**Research and Communications in Mathematics and Mathematical Sciences**  Vol. 7, Issue 1, 2016, Pages 11-30 ISSN 2319-6939 Published Online on November 30, 2016 2016 Jyoti Academic Press http://jyotiacademicpress.org

# **WELL-POSEDNESS AND ASYMPTOTIC BEHAVIOUR OF SOLUTIONS FOR THE MODEL OF STEM CELLS**

## **MENG BAI**

School of Mathematics and Information Sciences Zhaoqing University Zhaoqing, Guangdong 526061 P. R. China e-mail: 124204602@qq.com

#### **Abstract**

In this paper, we study the model of stem cells with two phases. We establish the well-posedness for this model and show that the solutions exhibit the phenomenon of asynchronous exponential growth if they don't decay in an exponential speed to 0 as the time goes to infinity.

## **1. Introduction**

In this paper, we consider the model of the stem cells, which is divided in two compartments: the proliferating and the nonproliferating (see [1], [2], and [3]). We denote by  $n(t, a)$  and  $p(t, a)$  the densities of the nonproliferating cells and the proliferating cells of the age *a* at the time *t*, respectively. The nonproliferating cells are assumed to differentiate at a rate  $\delta(a)$  and transit to the proliferating cells of the age 0 with a rate  $\beta(a)$ . As soon as a cell enters the proliferating phase, it is committed to

<sup>2010</sup> Mathematics Subject Classification: 35L02, 35P99.

Keywords and phrases: stem cell, well-posedness, asynchronous exponential growth. Communicated by Suayip Yuzbasi.

Received October 25, 2016

divide a time  $\tau$  (a constant) later. The proliferating cells also have a mortality rate  $\gamma(a)$ . The nonproliferating cells and the proliferating cells have the maximal ages  $\bar{a}$  and  $\tau$ , respectively. Then the evolution of the stem cell population is described by the following system:

$$
\begin{cases}\n\frac{\partial n}{\partial t}(t, a) + \frac{\partial n}{\partial a}(t, a) = -\delta(a)n(t, a) - \beta(a)n(t, a), 0 < a < \overline{a}, t > 0, \\
\frac{\partial p}{\partial t}(t, a) + \frac{\partial p}{\partial a}(t, a) = -\gamma(a)p(t, a), & 0 < a < \tau, t > 0, \\
n(t, 0) = 2p(t, \tau), & t > 0, \\
p(t, 0) = \int_0^{\overline{a}} \beta(a)n(t, a)da, & t > 0, \\
n(0, a) = n_0(a), & 0 < a < \overline{a}, \\
p(0, a) = p_0(a), & 0 < a < \tau,\n\end{cases}
$$
\n(1.1)

We shall prove that under suitable assumptions on  $δ$ ,  $β$ , and  $γ$  the problem (1.1) is globally well-posed, and analyze the large time behaviour of its solutions. We prove that the solutions exhibit the phenomenon of asynchronous exponential growth if they don't decay in an exponential speed to 0 as  $t \to \infty$ . The phenomenon of asynchronous exponential growth appears frequently in age-or size-structured population models (see [4], [5], [6], [7], [8], [9]). In the framework of semigroup theory, a strongly continuous semigroup  $(T(t))_{t\geq0}$  with infinitesimal generator A on the Banach space  $X$  is said to possess the property of asynchronous exponential growth if there exist  $\lambda_0 \in \mathbb{R}$ , which is an eigenvalue of *A* and a strictly positive associated eigenfunction  $\Phi \in X$  such that, for each  $u_0 \in X$ ,

$$
\lim_{t \to +\infty} e^{-\lambda_0 t} T(t) u_0 = C_0 \Phi,
$$

where  $C_0$  is a constant depending on the initial data  $u_0$  (see [4], [5], [6], [7], [8], [9]).

The theory of asynchronous exponential growth is well studied in [7], [8], and [9] where some applicable sufficient conditions are derived. In this paper, we shall use the theory developed in [7], [8], and [9] to prove that the solution operators of the model (1.1) possess this property.

Throughout this paper, the vital rates  $\delta(a)$ ,  $\beta(a)$ , and  $\gamma(a)$  are supposed to satisfy the following conditions:

(1)  $\delta(a)$  and  $\gamma(a)$  are nonnegative and continuous functions defined in  $[0, \overline{a}]$  and  $[0, \tau]$ .

(2)  $\beta(a)$  is a nonnegative and continuous function defined in [0,  $\overline{a}$ ] with  $\beta(a) > 0$  for almost all  $a \in (0, \overline{a})$ .

Our main result considers the well-posedness for the problem (1.1) and reads as follows:

**Theorem 1.1.** For  $(n_0(a), p_0(a)) \in W^{1,1}[0, \overline{a}] \times W^{1,1}[0, \tau]$  such that  $(n_0(a), p_0(a))$  *satisfies the boundary condition*  $n_0(0) = 2p_0(\tau)$  *and*  $p_0(0) = \int_0^{\overline{a}} \beta(a) n_0(a) da$ , the problem (1.1) has a unique solution  $(n, p) \in C([0, \infty), W^{1,1}(0, \overline{a}) \times W^{1,1}(0, \tau)) \cap C^1([0, \infty), L^1[0, \overline{a}] \times L^1[0, \tau]),$ *and for any*  $T > 0$ *, the mapping*  $(n_0, p_0) \mapsto (n, p)$  from the space

 $\{(n_0, p_0)\in W^{1,1}(0, \overline a)\times W^{1,1}(0, \tau): (n_0(0), p_0(0))=(2p_0(\tau), \int_0^{\overline a}\beta(a)n_0(a)da)\}$ 

*to*  $C([0, T], W^{1,1}(0, \overline{a}) \times W^{1,1}(0, \tau)) \cap C^1([0, T], L^1[0, \overline{a}] \times L^1[0, \tau])$  *is continuous*.

The proof of this result will be given in Section 2.

Before giving the main results about the asymptotic behaviour of the solutions of the problem (1.1), we define

$$
R := \exp\left\{-\int_0^{\tau} \gamma(s)ds\right\} \int_0^{\overline{a}} \beta(a) \exp\left\{-\int_0^a (\delta(s) + \beta(s))ds\right\} da.
$$

Then we give a statement of our first main result about the asymptotic behaviour of the solution of the problem (1.1):

**Theorem 1.2.** *Under the assumption*  $R < \frac{1}{2}$ , *there exists*  $\epsilon > 0$  *such* 

*that* 

$$
\lim_{t\to\infty}e^{\varepsilon t}(\|n(t,\cdot)\|_{L^1[0,\,\overline{a}]}+\|p(t,\cdot)\|_{L^1[0,\,\tau]})=0.
$$

The proof of this result will be given in Section 4.

Under the assumption  $R \ge \frac{1}{2}$ , we have that there exists an eigenvalue  $\lambda_0 \geq 0$  associated with the strongly positive eigenvector  $(\hat{n}(a), \hat{p}(a), \text{ i.e.,})$ 

$$
\begin{cases}\n\hat{n}'(a) + \lambda \hat{n}(a) = -\delta(a)\hat{n}(a) - \beta(a)\hat{n}(a), & 0 < a < \overline{a}, \\
\hat{p}'(a) + \lambda \hat{p}(a) = -\gamma(a)\hat{p}(a), & 0 < a < \tau, \\
\hat{n}(0) = 2\hat{p}(\tau), & \hat{p}(0) = \int_0^{\overline{a}} \beta(a)\hat{n}(a)da.\n\end{cases}
$$
\n(1.2)

Let  $(\varphi, \psi)$  be the eigenvector of the conjugate problem of (1.2), i.e.,

$$
\begin{cases}\n-\varphi'(a) + \lambda \varphi(a) = -\delta(a)\varphi(a) - \beta(a)\varphi(a) + \psi(0)\beta(a), & 0 < a < \overline{a}, \\
-\psi'(a) + \lambda \psi(a) = -\gamma(a)\psi(a), & 0 < a < \tau, \\
\psi(\tau) = 2\varphi(0), & 0 < a < \tau,\n\end{cases}
$$
\n(1.3)

We normalize  $(\varphi, \psi)$  such that

$$
\int_0^{\overline{a}} \hat{n}(a)\varphi(a)da + \int_0^{\tau} \hat{p}(a)\psi(a)da = 1.
$$

Then we give our second result about the asymptotic behaviour of the solutions of the problem (1.1):

**Theorem 1.3.** Under the assumption  $R \geq \frac{1}{2}$ , we have that

$$
\lim_{t\to\infty}e^{-\lambda_0t}(n, p) = \left(\int_0^{\overline{a}}n_0(a)\varphi(a)da + \int_0^{\tau}p_0(a)\psi(a)da\right)(\hat{n}, \hat{p}).
$$

The proof of this result will be given in Section 4. The parameter  $\lambda_0$ is called the intrinsic rate of natural increase or Malthusian parameter (see [7]). Theorems 1.2 and 1.3 show that the population densities  $n(t, a)$ and  $p(t, a)$  decay in an exponential speed to zero as  $t \to \infty$  when the  $R < \frac{1}{2}$  and the population densities  $n(t, a)$  and  $p(t, a)$  exhibit the phenomenon of asynchronous exponential growth as  $t \to \infty$  when the  $R \geq \frac{1}{2}$ .

The layout of the rest part is as follows. In Section 2, we reduce the problem (1.1) into an abstract Cauchy problem and establish the wellposedness for it by means of Hille-Yosida operator. In Section 3, we find the resolvent of the generator of the semigroup of the solutions of the problem (1.1) which is the preparation for the proof of the asynchronous exponential growth. In Section 4, we obtain the large time behaviour of the solutions.

#### **2. Reduction and Well-Posedness**

In this section, we reduce the problem (1.1) into an abstract Cauchy problem and establish the well-posedness for it. We choose as state spaces  $X := L^1[0, \overline{a}] \times L^1[0, \tau]$ . On this Banach space, we introduce the following operators:

$$
A\begin{pmatrix} u \\ v \end{pmatrix} := -\begin{pmatrix} u_0 \\ v_0 \end{pmatrix},\tag{2.1}
$$

the domain 
$$
D(A) = \left\{ \begin{pmatrix} u \\ v \end{pmatrix} \in W^{1,1}[0, \overline{a}] \times W^{1,1}[0, \tau] : \begin{pmatrix} u(0) \\ v(0) \end{pmatrix} = \begin{pmatrix} 2v(\tau) \\ \int_0^{\overline{a}} \beta(a)u(a)da \end{pmatrix} \right\},
$$

$$
(2.2)
$$

$$
B\begin{pmatrix} u \\ v \end{pmatrix} := \begin{pmatrix} -\delta(a) - \beta(a) & 0 \\ 0 & -\gamma(a) \end{pmatrix} \begin{pmatrix} u \\ v \end{pmatrix},
$$
(2.3)

$$
L = A + B
$$
, with domain  $D(L) := D(A)$ . (2.4)

We note that  $A \in \mathcal{L}(D(A), X)$ ,  $B \in \mathcal{L}(X, X)$ , and  $L \in \mathcal{L}(D(A), X)$ .

Using these notations, we rewrite the model (1.1) the following abstract differential equation in the Banach space *X*:

$$
\begin{cases}\n\frac{dU(t)}{dt} = LU(t), & t \ge 0, \\
U(0) = U_0,\n\end{cases}
$$
\n(2.5)

where 
$$
U(t) = \begin{pmatrix} n(t, \cdot) \\ p(t, \cdot) \end{pmatrix}
$$
 and  $U_0 = \begin{pmatrix} n_0(a) \\ p_0(a) \end{pmatrix}$ .

Since  $D(A)$  is nonlocal, we introduce a new abstract setting involving Hille-Yosida operator. Recall that (see [10]) a linear operator  $(A, D(A))$ 

acting on a Banach space *X* is called a Hille-Yosida operator if there exists  $\omega \in \mathbb{R}$  such that  $(\omega, +\infty) \subset \rho(A)$  and

$$
\sup\{\|(\lambda-\omega)^n(\lambda-A)^{-n}\|:\lambda > \omega,\,n\in\mathbb{N}\}=:M(A)<+\infty.
$$

For Hille-Yosida operators, we also recall the following important result (see [10]):

**Theorem 2.1.** *Let*  $(A, D(A))$  *be a Hille-Yosida operator on the Banach*  $space\ X\ and\ the\ set\ X_0\ \coloneqq (\overline{D(A)}, \|\cdot\|),\ D(A_0)\coloneqq \{x\in D(A): Ax\in X_0\},$  $A_0x = Ax$  for  $x \in D(A_0)$ . *Then the operator*  $(A_0, D(A_0))$ , *called the* part of the A in  $X_0$ , is the generator of a strongly continuous semigroup *on*  $X_0$  *denoted by*  $(T_0(t))_{t \geq 0}$ *.* 

In order to use Theorem 2.1, we introduce the following operators on the Banach space *X*:

$$
A_m \begin{pmatrix} u \\ v \end{pmatrix} := -\begin{pmatrix} u_a \\ v_a \end{pmatrix}, \tag{2.6}
$$

the domain 
$$
D(A_m) = \left\{ \begin{pmatrix} u \\ v \end{pmatrix} \in W^{1,1}[0, \overline{a}] \times W^{1,1}[0, \tau] \right\},
$$
 (2.7)

$$
P\begin{pmatrix} u \\ v \end{pmatrix} := \begin{pmatrix} u(0) \\ v(0) \end{pmatrix},
$$
 (2.8)

$$
\Phi\begin{pmatrix}u\\v\end{pmatrix} := \begin{pmatrix}2v(\tau)\\ \int_0^{\overline{a}} \beta(a)u(a)da\end{pmatrix},\tag{2.9}
$$

$$
L_m = A_m + B
$$
, with domain  $D(L_m) := D(A_m)$ . (2.10)

We consider the Banach space  $\chi := X \times \mathbb{R}^2$  and the operator

$$
\mathcal{A} := \begin{pmatrix} L_m & 0 \\ \Phi - P & 0 \end{pmatrix}
$$

,

with the domain  $D(A) := D(A_m) \times \{0\}$ . To the operator  $(A, D(A))$ , we have the following lemma:

**Lemma 2.2.** *The operator*  $(L, D(A))$  *is isomorphic to the part*  $({\cal A}_0, D({\cal A}_0))$  of the operator  $({\cal A}, D({\cal A}))$  in the closure of its domain  $\overline{D({\cal A})}$ .

**Proof.** Since  $\overline{D(A)} = X \times \{0\}$ , we have that

$$
D(A_0) = \left\{ \begin{pmatrix} U \\ \mathbf{0} \end{pmatrix} : U \in D(A_m), \mathcal{A} \begin{pmatrix} U \\ \mathbf{0} \end{pmatrix} \in \overline{D(A)} \right\}
$$

$$
= \left\{ \begin{pmatrix} U \\ \mathbf{0} \end{pmatrix} : U \in D(A_m), \Phi U - PU = 0 \right\}.
$$

The claim follows.  $\Box$ 

Then if we prove the part  $(A_0, D(A_0))$  of the operator  $(A, D(A))$  in the closure of its domain  $D(A)$  generates a strongly continuous semigroup, the operator  $(L, D(A))$  does the same. By Theorem 2.1, we need to prove that the operator  $(A, D(A))$  is a Hille-Yosida operator. To  $\backslash$ ſ 0

this aim, we split *A* into two operators  $A_1$  and  $A_2$ , where  $A_1 = \begin{bmatrix} 2m^2 \\ m \end{bmatrix}$ J  $\mathsf{I}$ I  $\setminus$ − = 0 1 *P*  $A_1 = \begin{pmatrix} L_m \end{pmatrix}$ 00  $\backslash$ ſ

and  $A_2 =$  | 0 2  $=$   $\begin{bmatrix} 2 & 1 \end{bmatrix}$  $\overline{\phantom{a}}$ J  $\mathsf{I}$ I J Φ  $A_2 =$  |  $\therefore$  Since  $A_2$  is a bounded operator on *X*, it suffices to prove

that  $A_1$  is a Hille-Yosida operator (see [11]).

**Lemma 2.3.** *The operator*  $(A_1, D(A))$  *is a Hille-Yosida operator on the Banach space X*.

**Proof.** The restriction  $(L_0, D(L_0))$  of *L* to the kernel of *P* generates the nilpotent semigroup  $(T_0(t))_{t\geq0}$  on *X* given by

$$
T_0(t)(f_1(a), f_2(a)) = \begin{cases} \left(\exp\{-\int_{a-t}^a (\delta(s) + \beta(s))ds\} f_1(a-t), \\ \exp\{-\int_{a-t}^a \gamma(s)ds\} f_2(a-t)\right), \text{ for } t \le a, \\ (0, 0), \text{ for } t > a. \end{cases}
$$
 (2.11)

It is easily to see that  $\sigma(L_0) = \emptyset$ . For  $\lambda > 0$ , its resolvent is

$$
R(\lambda, \mathcal{A}_1) = \begin{pmatrix} R(\lambda, L_0) & E_\lambda \\ 0 & 0 \end{pmatrix},
$$

where  $E_{\lambda} := (\varphi_{\lambda}, \psi_{\lambda}), \varphi_{\lambda}(a) = \exp\{-\int_0^a (\lambda + \delta(s) + \beta(s))ds\}$ , for  $a \in [0, \overline{a}],$ and  $\psi_{\lambda}(a) = \exp\{-\int_0^a (\lambda + \gamma(s))ds\}$ , for  $a \in [0, \tau]$ . For  $(F, H) \in X$ , *F*  $= ( f_1(a) , f_2(a) ) \in X \text{ and } H = ( h_1, h_2 ) \in \mathbb{R}^2,$  $\left\| R(\lambda,\ \mathcal{A}_1) (F,\ H)^t \right\| = \left\| R(\lambda,\ A) F \right\| + \left\| H E_{\lambda} \right\|$ 

$$
= \left\| \int_{0}^{a} \exp \left\{ - \int_{s}^{a} (\lambda + \delta(y) + \beta(y)) dy f_{1}(s) ds \right\|_{L^{1}[0, \overline{a}]} + \left\| \int_{0}^{a} \exp \left\{ - \int_{s}^{a} (\lambda + \gamma(y)) dy f_{2}(s) ds \right\|_{L^{1}[0, \tau]} + \left\| \exp \left\{ - \int_{0}^{a} (\lambda + \delta(s) + \beta(s)) ds h_{1} \right\|_{L^{1}[0, \overline{a}]} + \left\| \exp \left\{ - \int_{0}^{a} (\lambda + \gamma(s)) ds h_{2} \right\|_{L^{1}[0, \tau]} \leq \frac{1}{\lambda} (\| f_{1}(a) \|_{L^{1}(0, \overline{a})} + \| f_{2}(a) \|_{L^{1}(0, \tau)} + |h_{1}| + |h_{2}| ).
$$

Therefore  $\|\lambda R(\lambda, A_1)\| \leq 1$ . That completes the proof.

**Corollary 2.4.** *The operator*  $(A, D(A))$  *is a Hille-Yosida operator on the Banach space X*.

Then by Theorem 2.1 and Lemma 2.4, we have the following result:

**Corollary 2.5.** *The operator* (*L*, *D*(*A*)) *generates a strongly continuous semigroup*  $(T(t))_{t\geq0}$ *.* 

By the above Corollary 2.5 and a well-known result in the theory of strongly continuous semigroups, we immediately obtain the following result:

**Theorem 2.6.** For the initial data  $U_0 \in D(A)$ , the problem (2.5) has *a unique solution*  $U \in C^1([0, +\infty); X)$  given by

$$
U(t) = T(t)U_0.
$$
\n
$$
(2.12)
$$

By Theorem 2.6, we see that Theorem 1.1 follows.

# **3. The Resolvent of the Generator** *L*

In the section, we find the resolvent  $R(\lambda, L)$  of the generator *L*.

For each given  $F \in X$ , we solve the equation

$$
(\lambda I - L)U = F. \tag{3.1}
$$

By writing  $U = (u(a), v(a))$ , we can see that the Equation (3.1) can be rewritten as follows:

$$
\begin{cases}\nu'(a) + \lambda u(a) + \delta(a)u(a) + \beta(a)u(a) = f(a), & 0 < a < \overline{a}, \\
v'(a) + \lambda v(a) + \gamma(a)v(a) = g(a), & 0 < a < \tau, \\
u(0) = 2v(\tau), & \\
v(0) = \int_0^{\overline{a}} \beta(a)u(a)da.\n\end{cases}
$$
\n(3.2)

The solutions of the above equations are as follows:

$$
u(a) = 2\int_0^{\overline{a}} \beta(a)u(a)da\varepsilon_{1\lambda}(a)\varepsilon_{2\lambda}(\tau)
$$
  
+  $\varepsilon_{1\lambda}(a)\left(\int_0^a (\varepsilon_{1\lambda}(s))^{-1} f(s)ds + 2\varepsilon_{2\lambda}(\tau)\int_0^{\tau} (\varepsilon_{2\lambda}(s))^{-1} g(s)ds\right),$  (3.3)

$$
v(a) = \int_0^{\overline{a}} \beta(a)u(a)da\varepsilon_{2\lambda}(a) + \varepsilon_{2\lambda}(a)\int_0^a (\varepsilon_{2\lambda}(s))^{-1}g(s)ds,
$$
 (3.4)

where  $\varepsilon_{1\lambda}(x) = \exp\left\{-\int_0^x (\lambda + \delta(r) + \beta(r)) dr\right\}$  $\varepsilon_{1\lambda}(x) = \exp\left\{-\int_0^x (\lambda + \delta(r) + \beta(r))dr\right\}$  and  $\varepsilon_{2\lambda}(x) = \exp\left\{-\int_0^x (\lambda + \gamma(r))dr\right\}$ .  $\varepsilon_{2\lambda}(x) = \exp\left\{-\int_0^x (\lambda + \gamma(r)) dr\right\}.$ 

For each  $\lambda \in \mathbb{C}$ , we define the two operators on *X*:

$$
G_{\lambda}\left(\begin{matrix}f_{1}(a)\\f_{2}(a)\end{matrix}\right)=\left(\begin{matrix}2\int_{0}^{\overline{a}}\beta(a)u(a)da\varepsilon_{1\lambda}(a)\varepsilon_{2\lambda}(\tau)\\ \int_{0}^{\overline{a}}\beta(a)u(a)da\varepsilon_{2\lambda}(a)\end{matrix}\right),\tag{3.5}
$$

$$
S_{\lambda}\binom{f_1(a)}{f_2(a)} = \begin{pmatrix} \varepsilon_{1\lambda}(a) \left(\int_0^a (\varepsilon_{1\lambda}(s))^{-1} f_1(s) ds + 2\varepsilon_{2\lambda}(\tau) \int_0^{\tau} (\varepsilon_{2\lambda}(s))^{-1} f_2(s) ds \right) \\ \varepsilon_{2\lambda}(a) \int_0^a (\varepsilon_{2\lambda}(s))^{-1} f_2(s) ds \end{pmatrix}.
$$

(3.6)

Since

$$
\left\|G_{\lambda}\left(\begin{matrix}f_1(a)\\f_2(a)\end{matrix}\right)\right\| \leq c\epsilon_{2\lambda}(\tau)(\|f_1(a)\|_{L^1(0,\,\overline{a})} + \|f_2(a)\|_{L^1(0,\,\overline{a})} \to 0(\lambda \to +\infty),
$$

there exists  $\lambda_0 > 0$  such that  $||G_\lambda|| < 1$  for  $\lambda \ge \lambda_0$ . This implies  $(I - G<sub>λ</sub>)<sup>-1</sup>$  exists for  $λ ≥ λ<sub>0</sub>$ . Then the resolvent of *L* is

$$
R(\lambda, L)F = (I - L_{\lambda})^{-1} S_{\lambda} F, \text{ for } \lambda > \lambda_0. \tag{3.7}
$$

#### **4. Asynchronous Exponential Growth**

In this section, we consider the long-term behaviour of solutions of the problem (1.1). For this purpose, we shall analyze the spectrum of the operator  $(L, D(A))$  and prove that the semigroup  $(T(t))_{t\geq 0}$  is positive, eventually compact and irreducible. Recall (see [9] and [12]) that a strongly continuous semigroup  $(T(t))_{t\geq0}$  in a Banach lattice X is said to be positive if  $0 \le f \in X$  implies  $T(t)f \ge 0$  for all  $t \ge 0$ ; it is said to be eventually compact if there exists  $t_0 \geq 0$  such that the operator  $T(t)$  is compact for all  $t \ge t_0$ . Moreover,  $(T(t))_{t \ge 0}$  is said to be irreducible if  $∀$  $φ ∈ X, ψ ∈ X<sup>*</sup>$  (topological dual space of *X*),  $φ > 0, ψ > 0$ , we have that  $\langle T(t_0)\varphi, \psi\rangle > 0$  for some  $t_0 > 0$ , where  $\langle \cdot \rangle$  denotes the usual product of duality in *X*.

We denote by  $s(L)$  the spectral bound of  $L$ , i.e.,

$$
s(L) = \sup\{\text{Re }\lambda : \lambda \in \sigma(L)\}.
$$

We also denote by  $\omega_0$  the growth bound of the semigroup  $(T(t))_{t>0}$ , i.e.,

 $\omega_0 := \inf\{\omega \in \mathbb{R} : \text{there exists } M_\omega \geq 1 \text{ such that } ||T(t)|| \leq M_\omega e^{\omega t} \text{ for all } t\}$ 

$$
= \inf \{ \omega \in \mathbb{R} : \lim_{t \to \infty} e^{-\omega t} \|T(t)\| = 0 \}.
$$

**Lemma 4.1.** *The semigroup*  $(T(t))_{t\geq0}$  *is positive.* 

**Proof.** It suffices to prove that the resolvent  $R(\lambda, L)$  of the generator *L* is positive for all sufficiently large  $\lambda$  (see [[9], Theorem VI.1.8]). Using the expression (3.7) of  $R(\lambda, L)$ , we can see easily that for  $0 \leq F \in X$ ,  $R(\lambda, L)F \geq 0$  for all  $\lambda > \lambda_0$ . That completes the proof.  $\square$ 

**Lemma 4.2.** *The semigroup*  $(T(t))_{t\geq0}$  *is irreducible.* 

**Proof.** Since  $R(\lambda, L) = \int_0^{+\infty} e^{-\lambda t} T(t) dt$ , for all  $\text{Re }\lambda > s(L)$  (see [9], Lemma VI.1.9]), we have that  $\forall F = (f(a), g(a)) \in X$ ,  $\Psi = (\psi_1, \psi_2) \in X^*$ ,  $F > 0, \Psi > 0,$ 

$$
\langle \Psi, R(\lambda, L) F \rangle = \int_0^{+\infty} e^{-\lambda t} \langle \Psi, T(t) F \rangle dt.
$$

If we prove that  $\langle \Psi, R(\lambda, L)F \rangle > 0$  for some  $\lambda > 0$ , then from the above equation, it follows that there exists a  $t_0 > 0$  such that  $\langle \Psi, T(t) F \rangle > 0$ , and the desired assertion then follows. Let  $\pi_1$  and  $\pi_2$  be the projections onto the first and second coordinates, respectively. We will prove that  $\pi_1(R(\lambda, L)F)(a) > 0$  for almost all  $a \in [0, \bar{a}]$  and  $\pi_2(R(\lambda, L)F)(a) > 0$ for almost all  $a \in [0, \tau]$ . For  $0 \leq F$  and  $F \neq 0$ , without loss of generality, we can assume that  $0 \le f \in L^1[0, \overline{a}]$  and  $f(a) > 0$  for almost all  $a \in [x_0, x_1]$ . Using the expression (3.7) of  $R(\lambda, L)$ , we have that

$$
\pi_1(S_{\lambda}\begin{pmatrix}f\\g\end{pmatrix}(a) > 0, \text{ for almost all } a \in [x_0, \overline{a}],
$$
  

$$
\pi_1(G_{\lambda}S_{\lambda}\begin{pmatrix}f\\g\end{pmatrix}(a) > 0, \text{ for almost all } a \in [0, \overline{a}],
$$
  

$$
\pi_2(G_{\lambda}S_{\lambda}\begin{pmatrix}f\\g\end{pmatrix}(a) > 0, \text{ for almost all } a \in [0, \tau].
$$

Then we obtain  $\pi_1(R(\lambda, L)F)(a) > 0$  for almost all  $a \in [0, \bar{a}]$  and  $\pi_2(R(\lambda, L)F)(a) > 0$  for almost all  $a \in [0, \tau]$ . If we assume that  $g(a) > 0$  for almost all  $a \in [x_0, x_1]$ , the result is the same. This completes the proof.  $\Box$ 

**Lemma 4.3.** *The semigroup*  $(T(t))_{t\geq0}$  *is eventually compact.* 

**Proof.** We note that the abstract differential equation (2.5) is equivalent to the problem (1.1). For  $t_0 > 0$ , let us introduce  $n_1(a) = n(a, t(a))$  and  $p_1(a) = p(a, t(a))$ , where  $t(a) = t_0 + a$ . Then  $n_1(a)$  and  $p_1(a)$  satisfy the following equations:

$$
\begin{cases}\nn'_1(a) + \delta(a)n_1(a) + \beta(a)n_1(a) = 0, & 0 < a < \overline{a}, \\
p'_1(a) + \gamma(a)p_1(a) = 0, & 0 < a < \tau, \\
n_1(0) = 2p(t_0, \tau), \\
p_1(0) = \int_0^{\overline{a}} \beta(a)n(t_0, a)da.\n\end{cases}
$$
\n(4.1)

Hence

$$
n_1(a) = 2p(t_0, \tau) \exp\{-\int_0^a (\delta(s) + \beta(s))ds\},\tag{4.2}
$$

$$
p_1(a) = \int_0^{\overline{a}} \beta(a) n(t_0, a) da \exp\{-\int_0^a (\delta(s) + \beta(s)) ds\}.
$$
 (4.3)

For  $t - a > 0$ , this implies

$$
n(t, a) = 2p(t - a, \tau) \exp\{-\int_0^a (\delta(s) + \beta(s))ds\},
$$
\n(4.4)

$$
p(t, a) = \int_0^{\overline{a}} \beta(a) n(t - a, a) da \exp\{-\int_0^a (\delta(s) + \beta(s)) ds\}.
$$
 (4.5)

Therefore, if  $t > \max{\{\overline{a}, \tau\}}$ , p is continuous in a and t. Consequently, the second equation in problem  $(1.1)$  implies that  $p$  is continuously differentiable with respect to *a* if  $t > 2 \max{\{\overline{a}, \tau\}}$ . Then (4.5) implies that *n* is continuously differential with respect to *a* if  $t - a > 2 \max{\{\overline{a}, \tau\}}$ . Hence the semigroup  $(T(t))_{t\geq0}$  generated by *L* is differentiable for  $t > 3$ max $\{\overline{a}, \tau\}$ . Since  $W^{1,1}(0, \overline{a}) \times W^{1,1}(0, \tau)$  is compactly imbedded in  $L^1(0, \overline{a}) \times L^1(0, \tau)$ , the claim follows. **Corollary 4.4.**  $\sigma(L) \neq \phi$  *and*  $s(L) > -\infty$ .

**Proof.** This follows from Theorem C-III.3.7 of [12] that if the semigroup is positive, eventually compact and irreducible, then the spectrum of its generator is not  $\emptyset$ .

**Corollary 4.5.**  $\omega_0 = s(L) \in \sigma(L)$ .

**Proof.** Since the semigroup  $(T(t))_{t\geq0}$  is eventually compact, we have that the Spectral Mapping Theorem holds,  $\omega_0 = s(L)$  (see [[9], Corollary IV.3.12]). The positivity of the semigroup  $(T(t))_{t\geq0}$  and the fact  $s(L) > -\infty$  imply that  $s(L) \in \sigma(L)$  (see [[9], Theorem VI.1.10]).

In the sequel, we analyze the spectrum  $\sigma(L)$  of the generator  $(L, D(A)).$ 

**Lemma 4.6.** *The spectrum*  $σ(L)$  *of L consists of eigenvalues only and is determined by a characteristic equation*, *more precisely*,

$$
\lambda \in \sigma(L) \Leftrightarrow K(\lambda) - 1 = 0,\tag{4.6}
$$

*where* 

$$
K(\lambda) = 2 \exp \left\{-\int_0^{\tau} (\lambda + \gamma(s))ds\right\} \int_0^{\overline{a}} \beta(a) \exp \left\{-\int_0^a (\lambda + \delta(s) + \beta(s))ds\right\} da.
$$

**Proof.** Since the semigroup  $(T(t))_{t\geq0}$  is eventually compact, the spectrum of its generator is consists of eigenvalues only (see [[9], Corollary V.3.2]). Let  $n(t, a) = e^{\lambda t} \overline{n}(a)$  and  $p(t, a) = e^{\lambda t} \overline{p}(a)$ , substituting them into (1.1),

$$
\begin{cases}\n\overline{n}'(a) + \lambda \overline{n}(a) = -\delta(a)\overline{n}(a) - \beta(a)\overline{n}(a), & 0 < a < \overline{a}, \\
\overline{p}'(a) + \lambda \overline{p}(a) = -\gamma(a)\overline{p}(a), & 0 < a < \tau, \\
\overline{n}(0) = 2\overline{p}(\tau), & \overline{p}(0) = \int_0^{\overline{a}} \beta(a)\overline{n}(a)da.\n\end{cases}
$$
\n(4.7)

We have that

$$
\overline{n}(a) = 2\overline{p}(\tau) \exp\biggl\{-\int_0^a (\lambda + \delta(s) + \beta(s))ds\biggr\},\tag{4.8}
$$

$$
\overline{p}(a) = \int_0^{\overline{a}} \beta(a)\overline{n}(a)da \exp\left\{-\int_0^a (\lambda + \gamma(s))ds\right\}.
$$
 (4.9)

Substituting (4.9) into (4.8), we have that

$$
\overline{n}(a) = 2 \int_0^{\overline{a}} \beta(a) \overline{n}(a) da \exp \left\{-\int_0^{\tau} (\lambda + \gamma(s)) ds\right\} \exp \left\{-\int_0^a (\lambda + \delta(s) + \beta(s)) ds\right\}.
$$

Multiplying the above equation by  $\beta(a)$  and integrating from 0 to  $\overline{a}$ , we have that

$$
\int_0^{\overline{a}} \beta(a)\overline{n}(a)da = 2\int_0^{\overline{a}} \beta(a)\overline{n}(a)da \exp\left\{-\int_0^{\tau} (\lambda + \gamma(s))ds\right\}\int_0^{\overline{a}} \beta(a)
$$

$$
\exp\left\{-\int_0^a (\lambda + \delta(s) + \beta(s))ds\right\}da.
$$

We note that  $\int_0^{\overline{a}} \beta(a) \overline{n}(a) da \neq 0$ . Then

$$
1 = 2 \exp\left\{-\int_0^{\tau} (\lambda + \gamma(s))ds\right\} \int_0^{\overline{a}} \beta(a) \exp\left\{-\int_0^a (\lambda + \delta(s) + \beta(s))ds\right\} da. \tag{4.10}
$$

**Lemma 4.7.** *We have the following assertions*:

(i) *If* 

$$
\exp\left\{-\int_0^\tau \gamma(s)ds\right\}\int_0^{\overline{a}} \beta(a) \exp\left\{-\int_0^a (\delta(s) + \beta(s))ds\right\} da < \frac{1}{2},\tag{4.11}
$$

*then the spectral bound*  $s(L) < 0$ *.* 

(ii) *If* 

$$
\exp\left\{-\int_0^\tau \gamma(s)ds\right\}\int_0^{\overline{a}} \beta(a) \exp\left\{-\int_0^a (\delta(s) + \beta(s))ds\right\} da \ge \frac{1}{2},\tag{4.12}
$$

*then the spectral bound*  $s(L) \geq 0$ *.* 

**Proof.** We can easily see that  $\lim_{\lambda \to +\infty} K(\lambda) = 0$ ,  $\lim_{\lambda \to -\infty} K(\lambda) = +\infty$ and  $K'(\lambda) < 0$ . If (4.11) is satisfied, then we have  $K(0) < 1$ , so that the equation  $K(\lambda) = 1$  has no nonnegative root. Since  $s(L)$  is the largest root of this equation, it follows that  $s(L) < 0$ . Similarly, under the condition of the assertion (ii), we have that  $K(0) \geq 1$ , so that the equation  $K(\lambda) = 1$  has no negative root and, consequently,  $s(L) \geq 0$ . This completes the proof.  $\Box$ 

**Proof of Theorem 1.2.** By Corollary 4.5 and Lemma 4.7, we have that the growth bounds  $\omega_0 < 0$  under the assumption (4.11). Then there exists  $\varepsilon > 0$  such that

$$
\lim_{t\to\infty}e^{\varepsilon t}\|T(t)\|=0.
$$

We note that  $(n(t, a), p(t, a)) = T(t)(n_0(a), p_0(a))$ . Then Theorem 1.2 follows.  $\Box$ 

**Proof of Theorem 1.3.** By Corollary 4.5 and Lemma 4.6, we know that  $\lambda = s(L)$  is the dominant eigenvalue of the eigenvalue problem

$$
\begin{cases}\n\hat{n}'(a) + \lambda \hat{n}(a) = -\delta(a)\hat{n}(a) - \beta(a)\hat{n}(a), & 0 < a < \overline{a}, \\
\hat{p}'(a) + \lambda \hat{p}(a) = -\gamma(a)\hat{p}(a), & 0 < a < \tau, \\
\hat{n}(0) = 2\hat{p}(\tau), & \hat{p}(0) = \int_0^{\overline{a}} \beta(a)\hat{n}(a)da,\n\end{cases} \tag{4.13}
$$

and the corresponding eigenvector  $(\hat{n}, \hat{p})$  is strongly positive in  $(0, \bar{a})$ and  $(0, \tau)$ , i.e.,  $\hat{n}(a) > 0$  for almost all  $0 < a < \overline{a}$  and  $\hat{p}(a) > 0$  for almost all  $0 < a < \tau$ . We normalize  $(\hat{n}, \hat{p})$  such that

$$
\int_0^{\overline{a}} \hat{n}(a)da + \int_0^{\tau} \hat{p}(a)da = 1.
$$

Combining Lemmas 4.1-4.3, Corollary 4.4 and Corollary V.3.3 of [9], we have that

$$
\lim_{t \to +\infty} e^{-\lambda t} (n, p) = c(\hat{n}, \hat{p}). \tag{4.14}
$$

Let  $(\varphi, \psi)$  be the eigenvector of the conjugate problem of (4.13), i.e.,

$$
\begin{cases}\n-\varphi'(a) + \lambda \varphi(a) = -\delta(a)\varphi(a) - \beta(a)\varphi(a) + \psi(0)\beta(a), & 0 < a < \overline{a}, \\
-\psi'(a) + \lambda \psi(a) = -\gamma(a)\psi(a), & 0 < a < \tau, \\
\psi(\tau) = 2\varphi(0), & \varphi(\overline{a}) = 0.\n\end{cases}
$$
\n(4.15)

We normalize  $(\varphi, \psi)$  such that

$$
\int_0^{\overline{a}} \hat{n}(a)\varphi(a)da + \int_0^{\tau} \hat{p}(a)\psi(a)da = 1.
$$

Then  $\varphi$  and  $\psi$  are also strictly positive in  $(0, \bar{a})$  and  $(0, \tau)$ , due to a similar reason as that for  $\hat{n}$  and  $\hat{p}$ . Now we consider the function  $\int_0^{\overline{a}} n(t, a) \varphi(a) e^{-\lambda_0 t} da + \int_0^{\tau} p(t, a) \psi(a) e^{-\lambda_0 t} da$ . From (1.1) and (4.15), we easily obtain

$$
\frac{d}{dt}\bigg(\int_0^{\overline{a}} n(t, a)\varphi(a)e^{-\lambda_0 t}da + \int_0^{\tau} p(t, a)\psi(a)e^{-\lambda_0 t}da\bigg) = 0.
$$

Hence

$$
\int_0^{\overline{a}} n(t, a)\varphi(a)e^{-\lambda_0 t}da + \int_0^{\tau} p(t, a)\psi(a)e^{-\lambda_0 t}da = \int_0^{\overline{a}} n_0(a)\varphi(a)da
$$

$$
+ \int_0^{\tau} p_0(a)\psi(a)da,
$$

for all  $t \geq 0$ . Letting  $t \to \infty$  and using (4.14), we get

$$
c\int_0^{\overline{a}}\hat{n}(a)\varphi(a)da + \int_0^{\tau}\hat{p}(a)\psi(a)da = \int_0^{\overline{a}}n_0(a)\varphi(a)da + \int_0^{\tau}p_0(a)\psi(a)da.
$$

Since  $\int_{0}^{\overline{a}} \hat{n}(a) \varphi(a) da + \int_{0}^{\overline{a}} \hat{p}(a) \psi(a) da = 1$ , we obtain

$$
c = \int_0^{\overline{a}} n_0(a)\varphi(a)da + \int_0^{\tau} p_0(a)\psi(a)da.
$$

Hence, this completes the proof of Theorem 1.3.

# **Acknowledgement**

This work is supported by Foundation for Distinguished Young Talents in Higher Education of Guangdong, China (2014KQNCX223), Foundation for Distinguished Young Teacher in Higher Education of Guangdong, China (YQ2015167), Foundation of Science and Technology Innovation Project of Zhaoqing, China (2014G15), and Foundation of Zhaoqing University, China (201429).

#### **References**

- [1] M. C. Mackey, Unified hypothesis of the origin of aplastic anaemia and periodic hematopoiesis, Blood 51 (1978), 941-956.
- [2] G. Bradford, B. Williams, R. Rossi and I. Bertoncello, Quiescence, cycling, and turnover in the primitive haematopoietic stem cell compatment, Exper. Hematol. 25 (1997), 445-453.
- [3] F. J. Burns and I. F. Tannock, On the existence of a *G*0 phase in the cell cycle, Cell. Tissue Kinet. 19 (1970), 321-334.
- [4] O. Arina, E. Sánchez and G. F. Webb, Necessary and sufficient conditions for asynchronous exponential growth in age structured cell populations with quiescence, J. Math. Anal. Appl. 215 (1997), 499-513.
- [5] J. Dyson, R. Villella-Bressan and G. F. Webb, Asynchronous exponential growth in an age structured population of proliferating and quienscent cells, Math. Biosci. 177(178) (2002), 73-83.

- [6] O. Arino, A. Bertuzzi, A. Ganfolfi, E. Sánchez and C. Sinisgalli, The asynchronous exponential growth property in a model for the kinetic heterogeneity of tumour cell populations, J. Math. Anal. Appl. 302 (2005), 521-542.
- [7] H. R. Thieme, Balanced exponential growth of operator semigroups, J. Math. Anal. Appl. 223 (1998), 30-49.
- [8] Ph. Clément, H. Heijmans, S. Angenent, C. van Duijin and B. de Pagter, One-Parameter Semigroups, North-Holland, Amsterdam, 1987.
- [9] K.-J. Engel and R. Nagel, One-Parameter Semigroups for Linear Evolution Equations, Springer, New York, 2000.
- [10] G. Nickel and A. Rhandi, On the essential spectral radius of semigroups generated bu perturbations of Hille-Yosida operators, Tübinger Berichte zur Funktionalanalysis 4 (1994/95), 207-220.
- [11] A. Pazy, Semigroups of Linear Operators and Applications to Partial Differential Equations, Springer, New York, 1983.
- [12] W. Arendt, A. Grabosch, G. Greiner, U. Groh, H. P. Lotz, U. Moustakas, R. Nagel, F. Neubrander and U. Schlotterbeck, One-Parameter Semigroups of Positive Operators, Springer-Verlag, Berlin, (1986), North-Holland, Amsterdam, 1987.

g