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THE DYNAMICAL BEHAVIOUR OF THE AGE-SIZE-DISTRIBUTION OF A CELL POPULATION

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We study the model proposed by Bell and Anderson describing the dynamics of a proliferating cell population. This model assumes that the individual's behaviour is completely determined by its age and size. By the method of integration along characteristics the problem is reduced to a renewal type integral equation. Using Laplace transform techniques and results from positive operator theory we can describe the large time behaviour of the solution, if we impose a condition on the growth rate.

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Introduction

We investigate a mathematical model for cell growth and division. Our main assumption is that (chronological) age and size (by size we mean volume, length or any other quantity which is preserved at division) are the traits required to describe the cell's progress through its cycle properly. Age seems reasonable because some biochemical reactions (e.g. replication of DNA) proceed sequentially during the life time of a cell, while other reactions, such as the increase of structural materials, depend on such factors as diffusion times and surface to volume ratios, suggesting the indispensability of size as a parameter. (Bell & Anderson (1967)).

There is a vast amount of literature on cell cycle models and almost as many models have been proposed as there are papers on the subject, and the number of papers is enormous. We refer to chapter II and III of the monograph of Eisen (1979) for an overview. In this respect our paper can be seen as the umpteenth attempt to describe some features of proliferating cell populations. However, the main goal of this paper is to show how abstract results from functional analysis (in particular positive operator theory) can be exploited to "solve" a concrete problem.

This paper is subdivided into nine sections. In section 1 we present the model and we make some assumptions on the functions which describe the life of individual cells. In section 2 the problem is reduced to an integral equation (abstract renewal equation) from which the distribution of birth sizes can be calculated. Existence and uniqueness of a solution to this integral equation is proved in section 3. Then, in section 4 the abstract renewal equation is reduced to a family of operator equations by means of the Laplace transform. It turns out that the investigation of the large time behaviour of the solution of the renewal equation is very closely linked with the location of some set of singular points, in particular the position of the singular point with largest real part, the so-called dominant singularity (or, in another context, eigenvalue) which can be determined by employing methods from positive operator theory. We shall briefly discuss some results from positive operator theory in section 5, and these results are used in section 6 to prove existence of a dominant singularity under some extra condition on the growth rate (i.e. the function describing the dynamics of an individual's size). In section 7 we calculate the residue at this dominant singularity and the outcome is used in section 8, where we apply the inverse Laplace transform which gives us the large time behaviour of the birth function. Finally in section 9 we explain what this means for the solution of our original problem and why we cannot dispense with the assumptions made. In particular we will show what happens in case of exponential (individual) growth (i.e. growth of an individual is proportional to its size), and it will appear that these results reject a supposition of Bell (1968).

1. The model

Here we shall confine our attention to large populations so that fluctuations from the mean can be ignored. We assume that a cell is fully characterized by its age a and size x. Here size can mean volume, length, DNA-content or any other quantity which obeys a physical conservation law. Size increases with time and we assume that this process can be described by the ordinary differential equation

$$\frac{dx}{dt} = g(x). \tag{1.1}$$

This means in particular that the growth rate g does neither depend on age, which seems very reasonable from a biological point of view, nor on environmental factors (such as food density) which are influenced by the population itself, causing nonlinearities in the equation. Age also increases with time and obeys $\frac{da}{dt} = 1$. However our theory can be easily extended to the case where a denotes some physiological age, which does not necessarily increase linearly with time: $\frac{da}{dt} = f(a)$ where f is a bounded continuous positive function. We assume that if a cell divides, it produces two daughter cells, both having age zero and half the size of the mother. Let $n(t,a,x)$ be the cell density function, i.e. $\int_{x_1}^{x_2}\int_{a_1}^{a_2} n(t,a,x)dadx$ is the number of cells having age between a_1 and a_2, and size between x_1 and x_2. From the conservation principle it follows that the equation for the density function can be written as

$$\frac{\partial n}{\partial t} = -\nabla \cdot J - F - D, \tag{1.2}$$

where the flux $J = J(t,a,x)$ is given by $J = (n(t,a,x), g(x)n(t,a,x))$, and ∇ is the operator $(\frac{\partial}{\partial a}, \frac{\partial}{\partial x})$. The sinks F and D account for the individuals which "disappear" as a result of fission and death respectively. We refer to the forthcoming book of Metz & Diekmann (in preparation) for a more general description how to derive balance equations such as (1.2) (also see Eisen (1979)).

Let fission and death be described by the per capita probabilities per unit of time $b(a,x)$ and $\mu(a,x)$ respectively, then $F = F(t,a,x) = b(a,x)n(t,a,x)$ and $D = D(t,a,x) = \mu(a,x)n(t,a,x)$.

We shall now introduce a number of mathematical assumptions on the functions g, b and μ and discuss their biological meaning and/or mathematical motivation. With respect to the growth rate g we assume

g is a continuous function on $[0,\infty)$ *and there exist constants* $g_{\min}, g_{\max}$ (A_g)

such that $0 < g_{\min} \leq g_{\max} < \infty$ and $g_{\min} \leq g(x) \leq g_{\max}$ *for all* $x \in [0,\infty)$.

It follows from this assumption that certain combinations of a and x are forbidden in the sense that cells with such a combination of age and size will never come into existence. More precisely there exists a (continuous) curve in the (a,x)-plane starting from $(a,x) = (0,0)$ and tending towards (∞,∞) below which no individual will ever dwell. We can compute this curve explicitly. Consider a cell whose size at birth is $x (x \geq 0)$ (assuming that such cells indeed exist). Let $X(a,x)$ be its size at age a, if it has not died or divided before reaching that age. Then X is the solution of the initial value problem $\frac{dx}{da} = g(x)$, $x(0) = x$, which has a continuous (differentiable) solution tending to ∞ if a tends to ∞ because of assumption (A_g). The curve $\{(a,X(a,x))|a \geqslant 0\}$ is called the characteristic curve starting from $(0,x)$. (See figure 1) We refer to section 2 for more details.

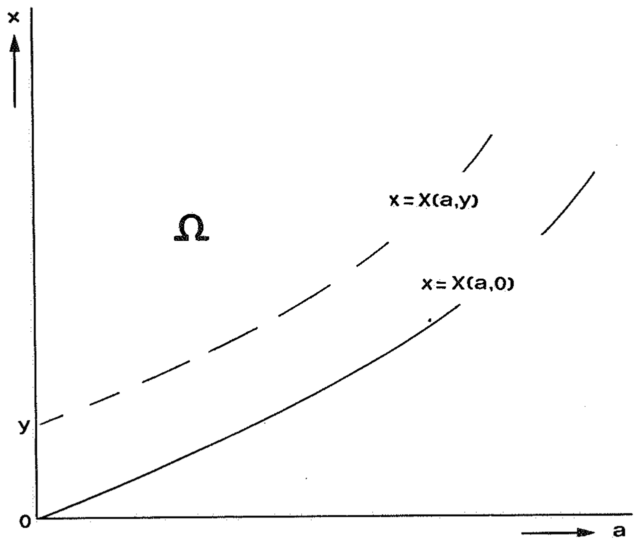

Figure 1. The set Ω. An individual with birth size x travels along the curve $\{X(a,x)|\ a \geqslant 0\}$ until it dies or divides. Individuals can only exist in the shaded region $\Omega = \{(a,x) \in \mathbb{R}^+ \times \mathbb{R}^+ | x \geqslant X(a,0)\}$. The actual state space Ω_s (i.e. the subset of $\mathbb{R}^+ \times \mathbb{R}^+$ in which indeed individuals do occur) is a subset of Ω, and in some cases Ω_s is smaller than Ω. (We refer to section 6 for more details.)

We impose the following conditions on b and μ:

$b \in L_\infty(\Omega)$ *(i.e. b is measurable and essentially bounded on* Ω*)*

$b(a,x) = 0,\ a \leqslant a_0,\ (a,x) \in \Omega,$ $\qquad (A_b)$

$b(a,x) > 0,\ a > a_0,\ (a,x) \in \Omega,$

$\liminf_{a \to \infty} b(a,X(a,x)) = \underline{b} > 0$ *uniformly in x.*

Here $a_0 > 0$ is some threshold below which cells cannot divide. The biological reason for this is that every cell has to go through a phase during which DNA is replicated, and the duration of this phase is more or less constant (see Bell & Anderson (1967), Eisen (1979)). Biologically, the last condition in (A_b) says that old individuals continue dividing at a positive rate.

$\mu \in L_\infty^{loc}(\Omega)$ *(i.e.* μ *is measurable and essentially bounded on compact subsets of* Ω*),* $\qquad (A_\mu)$

$\mu(a,x) \geqslant 0,\ (a,x) \in \Omega.$

Let

$$d(a,x) = b(a,x) + \mu(a,x). \tag{1.3}$$

We assume

There exists a constant d_∞ with $0 < d_\infty \leqslant \infty$ such that $\lim_{a \to \infty} d(a,X(a,x)) = d_\infty$ uniformly in x. Moreover, if $d_\infty < \infty$, there exists a constant $M \geqslant 0$ such that (A_d)

for all x: $\int_0^\infty |d(a,X(a,x)) - d_\infty| da \leqslant M$.

Biologically assumption (A_d) means that the probability for a cell to reach age a without dying or dividing decreases more or less exponentially if a becomes large. In section 9 it is explained why this assumption is needed.

We can rewrite (1.2) as

$$\frac{\partial}{\partial t} n(t,a,x) + \frac{\partial}{\partial a} n(t,a,x) + \frac{\partial}{\partial x}(g(x)n(t,a,x)) = -(\mu(a,x) + b(a,x))n(t,a,x), \tag{1.4}$$

$$t \geqslant 0,\ (a,x) \in \Omega.$$

The fact that dividing mothers of age a and size $2x$ give birth to two daughters of age a and size x is accounted for by the boundary condition

$$n(t,0,x) = 4\int_{a_0}^{\infty} b(a,2x)n(t,a,2x)da. \tag{1.5}$$

See Bell & Anderson (1967) or chapter II of Metz & Diekmann (in prep.) for an explanation of the factor 4.

Remark 1.1. In (1.5) we only have to integrate over those ages a that satisfy $X(a,0) \leqslant 2x$.

We specify an initial condition

$$n(0,a,x) = n_0(a,x),\ (a,x) \in \Omega. \tag{1.6}$$

Biological considerations yield that n_0 should satisfy

$$n_0(a,x) \geqslant 0,\ (a,x) \in \Omega \text{ and } n_0 \in L_1(\Omega). \tag{1.7}$$

2. Reduction to an abstract renewal equation

Usually age-dependent population models are reduced to a renewal equation (which is a Volterra integral equation of convolution type) for the birth function (see Hoppersteadt (1975)). Here we will show that this can also be done for our age-size-structured model (1.4)-(1.6). In this case, however, we obtain an abstract renewal equation, in the sense that solutions take values in some function space.

Let $m(t,a,x)$ be defined by

$$m(t,a,x) = g(x)n(t,a,x), \tag{2.1}$$

then m satisfies the equation

$$\frac{\partial m}{\partial t} + \frac{\partial m}{\partial a} + g(x)\frac{\partial m}{\partial x} = -(\mu(a,x) + b(a,x))m(t,a,x), \tag{2.2a}$$

$$m(t,0,x) = \frac{4g(x)}{g(2x)}\int_{a_0}^{\infty} b(a,2x)m(t,a,2x)da, \tag{2.2b}$$

$$m(0,a,x) = m_0(a,x) \overset{def}{=} g(x)n_0(a,x). \tag{2.2c}$$

By the method of integration along characteristics (See Courant & Hilbert (1962)) we can convert this system into an integral equation.

The characteristic curve through (t,a,x) is determined by $s \to (T(s,t),A(s,a),X(s,x))$, where s is an independent book-keeping variable and T,A,X are solutions of the ODE's $\frac{dT}{ds} = 1$, $T(0,t) = t$, $\frac{dA}{ds} = 1$, $A(0,a) = a$, $\frac{dX}{ds} = g(X)$, $X(0,x) = x$, thus $T(s,t) = s+t$, $A(s,a) = s+a$, and $X(s,x) = G^{-1}(s+G(x))$, where

$$G(x) = \int_0^x \frac{d\xi}{g(\xi)}, \quad x \geq 0, \tag{2.3}$$

and G^{-1} denotes the inverse function of $G \cdot G(x)$ can be interpreted as the time needed to grow from 0 to x. Observe that $G^{-1}(a) = X(a,0)$.

Now let t,a,x be fixed and let $\overline{m}(s) = m(T(s,t),A(s,a),X(s,x))$, then

$$\frac{d\overline{m}}{ds} = -d(A(s,a),X(s,x))\overline{m}(s), \tag{2.4}$$

where $d(a,x)$ is given by (1.3). Let

$$Q(s,a,x) \overset{def}{=} \exp\left[-\int_0^s d(A(\sigma,a),X(\sigma,x))d\sigma\right], \tag{2.5}$$

which can be interpreted as the probability that a cell with age a and size x reaches age $a+s$. From (2.4) we obtain that

$$\overline{m}(s) = \overline{m}(0)Q(s,a,x). \tag{2.6}$$

Let

$$t' = T(s,t),\ a' = A(s,a),\ x' = X(s,x). \tag{2.7}$$

(i) We choose $t = 0$. Then $a = a'-t'$, $x = X(-t',x')$. If we substitute this in (2.6) we obtain

$$m(t',a',x') = m(0,a'-t',X(-t',x'))\cdot Q(t',a'-t',X(-t',x')), \text{ if } a' \geq t'. \tag{2.8}$$

(ii) We choose $a = 0$. Then $t = t'-a'$, $x = X(-a',x')$, and we deduce from (2.6)

$$m(t',a',x') = m(t'-a',0,X(-a',x'))\cdot E(a',X(-a',x')), \text{if } a' \leq t', \tag{2.9}$$

where

$$E(a,x) \overset{def}{=} Q(a,0,x) = \exp\left[-\int_0^a d(\sigma,X(\sigma,x))d\sigma\right] \tag{2.10}$$

is the probability that a cell having size x at birth reaches age a.

If we drop the accents in (2.9) and (2.10), and use (2.1) and (2.2c) we find

$$n(t,a,x) = \frac{g(X(-t,x))}{g(x)} n_0(a-t,X(-t,x)) \cdot Q(t,a-t,X(-t,x)), \quad t < a, \tag{2.11}$$

$$n(t,a,x) = \frac{g(X(-a,x))}{g(x)} n(t-a,0,X(-a,x)) \cdot E(a,X(-a,x)), \quad t \geqslant a. \tag{2.12}$$

Let the birth function B be defined by

$$B(t,x) = n(t,0,x). \tag{2.13}$$

If we substitute (2.11)-(2.12) into (1.5), then we obtain the following integral equation for B:

$$B(t,x) = \Phi(t,x) + \int_{a_0}^{t} k(a,2x)B(t-a,X(-a,2x))da, \tag{2.14}$$

where

$$\Phi(t,x) = \frac{4g(X(-t,2x))}{g(2x)} \int_{t}^{\infty} b(a,2x)Q(t,a-t,X(-t,2x)) \cdot n_0(a-t,X(-t,2x))da, \tag{2.15}$$

and

$$k(a,x) = \frac{4g(X(-a,x))}{g(x)} b(a,x)E(a,X(-a,x)). \tag{2.16}$$

$\Phi(t,x)$ is only defined for values of x satisfying $G(2x) \geqslant t$, and one should read $\Phi(t,x) = 0$ if $G(2x) \leqslant t$. Furthermore $k(a,x) = 0$ if $a \leqslant a_0$ or $a \geqslant G(x)$, and $k(a,x) \geqslant 0$ if $a_0 \leqslant a \leqslant G(x)$.

The integral equation (2.14) was also found by Bell (1968) but he only solved it for the special case that all cells divide at the same age (see also Beyer (1970)).

It follows from (2.11)-(2.12) that knowledge of the solution $B(t,x)$ of (2.14) yields the solution $n(t,a,x)$ of (1.4)-(1.6). Therefore we shall concentrate on (2.14) during the rest of this chapter. In section 9 we shall interprete some result in terms of the density $n(t,a,x)$.

We can rewrite (2.14) as the abstract renewal equation

$$B(t) = \Phi(t) + \int_{0}^{t} K(a)B(t-a)da, \tag{2.17}$$

where, for fixed $t \geqslant 0$ $\Phi(t) \in L_1[0,\infty)$ and $K(t)$ defines a bounded operator from $L_1[0,\infty)$ into itself:

$$(K(t)\psi)(x) = k(t,2x)\psi(X(-t,2x)), \quad \psi \in L_1[0,\infty), \tag{2.18}$$

where one should read $\psi(X(-t,2x)) = 0$ if $G(2x) < t$.

Remark 2.1. Throughout this chapter we call a Banach space-valued function integrable if it is Bochner-integrable. This means the following: let E be a Banach space with norm $\|\cdot\|_E$ and let $f:(a,b) \to E$, where $-\infty \leqslant a < b \leqslant \infty$. Then $f(t)$ is Bochner-integrable if and only if f is strongly measurable and $\|f(t)\|_E$ is Lebesgue integrable (see Hille & Phillips (1957)).

We call $B(t)$ a solution of (2.17) if and only if

i) $B(t) \in L_1[0,\infty)$, $t \geqslant 0$,

ii) $B(t)$ is Bochner integrable on $[0,t_0)$ for all $t_0 \geqslant 0$,

iii) $B(t)$ obeys (2.17).

3. Existence and Uniqueness of solutions

It turns out that the proof of an existence and uniqueness result for the abstract renewal equation (2.17) is rather similar to the scalar case which has been extensively treated in the book of Bellman & Cooke (1963). First we shall prove a lemma.

Lemma 3.1. (a) *Let d_∞ (of assumption (A_d)) be finite. Then there exist positive constants T_0, m_K, M_K and M_Φ such that for all $t \geqslant T_0$: $\|\Phi(t)\| \leqslant M_\Phi e^{-d_\infty t}$, and for all $\psi \in L_1[0,\infty)$: $m_K e^{-d_\infty t}\|\psi\| \leqslant \|K(t)\psi\| \leqslant M_K e^{-d_\infty t}\|\psi\|$.*
(b) *Let $d_\infty = \infty$. For all $c > 0$ there exist constants $L_K(c), L_\Phi(c) > 0$ such that for all $t \geqslant 0$: $\|\Phi(t)\| \leqslant L_\Phi(c)e^{-ct}$, $\|K(t)\psi\| \leqslant L_K(c)e^{-ct}\|\psi\|$, for all $\psi \in L_1[0,\infty)$.*

Proof. (a) $E(a,x) = \exp[-\int_0^a d(\sigma,X(\sigma,x))d\sigma] = \exp[-\int_0^a \{d(\sigma,X(\sigma,x))-d_\infty\}d\sigma]\cdot\exp[-\int_0^a d_\infty d\sigma]$. Let M be the constant of assumption (A_d), then

$$e^{-M}e^{-d_\infty a} \leqslant E(a,x) \leqslant e^{M}e^{-d_\infty a}.$$

Part (a) of the lemma now follows immediately from these estimates and the assumptions (A_g) and (A_b). In an analogous manner we can prove part (b). □

The following existence and uniqueness result can be proved.

Theorem 3.2. *Let $t_0 > 0$. There exists a unique bounded integrable solution $B(t)$ of (2.17) on $[0,t_0]$.*

The existence result can be established by the method of successive approximations. Uniqueness then follows from a Gronwall-type lemma. We refer to Bellman & Cooke (1963) where the scalar case has been worked out in great detail, and the reader will have no difficulty to see that all proofs can be carried through. Because t_0 can be chosen arbitrarily large, theorem 3.2 implies global existence of the solution $B(t)$.

Remark 3.3. Strictly speaking condition (A_b) and (A_μ) are sufficient to prove existence and uniqueness.

In the next section we shall apply Laplace transformation to the integral equation (2.17). Therefore we need the following estimate.

Theorem 3.4. *There exists a $\beta \in \mathbb{R}$ such that $\|B(t)\| \leqslant M_B e^{\beta t}$, $t \geqslant 0$, where $M_B > 0$ is a constant.*

Proof. Let $\beta \in \mathbb{R}$ be such that $\|\Phi(t)\| \leqslant c_1 e^{\beta t}$ and $\int_0^\infty e^{-\beta t}\|K(t)\|dt = c_2 < 1$. From lemma 3.1 it is clear that such a β indeed exists. Then

$$\|B(t)\| \leqslant c_1 e^{\beta t} + \int_0^t \|K(a)\| \cdot \|B(t-a)\| da = c_1 e^{\beta t} + e^{\beta t} \int_0^t \{\|K(a)\| \cdot e^{-\beta a}\} \cdot \{\|B(t-a)\| \cdot e^{-\beta(t-a)}\} da.$$

Let $v(t) \overset{def}{=} \max_{0 \leqslant a \leqslant t} \|B(a) e^{-\beta a}\|$, then $v(t) \leqslant c_1 + v(t) \int_0^t e^{-\beta a} \|K(a)\| da \leqslant c_1 + c_2 v(t)$, hence $v(t) \leqslant \frac{c_1}{1-c_2}$, from which we obtain that $\|B(t)\| \leqslant \frac{c_1}{1-c_2} e^{\beta t}$. □

4. Laplace Transformation

A technique which turned out to be extremely useful in the study of scalar renewal equations is Laplace transformation (e.g. Bellman & Cooke (1963), Hoppensteadt (1975)). This technique can also be employed in the study of abstract renewal equations such as (2.17). First we shall introduce some notations. Let $I \subseteq \mathbb{R}$ be an interval, and E a Banach space. We define by $L_p(I,E)$, $1 \leqslant p \leqslant \infty$, the Banach space consisting of all functions $f: I \to E$ satisfying $\|f\|_p \overset{def}{=} \{\int_I \|f(t)\|^p dt\}^{\frac{1}{p}} < \infty$, if $p < \infty$ and $\|f\|_\infty \overset{def}{=} \text{ess sup} \|f(t)\| < \infty$, if $p = \infty$. If $I = [0,\infty)$ we shall write $L_p(0,\infty;E)$ instead of $L_p([0,\infty);E)$.

Remark 4.1. We have to distinguish between the norm of $f(t)$, $t \geqslant 0$, as an element of E and the norm of f being an element of $L_p(I;E)$. In the first case we write $\|f(t)\|$, in the second case $\|f\|_p$.

Definition. Let f be a function from $[0,\infty)$ to some Banach space E, then its Laplace transform $\hat{f}$ is defined by $\hat{f}(\lambda) = \int_0^\infty e^{-\lambda t} f(t) dt$, whenever this integral is defined with respect to the norm topology.

The following result is standard (Hille & Phillips (1957)).

Lemma 4.2. *If $f \in L_1(0,\infty;E)$ then $\hat{f}(\lambda)$ is analytic in* Re $\lambda > 0$ *and continuous in* Re $\lambda \geqslant 0$ *(with respect to the norm-topology).*

We shall state two results from Fourier theory which are generally known for the case that E is finite-dimensional. The first is the so-called Riemann-Lebesgue lemma (Hille & Phillips (1957), thm 6.4.2).

Lemma 4.3 (Riemann-Lebesgue). *Let $f \in L_1(0,\infty;E)$ and $\hat{f}$ its Laplace transform. Then* $\lim_{|\eta| \to \infty} \hat{f}(\xi + i\eta) = 0$, *uniformly for ξ in bounded closed subintervals of* $(0,\infty)$.

The second result which became known as Plancherel's theorem says that the Fourier transform of an L_2-function is again an L_2-function, and the mapping $f \to \hat{f}$ defines an isometry. We refer to Yosida (1980) for a proof in the scalar case, and the reader will have no difficulty to see that Yosida's proof can be carried through directly for Banach space-valued functions.

Lemma 4.4. *Let $f \in L_1(-\infty,\infty;E) \cap L_2(-\infty,\infty;E)$, then the function $\eta \to \hat{f}(i\eta)$ is an element of $L_2(-\infty,\infty;E)$ and $\int_{-\infty}^{\infty} \|f(t)\|^2 dt = \int_{-\infty}^{\infty} \|\hat{f}(i\eta)\|^2 d\eta$.*

This last equality is called Parseval's relation.

Let the right-half-plane Λ be defined by

$$\Lambda \stackrel{def}{=} \{\lambda \in \mathbb{C} | \mathrm{Re}\,\lambda > -d_\infty\} \tag{4.1}$$

(where $\Lambda = \mathbb{C}$ if $d_\infty = \infty$). Then it follows from lemma 3.1 and lemma 4.2 that $\hat{K}(\lambda)$ and $\hat{\Phi}(\lambda)$ are defined and analytic in Λ. Moreover it follows from lemma 3.1 that $\hat{K}(\lambda)$ is not defined if $\mathrm{Re}\,\lambda < -d_\infty$.

Remark 4.5. It is not a priori clear whether $\hat{K}(\lambda)$ is defined for λ on the vertical line $\mathrm{Re}\,\lambda = -d_\infty$. As to $\hat{\Phi}(\lambda)$ it depends on the initial age - size distribution $n_0(a,x)$ whether or not it is defined for values of λ satisfying $\mathrm{Re}\,\lambda \leqslant -d_\infty$. However this is not important for our purposes.

We define $\hat{B}(\lambda) = \int_0^\infty e^{-\lambda t} B(t)dt$ for those values of λ for which the integral converges. From theorem 3.3 we conclude that $\hat{B}(\lambda)$ exists if $\mathrm{Re}\,\lambda > \beta$. The convolution in (2.17) is converted by the Laplace transformation into a product of Laplace transforms. We wish to extend $\hat{B}(\lambda)$ to Λ minus some set Σ of singular points. More precisely

$$\hat{B}(\lambda) = \hat{\Phi}(\lambda) + \hat{K}(\lambda)\hat{B}(\lambda),\ \lambda \in \Lambda. \tag{4.2}$$

Let Σ be the set of all $\lambda \in \Lambda$ for which $I - \hat{K}(\lambda)$ is singular.

$$\Sigma = \{\lambda \in \Lambda | 1 \in \sigma(\hat{K}(\lambda))\}, \tag{4.3}$$

where $\sigma(\hat{K}(\lambda))$ denotes the spectrum of the operator $\hat{K}(\lambda)$. The condition $1 \in \sigma(\hat{K}(\lambda))$ is the usual precursor of a *characteristic equation* (Heijmans (to appear), Hoppersteadt (1975)).

For $\lambda \in \Lambda \setminus \Sigma$ we have

$$\hat{B}(\lambda) = (I - \hat{K}(\lambda))^{-1}\hat{\Phi}(\lambda). \tag{4.4}$$

In section 8 we shall prove that the element λ_d of Σ with largest real part determines the large time behaviour of the solution $B(t)$. Often λ_d turns out to be real, and the corresponding eigenvector of $\hat{K}(\lambda_d)$ to be positive. (See chapter II of Metz & Diekmann (in prep.).) The theory of positive operators is an important instrument to prove existence of λ_d, and has been succesfully exploited in a number of problems from population dynamics (Diekmann et al. (1984), Heijmans (to appear), Heijmans (1984), Metz & Diekmann (in prep.)). As an intermezzo we shall now present some results from positive operator theory with the emphasis on the existence and uniqueness of positive eigenvectors and eigenfunctionals.

5. Positive Operators

For the basic theory of order structures in a Banach space and positive operators, we refer to Schaefer (1974).

In the sequel E is some Banach space and E^* is it's dual, i.e. the space of all linear functionals (or linear forms) on E. We denote the duality pairing of $\psi \in E$, $F \in E^*$ with $<F,\psi>$. A subset $E_+ \subseteq E$ is called a cone if the following conditions are satisfied

(i) E_+ is closed,

(ii) $\alpha\phi + \beta\psi \in E_+$ if $\phi,\psi \in E_+$ and $\alpha,\beta \geqslant 0$

(iii) $\psi \in E_+$ and $-\psi \in E_+$ implies that $\psi = 0$.

The reader can easily verify that by virtue of "$\phi \leqslant \psi$ iff $\psi - \phi \in E_+$" each cone $E_+ \subseteq E$ defines an order relation on

E by which E becomes an ordered Banach space. We say that $\phi < \psi$ if $\phi \leqslant \psi$ and $\phi \neq \psi$. The cone E_+ is called total if the set $\{\psi - \phi | \psi, \phi \in E_+\}$ is dense in E. The dual set E_+^* is by definition the subset of E^* consisting of all positive functionals on E, i.e. $F \in E_+^*$ if and only if $F \in E^*$ and $<F,\psi> \geqslant 0$ for all $\psi \in E_+$. If E_+ is total then E_+^* is a cone as well. A positive functional F is said to be strictly positive if $<F,\psi> > 0$ for all $\psi \in E_+$, $\psi \neq 0$. A bounded linear operator $T: E \to E$ is called positive (with respect to the cone E_+) if $T\psi \in E_+$ for all $\psi \in E_+$. Notation $T \geqslant 0$. We denote the spectral radius of T by $r(T)$.

The first authors who systematically studied positive operators and their spectral properties were Krein and Rutman (1962). In that paper (which is a translation of a Russian paper which appeared already in 1948) they generalized the Frobenius theorem (which states that the spectral radius of a non-negative matrix is an eigenvalue of that matrix). They proved, among others, the following result.

Theorem 5.1 (Krein & Rutman (1962)). *Let $T: E \to E$ be compact and positive with respect to the total cone $E_+ \subseteq E$, and let $r = r(T) > 0$. Then there exists a $\psi \in E_+$, $\psi \neq 0$ such that $T\psi = r\psi$.*

They also introduced the notion of strong positivity. A positive operator $T: E \to E$ is called strongly positive if for all $\psi \in E_+$, $\psi \neq 0$ there is a natural number p such that $T^p\psi \in \overset{\circ}{E}_+$, where $\overset{\circ}{E}_+$ denotes the interior of the cone E_+ (assuming that E_+ has interior points). They proved that, if the assumptions of theorem 5.1 are fulfilled and, moreover, T is strongly positive, then

(a) T has (except for a constant) one and only one eigenvector $\psi \in E_+$. Moreover $\psi \in \overset{\circ}{E}_+$ and $T\psi = r\psi$.

(b) T^* has one and only one eigenvector $F \in E_+^*$, F is strictly positive and $T^*F = rF$.

(c) All other eigenvalues λ of T satisfy $|\lambda| < r(T)$.

Many years later their study was continued by a great number of authors, extending the ideas of Krein and Rutman in several directions. Among others they weakend the condition that T has to be compact. (In many cases it is sufficient that $\lambda = r(T)$ is a pole of the resolvent $R(\lambda,T) = (\lambda I - T)^{-1}$.) Furthermore several different concepts generalizing the concept of strong positivity have been introduced. We mention three of these generalizations. Schaefer (1974) introduced in the early sixties the concept of irreducible positive operators. Krasnoselskii (1964) studied u_0-positive operators, and finally Sawashima (1964) developed the theory of non-supporting operators. (Sawashima uses the terminology "non-support".) All three concepts have the advantage that the interior of the cone E_+ may be empty. It seems to us that Sawashima's definition is the most natural for our purposes. If E is a Banach lattice then there is a close relation between the concepts of Sawashima and Schaefer.

Definition (Sawashima (1964)). A bounded, positive operator $T: E \to E$ is called non-supporting with respect to E_+ if for all $\psi \in E_+$, $\psi \neq 0$, and $F \in F_+^*$, $F \neq 0$, there exists an integer p such that for all $n \geqslant p$ we have $<F,T^n\psi> > 0$.

The following result, which was proved by Sawashima (1964) is needed in the next section. The result can also be found in paper by Marek (1970) which provides a comprehensive overview of some of the developments in positive operator theory between 1950 and 1970.

Theorem 5.2. *Let the cone E_+ be total, let $T: E \to E$ be non-supporting with respect to E_+, and suppose that $r = r(T)$ is a pole of the resolvent, then*

(a) $r > 0$ *and* r *is an algebraically simple eigenvalue of* T.

(b) *The corresponding eigenvector* ψ *satisfies:* $\psi \in E_+$ *and* $<H,\psi> > 0$ *for all* $H \in E_+^*$, $H \neq 0$.

(c) *The corresponding dual eigenvector is strictly positive.*

(d) *All remaining elements* $\lambda \in \sigma(T)$ *satisfy* $|\lambda| < r$.

6. Location of the singular points

From now on we let $X = L_1[0,\infty)$. In section 4 we defined the analytic operator family $\hat{K}(\lambda)$, $\lambda \in \Lambda$, being the Laplace transform of $K(t)$. Evidently $\hat{K}(\lambda)$ defines a bounded operator on X for all $\lambda \in \Lambda$.

$$(\hat{K}(\lambda)\psi)(x) = \int_{a_0}^{G(2x)} e^{-\lambda a} k(a,2x)\psi(X(-a,2x))da, \ \psi \in X. \tag{6.1}$$

In the Appendix we shall prove the following result.

Lemma 6.1. *For all* $\lambda \in \Lambda$ *the operator* $\hat{K}(\lambda)$ *is compact.*

We can now apply the following result, proved by Steinberg (1968).

Lemma 6.2. *Let* E *be a Banach space and* Δ *a subset of the complex plane which is open and connected. If* $T(\lambda)$ *is an analytic family of compact operators on* E *for* $\lambda \in \Delta$, *then either* $(I - T(\lambda))$ *is nowhere invertible in* Δ *or* $(I - T(\lambda))^{-1}$ *is meromorphic in* Δ.

(A function $\phi(\lambda)$ defined on a set $V \subseteq \mathbb{C}$ is called meromorphic if it is analytic on V except for an at most countable set of elements of V which are poles of finite order of ϕ.) It is clear that $\|\hat{K}(\lambda)\| \to 0$ if $\mathrm{Re}\,\lambda \to \infty$, implying that $I - \hat{K}(\lambda)$ is invertible if $\mathrm{Re}\,\lambda$ is large enough. Thus lemma 6.1 and lemma 6.2 yield:

Theorem 6.3. *The function* $\lambda \to (I - \hat{K}(\lambda))^{-1}$ *is meromorphic in* Λ.

Therefore the set Σ defined by (4.3) is a discrete set whose elements are poles of $(I - \hat{K}(\lambda))^{-1}$ of finite order.

Now we shall employ positivity arguments to determine the so-called dominant singular point, i.e. the element of Σ with the largest real part. Before doing so we make an additional assumption on the growthrate g.

Assumption 6.4. *There exists a* $\delta > 0$ *such that* $2g(x) - g(2x) \geqslant \delta$, *all* $x \in [0,\infty)$.

In Diekmann et al. (1984) (see also chapter two of the forthcoming book Metz & Diekmann (in prep.)) a similar assumption has been made to establish compactness of the semigroup. In section 9 we shall explain why assumption 6.4 is imposed. A consequence of this assumption is that a baby call cell can not attain arbitrarily small sizes. We shall make this more explicit. If a cell is born with size x, than it can divide not earlier than a_0 time units later, and its daughers can not be smaller than

$$\gamma(x) \overset{def}{=} \tfrac{1}{2}X(a_0,x) = \tfrac{1}{2}G^{-1}(a_0 + G(x)). \tag{6.2}$$

A straightforward calculation shows that γ has precisely one fixed point x_0 if assumption 6.1 is satisfied. The following result shows that x_0 is a globally stable fixed point of the mapping γ.

Lemma 6.5. *Let for arbitrary $x_1 \geqslant 0$ the sequence $\{x_n\}$ be defined recursively as $x_{n+1} = \gamma(x_n)$, $n \geqslant 1$ then: $x_1 < x_0$ implies $x_0 < x_n$, $n \geqslant 1$, and $x_1 > x_0$ implies $x_n > x_0$, $n \geqslant 1$. Moreover $\lim_{n\to\infty} x_n = x_0$.*

Proof. Since $\gamma(0) > 0$, γ is continuous and x_0 is the unique solution of $\gamma(x) > x$ if $0 \leqslant x < x_0$. From assumption 6.4 we conclude that $\gamma'(x_0) = \dfrac{g(2x_0)}{2g(x_0)} < 1$, and this yields that $\gamma(x) < x$ if $x > x_0$. Since γ is increasing we have $x_n < x_0$ if $x_1 < x_0$ and $x_n > x_0$ if $x_1 > x_0$. Moreover $\lim_{n\to\infty} x_n$ exists and is a fixed point of γ. This yields the result. □

From this lemma and the observation that a baby cell attains the minimum birth size if all its ancestors have divided at age a_0, it follows that this minimum birth size is x_0 (which is positive if a_0 is positive), provided that there are infinitely many ancestors who all lived under the same growth regime.

Remark 6.6. The state space Ω_s indicated in section 1 is given by $\Omega_s = \{(a,x) \in \mathbb{R}^+ \times \mathbb{R}^+ | x \geqslant X(a,x_0)\}$.

However, we do not want to restrict ourselves à priori to initial data defined on Ω_s only, but admit that $n_0(a,x)$ defined in (1.6) is positive on $\Omega \setminus \Omega_s$. We can prove the following result.

Lemma 6.7. *If ψ is an eigenvector of $\hat{K}(\lambda)$, then $\psi(x) = 0$, $x < x_0$.*

Proof. Let $\psi \in X$. It follows from (6.1) that $(\hat{K}(\lambda)^n\psi)(x) = 0$ if $x \leqslant x_n$, where $x_1 = \gamma(0)$ and $x_{n+1} = \gamma(x_n)$, $n \geqslant 1$. If ψ is an eigenvector of $\hat{K}(\lambda)$ then ψ is an eigenvector of $\hat{K}(\lambda)^n$ for every positive integer n. As a consequence $\psi(x) = 0$ if $x \leqslant x_n$, and now the result follows from lemma 6.5. □

We denote with Y the subspace of X containing all $\psi \in L_1[0,\infty)$ which are identically zero on $[0,x_0)$. Obviously $\hat{K}(\lambda)Y \subseteq Y$. We let $\hat{K}_0(\lambda)$ be the restriction of $\hat{K}(\lambda)$ to Y. It is clear immediately that lemma 6.1 and theorem 6.3 remain valid if $\hat{K}(\lambda)$ is replaced by $\hat{K}_0(\lambda)$. Moreover (4.3) can be replaced by $\Sigma = \{\lambda \in \Lambda | 1 \in \sigma(\hat{K}_0(\lambda))\}$. Let Y_+ be the subset of Y containing all elements which are non-negative a.e. (almost everywhere). The following result is straightforward.

Theorem 6.8. *Y_+ defines a cone in Y which is total. Moreover $\hat{K}_0(\lambda)$ is positive with respect to Y_+ for all $\lambda \in \Lambda \cap \mathbb{R}$.*

We let Y_+^* be the dual of Y_+ and this defines a cone in Y^* because Y_+ is total. Clearly Y_+^* can be identified with $L_\infty^+[x_0,\infty)$, i.e. all measurable function on $[x_0,\infty)$ which are non-negative and essentially bounded.

The following lemma provides a useful characterization of the non-zero elements of Y_+^*.

Lemma 6.9. *If $F \in Y_+^*$, $F \neq 0$, then there exists an $\epsilon > 0$ such that for all $f \in Y_+$ satisfying $f(x) > 0$ for almost every $x \in [x_0+\epsilon,\infty)$ the relation $<F,f> > 0$ holds.*

Proof. $F \in Y_+^*$, $F \neq 0$ implies that there exists a measurable set $V \subset [x_0,\infty)$ with measure $\mu > 0$ such that $F(x) > 0$, $x \in V$. If we choose $\epsilon < \mu$, then the intersection $V \cap [x_0+\epsilon,\infty)$ has a measure which is greater than $\mu-\epsilon > 0$, and this yields the result. □

Now we can prove the following strong positivity result with respect to $\hat{K}_0(\lambda)$.

Theorem 6.10. *For all* $\lambda \in \Lambda \cap \mathbb{R}$ *the operator* $\hat{K}_0(\lambda)$ *is non-supporting with respect to* Y_+.

Proof. Let $\psi \in Y_+$, $\psi \neq 0$ and $\lambda \in \Lambda \cap \mathbb{R}$. If we substitute $z = X(-a,2x)$ in (6.1) we obtain

$$(\hat{K}_0(\lambda)\psi)(x) = \int_{x_0}^{X(-a_0,2x)} e^{-\lambda(G(2x)-G(z))} \cdot k(G(2x)-G(z),2x) \frac{\psi(z)}{g(z)}\, dz.$$

Let $F \in Y_+^*$, $F \neq 0$ and let $\epsilon > 0$ be given by lemma 6.9. There exists a $x_1 > x_0$ such that $\int_{x_0}^{X(-a_0,2x_1)} \psi(z)dz > 0$. This yields that $(\hat{K}_0(\lambda)\psi)(x) > 0$ if $x \geqslant x_1$. Let $x_2 = \gamma(x_1)$, where γ is defined by (6.2). Then $(\hat{K}_0(\lambda)^2\psi(x) > 0$, $x \geqslant x_2$. Recursively we find $(\hat{K}_0(\lambda)^n \psi)(x) > 0$, $x \geqslant x_n$, where $x_n = \gamma(x_{n-1})$, $n \geqslant 2$. We conclude from lemma 6.5 that there exists a $p \in \mathbb{N}$ such that $x_n < x_0 + \epsilon$ if $n \geqslant p$. Now we can apply lemma 6.9 which says that $<F, \hat{K}_0(\lambda)^n \psi > 0$ if $n \geqslant p$, and this proves the result. □

We can draw the following conclusions from theorem 5.2.

Let $r_\lambda = r(\hat{K}_0(\lambda))$, $\lambda \in \Lambda$. If $\lambda \in \Lambda \cap \mathbb{R}$, then

(a) r_λ is an algebraïcally simple eigenvalue of $\hat{K}_0(\lambda)$.

(b) The corresponding eigenvector $\psi_\lambda \in Y_+$ satisfies $\psi_\lambda(x) > 0$, $x \in [x_0,\infty)$ a.e. (We fix ψ_λ by the normalization $\|\psi_\lambda\| = 1$.)

(c) The corresponding eigenfunctional $F_\lambda \in Y_+^*$ satisfies $F_\lambda(x) > 0$, $x \in [x_0,,,\infty)$ a.e. (i.e. F_λ is strictly positive).

Hence, if $\lambda \in \Lambda$ is real and $r_\lambda = 1$, then $\lambda \in \Sigma$.

Lemma 6.11. *There exists a unique* $\lambda \in \Lambda \cap \mathbb{R}$ *such that* $r(\hat{K}_0(\lambda)) = 1$.

Proof. Let $\lambda, \mu \in \Lambda \cap \mathbb{R}$, $\lambda > \mu$ and $\psi \in Y_+$.

$$(\hat{K}_0(\mu)\psi)(x) = \int_{a_0}^{G(2x)} e^{-\mu a} k(a,2x)\psi(X(-a,2x))da$$

$$\geqslant e^{(\lambda-\mu)a_0} \int_{a_0}^{G(2x)} e^{-\lambda a} k(a,2x)\psi(X(-a,2x))da = e^{(\lambda-\mu)a_0}(\hat{K}_0(\lambda)\psi)(x).$$

If we substitute $\psi = \psi_\lambda$, then we obtain $\hat{K}_0(\mu)\psi_\lambda \geqslant e^{(\lambda-\mu)a_0} r_\lambda \psi_\lambda$. Taking duality pairings with F_μ on both sides yields

$$r_\mu \geqslant e^{(\lambda-\mu)a_0} \cdot r_\lambda \tag{6.3}$$

where we have used that $<F_\mu,\psi_\lambda>0$. Thus $\lambda \to r(\hat{K}_0(\lambda))$ is strictly decreasing in $\Lambda \cap \mathbb{R}$. Moreover this function is continuous. It follows easily that $\lim_{\lambda\to\infty} r(\hat{K}_0(\lambda)) = 0$. If we can prove that $\lim_{\lambda \downarrow -d_\infty} r(\hat{K}_0(\lambda)) = \infty$ then the conclusion of the lemma follows. We have to distinguish between two cases.

(a) $d_\infty = \infty$. Then (6.3) implies that $\lim_{\lambda\to-\infty} r(\hat{K}_0(\lambda)) = \infty$.

(b) $d_\infty < \infty$. Since $\|\psi_\lambda\| = 1$,

$$r(\hat{K}_0(\lambda)) = \|\hat{K}_0(\lambda)\psi_\lambda\| = \int_{x_0}^{\infty} \{ \int_0^{\infty} e^{-\lambda t}(K(t)\psi_\lambda)(x)dt \}dx = \int_0^{\infty} e^{-\lambda t} \{ \int_{x_0}^{\infty} (K(t)\psi_\lambda)(x)dx \}dt$$

$$= \int_0^{\infty} e^{-\lambda t} \|K(t)\psi_\lambda\| dt \geqslant \int_{T_0}^{\infty} e^{-\lambda t} \|K(t)\psi_\lambda\| dt \geqslant \int_{T_0}^{\infty} m_K e^{-d_\infty t} e^{-\lambda t} dt = \frac{m_K}{\lambda + d_\infty} e^{-(\lambda + d_\infty)T_0},$$

where we have used lemma 3.1. The change of order of integration was permitted because of Fubini's theorem (Dunford & Schwartz (1958)). It follows that $\lim_{\lambda \downarrow -d_\infty} r(\hat{K}_0(\lambda)) = \infty$. □

We denote the unique solution of $r(\hat{K}_0(\lambda)) = 1$ by λ_d, and we shall write ψ_d and F_d in stead of ψ_{λ_d} and F_{λ_d} respectively. We assume that ψ_d and F_d are normalized by

$$\|\psi_d\| = 1, \quad <F_d, \psi_d> = 1. \tag{6.4}$$

In order to prove that indeed λ_d is indeed the element of Σ with the largest real part, we need the following lemma.

Lemma 6.12. *Let $f \in L_1[0,\infty)$ be a complex-valued function. Then $|\int_0^\infty f(x)dx| = \int_0^\infty |f(x)|dx$ if and only if there exists a constant $\alpha \in \mathbb{C}$, $|\alpha| = 1$ such that $|f(x)| = \alpha f(x)$ a.e. on $[0,\infty)$.*

This result has been proved in Heijmans (to appear).

Theorem 6.13. *If $\lambda \in \Sigma$, $\lambda \neq \lambda_d$, then* $\text{Re}\,\lambda < \lambda_d$.

Proof. Suppose $\lambda \in \Sigma$ and $\hat{K}_0(\lambda)\psi = \psi$. Hence $|\hat{K}_0(\lambda)\psi| = |\psi|$, where $|\psi|(x) \overset{def}{=} |\psi(x)|$. This yields $\hat{K}_0(\lambda_R)|\psi| \geqslant |\psi|$, where $\lambda_R = \text{Re}\,\lambda$. Taking duality pairings with F_{λ_R} on both sides yields $r_{\lambda_R} <F_{\lambda_R}, |\psi|> \geqslant <F_{\lambda_R}, |\psi|>$, from which we conclude that $r_{\lambda_R} \geqslant 1$. In the proof of lemma 6.11 we have shown that $\lambda \rightarrow r_\lambda$ is decreasing in $\lambda \in \Lambda \cap \mathbb{R}$, and this implies that $\lambda_R = \text{Re}\,\lambda_d$. Now suppose that $\text{Re}\,\lambda = \lambda_d$ and $\text{Im}\,\lambda = \eta$. Thus $\hat{K}_0(\lambda_d)|\psi| \geqslant |\psi|$. Suppose that $\hat{K}_0(\lambda_d)|\psi| > |\psi|$. Taking duality pairings with F_d on both sides yields $<F_d, |\psi|> \; > \; <F_d, |\psi|>$ which is a contradiction. As a consequence $\hat{K}_0(\lambda_d)|\psi| = |\psi|$, from which we deduce that $|\psi| = c \cdot \psi_d$ for some constant c which we may assume to be one. Therefore $\psi(x) = \psi_d(x)e^{i\alpha(x)}$ for some real-valued function α. If we substitute this in $\hat{K}_0(\lambda_d)\psi_d = |\hat{K}_0(\lambda)\psi|$ we obtain

$$\int_{a_0}^{\infty} e^{-\lambda_d a} k(a,2x)\psi_d(X(-a,2x))da = |\int_{a_0}^{\infty} e^{-\lambda_d a - i\eta a} k(a,2x)\psi_d(X(-a,2x))e^{i\alpha(X(-a,2x))}da|.$$

From lemma 6.12 we conclude that $\alpha(X(-a,2x)) - \eta a = \beta$, for some constant β. If we substitute this in $\hat{K}_0(\lambda)\psi = \psi$ we obtain $e^{i\beta}\int_0^\infty e^{-\lambda_d a} k(a,2x))da = \psi_d(x)e^{i\alpha(x)}$, thus $\alpha(x) = \beta$ from which we conclude that $\eta = \text{Im}\,\lambda = 0$. □

This result, combined with the Riemann-Lebesgue lemma (lemma 4.3) and theorem 6.3, implies among others that there exists a positive horizontal distance between λ_d and the other points in Σ.

Corollary 6.14. *There exists an $\epsilon > 0$ such that $\lambda_d - \epsilon > -d_\infty$ and* $\text{Re}\,\lambda \leqslant \lambda_d - \epsilon$ *if $\lambda \in \Sigma$, $\lambda \neq \lambda_d$.*

Clearly $\hat{K}_0(\lambda)$ and $\hat{K}(\lambda)$ have the same eigenvectors (lemma 6.7). However $\hat{K}_0(\lambda)^*$ and $\hat{K}(\lambda)^*$ do not have the same eigenvectors. Let F_d' be the eigenvector of $\hat{K}(\lambda_d)^*$ corresponding to the eigenvalue one. Obviously, F_d' defines a positive functional on X. We can prove the following relation between F_d and F_d'. Let $<F_d', \psi_d> = 1$.

Theorem 6.15. *For all* $\psi \in Y$*, the equality* $<F_d,\psi> = <F_d',\psi>$ *holds.*

Proof. Let $\psi \in Y$, then $\psi = <F_d,\psi> \cdot \psi_d + \rho$, where $\rho \in \Re(\hat{K}_0(\lambda_d)-I) \overset{def}{=} Z$, i.e. the range of $\hat{K}_0(\lambda_d)-I$. Since the spectral radius of the restriction of $\hat{K}_0(\lambda_d)$ to the subspace Z is strictly less than one (theorem 5.2d) it follows that $\|\hat{K}_0(\lambda_d)^n\rho\| < \theta^n\|\rho\|$ for all $\rho \in Z$, where θ is some constant strictly less than one. Since $\hat{K}(\lambda_d)\psi = \hat{K}_0(\lambda_d)\psi$ we have $<F_d',\psi> = <\hat{K}(\lambda_d)^{*n}F_d',\psi> = <F_d',\hat{K}_0(\lambda_d)^n(<F_d,\psi>\psi_d + \rho)> = <F_d,\psi> + <F_d',\hat{K}_0(\lambda_d)^n\rho>$. If we let $n \to \infty$ then the second term at the right-hand-side tends to zero yielding that $<F_d',\psi> = <F_d,\psi>$. □

7. Computation of the residue in λ_d.

Here we shall concentrate on the behaviour of $(I-\hat{K}(\lambda))^{-1}$ in a neighbourhood of $\lambda = \lambda_d$, which is a pole of finite order (cf. theorem 6.3). The techniques exploited in this section are very similar to those in a paper by Schumitzky & Wenska (1975). We define

$$R(\lambda) = (I-\hat{K}(\lambda))^{-1}, \ \lambda \in \Lambda \setminus \Sigma. \tag{7.1}$$

Since $\hat{K}(\lambda)$ is analytic in a neighbourhood of λ_d we can write down its Taylor expansion.

$$\hat{K}(\lambda) = \sum_{n=0}^{\infty} (\lambda-\lambda_d)^n K_n, \tag{7.2}$$

where the series converges in the norm topology. Let $p \geqslant 1$ be the order of the pole of $R(\lambda)$ in $\lambda = \lambda_d$. In a neighbourhood of λ_d, $R(\lambda)$ can be represented by a Laurent series:

$$R(\lambda) = \sum_{n=-p}^{\infty} (\lambda-\lambda_d)^n R_n, \tag{7.3}$$

where by definition $R_{-p} \neq 0$. From

$$R(\lambda)(I-\hat{K}(\lambda)) = (I-\hat{K}(\lambda))R(\lambda) = I \tag{7.4}$$

if follows immediately that

$$R_{-p}(I-K_0) = (I-K_0)R_{-p} = 0. \tag{7.5}$$

From this relation and $K_0 = \hat{K}(\lambda_d)$ we obtain

$$\Re(R_{-p}) = \{\psi_d\}, \tag{7.6}$$

where $\Re(R_{-p})$ denotes the range of the operator R_{-p}, and $\{\psi_d\}$ stands for the span of the positive eigenvector ψ_d, i.e. $\{\psi_d\} = \{\gamma \cdot \psi_d | \gamma \in \mathbb{C}\}$. A relation similar to (7.4) is valid for the dual operators $K_0^* = \hat{K}(\lambda_d)^*$ and R_{-p}^*. Therefore

$$\Re(R_{-p}^*) = \{F_d\}. \tag{7.7}$$

From (7.4) we also deduce that

$$-R_{-p}K_1 + R_{-p+1}(I-K_0) = 0, \ \text{if}\ p > 1, \tag{7.8a}$$

$$-R_{-1}K_1 + R_0(I-K_0) = I, \ \text{if}\ p = 1. \tag{7.8b}$$

Together with (7.5) this implies

$$R_{-p}K_1R_{-p} = 0, \ \text{if } p > 1, \tag{7.9a}$$

$$R_{-1}K_1R_{-1} = -R_{-1}, \ \text{if } p = 1. \tag{7.9b}$$

We can state our main result now.

Theorem 7.1. *$R(\lambda)$ has a pole of order one in $\lambda = \lambda_d$ and the residue R_{-1} is given by*

$$R_{-1}\psi = \frac{<F_d',\psi>}{<F_d',-K_1\psi_d>} \cdot \psi_d, \ \psi \in X. \tag{7.10}$$

Observe that $-K_1 = [-\frac{d}{d\lambda}\hat{K}(\lambda)]_{\lambda=\lambda_d}$ defines a positive non-supporting operator on Y and thus it follows from theorem 6.15 that $<F_d',-K_1\psi_d> = <F_d,-K_1\psi_d> > 0$.

Proof of theorem 7.1. Let ϕ_d and H_d be solutions of $R_{-p}\phi = \psi_d$ and $R_{-p}^*H = F_d$ respectively. On account of (7.6) and (7.7) such solutions indeed exist. If $p > 1$ then (7.9a) yields $0 = <H_d, R_{-p}K_1R_{-p}\phi_d> = <F_d,K_1\psi_d>$ which is a contradiction since F_d is strictly positive and $-K_1\psi_d$ is positive and nonzero. Therefore $p = 1$, and $\Re(R_{-1}) = \{\psi_d\}$. Now let $R_{-1}\psi = f(\psi)\cdot\psi_d$ for some linear functional f. Then $<H_d,R_{-1}\psi> = <R_{-1}^*H_d,\psi> = <F_d,\psi> = <H_d,-R_{-1}KR_{-1}\psi> = <R_{-1}^*H_d, \ -K_1(f(\psi)\cdot\psi_d)> = f(\psi)\cdot <F_d,-K_1\psi_d>$, thus $f(\psi) = <F_d,\psi> / <F_d,-K_1\psi_d>$ which proves the result. □

It is not à priori clear whether or not $<F_d',\psi> > 0$ if $\psi \in X_+$, $\psi \neq 0$. This, however, is proved in the following lemma.

Lemma 7.2. *If $\psi \in X_+$, $\psi \neq 0$ then $<F_d',\psi> > 0$.*

Proof. If the restriction of ψ to $[x_0,\infty)$ is not identically zero, then the result follows from theorem 6.15. Now suppose that ψ is positive on a subset of $[0,x_0]$ with positive measure. Thus

$$(\hat{K}(\lambda_d)\psi)(x) \geq \int_{G(2x)-G(x_0)}^{G(2x)} e^{-\lambda_d a}k(a,2x)\psi(X(-a,2x))da$$

$$= \int_0^{x_0} e^{-\lambda_d(G(2x)-G(z))}\cdot k(G(2x)-G(z),2x)\frac{\psi(z)}{g(z)}\,dz > 0$$

for all $x \geq x_0$. Therefore $<F_d',\psi> = <\hat{K}(\lambda_d)^*F_d',\psi> = <F_d',\hat{K}(\lambda_d)\psi> > 0$. □

8. The inverse Laplace transform

Let E be a Banach space. The Hardy-Lebesgue class $H_p(\alpha;E)$ is the class of functions $g(\lambda)$ with values in E, which are analytic in $\mathrm{Re}\,\lambda > \alpha$ and satisfy the following conditions (cf. Friedman & Shinbrot (1967), Hille & Phillips (1957)).

$$\sup_{\zeta>\alpha}\left\{\int_{-\infty}^{\infty}\|g(\zeta+i\eta)\|^p\,d\eta\right\}^{\frac{1}{p}} < \infty, \tag{8.1a}$$

$$g(\alpha+i\eta) = \lim_{\zeta\downarrow\alpha} g(\zeta+i\eta) \text{ exists a.e. and is an element of } L_p(-\infty,\infty;E). \tag{8.1b}$$

The following inverse Laplace transform formula can be found in Friedman & Shinbrot (1967).

Lemma 8.1. *Let $g(\lambda) \in H_1(\alpha;E)$, then the function*

$$f(t) = \frac{1}{2\pi i}\int_{\gamma-i\infty}^{\gamma+i\infty} e^{\lambda t} g(\lambda)d\lambda, \ (\gamma \geqslant \alpha) \tag{8.2}$$

is defined and independent of γ, for all $t \in (-\infty,\infty)\cdot f(t) = 0$, $t < 0$, $f(t)$ is continuous and $\hat{f}(\lambda) = g(\lambda)$.

We rewrite the abstract renewal equation (2.17) as

$$B = \Phi + K{\star}B, \tag{8.3}$$

where $K{\star}B$ denotes the convolution product, i.e. $(K{\star}B)(t) = \int_0^t K(a)B(t-a)da$. If we substitute

$$B = \Phi + \nu, \tag{8.4}$$

we obtain

$$\nu = \Psi + K{\star}\nu, \tag{8.5}$$

where

$$\Psi = K{\star}\Phi. \tag{8.6}$$

Taking Laplace transforms on both sides of (8.5) gives us

$$\hat{\nu}(\lambda) = (I-\hat{K}(\lambda))^{-1}\hat{\Psi}(\lambda). \tag{8.7}$$

We can prove the following result.

Lemma 8.2. $\hat{\nu}(\lambda) \in H_1(\alpha;X)$, *if* $\alpha > \lambda_d$.

Proof. Let $\lambda \in \mathbb{C}$ be such that $\operatorname{Re}\lambda \geqslant \alpha$. It follows from lemma 3.1 and lemma 4.4 that the functions $\eta \to \hat{\Phi}(\zeta+i\eta)$ and $\eta \to \hat{K}(\zeta+i\eta)$ are element of $L_2(-\infty,\infty;X)$ and $L_2(-\infty,\infty;\mathcal{B}(X))$ respectively, if $\zeta > -d_\infty$, where $\mathcal{B}(X)$ is the space of bounded linear operators on X. Therefore the function $\eta \to \hat{\Psi}(\zeta+i\eta)$ is an element of $L_1(-\infty,\infty;X)$ if $\zeta > -d_\infty$. Moreover we know from the Riemann-Lebesgue lemma (lemma 4.3) that $\|(I-\hat{K}(\zeta+i\eta))^{-1}\| \leqslant 2$ if $|\eta|$ is large enough, say $|\eta| \geqslant \eta_0$. From the continuity of the function $\eta \to (I-\hat{K}(\zeta+i\eta))^{-1}$ on $[-\eta_0,\eta_0]$ (if $\zeta \geqslant \alpha$) we conclude that there exists a constant $C > 0$ such that $\|(I-\hat{K}(\zeta+i\eta))^{-1}\| < C$ for all $\eta \in (-\infty,\infty)$. Thus $\|\hat{\nu}(\zeta+i\eta)\| \leqslant C\|\hat{\Psi}(\zeta+i\eta)\|$ where we have used (8.7). The positivity of $K(t)$ and $\Psi(t)$ yields that

$$\|\hat{\Psi}(\zeta+i\eta)\| \leqslant \|\hat{\Psi}(\alpha+i\eta)\|, \ \zeta \geqslant \alpha,$$

and we conclude that condition (8.1a) is satisfied. The validity of condition (8.1b) follows from the analyticity of $(I-\hat{K}(\lambda))^{-1}$, $\hat{\Phi}(\lambda)$ and $\hat{K}(\lambda)$ on the region $\operatorname{Re}\lambda > \lambda_d$ and the fact that $\alpha > \lambda_d$. □

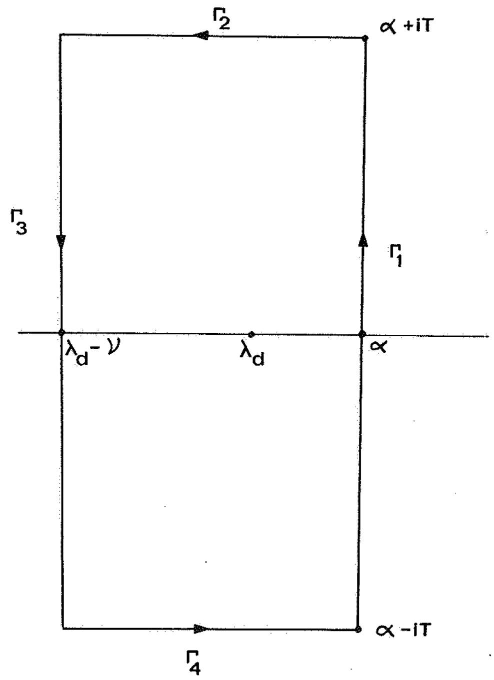

Figure 2. $\Gamma = \bigcup_{i=1}^{h} \Gamma_i$

Now let $\alpha > \lambda_d$, then lemma 8.1 yields that

$$v(t) = \frac{1}{2\pi i} \int_{\alpha-i\infty}^{\alpha+i\infty} e^{\lambda t} \hat{v}(\lambda) d\lambda \tag{8.8}$$

is well-defined. Some contributions to this integral can be evaluated by the method of residues. Therefore we shift the vertical integration curve Re $\lambda = \alpha$ to the left across the singularity $\lambda = \lambda_d$, such that it crosses no other elements of Σ (see fig. 2). Let $\epsilon > 0$ be given by corollary 6.14, and let $0 < \nu < \epsilon$. Let Γ be the rectangular contour in fig. 2. It follows immediately from the Riemann-Lebesgue lemma (lemma 4.3) that

$$\lim_{T\to\infty} \int_{\Gamma_i} e^{\lambda t} \hat{v}(\lambda) d\lambda = 0, \; i = 2,4.$$

Now it follows from Cauchy's theorem (which is also valid for vector-valued functions: see Hille & Phillips (1957)) that

$$v(t) = \frac{1}{2\pi i} \oint_{\Gamma} e^{\lambda t} \hat{v}(\lambda) d\lambda + \frac{1}{2\pi i} \lim_{T\to\infty} \int_{\lambda_d-\nu-iT}^{\lambda_d-\nu+iT} e^{\lambda t} \hat{v}(\lambda) d\lambda,$$

where we have used that the first integral does not depend on T. The residue theorem gives:

$$\frac{1}{2\pi i}\oint_{\Gamma} e^{\lambda t}\hat{\nu}(\lambda)d\lambda = \underset{\lambda=\lambda_d}{Res}\{e^{\lambda t}\hat{\nu}(\lambda)\} = e^{\lambda_d t}R_{-1}\hat{\Psi}(\lambda_d)$$

$$= e^{\lambda_d t}R_{-1}\hat{K}(\lambda_d)\hat{\Phi}(\lambda_d) = e^{\lambda_d t}\cdot\frac{<F_d',\hat{K}(\lambda_d)\hat{\Phi}(\lambda_d)>}{<F_d',-K_1\psi_d>}\cdot\psi_d$$

$$= e^{\lambda_d t}\,\frac{<F_d',-K_1\hat{\Phi}(\lambda_d)>}{<F_d',-K_1\psi_d>}\cdot\psi_d,$$

where we have used theorem 7.1, (8.6) and (8.7). As in the proof of lemma 8.2 we have that the function $\eta\rightarrow\hat{\nu}(\lambda_d-\nu+i\eta)$ is an element of $L_1(-\infty,\infty;X)$. Now

$$\|\frac{1}{2\pi i}\int_{\lambda_d-\nu-i\infty}^{\lambda_d-\nu+i\infty} e^{\lambda t}\hat{\nu}(\lambda)d\lambda\| \leqslant M\cdot e^{(\lambda_d-\nu)t},$$

where

$$M \stackrel{def}{=} \frac{1}{2\pi}\int_{-\infty}^{\infty}\|\hat{\nu}(\lambda_d-\nu+i\eta)\|d\eta \text{ depends on } \nu \text{ and } \Phi.$$

Remark 8.3. It follows from the boundedness of $(I-\hat{K}(\lambda))^{-1}$ on the vertical line $\mathrm{Re}\,\lambda = \lambda_d-\nu$, the Schwarz inequality and Parseval's relation (section 3) that

$$M \leqslant M_1\cdot\{\int_0^{\infty} e^{-2(\lambda_d-\nu)t}\|K(t)\|^2dt\}^{\frac{1}{2}}\cdot\{\int_0^{\infty} e^{-2(\lambda_d-\nu)t}\|\Phi(t)\|^2dt\}^{\frac{1}{2}},$$

where M_1 only depends on ν.

We can state our main result now.

Corollary 8.4. *Let $\epsilon > 0$ be given by corollary 6.12, and let $0 < \nu < \epsilon$, then $\|e^{-\lambda_d t}B(t)-c\cdot\psi_d\| \leqslant Le^{-\nu t}$, $t \geqslant 0$, for some constant L, where $c = \dfrac{<F_d',\hat{\Phi}(\lambda_d)>}{<F_d',-K_1\psi_d>}$ is a constant depending linearly on Φ.*

Proof. We have $B(t) = \Phi(t) + \nu(t)$, and $\nu(t) = e^{\lambda_d t}(c\cdot\psi_d+O(e^{-\nu t}))$. Now the result follows from lemma 3.1. □

Remark 8.5. Observe from corollary 8.4 that if t has become infinite, no cells with size less than x_0 are born, although such cells may be present at time zero.

9. Interpretation, conclusions and final remarks

For the sake of converience we repeat (2.11) and (2.12)

$$n(t,a,x) = \frac{g(X(-t,x))}{g(x)}\,Q(t,a-t,X(-t,x))n_0(a-t,X(-t,x)),\ t \leqslant a,$$

$$n(t,a,x) = \frac{g(X(-a,x))}{g(x)}\,E(a,X(-a,x))B(t-a,X(-a,x)),\ t > a.$$

This does not define a classical solution of (1.4)-(1.6). However it can be proved that n is differentiable along the characteristics of the partial differential operator $D = \frac{\partial}{\partial t} + \frac{\partial}{\partial a} + g(x)\frac{\partial}{\partial x}$, and in this sense indeed is a solution of (1.4)-(1.6).

Let

$$n_d(a,x) = e^{-\lambda_d a} \cdot \frac{g(X(-a,x))}{g(x)} E(a,X(-a,x))\psi_d(X(-a,x)). \tag{9.1}$$

Now we can restrate corollary 8.4 in terms of the solution n of (1.5)-(1.6).

Corollary 9.1. *Let* $\epsilon > 0$ *be given by corollary 6.14 and let* $0 < \nu < \epsilon$, *then the solution* $n(t,a,x)$ *of (1.4)-(1.6) satisfies* $\|e^{-\lambda_d t} n(t,\cdot,\cdot) - h(n_0) \cdot n_d\| \leq L' e^{-\nu t} \|n_0\|$, $t \geq 0$, *where* $\|\cdot\|$ *stands for the* $L_1(\Omega)$*-norm,* L' *is a positive constant, and* h *is a strictly positive linear functional on* $L_1(\Omega)$.

Remark 9.2. h can be computed from $h(n_0) = \dfrac{<F_d', \hat{\Phi}(\lambda_d)>}{<F_d', -K_1\psi_d>}$.

Corollary 9.1 is a typical renewal result. The population grows (or decays) exponentially with exponent λ_d (which is sometimes called the Malthusian parameter). As time increases an asymptotically stable age-size distribution is reached. If $t = \infty$ the dependence on the initial condition is only reflected by the scalar $h(h_0)$.

If in our model the rates b and μ depend on age only then we can integrate (1.4)-(1.6) over all sizes x and we find the age-dependent problem

$$\frac{\partial N}{\partial t} + \frac{\partial N}{\partial a} = -(\mu(a)+b(a))N(t,a), \tag{9.2a}$$

$$N(t,0) = 2\int_0^\infty b(a)N(t,a)da, \tag{9.2b}$$

$$N(0,a) = N_0(a), \tag{9.2c}$$

where $N(t,a) \stackrel{def}{=} \int_0^\infty n(t,a,x)dx$. If the assumptions (A_b), (A_μ) and (A_d) of section 1 are satisfied then a stable age-distribution is reached as $t \to \infty$:

$$N(t,a) \sim e^{\lambda_d t} N_d(a),\ t \to \infty,$$

(this result can also be found in Eisen (1979)) and the growthrate $g(x)$ has no effect on this stable age-distribution. More details can be found in Hannsgen et al. (1984).

Now we shall explain what can happen if assumption 6.4 is not fulfilled.

I. We expect that most of our result remain valid if $g(2x) < 2g(x)$, all x (but not necessarily $2g(x) - g(2x) > \delta$, for some $\delta > 0$). But probably one gets mixed up with great technical difficulties, which, however, do not provide additional insight.

II. If $g(2x) > 2g(x)$, for all x, then some sort of instability comes into the problem. Although γ defined by (6.3) again has a unique fixed point x_0, in this case it is unstable:

$$\frac{d\gamma}{dx}\Big|_{x=x_0} = \frac{g(2x_0)}{2g(x_0)} > 1.$$

For the sequence $\{x_n\}$ of lemma 6.4 this result in

$$x_n \to 0, \text{ if } x_1 < x_0,$$

$$x_n \to \infty, \text{ if } x_1 > x_0.$$

If we start with a population all of whose members have size $> \bar{x}(0)$, where $\bar{x}(0) > x_0$, then at time t all individuals have size $> \bar{x}(t)$, where $\bar{x}(t) \to \infty$. As a consequence there cannot exist a stable age-size distribution. A second problem arising in this case is caused by the fact that growth becomes very small if x tends to zero. As a consequence individuals can not grow away from zero.

III. Suppose that $g(2x) = 2g(x)$, all x. (Notice that this and also former case is actually excluded by the boundedness condition on g: however the same integral equation for the birth function $B(t)$ still holds.) Biologically this condition means that the time T needed to grow from x to $2x$ does not depend on x. We can prove that in this case the set of singular points Σ is periodic, i.e. there exists a $p > 0$ such that $\lambda \in \Sigma \Rightarrow \lambda + ikp \in \Sigma,\ k \in \mathbb{Z}$.

Lemma 9.3. *Let $g(2x) = 2g(x)$, for all x and let $T = G(2x) - G(x)$ (which does not depend on x), then Σ is periodic with period $p = \frac{2\pi}{T}$.*

Proof. Suppose $\lambda \in \Sigma$ and let $\psi \in X$ be determined by $\hat{K}(\lambda)\psi = \psi$:

$$\psi(x) = \int_{a_0}^{\infty} e^{-\lambda a} k(a,2x)\psi(X(-a,2x))da.$$

Let $T = G(2x) - G(x)$ and $p = \frac{2\pi}{T}$. Let $\psi_k(x) = e^{-ikpG(x)} \cdot \psi(x)$, then

$$(\hat{K}(\lambda + ikp)\psi_k)(x) = \int_{a_0}^{\infty} e^{-\lambda a} e^{-ikpa} k(a,2x)\psi(X(-a,2x))e^{-ikp(G(2x)-a)}da$$

$$= e^{-ikpG(2x)} \int_{a_0}^{\infty} e^{-\lambda a} k(a,2x)\psi(X(-a,2x))da =$$

$$= e^{-ikp(T+G(x))} \cdot \psi(x) = \psi_k(x), \text{ hence } \lambda + ikp \in \Sigma. \ \square$$

Now let $\psi_k(x) = e^{-ikpG(x)} \cdot \psi_d(x)$, where ψ_d is the positive eigenvector of $\hat{K}(\lambda_d)$ (assumed that a solution λ_d of $r(\hat{K}(\lambda)) = 1$ exists). Let

$$n_0^k(a,x) = e^{-\lambda_k a} \frac{g(X(-a,x))}{g(x)} E(a,X(-a,x)) \cdot \psi_k(X(-a,x)), \ k \in \mathbb{Z},$$

where $\lambda_k = \lambda_d + ikp$ (see (9.1)). Choose $\gamma_k \in \mathbb{C}$, $k \in \mathbb{Z}$ such that $\Sigma_{k=1}^{\infty} |\gamma_k| < \frac{1}{2}$, $\gamma_{-k} = \bar{\gamma}_k$, and define the initial age-size-distribution $n_0(a,x)$ by

$$n_0(a,x) \stackrel{def}{=} n_0^0(a,x) + \sum_{\substack{k=-\infty \\ k\neq 0}}^{\infty} \gamma_k n_0^k(a,x),$$

$$= (1 + 2Re \sum_{k=1}^{\infty} \gamma_k e^{-ikpG(x)}) \cdot n_0^0(a,x),$$

then $n_0(a,x) \geqslant 0$, $(a,x) \in \Omega$ and the solution $B(t,x)$ of the associated integral equation (2.14) is given by

$$B(t,x) = e^{\lambda_d t}\cdot\psi_d(x)\cdot\{1+2\,\mathrm{Re}\sum_{k=1}^{\infty}\gamma_k e^{ikp(t-G(x))}\} = e^{\lambda_d t}\cdot\psi_d(x)\cdot h(t,x)$$

where

$$h(t,x) \overset{def}{=} 1 + 2\,\mathrm{Re}\sum_{k=1}^{\infty}\gamma_k e^{ikp(t-G(x))}$$

satisfies

$$h(t+T,x) = h(t,x),$$
$$h(t,2x) = h(t,x).$$

This proves that there does not exist a stable age-size-distribution in this case.

This result disproves a remark of Bell (1968) which says that in case of exponential growth ($g(x)=c\cdot x$) there can exist a stable age-size-distribution if b depends in an appropriate manner on x and a. Trucco & Bell (1970) showed that in the case of dispersionless growth (i.e. $\frac{1}{x}X(a,x)$ depends on a only: this is satisfied if $g(x) = c\cdot x$) it is not possible that the first and second moments of the distribution of birth sizes both approach finite non-zero limits as $t \to \infty$, yielding that there does not exist a stable age-size distribution (see also Trucco (1970)). Hannsgen, Tyson & Watson (1984) proved that in case of exponential growth and under the assumption that the generation time (= age at which a cell divides) is a random variable with a given probability density function there cannot exist a stable, time-independent size distribution for the birth function.

IV. If $[0,\infty) = I_1 \cup I_2 \cup I_3$ such that $g(2x) < 2g(x)$, $x \in I_1$, $g(2x) = 2g(x)$, $x \in I_2$, $g(2x) > 2g(x)$, $x \in I_3$, then the question of existence of a stable distribution is a very hard one, but also a very interesting and exciting one from the mathematical point of view.

The reason for making assumption (A_d) is a technical one. It guarantees the existence of a dominant element λ_d of Σ (see lemma 6.11).

Undoubtedly our theory is also valid if a less restrictive condition than (A_g) is imposed. However, our main purpose is not generality but to give an idea how abstract results from functional analysis can be used in the study of concrete structured population models. The results that we obtained here can also be found using semigroup methods, and readers who are trying to do so, will find out that the two approaches are more closely linked then it seems at first sight.

Appendix

Here we shall prove that for all $\lambda\in\Lambda$ the operator $\hat{K}(\lambda)$ is compact. We need the following result of Krasnoselskii et al. (1976, chapter 2, § 5. 6). They proved that a linear integral operator which has a compact majorant is compact itself. We shall make this more precise. Let $\Omega\subseteq\mathbb{R}$ be a measurable set and let the linear integral operator $T:L_1(\Omega)\to L_1(\Omega)$ be given by

$$(T\phi)(x) = \int_{\Omega} h(x,y)\phi(y)dy.$$

Suppose that

$$|h(x,y)| \leqslant h^{+}(x,y),\ x,y \in \Omega,$$

and let the operator T^{+} be given by

$$(T^{+}\phi)(x) = \int_{\Omega} h^{+}(x,y)\phi(y)dy.$$

Then the following result holds (Krasnoselskii et al. (1976)):

Lemma 1. *If T^{+} is a bounded, compact operator from $L_1(\Omega)$ into itself then T is also compact.*

Now let $\lambda \in \Omega$, then

$$(\hat{K}(\lambda)\psi)(x) = \int_{0}^{X(-a_0,2x)} e^{-\lambda(G(2x)-G(z))}k(G(2x)-G(z),2x)\frac{\psi(z)}{g(z)}dz.$$

With (2.16), (A_g) and lemma 3.1 this yields

$$|e^{-\lambda(G(2x)-G(z))}.k(G(2x)-G(z),2x).\frac{1}{g(z)}| < e^{-(Re\,\lambda+d_\infty)(G(2x)-G(z))}.\frac{4}{g_{\min}}\,\|b\|_\infty \cdot e^{M}.$$

Let $p = \mathrm{Re}\lambda + d_\infty$, then $p>0$, since $\lambda \in \Lambda$. Let the operator $K^{+}(p)$ be defined as

$$(K^{+}(p)\psi)(x) = \int_{0}^{X(-a_0,2x)} e^{-p(G(2x)-G(z))}.\psi(z)dz.$$

If we can prove that $K^{+}(p)$ is compact for all $p>0$ then it follows from Lemma 1 that $\hat{K}(\lambda)$ is compact for all $\lambda \in \Lambda$.

Then following compactness criterium can be found in Kufner et al. (1977).

Lemma 2. *The bounded linear operator $T: L_1(\Omega) \to L_1(\Omega)$ is compact if for every $\epsilon>0$ there exists a $\delta>0$ such that $\int_\Omega |(T\phi)(x+h)-(T\phi)(x)|dx < \epsilon\|\phi\|$ for all $\phi \in L_1(\Omega)$ and $|h|<\delta$.*

We shall use this criterium to prove that $K^{+}(p)$ is compact for all $p>0$. For simplicity we assume that $g(x)=1$, for all x. The reader will have no difficulty to see that the proof can be carried through for more general g. Let $\psi \in L_1[0,\infty)$ and let $h>0$. Then

$$|(K^{+}(p)\psi)(x+h)-(K^{+}(p)\psi)(x)| =$$

$$|e^{-2p(x+h)}\int_{0}^{2(x+h)-a_0} e^{pz}\psi(z)dz - e^{-2px}\int_{0}^{2x-a_0} e^{pz}\psi(z)dz|$$

$$\leqslant |e^{-2p(x+h)} - e^{-2px}| \cdot \int_{0}^{2x-a_0} e^{pz}|\psi(z)|dz + e^{-2p(x+h)}\int_{2x-a_0}^{2(x+h)-a_0} e^{pz}|\psi(z)|dz \overset{def}{=} f_1(x)+f_2(x),$$

where $f_1(x) = (1-e^{-2ph})(K^{+}(p)|\psi|)(x)$, $f_2(x) = e^{-2p(x+h)}\int_{2x-a_0}^{2(x+h)-a_0} e^{pz}|\psi(z)|dz$, and $|\psi|(x) \overset{def}{=} |\psi(x)|$. Thus

$$\|f_2\| = \int_{0}^{\infty} f_2(x)dx = \int_{\frac{1}{2}a_0}^{\infty} e^{-2p(x+h)}.\{\int_{2x-a_0}^{2(x+h)-a_0} e^{pz}|\psi(z)|dz\}dx$$

$$= \int_0^\infty e^{pz}|\psi(z)|\cdot\{\int_{\frac{1}{2}(z+a_0)-h}^{\frac{1}{2}(z+a_0)} e^{-2p(x+h)}dx\}dx = \frac{1-e^{-2ph}}{2p}\, e^{-pa_0}\|\psi\|.$$

From these two estimates and Lemma 2, the compactness of $K^+(p)$ and thus $\hat{K}(\lambda)$ follows immediately.

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