Positive semigroups and perturbations of boundary conditions

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Abstract

We present a generation theorem for positive semigroups on an L^1 space. It provides sufficient conditions for the existence of positive and integrable solutions of initial-boundary value problems. An application to a two-phase cell cycle model is given.

Keywords Positive semigroup · Perturbation of boundary conditions · Steady state · Cell cycle models

Mathematics Subject Classification 47B65 · 47H07 · 47D06 · 92C40

1 Introduction

We study well-posedness of linear evolution equations on L^1 of the form

$$u'(t) = Au(t), \quad \Psi_0 u(t) = \Psi u(t), \quad t > 0, \quad u(0) = f, \quad (1)$$

where Ψ_0, Ψ are positive and possibly unbounded linear operators on L^1 , the linear operator A is such that Eq. (1) with $\Psi = 0$ generates a *positive semigroup* on L^1 , i.e., a C_0 -semigroup of positive operators on L^1 . We present sufficient conditions for the operators A, Ψ_0 , and Ψ under which there is a unique positive semigroup on L^1 providing solutions of the initial-boundary value problem (1). For a general theory of

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positive semigroups and their applications we refer the reader to [4,7,11,14,34]. An overview of different approaches used in studying initial-boundary value problems is presented in [13].

Our result is an extension of Greiner's [19] by considering unbounded Ψ and positive semigroups. Unbounded perturbations of the boundary conditions of a generator were studied recently in [1,2] by using extrapolated spaces and various admissibility conditions. In the proof of our perturbation theorem we apply a result about positive perturbations of resolvent positive operators [3] with non-dense domain in AL -spaces in the form given in [37, Theorem 1.4]. It is an extension of the well known perturbation result due to Desch [15] and by Voigt [41]. For positive perturbations of positive semigroups in the case when the space is not an AL -space we refer to [5,10]. We also present a result about stationary solutions of (1). We illustrate our general results with an age-size-dependent cell cycle model generalizing the discrete time model of [22,25,38]. This model can be described as a piecewise deterministic Markov process (see Sect. 5 and [34]). Our approach can also be used in transport equations [8,23].

2 General results

Let $(E, \mathcal{E}, m)$ and $(E_\partial, \mathcal{E}_\partial, m_\partial)$ be two σ -finite measure spaces. Denote by $L^1 = L^1(E, \mathcal{E}, m)$ and $L^1_\partial = L^1(E_\partial, \mathcal{E}_\partial, m_\partial)$ the corresponding spaces of integrable functions. Let $\mathcal{D}$ be a linear subspace of L^1 . We assume that $A: \mathcal{D} \rightarrow L^1$ and $\Psi_0, \Psi: \mathcal{D} \rightarrow L^1_\partial$ are linear operators satisfying the following conditions:

- (i) for each $\lambda > 0$, the operator $\Psi_0: \mathcal{D} \rightarrow L^1_\partial$ restricted to the nullspace $\mathcal{N}(\lambda I - A) = \{f \in \mathcal{D} : \lambda f - Af = 0\}$ of the operator $(\lambda I - A, \mathcal{D})$ has a positive right inverse, i.e., there exists a positive operator $\Psi(\lambda): L^1_\partial \rightarrow \mathcal{N}(\lambda I - A)$ such that $\Psi_0 \Psi(\lambda) f_\partial = f_\partial$ for $f_\partial \in L^1_\partial$;
- (ii) the operator $\Psi: \mathcal{D} \rightarrow L^1_\partial$ is positive and there exists $\omega \in \mathbb{R}$ such that the operator $I_\partial - \Psi \Psi(\lambda): L^1_\partial \rightarrow L^1_\partial$ is invertible with positive inverse for all $\lambda > \omega$, where I_∂ is the identity operator on L^1_∂ ;
- (iii) the operator $A_0 \subseteq A$ with $\mathcal{D}(A_0) = \{f \in \mathcal{D} : \Psi_0 f = 0\}$ is the generator of a positive semigroup on L^1 ;
- (iv) for each nonnegative $f \in \mathcal{D}$

$$\int_E Af(x) m(dx) - \int_{E_\partial} \Psi_0 f(x) m_\partial(dx) \leq 0. \quad (2)$$

Theorem 1 Assume conditions (i)–(iv). Then the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ defined by

$$A_\Psi f = Af, \quad f \in \mathcal{D}(A_\Psi) = \{f \in \mathcal{D} : \Psi_0(f) = \Psi(f)\}, \quad (3)$$

is the generator of a positive semigroup on L^1 . Moreover, the resolvent operator of A_Ψ at $\lambda > \omega$ is given by

$$R(\lambda, A_\Psi)f = (I + \Psi(\lambda)(I_\partial - \Psi \Psi(\lambda))^{-1}\Psi)R(\lambda, A_0)f, \quad f \in L^1. \quad (4)$$

Proof The space $\mathcal{X} = L^1 \times L^1_\partial$ is an AL -space with norm

$$\|(f, f_\partial)\| = \int_E |f(x)| m(dx) + \int_{E_\partial} |f_\partial(x)| m_\partial(dx), \quad (f, f_\partial) \in L^1 \times L^1_\partial.$$

We define operators $\mathcal{A}, \mathcal{B}: \mathcal{D}(\mathcal{A}) \rightarrow L^1 \times L^1_\partial$ with $\mathcal{D}(\mathcal{A}) = \mathcal{D} \times \{0\}$ by (see e.g. [34])

$$\mathcal{A}(f, 0) = (Af, -\Psi_0 f) \quad \text{and} \quad \mathcal{B}(f, 0) = (0, \Psi f) \quad \text{for } f \in \mathcal{D}.$$

We have $\mathcal{D}(A_0) \times \{0\} \subset \mathcal{D}(\mathcal{A}) \subset L^1 \times \{0\}$ and $\mathcal{D}(A_0)$ is dense in L^1 . Hence, $\overline{\mathcal{D}(\mathcal{A})} = L^1 \times \{0\}$. For every $\lambda > 0$ the resolvent of the operator $\mathcal{A}$ at $\lambda > 0$ is given by

$$R(\lambda, \mathcal{A})(f, f_\partial) = (R(\lambda, A_0)f + \Psi(\lambda)f_\partial, 0), \quad (f, f_\partial) \in L^1 \times L^1_\partial. \quad (5)$$

Thus $(\mathcal{A}, \mathcal{D}(\mathcal{A}))$ is resolvent positive, i.e., its resolvent operator $R(\lambda, \mathcal{A})$ is positive for all sufficiently large $\lambda > 0$. We now show that $\|\lambda R(\lambda, \mathcal{A})\| \leq 1$ for all $\lambda > 0$. Since the operator $\lambda R(\lambda, \mathcal{A})$ is positive, it is enough to show that

$$\|\lambda R(\lambda, \mathcal{A})(f, f_\partial)\| \leq \|(f, f_\partial)\| \quad \text{for nonnegative } (f, f_\partial) \in L^1 \times L^1_\partial. \quad (6)$$

The operator $R(\lambda, A_0)$ is positive, $R(\lambda, A_0)f \in \mathcal{D}(A_0) \subseteq \mathcal{D}$ and $\Psi_0 R(\lambda, A_0)f = 0$ for $f \in L^1$. From this and (2) we see that

$$\int_E AR(\lambda, A_0)f(x) m(dx) \leq \int_{E_\partial} \Psi_0 R(\lambda, A_0)f(x) m_\partial(dx) = 0$$

for all nonnegative $f \in L^1$. We have $AR(\lambda, A_0)f = \lambda R(\lambda, A_0)f - f$ for all $f \in L^1$, by (iii). Thus, we get

$$\begin{aligned} \int_E \lambda R(\lambda, A_0)f(x) m(dx) &= \int_E AR(\lambda, A_0)f(x) m(dx) + \int_E f(x) m(dx) \\ &\leq \int_E f(x) m(dx), \quad f \in L^1, f \geq 0. \end{aligned}$$

By assumption (i), $A\Psi(\lambda)f_\partial = \lambda\Psi(\lambda)f_\partial$ and $\Psi_0\Psi(\lambda)f_\partial = f_\partial$ for $f_\partial \in L^1_\partial$. This together with condition (2) implies that

$$\begin{aligned} \int_{E_\partial} \lambda\Psi(\lambda)f_\partial(x) m_\partial(dx) &= \int_E A\Psi(\lambda)f_\partial(x) m(dx) \leq \int_{E_\partial} \Psi_0\Psi(\lambda)f_\partial(x) m_\partial(dx) \\ &= \int_{E_\partial} f_\partial(x) m_\partial(dx) \end{aligned}$$

for all nonnegative $f_\partial \in L^1_\partial$, completing the proof of (6).

Let $\mathcal{I}$ be the identity operator on $\mathcal{X} = L^1 \times L^1_\partial$. We have $\mathcal{B}R(\lambda, \mathcal{A})(f, f_\partial) = (0, \Psi R(\lambda, A_0)f + \Psi\Psi(\lambda)f_\partial)$ for any (f, f_∂) . Thus, $\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A})$ is invertible if and only if $I_\partial - \Psi\Psi(\lambda)$ is invertible. In that case

$$(\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A}))^{-1}(f, f_\partial) = (f, (I_\partial - \Psi\Psi(\lambda))^{-1}(\Psi R(\lambda, A_0)f + f_\partial)).$$

Combining this with (ii) we conclude that $\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A})$ is invertible with positive inverse $(\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A}))^{-1}$ for all $\lambda > \omega$. Hence, the spectral radius of the positive operator $\mathcal{B}R(\lambda, \mathcal{A})$ is strictly smaller than 1 for some $\lambda > \omega$. It follows from [37, Theorem 1.4] that the part of $(\mathcal{A} + \mathcal{B}, \mathcal{D}(\mathcal{A}))$ in $\mathcal{X}_0 = \overline{\mathcal{D}(\mathcal{A})}$ denoted by $((\mathcal{A} + \mathcal{B})|_{\mathcal{X}_0}, \mathcal{D}((\mathcal{A} + \mathcal{B})|_{\mathcal{X}_0}))$ generates a positive semigroup on $\mathcal{X}_0$. We have $\mathcal{D}((\mathcal{A} + \mathcal{B})|_{\mathcal{X}_0}) = \mathcal{D}(A_\Psi) \times \{0\}$ and $(\mathcal{A} + \mathcal{B})|_{\mathcal{X}_0}(f, 0) = (A_\Psi f, 0)$, $f \in \mathcal{D}(A_\Psi)$. Consequently, the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ is densely defined and generates a positive semigroup on L^1 . Finally, the operator $(\mathcal{A} + \mathcal{B}, \mathcal{D}(\mathcal{A}))$ is resolvent positive with resolvent given by $R(\lambda, \mathcal{A} + \mathcal{B}) = R(\lambda, \mathcal{A})(\mathcal{I} - \mathcal{B}R(\lambda, \mathcal{A}))^{-1}$ for $\lambda > \omega$. Hence, the formula for $R(\lambda, A_\Psi)$ is also valid. $\square$

Remark 1 Condition (iv) ensures that the operator $(A_0, \mathcal{D}(A_0))$ satisfies

$$\int_E A_0 f(x) m(dx) \leq 0 \quad (7)$$

for all nonnegative $f \in \mathcal{D}(A_0)$. If, additionally,

(v) $(A_0, \mathcal{D}(A_0))$ is densely defined and resolvent positive,

then $(A_0, \mathcal{D}(A_0))$ is the generator of a *substochastic semigroup* on L^1 , i.e., a positive semigroup of contractions on L^1 . This is a consequence of the Hille–Yosida theorem, see e.g. [34, Theorem 4.4]. Thus it is enough to assume condition (v) instead of (iii). Observe also that (iii) and (iv) imply that $(0, \infty) \subseteq \rho(A_0)$.

Remark 2 Note that if $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a positive semigroup and

$$\int_E A_\Psi f(x) m(dx) = 0 \quad \text{for all nonnegative } f \in \mathcal{D}(A_\Psi), \quad (8)$$

then $(A_\Psi, \mathcal{D}(A_\Psi))$ generates a *stochastic semigroup*, i.e., a positive semigroup of operators preserving the L^1 norm of nonnegative elements (see e.g. [7, Section 6.2] and [34, Corollary 4.1]).

Remark 3 If we assume that

- (a) $(A, \mathcal{D})$ is closed,
- (b) Ψ_0 is onto and continuous with respect to the graph norm $\|f\|_A = \|f\| + \|Af\|$,

then $\Psi(\lambda)$ exists for each $\lambda > 0$ and is bounded, by [19, Lemma 1.2]. If Ψ_0 is positive, then $\Psi(\lambda)$ is positive. Thus condition (i) can be replaced by conditions (a) and (b).

Remark 4 Greiner [19, Theorem 2.1] establishes that $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a C_0 -semigroup for any bounded Ψ provided that conditions (a) and (b) hold true, $(A_0, \mathcal{D}(A_0))$ is the generator of a C_0 -semigroup, and that there exist constants $\gamma > 0$ and λ_0 such that

$$\|\Psi_0 f\| \geq \lambda \gamma \|f\|, \quad f \in \mathcal{N}(\lambda I - A), \lambda > \lambda_0. \quad (9)$$

This is condition (2.1) of Greiner [19, Theorem 2.1]. Some extensions of this result are provided in [20, 29] for unbounded Ψ , as well as in [1, 2].

Remark 5 Recall that a positive operator on an AL-space defined everywhere is automatically bounded. Thus our assumption (i) implies that $\Psi(\lambda)$ is bounded for each $\lambda > 0$. Moreover, its norm is determined through its values on the positive cone. From assumptions (i) and (iv) it follows that $\lambda \|\Psi(\lambda)\| \leq 1$ for each $\lambda > 0$, as was shown in the proof of Theorem 1. Thus, for $f = \Psi(\lambda) f_\partial$, we get (9) with $\gamma = 1$. Now suppose, as in [19], that Ψ is bounded. Then $\|\Psi \Psi(\lambda)\| \leq \|\Psi\|/\lambda$ for all $\lambda > 0$. Hence, the operator $I_\partial - \Psi \Psi(\lambda)$ is invertible for $\lambda > \|\Psi\|$. Since $I - \Psi(\lambda)\Psi$ is also invertible, we have $(I - \Psi(\lambda)\Psi)^{-1} = I + \Psi(\lambda)(I_\partial - \Psi \Psi(\lambda))^{-1}\Psi$ and, by (4),

$$R(\lambda, A_\Psi) = (I - \Psi(\lambda)\Psi)^{-1} R(\lambda, A_0).$$

Consequently, if Ψ is bounded and positive, then we get the same result as in [19].

We now look at a simple example where Theorem 1 can be easily applied and it should be compared with [1, Corollary 25].

Example 1 Consider the space $L^1 = L^1[0, 1]$ and the first derivative operator $A = \frac{d}{dx}$ with domain $\mathcal{D} = W^{1,1}[0, 1]$. Let E_∂ be the one point set $\{1\}$ and m_∂ be the point measure δ_1 at 1, so that the boundary space is $L^1_\partial = \{f_\partial : \{1\} \rightarrow \mathbb{R} : f_\partial(1) \in \mathbb{R}\}$ and can be identified with $\mathbb{R}$, by writing $f_\partial = f_\partial(1)$. Let the boundary operators Ψ_0 and Ψ be defined by

$$\Psi_0 f = f(1) \quad \text{and} \quad \Psi f = \int_{[0,1]} f(x) \mu(dx), \quad f \in W^{1,1}[0, 1],$$

where μ is a finite Borel measure. Note that for each $\lambda > 0$ and $f \in \mathcal{N}(\lambda I - A)$ we have $f' = \lambda f$. Thus f' is a continuous function. Consequently, for each $f_\partial \in L^1_\partial$ and $\lambda > 0$, the solution $f = \Psi(\lambda) f_\partial$ of equation $f' = \lambda f$ satisfying $\Psi_0(\lambda) f = f_\partial$ is of the form

$$\Psi(\lambda) f_\partial(x) = e^{\lambda(x-1)} f_\partial, \quad x \in [0, 1].$$

Hence condition (i) holds true. We have

$$\int_{[0,1]} A f(x) dx = f(1) - f(0), \quad f \in W^{1,1}[0, 1],$$

and the restriction A_0 of the operator A to

$$\mathcal{D}(A_0) = \{f \in W^{1,1}[0, 1] : f(1) = 0\}$$

is the generator of a positive semigroup. Thus conditions (iii) and (iv) hold true. If there exists $\lambda > 0$ such that

$$\int_{[0,1]} e^{\lambda(x-1)} \mu(dx) < 1, \quad (10)$$

then condition (ii) holds true and the operator $A_\psi \subseteq \frac{d}{dx}$ with domain

$$\mathcal{D}(A_\psi) = \{f \in W^{1,1}[0, 1] : f(1) = \int_{[0,1]} f(x) \mu(dx)\}$$

is the generator of a positive semigroup, by Theorem 1. Now suppose that μ is a probability measure, so that $\mu([0, 1]) = 1$. Then

$$\int_{[0,1]} e^{\lambda(x-1)} \mu(dx) \leq 1$$

for all $\lambda > 0$. Thus if (10) does not hold for any $\lambda > 0$ then $e^{\lambda(x-1)} = 1$ for all $\lambda > 0$ and μ -almost every $x \in [0, 1]$ implying that $\mu\{x \in [0, 1] : x = 1\} = 1$. Consequently, if μ is a probability measure such that $\mu \neq \delta_1$ then $(A_\psi, \mathcal{D}(A_\psi))$ is the generator of a positive semigroup.

It should be noted that in [34, Theorem 4.6] the assumption that the domain $\mathcal{D}(A_\psi)$ of the operator A_ψ is dense is missing. Making use of Theorem 1, we get the following result.

Theorem 2 *Assume conditions (i)–(iv). If B is a bounded positive operator such that*

$$\int_E (A_\psi f(x) + Bf(x)) m(dx) \leq 0 \quad \text{for all nonnegative } f \in \mathcal{D}(A_\psi),$$

then $(A_\psi + B, \mathcal{D}(A_\psi))$ is the generator of a substochastic semigroup.

We conclude this section with a result concerning the existence of steady states of the positive semigroup from Theorem 1. Note that given any $\lambda, \mu \in \rho(A_0)$ we have $\Psi(\lambda) = \Psi(\mu) + (\mu - \lambda)R(\lambda, A_0)\Psi(\mu)$, see [19, Lemma 1.3]. Thus $\Psi(\lambda) \geq \Psi(\mu)$ for $\lambda \leq \mu$. Consequently, for each nonnegative $f_\partial \in L^1_\partial$ the pointwise limit

$$\Psi(0)f_\partial = \lim_{\lambda \rightarrow 0^+} \Psi(\lambda)f_\partial \quad (11)$$

exists and $\Psi(0)f_\partial$ is nonnegative.

Theorem 3 Assume conditions (i)–(iv). Let $\Psi(0)$ be as in (11). If a nonnegative $f_{\partial} \in L^1_{\partial}$ satisfies $\Psi(0)f_{\partial} \in L^1$ and $f_{\partial} = \Psi\Psi(0)f_{\partial}$, then $\Psi(0)f_{\partial} \in \mathcal{D}(A_{\Psi})$ and $A_{\Psi}\Psi(0)f_{\partial} = 0$. Conversely, if $A_{\Psi}f = 0$ for a nonnegative $f \in \mathcal{D}(A_{\Psi})$ then $f_{\partial} = \Psi f$ satisfies $\Psi\Psi(\lambda)f_{\partial} \leq f_{\partial}$ for all $\lambda > \max\{0, \omega\}$, where ω is as in (ii).

Proof It follows from condition (i) that $\Psi(\lambda)f_{\partial} \in \mathcal{D}$, $\Psi_0\Psi(\lambda)f_{\partial} = f_{\partial}$, and $A\Psi(\lambda)f_{\partial} = \lambda f_{\partial}$ for all $\lambda > 0$. We have $\Psi(\lambda)f_{\partial} \rightarrow \Psi(0)f_{\partial}$ in L^1 , as $\lambda \rightarrow 0$. Thus $A\Psi(\lambda)f_{\partial} \rightarrow 0$ in L^1 , as $\lambda \rightarrow 0$. Recall from the proof of Theorem 1 that the operator $(\mathcal{A} + \mathcal{B})(f, 0) = (Af, \Psi f - \Psi_0 f)$, $f \in \mathcal{D}$, is a closed operator in the space $L^1 \times L^1_{\partial}$. The operators Ψ and Ψ_0 are positive and we have $\Psi\Psi(\lambda)f_{\partial} \rightarrow \Psi\Psi(0)f_{\partial} = f_{\partial} = \Psi_0\Psi(0)f_{\partial}$. Thus, $(\mathcal{A} + \mathcal{B})(\Psi(\lambda)f_{\partial}, 0) \rightarrow (0, 0)$ as $\lambda \rightarrow 0$. This implies that $\Psi(0)f_{\partial} \in \mathcal{D}(A_{\Psi})$ and $A_{\Psi}\Psi(0)f_{\partial} = 0$.

For the converse, suppose that $f \in \mathcal{D}(A_{\Psi})$ and $A_{\Psi}f = 0$. We have $R(\lambda, A_{\Psi})(\lambda f - A_{\Psi}f) = 0$. Thus $\lambda R(\lambda, A_{\Psi})f = f$ and $\Psi f = \Psi R(\lambda, A_{\Psi})(\lambda f) = \Psi R(\lambda, A_0)(\lambda f) + \Psi\Psi(\lambda)(I_{\partial} - \Psi\Psi(\lambda))^{-1}\Psi R(\lambda, A_0)(\lambda f)$, by (4). Since

$$\Psi R(\lambda, A_0)(\lambda f) = (I_{\partial} - \Psi\Psi(\lambda))(I_{\partial} - \Psi\Psi(\lambda))^{-1}\Psi R(\lambda, A_0)(\lambda f),$$

we conclude that $\Psi f = (I_{\partial} - \Psi\Psi(\lambda))^{-1}\Psi R(\lambda, A_0)(\lambda f)$. This implies that $(I_{\partial} - \Psi\Psi(\lambda))\Psi f = \Psi R(\lambda, A_0)(\lambda f) \geq 0$ for $\lambda > \max\{0, \omega\}$ and completes the proof. $\square$

3 A model of a two phase cell cycle in a single cell line

The cell cycle is the period from cell birth to its division into daughter cells. It contains four major phases: G_1 phase (cell growth before DNA replicates), S phase (DNA synthesis and replication), G_2 phase (post DNA replication growth period), and M (mitotic) phase (period of cell division). The Smith–Martin model [36] divides the cell cycle into two phases: A and B . The A phase corresponds to all or part of G_1 phase of the cell cycle and has a variable duration, while the B phase covers the rest of the cell cycle. The cell enters the phase A after birth and waits for some random time T_A until a critical event occurs that is necessary for cell division. Then the cell enters the phase B which lasts for a finite fixed time T_B . At the end of the B -phase the cell splits into two daughter cells. We assume that individual states of the cell are characterized by age $a \geq 0$ in each phase and by size $x > 0$, which can be volume, mass, DNA content or any quantity conserved through division. We assume that individual cells of size x increase their size over time in the same way, with growth rate $g(x)$ so that $dx/dt = g(x)$, and all cells age over time with unitary velocity so that $da/dt = 1$. We assume that the probability that a cell is still being in the phase A at age a is equal to $H(a)$, so the rate of exit from the phase A at age a is $\rho(a)$ given by

$$\rho(a) = -\frac{H'(a)}{H(a)}, \quad H(a) = \int_a^{\infty} h(r)dr, \quad (12)$$

where h is a probability density function defined on $[0, \infty)$, describing the distribution of the time T_A , the duration of the phase A . We make the following assumptions:

- (I) The function h in (12) is a probability density function so that $h: [0, \infty) \rightarrow [0, \infty)$ is Borel measurable and the function H in (12) satisfies: $H(0) = 1$, $H(\infty) = 0$.
- (II) The growth rate function $g: (0, \infty) \rightarrow (0, \infty)$ is globally Lipschitz continuous and $g(x) > 0$ for $x > 0$.

The Smith and Martin hypothesis [36] states that h is exponentially distributed with parameter $p > 0$, so that $\rho(a) = p$ for all $a > 0$. However, this does not agree with experimental data, see e.g. [18, 43] for recent results. The generation time of a cell, i.e. the time from birth to division, can be written as $T = T_A + T_B$. Thus the distribution of the generation time has a probability density of the form

$$h_T(t) = \begin{cases} 0, & t < T_B \\ h(t - T_B), & t \geq T_B. \end{cases}$$

Cell generation times can have lognormal or bimodal distribution (see [35]), exponentially modified Gaussian [17], or tempered stable distributions [30].

To describe the growth of cells we define

$$\Omega(x) := \int_{\bar{x}}^x \frac{1}{g(r)} dr, \quad x > 0, \quad (13)$$

where $\bar{x} > 0$ or $\bar{x} = 0$, if the integral is finite. The value $\Omega(x)$ has a simple biological interpretation. If $\bar{x}$ is the size of a cell, then $\Omega(x)$ is the time it takes the cell to reach the size x . It follows from assumption (II) that the function Ω is strictly increasing and continuous. We denote by Ω^{-1} the inverse of Ω . Define

$$\pi_t x_0 = \Omega^{-1}(\Omega(x_0) + t) \quad (14)$$

for $t \geq 0$ and $x_0 > 0$. Then $\pi_t x_0$ satisfies the initial value problem

$$x'(t) = g(x(t)), \quad x(0) = x_0 > 0.$$

If $\Omega(0) = -\infty$ then Ω^{-1} is defined on $\mathbb{R}$. Hence, formula (14) extends to all $t \in \mathbb{R}$ and $x_0 > 0$. We also set $\pi_t 0 = 0$ for $t > 0$ in this case. If $\Omega(0) = 0$ then Ω^{-1} is defined only on $(0, \infty)$ and we set $\pi_t 0 = \Omega^{-1}(t)$ for $t > 0$. We can extend formula (14) to all negative t satisfying $\Omega(x_0) + t > 0$; otherwise we set $\pi_t x_0 = 0$. Note that at time $t = T$, the generation time, a “mother cell” of size $\pi_T x_0$ divides into two daughter cells of equal size $\frac{1}{2}\pi_T x_0$.

In the probabilistic model of [22, 25, 38, 39] a sequence of consecutive descendants of a single cell was studied. Let f be the probability density function of the size distribution at birth at time t_0 of mother cells and let $t_1 > t_0$ be a random time of birth of daughter cells. Then the probability density function of the size distribution of daughter cells is given by [25, 38]

$$Pf(x) = - \int_0^{\lambda(x)} \frac{\partial}{\partial x} H(\Omega(\lambda(x)) - \Omega(r)) f(r) dr, \quad (15)$$

where

$$\lambda(x) = \max\{\pi_{-T_B}(2x), 0\} = \max\{\Omega^{-1}(\Omega(2x) - T_B), 0\}.$$

The iterates $P^2 f, P^3 f, \dots$ denote densities of the size distribution of consecutive descendants born at random times $t_2, t_3, \dots$. The operator P defined by (15) is a positive contraction on $L^1(0, \infty)$, the space of Borel measurable functions defined on $(0, \infty)$ and integrable with respect to the Lebesgue measure. Here we extend the probabilistic model to a continuous time situation by examining what happens at all times t and not only at $t_0, t_1, t_2, \dots$.

We denote by $p_1(t, a, x)$ and $p_2(t, a, x)$ the densities of the age and size distribution of cell in the A -phase and in the B -phase at time t , age a , and size x , respectively. Neglecting cell deaths the equations can be written as

$$\begin{aligned} \frac{\partial p_1(t, a, x)}{\partial t} + \frac{\partial p_1(t, a, x)}{\partial a} + \frac{\partial(g(x)p_1(t, a, x))}{\partial x} &= -\rho(a)p_1(t, a, x), \\ \frac{\partial p_2(t, a, x)}{\partial t} + \frac{\partial p_2(t, a, x)}{\partial a} + \frac{\partial(g(x)p_2(t, a, x))}{\partial x} &= 0, \end{aligned} \quad (16)$$

with boundary and initial conditions

$$p_1(t, 0, x) = 2p_2(t, T_B, 2x), \quad x > 0, t > 0, \quad (17)$$

$$p_2(t, 0, x) = \int_0^\infty \rho(a)p_1(t, a, x)da, \quad x > 0, t > 0, \quad (18)$$

$$p_1(0, a, x) = f_1(a, x), \quad p_2(0, a, x) = f_2(a, x). \quad (19)$$

In this model, cells in the A -phase enter the B -phase at rate ρ . This is taken into account by the boundary condition (18). All cells stay in the B -phase until they reach the age T_B . Then they divide their size into half (17). The model is complemented with initial conditions (19). The model we propose is different as compared to mass/maturity structured models [16,21,31,40] where a cell leaves the phase A with intensity being dependent on maturity, not age. In the case of $T_B = 0$ there is only one phase present; a maturity structured model being a continuous time extension of [24] is studied in [27], while age and volume/maturity structured population models of growth and division were studied extensively since the seminal work of [12,26,33]. We refer the reader to [28] for historical remarks concerning modeling of age structured populations and to [35,42] for recent reviews.

We look for positive solutions of (16)–(19) in the space $L^1 = L^1(E, \mathcal{E}, m)$ with $E = E_1 \times \{1\} \cup E_2 \times \{2\}$, where

$$E_1 = \{(a, x) \in (0, \infty) \times (0, \infty) : x > \pi_a 0\}$$

and

$$E_2 = \{(a, x) \in (0, T_B) \times (0, \infty) : x > \pi_a 0\},$$

m is the product of the two-dimensional Lebesgue measure and the counting measure on $\{1, 2\}$, and $\mathcal{E}$ is the σ -algebra of all Borel subsets of E . We identify $L^1 = L^1(E, \mathcal{E}, m)$ with the product of the spaces $L^1(E_1)$ and $L^1(E_2)$ of functions defined on the sets E_1 and E_2 , respectively, and being integrable with respect to the two-dimensional Lebesgue measure. We say that the operator P has a steady state in $L^1(0, \infty)$ if there exists a probability density function f such that $Pf = f$. Similarly, a semigroup $\{S(t)\}_{t \geq 0}$ has a steady state in L^1 if there exists a nonnegative $f \in L^1$ such that $S(t)f = f$ for all $t > 0$ and $\|f\|_1 = 1$ where $\|\cdot\|_1$ is the norm in L^1 .

Theorem 4 Assume conditions (I) and (II). There exists a unique positive semigroup $\{S(t)\}_{t \geq 0}$ on L^1 which provides solutions of (16)–(19) and $\{S(t)\}_{t \geq 0}$ is stochastic. If $H \in L^1(0, \infty)$ then the semigroup $\{S(t)\}_{t \geq 0}$ has a steady state in L^1 if and only if the operator P in (15) has a steady state in $L^1(0, \infty)$.

We give the proof of Theorem 4 in the next section. Theorem 4 combined with [9] implies the following sufficient conditions for the existence of steady states of (16)–(19).

Corollary 1 Assume conditions (I) and (II). Suppose that $H \in L^1(0, \infty)$ and that $|\Omega(0)| < \infty$. If

$$\mathbb{E}(T_A) := \int_0^\infty H(a)da < \liminf_{x \rightarrow \infty} (\Omega(\lambda(x)) - \Omega(x)) \quad (20)$$

then (16)–(19) has a steady state and it is unique if, additionally, $h(a) > 0$ for all sufficiently large a . Conversely, if there is $x_0 \geq 0$ such that $H(Q(\lambda(x_0))) > 0$ and $\mathbb{E}(T_A) > \sup_{x \geq x_0} (\Omega(\lambda(x)) - \Omega(x))$, then (16)–(19) has no steady states.

If the cell growth is exponential so that we have $g(x) = kx$ for all $x > 0$, where k is a positive constant, then it is known [22,38,39] that the operator P has no steady state. We now consider a linear cell growth and assume that $g(x) = k$ for all $x > 0$. We see that $\Omega(x) = x/k$, the operator P is of the form (see [39] or the last section)

$$Pf(x) = \frac{2}{k} \int_0^{2x-kT_B} h((2x-kT_B-r)/k) f(r) dr \mathbf{1}_{(0,\infty)}(2x-kT_B), \quad x > 0,$$

and condition (20) holds if and only if $\mathbb{E}(T_A) < \infty$. Combining Corollary 1 with Theorem 4 implies the following.

Corollary 2 Assume that $g(x) = k$ for $x > 0$ and that $h(a) > 0$ for all sufficiently large $a > 0$. If $\mathbb{E}(T_A) < \infty$ then the semigroup $\{S(t)\}_{t \geq 0}$ has a unique steady state.

4 Proof of Theorem 4

We will show that Theorem 4 can be deduced from Theorems 1 and 3. To this end, we introduce some notation. Let us define

$$\pi(t, a_0, x_0) = (a_0 + t, \pi_t x_0), \quad a_0, x_0 \geq 0, t \in \mathbb{R},$$

where π_t is given by (14). Then $t \mapsto \pi(t, a_0, x_0)$ solves the system of equations $a'(t) = 1$ and $x'(t) = g(x(t))$ with initial condition $a(0) = a_0$ and $x(0) = x_0$. Recall that E_1 is an open set. For any $x_0, a_0 \in E_1$ we define

$$t_-(a_0, x_0) = \inf\{s > 0 : \pi(-s, a_0, x_0) \notin \overline{E_1}\}$$

and the incoming part of the boundary ∂E_1

$$\Gamma_1^- = \{z \in \partial E_1 : z = \pi(-t_-(y), y) \text{ for some } y \in E_1 \text{ with } t_-(y) < \infty\}.$$

Observe that $t_-(a_0, x_0) = a_0$ for all $(a_0, x_0) \in E_1$ and that $\Gamma_1^- = \{0\} \times (0, \infty)$. We consider on Γ_1^- the Borel measure m_1^- being the product of the point measure δ_0 at 0 and the Lebesgue measure on $(0, \infty)$. We define the operator $T_{\max}$ on $L^1(E_1)$ by [6]

$$T_{\max} f(a, x) = -\frac{\partial(f(a, x))}{\partial a} - \frac{\partial(g(x)f(a, x))}{\partial x}$$

with domain

$$\mathcal{D}(T_{\max}) = \{f \in L^1(E_1) : T_{\max} f \in L^1(E_1)\},$$

where the differentiation is understood in the sense of distributions. Then it follows from [6] that for $f \in \mathcal{D}(T_{\max})$ the following limit

$$B^- f(z) = \lim_{t \rightarrow 0} f(\pi(t, z))$$

exists for almost every $z \in \Gamma_1^-$ with respect to the measure m_1^- on Γ_1^- . According to [6, Theorem 4.4] the operator $T_0 = T_{\max}$ with domain

$$\mathcal{D}(T_0) = \{f \in \mathcal{D}(T_{\max}) : B^- f = 0\}$$

is the generator of a substochastic semigroup on $L^1(E_1)$ given by

$$U_0(t)f(a, x) = \frac{g(\pi_{-t}x)}{g(x)} f(a-t, \pi_{-t}x) \mathbf{1}_{\{t < t_-(a, x)\}}(a, x), \quad (a, x) \in E_1, f \in L^1(E_1).$$

By [6, Proposition 5.1], the operator $(T, \mathcal{D}(T))$ defined by

$$Tf = T_{\max} f - \rho f, \quad f \in \mathcal{D}(T) = \{f \in \mathcal{D}(T_0) : \rho f \in L^1(E_1)\}$$

is the generator of a substochastic semigroup on $L^1(E_1)$ of the form

$$U_1(t)f(a, x) = e^{-\int_0^t \rho(a-r)dr} U_0(t)f(a, x), \quad (a, x) \in E_1, f \in L^1(E_1).$$

Note that we can identify the space $L^1(E_2)$ with the subspace

$$Y = \{f \in L^1(E_1) : f(a, x) = 0 \text{ for a.e. } (a, x) \in E_1 \setminus E_2\}$$

of $L^1(E_1)$ and we have $T_{\max}(\mathcal{D}(T_{\max}) \cap L^1(E_2)) \subseteq L^1(E_2)$. We set

$$t_-(a_0, x_0) = \inf\{s > 0 : \pi(-s, a_0, x_0) \notin \overline{E_2}\} = a_0, \quad (a_0, x_0) \in E_2,$$

and

$$\Gamma_2^- = \{z \in \partial E_2 : z = \pi(-t_-(y), y) \text{ for some } y \in E_2 \text{ with } t_-(y) < \infty\}.$$

We also define the exit time from the set E_2 by

$$t_+(a_0, x_0) = \inf\{s > 0 : \pi(s, a_0, x_0) \notin \overline{E_2}\}$$

and the outgoing part of the boundary ∂E_2

$$\Gamma_2^+ = \{z \in \partial E_2 : z = \pi(t_+(y), y) \text{ for some } y \in E_2\}.$$

We have $t_+(a_0, x_0) = T_B - a_0$ and $\Gamma_2^+ = \{(T_B, x) : x > \pi_{T_B} 0\}$. We define the Borel measure m_2^- on Γ_2^- as the measure m_1^- and the m_2^+ on Γ_2^+ as the product of the point measure at T_B and the one dimensional Lebesgue measure. Since $U_0(t)(L^1(E_2)) \subseteq L^1(E_2)$, the part of the operator $(T_0, \mathcal{D}(T_0))$ in $L^1(E_2)$ is the generator of a substochastic semigroup $\{U_2(t)\}_{t \geq 0}$ in $L^1(E_2)$. Moreover, the following pointwise limits exist

$$B^\pm f(z) = \lim_{t \rightarrow 0} f(\pi(\mp t, z)) \quad \text{for } f \in \mathcal{D}(T_{\max}) \cap L^1(E_2)$$

for almost every $z \in \Gamma_2^\pm$ with respect to the Borel measure $m_2^\pm$ on $\Gamma_2^\pm$.

Let $E_\partial = \Gamma_1^- \times \{1\} \cup \Gamma_2^- \times \{2\}$, $\mathcal{E}_\partial$ be the σ -algebra of Borel subsets of E_∂ and m_∂ be the product of the Lebesgue measure on the line $\{0\} \times (0, \infty)$ and the counting measure on $\{1, 2\}$. To simplify the notation we identify $L_\partial^1 = L^1(E_\partial, \mathcal{E}_\partial, m_\partial)$ with the product space $L^1(0, \infty) \times L^1(0, \infty)$. We define operators A_1 and A_2 by

$$A_1 f_1 = T_{\max} f_1 - \rho f_1, \quad f_1 \in \mathcal{D}_1 = \{f_1 \in L^1(E_1) : T_{\max} f_1, \rho f_1 \in L^1(E_1)\}, \quad (21)$$

$$A_2 f_2 = T_{\max} f_2, \quad f_2 \in \mathcal{D}_2 = \{f_2 \in L^1(E_2) : T_{\max} f_2 \in L^1(E_2)\}. \quad (22)$$

We set

$$\mathcal{D} = \{(f_1, f_2) \in \mathcal{D}_1 \times \mathcal{D}_2 : B^- f_1, B^- f_2 \in L^1(0, \infty)\}$$

and we define the operator A on $\mathcal{D}$ by setting $Af = (A_1 f_1, A_2 f_2)$ for $f = (f_1, f_2) \in \mathcal{D}$. We take operators $\Psi_0, \Psi : \mathcal{D} \rightarrow L^1_\partial$ of the form

$$\Psi_0 f = (B^- f_1, B^- f_2), \quad f = (f_1, f_2) \in \mathcal{D}, \quad (23)$$

and

$$\Psi f(x) = \left(2B^+ f_2(T_B, 2x) \mathbf{1}_{(\pi_{T_B}(0), \infty)}(2x), \int_0^\infty \rho(a) f_1(a, x) \mathbf{1}_{(0, \infty)}(\pi_{-a} x) da \right) \quad (24)$$

for $f = (f_1, f_2) \in \mathcal{D}$. We show that the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a positive semigroup on L^1 , where $A_\Psi f = Af$ for $f \in \mathcal{D}(A_\Psi) = \{f \in \mathcal{D} : \Psi_0 f = \Psi f\}$. To this end, we check that assumptions (i)–(iv) of Theorem 1 from Sect. 2 are satisfied.

We first show that conditions (iii) and (iv) hold. The operator A restricted to $\mathcal{D}(A_0) = \{(f_1, f_2) \in \mathcal{D}_1 \times \mathcal{D}_2 : B^- f_1 = 0, B^- f_2 = 0\}$ is the generator of the semigroup $\{S_0(t)\}_{t \geq 0}$ given by

$$S_0(t)f = (U_1(t)f_1, U_2(t)f_2), \quad t \geq 0, f = (f_1, f_2) \in L^1,$$

since $\{U_1(t)\}_{t \geq 0}$ and $\{U_2(t)\}_{t \geq 0}$ are semigroups on the spaces $L^1(E_1)$ and $L^1(E_2)$ with the corresponding generators. The semigroup $\{S_0(t)\}_{t \geq 0}$ is substochastic. For all nonnegative $f = (f_1, f_2) \in \mathcal{D}$ we have

$$\begin{aligned} \int_E Af dm - \int_{E_\partial} \Psi_0 f dm_\partial &= \int_{E_1} A_1 f_1(a, x) dadx + \int_{E_2} A_2 f_2(a, x) dadx \\ &\quad - \int_{\Gamma_1^-} B^- f_1(z) m_1^-(dz) - \int_{\Gamma_2^-} B^- f_2(z) m_2^-(dz). \end{aligned}$$

By [6, Proposition 4.6], this reduces to

$$\int_E Af dm - \int_{E_\partial} \Psi_0 f dm_\partial = - \int_{E_1} \rho(a) f_1(a, x) dadx - \int_{\Gamma_2^+} B^+ f_2(z) m_2^+(dz), \quad (25)$$

implying that condition (iv) holds.

For $f = (f_1, f_2) \in \mathcal{D}$ we can rewrite the equation $\lambda f - Af = 0$ as

$$\begin{aligned} \frac{\partial}{\partial a} \left(e^{\int_0^a \rho(r) dr} f_1(a, x) \right) &= - \frac{\partial}{\partial x} (g(x) f_1(a, x)) - \lambda f_1(a, x), \\ \frac{\partial}{\partial a} (f_2(a, x)) &= - \frac{\partial}{\partial x} (g(x) f_2(a, x)) - \lambda f_2(a, x). \end{aligned}$$

Hence, we see that the right inverse of Ψ_0 when restricted to the nullspace of $\lambda I - A$ is given by

$$\Psi(\lambda)f_{\partial}(a, x) = \left(e^{-\lambda a - \int_0^a \rho(r)dr} f_{\partial,1}(\pi_{-a}x), e^{-\lambda a} f_{\partial,2}(\pi_{-a}x) \mathbf{1}_{(0,T_B)}(a) \right) \frac{g(\pi_{-a}x)}{g(x)} \quad (26)$$

for $(a, x) \in E_1$ and $f_{\partial} = (f_{\partial,1}, f_{\partial,2}) \in L^1_{\partial}$. Moreover, if $(f_1, f_2) = \Psi(\lambda)f_{\partial}$ then

$$B^- f_1(0, x) = \lim_{t \rightarrow 0} f_1(t, \pi_t x) = \lim_{t \rightarrow 0} e^{-\lambda t - \int_0^t \rho(r)dr} f_{\partial,1}(x) = f_{\partial,1}(x).$$

Thus $f_1 \in \mathcal{D}_1$. Similarly, $f_2 \in \mathcal{D}_2$. Hence, condition (i) holds.

To check condition (ii) take $\lambda > 0$ and $f_{\partial} \in L^1_{\partial}$. For $(f_1, f_2) = \Psi(\lambda)f_{\partial}$ we have

$$f_2(a, x) = e^{-\lambda a} f_{\partial,2}(\pi_{-a}x) \frac{g(\pi_{-a}x)}{g(x)} \mathbf{1}_{(0,\infty)}(\pi_{-a}x) \mathbf{1}_{(0,T_B)}(a).$$

This implies that

$$\begin{aligned} B^+ f_2(T_B, x) &= \lim_{t \rightarrow 0} f_2(T_B - t, \pi_{-t}x) \\ &= \lim_{t \rightarrow 0} e^{-\lambda(T_B - t)} f_{\partial,2}(\pi_{-T_B}x) \frac{g(\pi_{-T_B}x)}{g(\pi_{-t}x)} \mathbf{1}_{(0,\infty)}(\pi_{-T_B}x) \\ &= e^{-\lambda T_B} f_{\partial,2}(\pi_{-T_B}x) \frac{g(\pi_{-T_B}x)}{g(x)} \mathbf{1}_{(0,\infty)}(\pi_{-T_B}x). \end{aligned}$$

Hence,

$$\Psi\Psi(\lambda)f_{\partial}(x) = ((\Psi\Psi(\lambda)f_{\partial})_1(x), (\Psi\Psi(\lambda)f_{\partial})_2(x)),$$

where

$$(\Psi\Psi(\lambda)f_{\partial})_1(x) = 2e^{-\lambda T_B} f_{\partial,2}(\pi_{-T_B}(2x)) \frac{g(\pi_{-T_B}(2x))}{g(2x)} \mathbf{1}_{(0,\infty)}(\pi_{-T_B}(2x))$$

and, by (12),

$$(\Psi\Psi(\lambda)f_{\partial})_2(x) = \int_0^{\infty} h(a) e^{-\lambda a} f_{\partial,1}(\pi_{-a}x) \frac{g(\pi_{-a}x)}{g(x)} \mathbf{1}_{(0,\infty)}(\pi_{-a}x) da.$$

For $f_{\partial} \in L^1_{\partial}$ we obtain

$$\begin{aligned} \|\Psi\Psi(\lambda)f_{\partial}\| &\leq e^{-\lambda T_B} \int_0^{\infty} |f_{\partial,2}(z)| dz + \int_0^{\infty} h(a) e^{-\lambda a} da \int_0^{\infty} |f_{\partial,1}(y)| dy \\ &\leq \max \left\{ e^{-\lambda T_B}, \int_0^{\infty} h(a) e^{-\lambda a} da \right\} \|f_{\partial}\|, \end{aligned}$$

showing that $\|\Psi\Psi(\lambda)\| < 1$ for all $\lambda > 0$. Consequently, it follows from Theorem 1 that the operator $(A_\Psi, \mathcal{D}(A_\Psi))$ is the generator of a positive semigroup $\{S(t)\}_{t \geq 0}$ on L^1 . The semigroup $\{S(t)\}_{t \geq 0}$ is stochastic, since (8) holds by (25).

Next assume that $H \in L^1(0, \infty)$. By Theorem 3, it remains to look for fixed points of the operator $\Psi\Psi(0)$. Here $\Psi(0)$ defined as in (11) is, by (26), of the form

$$\Psi(0)f_\partial(a, x) = \left(e^{-\int_0^a \rho(r)dr} f_{\partial,1}(\pi_{-a}x), f_{\partial,2}(\pi_{-a}x)\mathbf{1}_{[0,T_B)}(a) \right) \frac{g(\pi_{-a}x)}{g(x)} \quad (27)$$

for $(a, x) \in E_1$. Observe that $\Psi(0)f_\partial \in L^1$ for $f_\partial \in L^1_\partial$, since $e^{-\int_0^a \rho(r)dr} = H(a)$, by (12), and

$$\|\Psi(0)f_\partial\| \leq \int_0^\infty H(a)da \int_0^\infty |f_{\partial,1}(y)|dy + T_B \int_0^\infty |f_{\partial,2}(y)|dy.$$

We have $\pi_{-T_B}(2x) = \varOmega^{-1}(\varOmega(2x) - T_B) = \lambda(x)$ if $2x > \pi_{T_B}0$ and

$$\lambda'(x) = 2 \frac{g(\lambda(x))}{g(2x)} \mathbf{1}_{(0,\infty)}(\lambda(x)). \quad (28)$$

Hence

$$(\Psi\Psi(0)f_\partial)_1(x) = f_{\partial,2}(\lambda(x))\lambda'(x)$$

and

$$(\Psi\Psi(0)f_\partial)_2(x) = \int_0^\infty \rho(a)e^{-\int_0^a \rho(r)dr} f_{\partial,1}(\pi_{-a}x) \frac{g(\pi_{-a}x)}{g(x)} \mathbf{1}_{(0,\infty)}(\pi_{-a}x)da.$$

If $f_\partial = \Psi\Psi(0)f_\partial$ then $f_{\partial,2}(x) = (\Psi\Psi(0)f_\partial)_2(x)$ and $f_{\partial,1}$ satisfies

$$\begin{aligned} f_{\partial,1}(x) &= (\Psi\Psi(0)f_\partial)_1(x) \\ &= 2 \int_0^\infty h(a)f_{\partial,1}(\pi_{-a}(\lambda(x))) \frac{g(\pi_{-a}(\lambda(x)))}{g(2x)} \mathbf{1}_{(0,\infty)}(\pi_{-a}(\lambda(x)))da. \end{aligned}$$

By changing the variables $r = \pi_{-a}(\lambda(x))$, we arrive at the equation

$$f_{\partial,1}(x) = \frac{2}{g(2x)} \int_0^{\lambda(x)} h(\varOmega(\lambda(x)) - \varOmega(r))f_{\partial,1}(r)dr, \quad x > 0. \quad (29)$$

Equivalently, $f_{\partial,1} = Pf_{\partial,1}$ where P is as in (15). Consequently, equation $\Psi\Psi(0)f_\partial = f_\partial$ has a solution in L^1_∂ if and only if the equation $Pf_{\partial,1} = f_{\partial,1}$ has a solution in $L^1(0, \infty)$. Observe also that the operator $\Psi\Psi(0)$ preserves the L^1_∂ norm on nonnegative elements. Hence, if $f_\partial \in L^1_\partial$ is such that $\Psi\Psi(0)f_\partial \leq f_\partial$ then $\Psi\Psi(0)f_\partial = f_\partial$. Thus the assertion follows from Theorem 3.

5 Final remarks

Our model can be described as a piecewise deterministic Markov process $\{X(t)\}_{t \geq 0}$. We considered three variables (a, x, i) , where $i = 1$ if a cell is in the phase A , $i = 2$ if it is in the phase B , the variable x describes the cell size, and a describes the time which elapsed since the cell entered the i th phase. Let $t_0 = 0$. If we observe consecutive descendants of a given cell and the n th generation time is denoted by t_n , then $t_{n+1} = s_n + T_B$ where s_n is the time when the cell from the n th generation enters the phase B , $n \geq 0$. A newborn cell at time t_n is with age $a(t_n) = 0$ and with initial size equal to $x(t_n^-)/2$, where $x(t_n^-)$ is the size of its mother cell. The cell ages with velocity 1 and its size grows according to the equations $x'(t) = g(x(t))$ for $t \in (t_n, s_n)$. If the cell enters the phase B then its age is reset to 0 and its size still grows according to $x'(t) = g(x(t))$ for $t \in (s_n, s_n + T_B)$. We have

$$a(s_n) = 0, \quad x(s_n) = x(s_n^-), \quad i(s_n) = 2, \quad (30)$$

and at the end of the second phase the cell divides into two cells, so that we have

$$a(t_{n+1}) = 0, \quad x(t_{n+1}) = \frac{1}{2}x(t_{n+1}^-), \quad i(t_{n+1}) = 1. \quad (31)$$

Thus the process $X(t) = (a(t), x(t), i(t))$ satisfies the following system of ordinary differential equations

$$a'(t) = 1, \quad x'(t) = g(x(t)), \quad i'(t) = 0,$$

between consecutive times $t_0, s_0, t_1, s_1, \dots$, called *jump times*. At jump times the process is given by (30) and (31). If the distribution of $X(0)$ has a density f then $X(t)$ has a density $S(t)f$, i.e.,

$$\Pr(X(t) \in B_i \times \{i\}) = \int_{B_i} (S(t)f)_i(a, x) da dx$$

for any Borel set $B_i \subset E_i$, where $\{S(t)\}_{t \geq 0}$ is the stochastic semigroup from Theorem 4.

If $f_{\partial,1}$ is the density of the size distribution at time $t_0 = 0$ and $f_{\partial,2}$ is the density of the distribution of size at time s_1 , then the distribution of size at time t_1 is given by

$$\Pr(x(t_1) \leq x) = \Pr(\pi_{T_B} x(s_1) \leq 2x) = \Pr(x(s_1) \leq \lambda(x)) = \int_0^{\lambda(x)} f_{\partial,2}(z) dz$$

and

$$f_{\partial,2}(z) = \int_0^\infty h(a) \hat{\pi}_a f_{\partial,1}(z) da, \quad (32)$$

where

$$\hat{\pi}_a f_{\partial,1}(z) = f_{\partial,1}(\pi_{-a}z) \frac{g(\pi_{-a}z)}{g(z)} \mathbf{1}_{(0,\infty)}(\pi_{-a}z)$$

is the density of the size $x(a)$ of the cell at time a , if $x(0)$ has a density $f_{\partial,1}$. Thus the density of the mass $x(t_1)$ is given by

$$\frac{d}{dx} \Pr(x(t_1) \leq x) = f_{\partial,2}(\lambda(x))\lambda'(x) = P f_{\partial,1}(x)$$

for Lebesgue almost every $x \in (0, \infty)$, where P is as in (15). Now, if the operator P has a steady state $f_{\partial,1} \in L^1(0, \infty)$ so that $f_{\partial,1}$ satisfies (29) and if $f_{\partial,2}$ is as in (32), then $f^* = (f_1^*, f_2^*)$ given by

$$f_1^*(a, x) = e^{-\int_0^a \rho(r)dr} \hat{\pi}_a f_{\partial,1}(x), \quad f_2^*(a, x) = \hat{\pi}_a f_{\partial,2}(x) \mathbf{1}_{(0,T_B)}(a) \quad (33)$$

is the steady state for the semigroup $\{S(t)\}_{t \geq 0}$ existing by Theorem 4. Moreover, it is unique if P has a unique steady state.

Remark 6 It should be noted that in the two-phase cell cycle model in [31] the rate of exit from the phase A depends on x , not on a , and that there is no such equivalence between the existence of steady states as presented in Theorem 4. Our results remain true if we assume as in [31] that division into unequal parts takes place. Methods as in [31,34] can also be used in our model to study asymptotic behaviour of the semigroup $\{S(t)\}_{t \geq 0}$. For a different approach to study positivity and asymptotic behaviour of solutions of population equations in L^1 we refer to [32].

We conclude this section with an extension of the age-size dependent model from [12] to a model with two phases. Let $p_i(t, a, x)$ be the function representing the distribution of cells over all individual states a and x at time t in the phase A for $i = 1$ or B for $i = 2$, i.e., $\int_{a_1}^{a_2} \int_{x_1}^{x_2} p_i(t, a, x) da dx$ is the number of cells with age between a_1 and a_2 and size between x_1 and x_2 at time t in the given phase. Then p_1 and p_2 satisfy Eqs. (16), (18), (19) while the boundary condition (17) takes the form

$$p_1(t, 0, x) = 4p_2(t, T_B, 2x), \quad x > 0, t > 0, \quad (34)$$

since a mother cell at the moment of division T_B has size $2x$ and gives birth to two daughters of size x entering the phase A at age 0.

Theorem 5 Assume conditions (I) and (II). Then there exists a unique positive semigroup on L^1 which provides solutions of (16), (34), (18), (19).

This follows from Theorem 1 in the same way as Theorem 4, where now to check condition (ii) we note that

$$\|\Psi \Psi(\lambda) f_{\partial}\| \leq \max \left\{ 2e^{-\lambda T_B}, \int_0^\infty h(a) e^{-\lambda a} da \right\} \|f_{\partial}\|$$

for all $f_{\partial} \in L^1_{\partial}$ and $\lambda > 0$, implying that $\|\Psi\psi(\lambda)\| < 1$ for all $\lambda > \omega$ with $\omega = \log 2/T_B$.

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