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AFDELING TOEGEPASTE WISKUNDE  
(DEPARTMENT OF APPLIED MATHEMATICS)

TW 242/83

JULI

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ON THE STABILITY OF THE CELL SIZE DISTRIBUTION

Preprint

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**kruislaan 413 1098 SJ amsterdam**

BIBLIOTHEEK MATHEMATISCH CENTRUM  
—AMSTERDAM—

**Printed at the Mathematical Centre, Kruislaan 413, Amsterdam, The Netherlands.**

**The Mathematical Centre, founded 11 February 1946, is a non-profit institution for the promotion of pure and applied mathematics and computer science. It is sponsored by the Netherlands Government through the Netherlands Organization for the Advancement of Pure Research (Z.W.O.).**

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1980 Mathematics subject classification: 92A15

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On the stability of the cell size distribution \*)

by

O. Diekmann, H.J.A.M. Heijmans & H.R. Thieme \*\*)

#### ABSTRACT

A model for the growth of a size-structured cell population reproducing by fission into two identical daughters is formulated and analysed. The model takes the form of a linear first order partial differential equation (balance law) in which one term has a transformed argument. Using semigroup theory and compactness arguments we establish the existence of a stable size distribution under a certain condition on the growth rate of the individuals. An example shows that one cannot dispense with this condition.

KEY WORDS & PHRASES: *size-dependent population growth, reproduction by fission, balance equation, first order partial differential equation, transformed arguments, stable size distribution*

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\*) This report will be submitted for publication elsewhere.

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## 1. INTRODUCTION

In their paper "A model for populations reproducing by fission" [18], J.W. Sinko and W. Streifer presented a deterministic model describing the dynamics of single species populations of organisms reproducing by binary fission. Starting from the assumption that the important physiological characteristics of these organisms can be described by their size alone, they derived a complicated nonlinear evolution equation which they solved numerically (moreover, the model is applied to populations of the planarian worm *Dugesia tigrina* and theory and experiments are compared with each other). Similar models for the growth of procaryotic cell populations have been formulated by A.G. Fredrickson, D. Ramkrishna and H.M. Tsuchiya [5].

Although our long-term objective is the analysis of such complicated systems of nonlinear equations describing the dynamics of structured populations, we shall here concentrate on some aspects of a related but much simpler linear problem. More precisely, we study a variant of the Bell-Anderson [1,2] model for size-dependent cell population growth when reproduction occurs by fission into two equal parts. (Here one may replace "size" by weight, volume, length or, in fact, by any quantity which obeys a physical conservation law.) The environment is supposed to be unlimited and all possible (nonlinear) feedback mechanisms are ignored. It is well-known that under such circumstances the solution of the initial-value problem for *age-dependent* population growth behaves asymptotically for  $t \rightarrow \infty$  as

$$n(t,a) \sim Ce^{\sigma t} \bar{n}(a)$$

- where i)  $\sigma$  is the Malthusian parameter (intrinsic rate of natural increase),  
 ii)  $\bar{n}(a)$  is the so-called stable age-distribution,  
 iii)  $\sigma$  and  $\bar{n}(a)$  do not depend on the initial condition  
 iv)  $C$  is a constant which depends on the initial condition only.

(See [10,11,16]). Here we address the question whether reproduction by fission results similarly into convergence towards a stable size-distribution. As anticipated by Bell & Anderson [0,1,2] we find that the answer depends heavily on the functional relationship (described by a function  $g$ ) between

the growth of organisms and their size  $x$ . For instance, the answer is yes if  $g(2x) < 2g(x)$  for all relevant  $x$ , but no if  $g(2x) = 2g(x)$ . Two of us conjecture that the answer remains yes, if the relation  $g(2x) < 2g(x)$  is satisfied for values of  $x$  in a set of nonzero measure. This is proved for a special case.

The organization of the paper is as follows. In section 2 we present the balance law for size dependent reproduction by fission into two identical parts and we rewrite it as a linear evolution problem in a Banach space. In section 3 we prove the existence and uniqueness of a solution and we reformulate that result in terms of a strongly continuous semigroup of bounded linear operators. In section 4 we present a representation of the solution in terms of a *finite* sum of generations. In section 5 we show that the semigroup is compact after finite time if  $g(2x) < 2g(x)$ . In section 6 we discuss the eigenvalues of the infinitesimal generator and we derive a characteristic equation for an important special case (the general case is treated in [8]). In section 7 we reap the fruits of our preparations and prove the existence of a stable size distribution under the condition  $g(2x) < 2g(x)$ . In section 8 we investigate what happens if the condition  $g(2x) < 2g(x)$  is not satisfied for all  $x$ . Finally in section 9, we make some concluding remarks.

## 2. THE EQUATION AND ITS INTERPRETATION

The subject of our investigation is the equation

$$(2.1) \quad \frac{\partial n}{\partial t}(t, x) + \frac{\partial}{\partial x}(g(x)n(t, x)) = -\mu(x)n(t, x) - b(x)n(t, x) + 4b(2x)n(t, 2x).$$

Here the independent variables  $t$  and  $x$  denote, respectively, time and size. The unknown  $n$  is a density function:  $\int_{x_1}^{x_2} n(t, \xi) d\xi$  is the number of cells with size between  $x_1$  and  $x_2$  at time  $t$ . The functions  $\mu, b$  and  $g$  (which are assumed to be known) are the rates at which cells of size  $x$  die, divide and grow, respectively. The second term at the left hand side describes changes due to the growth of individuals and the first term at the right hand side describes changes due to death or dilution. The last two terms describe the reproduction process. At first sight the factor 4 in the source term may seem strange. But a moment of reflection should bring about that

$4 = 2 \times 2$ , where the first factor accounts for the doubling of numbers and the second for the doubling of intervals (those who originate from splitting in  $(2x, 2x+2dx)$  enter into  $(x, x+dx)$ ); a convincing check can be made as follows: multiply by the size  $x$  and integrate, then the contributions of the last two terms have to cancel each other because of conservation of "size". For the sake of completeness we present a derivation of (2.1) in the Appendix.

We assume that the cells cannot divide before they have reached a minimal size  $a > 0$ . Consequently, cells with size less than  $\frac{1}{2}a$  cannot exist. Mathematically we express this fact by the boundary condition

$$(2.2) \quad n(t, \frac{1}{2}a) = 0$$

which supplements (2.1).

From each "cohort" passing size  $y$  a fraction  $\frac{E(x)}{E(y)}$  will reach size  $x$ , where

$$(2.3) \quad E(x) = M(x)\Gamma(x),$$

$$(2.4) \quad M(x) = \exp - \int_{\frac{1}{2}a}^x \frac{\mu(\xi)}{g(\xi)} d\xi,$$

$$(2.5) \quad \Gamma(x) = \exp - \int_a^x \frac{b(\xi)}{g(\xi)} d\xi.$$

Note that  $M$  describes the loss due to mortality and  $\Gamma$  the "loss" due to splitting. Since we want to describe that the cells have to divide before they reach a maximal size, which we normalize to be  $x = 1$ , we are led to require that the integral  $\int_a^x \frac{b(\xi)}{g(\xi)} d\xi$  diverges for  $x \uparrow 1$  and to interpret the term  $4b(2x)n(t, 2x)$  in equation (2.1) as zero whenever  $x \geq \frac{1}{2}$ . Clearly we now require  $a < 1$ . If  $a \geq \frac{1}{2}$  the maximal size of a daughter is less than the minimal size of a mother. This realistic case is relatively easy and we will pay special attention to it. However, at this point we do not yet exclude the case  $a < \frac{1}{2}$  in which a large cell can undergo two divisions immediately after each other so that effectively a division into four parts occurs.

Clearly we now choose the domain of  $x$  to be the interval  $[\frac{1}{2}a, 1]$ . Concerning the growth, death and division rates we assume

$H_g$ :  $g$  is a strictly positive continuous function

$H_\mu$ :  $\mu$  is a nonnegative continuous function

$H_b$ :  $b(x) = 0$  for  $x \in [\frac{1}{2}a, a]$  and  $b(x) > 0$  for  $x \in (a, 1)$ .

Moreover  $b$  is continuous and satisfies  $\lim_{x \uparrow 1} \int_a^x b(\xi) d\xi = +\infty$ .

In all these assumptions we can weaken the continuity requirement at the expense of some small technical difficulties.

Strictly speaking the interpretation suggests no other condition on  $n(t, x)$  as a function of  $x$  than the integrability of the functions  $b(\cdot)n(t, \cdot)$  and  $n(t, \cdot)$ . Nevertheless we shall assume that the initial condition  $n_0$  in

$$(2.6) \quad n(0, x) = n_0(x)$$

is such that  $n_0(\cdot)/\Gamma(\cdot)$  is continuous (in particular this assumption requires that  $n_0(x) \rightarrow 0$  at a certain rate as  $x \uparrow 1$ ) and we shall show that  $n(t, \cdot)$  inherits this property. Here we are guided by the interpretation of  $\Gamma$  and by the desire to avoid technical details. As a side remark we mention that the smoothing properties of (2.1) hinge upon properties of  $g(2x) - 2g(x)$  on the one hand (cf. sections 5 and 8) and the behaviour of  $\Gamma'(x)$  for  $x \uparrow 1$  on the other.

The transformation

$$(2.7) \quad m(t, x) = \frac{g(x)}{E(x)} n(t, x)$$

leads to the evolution problem

$$(EP) \quad \begin{cases} \frac{\partial m}{\partial t} = -g(x) \frac{\partial m}{\partial x}(t, x) + k(x)m(t, 2x) \\ m(t, \frac{1}{2}a) = 0 \\ m(0, x) = \phi(x) \end{cases}$$

where by definition  $\phi(x) = \frac{g(x)}{E(x)} n_0(x)$  and

$$(2.8) \quad k(x) = 4 \frac{g(x)}{E(x)} \frac{b(2x)}{g(2x)} E(2x)$$



and where, here and in the following, one should interpret  $k(x)m(t,2x)$  as zero for  $x \geq \frac{1}{2}$ . Note that  $g(x)n(t,x)$  is the flux of individuals at  $(t,x)$  and that  $E(x)$  is a factor which, in some sense, accounts for the "loss" due to mortality and fission.

Although  $b$  has a non-integrable singularity,  $k$  is integrable and we shall exploit this property in, e.g., the proof of lemma 3.1. In fact this "reduction of the singularity" is an extra motivation for the transformation (2.7).

Our approach will be to look for solutions as functions of  $t$  with values in the space

$$X = \{\psi \in C[\frac{1}{2}a, 1] \mid \psi(\frac{1}{2}a) = 0\}$$

provided with the supremum norm. Thus we can rewrite (EP) as the abstract Cauchy problem

$$(ACP) \quad \begin{cases} \frac{dm}{dt} = Am \\ m(0) = \phi \end{cases}$$

where  $A$  is the unbounded operator defined by

$$(2.9) \quad \begin{cases} (A\psi)(x) = -g(x)\psi'(x) + k(x)\psi(2x) \\ \mathcal{D}(A) = \{\psi \in X \mid \psi \text{ is } C^1 \text{ on } [\frac{1}{2}a, \frac{1}{2}) \cup (\frac{1}{2}, 1]; \text{ the limits} \\ \lim_{x \uparrow \frac{1}{2}} -g(x)\psi'(x) + k(x)\psi(2x) \text{ and } \lim_{x \downarrow \frac{1}{2}} -g(x)\psi'(x) \text{ exist and} \\ \text{equal each other; } -g(\frac{1}{2}a)\psi'(\frac{1}{2}a) + k(\frac{1}{2}a)\psi(a) = 0\} \end{cases}$$

$A$  is a closed, densely defined operator on  $X$ . Now we are ready to apply the theory of semigroups of operators [12,15].

### 3. EXISTENCE AND UNIQUENESS OF A SOLUTION

One possibility to show that  $A$  generates a strongly continuous semigroup of bounded linear operators on  $X$  is to verify the Hille-Yosida

conditions [12,15]. Although this is not too difficult (one can use the results of [8]) we prefer another approach. Formally  $A = B + C$  where

$$(3.1) \quad (B\psi)(x) = -g(x)\psi'(x)$$

$$(3.2) \quad (C\psi)(x) = k(x)\psi(2x).$$

We consider  $B$  as an unbounded operator from  $L_1[\frac{1}{2}a, 1]$  into itself, with domain of definition

$$\mathcal{D}(B) = \{\psi \mid \psi \text{ is absolutely continuous and } \psi(\frac{1}{2}a) = 0\}$$

and  $C$  as a bounded operator from  $X$  into  $L_1[\frac{1}{2}a, 1]$ . Clearly  $B$  generates the semigroup  $e^{Bt}$  defined by

$$(3.3) \quad (e^{Bt}\psi)(x) = \psi(G^{-1}(G(x)-t))$$

where by definition

$$(3.4) \quad G(x) = \int_{\frac{1}{2}a}^x \frac{d\xi}{g(\xi)}$$

and  $G^{-1}$  is the inverse of the monotone function  $G$  on  $[0, G(1)]$  and defined to be  $\frac{1}{2}a$  on  $(-\infty, 0]$ . Note that  $G(x)$  is the time which a cell needs to grow from  $\frac{1}{2}a$  to  $x$  and that  $G^{-1}(t)$  is the size at time  $t$  when the cell had size  $\frac{1}{2}a$  at time zero; so  $G^{-1}$  is the solution of  $\frac{du}{dt} = g(u)$  with initial condition  $u(0) = \frac{1}{2}a$ .

We observe that  $e^{Bt}$  leaves (the embedding of)  $X$  invariant. Moreover,  $(e^{Bt}\phi)(x) = 0$  for  $t \geq G(x)$  and so, in particular,  $e^{Bt} = 0$  for  $t \geq G(1)$ .

Again formally the problem

$$\frac{dm}{dt} = (B+C)m$$

$$m(0) = \phi$$

leads to the integral equation (variation-of-constants formula)

$$(3.5) \quad m(t) = e^{Bt}\phi + \int_0^t e^{B(t-\tau)} C m(\tau) d\tau.$$

Our plan is as follows. First we shall show that (3.5) has a unique solution  $m = m(t; \phi)$ . Next we prove that  $T(t)\phi = m(t; \phi)$  defines a semigroup on  $X$  and, finally, that  $A$  is the generator of  $T(t)$ .

If  $m$  is an  $X$ -valued function then  $e^{B(t-\tau)} C m(\tau)$  is a  $L_1$ -valued function. It turns out that the integration with respect to  $\tau$  produces a continuous function of  $x$ :

LEMMA 3.1. *The formula*

$$(3.6) \quad (Lm)(t) = \int_0^t e^{B(t-\tau)} C m(\tau) d\tau$$

*defines a bounded linear operator from  $C([0, T]; X)$  into itself. For  $T$  sufficiently small, the norm of  $L$  is less than one.*

PROOF. Explicitly we have the following expressions for  $(Lm)(t)(x)$ :

$$\begin{aligned} & \int_{G^{-1}(G(x)-t)}^x k(\xi) m(G(\xi) - G(x) + t, 2\xi) \frac{d\xi}{g(\xi)}, \quad \text{for } x \leq \frac{1}{2} \\ & \int_{G^{-1}(G(x)-t)}^{\frac{1}{2}} k(\xi) m(G(\xi) - G(x) + t, 2\xi) \frac{d\xi}{g(\xi)}, \quad \text{for } x \geq \frac{1}{2} \quad \text{and} \\ & \quad t \geq G(x) - G(\frac{1}{2}), \\ & 0, \quad \text{for } x \geq \frac{1}{2} \quad \text{and} \quad t \leq G(x) - G(\frac{1}{2}) \end{aligned}$$

(here we used the transformation  $\xi = G^{-1}(G(x) - t + \tau)$ ). Hence it follows that:

- i) for fixed  $t$  this is a continuous function of  $x$  (which is zero for  $x = \frac{1}{2}a$ );
- ii) the supremum norm with respect to  $x$  depends continuously on  $t$ ;
- iii) for  $T \downarrow 0$  the supremum norm with respect to  $x$  and  $t$  goes to zero uniformly for  $m$  in the unit-ball of  $C([0, T]; X)$ .  $\square$

A standard contraction mapping and continuation argument yields

COROLLARY 3.2. *For arbitrary  $\phi \in X$  and  $T > 0$  equation (3.5) has a unique solution in  $C([0, T]; X)$ . This solution depends continuously and linearly on  $\phi$ .*

On the basis of this result we define bounded linear operators  $T(t)$  on  $X$  by

$$(3.7) \quad T(t)\phi = m(t;\phi),$$

where  $m(t;\phi)$  is the solution of (3.5). If we take in (3.5) the argument  $t+s$  and subsequently rearrange the terms a little bit, we arrive at the identity

$$m(s+t) = e^{Bt}m(s) + \int_0^t e^{B(t-\tau)} Cm(s+\tau) d\tau.$$

Consequently, uniqueness of solutions implies the semigroup relation

$$T(t+s) = T(t)T(s).$$

COROLLARY 3.3.  $\{T(t)\}$  forms a strongly continuous semigroup of bounded linear operators on  $X$ .

THEOREM 3.4.  $A$  is the infinitesimal generator of  $T(t)$ .

PROOF. Let  $\tilde{A}$  be the infinitesimal generator of  $T(t)$ . In order to show that  $A = \tilde{A}$ , we let  $u \in D(\tilde{A})$ ,  $\tilde{A}u = v$ . Then, if  $\text{Re } \lambda$  is large enough,  $u = (\lambda I - \tilde{A})^{-1}(\lambda u - v) = \int_0^\infty e^{-\lambda t} T(t)(\lambda u - v) dt$ . (See [15]). The Laplace transformation of (3.5) with  $\phi = \lambda u - v$  yields

$$u = (\lambda I - B)^{-1}(\lambda u - v) + (\lambda I - B)^{-1} Cu$$

with  $B$  and  $C$  regarded as operators from  $X$  to  $L_1$ . Thus  $u \in \mathcal{D}(B)$  and  $(B+C)u = v$ . Since  $v \in X$ ,  $u \in \mathcal{D}(A)$  and  $Au = v$ . This consideration implies that  $\mathcal{D}(\tilde{A}) \subset \mathcal{D}(A)$  and  $\tilde{A}u = Au$  for  $u \in \mathcal{D}(\tilde{A})$ .

$\mathcal{D}(A) \subset \mathcal{D}(\tilde{A})$  is proved by reading these arguments backwards.  $\square$

Thus we showed that  $A$  generates a semigroup which corresponds exactly to solving the integral equation (3.5).

The solution  $m(t,x)$  is not necessarily differentiable with respect to  $t$  and  $x$  separately. So the question arises in what sense it satisfies the first order p.d.e.. The following two observations clarify the situation:

- i) the solution is differentiable along the characteristics  $t-G(x) = \text{constant}$ ,
- ii) but in  $x = \frac{1}{2}$  one has to distinguish between the right- and left derivative since  $k(x)m(t, 2x)$  (interpreted as zero for  $x \geq \frac{1}{2}$ ) is not necessarily continuous in  $x = \frac{1}{2}$ .

Mathematically this amounts to the relation:

$$\lim_{\epsilon \rightarrow 0} \frac{m(t+\epsilon, G^{-1}(G(x)+\epsilon)) - m(t, x)}{\epsilon} = k(x)m(t, 2x)$$

where for  $x = \frac{1}{2}$  the two limits  $\epsilon \uparrow 0$  and  $\epsilon \downarrow 0$  have to be taken separately if  $k(\frac{1}{2}) \neq 0$ .

#### 4. REPRESENTATION OF THE SOLUTION: THE GENERATION EXPANSION

Defining  $m_0(t) = e^{Bt} \phi$  we can rewrite (3.5) as

$$(4.1) \quad m = m_0 + Lm.$$

By the method of successive approximations we find formally

$$(4.2) \quad m = m_0 + \sum_{n=1}^{\infty} L^n m_0.$$

It turns out that the infinite sum contains, in fact, a finite number of terms only.

LEMMA 4.1. Fix  $T > 0$ .  $L$ , as an operator from  $C([0, T]; X)$  into itself, is nilpotent. More precisely,  $L^n = 0$  for  $n \geq \frac{2T}{a} |g| + k$  where  $k$  is such that

$$2^{-k} \leq \frac{a}{2} < 2^{-k+1}$$

and  $|g| := \max\{|g(x)| \mid \frac{1}{2}a \leq x \leq 1\}$ .

PROOF. We shall first deal with the special case that  $g$  is identically one. We split the iterative procedure into two steps:

$$w_n(t) = C m_n(t), \quad n = 0, 1, 2, \dots$$

$$m_n(t) = \int_0^t e^{B(t-\tau)} w_{n-1}(\tau) d\tau, \quad n = 1, 2, 3, \dots$$

From (3.2) and (3.3) we deduce that

$$w_0(t)(x) = 0 \quad \text{for } x \geq \frac{1}{2} \Rightarrow m_1(t)(x) = 0 \quad \text{for } x \geq \frac{1}{2} + t$$

$$\Rightarrow w_1(t)(x) = 0 \quad \text{for } x \geq \frac{1}{4} + \frac{1}{2}t \Rightarrow m_2(t)(x) = 0 \quad \text{for } x \geq \frac{1}{4} + t$$

$$\Rightarrow w_{\ell-1}(t)(x) = 0 \quad \text{for } x \geq 2^{-\ell} + \frac{1}{2}t \Rightarrow m_{\ell}(t)(x) = 0 \quad \text{for } x \geq 2^{-\ell} + t.$$

So  $w_k(t)(x) = 0$  for  $x \geq \frac{a}{4} + \frac{1}{2}t$ . But, since also  $w_k(t)(x) = 0$  for  $x \leq \frac{a}{2}$ , it follows that

$$w_k(t) = 0 \quad \text{for } x \geq \frac{a}{4} + \frac{1}{2}t \quad \text{and for } t \leq \frac{a}{2}.$$

Hence  $m_{k+1}(t)(x) = 0$  for those combinations of  $x$  and  $t$  for which  $x - t + \tau \geq \frac{a}{4} + \frac{1}{2}\tau$  for all  $\tau \in [\frac{a}{2}, 1] \cap [0, t]$ , i.e. for  $x \geq t$  and for  $t \leq \frac{a}{2}$ . Continuing like above we find that  $m_{k+\ell}(t)(x) = 0$  for  $x \geq t - (\ell-1)\frac{a}{2}$  and for  $t \leq \ell\frac{a}{2}$ . As soon as  $\ell\frac{a}{2} \geq T$ ,  $m_{k+\ell}$  is identically zero. For the special case this concludes the proof.

In the general case we have

$$m_n(t)(x) = \int_0^t w_{n-1}(\tau) (G^{-1}(G(x) - t + \tau)) d\tau.$$

We claim that for  $t \geq \tau$  and  $x \geq |g|(t-\tau) + \xi$ , the inequality  $G^{-1}(G(x) - t + \tau) \geq \xi$ , holds. Indeed, the definition (3.4) of  $G$  implies that

$$G(x) - G(\xi) \geq |g|^{-1}(x - \xi) \quad \text{for } x \geq \xi$$

and consequently

$$G(x) - G(\xi) - t + \tau \geq |g|^{-1}(x - \xi) - t + \tau \geq 0$$

from which it follows that

$$G^{-1}(G(x)-t+\tau) \geq \xi.$$

Using this result one can repeat the induction steps above. In all (intermediate) formulas one has to replace  $t$  and  $\tau$  by  $|g|t$  and  $|g|\tau$ .  $\square$

We conclude that (4.2) gives a valid and useful representation of the solution. Moreover, each term has a clear interpretation which we now describe.

The contribution to the solution of those cells which were present at  $t = 0$ , but have not yet divided, is given by  $m_0$ , the zero'th generation. Inductively the  $\ell$ 'th generation  $m_\ell = L^\ell m_0$  gives the contribution of those organisms which arose from divisions of the  $(\ell-1)$ 'th generation and have not yet divided themselves. Lemma 4.1 expresses the intuitively obvious fact that at each time instant at most finitely many generations are present in the population. We note that each generation will go extinct in finite time, but that still the number of generations present in the population becomes unbounded as  $t \rightarrow +\infty$ .

## 5. COMPACTNESS

From the generation expansion (4.2) one can compute the solution for finite (and especially small) times, but this does not give any information about the asymptotic behaviour for  $t \rightarrow +\infty$ . In order to obtain such information we shall try to characterize the spectrum of  $T(t)$  in terms of the spectrum of  $A$ , about which we know a lot (see [8] and the next section). It is known that this characterization is easy when there is compactness in the problem [7,15].

Somewhat unprecisely one can say that growth and division lead to shift and multiplication operators, and these are not compact. However, when division occurs distributed, some kind of smoothing may (but need not to) take place. We shall show that the way in which the growth rate  $g$  depends on  $x$  has a decisive influence.

LEMMA 5.1. Assume that  $2g(x) > g(2x)$  for  $\frac{1}{2}a \leq x \leq \frac{1}{2}$ . Fix  $t > 0$ . The mapping

$$\phi \mapsto \int_0^t e^{B(t-\tau)} C e^{B\tau} \phi d\tau$$

from  $X$  into itself is compact.

PROOF. Let  $F = F(x, \phi)$  and  $\alpha = \alpha(x, t)$  be defined by

$$F(x, \phi) = \int_0^t (e^{B(t-\tau)} C e^{B\tau} \phi)(x) d\tau$$

$\alpha(x, t) = G^{-1}(G(x) - t)$ . (This quantity has a clear biological interpretation: it is the size of an individual at time 0 given that its size at time  $t$  equals  $x$ .) By definition  $\alpha(x, t) = \frac{1}{2}a$  if  $G(x) < t$ . Now

$$F(x, \phi) = \int_0^t k(\alpha(x, t-\tau)) \phi(G^{-1}(G(2\alpha(x, t-\tau)) - \tau)) d\tau,$$

where the integrand should be interpreted as zero whenever  $\alpha \leq \frac{1}{2}a$  or  $\alpha \geq \frac{1}{2}$ . Putting

$$\xi = G(2\alpha(x, t-\tau)) - \tau$$

we find

$$\frac{d\xi}{d\tau} = \frac{2g(\alpha)}{g(2\alpha)} - 1 > 0.$$

So we can use  $\xi$  as a new integration variable:

$$F(x, \phi) = \int_{G(2G^{-1}(G(x)-t))}^{G(2x)-t} k(\alpha(x, t-\tau(\xi))) \phi(G^{-1}(\xi)) \cdot \frac{g(2\alpha(x, t-\tau(\xi)))}{2g(\alpha(x, t-\tau(\xi))) - g(2\alpha(x, t-\tau(\xi)))} d\xi.$$

Since now  $x$  does not appear in the argument of  $\phi$  anymore, it is easy to show, using the continuity of  $g, G, G^{-1}$  and  $\alpha$  and the fact that  $k \in L_1$ , that



$$|F(x_1, \phi) - F(x_2, \phi)| \leq \|\phi\| \varepsilon(x_1, x_2)$$

where  $\varepsilon(x_1, x_2) \downarrow 0$  as  $|x_1 - x_2| \downarrow 0$ . (In view of the proof of Lemma 5.2 we remark that for each  $T > 0$ ,  $\varepsilon(x_1, x_2)$  can be chosen such that the estimate holds for any  $t \in [0, T]$ .) Hence, on account of the Arzela-Ascoli theorem, we conclude that each bounded set is mapped onto a precompact set.  $\square$

Lemma 5.1 gives a compactness criterion for the first generation  $m_1(t, \phi) = \int_0^t e^{B(t-\tau)} C e^{B\tau} \phi d\tau$ . Essentially the same argument leads to

LEMMA 5.2. Assume that  $2g(x) > g(2x)$  for  $\frac{1}{2}a \leq x \leq \frac{1}{2}$ . Define, as before, the  $n$ -th generation by

$$m_n(t, \phi) = \int_0^t e^{B(t-\tau)} C m_{n-1}(\tau, \phi) d\tau, \quad n \geq 1.$$

Fix  $t > 0$  and  $n \in \mathbb{N}$ . The mapping

$$\phi \mapsto m_n(t, \phi)$$

from  $X$  into itself is compact.

COROLLARY 5.3. If  $g(2x) < 2g(x)$  for all  $x \in [\frac{1}{2}a, \frac{1}{2}]$ , then  $T(t)$  is compact for  $t \geq G(1)$ .

PROOF. For  $t \geq G(1)$ ,  $m_0(t, \cdot) = 0$  and consequently  $T(t)$  equals a finite sum of compact operators.  $\square$

Precisely the same conclusion follows from the biologically unrealistic assumption  $2g(x) < g(2x)$ . The importance of such a condition on  $g$  becomes clear in section 8.

## 6. THE SPECTRUM OF A

In this section we restrict our attention to the case  $a \geq \frac{1}{2}$  (i.e., the maximal size of a daughter cell is less than the minimal size of a mother cell). We refer to Heijmans [8] for a detailed study of the general case, which turns out to be essentially the same but computationally much more

difficult.

The inhomogeneous equation  $(A-\lambda I)\psi = f$  can be rewritten as

$$-g(x)\psi'(x) - \lambda\psi(x) = f(x), \quad \frac{1}{2} \leq x \leq 1,$$

$$-g(x)\psi'(x) - \lambda\psi(x) = f(x) - k(x)\psi(2x), \quad \frac{1}{2}a \leq x \leq \frac{1}{2}, \quad \psi(\frac{1}{2}a) = 0.$$

The solution of the first equation is given by

$$(6.1) \quad \psi(x) = \psi(\frac{1}{2})e^{\lambda(G(\frac{1}{2})-G(x))} - \int_{\frac{1}{2}}^x e^{\lambda(G(\xi)-G(x))} \frac{f(\xi)}{g(\xi)} d\xi, \quad \frac{1}{2} \leq x \leq 1.$$

Using this expression we can solve the second equation:

$$(6.2) \quad \psi(x) = \int_{\frac{1}{2}a}^x e^{\lambda(G(\xi)-G(x))} \left\{ \psi(\frac{1}{2})e^{\lambda(G(\frac{1}{2})-G(2\xi))} k(\xi) - f(\xi) - k(\xi) \int_{\frac{1}{2}}^{2\xi} e^{\lambda(G(\eta)-G(2\xi))} \frac{f(\eta)}{g(\eta)} d\eta \right\} \frac{d\xi}{g(\xi)}.$$

Finally, the requirement of continuity in  $x = \frac{1}{2}$  yields the compatibility condition

$$(6.3) \quad (\pi(\lambda)-1)\psi(\frac{1}{2}) = \zeta(\lambda, f)$$

where

$$(6.4) \quad \pi(\lambda) = \int_{\frac{1}{2}a}^{\frac{1}{2}} e^{\lambda(G(\xi)-G(2\xi))} \frac{k(\xi)}{g(\xi)} d\xi$$

and

$$(6.5) \quad \zeta(\lambda, f) = \int_{\frac{1}{2}a}^{\frac{1}{2}} e^{\lambda(G(\xi)-G(\frac{1}{2}))} \left\{ f(\xi) + k(\xi) \int_{\frac{1}{2}}^{2\xi} e^{\lambda(G(\eta)-G(2\xi))} \frac{f(\eta)}{g(\eta)} d\eta \right\} \frac{d\xi}{g(\xi)}.$$

If  $\pi(\lambda) \neq 1$  we can solve (6.3) for  $\psi(\frac{1}{2})$  and for that special value  $\psi$  defined by (6.1)-(6.2) is a solution of  $(A-\lambda I)\psi = f$  which depends continuously on  $f$ . Hence  $\lambda$  is an element of the resolvent set if  $\pi(\lambda) \neq 1$ . If, on the other hand,  $\pi(\lambda) = 1$  (6.1)-(6.2) with  $f \equiv 0$  defines for arbitrary  $\psi(\frac{1}{2})$  a solution of  $(A-\lambda I)\psi = 0$ . It follows that  $\lambda$  is an eigenvalue if  $\pi(\lambda) = 1$ . For obvious reasons we shall call the equation

$$(6.6) \quad \pi(\lambda) = 1$$

the *characteristic equation*. Since  $\pi$  is analytic its roots are isolated points.

Using the definitions (2.3)-(2.5) and (2.8) we can rewrite the definition of  $\pi(\lambda)$  as follows

$$(6.7) \quad \begin{aligned} \pi(\lambda) &= 2 \int_a^1 \frac{b(\xi)}{g(\xi)} \exp\left(- \int_{\frac{1}{2}\xi}^{\xi} \frac{\lambda + \mu(\eta) + b(\eta)}{g(\eta)} d\eta\right) d\xi \\ &= 2 \int_a^1 \exp\left( \int_{\frac{1}{2}\xi}^{\xi} \frac{\lambda + \mu(\eta)}{g(\eta)} d\eta \right) d\Gamma(\xi) \end{aligned}$$

(here we also used that the support of  $b$  is contained in  $[a, 1]$ ). As an intermezzo we now show that  $\pi(0)$  admits a simple biological interpretation.

Clearly any newborn cell has to pass size  $a$  before it can possibly produce offspring. So the contribution of an arbitrary cell passing size  $a$  to the growth of the population can be effectively measured by the number of her daughters that will grow up to at least size  $a$ . If we consider a large number of cells passing size  $a$ , the average number of daughters which grow up safely to size  $a$  can be calculated as follows:

i. The chance that the potential mother reaches size  $\xi$  is given by

$$\exp\left(- \int_a^{\xi} \frac{\mu(\eta) + b(\eta)}{g(\eta)} d\eta\right).$$

ii. The chance density that fission occurs at  $\xi$  is given by  $\frac{b(\xi)}{g(\xi)}$  (here the factor  $\frac{1}{g(\xi)}$  accounts for the conversion of chance per unit of time to chance per unit of size). The number of daughters is exactly two.

iii. The chance that a daughter born with size  $\frac{1}{2}\xi$  does not die before reaching size  $a$  is given by

$$\exp\left(- \int_{\frac{1}{2}\xi}^a \frac{\mu(\eta)}{g(\eta)} d\eta\right).$$

Summing all contributions with respect to  $a < \xi < 1$  we find that the average number of daughters at  $a$  is precisely  $\pi(0)$ .

The characteristic function  $\pi$  is monotone decreasing as a function of real  $\lambda$ . Since  $\pi(-\infty) = +\infty$  as and  $\pi(+\infty) = 0$  there exists precisely one real

root of the characteristic equation, which we shall call  $\lambda_d$ . Clearly  $\lambda_d > 0$  if  $\pi(0) > 1$  and  $\lambda_d < 0$  if  $\pi(0) < 1$ . Other roots occur in complex conjugate pairs. Their position relative to  $\lambda_d$  depends heavily on the function  $g(x)$  (see section 8).

If  $g(2x) < 2g(x)$ , one can use the transformation  $\tau = G(\xi) - G(\frac{1}{2}\xi)$  to rewrite  $\pi(\lambda)$  as the Laplace transform of a nonnegative function and, consequently, all complex roots satisfy  $\text{Re } \lambda \leq \lambda_d - \epsilon$  for some  $\epsilon > 0$  (and, moreover, there are at most finitely many roots in any vertical strip).

A straightforward computation based on (6.1)-(6.5) shows that a root of  $\pi(\lambda) = 1$  corresponds to an algebraically simple eigenvalue of  $A$  if and only if  $\pi'(\lambda) \neq 0$ . Hence  $\lambda_d$  is a simple eigenvalue. The corresponding eigenvector of  $A$  which we denote by  $\psi_d$  is positive. One can decompose the whole space as the direct sum of the null space and the range of  $A - \lambda_d I$ :

$$(6.8) \quad X = N(A - \lambda_d I) \oplus R(A - \lambda_d I)$$

(here we use that  $A$  has a compact resolvent: if  $\pi(\lambda) \neq 1$ , (6.1)-(6.2) with  $\psi(\frac{1}{2})$  the solution of (6.3) defines a compact inverse of  $A - \lambda I$ ).  $\psi_d$  can be found from (6.1)-(6.2) with  $\lambda = \lambda_d$  and  $f \equiv 0$ . We normalize  $\psi_d$  by the condition  $\psi_d(\frac{1}{2}) = e^{-\lambda_d G(\frac{1}{2})}$ . Then  $N(A - \lambda_d I)$  is the one-dimensional subspace spanned by  $\psi_d$  and the projection on this subspace according to (6.8) is given by

$$(6.9) \quad P\phi = \frac{\zeta(\lambda_d, \phi)}{\pi'(\lambda_d)} \psi_d.$$

This formula follows directly from our explicit calculations, but a more systematic derivation can be based on the theory of adjoint operators. See [8, section 7]. In that paper it has been shown that there exists an  $L_\infty$ -function  $\psi_d^*$  which is positive almost everywhere, such that

$$(6.10) \quad P\phi = \left( \int_{\frac{1}{2}a}^1 \psi_d^*(x) \phi(x) dx \right) \psi_d.$$

As a side remark we mention that Sudbury [19] has studied related models starting from the adjoint formulation. (He considers the backward equation whereas our starting point has been the forward equation,

cf. Feller [4, Ch.X]).

We summarize those results of this section which remain true if the restriction on  $a$  is dropped.

**THEOREM 6.1** [8]. *The spectrum of  $A$  consists of isolated points which are eigenvalues. On the real axis there is a greatest eigenvalue  $\lambda_d$ , which is algebraically simple. The corresponding eigenvector  $\psi_d$  is positive on  $(\frac{1}{2}a, 1]$  and no other eigenvector has this property. The decomposition (6.8) holds. If  $2g(x) > g(2x)$  all other eigenvalues satisfy  $\operatorname{Re} \lambda \leq \lambda_d - \epsilon$  for some  $\epsilon > 0$  and in each vertical strip there are at most finitely many of them.*

## 7. THE STABLE SIZE DISTRIBUTION

Let, as before,  $\psi_d$  denote the eigenvector spanning  $N(A - \lambda_d I)$  and let  $P$  denote the projection operator on  $\psi_d$  according to the decomposition (6.8). Then  $P$  commutes with  $T(t)$  and one can study the action of  $T(t)$  on the two invariant subspaces separately. The action on  $\psi_d$  is rather simple:

$$T(t)\psi_d = e^{\lambda_d t} \psi_d.$$

Our aim is to deduce an exponential estimate for the action of  $T(t)$  on  $R(A - \lambda_d I)$  from information about the position of the remaining eigenvalues of  $A$  relative to  $\lambda_d$ .

**THEOREM 7.1.** *Assume  $g(2x) < 2g(x)$  then there exist positive constants  $\epsilon$  and  $K$  such that*

$$\|(I-P)T(t)\phi\| \leq Ke^{(\lambda_d - \epsilon)t} \|\phi\|.$$

**PROOF.** Take some  $s \geq G(1)$ . Corollary 5.3 implies that  $T(s)$  is compact. It follows that the nonzero part of the spectrum of  $T(s)$  consists of eigenvalues. Eigenvalues of  $T(s)$  are necessarily of the form  $e^{\lambda s}$  with  $\lambda$  some eigenvalue of  $A$  (the point spectrum of the semigroup is "faithful" to the point spectrum of the generator, see [15, §2.2]). Theorem 6.1 implies that for the restriction to  $R(A - \lambda_d I)$  the inequality  $\operatorname{Re} \lambda \leq \lambda_d - \epsilon$  holds for some

$\varepsilon > 0$ . Exploitation of the semigroup property then yields the required estimate, see Hale [7, §7.4].  $\square$

The constant  $\varepsilon$  has to be estimated by analysing the characteristic function  $\pi(\lambda)$ .

COROLLARY 7.2. *Assume  $g(2x) < 2g(x)$  then*

$$m(t, \cdot; \phi) = T(t)\phi = e^{\lambda_d t} (P\phi + o(1)), \quad t \rightarrow +\infty.$$

In words this says that the dominant term in the asymptotic expansion for  $t \rightarrow +\infty$  is factorized as the product of an exponential function of  $t$ , a function  $\psi_d(x)$  and a scalar factor. The initial function manifests itself in the scalar factor only. Note that for nonnegative  $\phi$ ,  $P\phi \neq 0$  unless  $\phi = 0$  (see (6.9) or [8]). Since  $e^{-\lambda_d t} m(t, \cdot; \phi)$  converges to a multiple of  $\psi_d$  we call  $\psi_d$  the *stable size distribution* of  $m$ . If  $a \geq \frac{1}{2}$  then  $\psi_d$  is given by (6.1)-(6.2) with  $f \equiv 0$  and  $\lambda = \lambda_d$  the real root of (6.6). The computation of  $\psi_d$  for  $a < \frac{1}{2}$  is presented in [8]. From  $\psi_d$  one can compute the stable size distribution  $\Psi_d$  of  $n$ :  $\Psi_d = \frac{E}{g} \psi_d$  (See (2.7)).

Let  $n(t, x; n_0)$  be the solution of our original equation (2.1) supplied with the boundary condition (2.2) and initial condition (2.6) where  $n_0$  is such that  $n_0(\cdot)/\Gamma(\cdot)$  is continuous on  $[\frac{1}{2}a, 1]$ , then we have the following result.

COROLLARY 7.3. *Assume  $g(2x) < 2g(x)$  for all  $x \in [\frac{1}{2}a, \frac{1}{2}]$ , then*

$n(t, \cdot; n_0) = e^{\lambda_d t} (C \cdot \Psi_d + o(1))$ ,  $t \rightarrow \infty$ , where  $C$  is a constant depending (linearly) on the initial condition only.

Since the total population size behaves like  $\exp(\lambda_d t)$  we call  $\lambda_d$  the Malthusian parameter.

REMARK 1. The relation between  $n$  and  $m$  can be formulated more precisely in the following way. A function  $\psi \in X$  is called  $E$ -bounded if  $\psi(\cdot)/E(\cdot)$  is a bounded function. (This is equivalent to saying that  $\psi(\cdot)/\Gamma(\cdot)$  is bounded). Let  $X_0$  be the space of  $E$ -bounded functions in  $X$  supplied with the norm

$$\|\psi\|_E = \sup \left\{ \frac{|\psi(x)|}{E(x)} \mid \frac{1}{2}a \leq x \leq 1 \right\}.$$

Then  $X_0$  is a Banach-space and the linear mapping  $H: X_0 \rightarrow X$  given by

$$(H\psi)(x) = \frac{g(x)\psi(x)}{E(x)}$$

is an isomorphism. Now the transformation from  $n$  to  $m$  can be written abstractly as

$$m(t, \cdot) = Hn(t, \cdot).$$

Now  $\tilde{T}(t) = H^{-1} T(t) H$ ,  $t \geq 0$ , defines a strongly continuous semigroup on  $X_0$  and the solution of the original equation is  $n(t, \cdot; n_0) = \tilde{T}(t)n_0$ , if  $n_0 \in X_0$ .

2) Using expression (6.10) the constant  $C$  in corollary 7.3 can be computed explicitly

$$C = \int_{\frac{1}{2}a}^1 \frac{g(x)}{E(x)} \psi_d^*(x) n_0(x) dx.$$

## 8. EXPONENTIAL INDIVIDUAL GROWTH

In the former section it has been proved that the semigroup  $T(t)$  is compact after finite time if  $g$  satisfies the condition

$$g(2x) < 2g(x), \quad \frac{1}{2}a \leq x \leq \frac{1}{2}$$

(or  $g(2x) > 2g(x)$ ). In this section we shall investigate what happens if this condition is not satisfied for all  $x$ . We will distinguish between two cases

$$A) \quad g(2x) = 2g(x), \quad \text{all } x \in [\frac{1}{2}a, \frac{1}{2}]$$

$$B) \quad g(2x) = 2g(x), \quad x \in Q_1$$

$$g(2x) < 2g(x), \quad x \in Q_2$$

where  $Q_1 \cup Q_2 = [\frac{1}{2}a, \frac{1}{2}]$  and both sets have a non-zero measure.

The general solution of the functional equation  $g(2x) = 2g(x)$  is  $g(x) = x\phi(\ell_n x)$  where  $\phi$  is a  $\ell_n$  2-periodic function. We restrict ourselves

to a special solution, namely  $g(x) = cx$  where  $c$  is some constant. By scaling the time we may set  $c = 1$ . This case which is characterized by exponential individual growth seems to be the most relevant from a biological point of view. See [0,1,2]. (However, our method of proof works equally well in the general case.)

Let us first deal with case A.

$$g(x) = x, \quad \frac{1}{2}a \leq x \leq 1.$$

Clearly

$$G(x) = \ln \frac{2x}{a} \text{ and } G^{-1}(t) = \frac{a}{2} e^t.$$

For the 0<sup>th</sup> and 1<sup>st</sup> generation of the population we find, respectively, (See section 4)  $m_0(t, x; \phi) = \phi(xe^{-t})$  and

$$m_1(t, x; \phi) = \phi(2xe^{-t}) \int_0^t k(xe^{-\tau}) d\tau$$

where by definition  $\phi(x) = 0$  if  $x \leq \frac{1}{2}a$ . Similar expressions for higher generations show that the solution is related to the initial condition by periodic continuation and multiplication. No information is lost, no smoothing occurs. Although non-negativity is preserved, it is not reinforced: the solution has zero's for arbitrary large times if it has zero's initially.

The exceptional position of exponential individual growth is found once more if one looks at the characteristic equation. A straightforward calculation shows that for  $a \geq \frac{1}{2}$  (See (6.7)):

$$\pi(\lambda) = 2^{-\lambda} C$$

where

$$C = 2 \int_a^1 \exp\left(- \int_{\frac{1}{2}\xi}^{\xi} \frac{\mu(\eta)}{g(\eta)} d\eta\right) d\Gamma(\xi)$$

and all roots  $\lambda = \frac{1}{\ln 2} (\ln C + 2k\pi i)$ ,  $k \in \mathbb{Z}$  lie on the vertical line  $\text{Re } \lambda = \lambda_d = \frac{\ln C}{\ln 2}$ ; in other words, there is no distance  $\epsilon > 0$  between the dominant (real) eigenvalue  $\lambda_d$  and the real parts of the other eigenvalues of A. The total population size still behaves like  $\exp \lambda_d t$  but convergence in



shape does not take place. Instead the initial size distribution turns around and around while numbers are multiplied.

This striking behaviour in the case of exponential individual growth has already been noticed by Bell & Anderson [1,2]. The following "thought-experiment" illustrates the biological reason. Consider two cells A and B with equal size and assume that at some time instant  $t_0$  cell A splits into a and a. During the time interval  $[t_0, t_1]$ , a, a and B grow and at  $t_1$  cell B splits into b and b. If  $g(x) = cx$ , the daughter cells a and b will have equal sizes just as their mothers A and B. In other words, the relation "equal size" is hereditary and extends over the generations. The growth model behaves like a multiplying machine which copies the size distribution.

Of course the situation changes if we abandon the point of view that fission results into two exactly equal daughters. One of us (Heijmans) currently investigates a model with  $g(x) = cx$  and a smooth probability density function for the mother-daughter size ratio [9].

Now a very interesting question arises: what happens in situation B, i.e. the situation that the functional equation  $g(2x) = 2g(x)$  is satisfied on a subset of  $[\frac{1}{2}a, \frac{1}{2}]$ ?

Heuristic reasoning in terms of probabilities can give some insight (the characteristic equation appears to be very helpful. See below.)

To begin, let us restrict ourselves to the following situation.

$$\begin{aligned}
 B') \quad & a \geq \frac{1}{2} \\
 & g(x) = x, \quad \frac{1}{2}a \leq x \leq \beta \\
 & g(x) < x, \quad \beta < x \leq 1
 \end{aligned}$$

where  $\beta$  is some value between a and 1. We shall prove that in this case there exists a stable size distribution.

The idea is the following. Suppose  $\lambda_d = 0$ , then the average cell which undergoes fission has one viable descendant. (i.e. a daughter which undergoes fission as well). The population can be seen as the union of two distinct groups. A cell is a member of the first group iff all of its ancestors have been dividing before reaching the size  $x = \beta$ . If at least one of its ancestors has divided at a size  $x > \beta$ , then it is a member of the second

group. The semigroup  $T(t)$  corresponding to the total population never becomes compact because the first group (the reproduction of whose members should be compared to a copying-machine, as mentioned in the first part of this section) never goes extinct (assumed that it had members at  $t = 0$ ). The membership in the first group, however, decreases to zero as  $t \rightarrow \infty$ , because the probability that a member's descendant  $n$  generations afterwards is also member of the first group is  $p^n$ , where  $p$  is the probability that a daughter cell born at a size smaller than  $\beta$  will divide before reaching size  $\beta$ . Note that there is only a one-way traffic from the first to the second group. Members of the second group have at least one ancestor which has run through the dispersion-machine generated by the non-exponential individual growth, which is enough "to make this group compact".

The rest of this section is devoted to the precise elaboration of this idea. Let us assume that  $\lambda_d = 0$ . (This can always be achieved by the transformation  $\tilde{n}(t, x) = e^{-\lambda_d t} n(t, x)$  in the original equation (2.1) and replacement of  $\mu(x)$  by  $\mu(x) + \lambda_d$ ).

We are going to investigate solutions  $m(t, x)$  of the evolution problem (EP). At each instant  $t$  the population is composed of two so-called subpopulations.

$$(8.1) \quad m(t, x) = \bar{m}(t, x) + \hat{m}(t, x)$$

where  $\bar{m}(t, x)$  represents the members of the first group and  $\hat{m}(t, x)$  the members of the second group. As has been done in section four we can write down a generation expansion for both  $\bar{m}(t, x)$  and  $\hat{m}(t, x)$

$$(8.2a) \quad \bar{m}(t, x) = \sum_{i=0}^{\infty} \bar{m}_i(t, x)$$

$$(8.2b) \quad \hat{m}(t, x) = \sum_{i=1}^{\infty} \hat{m}_i(t, x).$$

Note that the 0<sup>th</sup> generation is not present in the subpopulation  $\hat{m}(t, x)$ , which should be clear from the assumptions. Thus

$$(8.3) \quad \bar{m}_0(t, x) = \phi(G^{-1}(G(x) - t)).$$

We can write down the following recurrent relations for  $\bar{m}_i$  and  $\hat{m}_i$ . Let, as in section five

$$(8.4) \quad \alpha(x, t) = G^{-1}(G(x) - t) \\ (t, t + G(\frac{1}{2}\beta) - G(x))^- \\ \bar{m}_{i+1}(t, x) = \int_0^t k(\alpha(x, t-\tau)) \bar{m}_i(\tau, 2\alpha(x, t-\tau)) d\tau$$

$$(8.5) \quad \hat{m}_{i+1}(t, x) = \int_0^t k(\alpha(x, t-\tau)) \hat{m}_i(\tau, 2\alpha(x, t-\tau)) d\tau \\ + \int_{(t, t + G(\frac{1}{2}\beta) - G(x))^-}^t k(\alpha(x, t-\tau)) \bar{m}_i(\tau, 2\alpha(x, t-\tau)) d\tau$$

where  $(t_1, t_2)^- = \min(t_1, t_2)$ . Note that  $\tau \geq t + G(\frac{1}{2}\beta) - G(x)$  implies  $\alpha(x, t-\tau) \leq \frac{1}{2}\beta$ . So, it should be clear that these expressions are in conformity with the interpretation. Note that the second term at the right-hand side of (8.5) is identically zero if  $x < \frac{1}{2}\beta$ . The assumption  $\lambda_d = 0$  together with (6.7) yields

$$\int_{\frac{1}{2}a}^{\frac{1}{2}\beta} \frac{k(\xi)}{g(\xi)} d\xi = 1. \quad \text{Now let} \\ (8.6) \quad p = \int_{\frac{1}{2}a}^{\frac{1}{2}\beta} \frac{k(\xi)}{g(\xi)} d\xi, \quad \text{then } p < 1.$$

LEMMA 8.1.  $|\bar{m}_i(t, x)| \leq p^i \|\phi\|$ ,  $i = 0, 1, 2, \dots$  and  $\bar{m}_i(t, x) = 0$  (i.e. the  $i^{\text{th}}$   $\bar{m}$  generation goes extinct) for

$$t \geq \ln \left( \frac{2^{i+1}\beta}{a} \right) + \int_{\beta}^1 \frac{d\xi}{g(\xi)}.$$

PROOF. Let  $\bar{u}_i(t, x)$  be the restriction of  $\bar{m}_i(t, x)$  to the subinterval  $[\frac{1}{2}a, \beta]$ . Let  $\bar{u}(t, x) = \sum_{i=0}^{\infty} \bar{u}_i(t, x)$  then  $\bar{u}(0, x) = \bar{\phi}(x)$  where  $\bar{\phi}$  is the restriction of  $\phi$  to  $[\frac{1}{2}a, \beta]$ . Using the recurrence relation (8.4) we find

$$\bar{u}_1(t, x) = \bar{\phi}(2xe^{-t}) \int_0^t \bar{k}(xe^{-\tau}) d\tau.$$

where  $\bar{k}(x) = k(x)$  if  $x \leq \frac{1}{2}\beta$  and  $\bar{k}(x) = 0$  elsewhere.

By iteration we find

$$\bar{u}_i(t, x) = \bar{\phi}(2^i x e^{-t}) \bar{k}_i(t, x), \quad i = 0, 1, 2, \dots$$

where  $\bar{k}_0(t, x) = 1$  and

$$\bar{k}_i(t, x) = \int_0^t \bar{k}(x e^{-\tau}) \bar{k}_{i-1}(t-\tau, 2x e^{-\tau}) d\tau.$$

Using these expressions for  $\bar{u}_i$  we find

$$|\bar{u}_0(t, x)| \leq \|\bar{\phi}\|$$

$$|\bar{u}_1(t, x)| \leq \|\bar{\phi}\| \int_{\frac{1}{2}a}^{\frac{1}{2}\beta} \frac{\bar{k}(\xi)}{\xi} d\xi = p \|\bar{\phi}\|$$

and by iteration we find

$$(8.7) \quad |\bar{u}_i(t, x)| \leq p^i \|\bar{\phi}\|.$$

One can also see from the expressions above that  $\bar{u}_i(t, x)$  vanishes identically from time

$$t_i = \ln\left(\frac{2^{i+1}\beta}{a}\right) \text{ on. Let } i \geq 1.$$

All individuals contained in  $\bar{m}_i(t, x)$  are daughters of individuals contained in  $\bar{u}_{i-1}(t, x)$ . From (8.4) we find

$$\bar{m}_i(t, x) = \int_0^{(t, t+G(\frac{1}{2}\beta)-G(x))^-} k(\alpha(x, t-\tau)) \bar{u}_{i-1}(\tau, 2\alpha(x, t-\tau)) d\tau$$

and this together with (8.7) gives us

$$|\bar{m}_i(t, x)| \leq p^{i-1} \|\bar{\phi}\| \cdot \int_{\frac{1}{2}a}^{\frac{1}{2}\beta} \frac{k(\xi)}{g(\xi)} d\xi = p^i \|\bar{\phi}\| \leq p^i \|\bar{\phi}\|.$$

The generation  $\bar{m}_i$  goes extinct a time  $\int_{\beta}^1 \frac{d\xi}{g(\xi)}$  after  $\bar{u}_i$ . This proves the lemma.  $\square$

Now we are able to prove that the contribution of  $\bar{m}(t,x)$  to the total population becomes very small for large  $t$ .

**THEOREM 8.2.**  $\|\bar{m}(t, \cdot; \phi)\| \leq M e^{-qt} \|\phi\|$ ,  $t \geq 0$ , where  $M > 0$  is some constant not depending on  $t$  or  $\phi$  and  $q = -\frac{\ln p}{\ln 2} > 0$ .

**PROOF.** Suppose  $t > 0$ . There are finitely many generations  $i, i+1, \dots, j$  present in the sub-population  $\bar{m}(t,x)$  where  $i$  is larger or equal to the smallest integer  $v$  satisfying

$$\ln\left(\frac{2^v \beta}{a}\right) + \int_{\beta}^1 \frac{d\xi}{g(\xi)} \geq t$$

(The precise value of  $j$  is not important for our purposes).

Hence  $\bar{m}(t,x) = \sum_{\ell=i}^j \bar{m}_{\ell}(t,x)$  from which it follows that

$$|\bar{m}(t,x)| \leq \sum_{\ell=v}^{\infty} \|\bar{m}_{\ell}(t, \cdot)\| \leq \sum_{\ell=v}^{\infty} p^{\ell} \|\phi\| = \frac{p^v}{1-p} \|\phi\|.$$

The definition of  $v$  yields

$$v-1 \leq \frac{t}{\ln 2} + \theta \leq v \quad \text{where} \quad \theta = \frac{\ln a/\beta}{\ln 2}$$

and the result follows.  $\square$

For the remaining sub-population  $\hat{m}(t,x)$  we can prove a compactness result.

**THEOREM 8.3.** The linear map  $\phi \mapsto \hat{m}(t, \cdot; \phi)$  is compact for all  $t \geq 0$ .

**PROOF.**  $\hat{m}_0(t,x) = 0$  by assumption (8.3) and (8.5) yield that

$$\hat{m}_1(t,x) = \int_{(t, t+G(\frac{1}{2}\beta)-G(x))^-}^t k(\alpha(x, t-\tau)) \phi(G^{-1}(G(2\alpha(x, t-\tau))-\tau)) d\tau.$$

As in lemma 5.1 we substitute

$$\xi = G(2\alpha(x, t-\tau))-\tau$$

and find that  $\frac{d\xi}{d\tau} > 0$  for all values of  $x, t$  and  $\tau$  where  $\alpha(x, t-\tau) \geq \frac{1}{2}\beta$ . Now

arguments similar to those used to prove lemma 5.1 yield the result.  $\square$

Corresponding to the subpopulations  $\bar{m}(t, x)$  and  $\hat{m}(t, x)$  we define two families of operators  $\bar{T}(t)$  and  $\hat{T}(t)$ :

$$\bar{T}(t)\phi = \bar{m}(t, \cdot; \phi),$$

$$\hat{T}(t)\phi = \hat{m}(t, \cdot; \phi).$$

One should note that neither of them defines a semigroup.

Theorem 8.2 states

$$(8.8) \quad \|\bar{T}(t)\| \leq Me^{-qt}$$

and theorem 8.3 can be summarized by saying that

$$(8.9) \quad \hat{T}(t) \text{ is compact for all } t \geq 0.$$

Now we introduce some notions which might not be known to the reader. We refer to [14] for more details.

Let  $B$  be a Banach-space, and  $V$  be a bounded subset of  $B$ . The measure of noncompactness (or Kuratowski-measure)  $\gamma(V)$  of  $V$  is defined to be

$$\gamma(V) = \inf\{d > 0 \mid \text{there exist a finite number of sets } S_1, \dots, S_n \text{ such that diameter } (S_i) \leq d \text{ and } V = \bigcup_{i=1}^n S_i\}.$$

Two important properties are

$$(8.10a) \quad \gamma(V) = 0 \text{ iff } V \text{ has a compact closure}$$

$$(8.10b) \quad \gamma(V+W) \leq \gamma(V) + \gamma(W) \text{ where } V + W = \{v+w \mid v \in V \text{ and } w \in W\} \text{ and } V, W \text{ are bounded subsets of } B.$$

The measure of non-compactness of a bounded operator  $L: B \rightarrow B$  is defined to be

$$(8.11) \quad \hat{\gamma}(L) = \inf\{\varepsilon \geq 0 \mid \gamma(L(V)) \leq \varepsilon \gamma(V), \text{ for all bounded sets } V \subset B\}.$$

(8.10a) and (8.10b) yield

$$(8.12a) \quad \hat{\gamma}(L) = 0 \text{ iff } L \text{ is compact,}$$

$$(8.12b) \quad \hat{\gamma}(L_1 + L_2) \leq \hat{\gamma}(L_1) + \hat{\gamma}(L_2),$$

where  $L_1, L_2$  are bounded operators on  $B$ .

Moreover, it is obvious that

$$(8.12c) \quad \hat{\gamma}(L) \leq \|L\|.$$

The Browder essential spectrum  $\sigma_{\text{ess}}(L)$  of the operator  $L$  is defined by

$\lambda \in \sigma_{\text{ess}}(L)$  if at least one of the following conditions holds

- (1)  $\mathcal{R}(\lambda I - L)$  is not closed
- (2)  $\lambda$  is a limit point of  $\sigma(L)$
- (3)  $\bigcup_{k \geq 1} N((\lambda I - L)^k)$  is infinite dimensional.

It can be proved that

$$(8.13) \quad \lambda \in \sigma(L) \setminus \sigma_{\text{ess}}(L) \Rightarrow \lambda \in P\sigma(L)$$

(These are called normal eigenvalues).

Let  $r_{\text{ess}}(L)$  be the radius of the essential spectrum

$$r_{\text{ess}}(L) = \sup\{|\lambda| \mid \lambda \in \sigma_{\text{ess}}(L)\}$$

Nussbaum [14] proved the following result.

LEMMA 8.4.  $r_{\text{ess}}(L) = \lim_{n \rightarrow \infty} (\hat{\gamma}(L^n))^{1/n}$ .

Now we can prove the following important result.

THEOREM 8.5. Suppose  $\mu \in \sigma(T(t))$  and  $|\mu| > e^{-qt}$  then there exists a  $\lambda \in P\sigma(A)$  such that  $\mu = e^{\lambda t}$ .

PROOF.  $r_{\text{ess}}(T(t)) = \lim_{n \rightarrow \infty} (\hat{\gamma}(T(nt)))^{1/n}$ .

$\hat{\gamma}(T(nt)) \leq \hat{\gamma}(\bar{T}(nt)) + \hat{\gamma}(\hat{T}(nt)) = \hat{\gamma}(\bar{T}(nt)) \leq \|\bar{T}(nt)\| \leq Me^{-qnt}$ , where we have used (8.8), (8.9) and (8.12a,b,c). Consequently  $r_{\text{ess}}(T(t)) \leq e^{-qt}$ . Now suppose  $\mu \in \sigma(T(t))$  and  $|\mu| > e^{-qt}$ , then it must be that  $\mu \in P\sigma(T(t))$ , and

as we already saw in the proof of theorem 7.1 there must be some  $\lambda \in \rho\sigma(A)$  such that  $\mu = e^{\lambda t}$ .  $\square$

The characteristic equation in situation B' is given by

$$1 = \pi(\lambda) = p \cdot 2^{-\lambda} + \int_{\frac{1}{2}\beta}^{\frac{1}{2}} \frac{k(\xi)}{g(\xi)} e^{-\lambda(G(2\xi)-G(\xi))} d\xi$$

(where  $p$  was given by (8.6)) and it follows that the results of theorem 6.1 remain valid for this wider class of functions  $g$ . Hence there exists an  $\varepsilon_1 > 0$  such that

$$\operatorname{Re} \lambda \leq -\varepsilon_1, \quad \lambda \in \sigma(A) \setminus \{0\}$$

(recall that  $\lambda_d = 0$ ) and the conclusion of theorem 7.1 remains valid if we chose  $\varepsilon = \min(\varepsilon_1, q)$ .

We can state our main result now

COROLLARY 8.6. *If B' is satisfied then  $m(t, \cdot; \phi) = e^{\lambda_d t} (P\phi + o(1))$ ,  $t \rightarrow +\infty$*

Of course the conclusion of corollary 7.3 remains valid as well, if B' is satisfied.

If  $a \geq \frac{1}{2}$ , extension to the more general case B is straightforward. In that case (8.6) should be replaced by

$$p = \int_{Q_1} \frac{k(\xi)}{g(\xi)} d\xi.$$

Furthermore we were able to prove that the result stated in corollary 8.6 remains valid if the first condition in B' is replaced by  $a \geq \frac{1}{2}\beta$ . In their study of the inverse problem in [0], Anderson et al found that the growth-rate  $g$  satisfied the condition in B'; but unfortunately figure 4.B in [0] suggests that neither  $a \geq \frac{1}{2}$  nor  $a \geq \frac{1}{2}\beta$  is satisfied. It seems to two of us that extension to situations where  $a < \frac{1}{2}\beta$  should be possible, although one probably has to deal with intransparent and troublesome technical problems which do not provide new insight; the third of us has some doubts about it.



## 9. CONCLUDING REMARKS

It is rather difficult to make dynamic observations of individual micro-organisms and consequently the "data"  $b$ ,  $g$  and  $\mu$  are hard to obtain. In fact it might be easier to measure the stable distribution and one may want to derive information about  $b$ ,  $g$  and  $\mu$  from such measurements. We refer to Bell & Anderson [0,1,2] for a discussion of this inverse problem (also see [3]).

The present study can serve as a starting point for an investigation of nonlinear problems. More precisely we think of situations where the growth of the individuals depends on the availability of a certain substrate, which in turn is influenced by the consumption [5,6,13]. In [3] Diekmann et al. argue that there are several ways to describe reproduction by fission under changing conditions, each of them corresponding to a different intrinsic mechanism. Using the results of this paper they show that for one of these mechanisms the stable distribution in a chemostat is independent of controllable parameters like the dilution rate and the inflowing substrate concentration.

We shall deal with other generalizations such as fission into not necessarily equal parts and time-periodic (seasonal) growth, death, and fission rates in forthcoming publications. We intend to study models of size- and age-dependent population growth [1,2,17] in the near future.

Acknowledgement. We are grateful to T. Aldenberg and J.A.J. Metz for many discussions which have been the starting point for this investigation. H.Thieme thanks P. Wolf for useful conversations.

## APPENDIX

Choose  $x_1$  and  $x_2$  with  $x_1 < x_2$  and let  $h > 0$  be small. Individuals which have at time  $t+h$  a size between  $x_1$  and  $x_2$  fall into two different categories:

- i) those who had at time  $t$  a size between  $x_1 - hg(x_1) + o(h)$  and  $x_2 - hg(x_2) + o(h)$  and which have neither split nor died
- ii) those which were born between  $t$  and  $t+h$  as daughters of mothers with a size between  $2x_1 + 0(h)$  and  $2x_2 + 0(h)$ . Or, in formula

$$\int_{x_1}^{x_2} n(t+h, x) dx = \int_{x_1 - hg(x_1)}^{x_2 - hg(x_2)} n(t, x) [1 - h(\mu(x) + b(x))] dx + 2h \int_{2x_1 + 0(h)}^{2x_2 + 0(h)} b(x) n(t, x) dx + o(h).$$

Rearranging the term and dividing by  $h$  we find

$$\begin{aligned} \frac{1}{h} \int_{x_1}^{x_2} [n(t+h, x) - n(t, x)] dx + \frac{1}{h} \left\{ \int_{x_2 - hg(x_2)}^{x_2} n(t, x) dx - \int_{x_1 - hg(x_1)}^{x_1} n(t, x) dx \right\} \\ + o(1) \\ = - \int_{x_1}^{x_2} (\mu(x) + b(x)) n(t, x) dx + 4 \int_{x_1}^{x_2} b(2x) n(t, 2x) dx. \end{aligned}$$

The right hand side is independent of  $h$ . In the limit  $h \rightarrow 0$  the left hand side yields

$$\int_{x_1}^{x_2} \frac{\partial n}{\partial t}(t, x) dx + g(x_2) n(t, x_2) - g(x_1) n(t, x_1).$$

If we now divide both sides by  $x_2 - x_1$  and subsequently take the limit  $x_2 - x_1 \downarrow 0$  we find the balance law (2.1).

Of course taking the limits  $h \rightarrow 0$  and  $x_2 - x_1 \downarrow 0$  is not justified a priori and, in fact, not even a posteriori (see the end of section 3). Nevertheless this formal procedure is a helpful intermediate step towards the calculation of  $n(t, x)$ . In section 3 we employ the concepts of a semi-group of bounded linear operators and its infinitesimal generator to give

a precise mathematical formulation of the relation between the balance law and its solution.

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