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ON THE STABILITY OF THE CELL-SIZE DISTRIBUTION II: TIME-PERIODIC DEVELOPMENTAL RATES

O. DIEKMANN
Centrum voor Wiskunde en Informatica, Kruislaan 413, 1098 SJ Amsterdam, The Netherlands

H. J. A. M. HEIJMANS
Centrum voor Wiskunde en Informatica, Kruislaan 413, 1098 SJ Amsterdam, The Netherlands

and

H. R. THIEME
Sonderforschungsbereich 123, Universität Heidelberg, Im Neuenheimer Feld 293, D-6900 Heidelberg, F.R.G.

Abstract—A deterministic model for the growth of a size-structured proliferating cell population is analyzed. The developmental rates are allowed to vary with time. For periodically varying rates stability of the cell-size distribution is shown under similar conditions for the growth rate of individual cells as found before in the time-homogeneous case. Strongly positive quasicompact linear operators on Banach lattices serve as powerful abstract tools. Finally, the autonomous case is revisited and the conditions for stability found in [1] are relaxed.

INTRODUCTION

The growth of a size-structured population of cells which reproduce by fission into two equal parts can be described by the partial differential equation

$$\partial_t n(t, x) + \partial_x(g \cdot n)(t, x) + (\mu + b) \cdot n(t, x) = 4b \cdot n(t, 2x). \tag{1a}$$

Here $\partial_x(g \cdot n)(t, x)$ denotes $(\partial/\partial x)(g(t, x)n(t, x))$, $(\mu + b) \cdot n(t, x)$ denotes $(\mu(t, x) + b(t, x))n(t, x)$. The independent variables t and x denote, respectively, time and cell size (e.g. the length, volume, weight, protein content, etc. of a cell). At fixed time t, $n(t, x)$ describes the size density of the population. The development of an individual cell is governed by three processes: growth (i.e. increase in size), death (or dilution), and reproduction by splitting into two parts of equal size. $g(t, x)$, $\mu(t, x)$ and $b(t, x)$ indicate the respective rates in dependence on time t and cell size x. Equation (1a) relates these individual changes to the change of the population density. For a further explanation and a derivation of (1a) see [1, Sec. 2 and Appendix].

We assume that cells can only divide between a minimum size $a > 0$ and a maximum size which has been normalized to be 1, i.e.

$$b \cdot n(t, x) = 0 \quad \text{if } x \notin [a, 1), \tag{1b}$$

with $a < 1$. Consequently there are no cells with size less than $a/2$, so we require

$$n(t, a/2) = 0. \tag{1c}$$

Usually we consider (1) as an initial-value problem, i.e. (1a–c) are assumed to hold for $t > t_0$ with $t_0 \in \mathbb{R}$, and

$$n(t_0, x) = n_0(x) \tag{2}$$

with a given initial cell density n_0.

In [1] we impose conditions on the splitting rate b which guarantee that all cells die or divide before reaching the maximum size 1. But this is an unnecessary restriction. We confine the size interval to $[a/2, 1]$ in (1a), however, and so assume that cells with a size exceeding the maximum splitting size 1 do not affect the further development of the population. This assumption, as well as the linear character of Eq. (1), is justified if the environment of the population is unlimited (this can be artificially achieved in a laboratory) such that density-dependent feedback mechanisms can be ignored.

In [1] we considered (1) for time-independent rates g, μ, b and found conditions under which a cell population (with an arbitrary cell-size distribution at the beginning) asymptotically ($t \to \infty$) exhibits exponential growth with a stationary cell-size distribution, i.e.

$$n(t, x) \sim Ce^{\sigma t}\bar{n}(x), \quad t \to \infty. \tag{3}$$

Here σ and $\bar{n}$ do not depend on the initial state of the population, whereas the positive scalar C depends on the initial function in a linear and strictly positive way. The conditions mainly concerned the individual growth rate g: (3) holds, for example, if $g(2x) < 2g(x)$ for $x \in [a/2, \frac{1}{2}]$, whereas (3) does not hold if $g(2x) = 2g(x)$ for $x \in [a/2, \frac{1}{2}]$.

We generalize the results of [1] to the case of time-periodic rates g, μ, b (with the same period for b, g, μ) in presenting similar conditions under which

$$n(t, x) \sim Ce^{\sigma t}\bar{n}(t, x), \quad t \to \infty, \tag{4}$$

with C, σ, $\bar{n}$ having the same characteristics as in the time-homogeneous case and $\bar{n}(t, x)$ being periodic in t (having the same period as g, b, μ) (see Sec. 6). In Sec. 7 we revisit the time-homogeneous case and prove the conjecture at the end of Sec. 8 in [1], namely that $g(2x) \neq 2g(x)$ on an open subinterval of $[a/2, \frac{1}{2}]$ is sufficient for (3) to hold. In [1] we already showed that (3) does not hold for arbitrary initial values if $g(2x) = 2g(x)$ on $[a/2, \frac{1}{2}]$, e.g. in the case of exponential individual cell growth. So a complete characterization of those growth rates g has been achieved which cause convergence to steady-state exponential growth from arbitrary initial states. This improvement of our former result is of particular importance because the stronger assumptions in [1, Sec. 8] are not satisfied by data found for g by Anderson *et al.* (see [2, Fig. 4.B]) whose work[2–5] (besides the work of Sinko and Streifer[6,7], see also [8]) has been the main motivation for our study. See [1] for some more references. We mention that splitting into two unequal parts of fixed ratio (as it is considered in Sinko and Streifer's work[7] on planarian worms) can be dealt with in essentially the same way. Heijmans[9] deals with a model in which the ratio of mother size and daughter size is described by a probability distribution.

Recently, related models of proliferating cell populations have been studied by Lasota and Mackey[10] and by Tyson and coworkers[11–16]. Hannsgen, Tyson and Watson[16] examine the stationary size distribution for populations growing under steady-state conditions and they find, among other things, that such a distribution does not exist if growth is proportional to size and division is governed by the (purely age-dependent) transition probability model. In [13] Tyson and Hannsgen analyse the "Tandem Model," which is obtained from the transition probability model by adding a critical size requirement. Lasota and Mackey[10] consider the size distribution at birth in successive generations (so they are not concerned with the evolution in time of the size distribution of extant cells). Their assumptions about the dynamics of individual cells resemble ours and they prove that the birth-size distribution converges to a unique globally stable distribution when the generation number tends to infinity. In [15] Tyson and Hannsgen derive a similar result for the case that the probability of division is governed by age (and not size) and individual cell growth is linear. Moreover, they show that such a result does not hold if one assumes that individual cell growth is exponential instead of linear. In [11,12] finally, Tyson makes a comparison of the generation time distribution and the division-size distribution predicted by various models and observed for a population of fission yeast cells.

The organisation of our paper is as follows: In Sec. 1 we study the characteristic curves associated with the first-order partial differential equation (1a). These are important tools to transform (1), (2) into an integral equation, the solutions of which can be considered weak solutions of (1), (2) (see Sec. 2). In Sec. 3 we prove uniqueness and existence of solutions to the integral equation and derive some properties. In Sec. 4 we study the solution operators corresponding to the integral equations, in particular their positivity and compactness properties. In Sec. 5 we investigate their spectral properties, if the rates g, μ, b are time-periodic. Here we make substantial use of the theory of strongly positive linear operators on Banach lattices (see, e.g. [17,18]). In Secs. 6 and 7 we formulate and prove our results, first for the periodic and, under less restrictive assumptions, for the time-homogeneous case. In the appendix we present some material from the theory of Banach lattices.

Finally, we mention that the extensions and improvements of the results in [1], which we achieved in this paper, lead to corresponding extensions and improvements of the results in [19] for a rather special nonlinear variant of the model.

1. THE CHARACTERISTIC CURVES

The growth of an individual cell

In dealing with PDEs of first order, integration along characteristic curves plays an important role (see, e.q., [20,21]). In our case these characteristic curves describe the growth of an individual cell.

Throughout this paper we impose the following conditions on the growth rate g.

ASSUMPTION 1.1

g is a continuous nonnegative function on $\mathrm{R} \times [a/2, 1]$ with the following properties:

(a) g is bounded and bounded away from zero, i.e.

$$0 < g_{\min} \leqslant g(t, x) \leqslant g_{\max} < \infty \quad \text{for } t \in \mathrm{R},\ x \in [a/2, 1].$$

(b) The partial derivatives $\partial_t g(t, x)$, $\partial_t^2 g(t, x)$, $\partial_x g(t, x)$ exist and are continuous and bounded on $\mathrm{R} \times [a/2, 1]$.

We recall that even if cells should grow beyond the maximum splitting size 1, only cells of size $x \in [a/2, 1)$ affect the further development of the population [see (1b, c)]. So it is sufficient to know g on $\mathrm{R} \times [a/2, 1]$. For convenience we extend g to R^2 by

$$\begin{aligned} g(t, x) &= g(t, 1) && \text{for } x \geqslant 1, \\ g(t, x) &= g(t, a/2) && \text{for } x \leqslant a/2. \end{aligned} \tag{5}$$

The derivatives $\partial_t g$ and $\partial_t^2 g$ now exist and are continuous on R^2, $\partial_x g$ still exists in a generalized sense and is bounded.

So g is smooth enough such that the following ODE initial-value problems can be solved:

$$\begin{aligned} \partial_y T(t, x, y) &= 1/g(T(t, x, y), y), \\ T(t, x, x) &= t, \end{aligned} \tag{6}$$

$$\begin{aligned} \partial_t X(t, s, x) &= g(t, X(t, s, x)), \\ X(s, s, x) &= x, \end{aligned} \tag{7}$$

for $t, s, x, y \in \mathrm{R}$.

T and X can be interpreted biologically: A cell with size x at time s has size $X(t, s, x)$ at time t; a cell with size x at time t has size y at time $T(t, x, y)$. The following lemma lists a number of properties of the unique solutions T and X to (6) and (7). These will serve as paramount tools in our analysis of problem (1). A proof can be established by standard methods or can be found in textbooks dealing with differential equations (see, e.g. [22, Chap. VI]).

LEMMA 1.2

There exist unique continuously differentiable solutions T of (6) and X of (7) on $\mathbb{R}^3$. They have the following properties:

(a) $T(t, x, y)$ and $X(t, s, y)$ strictly increase as t and y increase and x and s decrease.
(b) $T(T(t, x, y), y, z) = T(t, x, z)$, $X(t, r, X(r, s, x)) = X(t, s, x)$.
(c) $T(s, x, X(t, s x)) = t$, $T(t, X(t, s, x), x) = s$, $T(t, X(t, s, x), y) = T(s, x, y)$.
(d) $X(s, T(s, x, y), y) = x$, $X(T(s, y, x), s, y) = x$, $X(t, T(s, x, y), y) = X(t, s, x)$.
(e) $\partial_t T(t, x, y) = \exp\left(-\int_x^y \frac{\partial_1 g(T(t, x, z), z)}{(g(T(t, x, z), z))^2}\, dz\right)$.
(f) $\partial_x X(t, s, x) = \exp\left(\int_s^t \partial_2 g(r, X(r, s, x))\, dr\right)$.
(g) $\partial_x T(t, x, y) + g(t, x)\partial_y T(t, x, y) = 0$.
(h) $\partial_s X(t, s, x) + g(s, x)\partial_x X(t, s, x) = 0$.

As an exercise the reader might verify (a)–(d) from the biological interpretation of T and X. Because of their permanent use these properties will not explicitly be quoted in the sequel.

Since we extended g from $\mathbb{R}^2 \times [a/2, 1]$ to $\mathbb{R}^2$ we should be aware of the domains in which T and X only depend on the values of g on $\mathbb{R} \times [a/2, 1]$: Eq. (6) tells us that this is the case for $T(t, x, y)$ iff $x, y \in [a/2, 1]$. It follows from (7) that, if $x \in [a/2, 1]$, $X(t, s, x)$ depends on the values of g on $\mathbb{R} \times [a/2, 1]$ iff $X(t, s, x) \in [a/2, 1]$, i.e. iff $t \in [T(s, x, a/2), T(s, x, 1)]$ or, equivalently, iff $s \in [T(t, a/2, x), T(t, 1, x)]$.

2. TRANSFORMATION OF THE PROBLEM

Weak solutions

As we shall see in Sec. 3 one cannot find classical solutions of (1) for $t > t_0$ if the initial values $n(t_0, \cdot)$ and the rates μ and b are not differentiable. Since we want to include initial values and rates which are continuous only, we look for a reformulation of (1) which is equivalent to the original one for differentiable data and solutions, but makes sense for continuous non-differentiable data and solutions as well.

Throughout this paper we make the following assumptions on the splitting and mortality rates b and μ.

ASSUMPTION 2.1

(a) μ is a continuous nonnegative function on $\mathbb{R} \times [a/2, 1]$.
(b) b is a nonnegative function on $\mathbb{R}^2$ with the following properties:
  (i) b is continuous on $\mathbb{R} \times [a, 1)$.
  (ii) $b(t, x) > 0$ if $x \in (a, 1)$, $b(t, x) = 0$ if $x \notin [a, 1)$.
  (iii) There exists a continuous function b_0 on $(a, 1)$ and some $c > 0$ such that

$$b_0(x) \leq b(t, x) \leq cb_0(x).$$

By assumption (b) cells can divide at any size in $(a, 1)$, but at no size outside $[a, 1)$. If $\int_a^1 b_0(x)\, dx = \infty$, then every cell dies or divides before reaching the maximum size 1.

In a first step we transform (1) to a simpler equation. We define

$$m = g \cdot n \cdot E \tag{8}$$

with

$$E(t, x) = \exp\left(\int_{a/2}^{x} \left[\frac{\partial_1 g}{g^2} - \frac{\mu - b}{g}\right](T(t, x, z), z)\, dz\right). \tag{9}$$

If $(\mu + b)(s, z)$ is differentiable in s, by Lemma 1.2(g),

$$(\partial_t + g(t, x)\partial_x)E = \left[\frac{\partial_1 g}{g} - (\mu + b)\right] E;$$

hence Eq. (1) is equivalent to the following equations for m:

$$(\partial_t m/g)(t, x) + \partial_x m(t, x) = D(t, x)m(t, 2x), \quad x \in (a/2, 1); \tag{10a}$$

$$D(t, x)m(t, 2x) = 0, \quad x \notin [a/2, \tfrac{1}{2}); \tag{10b}$$

$$m(t, a/2) = 0; \tag{10c}$$

with

$$D(t, x) = 4\,\frac{b(t, 2x)E(t, 2x)}{g(t, 2x)E(t, x)}, \quad a/2 \leqslant x \leqslant \tfrac{1}{2}. \tag{11}$$

The initial function takes the form

$$m(t_0, x) = (g \cdot n/E)(t_0, x) =: \Phi(x). \tag{12}$$

The following properties of D follow from Assumptions 1.1 and 2.1.

LEMMA 2.2

(a) D is continuous on $\mathbb{R} \times [a/2, \tfrac{1}{2})$.

(b) $D(t, x) > 0$ if $x \in (a/2, \tfrac{1}{2})$, $D(t, x) = 0$ if $x \notin [a/2, \tfrac{1}{2})$.

(c) There exists a continuous function D_0 on $[a/2, \tfrac{1}{2}]$ such that $D(t, x) \leqslant D_0(x)$, $\int_{a/2}^{1/2} D_0(x)\,\mathrm{d}x < \infty$.

Note that Lemma 2.2 even holds if $\int_a^1 b_0(x)\,\mathrm{d}x = \infty$. This "reduction in the singularity" will be very useful in the next section and is an extra motivation for the transformation (8).

The transformation from (1) to (10) does not yet settle the problems we mentioned at the beginning of this section. So, in a next step, we integrate (10a) along the characteristic curves T. To this end we define

$$u(s, z, x) = m(T(s, z, x), x). \tag{13}$$

By (10a) and (6),

$$\partial_x u(s, z, x) = D(T(s, z, x), x).m(T(s, z, x), 2x).$$

Hence, since $T(s, z, z) = s$,

$$u(s, z, x) = \int_z^x D(T(s, z, y), y).m(T(s, z, y), 2y)\,\mathrm{d}y + m(s, z). \tag{14}$$

In order to return to an equation for m, we use that $m(t, x) = u(s, z, x)$ with $s = T(t, x, z)$ by (13). But, dealing with an initial-value problem, we have to avoid that $s < t_0$. So, if $x < X(t, t_0, a/2)$ we choose $z = a/2$ and $s = T(t, x, a/2) > t_0$.

If $x \geqslant X(t, t_0, a/2)$, we choose $z = X(t_0, t, x) \geqslant a/2$ and $s = T(t, x, z) = t_0$. In this way we arrive at the following integral equation for m on which we will focus in the sequel:

$$m(t, x) = \int_{a/2}^{1/2} K(t, x, y)m(T(t, x, y), 2y)\,\mathrm{d}y + m_0(t, x) \tag{15a}$$

for $t \geq t_0$, $x \in [a/2, 1)$, with

$$K(t, x, y) = D(T(t, x, y), y), \quad \text{if } X(t_0, t, x) \leq y \leq x, \text{ and}$$
$$K(t, x, y) = 0 \quad \text{otherwise.} \tag{15b}$$

m_0 contains the information about the initial function Φ:

$$m_0(t, x) = \Phi(X(t_0, t, x)) \quad \text{if } X(t, t_0, a/2) \leq x < 1, \quad m_0(t, x) = 0 \quad \text{otherwise}, \tag{16}$$

with Φ being the initial values of m at $t = t_0$.

Let us summarize what we have done so far. We have shown that, if $(\mu - b)(s, x)$ is differentiable in s, solutions n of (1) correspond to solutions m of (10) via the transformation (8) and conversely. Furthermore, any solution of (10) with initial function $m(t_0, \cdot) = \Phi$ at $t = t_0$ solves (15), (16). Conversely, if m is a solution of (15), (16) and $m(t, x)$, $D(t, x)$ are differentiable in t and $\Phi(x)$ is differentiable in x, then m is a solution of (10) by Lemma 1.2 (g, h). But Eq. (15) also makes sense, if m and m_0 are continuous (without the special form of m_0 in (16)) and D has the properties listed in Lemma 2.2. So (15), (16) can be considered a weak version of (10), (12) or (1), (2) respectively, and we define the following.

Definition 2.3. A continuous solution m of (15), (16) is called a "weak solution of (10) with initial function Φ at $t = t_0$". If $m(t_0, \cdot) = \Phi$ is given by (12), $n = m \cdot E/g$ is called a weak solution of (1) with initial function $n(t_0, \cdot)$ at $t = t_0$.

Remarks

(a) Since

$$K(t, x, y) \leq D_0(y), \quad \int_{a/2}^{1/2} D_0(y)\, dy < \infty \tag{17}$$

by (15b) and Lemma 2.2(c), it will be appropriate to handle (15) with m, m_0 being continuous on $[t_0, T] \times [a/2, 1]$, $T > t_0$. This involves that, in order to obtain weak solutions n of (1) for initial functions $n(t_0, \cdot)$, we must assume $(g \cdot n/E)(t_0, \cdot)$ to be continuous on $[a/2, 1]$. As a kind of tradeoff we obtain that $g \cdot n/E$ is continuous in $[t_0, t] \times [a/2, 1]$, $t > t_0$.

(b) There are two other ways of defining and/or handling weak solutions of (10). The first one approximates the initial function and the other data of the equation by sufficiently smooth ones, and finds "strong" solutions of the approximating equations which have a limit: the weak solution. This can be done, for example, by studying Eq. (15). The second way studies (10) as a temporally inhomogeneous evolution equation (see, e.g. [23, XIV.4] or [24,25]) of the form

$$m'(t) = A(t)m(t), \; m(t_0) = \Phi$$

and joins an "evolutionary system" $U(t, s)$ with the operators $A(t)$. Since $U(t, t_0)\Phi$ provides "strong" solutions of (10) for sufficiently smooth data and initial values Φ, $U(t, t_0)\Phi$ can be considered a weak solution of (10). Whereas the first alternative only provides an additional characterization of weak solutions, the second also suggests a different mathematical approach.

In this paper we concentrate on (15). In a second step we show that the solution operators associated with (15), (16) form an evolutionary system. In the temporally homogeneous case [1] we subsequently refer to the underlying evolution equation and consider the infinitesimal generator A and its spectrum in order to derive conclusions about the asymptotic behaviour of the semigroup. Here the corresponding approach would consist in considering the generating operators $A(t)$ and deriving information about the qualitative behaviour of $U(t, t_0)$ from spectral properties of $A(t)$. Since the theory of abstract evolutionary systems has not yet been developed so far as the theory of semigroups, we will not do so. Instead we draw the required information about the spectrum of $U(t, t_0)$ more or less directly from (15), (16) by means of positivity and compactness arguments.

3. EXISTENCE AND UNIQUENESS OF WEAK SOLUTIONS

In the preceding section we revealed a one-to-one correspondence between weak solutions of (1), (2) and solutions of (15), (16). In this section we look for solutions m of (15) in the space $Y = C([t_0, t_1] \times [a/2, 1])$ of real-valued continuous functions with $m_0 \in Y$ being given. By Lemma 2.2 and (17) the integral in the right-hand side of (15a) provides a bounded linear operator F on Y. We show that the spectral radius of F is zero by finding equivalent norms $\|\cdot\|_\lambda$, $\lambda > 0$, on Y such that, for the associated operator norms $\|F\|_\lambda \to 0$ for $\lambda \to \infty$. We take

$$\|m\|_\lambda = \sup\{e^{-\lambda t}|m(t, x)|;\ t_0 \leq t \leq t_1,\ a/2 \leq x \leq 1\}.$$

Then, by (15) and (17),

$$|e^{-\lambda t}(Fm)(t, x)| \leq \|m\|_\lambda \int_{a/2}^{x} e^{\lambda(T(t,x,y)-t)} D_0(y)\, dy.$$

We have to show that the integrals $I_\lambda(t, x)$ on the right-hand side of this equation converge to zero for $\lambda \to \infty$ uniformly in t. Since $T(t, x, y) < t$ for $y < x$ and D_0 is integrable, pointwise decreasing convergence follows from Lebesgue's theorem of dominated convergence. As $I_\lambda(t, x)$ continuously depends on t and x, uniform convergence follows from Dini's lemma. Thus (15) takes the abstract form

$$m = Fm + m_0$$

with the bounded linear operator F having zero spectral radius. Hence $(I - F)^{-1}$ exists (with I being the identity operator on Y) and can be represented by the Neumann series ΣF^j with convergence in the operator topology. Note that the operator F preserves continuity and non-negativity and so does $(I - F)^{-1}$. So we obtain the following.

THEOREM 3.1

Let m_0 be a continuous function from $[t_0, \infty) \times [a/2, 1]$ to R. Then there exists a unique continuous solution m of (15) on $[t_0, \infty) \times [a/2, 1]$. m can be represented as

$$m(t, x) = \sum_{j=0}^{\infty} m_j(t, x) \tag{18}$$

with

$$m_j(t, x) = \int_{a/2}^{1/2} K(t, x, y) m_{j-1}(T(t, x, y), 2y)\, dy \tag{19}$$

for $j = 1, 2, \ldots$. The convergence of the series in (18) is uniform on $[t_0, t_1] \times [a/2, 1]$ for any $t_1 > t_0$. If m_0 is nonnegative, so is m.

We have not yet stated that m depends continuously on m_0. To make this precise let $\| \|_{0,t}$ be the sup-norm on $[t_0, t] \times [a/2, 1]$ for $t < \infty$.

PROPOSITION 3.2

Let m_0 and m be as in Theorem 3.1. Then

$$\|m\|_{0,t} \leq c(t)\|m_0\|_{0,t} \quad \text{for } t \geq t_0$$

with constants $c(t)$ depending continuously on t, but not depending on m_0.

This boundedness result can be sharpened. To this end we define

$$v_0(t, x) = \int_{a/2}^{x} D(T(t, x, y), y)\, dy, \quad a/2 \leq x \leq 1, \tag{20}$$

with D from (11), $D(t, y) = 0$ for $y > \frac{1}{2}$. It follows from assumption 2.1(b) (iii) that

$$v_0(t, x) \leqslant \int_{a/2}^{x} D_0(y)\, dy \tag{21}$$

for $t \in \mathbb{R}$, $x \in [a/2, 1]$, with D_0 from Lemma 2.2(c). Hence we obtain the following estimate from proposition 3.2 and (15a).

COROLLARY 3.3

Let m_0 and m be as in Theorem 3.1. Then

$$|m(t, x)| \leqslant c(t) \|m_0\|_{0,t} \cdot v_0(t, x) + |m_0(t, x)|$$

with constant $c(t)$ depending continuously on t, but not on m_0.

In order to let the reader appreciate this estimate we recall that $m_0(t, \cdot) \equiv 0$, if m_0 is given by (16) and $t \geqslant T(t_0, a/2, 1)$.

Remark 3.4

(a) As in [1], Sec. 4, m_j in (18) can be considered the j^{th} generation of cells and for any $t_1 > t_0$ it can be shown that there exists $j_0 \in \mathbb{N}$ with $m_j(t, x) = 0$ for $j \geqslant j_0$, $t \in [t_0, t_1]$, $x \in [a/2, 1]$. So at any time only finitely many generations are present.

(b) The last observation helps to find conditions under which a solution m of (15), (16), i.e. a weak solution of (10) with initial function Φ, actually is a strong solution of (10) and so provides a strong solution of (1). As we mentioned in Sec. 2 the crucial step consists in proving the differentiability of $m(t, x)$ in t. If m_0 is given by (16), it is differentiable if Φ is differentiable and $\Phi(a/2) = \Phi'(a/2) = 0$. The operator F defined by (19) preserves differentiability except at $x = \frac{1}{2}$, if D is differentiable in t, i.e. if b and μ are differentiable with respect to time. Thus all m_j are differentiable and so is m because the series (18) is locally finite.

4. PROPERTIES OF THE SOLUTION OPERATORS

In studying the asymptotic behaviour of weak solutions n to (1), (2), or, equivalently, of solutions m to (15), (16) in the case of time-periodic developmental rates, we want to apply the spectral theory of strongly positive, quasicompact operators on Banach lattices (see, e.g. [18]). To this end it is convenient to consider the solution operators belonging to Eqs. (15), (16).

Let Z be the Banach space of continuous real-valued functions u on $[a/2, 1]$ with $u(a/2) = 0$. The norm $\|\cdot\|$ on Z is provided by the supremum-norm. Note that the continuity of u at $x = 1$, in view of Eq. (1), involves for the initial values of n that $(g \cdot n/E)(t_0, x)$ converges for $x \uparrow 1$.

For $\Phi \in Z$ there exists a unique solution m of (15), (16) by Theorem 3.1. The solution operators $U(t, t_0)$, $t \geqslant t_0$ are now defined by

$$U(t, t_0)\Phi = m(t, \cdot). \tag{22}$$

It turns out that the operators $U(t, t_0)$, $t \geqslant t_0$, form an evolutionary system.

PROPOSITION 4.1

(a) $U(t, t_0)$ is a bounded linear operator on Z.

(b) $U(t, s)U(s, t_0) = U(t, t_0)$, $t_0 \leqslant s \leqslant t$, $U(t, t)u = u$, $u \in Z$.

(c) For $u \in Z$, $U(t, t_0)u$ continuously depends on t, $t \geqslant t_0$.

(a) and (c) follow from Theorem 3.1 immediately. (b) can also be formulated in this way: if m is a weak solution of (10) with initial values at $t = t_0$, then

$$m(t, \cdot) = U(t, s)m(s, \cdot), \; t \geqslant s \geqslant t_0. \tag{23}$$

Since solutions of (15) are unique by Theorem 3.1, (23) follows by showing that $m(t, x)$ is a weak solution of (10) for $t > s$ with initial values $m(s, \cdot)$ at $t = s$. This is easily done by using the properties of T and X in Lemma 1.2.

In order to prepare the application of the theory of strongly positive operators we recall that Z is a Banach lattice. The cone Z_+ is formed by the nonnegative functions, the ordering '$\leqslant$' is the point-wise ordering and the modulus (or absolute value) of $u \in Z$ is given by $|u|(x) = |u(x)|$, $x \in [a/2, 1]$ (see the Appendix and [18]).

First we note that the boundedness of $U(t, t_0)$ holds in a stricter, order-theoretic way if t is large enough.

PROPOSITION 4.2

For $t \geqslant T(t_0, a/2, 1)$ we have $|U(t, t_0)u| \leqslant c\|u\|v_0$ for $u \in Z$ with c depending on t and t_0, and v_0 given by (20).

In other words $U(t, t_0)$ continuously maps Z into the Banach space $Z_{v_0(t)}$ (see Appendix 2), if $t \geqslant T(t_0, a/2, 1)$. For then $m_0(t, \cdot) = 0$, if m_0 is given by (16), and so the proposition easily follows from Corollary 3.3. Finding conditions under which the operators $U(t, t_0)$ are strongly positive is much more involved.

Strong positivity of the solution operators

We look for conditions under which, after a sufficiently long time t, cells of every size in $(a/2, 1)$ are present in the population, i.e.

$$m(t, x) > 0 \quad \text{for } x \in (a/2, 1]. \tag{24}$$

We claim that the following assumption will work.

ASSUMPTION 4.3

For any $x \in [\frac{1}{2}, 1)$ there exist $\epsilon > 0$, $y, z \in [a, 1]$, $y \geqslant x$, $z \geqslant \frac{1}{2}$ such that

$$T(T(s, x, y), y/2, x) + \epsilon \leqslant T(T(s, \tfrac{1}{2}, z), z/2, \tfrac{1}{2})$$

for all $s \in \mathbb{R}$.

Assumption 4.3 roughly states the following: consider a cohort (group) of cells all having the same size $x \in [\frac{1}{2}, 1)$ and a cohort of cells having size $\frac{1}{2}$, at time s. Then *some* daughters of the first cohort have reached size x again before *all* daughters of the second cohort (either have divided or) have reached $\frac{1}{2}$.

In order to show that Assumption 4.3 actually implies (24) for large t, we define $\bar{T}(s, x)$ to be the latest possible time at which a daughter of a cell having size x at time s can reach size x again, formally

$$\bar{T}(s, x) = \sup\{T(T(s, x, y), y/2, x); x, a \leqslant y \leqslant 1, 2x\}. \tag{25}$$

Remember that the mother cell can split at any size y with $x, a < y < 1$. We also define $\bar{X}(t, s, x)$ and $\underline{X}(t, s, x)$ to be the maximum and the minimum size which daughters of a cell having size x at time s can reach up to time t, formally

$$\bar{X}(t, s, x) = \sup\{X(t, T(s, x, y), y/2); x, a \leqslant y \leqslant X(t, s, x), 1\} \tag{26}$$

for $t \geqslant s$, $t \geqslant T(s, x, a)$. $\underline{X}(t, s, x)$ is the corresponding infimum. Equation (26) only makes sense if the mother cell can reach the minimum splitting size a up to time t, i.e. for $t > T(s, x, a)$, or equivalently, $a \leqslant X(t, s, x)$. We mention that $\bar{X}$, $\underline{X}$ are continuous and that $X(t, s, x)$ and $\underline{X}(t, s, x)$ strictly monotone increase if t, x increase and s decreases. More precisely, there is some $\bar{\epsilon} > 0$ such that

$$\bar{X}(t_2, s, x) - \bar{X}(t_1, s, x) \geqslant \bar{\epsilon}(t_2 - t_1) \text{ for all } t_2 \geqslant t_1 \geqslant s, x \in [a/2, 1] \text{ with } t_1 \geqslant T(s, x, a).$$

Furthermore, for any $r > 0$, $1 \geq x_2 > x_1 > a/2$ there exists $\epsilon > 0$ such that

$$\bar{X}(t, s, x_2) - \bar{X}(t, s, x_1) \geq \epsilon, \quad \text{if } 0 \leq t - s \leq r, t \geq T(s, x_1, a).$$

The same statements hold for $\underset{\sim}{X}$. They follow from the Assumptions 1.1 and from Lemma 2.2.

Since Assumption 4.3 states that daughters of a cell having size $x \in [\frac{1}{2}, 1)$ at time s can reach size x again before time $\bar{T}(s, \frac{1}{2})$, it follows that $\bar{T}(s, \frac{1}{2}) \geq T(s, x, a)$ and

$$\bar{X}(\bar{T}(s, \tfrac{1}{2}), s, x) \geq x + \delta \quad \text{for } x \in [\hat{x}, 1), \tag{27}$$

where $a/2 < \hat{x} < \frac{1}{2}$ and $\delta > 0$ can be chosen independently of $s \in \mathbb{R}$ and of x in any compact subset of $[\hat{x}, 1)$. Equation (27) can be derived from Assumption 4.3 rigorously by exploiting Lemma 1.2. Similarly, it is intuitively clear and can rigorously be derived from Lemma 1.2 that

$$\underset{\sim}{X}(\bar{T}(s, \tfrac{1}{2}), s, \tfrac{1}{2}) = \tfrac{1}{2}. \tag{28}$$

Before we actually dive into the proof of (24) we state a couple of useful lemmas.

The following statement is intuitively evident from the interpretation of X.

LEMMA 4.4

Let m be a weak solution of (10) for $t > t_0$. If $s \geq t_0$, $a/2 < x_1 \leq x_2 \leq 1$, and $m(s, y) > 0$ for $x_1 \leq y \leq x_2$, then $m(t, x) > 0$ for $t \geq s$, $X(t, s, x_1) \leq x \leq X(t, s, x_2)$, $x \leq 1$.

In order to prove Lemma 4.4 take into account that $m(t, x)$ is a weak solution of (10) with initial function $m(s, \cdot)$ at $t = s$ (see Proposition 4.1 and the subsequent remarks). Hence, by (15) and (16), $m(t, x) \geq m(s, X(s, t, x))$ if $X(t, s, a/2) \leq x \leq 1$.

The next lemma states that the presence of cells of size x, $a < x < 1$, implies the presence of cells of size $x/2$ by splitting. It is an obvious consequence of the continuity of m and of (15a).

LEMMA 4.5

Let m be as in Lemma 4.4, $s > t_0$, $x \in (a, 1]$. If $m(s, x) > 0$, then $m(s, x/2) > 0$.

Combining Lemmas 4.4 and 4.5 yields the following statement, which is intuitively evident from the interpretation of $\bar{X}$ and $\underset{\sim}{X}$.

LEMMA 4.6

Let m be as in Lemma 4.4. Let $t > s > t_0$, $a/2 < x_1 \leq x_2 \leq 1$, $t \geq T(s, x_1, a)$. If $m(s, x) > 0$ for $x_1 \leq x \leq x_2$, then $m(t, z) > 0$ for $\underset{\sim}{X}(t, s, x_1) \leq z \leq \bar{X}(t, s, x_1)$, $z \leq 1$.

Actually combining Lemmas 4.4 and 4.5 leads to the following conclusion: if $s > t_0$, $a/2 < x < 1$ and $m(s, x) > 0$, then $m(t, z) > 0$ for all $z = X(t, r, X(r, s, x)/2)$ with $z \leq 1$, $s \leq r \leq t$, $a \leq X(r, s, x) \leq 1$, or, equivalently for all $z = X(t, T(s, x, y), y/2)$ with $z \leq 1$, x, $a \leq y \leq 1$. Lemma 4.6 now follows from the definitions of $\bar{X}$ and $\underset{\sim}{X}$ in (26).

From (27) and (28) we can now derive Lemma 4.7.

LEMMA 4.7

Let m be as in Lemma 4.4, $s > t_0$, $t = \bar{T}(s, \frac{1}{2})$, $x \in [\frac{1}{2}, 1)$. If $m(s, y) > 0$ for $\frac{1}{2} \leq y \leq x$ then $m(t, z) > 0$ for $z \in [\frac{1}{2}, \bar{x}] \cap [\frac{1}{2}, 1]$ with $\bar{x} = \bar{X}(t, s, x)$.

Remark

Note that $\bar{x} > x + \delta$ and that $\delta > 0$ can be chosen independently of $s \in \mathbb{R}$ and of x in compact subsets of $[\frac{1}{2}, 1)$.

After these preparations we are ready for the proof of (24).

First we note from Lemmas 4.4 and 4.5 that, if the initial value $\Phi \in Z_+$ at time $t = t_0$ satisfies $\Phi \neq 0$, then

$$m(s_0, \tfrac{1}{2}) > 0$$

with some $s_0 \in (t_0, T(t_0, a/2, 1)]$. Guided by Lemma 4.5 we define

$$\begin{aligned} s_{j+1} &= \bar{T}(s_j, \tfrac{1}{2}), \\ x_{j+1} &= \min(1, \bar{X}(s_{j+1}, s_j, x_j)), \\ x_0 &= \tfrac{1}{2}, \end{aligned}$$

It follows that

$$x^* = \lim_{j\to\infty} x_j = 1,$$

for $j = 0, 1, \ldots$, and find a strictly increasing sequence $x_j \leqslant 1$ with

$$m(s_j, x) > 0 \quad \text{for } x \in [\tfrac{1}{2}, x_j].$$

for, if $x^* < 1$, by Lemma 4.7 and the subsequent remark, $x_{j+1} \geqslant x_j + \delta$ with $\delta > 0$ for all $j \in \mathbb{N}$, in contradiction to the convergence of x_j. Now, by Lemma 4.5,

$$m(s_j, x) > 0 \quad \text{for } x \in (\underset{\sim}{x}, x_j/2] \cup [\tfrac{1}{2}, x_j] \tag{29}$$

with $\underset{\sim}{x} = \max(a/2, \tfrac{1}{4})$ and $x_j \to 1$ for $j \to \infty$. By (27) there exists $\hat{x} \in [\hat{x}, \tfrac{1}{2})$ such that

$$\bar{X}(\bar{T}(s, \tfrac{1}{2}), s, \hat{x}) \geqslant \tfrac{1}{2}$$

for all $s \in \mathbb{R}$, in particular

$$\bar{X}(s_{j+1}, s_j, \hat{x}) \geqslant \tfrac{1}{2}.$$

By the remarks following the definition of $\bar{X}$, $\underset{\sim}{X}$ in (26) we obtain

$$\underset{\sim}{X}(s_{j+1}, s_j, \hat{x}) \leqslant \underset{\sim}{X}(s_{j+1}, s_j, \tfrac{1}{2}) - \delta = \tfrac{1}{2} - \delta$$

with $\delta > 0$ not depending on j. Since, for large j, $x_j/2 > \hat{x}$ and $x_{j+1}/2 > \frac{1}{2} - \delta$ we obtain from (29) and Lemma 4.6 that

$$m(s_{j+1}, x) > 0 \quad \text{for } x \in (\underset{\sim}{x}, x_{j+1}],$$

for sufficiently large j, with $x_j \to 1$ for $j \to \infty$. If j is large enough, $T(s_j, x_j, 1) < T(s_j, \underset{\sim}{x}, \tfrac{1}{2})$; hence

$$m(\bar{s}, x) > 0 \quad \text{for } \tfrac{1}{2} \leqslant x \leqslant 1,$$

with some large $\bar{s} > s_0$. By Lemma 4.5,

$$m(\bar{s}, x) > 0 \quad \text{for } a/2 < x \leqslant 1.$$

The continuity of m and Lemma 4.5 yield

$$m(s, x) > 0 \quad \text{for } a/2 < x \leqslant 1,\ s \geqslant \bar{s}.$$

We formulate this result in terms of the solution operators $U(t, t_0)$. $v \in Z_+$ is a quasi-interior point of Z_+ (see the Appendix, point 4) iff v is continuous on $[a/2, 1]$ and $v(x) > 0$ for $x \in (a/2, 1]$.

PROPOSITION 4.8

Let the assumption 4.3 be satisfied. Then, for $t_0 \in \mathbb{R}$, there exists $t_1 > t_0$ such that $U(t, t_0)\Phi$ is a quasiinterior point of Z_+ if $t \geq t_1$, $\Phi \in Z_+$, $\Phi \neq 0$.

Note that t_1 is independent of Φ.

After having established this positivity property of the operators $U(t, t_0)$ for $t - t_0$ being large we now turn to compactness.

Compactness of the solution operators

In order to show that the operators $U(t, t_0)$ are compact on Z if $t - t_0$ is large enough, we consider an arbitrary bounded subset M of Z and consider the weak solutions m of (10) with initial function $\Phi \in M$ for $t = t_0$. By the Arzela–Ascoli theorem we have to show that $m(t, \cdot)$ is bounded and continuous uniformly in $\Phi \in M$ for $t - t_0$ being large. Boundedness is obvious from Theorem 3.1 and (16). For the proof of equicontinuity we set

$$v(s, x) = m(T(s, a/2, x), x) \quad \text{for } s \geq t_0.$$

It follows from (14) and Theorem 3.1 that $v(s, x)$ is continuous in x uniformly for s ranging in a bounded interval and $\Phi \in M$. Transforming (14) into an equation for v we obtain

$$v(s, x) = \int_{a/2}^{\min(x, 1/2)} D(T(s, a/2, y), y)v(f(s, y), 2y)\, dy \tag{30}$$

for $s \geq T(t_0, a/2, 1)$, with

$$f(s, y) = T(T(s, a/2, y), 2y, a/2). \tag{31}$$

Since $m(t, x) = v(T(t, x, a/2), x)$ for $t \geq T(t_0, a/2, x)$ we are done, if v can be shown to be continuous in (s, x) uniformly in $\Phi \in M$. This follows from the uniform (with respect to s and $\Phi \in M$) continuity in x, if a change of variables $f(s, y) = r$ can be performed in the right-hand side of (30). To this end we differentiate f with respect to y and obtain, with $\bar{s} = T(s, a/2, y)$ from Lemma 1.2(g),

$$\partial_y f(s, y) = 2\partial_1 T(\bar{s}, 2y, a/2) \cdot \left(\frac{1}{2g(\bar{s}, y)} - \frac{1}{g(\bar{s}, 2y)}\right). \tag{32}$$

Guided by this formula we make the following assumption.

ASSUMPTION 4.9

There exist at most finitely many points $x_i \in [a/2, \frac{1}{2}]$ such that $2g(s, x_i) = g(s, 2x_i)$ for some $s \in \mathbb{R}$.

By this assumption the interval $[a/2, \frac{1}{2}]$ can be divided into intervals $[x_i, x_{i-1}]$ such that $2g(s, y) - g(s, 2y)$ is either strictly positive on (x_i, x_{i-1}) or strictly negative.

We want to solve the equation

$$f(s, h_i(s, r)) = r \tag{33}$$

with $h_i(s, r) \in (x_i, x_{i-1})$. To this end we differentiate (33) with respect to r and obtain the following differential equation for h_i:

$$\partial_r h_i(s, r) = \frac{1}{\partial_2 f(s, h_i(s, r))}. \tag{34}$$

Since $\partial_1^2 g$ exists and is continuous by Assumption 1.1, $\partial_2 f(s, y)$ is Lipschitz continuous in (s, y) by Lemma 1.2(e) and (32). So we find a continuous solution $h_i(s, r)$ of (34) and thus of (33) for $s \in \mathrm{R}$, r in the interval with endpoints $f(s, x_i)$, $f(s, x_{i+1})$. We now split up the integral (30) into integrals

$$\int_{\min\{x, x_i\}}^{\min\{x, x_{i+1}\}} D(T(s, a/2, y), y) v(f(s, y), 2y)\, \mathrm{d}y$$

$$= \int_{f(s, \min\{x, x_i\})}^{f(s, \min\{x, x_{i+1}\})} \frac{D(T(s, a/2, h_i(s, r)), h_i(s, r))}{\partial_2 f(s, h_i(s, r))} v(r, 2h_i(s, r))\, \mathrm{d}r.$$

Since the first integral exists if we take absolute values of the integrand, so does the second. We conclude that the integrals are continuous in (s, x) uniformly for $\Phi \in M$.

Summarizing our preceding considerations we conclude that $v(s, x)$ is continuous in (s, x), $s \geqslant T(t_0, a/2, 1)$, $a/2 \leqslant x \leqslant 1$, uniformly for $\Phi \in M$. Since $m(t, x) = v(T(t, x, a/2), x)$ for $t \geqslant T(t_0, a/2, x)$, $m(t, x)$ is continuous in (t, x) uniformly for $\Phi \in M$, provided that $T(t, x, a/2) \geqslant T(t_0, a/2, 1)$, $a/2 \leqslant x \leqslant 1$, thus in particular if $t \geqslant \phi(\phi(t_0))$ with $\phi(s) = T(s, a/2, 1)$. By the Arzela–Ascoli theorem (see, e.g. [22, IX, Sec. 4]) we obtain the following result.

PROPOSITION 4.10

Let Assumptions 4.9 be satisfied. Then the operators $U(t, t_0)$ are compact on Z for $t \geqslant \phi(\phi(t_0))$.

One can presumably prove that the operators $U(t, t_0)$ are compact on Z for $t \geqslant \phi(t_0)$ by studying the generation expansion (18), (19) (see [1], Sec. 5). Recall that at time $\phi(t_0)$ all cells from the initial population (i.e. the cells of the zero generation) have divided or died.

Furthermore, Assumption 4.9 can be relaxed, e.g. by assuming that the set $\{(s, y): s \in \mathrm{R}, a/2 \leqslant y \leqslant \frac{1}{2}, 2g(s, y) = g(s, 2y)\}$ is contained in the union of finitely many graphs of continuous functions $x_i\colon \mathrm{R} \to [a/2, \frac{1}{2}]$.

5. THE SOLUTION OPERATORS UNDER PERIODICITY

In this section we study the operator

$$B = U(t_0 + p, t_0) \tag{35}$$

the properties of which are of crucial importance for the asymptotic behaviour of weak solutions of (10), if the developmental rates are time-periodic with period p. We will use the language of Banach lattices which is summarized in the Appendix.

From now on we make the following assumption.

ASSUMPTION 5.1

$g(t, x)$, $\mu(t, x)$, $b(t, x)$ are periodic in $t \in \mathrm{R}$ with the same period $p > 0$ for g, b, μ.

This periodicity assumption has the following consequence for the solution operators.

PROPOSITION 5.2

$U(t + p, t_0 + p) = U(t, t_0)$ for all $t, t_0 \in \mathrm{R}$, $t \geqslant t_0$.

Proof. Let m be the weak solution of (10) with initial function $\Phi \in Z$ at $t = t_0$. By the uniqueness of solutions it is sufficient to show that $\tilde{m}(t, \cdot) = m(t - p, \cdot)$ is a weak solution of (10) with initial values Φ at $t = t_0 + p$. This easily follows from Lemma 5.3.

LEMMA 5.3

$T(t + p, x, y) = T(t, x, y) + p$, $X(t + p, s + p, x) = X(t, s, x)$.

The lemma follows from the uniqueness of solutions to the differential equations (6), (7). Proposition 4.1 now implies the following.

PROPOSITION 5.4

(a) B is a positive bounded linear operator on Z.

(b) For $k \in \mathbb{N}$, $t \in [0, p]$, $U(t_0 + kp + t, t_0) = U(t_0 + t, t_0)B^k$.

Assumptions 4.3 now take the following seemingly weaker form (see Lemma 5.3).

ASSUMPTION 5.5

For any $x \in [\frac{1}{2}, 1)$ there exist $y, z \in [a, 1]$, $y \geq x$, $z \geq \frac{1}{2}$ such that $T(T(s, x, y), y/2, x) < T(T(s, \frac{1}{2}, z), z/2, \frac{1}{2})$ for all $s \in \mathbb{R}$.

Recall the interpretation we gave after Assumption 4.3. Propositions 4.2, 4.8 and 4.10 imply the following properties of B.

PROPOSITION 5.6

(a) If Assumption 4.9 holds then B^j is a compact operator on Z for sufficiently large j.

(b) For large enough j, B^j maps Z continuously into the Banach lattice $Z_{v_0(t_0)}$ with $v_0(t_0)$ being the quasi-interior point of Z_+ defined in (20).

(c) If Assumption 5.5 holds then B^j maps $Z_+\backslash\{0\}$ into the quasi-interior points of Z_+ for large enough j. In particular B is strongly positive on Z (see Appendix, points 4, 7).

The following spectral properties of B now follow easily from the theory of power compact strongly positive operators (see [18, Chap. V]).

PROPOSITION 5.7

Let Assumptions 4.9 and 5.5 be valid. Then the following holds:

(a) The spectral radius $r_0 = \text{spr } B$ of B is different from zero.

(b) r_0 is an algebraically simple eigenvalue of B and B'.

(c) There is an eigenvector w_0 of B belonging to r_0 which is a quasi-interior point of Z_+.

(d) There is a strictly positive eigenfunctional $w_0' \in Z'$ of B' belonging to r_0, $w_0' = 0$ on $(r_0 I - B)Z$.

(e) All spectral values of B different from r_0 lie in a circle around $0 \in \mathbb{C}$ with radius strictly smaller than r_0.

(f) r_0 is the unique eigenvalue of B with an eigenvector in Z_+.

See the Appendix, point 5. Since r_0 is a pole of the resolvent of B, we can split up the space Z into a direct sum

$$Z = \text{span}\{w_0\} \oplus \tilde{Z},$$

with the eigenvector w_0 being provided by Proposition 5.7(c) and the B-invariant closed subspace $\tilde{Z} = (r_0 I - B)Z$ (see, e.g. [26, Chap. 1]). The spectral radius of B restricted to $\tilde{Z}$ is strictly smaller than r_0 by Proposition 5.7(e). In (d) it is stated that $w_0' = 0$ if restricted to $\tilde{Z}$. So we obtain the following result.

PROPOSITION 5.8

Let w_0' be normalized such that $w_0' w_0 = 1$. Then there exists a bounded linear projection P on Z with the following properties:

(a) $PB = BP$.

(b) $Pw_0 = 0$, $w_0' P = 0$.

(c) $r_1 := \text{spr } BP < r_0 := \text{spr } B$.

(d) Any $w \in Z$ has the unique representation $w = w_0'(w)w_0 + Pw$.

We conclude this section by characterizing the nonzero eigenvalues and eigenvectors of B. Let $Bw = qw$, $q \neq 0$ and let m be the weak solution of (10) with initial value w at $t = t_0$, i.e. $m(t, \cdot) = U(t, t_0)w$. Let $\lambda \in \mathbb{C}$ be such that $e^{\lambda p} = q$ and set

$$\tilde{m}(t, \cdot) = e^{-\lambda t} m(t, \cdot).$$

Then

$$\tilde{m}(t + p, \cdot) = e^{-\lambda(t+p)}U(t + p, t_0)w = e^{-\lambda t}U(t + p, t_0 + p)w = e^{-\lambda t}U(t, t_0)w = \tilde{m}(t, \cdot)$$

by Proposition 5.4(b). We extend $\tilde{m}$ for $t < t_0$ in a p-periodic way. If $t \geq T(t_0, a/2, 1)$

$$\tilde{m}(t, x) = \int_{a/2}^{\min\{x, 1/2\}} D(T(t, x, y), y)e^{\lambda(T(t,x,y)-t)}\tilde{m}(T(t, x, y), 2y)\,\mathrm{d}y \tag{36}$$

by (15a). Since $\tilde{m}(t, x)$ is p-periodic in t, this equality holds for all $t \in \mathrm{R}$ (see Lemma 5.3). Moreover, $\tilde{m}$ is continuous.

Conversely, if $\tilde{m}$ is a continuous p-periodic solution of (36) on $\mathrm{R} \times [a/2, 1]$, then $m(t, x) = e^{\lambda t}\tilde{m}(t, x)$ is a weak solution of (10) with initial value $w = e^{\lambda t_0}\tilde{m}(t_0, \cdot)$ at $t = t_0$ satisfying $Bw = e^{\lambda p}w$. (Use Lemma 1.2.)

Thus we have obtained the following relation between eigenvalues of B and p-periodic solutions of (36).

PROPOSITION 5.9

Let $q, \lambda \in \mathrm{C}$, $q = e^{\lambda p}$. Then q is an eigenvalue of B iff there exists a p-periodic continuous solution $\tilde{m}$ on $\mathrm{R} \times [a/2, 1]$ of (36). The eigenvectors w of B belonging to q are related to the periodic solutions $\tilde{m}$ of (36) by

$$U(t, t_0)w = e^{\lambda t}\tilde{m}(t, \cdot) \quad \text{for } t \geq t_0.$$

6. ASYMPTOTIC BEHAVIOUR OF SOLUTIONS

In order to prove our main result on the asymptotic behaviour of weak solutions to (10) or to (1) respectively, we continue the considerations of the last section.

Let $\Phi \in Z$ and let m be the weak solution to (10) with initial value Φ at $t = t_0$. Furthermore, let $t > t_0 + kp$, $k \in \mathrm{N}$. Then, by Propositions 5.4 and 5.8,

$$m(t, \cdot) = U(t, t_0)\Phi = U(t - kp, t_0)B^k\Phi = w_0'(\Phi)U(t, t_0)w_0 + U(t - kp, t_0)(PB^k\Phi),$$

and $\|PB^k\| \leq cr^k$ for any $r \in (r_1, r_0)$ with $c > 0$ depending on r, but not on k.

By Proposition 5.9 $\tilde{m}(t, \cdot) = e^{-\lambda t}U(t, t_0)w_0$ is a p-periodic continuous solution of (36) on $\mathrm{R} \times [a/2, 1]$. Since w_0 is strictly positive on $(a/2, 1]$ by Proposition 5.7(a), $\tilde{m}(t, x) > 0$ for $t \in \mathrm{R}$, $x \in (a/2, 1]$ by Proposition 4.8. Now (36), (20), and the periodicity of $\tilde{m}$ imply that

$$\epsilon v_0(t, x) \leq \tilde{m}(t, x) \leq c v_0(t, x)$$

for $t \in \mathrm{R}$, $x \in [a/2, 1]$ with ϵ, $c > 0$ not depending on t and x. On the other hand, $|U(t - kp, t_0)PB^k\Phi| \leq cr^k\|\Phi\|v_0(t)$ by Proposition 4.2, if $t - kp \geq T(t_0, a/2, 1)$ with c depending on r. Combining these observations and Corollary 3.3 yields the following.

THEOREM 6.1

Let Assumptions 1.1, 2.1, 4.9, 5.1 and 5.5 be satisfied. Then the following holds:

(a) There exists a unique $\lambda \in \mathrm{R}$ such that (36) admits a continuous nonnegative time-periodic (with period p) solution $\tilde{m} \neq 0$ on $\mathrm{R} \times [a/2, 1]$. $\tilde{m}$ is uniquely determined up to a scalar factor.

(b) If m is a weak solution of (10) with continuous initial function Φ on $[a/2, 1]$ at $t = t_0$, $\Phi(a/2) = 0$, then, for $t \to \infty$,

$$m(t, x) = e^{\lambda t}\tilde{m}(t, x).(\alpha + e^{-\epsilon t}\mathcal{O}(1))$$

with some $\epsilon > 0$. The scalar α depends in a linear and strictly positive way on the initial function Φ.

More precisely, one can say that $\alpha(\Phi)$ is a strictly positive bounded linear functional on Z. The Landau symbol $\mathcal{O}(1)$ represents a bounded function $m(t, x)$. Actually $\underset{\sim}{m}(t, \cdot) = \tilde{U}(t, t_0)\Phi$ with bounded linear operators $\tilde{U}(t, t_0)$ on Z and $\|\tilde{U}(t, t_0)\|$ is bounded on $[t_0, \infty)$.

We now translate this result to weak solutions of (1) via (8), (9). We define

$$\bar{E}(t, x) = \exp\left(-\int_{a/2}^{x} (b/g)(T(t, x, z), z)\,dz\right).$$

COROLLARY 6.2

Under the assumptions of Theorem 6.1 the following holds.

Let n be a weak solution of (1) for $t > t_0$ such that $n(t_0, x)/\bar{E}(t_0, x)$ is continuous in $x \in [a/2, 1]$ and $n(t_0, a/2) = 0$. Then, for $t \to \infty$,

$$n(t, x) = e^{\lambda t}\bar{n}(t, x)(\alpha - e^{-\epsilon t}\mathcal{O}(1))$$

with some $\epsilon > 0$. In this expression λ and the time-periodic (with period p) function $\bar{n}$ do not depend on the initial function $n(t_0, \cdot)$. The scalar α, however, depends linearly and strictly positive on the initial function.

More precisely, $\alpha(\Psi)$, $\Psi = n(t_0, \cdot)$, is a strictly positive bounded linear functional on the Banach space $Z_{\bar{E}(t_0,\cdot)}$. $\mathcal{O}(1)$ stands for a bounded function $\underset{\sim}{n}(t, x)$. Actually $\underset{\sim}{n}(t, \cdot) = \tilde{U}(t, t_0)\Psi$ with $\tilde{U}(t, t_0)$ now being bounded linear operators from $Z_{\bar{E}(t_0,\cdot)}$ to Z and $\|\tilde{U}(t, t_0)\| \leqslant$ const for all $t \geqslant t_0$.

Though Assumption 5.5 has a clear biological meaning (see the interpretation following Assumption 4.3) one would like to have an assumption in terms of the growth rate g as well. Unfortunately a condition of that kind which is not too complicated can only be given in the very special case

$$g(t, x) = \gamma(t)g(x).$$

Then, by (6),

$$\int_t^{T(t,x,y)} \gamma(s)\,ds = \int_x^y \frac{dz}{g(z)},$$

and Assumption 5.5 takes the following form.

For any $x \in [\frac{1}{2}, 1)$ there exist $y, z \in [a, 1]$, $y \geqslant x$, $z \geqslant \frac{1}{2}$ such that

$$\int_{y/2}^{x} \frac{d\zeta}{g(\zeta)} < \int_{z/2}^{z} \frac{d\zeta}{g(\zeta)}, \quad \text{i.e.} \quad \int_{z/2}^{x/2} \left\{\frac{1}{g(2\zeta)} - \frac{1}{2g(\zeta)}\right\} < 0.$$

But this already follows from Assumption 4.9. So we obtain the following result.

COROLLARY 6.3

Let Assumptions 1.1, 2.1 and 5.1 be satisfied, $g(t, x) = \gamma(t)g(x)$ with $g(2x) \neq 2g(x)$ for all but finitely many $x \in [a/2, \frac{1}{2}]$. Then the statements (a) and (b) of Theorem 6.1 and Corollary 6.2 are valid.

7. THE TIME-HOMOGENEOUS CASE REVISITED

For time-independent developmental rates one expects Theorem 6.1 and Corollary 6.2 to hold with $\bar{m}(t, x)$ and $\bar{n}(t, x)$ not depending on t. In fact, we established the theorems in this form in [1] under one of the following conditions on the growth rate g:

(i) $g(2x) < 2g(x)$, $x \in [a/2, \frac{1}{2}]$.

(ii) $a \geqslant \frac{1}{2}$, $g(x) = x$ for $x \in [a/2, \beta]$; $g(x) < x$ for $x \in (\beta, 1]$ with $\beta < 1$.

Unfortunately neither condition is satisfied by the experimental data for g of Anderson *et al.* [2]; in particular they found $a < \frac{1}{2}$. This situation is especially unsatisfactory because Anderson *et al.* gathered their data from cell populations which, after the experiment had run for some time, showed exponential growth with a stationary size distribution. So our theorem should hold for their data. In [1] we guessed that a substantial generalization of conditions (i) or (ii) would be very laborious or even impossible. Fortunately, this fear is unfounded. Let us assume that

$$g(2x) \neq 2g(x) \quad \text{for } x \in J, \tag{37}$$

J being a nonempty open subinterval of $[a/2, \frac{1}{2}] =: I$. Since g is continuous, (37) is a necessary condition for asymptotic exponential growth with stationary size distribution, as we pointed out at the beginning of [1, Sec. 8]. Replacing Assumption 4.9 by (37) we in general lose the compactness of the operators $U(t, t_0)$ even if $t - t_0$ is large. The hope, however, is that (37) is strong enough to imply that the radius of the essential spectrum of $U(t, t_0)$ is strictly smaller than the spectral radius of $U(t, t_0)$. The spectral values in the complement of the essential spectrum essentially behave like the spectral values of a compact operator. We proceed as in Sec. 8 of [1] where the reader can also find details and references concerning the essential spectrum. (The essential spectrum consists of all elements of the spectrum which are not poles of the resolvent with a residue of finite rank.)

A solution m of (15) can be split up as follows:

$$m(t, x) = \overline{m}(t, x) + \hat{m}(t, x), \tag{38}$$

with

$$\overline{m}(t, x) = \int_{I \setminus J} K(t, x, y)\overline{m}(T(t, x, y), 2y)\, dy + m_0(t, x), \tag{39}$$

$$\hat{m}(t, x) = \int_I K(t, x, y)\hat{m}(T(t, x, y), 2y)\, dy + \int_J K(t, x, y)\overline{m}(T(t, x, y), 2y)\, dy. \tag{40}$$

With m_0 being given by (16) we define solution operators $\overline{U}(t, t_0)$ and $\hat{U}(t, t_0)$ by

$$\begin{aligned} \overline{U}(t, t_0)\Phi &= \overline{m}(t, \cdot), \\ \hat{U}(t, t_0)\Phi &= \hat{m}(t, \cdot). \end{aligned} \tag{41}$$

In particular

$$U(t, t_0) = \overline{U}(t, t_0) + \hat{U}(t, t_0). \tag{42}$$

Observe that $\overline{U}(t, t_0)$ defines an evolutionary system.

We claim that (37) implies compactness of the operators $\hat{U}(t, t_0)$ for $t - t_0$ being large enough. We proceed as in the proof of the compactness of the operators $U(t, t_0)$ for large $t - t_0$ in Sec. 4.

We find that

$$\overline{v}(s, x) = \overline{m}(T(s, a/2, x), x)$$

is continuous in x uniformly for s ranging in a bounded interval in $[t_0, \infty)$ and for initial values Φ in a bounded subset M of Z. Let $\tilde{m}(t, x)$ denote the second integral on the right-hand side of (40). Then

$$\tilde{m}(T(s, a/2, x), x) = \int_{J \cap [0, x]} D(T(s, a/2, y), y)\overline{v}(f(s, y), 2y)\, dy$$

for $s \geq T(t_0, a/2, 1)$, with f in (31). By (37) we can perform the transformation $f(s, y) = r$ and find that $\tilde{m}(t, x)$ is jointly continuous in $t \geq \phi(\phi(t_0))$, $x \in [a/2, 1]$ uniformly in $\Phi \in M$. Here, as before,

$$\phi(t) = T(t, a/2, 1). \tag{43}$$

By (40) $\hat{m}(t, x)$ is jointly continuous in $t \geq \phi(\phi(\phi(t_0)))$, $x \in [a/2, 1]$, uniformly in $\Phi \in M$. Note that $\hat{m}$ can be given as a convergent series as in Theorem 3.1. By the Arzela–Ascoli theorem we obtain the following.

LEMMA 7.1

The operators $\hat{U}(t, t_0)$ are compact on Z for $t \geq \phi(\phi(\phi(t_0)))$.

For Lemma 7.1 to hold we did not need that the developmental rates are time independent. This is different for the next lemma.

LEMMA 7.2

Let g, μ, b be time independent. If $t \geq \phi(\phi(\phi(t_0)))$, the spectral radius of $\overline{U}(t, t_0)$ is strictly smaller than the spectral radius of $U(t, t_0)$, in particular the radius of the essential spectrum of $U(t, t_0)$ is strictly smaller than the spectral radius of $U(t, t_0)$.

In order to prove Lemma 7.2 we first note that, if the developmental rates do not depend on t,

$$D(t, y) = D(y) \tag{44}$$

is independent of t [see (11)]. Furthermore,

$$T(t, x, y) - t =: T_0(x, y) \tag{45}$$

does not depend on t. We note that (39) can be written in the form of (15) if D is replaced by D^J:

$$\begin{aligned} D^J(y) &= D(y) \quad \text{for } a/2 \leq y \leq \tfrac{1}{2},\ y \notin J; \\ D^J(y) &= 0 \qquad \text{otherwise.} \end{aligned} \tag{46}$$

Though the positivity and compactness results in Secs. 4, 5 may cease to be valid under this modification, Propositions 4.1, 4.2 and 5.9 equally hold for $\overline{U}$.

In Sec. 5 we found p-periodic solutions of (36) from the properties of the operators $U(t, t_0)$. We now go this way backwards and try to obtain information on the operators $U(t, t_0)$, $\overline{U}(t, t_0)$ by looking for special periodic, namely t-independent solutions of (36). This is possible because of (44) and (45). To this end we define operators V^J_λ on Z by

$$(V^J_\lambda u)(x) = \int_{a/2}^{\min(x, 1/2)} D^J(y) e^{\lambda T_0(x, y)} u(2y)\, dy \tag{47}$$

for $\lambda \in \mathbb{R}$, $u \in Z$. Here we admit any open subinterval J of $[a/2, \frac{1}{2}]$, in particular $J = \emptyset$, i.e. $D^J = D$. Recall that $D^J(y) > 0$ if a $a/2 < y < \frac{1}{2}$, $y \notin J$ (see Lemma 2.2). We now study the eigenvalues and the positive eigenvectors of V^J_λ in dependence on λ. Since Proposition 5.9 also holds if D is replaced by D^J, any pair $\lambda \in \mathbb{C}$, $u \in Z$ with $u = V^J_\lambda u$ provides an eigenvalue $e^{\lambda p}$ of $U^J(t_0 + p, t_0)$ with eigenvector u. Here $U^J(t, t_0)$, $t \geq t_0$, denote the solution operators associated with Eq. (39).

LEMMA 7.3

(a) Let J be an open subinterval of $(a/2 + \epsilon, \frac{1}{2} - \epsilon)$ for some $\epsilon > 0$. Then there exists $\lambda = \lambda_J \in \mathbb{R}$ such that the spectral radius of V^J_λ is equal to 1. Furthermore, for $\lambda = \lambda_J$, there are $v_J \in Z_+$, $v_J \neq 0$ and $v'_J \in Z'_+$, $v'_J \neq 0$ such that $V^J_\lambda v_J = v_J$ and $(V^J_\lambda)' v'_J = v'_J$.

(b) Let, in addition, the length of J be strictly smaller than

$$\frac{1}{n+1} - \frac{1}{2n}$$

for any $n \in \mathbb{N}$ with $a < 1/n$. Then v_J is comparable with v_0 in (20) and $v_J'(v) > 0$ for every $v \in Z_+$ with $V_\lambda^J(v) \neq 0$. If $J = \emptyset$, i.e. $D^J = D$, v_J' is strictly positive.

Remark

The notation λ_J, v_J, v_J' may be misleading insofar as it suggests that these entities are uniquely determined (in the case of v_J, v_J' up to normalization). In general this might not be the case. It will be the case, however, if J satisfies both the conditions of Lemma 7.3(a) and (b). Note that v_0 in (20) is now time independent. The case $J = \emptyset$ has already been dealt with by one of us in [27].

Proof of Lemma 7.3. Drop the index J for convenience. Let r_λ denote the spectral radius of V_λ. It can readily be seen that $\|V_\lambda\| \to 0$ for $\lambda \to \infty$. Recall that $T_0(x, y) < 0$ for $x > y$. Thus $r_\lambda \to 0$ for $\lambda \to \infty$. In order to see that $r_\lambda \to \infty$ for $\lambda \to -\infty$ we choose $v \in Z_+$, $v(x) = 0$ for $x \leq \frac{1}{2}$, $v(1) > 0$. Then

$$(V_\lambda v)(x) \geq \int_{a/2}^{1/2} D^J(y) e^{\lambda T_0(x,y)} v(2y)\, dy > 0$$

for $\frac{1}{2} \leq x \leq 1$, in particular $V_\lambda v \geq c_\lambda v$ with $c_\lambda > 0$ for $\lambda \in \mathbb{R}$ and $c_\lambda \to \infty$ for $\lambda \to -\infty$. This implies that $r_\lambda \geq c_\lambda > 0$ for $\lambda \in \mathbb{R}$ and $c_\lambda \to \infty$ for $\lambda \to -\infty$. Note that V_λ continuously depends on λ in the uniform operator topology. The formula $r_\lambda = \inf_n \|V_\lambda^n\|^{1/n} = \lim_{n\to\infty} \|V_\lambda^n\|^{1/n}$ reveals that r_λ is continuous from above, i.e. $\overline{\lim}_{\hat\lambda\to\lambda} r_{\hat\lambda} \leq r_\lambda$. Since every nonzero spectral value of the compact operator V_λ is an isolated point of the spectrum, the perturbation result in Theorem 3.16 in [28, Chap. IV] implies the continuity of r_λ from below, i.e. $\underline{\lim}_{\hat\lambda\to\lambda} r_{\hat\lambda} \geq r_\lambda$. The intermediate value theorem now implies the existence of some $\lambda \in \mathbb{R}$ with $r_\lambda = 1$. The existence of v_J and v_J' follows from the Krein–Rutman theorem (see, for example, [29]).

Part (b) follows from the fact that there is some $j \in \mathbb{N}$ such that $(V_\lambda^j v)(x) > 0$ for $a/2 < x \leq 1$, if $v \in Z_+$ and $V_\lambda v \neq 0$. In fact, if $V_\lambda v \neq 0$, $v \in Z_+$, then $(V_\lambda v)(x) > 0$ for $\frac{1}{2} \leq x \leq 1$. Let us suppose that we have already proved

$$(V_\lambda^{j-1} v)(x) > 0 \text{ for } \frac{a}{2} < \frac{1}{j} \leq x \leq 1, j \geq 2.$$

Then

$$D^J(y)(V_\lambda^{j-1} v)(2y) > 0 \quad \text{for } \tfrac{1}{2}j,\ a/2 \leq y \leq \tfrac{1}{2};\ y \in J.$$

If $\frac{1}{2}j \leq a/2$, $D^J(y)(V_\lambda^{j-1} v)(2y) > 0$ for $a/2 \leq y \leq a/2 + \epsilon$; hence $(V_\lambda^j v)(x) > 0$ for $a/2 < x \leq \frac{1}{2}$. If $\frac{1}{2}j > a/2$, $D^J(y)(V_\lambda^{j-1} v)(2y)$ cannot vanish a.e. on $[\frac{1}{2}j, 1/(j+1)]$ because, by assumption, the length of J is strictly smaller than the length of $[\frac{1}{2}j, 1/(j+1)]$; hence $(V_\lambda^j v)(x) > 0$ for $1/(j+1) < x < \frac{1}{2}$. Repeating this step several times we find some j such that $(V_\lambda^j v)(x) > 0$ for $a/2 < x \leq 1$. ■

We now prove the crucial result which will imply that the spectral radius of $\overline{U}(t, t_0)$ is strictly smaller than the spectral radius of $U(t, t_0)$, $t > t_0$.

LEMMA 7.4

Let J be an interval satisfying the assumptions in Lemma 7.3(a, b). Let $\lambda, \lambda_J \in \mathbb{R}$ be such that the spectral radius of V_λ^0 and $V_{\lambda_J}^J$ equal 1. Then $\lambda > \lambda_J$.

Proof. We suppose that $\lambda \leq \lambda_J$. Choose $v_J \in Z_+$, $v_J \neq 0$ such that $V_{\lambda_J}^J v_J = v_J$. Since v_J is strictly positive by Lemma 7.3(b), $V_\lambda^0 v_J > V_\lambda^J v_J \geq V_{\lambda_J}^J v_J = v_J$. Recall that $T_0(x, y) \leq 0$ for

$y \leq x$. Now choose a strictly positive functional $v' = V_\lambda^{*} v'$ according to Lemma 7.3(b). Then

$$1 = \frac{(V_\lambda^{*} v')(v_J)}{v'(v_J)} = \frac{v'(V_\lambda^{*} v_J)}{v'(v_J)} > \frac{v'(v_J)}{v'(v_J)} = 1,$$

a contradiction. ∎

Let us now fix the nonempty open subinterval J of $I = [a/2, 1]$ such that J satisfies both the assumptions in Lemma 7.3 and in (37). Choose an arbitrary $p > 0$. Proposition 5.9 and Lemmas 7.3, 7.4 now imply that $e^{p\lambda}$ and $e^{p\lambda_J}$ are positive eigenvalues of $B = U(t_0 + p, t_0)$ and $\bar{B} = \bar{U}(t_0 + p, t_0)$ respectively with eigenvectors $v, \bar{v}$ which are comparable to v_0 in (20), and that $e^{p\lambda} > e^{p\lambda_J}$. Thus $Z_{v_0} = Z_v = Z_{\bar{v}}$ as Banach spaces. Obviously B and $\bar{B}$ map Z_v and $Z_{\bar{v}}$ continuously into themselves and have the spectral radii $e^{p\lambda}$ and $e^{p\lambda_J}$ on these spaces (see the Appendix, point 8). It follows from proposition 4.2 that B and $\bar{B}$ map Z continuously into Z_{v_0} for $p \geq T_0(a/2, 1)$. The next lemma will imply that B and $\bar{B}$ have the spectral radii $e^{p\lambda} > e^{p\lambda_J}$ on Z so that Lemma 7.2 follows from Lemma 7.1.

LEMMA 7.5

Let W, Z be Banach spaces, W a linear subspace of Z. Let B be a bounded linear operator on Z such that $BZ \subseteq W$ and B is also a bounded operator on W. Then, with the possible exception of $0 \in \mathbb{C}$, B has the same spectrum on Z and on W.

By the open mapping theorem the proof of the lemma reduces to showing that, for $q \neq 0$, $qI - B$ is a bijection on Z iff it is a bijection on W. But proving this is almost trivial and left to the reader.

In order to conclude the consideration of the time-homogeneous case we remind that (37) implies Assumption 5.5, as we have seen in the remarks preceding Corollary 6.3. Thus Propositions 5.6(b, c) hold. The power compactness of B stated in proposition 5.6(a) was only needed to guarantee that the spectral radius r_0 of $B = U(t_0 + p, t_0)$ is a pole of the resolvent of B. In order to realize that r_0 keeps this property under the present conditions we first note that r_0 is a spectral value of the positive operator B (see [18, V.4.1]). By Lemma 7.2 r_0 has the same properties as a nonzero spectral value of a compact operator, in particular r_0 is an eigenvalue and even a pole of the resolvent of B (see [1, Sec. 8]). Thus Propositions 5.7 and 5.8 are valid (see [18, Chap. V]) and so are Theorem 6.1 and Corollary 6.2, if we replace Assumptions 4.8, 5.1 and 5.5 by (37) and the time independence of g, b, μ. Note that $\bar{m}$ in Theorem 6.1 is now a time-independent solution of $\bar{m} = V_\lambda^{*}\bar{m}$. Thus, by (47), $\bar{m}$ is differentiable for $a/2 < x < 1$, $x \neq \frac{1}{2}$ and satisfies the differential equation

$$\left(\frac{\lambda}{g(x)} + \frac{d}{dx}\right)\bar{m}(x) = D(x)\bar{m}(2x) \quad \text{for } a/2 < x < 1, \ x \neq \tfrac{1}{2}, \tag{48a}$$

$$D(x)\bar{m}(2x) = 0, \quad x \geq \tfrac{1}{2}, \tag{48b}$$

and the boundary condition

$$\bar{m}(a/2) = 0. \tag{49}$$

So Theorem 6.1 takes the following form.

THEOREM 7.6

Let Assumptions 1.1, 2.1 be satisfied. Let g, μ, b be time independent and $g(2x) \neq 2g(x)$ for some $x \in (a/2, \frac{1}{2})$. Then the following holds.

(a) There exists a unique $\lambda \in \mathbb{R}$ with a nonnegative solution $\bar{m} \neq 0$ of (48), (49). $\bar{m}$ is uniquely determined up to a scalar factor.

(b) If m is a weak solution of (10) with a continuous initial function Φ on $[a/2, 1]$ at $t = t_0$, $\Phi(a/2) = 0$, then for $t \to \infty$,

$$m(t, x) = e^{\lambda t}\bar{m}(x) \cdot (\alpha - e^{-\epsilon t} O(1))$$

with $\epsilon > 0$ and α as in Theorem 6.1.

Again the dependence of α and $\mathcal{O}(1)$ on the initial values u can be described in more detail, as we did in the sequel of Theorem 6.1.

When Theorem 7.6 is translated to Eq. (1), we note that $\tilde{n}(t, x)$ in Corollary 6.2 is time independent, continuous in x, differentiable in $x \neq a, \frac{1}{2}$ and a solution of the differential equation

$$\lambda \tilde{n}(x) + \frac{d}{dx}(g \cdot \tilde{n})(x) + (\mu + b) \cdot \tilde{n}(x) = 4b \cdot \tilde{n}(2x), \quad x \in (a/2, 1), x \neq a, \tfrac{1}{2}, \tag{50a}$$

$$b \cdot \tilde{n}(x) = 0 \quad \text{if } x \notin [a, 1), \tag{50b}$$

and the boundary condition

$$\tilde{n}(a/2) = 0. \tag{51}$$

Furthermore, $\tilde{n}(x)/\bar{E}(x)$ is bounded in $x \in (a/2, 1)$ with

$$\bar{E}(x) = \exp\left(-\int_{a/2}^{x} (b/g)(z)\,dz\right). \tag{52}$$

So Corollary 6.2 takes the following form.

COROLLARY 7.7

Let the assumptions of Theorem 7.6 be satisfied. Then the following holds.

(a) There exists a unique $\lambda \in R$ with a nonnegative solution $\tilde{n} \neq 0$ of (50), (51) such that $\tilde{n}(x)/\bar{E}(x)$ is continuous on $[a/2, 1]$. $\tilde{n}$ is uniquely determined up to a scalar factor.

(b) Let n be a weak solution of (1) for $t > t_0$ such that $n(t_0, x)/\bar{E}(x)$ is continuous in $x \in [a/2, 1]$. Then, for $t \to \infty$,

$$n(t, x) = e^{\lambda t}\tilde{n}(x) \cdot (\alpha + e^{-\epsilon t}\mathcal{O}(1))$$

with $\epsilon > 0$ and α as in Corollary 6.2.

We remark that these results for the time-homogeneous model can also be obtained using the semigroup theory we applied in [1]. The proof of the strong positivity of the solution operators could then be replaced by a more thorough analysis of the operators V_λ in (47), in particular by the considerations in [27, Sec. 7]. Though $g(2x) < 2g(x)$ for all $x \in [a/2, 1]$ is supposed there, the proof of Theorem 7.2 reveals that (37) is sufficient because the eigenfunction Φ_0 is strictly positive. For time-dependent developmental rates a direct proof of the strong positivity of $U(t, t_0)$ seems unavoidable.

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APPENDIX: SOME VOCABULARY FROM THE THEORY OF BANACH LATTICES

1. A Banach lattice Z is a Banach space with norm $\|\cdot\|$ and a vector lattice with cone Z_+, ordering "$\leq$" and absolute value (or modulus) $|\cdot|$ with these two structures being interlinked by

$$|u| \leq |v| \quad \text{implies} \quad \|u\| \leq \|v\| \tag{A1}$$

for all $u, v \in Z$ (see [18]).

2. Let $v \in Z_+$, $v \neq 0$. $u \in Z$ is called *v-bounded* iff

$$|u| \leq cv \quad \text{for some } c > 0. \tag{A2}$$

The set Z_v of v-bounded elements is a linear subspace of Z and becomes a Banach space itself by the v-norm $\|u\|_v$, which is by definition the smallest c such that (A2) is satisfied (see [17, Secs. 1.2, 1.3]). The Banach space Z_v becomes a Banach lattice by restricting the lattice structure of Z to Z_v, in particular $Z_{v,+} = Z_v \cap Z_+$. If Z is a function space, then $\|u\|_v = \sup\{|(u/v)(x)|;\ v(x) \neq 0\}$. The cone $Z_{v,+}$ has interior points in the Z_v-topology.

3. Let $u, v \in Z_+$. u is called *v-positive* iff $u \geq \epsilon v$ for some $\epsilon > 0$. u and v are called *comparable* (or order-equivalent) iff u is v-bounded and v-positive. u and v are comparable iff Z_v and Z_u are equal as Banach lattice (in particular $Z_u = Z_v$ as sets and $\|\cdot\|_v$ and $\|\cdot\|_u$ are equivalent norms); furthermore, u and v are comparable iff u is an interior point in Z_v and *vice versa*.

4. $v \in Z_+$ is called a *quasi-interior point* iff Z_v is dense in Z, or equivalently, iff $v'v > 0$ for any $v' \in Z'_+$, $v' \neq 0$ (see [18, Thm. II.6.3]).

5. A functional v' on Z is called *positive* iff $v'(u) \geq 0$ for all $u \in Z_+$. v' is called *strictly positive* iff $v'(u) > 0$ for all $u \in Z_+$, $u \neq 0$.

6. A linear operator A from one Banach lattice into another is called *positive* iff it maps one cone into the other. Positive linear operators between Banach lattices are automatically bounded (see [18, Sec. II.5.3]).

7. A positive linear operator A is called *strongly positive* iff for any $u \in Z_+$, $u \neq 0$, $A^n u$ is a quasi-interior point of Z_+ for some $n \in \mathbb{N}$.

8. A positive operator A on Z maps Z_v, $v \in X_+$, into itself iff Av is v-bounded (i.e. $Av \in Z_v$). The operator norm $\|A\|_v$ of A on X_v satisfies $\|A\|_v = \|Av\|_v$. If $Av = rv$ for some $r > 0$, then $\|A\|_v = v$ and r is the spectral radius of A on Z_v.