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Necessary and Sufficient Conditions for Asynchronous Exponential Growth in Age Structured Cell Populations with Quiescence

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A linear model on age structured cell population is analyzed. The population is divided into proliferating and quiescent compartments. Necessary and sufficient conditions are established for the population to exhibit the asymptotic behavior of asynchronous exponential growth. The model is analyzed as a semigroup of linear operators which is shown to be eventually compact and irreducible.

1. INTRODUCTION

In the investigation of cell population dynamics it is important to consider the structure of the population with respect to individual properties such as age, size, or other physical characteristics. In structured cell

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population dynamics the property of asynchronous (or balanced) exponential growth is frequently observed. Asynchronous exponential growth occurs when a proliferating cell population converges (after multiplication by an exponential factor in time) to a characteristic distribution of structure that depends on the initial distribution of structure through a one-dimensional strictly positive projection. This behavior means that the ultimate distribution of the structure of cells will be strictly positive through all possible structure values no matter how the structure is initially distributed. The property of asynchronous exponential growth has been investigated in models of age structured cell populations by Webb [11], Clement *et al*. [1], and Iannelli [8]. The property of asynchronous exponential growth has been investigated in models of size structured cell populations by Diekmann *et al*. [2] and Greiner and Nagel [3].

In many cell populations not all cells are progressing to mitosis, but some are in a quiescent or resting state for an extended period of time. The property of asynchronous exponential growth has been investigated in models of size structured cell populations with proliferating and quiescent compartments in [5–7, 10]. In this paper we develop a model of an age structured cell population with proliferating and quiescent subpopulations. We establish necessary and sufficient conditions on the functions controlling transition between the two compartments to assure that the population has the property of asynchronous exponential growth. These conditions have the following interpretation: Asynchronous exponential growth occurs if and only if the youngest proliferating cells have the possibility to transit to the quiescent compartment and the oldest quiescent cells have the possibility to transit to the proliferating compartment. The techniques we use to prove this result are drawn from the theory of semigroups of positive linear operators in Banach lattices.

2. THE MODEL

In this paper we analyze a linear model of cell population dynamics structured by age with two interacting compartments: proliferating cells and quiescent cells. Proliferating cells grow, divide, and transit to the quiescent compartment, whereas quiescent cells do not grow and can only transit back and forth to proliferation.

We assume that an individual is fully characterized by its age and the state (either proliferating or quiescent) it is in. This means that all quantities that determine the development of an individual, such as growth and death rates and transition rates from one state to the other, depend only on age and state.

We assume that division is the only cause of cell loss and all daughter cells are born in the proliferating state. An individual in the quiescent compartment cannot divide as long as it stays in this state.

We let t denote time, a age, and we denote the densities of cells in the proliferating and the quiescent state by $p(a,t)$ and $q(a,t)$, respectively. Thus, for instance, $\int_{a_1}^{a_2} p(a,t)\,da$ is the number of proliferating cells which at time t have age between a_1 and a_2.

We can now write the balance equations for the two compartments:

$$\begin{aligned}
\frac{\partial p}{\partial t} + \frac{\partial p}{\partial a} &= -\mu(a)p - \sigma(a)p + \tau(a)q, \qquad 0 < a < a_1,\, t > 0\\
\frac{\partial q}{\partial t} + \frac{\partial q}{\partial a} &= \sigma(a)p - \tau(a)q, \qquad 0 < a < a_1,\, t > 0\\
p(0,t) &= 2\int_0^{a_1} \mu(a)p(a,t)\,da, \qquad t > 0\\
q(0,t) &= 0, \qquad t > 0\\
p(a,0) &= \varphi(a), \qquad 0 < a < a_1\\
q(a,0) &= \psi(a), \qquad 0 < a < a_1,
\end{aligned} \tag{PQ}$$

where μ is the division rate, σ is the transition rate from proliferating stage to the quiescent stage, and τ is the transition rate from quiescent stage to proliferating stage. We assume that there exists a maximal age of division a_1, that is, cells older than a_1 do not contribute to the renewal of the population. So, we simply neglect them and consider only the population of proliferating and quiescent individuals of age less than or equal to a_1.

Throughout the paper we make the following assumptions:

HYPOTHESIS (H1). $\mu \in L^{\infty}_{+}(0, a_1)$. *There exists* ϵ_0, $0 < \epsilon_0 < a_1$, *such that*

$$\forall \epsilon \in]0, \epsilon_0[, \qquad \int_{a_1-\epsilon}^{a_1} \mu(a)\,da > 0.$$

HYPOTHESIS (H2). $\sigma, \tau \in L^1_{+}(0, a_1)$. *The functions* σ, τ *do not vanish identically.*

The natural choice for the state space is $X = L^1(0,a_1) \times L^1(0,a_1)$. The solutions of the model (PQ) form a strongly continuous semigroup of positive linear bounded operators $\{U(t)\}_{t \geq 0}$ in X, according to the formula

$$U(t)\begin{pmatrix}\varphi\\ \psi\end{pmatrix} = \begin{pmatrix}p(.,t)\\ q(.,t)\end{pmatrix}, \qquad t \geq 0,$$

where $p(.,t)$, $q(.,t)$ are the solutions of (PQ) corresponding to given initial age distributions

$$p(a,0) = \varphi(a); \qquad q(a,0) = \psi(a), \qquad a > 0$$

$\varphi, \psi \in L^1(0, a_1)$.

Using the general theory of positive operator semigroups in Banach lattices, we can obtain the asymptotic behavior of solutions of (PQ). In fact, we prove here that these solutions have *asynchronous exponential growth*. This means that there exist a real constant λ^* and a strictly positive rank one projection Π on X such that

$$\forall \begin{pmatrix} \varphi \\ \psi \end{pmatrix} \in X, \qquad \lim_{t \to +\infty} e^{-\lambda^* t} U(t) \begin{pmatrix} \varphi \\ \psi \end{pmatrix} = \Pi \begin{pmatrix} \varphi \\ \psi \end{pmatrix}.$$

λ^* is the *Maltusian parameter* and $\Pi(\varphi, \psi)^T$ the *exponential steady state*.

We refer the reader to [9, 1] for the general theory of C_0-semigroups of positive operators in Banach lattices. Asynchronous exponential growth of the semigroup $\{U(t)\}_{t \geq 0}$ results from two important properties it possesses: compactness and irreducibility. The main result we obtain here is to characterize the irreducibility of the semigroup in terms of the support of rates σ and τ.

It will be useful in the following sections to consider (PQ) as a perturbation of two uncoupled problems:

$$\begin{aligned} &\frac{\partial p}{\partial t} + \frac{\partial p}{\partial a} = -\mu(a)p - \sigma(a)p, \qquad 0 < a < a_1, t > 0 \\ &p(0,t) = 2\int_0^{a_1} \mu(a)p(a,t)\,da, \qquad t > 0 \\ &p(a,0) = \hat{p}(a), \qquad 0 < a < a_1 \end{aligned} \tag{P}$$

$$\begin{aligned} &\frac{\partial q}{\partial t} + \frac{\partial q}{\partial a} = -\tau(a)q, \qquad 0 < a < a_1, t > 0 \\ &q(0,t) = 0, \qquad t > 0 \\ &q(a,0) = \hat{q}(a), \qquad 0 < a < a_1. \end{aligned} \tag{Q}$$

Problem (P) can be reduced to an integral equation for $B(t) = p(0,t)$. In fact, we have

$$p(a,t) = \begin{cases} \hat{p}(a-t)\exp\left(-\int_{a-t}^{a} (\mu(s) + \sigma(s))\,ds\right), & a > t \\ B(t-a)\exp\left(-\int_0^{a} (\mu(s) + \sigma(s))\,ds\right), & a < t, \end{cases}$$

where $\hat{p} \in L^1(0, a_1)$ is the initial age distribution, and

$$B(t) = 2\int_0^{a_1} \mu(a) e^{-\int_0^a (\mu(s) + \sigma(s))\,ds} B(t-a)\,da, \qquad a < t.$$

Let $\{T(t)\}_{t \geq 0}$ be the semigroup associated for problem (P) in $L^1(0, a_1)$. $\{T(t)\}_{t \geq 0}$ is positive, eventually compact (compact for $t \geq a_1$), and irreducible [1, Sect. 10.2]. Also, we can write

$$(T(t)\hat{p})(a) = (T(t-a)\hat{p})(0)\exp\left(-\int_0^a (\mu(s) + \sigma(s))\,ds\right), \qquad t > a. \tag{1}$$

The solution of problem (Q) is

$$q(a,t) = \begin{cases} \hat{q}(a-t)\exp\left(-\int_{a-t}^a \tau(s)\,ds\right), & a > t \\ 0, & a < t, \end{cases}$$

where $\hat{q} \in L^1(0, a_1)$ is the initial age distribution. We denote by $\{S(t)\}_{t \geq 0}$ the associated semigroup. It is obvious that $\forall t > a_1$, $S(t) = 0$.

Using a *variation of constants formula*, we can express the semigroup $\{U(t)\}_{t \geq 0}$ in terms of the semigroups $\{T(t)\}_{t \geq 0}$, $\{S(t)\}_{t \geq 0}$,

$$p(.,t) = T(t)\hat{p} + \int_0^t T(t-s)(\tau(.)q(.,s))\,ds \tag{2}$$

$$q(.,t) = S(t)\hat{q} + \int_0^t S(t-s)(\sigma(.)p(.,s))\,ds \tag{3}$$

or, in vector form

$$U(t)\begin{pmatrix} \hat{p} \\ \hat{q} \end{pmatrix} = \begin{pmatrix} T(t) & 0 \\ 0 & S(t) \end{pmatrix}\begin{pmatrix} \hat{p} \\ \hat{q} \end{pmatrix} + \int_0^t \begin{pmatrix} T(t-s) & 0 \\ 0 & S(t-s) \end{pmatrix}\begin{pmatrix} 0 & \tau(.) \\ \sigma(.) & 0 \end{pmatrix} U(s)\begin{pmatrix} \hat{p} \\ \hat{q} \end{pmatrix} ds.$$

3. COMPACTNESS OF THE SEMIGROUP $U(t)$

Let $W(.) = (w_{ij}(.))_{i,j=1,2}$, $W(0) = \mathrm{Id}$, be the fundamental matrix of the linear differential system

$$\begin{pmatrix} p'(a) \\ q'(a) \end{pmatrix} = \begin{pmatrix} -\mu(a) - \sigma(a) & \tau(a) \\ \sigma(a) & -\tau(a) \end{pmatrix}\begin{pmatrix} p \\ q \end{pmatrix}.$$

We make a change of the unknown variables p, q into new variables $\tilde{p}$, $\tilde{q}$, defined by

$$\begin{pmatrix} p \\ q \end{pmatrix} = W(a)\begin{pmatrix} \tilde{p} \\ \tilde{q} \end{pmatrix}.$$

Then (PQ) is transformed to

$$\begin{aligned}
&\frac{\partial \tilde{p}}{\partial t} + \frac{\partial \tilde{p}}{\partial a} = 0, \qquad 0 < a < a_1,\ t > 0\\
&\frac{\partial \tilde{q}}{\partial t} + \frac{\partial \tilde{q}}{\partial a} = 0, \qquad 0 < a < a_1,\ t > 0\\
&\quad \tilde{p}(0,t) = 2\int_0^{a_1} \mu(a)\big(w_{11}(a)\tilde{p}(a,t) + w_{12}(a)\tilde{q}(a,t)\big)\,da, \qquad t > 0\\
&\quad \tilde{q}(0,t) = 0, \qquad t > 0\\
&\quad \tilde{p}(a,0) = \varphi(a), \qquad 0 < a < a_1\\
&\quad \tilde{q}(a,0) = \psi(a), \qquad 0 < a < a_1.
\end{aligned} \tag{$\widetilde{\mathrm{PQ}}$}$$

This problem can be reduced to an integral equation in $\tilde{p}(0,t)$, since the solutions are

$$\tilde{q}(a,t) = \begin{cases} \tilde{q}(a-t,0) = \psi(a-t), & a > t\\ 0, & a < t \end{cases}$$

$$\tilde{p}(a,t) = \begin{cases} \tilde{p}(a-t,0) = \varphi(a-t), & a > t\\ \tilde{p}(0,t-a), & a < t \end{cases}$$

with

$$\tilde{p}(0,t) = \begin{cases} 2\int_0^t \mu(a) w_{11}(a)\tilde{p}(0,t-a)\,da \\ \quad + 2\int_t^{a_1} \mu(a)\big[w_{11}(a)\varphi(a-t) + w_{12}(a)\psi(a-t)\big]\,da, \\ \qquad\qquad t < a_1 \\ 2\int_0^{a_1} \mu(a) w_{11}(a)\tilde{p}(0,t-a)\,da, \qquad t > a_1, \end{cases}$$

where

$$\begin{pmatrix} \varphi(a) \\ \psi(a) \end{pmatrix} = \begin{pmatrix} \tilde{p}(a,0) \\ \tilde{q}(a,0) \end{pmatrix} = W^{-1}(a)\begin{pmatrix} \hat{p}(a) \\ \hat{q}(a) \end{pmatrix}$$

are the initial age distributions.

We introduce the notations

$$K(a) = \begin{cases} \mu(a) w_{11}(a), & a \in [0, a_1] \\ 0, & a > a_1 \end{cases}$$

$$G_{\varphi\psi}(t) = \begin{cases} 2\int_t^{a_1} \mu(a)\left[w_{11}(a)\varphi(a-t) + w_{12}(a)\psi(a-t)\right] da, & t < a_1 \\ 0, & t > a_1 \end{cases}$$

so, $\tilde{p}(0,.)$ is the unique solution of

$$\tilde{p}(0,t) = G_{\varphi\psi}(t) + 2\int_0^t K(a)\tilde{p}(0,t-a)\,da, \qquad t > 0.$$

LEMMA 1. *The operator $H : X \to L^1(0, 2a_1)$ defined by*

$$H\begin{pmatrix} \varphi \\ \psi \end{pmatrix} = \tilde{p}(0,.)$$

is linear and bounded.

Proof. Hypotheses (H1), (H2) imply

$$K \in L^\infty(\mathbf{R}_+) \cap L^1(\mathbf{R}_+); \qquad \forall T > 0, G_{\varphi\psi} \in C([0,T]).$$

Then $\forall T > 0, \tilde{p}(0,.) \in C([0,T])$ and there exists $R \in L^1_{loc}(\mathbf{R}_+)$ such that

$$\tilde{p}(0,t) = G_{\varphi\psi}(t) - \int_0^t R(t-s) G_{\varphi\psi}(s)\,ds$$

(see [8, Appendix II, Theorem 1.1]) and the lemma follows.

THEOREM 1. *The semigroup $\{U(t)\}_{t \geq 0}$ is eventually compact, that is, the operators $U(t)$ are compact for $t \geq 2a_1$.*

Proof. It suffices to prove that $\tilde{U}(2a_1)$ is a compact operator, where $\{\tilde{U}(t)\}_{t \geq 0}$ is the semigroup associated with the problem $(\widetilde{\mathrm{PQ}})$. Consider the operators defined by

$$S : L^1(a_1, 2a_1) \to L^1(0, a_1), \qquad (S\psi)(.) = \psi(2a_1 - .)$$

$$T : L^1(0, 2a_1) \to L^1(a_1, 2a_1),$$

$$(T\varphi)(t) = 2\int_0^{a_1} K(a)\varphi(t-a)\,da.$$

S is linear, bounded, and T is compact (it is a convolution in L^1, see [4, Sect. 2.2, Theorem 2.5]). Therefore, $H \circ T \circ S$ is compact, which proves the compactness of

$$\tilde{U}(2a_1)\begin{pmatrix}\varphi\\ \psi\end{pmatrix} = \begin{pmatrix}(H \circ T \circ S)(\varphi, \psi)^T\\ 0\end{pmatrix}.$$

4. IRREDUCIBILITY OF THE SEMIGROUP

We devote this section to establishing the main result of this paper, namely the characterization of irreducibility of the semigroup associated with (PQ) in terms of the support of the rates σ, τ.

DEFINITION. A C_0-linear semigroup $\{T(t)\}_{t \geq 0}$ in the Banach space X is irreducible iff $\forall x \in X_+$, $x \neq 0$, and $x^* \in X^*_+$, $x^* \neq 0$, there is $t > 0$ such that $\langle x^*, T(t)x \rangle > 0$.

THEOREM 2. *Under Hypotheses* (H1), (H2), *the semigroup* $\{U(t)\}_{t \geq 0}$ *is irreducible iff there are* $\epsilon_1 > 0$, $\epsilon_2 > 0$ *such that both the following conditions hold*

$$\forall \epsilon \in]0, \epsilon_1[, \qquad \int_{a_1-\epsilon}^{a_1} \tau(a)\, da > 0, \tag{H3}$$

$$\forall \epsilon \in]0, \epsilon_2[, \qquad \int_0^{\epsilon} \sigma(a)\, da > 0. \tag{H4}$$

Proof. *Sufficiency*. We first claim that if the initial age distribution $\hat{q} \neq 0$, then there exists $t_0 > 0$ such that $p(., t_0) \neq 0$.

If this is not true, we should have $\forall t \geq 0$, $p(., t) = 0$. Then

$$0 = \frac{\partial p}{\partial t} + \frac{\partial p}{\partial a} = \tau(a) q.$$

Therefore

$$\frac{\partial q}{\partial t} + \frac{\partial q}{\partial a} = \sigma(a) p - \tau(a) q = 0$$

from which

$$q(a,t) = \begin{cases} \hat{q}(a-t), & a > t\\ 0, & a < t. \end{cases}$$

This is a contradiction to (H3), since this implies

$$0 = \int_{a_1 - a_0 - \epsilon}^{a_1 - a_0} \tau(a_0 + t)\hat{q}(a_0)\, dt = \int_{a_1 - \epsilon}^{a_1} \hat{q}(a_0)\tau(a)\, da > 0$$

for some $a_0 \in [0, a_1]$ such that $\hat{q}(a_0) \neq 0$ and $\epsilon \in]0, \epsilon_1[$.

Thus, without loss of generality we can suppose that initial age distribution $\hat{p} \neq 0$.

Let $(\varphi, \psi)^T \in L_+^\infty(0, a_1) \times L_+^\infty(0, a_1)$, where φ, ψ are not both zero and let $(\hat{p}, \hat{q})^T \in X$ with $\hat{p} \neq 0$.

Case 1. $\varphi \neq 0$.

Since $\{T(t)\}_{t \geq 0}$ is irreducible, there is $t_0 \geq 0$ such that $\langle \varphi, T(t_0)\hat{p} \rangle > 0$, where $\langle ., . \rangle$ means the usual duality product.

Then,

$$\begin{aligned} \left\langle (\varphi, \psi)^T, U(t_0)(\hat{p}, \hat{q})^T \right\rangle &= \left\langle \varphi, p(., t_0) \right\rangle + \left\langle \psi, q(., t_0) \right\rangle \\ &\geq \left\langle \varphi, p(., t_0) \right\rangle \\ &\geq \left\langle \varphi, T(t_0)\hat{p} \right\rangle > 0 \end{aligned}$$

and the irreducibility of the semigroup $\{U(t)\}_{t \geq 0}$ is proved.

Case 2. $\psi \neq 0$.

Denote $J(t) = \langle (\varphi, \psi)^T, U(t)(\hat{p}, \hat{q})^T \rangle$. Then,

$$\begin{aligned} J(t) &= \langle \varphi, p(., t) \rangle + \langle \psi, q(., t) \rangle \\ &\geq \langle \psi, q(., t) \rangle \\ &\geq \left\langle \psi, \int_0^t S(t - s)(\sigma(.)p(., s))\, ds \right\rangle \\ &= \int_0^{a_1} \psi(a) \left(\int_{t-a}^t \sigma(a - t + s) p(a - t + s, s) \right. \\ &\qquad \left. \times \exp\left(- \int_{a-t+s}^a \tau(w)\, dw \right) ds \right) da. \end{aligned}$$

From (1), (2), (3), we obtain for $a < t < a + s$,

$$\begin{aligned} p(a - t + s, s) &\geq (T(s)\hat{p})(a - t + s) \\ &= (T(t - a)\hat{p})(0) \exp\left(- \int_0^{a-t+s} (\mu(w) + \sigma(w))\, dw \right) \\ &= (T(t)\hat{p})(a) \exp\left(\int_{a-t+s}^a (\mu(w) + \sigma(w))\, dw \right) \end{aligned}$$

and then

$$J(t) \geq \int_0^{a_1} \psi(a)(T(t)\hat{p})(a) \cdot \left(\int_{t-a}^{t} \sigma(a-t+s) \exp\left(\int_{a-t+s}^{a} (\mu(w) + \sigma(w) - \tau(w))\, dw \right) ds \right) da.$$

Notice that, $\forall a \in [0, a_1]$,

$$\int_{t-a}^{t} \sigma(a-t+s) \exp\left(\int_{a-t+s}^{a} (\mu(w) + \sigma(w) - \tau(w))\, dw \right) ds \geq \left[\exp\left(-\int_0^a \tau(w)\, dw \right) \right] \cdot \int_0^a \sigma(\alpha)\, d\alpha.$$

If we denote this last term by $C(a)$, using (H4) we conclude that

$$\forall a \in [0, a_1], \qquad C(a) > 0.$$

Therefore

$$J(t) \geq \int_0^{a_1} C(a) \psi(a)(T(t)\hat{p})(a)\, da, \qquad t > a_1.$$

Since $\{T(t)\}_{t \geq 0}$ is irreducible, there is $t_0 > a_1$ such that $J(t_0) > 0$. Q.E.D.

Necessity. (a) Suppose that (H4) does not hold. Then, for some $\epsilon > 0$, we have $\sigma(a) = 0$, for a.e. $a \in [0, \epsilon]$.

We look for the solution $q(a, t)$ of problem (PQ) in $[0, \epsilon] \times \mathbf{R}_+$, associated with the initial age distribution $\hat{q}(a) = 0$, $a \in [0, \epsilon]$, and $\hat{q}(a) \neq 0$, $a \in (\epsilon, a_1]$.

It is straightforward to obtain from the equations of (PQ) that

$$\forall (a, t) \in [0, \epsilon] \times \mathbf{R}_+, \qquad q(a, t) = 0,$$

so, $\{U(t)\}_{t \geq 0}$ is not irreducible.

(b) Suppose that (H3) does not hold. Then, for some $\epsilon > 0$, we have $\tau(a) = 0$, $a \in [a_1 - \epsilon, a_1]$.

The initial age distributions $\hat{p} = 0$, and

$$\hat{q}(a) = 0, a \in [0, a_1 - \epsilon]; \qquad \hat{q}(a) \neq 0, a \in [a_1 - \epsilon, a_1]$$

have the solutions of (PQ),

$$p(a,t) = 0, \qquad 0 < a < a_1, t \geq 0$$

$$q(a,t) = \begin{cases} 0, & a < t \\ \hat{q}(a-t)\exp\left(-\int_{a-t}^{a} \tau(s)\,ds\right), & a > t \end{cases}$$

(since $\tau(a)q(a,t) = 0$ for $0 < a \langle a \langle a_1, t \rangle 0$).

Therefore, the semigroup $\{U(t)\}_{t \geq 0}$ is not irreducible.

The theorem is proved.

The above characterization of irreducibility has the following biological interpretation: In order for the population to have a dispersion of any initial age distribution in p and q to an ultimate age distribution through all ages between 0 and a_1 for both p and q, it is necessary and sufficient for (H3) and (H4) to hold. Condition (H3) prohibits the quiescent population from going extinct if $\hat{q}(a) = 0$ for $a \in [0, a_1 - \epsilon]$. Condition (H4) prohibits the quiescent population from staying at 0 for $(a,t) \in [0, \epsilon] \times \mathbf{R}_+$ if $\hat{q}(a) = 0$ for $a \in [0, \epsilon]$.

5. ASYNCHRONOUS EXPONENTIAL GROWTH OF THE SOLUTIONS

The asymptotic behavior of the semigroup $\{U(t)\}_{t \geq 0}$ follows immediately from Theorems 1 and 2 (see [1, Sect. 9.3]).

THEOREM 3. *Under Hypotheses* (H1), (H2), (H3), (H4), *the semigroup* $\{U(t)\}_{t \geq 0}$ *has asynchronous exponential growth*: *There exists a real constant* λ^* *and a rank one projection* Π *on* X *such that*

$$\forall \begin{pmatrix} \varphi \\ \psi \end{pmatrix} \in X, \qquad \lim_{t \to +\infty} e^{-\lambda^* t} U(t) \begin{pmatrix} \varphi \\ \psi \end{pmatrix} = \Pi \begin{pmatrix} \varphi \\ \psi \end{pmatrix}.$$

Moreover, $\lambda^* = \omega_0(A)$ (*the growth bound of* A, *where* A *is the infinitesimal generator of the semigroup*), *and there exists* $(\Phi, \Psi)^T \in L^1_+(0, a_1) \times L^1_+(0, a_1)$ *and a strictly positive functional* $(\Phi^*, \Psi^*)^T \in L^\infty_+(0, a_1) \times L^\infty_+(0, a_1)$ *such that*

$$\forall \begin{pmatrix} \varphi \\ \psi \end{pmatrix} \in X, \qquad \Pi \begin{pmatrix} \varphi \\ \psi \end{pmatrix} = [\langle \Phi^*, \varphi \rangle + \langle \Psi^*, \psi \rangle] . \begin{pmatrix} \Phi \\ \Psi \end{pmatrix}.$$

The general analysis of asymptotic behavior of solutions in the nonirreducible case is very complicated. We complete this section with an example showing what can happen when (H3), (H4) are not satisfied.

We make the following hypothesis

HYPOTHESIS (H5). *There exists* $a_0 \in]0, a_1[$ *such that*

$$\forall a \in [0, a_0],\ \mu(a) = 0; \qquad \forall a \in [a_0, a_1],\ \tau(a) = 0.$$

We will obtain the asymptotic behavior of the nonirreducible semigroup $\{U(t)\}_{t \geq 0}$ associated with this problem, from the analysis of its infinitesimal generator.

The infinitesimal generator is the operator defined by

$$A\begin{pmatrix} \varphi \\ \psi \end{pmatrix} = -\begin{pmatrix} \varphi' \\ \psi' \end{pmatrix} + \begin{pmatrix} \mu - \sigma & \tau \\ \sigma & -\tau \end{pmatrix} \cdot \begin{pmatrix} \varphi \\ \psi \end{pmatrix}$$

with domain

$$D(A) = \Big\{ (\varphi, \psi)^T \in X; (\varphi', \psi')^T \in X, \varphi(0) = 2\int_0^{a_1} \mu(a)\varphi(a)\, da, \psi(0) = 0 \Big\}.$$

First of all, we look for the fundamental matrix of the differential problem

$$\begin{pmatrix} \varphi' \\ \psi' \end{pmatrix} = \begin{pmatrix} -\mu - \sigma & \tau \\ \sigma & -\tau \end{pmatrix} \cdot \begin{pmatrix} \varphi \\ \psi \end{pmatrix}.$$

(1) On $[0, a_0]$, we have $\mu(a) = 0$, and then $\varphi + \psi$ is constant. It is easy to obtain

$$\begin{pmatrix} \varphi(a) \\ \psi(a) \end{pmatrix} = W(a)\begin{pmatrix} \varphi(0) \\ \psi(0) \end{pmatrix},$$

where

$$W(a) = E(a)^{-1}\begin{pmatrix} 1 + \int_0^a \tau(b)E(b)\, db & \int_0^a \tau(b)E(b)\, db \\ E(a) - 1 - \int_0^a \tau(b)E(b)\, db & E(a) - \int_0^a \tau(b)E(b)\, db \end{pmatrix}$$

and

$$E(x) = \exp\left(\int_0^x (\sigma(s) + \tau(s))\, ds\right).$$

(2) On $[a_0, a_1]$ we have $\tau(a) = 0$ and then we obtain

$$\begin{pmatrix} \varphi(a) \\ \psi(a) \end{pmatrix} = V(a) \begin{pmatrix} \varphi(a_0) \\ \psi(a_0) \end{pmatrix},$$

where

$$V(a) = \begin{pmatrix} \exp\left(-\int_{a_0}^{a} (\mu(s) + \sigma(s))\, ds \right) & 0 \\ \int_{a_0}^{a} \sigma(s) \exp\left(-\int_{a_0}^{s} (\mu(w) + \sigma(w))\, dw \right) ds & 1 \end{pmatrix}.$$

This implies that the fundamental matrix H ($H(0) = \mathrm{Id}$) is

$$H(a) = \begin{pmatrix} h_{11}(a) & h_{12}(a) \\ h_{21}(a) & h_{22}(a) \end{pmatrix} = \begin{cases} W(a), & a \in [0, a_0] \\ V(a) W(a_0), & a \in [a_0, a_1]. \end{cases}$$

Consider the eigenvalue problem

$$(A - \lambda I) \begin{pmatrix} \varphi \\ \psi \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}.$$

The general solution is

$$\begin{pmatrix} \varphi(a) \\ \psi(a) \end{pmatrix} = e^{-\lambda a} H(a) \begin{pmatrix} \varphi(0) \\ \psi(0) \end{pmatrix}.$$

The condition $(\varphi, \psi)^T \in D(A)$ provides a characteristic equation for the determination of the eigenvalues λ:

$$\varphi(0) = 2 \int_0^{a_1} e^{-\lambda a} h_{11}(a) \mu(a) \varphi(0)\, da, \qquad \psi(0) = 0.$$

That is,

$$\begin{aligned} 1 = 2 \exp&\left(-\int_0^{a_0} (\sigma(s) + \tau(s))\, ds \right) \\ &\times \left(1 + \int_0^{a_0} \tau(b) \exp\left(\int_0^{b} (\sigma(s) + \tau(s))\, ds \right) db \right) \\ &\times \left(\int_{a_0}^{a_1} e^{-\lambda a} \mu(a) \exp\left(-\int_{a_0}^{a} (\mu(s) + \sigma(s))\, ds \right) da \right). \end{aligned} \tag{4}$$

LEMMA 2. *The characteristic equation* (4) *has a unique real root* $\tilde{\lambda}$.

Proof. Denote by $F(\lambda)$ the right hand side of Eq. (4). Notice that F is a decreasing function,

$$\lim_{\lambda \to -\infty} F(\lambda) = +\infty; \qquad \lim_{\lambda \to +\infty} F(\lambda) = 0.$$

Then, the characteristic equation $F(\lambda) = 1$ has a unique real root $\tilde{\lambda} < 0$.

THEOREM 4. *Under Hypotheses* (H1), (H2), (H5), *the semigroup* $\{U(t)\}_{t \geq 0}$ *has the asymptotic behavior*

$$\lim_{t \to +\infty} e^{-\tilde{\lambda} t} U(t) = \tilde{\Pi},$$

where $\tilde{\Pi}$ *is a one dimensional projection on* X (*but not strictly positive*).

Proof. From the general theory [11, Chap. 4] we can conclude that there exists a finite rank projection $\tilde{\Pi} \neq 0$ on X such that

$$\left\| U(t)(\mathrm{Id} - \tilde{\Pi}) \right\| \leq M_\epsilon e^{(\tilde{\lambda} - \epsilon)t}, \qquad t \geq 0$$

for some constants $\epsilon > 0$, $M_\epsilon > 0$.

From the solution of the eigenvalue problem we obtain that the geometric multiplicity of $\tilde{\lambda}$ (i.e., the dimension of associate eigenspace) is one.

It suffices to prove that

$$\ker(A - \tilde{\lambda}\,\mathrm{Id})^2 = \ker(A - \tilde{\lambda}\,\mathrm{Id})$$

since then, the algebraic multiplicity of $\tilde{\lambda}$ is also one.

To obtain $\ker(A - \tilde{\lambda}\,\mathrm{Id})^2$, we start solving

$$(A - \tilde{\lambda}\,\mathrm{Id}) \begin{pmatrix} u \\ v \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \end{pmatrix}, \qquad \begin{pmatrix} u \\ v \end{pmatrix} \in D(A) \tag{5}$$

and then we consider

$$(A - \tilde{\lambda}\,\mathrm{Id}) \begin{pmatrix} \varphi \\ \psi \end{pmatrix} = \begin{pmatrix} u \\ v \end{pmatrix}, \qquad \begin{pmatrix} \varphi \\ \psi \end{pmatrix} \in D(A). \tag{6}$$

The solution of (5) is

$$\begin{pmatrix} u \\ v \end{pmatrix} = e^{-\tilde{\lambda} a} H(a) \begin{pmatrix} k \\ 0 \end{pmatrix},$$

where k is an arbitrary constant.

The solution of (6) is then

$$\begin{pmatrix} \varphi(a) \\ \psi(a) \end{pmatrix} = e^{-\tilde{\lambda} a} H(a) \begin{pmatrix} \varphi(0) + ak \\ 0 \end{pmatrix}.$$

We impose $(\varphi, \psi)^T \in D(A)$,

$$\varphi(0) = 2\varphi(0)\int_0^{a_1} e^{-\tilde{\lambda}a} h_{11}(a)\mu(a)\,da + 2k\int_0^{a_1} ae^{-\tilde{\lambda}a} h_{11}(a)\mu(a)\,da$$

which, in view of (4), immediately implies $k = 0$. Then, the algebraic multiplicity of $\tilde{\lambda}$ is also one and the theorem is proved. The claim that Π is not strictly positive follows from part (b) of the necessity proof of Theorem 2.

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