.

[65] A. Ulikowska. Structured population models in metric spaces. 2013.

[66] F. W. Van Delft, S. Horsley, S. Colman, K. Anderson, C. Bateman, H. Kempski, J. Zuna, C. Eckert, V. Saha, L. Kearney, et al. Clonal origins of relapse in etv6-runx1 acute lymphoblastic leukemia. *Blood*, 117:6247–54, 2011.

[67] C. Villani. *Optimal transport: old and new*, volume 338. Springer Science & Business Media, 2008.

[68] W. Walter. Gewöhnliche differentialgleichungen–eine einführung, 7. aufl, 2000.

[69] G. F. Webb. *Theory of nonlinear age-dependent population dynamics*. CRC Press, 1985.

[70] D. Werner. *Funktionalanalysis*. Springer, 2006.