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A Cell-Cycle Model Revisited

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Abstract

A perturbation theory for strongly continuous semigroups of operators and their adjoints, recently developed by the authors, is explained in the context of a cell division model involving size structure. The theory is based on renewal equations describing the cumulative effect of divisions, rather than on infinitesimal generators.

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1. Introduction

Some years ago a certain size structured cell cycle model, originally due to Bell & Anderson (1967) and Sinko & Streifer (1971), was analysed by Diekmann, Heijmans & Thieme (1984), Heijmans (1985, 1986a, 1986b), Metz & Diekmann (1986), Greiner & Nagel (1988). The model was formulated as the forward Kolmogorov functional partial differential equation

$$\frac{\partial}{\partial t}n(t,x) = -\frac{\partial}{\partial x}(g(x)n(t,x)) - \mu(x)n(t,x) - b(x)n(t,x) + 4b(2x)n(t,2x) \qquad (1.1)$$

where t denotes time, x denotes cell size and $n(t,\cdot)$ is the cell size density function at time t. The coefficients g, μ and b have the following interpretation:

g is the size-specific individual growth rate

μ is the size-specific per capita death rate

b is the size-specific probability per unit of time of division.

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The last term of equation (1.1) reflects the assumption that a dividing cell produces two daughters, each of which has exactly half the size of the mother. (For completeness we note that Bell & Andersson (1967) had "age" as an additional structuring variable.)

The basic idea of the cited mathematical papers is to write (1.1) abstractly in the form

$$\frac{d}{dt}n = (A_0 + B)n \tag{1.2}$$

where the operator A_0 incorporates the first three terms at the right-hand side (the "local" terms) and the operator B corresponds to the non-local last term. The fact that A_0 generates a semigroup of operators can be checked by explicit integration. Next perturbation theory (the Phillips-Dyson expansion) is used to show that $A_0 + B$ generates a semigroup as well. Finally the spectral theory of positive semigroups (see Nagel et al., 1986 or Clément, Heijmans et al., 1987, for systematic expositions) yields strong results concerning the asymptotic behaviour for $t \to \infty$.

Different authors have made different assumptions concerning g, μ and b as well as different choices for the (population) state space, ranging from L_1 (with or without a weight function related to g and b) to the space of finite Borel measures considered as the dual space of the space of continuous functions. Jagers (preprint) shows how the model fits into the framework of multi-type branching processes and he obtains strong conclusions from the general theory of such processes.

Similar cell cycle models have been formulated by Arino & Kimmel (1987) as integral equations; in Arino & Kimmel (preprint) these authors have elaborated in detail the relationship between various formulations. See Kimmel (1982, 1983) for early work in the spirit of the present paper. See Tyson & Diekmann (1986) for an application to actual data.

Recently Diekmann, Gyllenberg & Thieme (1993, preprint) and Diekmann, Gyllenberg, Metz & Thieme (to appear) argued that abstract Stieltjes renewal equations are an attractive alternative to functional partial differential equations, like (1.1), to formulate structured population models. Although the full strength of the alternative manifests itself only in time-dependent linear and in nonlinear problems, some of the advantages are evident in the context of autonomous linear problems. The aim of the present paper is two-fold:

(i) to elaborate the cell cycle model in the new setting as a concrete example of the general approach

(ii) to demonstrate that within the new framework one can work with measures and yet require very little regularity for the coefficients.

2. Ingredients at the individual level

We assume:

i. cells never exceed a maximal size, which we normalize to be 1

ii. cells cannot divide before reaching a threshold size $\alpha > 0$ and consequently $\frac{\alpha}{2}$ is the minimal size

iii. the "state" of an individual cell is adequately described by its size

iv. a dividing cell produces two daughter cells, each of which has exactly half the size of the mother.

The following ingredients suffice to describe the behaviour of individual cells:

1. $\mathcal{G}(x)$:= the time a cell needs to grow from size $\frac{\alpha}{2}$ to size x.
2. $\mathcal{F}(x)$:= the probability that a cell of size $\frac{\alpha}{2}$ will neither die nor divide before reaching size x.
3. $L(x)$:= the expected number of daughter cells that a cell of size $\frac{\alpha}{2}$ will produce before reaching size x.

Concerning these ingredients we make the following technical assumptions:

A1 : $\mathcal{G}$ is continuous and strictly increasing. $\mathcal{G}(\frac{\alpha}{2}) = 0$.
A2 : $\mathcal{F}$ is strictly positive for $x < 1$, continuous and non-increasing. $\mathcal{F}(\frac{\alpha}{2}) = 1$.
A3 : L is continuous and non-decreasing. $L(x) = 0$ for $\frac{\alpha}{2} \le x \le \alpha$ and $L(1) \le 2$.
A4 : $\frac{L(1)-L(x)}{\mathcal{F}(x)} \to 0$ for $x \uparrow 1$.

Except for A4, the logic of these assumptions should be clear from the biological interpretation of $\mathcal{G}, \mathcal{F}$ and L. We shall discuss A4 below.

From the basic ingredients we construct the following composite ingredients:

4. $X(t,x)$:= the size of a cell at time t, given that the size is x at time zero.

   Then

$$X(t,x) = \mathcal{G}^{-1}(t + \mathcal{G}(x)), \quad x \ge \frac{\alpha}{2}$$

   (with the convention that $X(t,x) = 1$ for $t > \mathcal{G}(1) - \mathcal{G}(x)$; note that this possibility does not occur when $\mathcal{G}(1) = \infty$, i.e. when it takes infinite time to reach the maximal size).

5. $\frac{\mathcal{F}(y)}{\mathcal{F}(x)}$ = the probability that a cell of size x will neither die nor divide before reaching size $y \ge x$.

6. $\frac{L(y)-L(x)}{\mathcal{F}(x)}$ = the expected number of daughter cells that a cell of size x will produce before reaching size y. (So we can now understand what (A4) means in biological terms.)

7. $\Lambda(x, x_0)(\omega)$:= the expected number of daughter cells with birth size in ω (a measurable subset of $[\frac{\alpha}{2}, \frac{1}{2}]$), that a cell of size x_0 produces before reaching size x.

   Then

$$\Lambda(x, x_0)(\omega) = \int_{2\omega \cap \{\xi : x_0 \le \xi < x\}} \frac{L(d\xi)}{\mathcal{F}(x_0)} = \frac{1}{\mathcal{F}(x_0)} \int_{2\omega} \chi_{[x_0, x)}(\xi) L(d\xi)$$

   where χ_I denotes the characteristic function of the set I.

8. The expected number of daughter cells, and their distribution with respect to birth size, that a cell of size x_0 produces in a time interval of length t, is described by the measure $\Lambda(X(t, x_0), x_0)$ with support in $[\frac{\alpha}{2}, \frac{1}{2}]$.

We now present, as an interlude, the relationship between the present ingredients $\mathcal{G}, \mathcal{F}$ and L on the one hand, and the rates g, μ and b occuring in (1.1) on the other hand. Formally we have

$$\frac{d}{dx}\mathcal{G}(x) = (g(x))^{-1}$$

$$\frac{1}{\mathcal{F}(x)} \frac{d}{dx}\mathcal{F}(x) = -\frac{b(x) + \mu(x)}{g(x)}$$

$$\frac{1}{\mathcal{F}(x)} \frac{d}{dx} L(x) = -2\frac{b(x)}{g(x)}$$

but of course these relations can only be made precise under additional regularity assumptions on $\mathcal{G}, \mathcal{F}$ and L. The inverse relations are

$$\mathcal{F}(x) = \exp\Big(-\int_{\alpha/2}^{x} \frac{b(\xi)+\mu(\xi)}{g(\xi)} d\xi\Big) \tag{2.1}$$

$$L(x) = 2\int_{\alpha/2}^{x} \frac{b(\xi)}{g(\xi)} \mathcal{F}(\xi) d\xi \tag{2.2}$$

$$\mathcal{G}(x) = \int_{\alpha/2}^{x} \frac{d\xi}{g(\xi)} \tag{2.3}$$

Note that, for given nonnegative and integrable rates b, μ and strictly positive rate g, the functions $\mathcal{F}, L$ and $\mathcal{G}$ defined by, respectively, (2.1)–(2.3), satisfy the assumptions A1–A3. In conclusion of this section we try to relate the biological interpretation of A4 to its mathematical function.

Condition A4 means that a very large cell (i.e. a cell with size close to the maximum observed size, which is normalized to be one) will with high probability not produce any daughter cells. Actually that condition is not satisfied in the setting of Diekmann, Heijmans & Thieme (1984). These authors assumed that μ is bounded while $b(x)$ tends to infinity as x tends to one in such a way that the integral diverges (i.e. $\mathcal{F}(x) \downarrow 0$ as $x \uparrow 1$) and in that case $\frac{L(1)-L(x)}{\mathcal{F}(x)} \to 2$ for $x \uparrow 1$, which means that a large cell will, with high probability, divide before dying. We think that A4 is probably better warranted since in real cell populations an extremely large cell has usually, for some reason, failed to divide in the "normal" way so it seems reasonable to assume that such a cell will not be able to divide at any later instant. Mathematically, the behaviour of individual cells near the singular point $x = 1$ reflects itself at the population level in the continuity properties of the orbits, in particular at $t = 0$. Here we make assumption A4 in order to stay in the realm of (adjoints of) strongly continuous semigroups (see the remark following Lemma 3.2). This is, of course, not a real necessity and various alternatives present themselves: work with integrated semigroups, accept discontinuities and analyse them, restrict to an invariant subspace that attracts all orbits and on which we have strong continuity, ... We may return to such approaches in a later publication, but at this moment we have chosen to make assumption A4.

3. Building blocks at the population level

Again we adopt a perturbation approach. That is, we begin by neglecting births.

Let, at some time t_0, the population size and composition be described by a measure m on the interval $[\frac{\alpha}{2}, 1)$. Then m qualifies as the population state at time t_0. A time interval of length t later, the population state is given by the measure $T_0^*(t)m$ defined as follows (cf. points 4 and 5 of section 2):

$$(T_0^*(t)m)(\omega) = \int_{[\frac{\alpha}{2},1)} \chi_\omega(X(t,z)) \frac{\mathcal{F}(X(t,z))}{\mathcal{F}(z)} m(dz). \tag{3.1}$$

The use of the $*$ is justified by the observation that indeed the linear operator so defined is the adjoint of the operator $T_0(t)$ acting on $C_0([\frac{\alpha}{2},1);\mathbb{C})$, respectively $C_0([\frac{\alpha}{2},1);\mathbb{R})$, according to

$$(T_0(t)\varphi)(x) = \varphi(X(t,x)) \frac{\mathcal{F}(X(t,x))}{\mathcal{F}(x)}. \tag{3.2}$$

(We introduce complex valued functions since later on we use spectral theory. For completeness we also recall that $C_0([\frac{\alpha}{2},1);\mathbb{C})$ denotes the space of complex-valued functions on the interval $[\frac{\alpha}{2},1)$ which are continuous and tend to zero when the argument tends to 1, equipped with the supremum norm.

So alternatively we can think of elements of this space as continuous functions defined on $[\frac{\alpha}{2}, 1]$ which are zero at 1. As is well known, the dual space can be represented by the space of complex regular Borel measures m on $[\frac{\alpha}{2}, 1)$, provided with the total variation norm. The pairing is given by

$$< m, \varphi > = \int_{\alpha/2}^{1} \varphi(x) m(dx).$$

Alternatively one can think of elements of the dual space as normalized bounded variation functions on $[\frac{\alpha}{2}, 1]$ which are continuous at $x = 1$, but we will not do so in this paper.)

LEMMA 3.1. $T_0(t)$ defined by (3.2) constitutes a C_0-semigroup of bounded linear operators on $C_0([\frac{\alpha}{2}, 1); \mathbb{C})$.

PROOF. Note that $X(t,x) \geq x$ for $t \geq 0$. So the expression (3.2) implies at once that

(i) $T_0(t)\varphi$ is a continuous function on $[\frac{\alpha}{2}, 1)$ which tends to zero as $x \uparrow 1$;

(ii) since $\frac{\mathcal{F}(X(t,x))}{\mathcal{F}(x)} \leq 1$, $T_0(t)$ is a bounded linear operator of norm less than or equal to one;

(iii) $T_0(0) = I$;

(iv) $T_0(t)T_0(s) = T_0(t+s)$, since $X(t+s,x) = X(t, X(s,x))$;

(v) for every $\varphi \in C_0([\frac{\alpha}{2}, 1); \mathbb{C})$ we have that

$$||T_0(t)\varphi - \varphi|| \to 0 \text{ as } t \downarrow 0$$ □

In order to describe births we recall point 8 of section 2 and introduce the *reproduction operators*

$$(U_0^*(t)m)(\omega) = \int_{\alpha/2}^{1} \Lambda(X(t,z), z)(\omega) m(dz) \tag{3.3}$$

and their pre-adjoints

$$(U_0(t)\varphi)(x) = \int_{\alpha/2}^{1} \varphi(y) \Lambda(X(t,x), x)(dy) = \frac{1}{\mathcal{F}(x)} \int_{\alpha}^{1} \varphi(\frac{1}{2}\xi) \chi_{[x, X(t,x))}(\xi) L(d\xi). \tag{3.4}$$

Note that $U_0(0) = 0$ and that $U_0^*(t)m$ gives the expected total number of daughter cells, produced in a time interval of length t, by the cells collectively described by m, as well as their distribution with respect to size at birth.

The remainder of this section is devoted to certain technical properties of the operators $U_0(t)$.

We define a function $Q = Q(t,x)$ by

$$Q(t,x) = \begin{cases} \dfrac{L(X(t,x)) - L(x)}{\mathcal{F}(x)} & \text{for } \dfrac{\alpha}{2} \leq x < 1 \\ 0 & \text{for } x = 1 \end{cases} \tag{3.5}$$

Note that A4 guarantees that $Q(t, \cdot)$ is a continuous function. We claim that $t \mapsto Q(t, \cdot)$ is continuous from $\mathbb{R}_+$ into $C_0([\frac{\alpha}{2}, 1); \mathbb{C})$. To prove the claim we choose $\epsilon > 0$ and then $\bar{x} < 1$ such that

$$\frac{L(1)-L(x)}{\mathcal{F}(x)} < \frac{\epsilon}{2} \quad \text{for all} \quad x \in [\bar{x}, 1).$$

We can subsequently choose $\delta > 0$ such that

$$|L(X(t_1, x)) - L(X(t_2, x))| < \epsilon \mathcal{F}(\bar{x})$$

for all $x \in [\frac{\alpha}{2}, \bar{x}]$ and $|t_1 - t_2| < \delta$. Then, provided $|t_1 - t_2| < \delta$, we have, for $x \in [\frac{\alpha}{2}, \bar{x}]$, the estimate

$$|Q(t_1, x) - Q(t_2, x)| \leq \frac{|L(X(t_1, x)) - L(X(t_2, x))|}{\mathcal{F}(\bar{x})} < \epsilon$$

while for all t_1, t_2 and $\bar{x} \leq x < 1$

$$|Q(t_1, x) - Q(t_2, x)| \leq Q(t_1, x) + Q(t_2, x) \leq 2\frac{L(1) - L(x)}{\mathcal{F}(x)} < \epsilon.$$

LEMMA 3.2. Formula (3.4) defines bounded linear operators $U_0(t)$ on $C_0([\frac{\alpha}{2}, 1); \mathbb{C})$ and the mapping $t \mapsto U_0(t)$ is continuous from $\mathbb{R}_+$ into $\mathcal{L}(C_0([\frac{\alpha}{2}, 1); \mathbb{C}))$.

PROOF. From the estimate

$$|(U_0(t)\varphi)(x)| \leq \|\varphi\| Q(t, x)$$

we infer that $U_0(t)$ is a bounded linear operator on $C_0([\frac{\alpha}{2}, 1); \mathbb{C})$, with norm $L(1) \leq 2$. Likewise the estimate

$$\|U_0(t_1)\varphi - U_0(t_2)\varphi\| \leq \|\varphi\| \|Q(t_1, \cdot) - Q(t_2, \cdot)\|$$

and the observations above show that $t \mapsto U_0(t)$ is continuous. □

It should now be clear why we made assumption A4: it guarantees that $(U_0(t)\varphi)(x)$ tends to zero for $x \uparrow 1$, i.e. that $U_0(t)$ maps $C_0([\frac{\alpha}{2}, 1); \mathbb{C})$ into itself.

LEMMA 3.3. U_0 is locally of bounded semi-variation, i.e. for given $t > 0$

$$V_t(U_0) := \sup \| \sum_{i=1}^{n} (U_0(t_i) - U_0(t_{i-1}))\varphi_i \| < \infty$$

where the supremum is taken over all partitions $0 = t_0 < t_1 < \cdots < t_n = t$ and all $\varphi_i \in C_0([\frac{\alpha}{2}, 1); \mathbb{C})$ with $\|\varphi_i\| \leq 1$.

PROOF. $| \sum_{i=1}^{n} (U_0(t_i) - U_0(t_{i-1}))\varphi_i(x)| \leq \frac{1}{\mathcal{F}(x)} \sum_{i=1}^{n} (L(X(t_i, x)) - L(X(t_{i-1}, x)))$

$$= \frac{L(X(t_n, x)) - L(x)}{\mathcal{F}(x)} = Q(t_n, x) = Q(t, x)$$

since $\|\varphi_i\| \leq 1$ and L is non-decreasing. □

LEMMA 3.4. $V_t(U_0) \downarrow 0$ for $t \downarrow 0$.

PROOF. Combine the estimate in the proof of Lemma 3.3 with the continuity of $t \mapsto Q(t, \cdot)$ and the fact that $Q(0, \cdot)$ is identically zero. □

4. The abstract renewal equation

The reproduction operators tell us how many (and what kind of) daughter cells are produced by some given group of cells, which we might call the zeroth generation. In other words, applying the reproduction operators to the zeroth generation we find the first generation. In order to find all births we should iterate this procedure indefinitely and sum the results. So let us define for $n \geq 0$

$$U^*_{n+1}(t) = \int_0^t U^*_0(t-\tau)U^*_n(d\tau) \tag{4.1}$$

and

$$U^*(t) = \sum_{n=0}^{\infty} U^*_n(t) \tag{4.2}$$

then $U^*(t)$ deserve to be called the (accumulated) ***birth operators***. Note that in our situation the sum in (4.2) is actually finite (though the number of terms depends on t and tends to infinity for $t \to \infty$) since, after one or more divisions, a newborn cell has a size less than α and so needs time before being able to divide.

Alternatively and equivalently we can write (4.1)–(4.2) as the *renewal equation*

$$U^*(t) = U^*_0(t) + \int_0^t U^*_0(t-\tau)U^*(d\tau) \tag{4.3}$$

which states that the births fall into two categories: those produced by cells present at time zero and those produced by cells which themselves were born after time zero. It is easier to study (4.3) in its pre-adjoint form

$$U(t) = U_0(t) + \int_0^t U(d\tau)U_0(t-\tau) \tag{4.4}$$

In Diekmann, Gyllenberg & Thieme (1993, preprint) it is shown that the Stieltjes convolution product is well-defined on the set $\mathcal{A}$ of all uniformly continuous families U of bounded linear operators which are locally of bounded semi-variation and satisfy $U(0) = 0$, and that the equation (4.4) admits a unique solution $U \in \mathcal{A}$ for given $U_0 \in \mathcal{A}$ with $\lim_{t\downarrow 0} V_t(U_0) = 0$. In this context U is called the ***resolvent kernel*** for U_0 and U is given by the appropriate series of iterated convolutions of U_0 with itself (with, in general, convergence on $\mathbb{R}_+$ with respect to some exponentially weighted norm). Recalling Lemmas 3.2, 3.3 and 3.4 and taking adjoints we arrive at the following conclusion:

THEOREM 4.1. The renewal equation (4.3) admits a unique solution, which is given by (4.2) with $U^*_n(t)$ defined by (4.1).

5. Population development

The operators $T^*_0(t)$ tell us how the zeroth generation changes in number (due to death and division) and in cell size (due to cell growth). In order to obtain this information for the whole population, we have to take newborns and their subsequent fate into account. So we introduce operators

$$T^*(t) = T^*_0(t) + \int_0^t T^*_0(t-\tau)U^*(d\tau) \tag{5.1}$$

and their pre-adjoints

$$T(t) = T_0(t) + \int_0^t U(d\tau)T_0(t-\tau). \tag{5.2}$$

The interpretation guarantees that these operator families have the semi-group property. Distrustful as mathematicians are, we shall now verify this formally. As a bonus we pinpoint the crucial relationship between T_0 and U_0.

LEMMA 5.1. U_0 is a *step response* for T_0, i.e.

$$U_0(t+s) = U_0(s) + T_0(s)U_0(t)$$

By duality U_0^* is a *cumulative output* family for T_0^*, i.e.

$$U_0^*(t+s) = U_0^*(s) + U_0^*(t)T_0^*(s)$$

PROOF. $$(T_0(s)U_0(t)\varphi)(x) = \frac{\mathcal{F}(X(s,x))}{\mathcal{F}(x)}\frac{1}{\mathcal{F}(X(s,x))}\int_\alpha^1 \varphi(\frac{1}{2}\xi)\chi_{[X(s,x),X(t,X(s,x)))}(\xi)L(d\xi)$$

$$= \frac{1}{\mathcal{F}(x)}\int_\alpha^1 \varphi(\frac{1}{2}\xi)\chi_{[X(s,x),X(t+s,x))}(\xi)L(d\xi)$$

$$= \frac{1}{\mathcal{F}(x)}\int_\alpha^1 \varphi(\frac{1}{2}\xi)\Big\{\chi_{[x,X(t+s,x))}(\xi) - \chi_{[x,X(s,x))}(\xi)\Big\}L(d\xi) = (U_0(t+s)\varphi)(x) - (U_0(s)\varphi)(x) \quad \square$$

THEOREM 5.2. U is a step response for T and $\{T(t)\}_{t\geq 0}$ is a C_0-semigroup.

PROOF. Using (4.4) and the fact that U_0 is a step response for T_0 we can write

$$U(t+s) = U_0(t+s) + \int_0^{t+s} U(d\tau)U_0(t+s-\tau) = U_0(t) + T_0(t)U_0(s)$$

$$+ \int_0^t U(d\tau)\{U_0(t-\tau) + T_0(t-\tau)U_0(s)\} + \int_0^s d_\tau[U(t+\tau) - U(t)]U_0(s-\tau) = U_0(t)$$

$$+ \int_0^t U(d\tau)U_0(t-\tau) + \{T_0(t) + \int_0^t U(d\tau)T_0(t-\tau)\}U_0(s) + \int_0^s d_\tau[U(t+\tau) - U(t)]U_0(s-\tau)$$

So, if we fix t and set

$$W(s) = U(t+s) - U(t)$$

$$W_0(s) = T(t)U_0(s)$$

we have

$$W = W_0 + W \star U_0$$

where $\star$ denotes the Stieltjes convolution product. Since U is the resolvent kernel corresponding to U_0 we know that (cf. Gripenberg et al., 1990, section 9.3)

$$W = W_0 + W_0 \star U$$

which, in terms of the original variables, reads

$$U(t+s) - U(t) = T(t)U_0(s) + \int_0^s T(t)U_0(d\sigma)U(s-\sigma) = T(t)U(s).$$

Now $T(0) = T_0(0) = I$ and the strong continuity of T_0 follows from the strong continuity of $t \mapsto U(t)$. It remains to verify that $T(t+s) = T(t)T(s)$, which we do by formula manipulation:

$$T(t+s) = T_0(t+s) + \int_0^{t+s} U(d\tau)T_0(t+s-\tau) = T_0(t)T_0(s) + \int_0^t U(d\tau)T_0(t-\tau)T_0(s)$$

$$+ \int_0^s d_\tau[U(\tau+t) - U(t)]T_0(s-\tau) = [T_0(t) + \int_0^t U(d\tau)T_0(t-\tau)]T_0(s)$$

$$+ \int_0^s T(t)U(d\tau)T_0(s-\tau) = T(t)[T_0(s) + \int_0^t U(d\tau)T_0(s-\tau)] = T(t)T(s) \qquad \square$$

6. Asymptotic behaviour

The standard approach in the analysis of the large time behaviour of a semigroup of operators is to analyse the spectrum of the infinitesimal generator. So it may seem that one has to determine this generator and, in particular, characterize its domain of definition. This task is afflicted with technical difficulties related to regularity matters. Therefore we prefer to avoid it. And indeed, as we now show, it is possible to determine the *resolvent* of the generator more or less directly by applying the Laplace transform to the defining equations of the semigroup. Subsequently it only remains to analyse the singularities of the resolvent.

Throughout this section we concentrate on the case $\mathcal{G}(1) < \infty$. In most of this section we assume that $\alpha > \frac{1}{2}$.

Recalling the identity

$$(\lambda I - A)^{-1} = \int_0^\infty e^{-\lambda\tau}T(\tau)d\tau, \quad \text{Re}\lambda \text{ sufficiently large,} \tag{6.1}$$

we find, upon applying the Laplace transform to (5.2) and (4.4), the equations

$$(\lambda I - A)^{-1} = (\lambda I - A_0)^{-1} + \hat{U}(\lambda)(\lambda I - A_0)^{-1} \tag{6.2}$$

$$\hat{U}(\lambda) = \hat{U}_0(\lambda) + \hat{U}(\lambda)\hat{U}_0(\lambda) \tag{6.3}$$

where $\hat{U}$ is, by definition, the Laplace-Stieltjes transform of U, i.e.

$$\hat{U}(\lambda) = \int_0^\infty e^{-\lambda\tau} U(d\tau) \tag{6.4}$$

and with identical definitions for the objects with index zero (see Diekmann, Gyllenberg & Thieme, 1993, Proposition 3.2.d. for the proof that U and U_0 are necessarily exponentially bounded). Combining (6.2) and (6.3) we deduce at once that

$$(\lambda I - A)^{-1} = (I - \hat{U}_0(\lambda))^{-1}(\lambda I - A_0)^{-1} \tag{6.5}$$

Our next step is to derive explicit representations for the operators at the right hand side of (6.5). Combining (6.1), with index zero, and (3.2) we find

$$((\lambda I - A_0)^{-1}\psi)(x) = \frac{e^{\lambda \mathcal{G}(x)}}{\mathcal{F}(x)} \int_x^1 e^{-\lambda \mathcal{G}(\xi)} \mathcal{F}(\xi)\psi(\xi)\mathcal{G}(d\xi). \tag{6.6}$$

So if $\mathcal{G}(1) < \infty$ the function $\lambda \mapsto (\lambda I - A_0)^{-1}$ is entire and, as far as singularities are concerned, we can concentrate on $(I - \hat{U}_0(\lambda))^{-1}$.

Combining (6.4), with index zero, and (3.4) we find after a simple computation that

$$(\hat{U}_0(\lambda)\psi)(x) = \frac{e^{\lambda \mathcal{G}(x)}}{\mathcal{F}(x)} \int_\alpha^1 H(\xi - x)\psi(\frac{1}{2}\xi)e^{-\lambda \mathcal{G}(\xi)} L(d\xi) \tag{6.7}$$

where, as usual, H denotes the Heaviside function. Note that the image of ψ under $\hat{U}_0(\lambda)$ depends only on the restriction of ψ to the interval $[\frac{\alpha}{2}, \frac{1}{2}]$. This can be exploited when studying the invertibility of $I - \hat{U}_0(\lambda)$.

In the remainder of this paper we restrict our attention to the relatively simple case $\alpha \geq \frac{1}{2}$ while noting that, provided one adds some notation and a bit of linear algebra, essentially the same ideas allow us to handle any case $\alpha \geq 2^{-k}$, $k \in \mathbb{N}$ (see in particular Heijmans, 1985).

When $\alpha \geq \frac{1}{2}$, $\xi \geq \alpha$ and $x \leq \frac{1}{2}$, necessarily $\xi \geq x$ and the Heaviside function in (6.7) always takes the value one. As a consequence $\hat{U}_0(\lambda)$, considered as an operator on $C([\frac{\alpha}{2}, \frac{1}{2}]; \mathbb{C})$, has one-dimensional range. Exploiting this fact we derived the following explicit representation for the inverse of $I - \hat{U}_0(\lambda)$.

Lemma 6.1. Let, for $\lambda \in \mathbb{C}$, $\hat{V}(\lambda) : X \to \mathbb{C}$, $\hat{W}(\lambda) \in X$ and $\hat{k}(\lambda) \in \mathbb{C}$ be defined by

$$\hat{V}(\lambda)\psi = e^{\lambda \mathcal{G}(\alpha)} \int_\alpha^1 \psi(\frac{1}{2}\xi)e^{-\lambda \mathcal{G}(\xi)} L(d\xi) \tag{6.8}$$

$$\hat{W}(\lambda)(x) = \frac{e^{\lambda(\mathcal{G}(x) - \mathcal{G}(\alpha))}}{\mathcal{F}(x)} \int_\alpha^1 \frac{e^{\lambda(\mathcal{G}(\frac{1}{2}\xi) - \mathcal{G}(\xi))}}{\mathcal{F}(\frac{1}{2}\xi)} H(\xi - x)L(d\xi) \tag{6.9}$$

$$\hat{k}(\lambda) = \int_\alpha^1 \frac{e^{\lambda(\mathcal{G}(\frac{1}{2}\xi) - \mathcal{G}(\xi))}}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi) \tag{6.10}$$

then for Reλ sufficiently large

$$(I - \hat{U}_0(\lambda))^{-1} = I + \hat{U}_0(\lambda) + (1 - \hat{k}(\lambda))^{-1}\hat{W}(\lambda)\hat{V}(\lambda) \tag{6.11}$$

(where we consider elements of $\mathbb{C}$ as the corresponding multiplication operators on X).

COROLLARY 6.2. $\sigma(A) = P\sigma(A) = \{\lambda \in \mathbb{C} : \hat{k}(\lambda) = 1\}$.

PROOF. The assumption $\mathcal{G}(1) < \infty$ guarantees that $\hat{V}$ and $\hat{W}$ are entire functions of λ. The same is true for $(\lambda I - A_0)^{-1}$, see (6.6). So combining (6.5) with (6.11) we see that the resolvent of A is regular for all λ with $\hat{k}(\lambda) \neq 1$ and that it has (non-removable) singularities at those λ for which $\hat{k}(\lambda) = 1$. Since $\hat{k}$ is an analytic function of λ, these singularities are necessarily isolated poles of finite order. The associated projection operator has finite rank, hence all points in the spectrum are eigenvalues.□

In order to justify the suggestive notation and for future use we introduce functions of time $V(t) : X \to \mathbb{C}$, $W(t) \in X$ and $k(t) \in \mathbb{C}$:

$$V(t)\psi = \int_{\alpha}^{\mathcal{G}^{-1}(t+\mathcal{G}(\alpha))} \psi(\frac{1}{2}\xi)L(d\xi) = \int_{\alpha}^{1} H(t + \mathcal{G}(\alpha) - \mathcal{G}(\xi))\psi(\frac{1}{2}\xi)L(d\xi) \tag{6.12}$$

$$\begin{aligned} W(t)(x) &= \frac{1}{\mathcal{F}(x)} \int_{\{\xi\in[\alpha,1):\mathcal{G}(\xi)-\mathcal{G}(\frac{1}{2}\xi)<t+\mathcal{G}(x)-\mathcal{G}(\alpha)\}} \frac{H(\xi - x)}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi) \\ &= \frac{1}{\mathcal{F}(x)} \int_{\alpha}^{1} \frac{H(t + \mathcal{G}(x) - \mathcal{G}(\alpha) - \mathcal{G}(\xi) + \mathcal{G}(\frac{1}{2}\xi))H(\xi - x)}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi) \end{aligned} \tag{6.13}$$

$$k(t) = \int_{\{\xi\in[\alpha,1):\mathcal{G}(\xi)-\mathcal{G}(\frac{1}{2}\xi)<t\}} \frac{1}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi) = \int_{\alpha}^{1} \frac{H(t + \mathcal{G}(\xi) - \mathcal{G}(\frac{1}{2}\xi))}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi) \tag{6.14}$$

One can use either Theorem C on page 163 of Halmos (1950) or, alternatively, apply the inverse Laplace transform to the functions of λ, cf. Widder (1946), to verify the assertion of the next lemma that $\hat{f}$ is indeed the Laplace-Stieltjes transform of f for $f = V, W$ and k. Note that we have incorporated a factor $e^{\lambda\mathcal{G}(\alpha)}$ in $\hat{V}(\lambda)$, compensated by a factor $e^{-\lambda\mathcal{G}(\alpha)}$ in $\hat{W}(\lambda)$, in order that V has support in $[0, \infty)$ (and without "destroying" that property for W, since $\mathcal{G}(x) - \mathcal{G}(\alpha) + \mathcal{G}(\frac{1}{2}\xi) - \mathcal{G}(\xi) < 0$ for $\xi \geq \max(\alpha, x)$).

LEMMA 6.3.

i) $\hat{V}(\lambda) = \int_0^\infty e^{-\lambda t} V(dt)$

ii) $\hat{W}(\lambda) = \int_0^\infty e^{-\lambda t} W(dt)$

iii) $\hat{k}(\lambda) = \int_0^\infty e^{-\lambda t} k(dt)$

There are now two cases to be distinguished:

1. The lattice case.

2. The non-lattice case.

In the lattice case the kernel k is constant except for (finitely many) jumps which all occur at integer multiples of some number c. In other words, considered as a measure k is concentrated on a set of points which are commensurable, with a greatest common factor which we call c (since k has compact support the set of points is actually finite). As a consequence, $\hat{k}(\lambda)$ is periodic along lines $\mathrm{Re}\lambda =$ constant, with period $\frac{2\pi}{c}$. Therefore the roots of $\hat{k}(\lambda) = 1$ occur in countably infinite groups on vertical lines in the complex plane. Since k is a nontrivial non-decreasing function of t, there exists precisely one real root, which we call λ_d. On the line $\mathrm{Re}\lambda = \lambda_d$ we have roots $\lambda = \lambda_d + \frac{2k\pi i}{c}$, $k \in \mathbb{Z}$, which form a group under addition. All other roots have real part less than λ_d (which explains the use of the index d, denoting "dominant").

As we shall show below by explicit calculations for a special lattice case, asymptotically for $t \to \infty$ we have

$$T(t)\phi \sim e^{\lambda_d t} S(t) P_\infty \phi \tag{6.15}$$

where P_∞ is a projection onto an infinite dimensional subspace which is isomorphic to the space of c-periodic continuous functions and $S(t)$ is a group of operators conjugate to translation as a group acting on the c-periodic functions.

The argument which shows that there exists precisely one real root λ_d of the characteristic equation $\hat{k}(\lambda) = 1$ does not require k to be lattice. In the non-lattice case there are no other roots on the line $\mathrm{Re}\lambda = \lambda_d$ and *all* roots different from λ_d satisfy $\mathrm{Re}\lambda < \lambda_d$. We shall then find that

$$T(t)\phi \sim e^{\lambda_d t} P_1 \phi, \quad t \to \infty, \tag{6.16}$$

where P_1 is a projection operator with *one-dimensional* range.

This dichotomy of two types of possible behaviour, (6.16) the rule and (6.15) the exception, is a general phenomenon for *positive* semigroups, see Nagel (ed., 1986) section C–IV.2, Kerscher & Nagel (1984), Greiner & Nagel (1988), where results are stated and proved for positive semigroups on $L^p(X,\mu)$, $1 \le p < \infty$; the same dichotomy is known in the theory of multi-type branching processes (see, in particular, Theorems 1 and 2 in Jagers, preprint).

In order to gain some intuitive understanding of (6.15) and (6.16) we shall first analyse the problem from the point of view of inverse Laplace transformation applied to (6.5), using (6.11). Since k is a non-decreasing function of t, $\hat{k}'(\lambda_d) \neq 0$ or, in other words, λ_d is a simple root of the equation $\hat{k}(\lambda) = 1$. Hence $(\lambda I - A)^{-1}$ has a first order pole in $\lambda = \lambda_d$ with residue

$$P_1 = \frac{\hat{W}(\lambda_d)\hat{V}(\lambda_d)(\lambda_d I - A_0)^{-1}}{-\hat{k}'(\lambda_d)} \tag{6.17}$$

The range of this operator P_1 is spanned by $\hat{W}(\lambda_d)$. More precisely we have

$$P_1 \psi = C(\psi)\hat{W}(\lambda_d) \tag{6.18}$$

where

$$C(\psi) = \frac{e^{\lambda \mathcal{G}(\alpha)} \int_\alpha^1 \frac{e^{\lambda(\mathcal{G}(\frac{1}{2}\xi) - \mathcal{G}(\xi))}}{\mathcal{F}(\frac{1}{2}\xi)} \int_{\frac{1}{2}\xi}^1 e^{-\lambda \mathcal{G}(\eta)} \mathcal{F}(\eta)\psi(\eta)\mathcal{G}(d\eta) L(d\xi)}{\int_\alpha^1 (\mathcal{G}(\xi) - \mathcal{G}(\frac{1}{2}\xi)) \frac{e^{\lambda(\mathcal{G}(\frac{1}{2}\xi) - \mathcal{G}(\xi))}}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi)} \tag{6.19}$$

So either invoking general results about Dunford integrals (see Yosida, 1980, section VIII.7,8) or checking that $\hat{k}(\lambda_d) = 1$ implies that $C(\hat{W}(\lambda_d)) = 1$, we conclude that P_1 is a projection operator with one-dimensional range.

When the real parts of all other roots of $\hat{k}(\lambda) = 1$ are uniformly bounded away from λ_d one can prove that

$$\|e^{-\lambda_d t}T(t) - P_1\| \to 0 \quad \text{as} \quad t \to \infty \tag{6.20}$$

(i.e. convergence in the operator norm) provided one can show that $1 - \hat{k}(\lambda)$ is bounded away from zero for $\mathrm{Im}\lambda \to \pm\infty$, uniformly for $\mathrm{Re}\lambda$ in some interval to the left of λ_d (see e.g. Chapter V, written by Heijmans, in Metz & Diekmann (eds.), 1986, Webb, 1987, and, in particular, Kaashoek & Verduyn Lunel, preprint, and the references given there). In the present generality, however, this need not be the case. The behaviour of $\hat{k}(\lambda)$ for $\mathrm{Im}\lambda \to \pm\infty$ may be quite complicated if k has a non-discrete singular part (see Lyons, 1985, Rudin, 1962; also see section 4.4 in Gripenberg, Londen & Staffans, 1990). Moreover, if, for instance, k is constant except for two jumps which occur in points which are *incommensurable* (i.e. rationally independent) then there must exist a sequence of roots λ_n such that $\mathrm{Im}\lambda_n \to \pm\infty$, $\mathrm{Re}\lambda_n \uparrow \lambda_d$, essentially since $\hat{k}(\lambda)$ is almost periodic as a function of $\mathrm{Im}\lambda$ (see the proof of Proposition 4.1 in Gyllenberg, 1986; as far as we know this is the first paper dealing explicitly, in a population dynamical context, with the situation of a strictly dominant root without uniform separation). As we shall show below using a result of Feller, 1966, on the renewal equation, we then still can have that (6.16) holds (i.e. strong convergence) but (6.20) is no longer true (indeed, Webb, 1987, proves that uniform convergence implies exponential estimates for the remainder and these cannot hold in the situation described above; see Gyllenberg & Webb, 1992, for another example of strong but non-uniform convergence).

In order to have a lattice kernel k we should have that $\mathcal{G}(\frac{1}{2}\xi) - \mathcal{G}(\xi)$ is constant on intervals on which L is strictly increasing. In order to simplify both the discussion and the calculations we shall restrict our attention to the case that $\mathcal{G}(\xi) - \mathcal{G}(\frac{1}{2}\xi) = c$ for $\alpha \leq \xi < 1$. It is then immediate that the residues in $\lambda = \lambda_d + \frac{2k\pi i}{c}$ are of the form

$$c_k e^{\frac{2k\pi i}{c}\mathcal{G}(x)} \frac{e^{\lambda_d \mathcal{G}(x)}}{\mathcal{F}(x)} \int_\alpha^1 \frac{H(\xi - x)}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi) \tag{6.21}$$

So, provided the c_k are indeed the Fourier coefficients of a c-periodic function z, which depends on the initial condition ψ, we find that one can associate with the whole group of poles the operator P_∞ "defined" by

$$(P_\infty\psi)(x) = \frac{e^{\lambda_d \mathcal{G}(x)}}{\mathcal{F}(x)} \int_\alpha^1 \frac{H(\xi - x)}{\mathcal{F}(\frac{1}{2}\xi)} L(d\xi) z_\psi(\mathcal{G}(x)). \tag{6.22}$$

Below we shall derive, by explicit calculations, an expression for z_ψ from which it then directly follows that P_∞ is a projection operator. In addition these calculations will show that (6.15) holds. Under additional regularity conditions on k an alternative proof follows from the results of Kaashoek & Verduyn Lunel, preprint.

After this long exposition about the singularities of the resolvent and their relation to the two types of behaviour (either a stable distribution or periodic continuation of an infinite dimensional amount of information about the initial condition), we shall now finally formulate and prove two theorems. The method of proof is slightly different: we use the resolvent kernel r of the kernel k to translate (6.5) & (6.11) into an explicit representation for $T(t)$ and subsequently use results of Feller (1966) about the one-dimensional renewal equation to deduce the asymptotic behaviour of $T(t)$ for $t \to \infty$.

THEOREM 6.4. Assume that k is non-lattice. Let λ_d be the unique real root of the equation $\hat{k}(\lambda) = 1$. Then for any $\phi \in X$

$$\lim_{t\to\infty} \|e^{-\lambda_d t}T(t)\phi - P_1\phi\| = 0.$$

where P_1 is defined by (6.18)–(6.19).

PROOF. Let r denote the *resolvent kernel* of k, i.e.

$$r = \sum_{n=0}^{\infty} k^{n\star} \tag{6.23}$$

where by definition $r^{0\star} = H$, the Heaviside function, and $r^{(n+1)\star} = r^{n\star} \star r$, $n \geq 0$. So equivalently r is the unique solution of the renewal equation

$$r = H + k \star r \tag{6.24}$$

and from this we infer that

$$\hat{r}(\lambda) = (1 - \hat{k}(\lambda))^{-1} \tag{6.25}$$

or, in words, $(1 - \hat{k}(\lambda))^{-1}$ is the Laplace-Stieltjes transform of r. Combining (6.5), (6.11) and (6.25) we find the representation

$$T(t) = T_0(t) + \int_0^t U_0(d\tau)T_0(t-\tau) + \int_0^t r(d\tau) \int_0^{t-\tau} W(d\sigma) \int_0^{t-\tau-\sigma} V(d\eta)T_0(t-\tau-\sigma-\eta) \tag{6.26}$$

Since $\mathcal{G}(1) < \infty$, the first two terms become zero in finite time whereas the operators $V(t)$ and $W(t)$ are independent of t, once t is large enough. It follows that the asymptotic behaviour of $T(t)$ is completely determined by the asymptotic behaviour of $r(t)$. For this we consult Feller (1966), Chapter XI. In order to adjust to the setting of that chapter we define

$$\tilde{r}(t) = \int_0^t e^{-\lambda_d \tau} r(d\tau), \quad \tilde{k}(t) = \int_0^t e^{-\lambda_d \tau} k(d\tau). \tag{6.27}$$

Then $\tilde{k}(\infty) = 1$ and (6.24) can be reformulated as

$$\tilde{r} = H + \tilde{k} \star \tilde{r} \tag{6.28}$$

Since, by assumption, k is non-lattice (or non-arithmetic in the terminology of Feller) we deduce from Feller's first form of the Renewal Theorem that for every $h > 0$

$$\tilde{r}(t) - \tilde{r}(t-h) \to \frac{h}{\mu} \quad \text{as} \quad t \to \infty \tag{6.29}$$

where

$$\mu := \int_0^\infty \tau e^{-\lambda_d \tau} k(d\tau). \tag{6.30}$$

It follows that for any f with compact support

$$\lim_{t\to\infty} e^{-\lambda_d t}\int_0^t r(d\tau)f(t-\tau) = \frac{1}{\mu}\int_0^\infty f(\tau)e^{-\lambda_d\tau}d\tau \tag{6.31}$$

which is (a weak version of) Feller's alternative form of the Renewal Theorem. Applying this to (6.26) we find that

$$\lim_{t\to\infty} e^{-\lambda_d t}T(t)\phi = \frac{1}{\mu}\hat{W}(\lambda_d)\hat{V}(\lambda_d)(\lambda_d I - A_0)^{-1}\phi \tag{6.32}$$

Using the explicit formulas for all factors we finally conclude that the right-hand side of (6.32) equals $P_1\phi$, where P_1 is defined by (6.18)–(6.19). □

THEOREM 6.5. Assume that $\mathcal{G}(\xi) - \mathcal{G}(\frac{1}{2}\xi) = c$ for $\alpha \le \xi < 1$. For given $\phi \in X$ define a c-periodic function $z_\phi : \mathbb{R} \to \mathbb{R}$ by the formulas

$$z_\phi(\sigma) = \theta^{-2}e^{-\lambda_d\sigma}\Big\{\phi(2\mathcal{G}^{-1}(\sigma))\mathcal{F}(2\mathcal{G}^{-1}(\sigma))$$

$$+\phi(\mathcal{G}^{-1}(\sigma))\mathcal{F}(\mathcal{G}^{-1}(\sigma))\int_\alpha^{2\mathcal{G}^{-1}(\sigma)}\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)}\Big\}, \qquad 0 \le \sigma \le \mathcal{G}(\frac{1}{2}) \tag{6.33}$$

$$z_\phi(\sigma) = \theta^{-1}e^{-\lambda_d\sigma}\phi(\mathcal{G}^{-1}(\sigma))\mathcal{F}(\mathcal{G}^{-1}(\sigma)), \qquad \mathcal{G}(\frac{1}{2}) \le \sigma \le c \tag{6.34}$$

and periodic continuation. Here

$$\theta := \int_\alpha^1 \frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)} \tag{6.35}$$

Then for sufficiently large t we have explicitly

$$(T(t)\phi)(x) = e^{\lambda_d t}z_\phi(t+\mathcal{G}(x))\frac{e^{\lambda_d\mathcal{G}(x)}}{\mathcal{F}(x)}\int_\alpha^1 \frac{H(\xi - x)}{\mathcal{F}(\frac{1}{2}\xi)}L(d\xi). \tag{6.36}$$

PROOF. First recall that $\mathcal{G}(\frac{\alpha}{2}) = 0$ and therefore $c = \mathcal{G}(\alpha) > \mathcal{G}(\frac{1}{2})$. Next recall that $\phi(1) = 0$, which guarantees that z is continuous in $\sigma = \mathcal{G}(\frac{1}{2})$ and $z_\phi(0) = z_\phi(c)$.

Under our assumption that $\mathcal{G}(\xi) - \mathcal{G}(\frac{1}{2}\xi) = c$ we find that

$$\Big(\int_0^t V(d\eta)T_0(t-\eta)\phi\Big)(x) = \phi(\mathcal{G}^{-1}(t))\mathcal{F}(\mathcal{G}^{-1}(t))\int_\alpha^{\mathcal{G}^{-1}(t+c)}\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)} \tag{6.37}$$

and subsequently that

$$\Big(\int_0^t W(d\tau)\int_0^{t-\tau} V(d\eta)T_0(t-\tau-\eta)\phi\Big)(x) =$$

$$\phi(\mathcal{G}^{-1}(t+\mathcal{G}(x)-2c))\mathcal{F}(\mathcal{G}^{-1}(t+\mathcal{G}(x)-2c))\frac{1}{\mathcal{F}(x)}\int_\alpha^1 \frac{H(\xi-x)}{\mathcal{F}(\frac{1}{2}\xi)}L(d\xi)\int_\alpha^{\mathcal{G}^{-1}(t+\mathcal{G}(x)-c)}\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)} \tag{6.38}$$

(where the expression should be interpreted as zero for $t+\mathcal{G}(x)<2c$ and $t+\mathcal{G}(x)>2c+\mathcal{G}(1)$). Since $k(t)=\theta H(t-c)$ we find for the resolvent r defined by (6.23) that

$$r(t)=\sum_{j=0}^{\infty}\theta^j H(t-jd) \tag{6.39}$$

Combining (6.26), (6.38) and (6.39) we see that for $t>2\mathcal{G}(1)$, when the first two terms at the right hand side of (6.26) are zero, we have

$$(T(t)\phi)(x)=\frac{1}{\mathcal{F}(x)}\int_\alpha^1\frac{H(\xi-x)}{\mathcal{F}(\frac{1}{2}\xi)}L(d\xi) \tag{6.40}$$

$$\sum_{j=0}^{\infty}\theta^j\phi(\mathcal{G}^{-1}(t+\mathcal{G}(x)-(2+j)c))\mathcal{F}(\mathcal{G}^{-1}(t+\mathcal{G}(x)-(2+j)c))$$

$$\int_\alpha^{\mathcal{G}^{-1}(t+\mathcal{G}(x)-(1+j)c))}\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)}$$

where the k-th term of the sum is different from zero if and only if

$$(2+k)c<t+\mathcal{G}(x)<(2+k)c+\mathcal{G}(1). \tag{6.41}$$

Now note that at most two terms can contribute at the same time since $\mathcal{G}(1)=c+\mathcal{G}(\frac{1}{2})<c+\mathcal{G}(\alpha)=2c$. In fact only the k-th term contributes for $(k+1)c+\mathcal{G}(1)<t+\mathcal{G}(x)<(k+3)c$, whereas both the k-th and $(k+1)$-th term contribute for $(k+3)c<t+\mathcal{G}(x)<(k+2)c+\mathcal{G}(1)$. It follows that we have periodicity of period c modulo multiplication by θ. It only remains to note that $\theta e^{-\lambda_d c}=\hat{k}(\lambda_d)=1$ and to exploit the periodicity to rewrite (6.40) as (6.36) with z_ϕ given by (6.33) & (6.34). □

COROLLARY 6.6. When $\mathcal{G}(\xi)-\mathcal{G}(\frac{1}{2}\xi)=c$ for $\alpha\le\xi<1$, the projection operator P_∞ takes the form

$$(P_\infty\psi)(x)=\begin{cases}\theta^{-1}\Big(\frac{\mathcal{F}(2x)}{\mathcal{F}(x)}\psi(2x)+\int_\alpha^{2x}\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)}\psi(x)\Big) & ,\ \frac{\alpha}{2}\le x<\frac{1}{2}\\ \psi(x) & ,\ \frac{1}{2}\le x<\alpha\\ \theta^{-1}\Big(\frac{\mathcal{F}(\frac{x}{2})}{\mathcal{F}(x)}\int_\alpha^x\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)}\int_x^1\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)}\psi(\frac{x}{2})+\int_\alpha^1\frac{L(d\xi)}{\mathcal{F}(\frac{1}{2}\xi)}\psi(x)\Big) & ,\ \alpha\le x<1\end{cases}$$

To conclude, let us try to understand in biological terms what the condition $\mathcal{G}(\xi)-\mathcal{G}(\frac{1}{2}\xi)=c$ means. When $\alpha\ge\frac{1}{2}$, every newborn cell necessarily has to pass the size $\frac{1}{2}$ before it can possibly divide. So we can base our book-keeping as well on the "traffic" of cells at $x = \frac{1}{2}$ (actually this is the biological "reason" for the "essentially one-dimensional range" property of $\hat{U}_0(\lambda)$ and the fact that the problem reduces to a *one-dimensional* renewal equation). Let us start a clock when a cell passes $x = \frac{1}{2}$ and stop that clock when any of its daughters passes $\frac{1}{2}$. Suppose the cell devides at $\xi \geq \alpha$. Then the clock shows time $\mathcal{G}(\xi) - \mathcal{G}(\frac{1}{2})$. At that time the two daughters start to grow with size $\frac{1}{2}\xi$ and so they will reach size $\frac{1}{2}$ after a time interval of length $\mathcal{G}(\frac{1}{2}) - \mathcal{G}(\frac{1}{2}\xi)$. Hence the clock will stop at time $\mathcal{G}(\xi) - \mathcal{G}(\frac{1}{2}\xi)$. Clearly when this time is independent of ξ, all cells that pass $x = \frac{1}{2}$ simultaneously will have offspring that pass $x = \frac{1}{2}$ simultaneously and likewise time differences are preserved from generation to generation (in fact the renewal equation reduces to a difference equation in this case; see also Metz & Diekmann (eds.), 1986, section V.11). So there is no "smoothing", no (eventual) compactness. Clearly any modification of our assumptions, however slight, may introduce some smoothing and thereby change the "periodic" asymptotic behaviour into the "normal" (for positive semigroups) one of convergence to a stable distribution. Such perturbations were studied by Heijmans (1984), who considered asymmetric division, and Gyllenberg & Webb (1987, 1990), Rossa (1991), who considered the effect of quiescence (see also Grabosch, preprint).

We hope that this section has convinced our readers that the formulation of structured population models in terms of abstract renewal equations is very well suited for a subsequent study of the asymptotic behaviour, since we obtain an explicit expression for the resolvent of the generator in terms of Laplace transforms of the building blocks at the population level. By inverse Laplace transformation we then find a representation of the semigroup itself from which it is possible, or even easy, to deduce the asymptotic behaviour for large time.

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