Electronic Journal of Differential Equations, Vol. 2010(2010), No. 47, pp. 1–12.
ISSN: 1072-6691. URL: http://ejde.math.txstate.edu or http://ejde.math.unt.edu
ftp ejde.math.txstate.edu

WELL-POSEDNESS AND ASYNCHRONOUS EXPONENTIAL GROWTH OF SOLUTIONS OF A TWO-PHASE CELL DIVISION MODEL

MENG BAI, SHANGBIN CUI

Abstract. In this article we study a two-phase cell division model. The cells of the two different phases have different growth rates. We mainly consider the model of equal mitosis. By using the semigroup theory, we prove that this model is well-posed in suitable function spaces and its solutions have the property of asynchronous exponential growth as time approaches infinity. The corresponding model of asymmetric mitosis is also studied and similar results are obtained.

1. Introduction

In the study of cell division, it has been recognized that the cell cycle can be divided into two major phase: The interphase and the **M** (mitosis) phase (cf. [14, 15]). In the interphase cells only increase their size and replicate their DNA, and do not undergo mitosis, whereas in the M phase the fully grown cells segregate the replicated chromosomes to opposite ends of the molecular scaffold (termed the spindle) and then cleave between them in a process known as cytokinesis to produce two daughter cells. The cells in the two phases are observably different.

In this paper we study a mathematical model describing the proliferation of cells which are divided into two different phases: mitotic phase and non-mitotic phase. We refer these two phases as m-phase and n-phase, respectively. We denote by $m(t,x)$ and $n(t,x)$ the densities of m-phase cells and n-phase cells, respectively, of size x (with a maximal size normalized to $x=1$) at time t. We assume that two daughter cells have equal sizes (i.e. *equal mitosis*). In particular, we assume that the two phases have different growth rates $\gamma_1(x)$ and $\gamma_2(x)$, respectively. Then the

2000 *Mathematics Subject Classification.* 35L02, 35P99.
Key words and phrases. Cell division model; two-phase; well-posedness;
asynchronous exponential growth.

Submitted March 3, 2010. Published April 6, 2010.
Supported by grant 10771223 from the National Natural Science Foundation of China.

model reads as follows:

$$\begin{aligned}
&\frac{\partial m}{\partial t}+\frac{\partial(\gamma_1(x)m)}{\partial x}=-B(x)m(t,x)-\nu(x)m(t,x)+\mu(x)n(t,x),\\
&\qquad 0<x<1,\ t>0,\\
&\frac{\partial n}{\partial t}+\frac{\partial(\gamma_2(x)n)}{\partial x}=-\nu(x)n(t,x)-\mu(x)n(t,x)\\
&\qquad +\begin{cases}4B(2x)m(t,2x), & 0\le x\le \frac{1}{2},\ t>0\\ 0, & \frac{1}{2}<x\le 1,\ t>0,\end{cases}\\
&m(t,0)=0,\quad n(t,0)=0,\quad t>0,\\
&m(0,x)=m_0(x),\quad n(0,x)=n_0(x),\quad 0<x<1.
\end{aligned} \tag{1.1}$$

Here $\mu(x)$ represents the transferring rate of cells from n-phase to m-phase, $\nu(x)$ represents the death rate of the cells, and $B(x)$ represents the mitosis rate of the cells in m-phase.

For the one-pase cell division model, it has been proved by Perthame and Ryzhik in [1] (see also [10, Chapter 4]) and Michel, Mischler and Perthame in [2] by using the generalized relative entropy method that the problems are globally well-posed and the solutions exhibit so called *asynchronous exponential growth* (cf. [5, 8, 9, 11, 13]). The purpose of this work is to extend these results to model (1.1), but using a different method – the semigroup method. We shall prove that under suitable assumptions on μ, ν and B, problem (1.1) is globally well-posed, and its solution possesses the properties of asynchronous exponential growth.

The anonymous referee called our attention to a recent work by Perthame and Touaoula [4], where a different multi-species cell division model is studied. In that model it is assumed that each cell can divide at most I times in its lifespan, so that all cells are divided into I-generations. All cells grow at a same constant rate and each of the cells in the i-th ($1\le i\le I-1$) generation divide into two cells of equal size at a rate $B_i(x)$ when mitosis occurs. One of the two cells, called the daughter cell, resumes a cycle at the generation 1, while the other cell, called the mother cell, enters the generation $i+1$. By establishing existence of eigenvalues with positive eigenvectors of the eigenvalue problem and its adjoint problem and using the general relative entropy method, those authors proved that the solutions of their model have the property of asynchronous exponential growth. Unlike that model, in the model under this study we assume that cells consist of two different phases: the mitotic phase and the non-mitotic phase. Cells in the mitotic phase can divide into two cells of non-mitotic phase, while cells in the non-mitotic phase do not undergo mitotic. This is the main difference between this work and the reference [4].

Throughout this paper, the transferring rate $\mu(x)$, the death rate $\nu(x)$, the equal mitosis rate $B(x)$, and the growth rates $\gamma_1(x)$ and $\gamma_2(x)$ are supposed to satisfy the following conditions:

- (H1) μ and ν are nonnegative and continuous functions defined in $[0,1]$. Moreover, $\mu(x)>0$ for almost all $x\in(0,1)$;
- (H2) B is a nonnegative and continuous function defined in $[0,1]$ with $B(x)>0$ for $x\in(0,1)$ and $B(x)=0$ for otherwise.
- (H3) $\gamma_1,\gamma_2\in C^1[0,1]$; $\gamma_1(x),\gamma_2(x)>0$ for almost all $x\in[0,1]$; Moreover, $\gamma_1(x)\ne\gamma_2(x)$ for $x\in[0,1]$ and $\gamma_2(2x)\ne 2\gamma_1(x)$ for $x\in[0,1]$.

Our first main result considers well-posedness of (1.1) and reads as follows.

Theorem 1.1. *For any pair of functions $(m_0, n_0) \in W^{1,1}(0,1) \times W^{1,1}(0,1)$ such that $(m_0(0), n_0(0)) = (0,0)$, problem (1.1) has a unique solution*

$$(m,n) \in C([0,\infty), W^{1,1}(0,1) \times W^{1,1}(0,1)) \cap C^1([0,\infty), L^1[0,1] \times L^1[0,1]),$$

and for any $T > 0$, the mapping $(m_0, n_0) \mapsto (m,n)$ from the space

$$\{(m_0,n_0) \in W^{1,1}(0,1) \times W^{1,1}(0,1) : (m_0(0), n_0(0)) = (0,0)\}$$

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

The proof of this result will be given in Section 2. From the proof of this theorem we shall see that for any $(m_0,n_0) \in W^{1,1}(0,1) \times W^{1,1}(0,1)$ we have $(m(t), n(t)) = T(t)(m_0, n_0)$, for all $t \geq 0$, where $(T(t))_{t\geq 0}$ is a strongly continuous semigroup in the space $X = L^1[0,1] \times L^1[0,1]$. Thus, for any $(m_0, n_0) \in X = L^1[0,1] \times L^1[0,1]$, $(m(t), n(t)) = T(t)(m_0, n_0)$ is well-defined for all $t \geq 0$, and $(m,n) \in C([0,\infty), X)$. As usual, for any $(m_0,n_0) \in X$ we call the vector function $t \mapsto (m(t), n(t)) = T(t)(m_0,n_0)$ (for $t \geq 0$) a *mild solution* of (1.1).

Our second main result studies the asymptotic behavior of the solution of (1.1). Before stating this result, we introduce the eigenvalue problem

$$\begin{gathered}
(\gamma_1(x)\hat{m}(x))' + \lambda\hat{m}(x) = -B(x)\hat{m}(x) - \nu(x)\hat{m}(x) + \mu(x)\hat{n}(x), \quad 0 < x < 1, \\
(\gamma_2(x)\hat{n}(x))' + \lambda\hat{n}(x) = -\nu(x)\hat{n}(x) - \mu(x)\hat{n}(x) + \begin{cases} 4B(2x)\hat{m}(2x), & 0 \leq x \leq \frac{1}{2}, \\ 0, & \frac{1}{2} < x \leq 1, \end{cases} \\
\hat{m}(0) = 0, \quad \hat{n}(0) = 0, \\
\int_0^1 \hat{m}(x)dx + \int_0^1 \hat{n}(x)dx = 1.
\end{gathered} \tag{1.2}$$

and its conjugate problem

$$\begin{gathered}
-\gamma_1(x)\varphi'(x) + \lambda\varphi(x) = -B(x)\varphi(x) - \nu(x)\varphi(x) + 2B(x)\psi(\frac{x}{2}), \quad 0 < x < 1, \\
-\gamma_2(x)\psi'(x) + \lambda\psi(x) = -\nu(x)\psi(x) - \mu(x)\psi(x) + \mu(x)\varphi(x), \quad 0 < x < 1, \\
\varphi(1) = 0, \quad \psi(1) = 0, \\
\int_0^1 [\hat{m}(x)\varphi(x)dx + \hat{n}(x)\psi(x)]dx = 1.
\end{gathered} \tag{1.3}$$

Then the second main result reads as follows.

Theorem 1.2. *There exists a constant λ and a strongly positive vector $(\hat{m}, \hat{n}) \in L^1[0,1] \times L^1[0,1]$ satisfying (1.2) such that*

$$\lim_{t\to\infty} e^{-\lambda t}(m(t,\cdot), n(t,\cdot)) = \int_0^1 [m_0(x)\varphi(x) + n_0(x)\psi(x)]dx(\hat{m}, \hat{n}).$$

where $(\varphi(x), \psi(x)) \in L^\infty[0,1] \times L^\infty[0,1]$ is the strongly positive solution of (1.3).

The proof of this result will be given in Section 3. The parameter λ is called the *intrinsic rate of natural increase* or *Malthusian parameter* (see [7]).

The layout of the rest part is as follows. In Section 2 we reduce model (1.1) into an abstract Cauchy problem and establish the well-posedness of it by means of strongly continuous semigroups. In Section 3 we prove that the solution of model

(1.1) has asynchronous exponential growth. In section 4 we consider extensions of the above results to the asymmetric counterpart of model (1.1), and establish similar results as Theorems 1.1 and 1.2.

2. Well-posedness

In this section we use the semigroup theory to study well-posedness of (1.1). We introduce the following spaces:

$$X = L^1[0,1] \times L^1[0,1], \quad \text{with norm } \|(u,v)\|_X = \|u\|_1 + \|v\|_1,$$
$$E = \{(u,v) \in W^{1,1}(0,1) \times W^{1,1}(0,1) : u(0) = 0, v(0) = 0\},$$

with norm $\|(u,v)\|_E = \|u\|_{W^{1,1}} + \|v\|_{W^{1,1}}$.

We first reduce problem (1.3) into an initial value problem of an abstract differential equation in the space X. For this purpose we introduce the linear operators A, B and C in X as follows:

$$A(u,v) = (-(\gamma_1(x)u(x))', -(\gamma_2(x)v(x))'), \quad \text{with domain } D(A) = E,$$
$$B(u,v) = (B_1(u,v), B_2(u,v)), \quad \text{for } (u,v) \in X,$$
$$C(u,v) = (C_1(u,v), C_2(u,v)), \quad \text{for } (u,v) \in X,$$

where

$$B_1(u,v) = -B(x)u(x) - \nu(x)u(x),$$
$$B_2(u,v) = -\mu(x)v(x) - \nu(x)v(x)$$
$$C_1(u,v) = -\mu(x)v(x),$$
$$C_2(u,v) = \begin{cases} 4B(2x)u(2x) & \text{for } 0 \le x \le \frac{1}{2}, \\ 0 & \text{for } \frac{1}{2} < x \le 1\,. \end{cases}$$

We now let $L = A + B + C$ with domain $D(L) = D(A) = E$. We note that $A \in \mathcal{L}(E,X)$, $B \in \mathcal{L}(X)$, $C \in \mathcal{L}(X)$, and $L \in \mathcal{L}(E,X)$. Later on we shall regard A and L as unbounded linear operators in X.

Using these notation, we see that (1.1) can be rewritten as the following abstract initial value problem of an ordinary differential equation in the Banach space X:

$$\begin{gathered} U'(t) = LU(t) \quad \text{for } t > 0, \\ U(0) = U_0, \end{gathered} \tag{2.1}$$

where $U(t) = (m(t), n(t))$ and $U_0 = (m_0(x), n_0(x))$.

Thus, to prove that (1.1) is well-posed in X, we only need to show that the operator L generates a strongly continuous semigroup in X.

Lemma 2.1. *The operator $A + B$ generates a strongly continuous semigroup $\{T_1(t)\}_{t\ge 0}$ in X.*

Proof. Let $F \in X$ and $U(t) = T_1(t)F$. We write $F = (f,g)$, $U(t) = (u(t,\cdot), v(t,\cdot))$. Then (u,v) is the solution of the problem

$$\frac{\partial u}{\partial t} + \frac{\partial(\gamma_1(x)u)}{\partial x} = -a_1(x)u(t,x), \quad 0 \le x \le 1,\ t > 0,$$
$$\frac{\partial v}{\partial t} + \frac{\partial(\gamma_2(x)v)}{\partial x} = -a_2(x)v(t,x), \quad 0 \le x \le 1,\ t > 0,$$
$$u(t,0) = 0, \quad v(t,0) = 0, \quad t > 0,$$

$$u(0,x) = f(x), \quad v(0,x) = g(x), \quad 0 \le x \le 1,$$

where $a_1(x) = B(x) + \nu(x)$ and $a_2(x) = \mu(x) + \nu(x)$. Let $S_1(t,x)$ and $S_2(t,x)$ be the solution of the following two equations

$$\begin{gathered} \frac{dS_1}{dt}(t,x) = \gamma_1(S_1(t,x)), \quad S_1(0,x) = x, \\ \frac{dS_2}{dt}(t,x) = \gamma_2(S_2(t,x)), \quad S_2(0,x) = x \end{gathered} \tag{2.2}$$

Then

$$S_1(t,x) = G_1^{-1}(t + G_1(x)), \quad S_2(t,x) = G_2^{-1}(t + G_2(x)) \tag{2.3}$$

where

$$G_1(x) = \int_0^x \frac{d\xi}{\gamma_1(\xi)}, \quad G_2(x) = \int_0^x \frac{d\xi}{\gamma_2(\xi)} \tag{2.4}$$

By using the standard characteristic method, we obtain

$$u(t,x) = \begin{cases} \frac{E_1(x)}{\gamma_1(x)} \frac{\gamma_1(S_1(-t,x))}{E_1(S_1(-t,x))} f(S_1(-t,x)), & 0 < S_1(-t,x) \\ 0, & \text{elsewhere}, \end{cases} \tag{2.5}$$

$$v(t,x) = \begin{cases} \frac{E_2(x)}{\gamma_2(x)} \frac{\gamma_2(S_2(-t,x))}{E_2(S_2(-t,x))} g(S_2(-t,x)), & 0 < S_2(-t,x), \\ 0, & \text{elsewhere}, \end{cases} \tag{2.6}$$

where

$$E_1(x) = \exp\Big(-\int_0^x \frac{a_1(s)}{\gamma_1(s)} ds\Big), \quad E_2(x) = \exp\Big(-\int_0^x \frac{a_2(s)}{\gamma_2(s)} ds\Big).$$

Obviously, $\{T_1(t)\}_{t\ge 0}$ is a strongly continuous semigroup in X. □

Since $L = A + B + C$ and $C \in \mathcal{L}(X)$, by using the above lemma and a well-known perturbation theorem for generators of strongly continuous semigroups in Banach spaces, we get the following result.

Lemma 2.2. *The operator L generates a strongly continuous semigroup $\{T(t)\}_{t\ge 0}$ in X.*

By this lemma and a well-known result in the theory of strongly continuous semigroups, we have the following result.

Theorem 2.3. *For any given initial data $U_0 \in E$, the initial value problem* (2.1) *has a unique solution $U \in C([0,+\infty); E) \cap C^1([0,+\infty); X)$, given by*

$$U(t) = T(t)U_0 \quad \textit{for } t \ge 0.$$

Since (2.1) is an abstractly rewritten form of (1.1), by this theorem we see that Theorem 1.1 follows.

3. Asynchronous exponential growth

In this section we study the asymptotic behavior of the solution of (1.1). We shall prove that the semigroup $(T(t))_{t\ge 0}$ has the property of asynchronous exponential growth on X. For this purpose, we shall prove that the semigroup $(T(t))_{t\ge 0}$ is *positive, eventually norm continuous, eventually compact* and *irreducible*. Recall (see [11] and [13]) that a strongly continuous semigroup $(T(t))_{t\ge 0}$ 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 continuous* if there exists $t_0 \ge 0$ such that the mapping

$t \mapsto T(t)$ is continuous from $[t_0, \infty)$ to $\mathcal{L}(X)$; it is said to be *eventually compact* if there exists $t_0 \geq 0$ such that the operator $T(t)$ is compact for all $t \geq t_0$. Moreover, $(T(t))_{t\geq 0}$ is said to be *irreducible* if $\forall\ \varphi \in X$, $\psi \in X^*$ (the linear and topological dual of X), $\varphi > 0$, $\psi > 0$, we have that $\langle T(t_0)\varphi, \psi\rangle > 0$ for some $t_0 > 0$, where $\langle \cdot, \cdot\rangle$ denotes the dual product between X and X^*.

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

$$s(L) = \sup\{\operatorname{Re}\lambda : \lambda \in \sigma(L)\}. \tag{3.1}$$

If the above assertions on the semigroup $(T(t))_{t\geq 0}$ are proved, then by a well-known result in the theory of semigroups we see that $s(L)$ is a dominant eigenvalue of L (i.e., $s(L) \in \sigma(L)$ and $\operatorname{Re}\lambda < s(L)$ for all $\lambda \in \sigma(L)\backslash\{s(L)\}$), and it is a first-order pole of $R(\lambda, L)$ with an one-dimensional residue P (see Corollary V.3.2, Theorem VI.1.12 and Corollary VI.1.13 in [11]). By [11, Corollary V.3.3], we then obtain the assertion in Theorem 1.2. Thus, in the sequel we step by step prove the above assertions about the semigroup $(T(t))_{t\geq 0}$.

Lemma 3.1. *The semigroup $(T(t))_{t\geq 0}$ is positive.*

Proof. From (2.5) and (2.6), we see that $\{T_1(t)\}_{t\geq 0}$ is positive. Since C is a positive operator on X, then the claim follows from [11, Corollary 1.11]. □

Lemma 3.2. *The semigroup $(T(t))_{t\geq 0}$ is eventually norm continuous.*

Proof. From (2.5) and (2.6) we see that $T_1(t) = 0$ for $t > \max\{G_1(1), G_2(1)\}$. This particularly implies that $(T_1(t))_{t\geq 0}$ is norm continuous for $t > \max\{G_1(1), G_2(1)\}$. Thus, by [11, Theorem III.1.16], the desired assertion follows if we prove that the mapping $t \mapsto K(t) \in \mathcal{L}(X)$ is continuous for $t > 0$, where $K(t)$ is the operator in X defined by

$$K(t)F = \int_0^t T_1(t-r)CT_1(r)F dr \quad \text{for } F \in X.$$

Using the representations of $T_1(t)$ (given by (2.5) and (2.6)) and C we see that for $F = (f, g) \in X$,

$$\begin{aligned} &T_1(t-r)CT_1(r)F \\ &= \Big(c_1(x,t,r)g(S_1(-t+r, S_2(-r,x))), c_2(x,t,r)f(S_2(-t+r, 2S_1(-r,x)))\Big), \end{aligned}$$

where $c_i(x,t,r)$ $(i = 1, 2)$ are continuous functions. Hence

$$\begin{aligned} K(t)F = \Big(&\int_0^t c_1(x,t,r)g(S_1(-t+r, S_2(-r,x)))dr, \\ &\int_0^t c_2(x,t,r)f(S_2(-t+r, 2S_1(-r,x)))dr\Big), \end{aligned}$$

We substitute $\xi_1 = S_1(-t+r, S_2(-r,x))$ for r in the first term of $K(t)F$ and $\xi_2 = S_2(-t+r, 2S_1(-r,x))$ for r in the second term of $K(t)F$. Because of the assumption (H3), We can find that

$$\begin{gathered} \frac{d\xi_1}{dr} = \gamma_1(\xi_1)\Big(1 - \frac{\gamma_2(S_2(-r,x))}{\gamma_1(S_2(-r,x))}\Big) \neq 0, \\ \frac{d\xi_2}{dr} = \frac{\gamma_2(\xi_2)}{\gamma_2(2S_1(-r,x))}(\gamma_2(2S_1(-r,x)) - 2\gamma_1(S_1(-r,x))) \neq 0. \end{gathered}$$

Then we can easily verify that the mapping $t \mapsto K(t)$ from $(0,+\infty)$ to $\mathcal{L}(X)$ is continuous. Hence the desired assertion follows. This proves lemma 3.2. □

Lemma 3.3. *The semigroup* $(T(t))_{t\geq 0}$ *is eventually compact.*

Proof. Since $R(\lambda, A)$ is compact and $B + C$ is the bounded operator, we conclude that $R(\lambda, L) = R(\lambda, A + B + C)$ is compact. Consequently, $R(\lambda, L)T(t)$ is compact for all $t > 0$. Since $(T(t))_{t\geq 0}$ is eventually norm continuous, by [11, Lemma II.4.28], it follows that $(T(t))_{t\geq 0}$ is eventually compact. This completes the proof. □

Lemma 3.4. *The semigroup* $(T(t))_{t\geq 0}$ *is irreducible.*

Proof. Since $R(\lambda, L) = \int_0^{+\infty} e^{-\lambda t}T(t)dt$, for all $Re\lambda > s(L)$ (see [[11],Lemma VI.1.9]), we have that for all $F = (f(x), g(x)) \in X$, $\Psi = (\psi_1, \psi_2) \in X^*$, $F > 0$, $\Psi > 0$,

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

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 π_1 and π_2 be the projections onto the first and second coordinates, respectively. We will prove that $\pi_1(R(\lambda, L)F)(x) > 0$ and $\pi_2(R(\lambda, L)F)(x) > 0$ for almost all $x \in [0, 1]$. In the sequel we find the expression of $R(\lambda, L)$. For $F = (f(x), g(x)) \in X$, we solve the equation

$$(\lambda I - L)U = F. \tag{3.2}$$

By writing $U = (u(x), v(x))$ and $F = (f(x), g(x))$, we see that (3.2) can be rewritten as

$$(\gamma_1(x)u(x))' + \lambda u(x) + a_1(x)u(x) = f(x) + \mu(x)v(x) \quad \text{for } 0 < x < 1,$$

$$(\gamma_2(x)u(x))' + \lambda v(x) + a_2(x)v(x) = g(x) + \begin{cases} 4B(2x)u(2x) & \text{for } 0 < x \leq \frac{1}{2}, \\ 0 & \text{for } \frac{1}{2} < x < 1, \end{cases}$$

$$u(0) = 0, \quad v(0) = 0$$

where $a_1(x) = B(x) + \nu(x)$, $a_2(x) = \mu(x) + \nu(x)$. Then, we have

$$u(a) = \int_0^x \frac{\varepsilon_{1\lambda}(x)f(s)}{\varepsilon_{1\lambda}(s)\gamma_1(s)}ds + \int_0^x \frac{\varepsilon_{1\lambda}(x)\mu(s)v(s)}{\varepsilon_{1\lambda}(s)\gamma_1(s)}ds \tag{3.3}$$

$$v(a) = \begin{cases} \int_0^x \frac{\varepsilon_{2\lambda}(x)g(s)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}ds + 4\int_0^x \frac{\varepsilon_{2\lambda}(x)B(2s)u(2s)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}ds & \text{for } 0 < x \leq \frac{1}{2}, \\ \int_0^x \frac{\varepsilon_{2\lambda}(x)g(s)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}ds + 4\int_0^{\frac{1}{2}} \frac{\varepsilon_{2\lambda}(x)B(2s)u(2s)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}ds & \text{for } \frac{1}{2} < x < 1, \end{cases} \tag{3.4}$$

where

$$\varepsilon_{1\lambda}(x) = \exp\big\{-\int_0^x \frac{\lambda + a_1(y) + \gamma_1'(y)}{\gamma_1(y)}dy\big\},$$
$$\varepsilon_{2\lambda}(x) = \exp\big\{-\int_0^x \frac{\lambda + a_2(y) + \gamma_2'(y)}{\gamma_2(y)}dy\big\}.$$

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

$$H_\lambda(f_1(x), f_2(x)) = \left(\int_0^x \frac{\varepsilon_{1\lambda}(x)\mu(s)f_2(s)}{\varepsilon_{1\lambda}(s)\gamma_1(s)}ds, \begin{cases} 4\int_0^x \frac{\varepsilon_{2\lambda}(x)B(2s)f_1(2s)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}ds & \text{for } 0 < x \leq \frac{1}{2}, \\ 4\int_0^{\frac{1}{2}} \frac{\varepsilon_{2\lambda}(x)B(2s)f_1(2s)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}ds & \text{for } \frac{1}{2} < x < 1, \end{cases}\right) \tag{3.5}$$

$$S_\lambda(f_1(x), f_2(x)) = \Big(\int_0^x \frac{\varepsilon_{1\lambda}(x) f_1(s)}{\varepsilon_{1\lambda}(s)\gamma_1(s)} ds, \int_0^x \frac{\varepsilon_{2\lambda}(x) f_2(s)}{\varepsilon_{2\lambda}(s)\gamma_2(s)} ds \Big) . \tag{3.6}$$

Since

$$\|H_\lambda(f_1(x), f_2(x))\| \to 0 (\lambda \to +\infty)$$

there exists $\lambda^* > 0$ such that $\|H_\lambda\| < 1$ for $\lambda \geq \lambda^*$. This implies $(I - H_\lambda)^{-1}$ exists for $\lambda \geq \lambda^*$. Then the resolvent of L is

$$R(\lambda, L)F = (I - H_\lambda)^{-1} S_\lambda F = \sum_{n=0}^{\infty} (H_\lambda)^n S_\lambda F, \quad \text{for } \lambda > \lambda^* \tag{3.7}$$

For $0 \leq (f(x), g(x)) \in \mathbf{X}$ and $(f(x), g(x)) \neq 0$, without loss of generality, we can assume that $0 \leq f \in L^1[0,1]$ and $f(x) > 0$ for almost all $x \in [x_0, x_1]$. Then

$$\begin{gathered}
\pi_1(S_\lambda(f,g))(x) > 0, \quad \text{for } x \in [x_0, 1] \\
\pi_2(H_\lambda S_\lambda(f,g))(x) > 0, \quad \text{for } x \in [\frac{x_0}{2}, 1] \\
\pi_1(H_\lambda H_\lambda S_\lambda(f,g))(x) > 0, \quad \text{for } x \in [\frac{x_0}{2}, 1] \\
\pi_2(H_\lambda H_\lambda H_\lambda S_\lambda(f,g))(x) > 0, \quad \text{for } x \in [\frac{x_0}{4}, 1]
\end{gathered}$$

Continuing in this way, we obtain $\pi_1(R(\lambda, L)F)(x) > 0$ and $\pi_2(R(\lambda, L)F)(x) > 0$ for almost all $x \in [0,1]$. If we assume that $g(x) > 0$ for almost all $x \in [x_0, x_1]$, the result is the same. This completes the proof. □

Corollary 3.5. *$\sigma(L) \neq \emptyset$.*

Proof. This follows from [13, Theorem C-III.3.7], which states that if a semigroup is irreducible, positive and eventually compact, then the spectrum of its generator is not empty. □

Corollary 3.6. *$s(L) > -\infty$ and $s(L) \in \sigma(L)$.*

Proof. The first assertion is an immediately consequence of Corollary 3.5. The second assertion follows from the positivity of the semigroup $(T(t))_{t\geq 0}$ and the fact $s(L) > -\infty$; see [11, Theorem VI.1.10]. □

By Lemmas 3.1–3.4, Corollary 3.6 and [11, Corollary V.3.3], we conclude that there exists an eigenvalue λ of L associated with a strictly positive eigenvector $(\hat{m}, \hat{n})$ such that

$$\lim_{t\to+\infty} e^{-\lambda t}(m(t,x), n(t,x)) = C(\hat{m}(x), \hat{n}(x)) \tag{3.8}$$

where $\lambda = s(L)$. In the sequel we find the constant C. we know that $\lambda = s(L)$ is the dominant eigenvalue of the eigenvalue problem

$$\begin{gathered}
(\gamma_1(x)\hat{m}(x))' + \lambda \hat{m}(x) = -B(x)\hat{m}(x) - \nu(x)\hat{m}(x) + \mu(x)\hat{n}(x), \quad 0 < x < 1, \\
(\gamma_2(x)\hat{n}(x))' + \lambda \hat{n}(x) = -\nu(x)\hat{n}(x) - \mu(x)\hat{n}(x) + \begin{cases} 4B(2x)\hat{m}(2x), & 0 \leq x \leq \frac{1}{2}, \\ 0, & \frac{1}{2} < x \leq 1, \end{cases} \\
\hat{m}(0) = 0, \quad \hat{n}(0) = 0,
\end{gathered} \tag{3.9}$$

and the corresponding eigenvector $(\hat{m}, \hat{n})$ is strongly positive in $(0,1)$; i.e., $\hat{m}(x) > 0$ and $\hat{n}(x) > 0$ for all $0 < x < 1$. We normalize $(\hat{m}, \hat{n})$ such that

$$\int_0^1 \hat{m}(x)dx + \int_0^1 \hat{n}(x)dx = 1.$$

Let (φ, ψ) be the eigenvector of the conjugate problem of (3.9); i.e.,

$$\begin{gathered}
-\gamma_1(x)\varphi'(x) + \lambda\varphi(x) = -B(x)\varphi(x) - \nu(x)\varphi(x) + 2B(x)\psi(\frac{x}{2}), \quad 0 < x < 1, \\
-\gamma_2(x)\psi'(x) + \lambda\psi(x) = -\nu(x)\psi(x) - \mu(x)\psi(x) + \mu(x)\varphi(x), \quad 0 < x < 1, \\
\varphi(1) = 0, \quad \psi(1) = 0.
\end{gathered} \tag{3.10}$$

We normalize (φ, ψ) such that

$$\int_0^1 \hat{m}(x)\varphi(x)dx + \int_0^1 \hat{n}(x)\psi(x)dx = 1.$$

Then φ and ψ are also strictly positive in $(0,1)$, due to a similar reason as that for $\hat{m}$ and $\hat{n}$. Now we consider the function $\int_0^1 [m(t,x)\varphi(x) + n(t,x)\psi(x)]e^{-\lambda t}dx$. From (1.1) and (3.10) we easily obtain

$$\frac{d}{dt}\int_0^1 [m(t,x)\varphi(x) + n(t,x)\psi(x)]e^{-\lambda t}dx = 0.$$

Hence

$$\int_0^1 [m(t,x)\varphi(x) + n(t,x)\psi(x)]e^{-\lambda t}dx = \int_0^1 [m_0(x)\varphi(x) + n_0(x)\psi(x)]dx$$

for all $t \geq 0$. Letting $t \to \infty$ and using (3.8), we get

$$C\int_0^1 [\hat{m}(x)\varphi(x)dx + \hat{n}(x)\psi(x)]dx = \int_0^1 [m_0(x)\varphi(x) + n_0(x)\psi(x)]dx.$$

Since $\int_0^1 [\hat{m}(x)\varphi(x)dx + \hat{n}(x)\psi(x)]dx = 1$, we obtain

$$C = \int_0^1 [m_0(x)\varphi(x) + n_0(x)\psi(x)]dx.$$

This completes the proof of Theorem 1.2.

4. Two-phase Asymmetric Cell Division Model

In this section we study the two-phase cell division model

$$\begin{gathered}
\frac{\partial m}{\partial t} + \frac{(\gamma_1(x)\partial m)}{\partial x} = -\nu(x)m(t,x) - B(x)m(t,x) + \mu(x)n(t,x), \\
0 < x < 1, \ t > 0, \\
\frac{\partial n}{\partial t} + \frac{(\gamma_2(x)\partial n)}{\partial x} = -\nu(x)n(t,x) - \mu(x)n(t,x) + \int_0^1 b(x,y)m(t,y)dy, \\
0 < x < 1, \ t > 0, \\
m(t,0) = 0, \quad n(t,0) = 0, \\
m(0,x) = m_0(x), \quad n(0,x) = n_0(x), \quad 0 < x < 1,
\end{gathered} \tag{4.1}$$

This model describes asymmetric division of cells; i.e., the m-phase cell of size y is divided into one n-phase cell of size x and another n-phase cell of size $y - x$. The notations $\gamma_1(x)$, $\gamma_2(x)$, $\mu(x)$, $\nu(x)$, and $B(x)$ have the same meaning as the corresponding notation in (1.1). For consistency with the modelling we have to impose

$$b(x,y) \geq 0 \quad \text{for } y \geq x \quad \text{and} \quad b(x,y) = 0 \quad \text{for } y < x, \tag{4.2}$$

$$\int_0^y b(x,y)dx = 2B(y), \tag{4.3}$$

$$\int_0^y xb(x,y)dx = yB(y), \tag{4.4}$$

$$b(x,y) = b(y-x,y). \tag{4.5}$$

We still assume that $\mu(x)$, $\nu(x)$ and $B(x)$ satisfy the assumptions (H1) and (H2). We only assume that $\gamma_1, \gamma_2 \in C^1[0,1]$ and $\gamma_1(x), \gamma_2(x) > 0$ for almost all $x \in [0,1]$ in this section. Besides, we assume that $b(\cdot, y) \in C[0,1]$ for any fixed $y \in [0,1]$.

To establish well-posedness of (4.1), we redefine the operator C_2 in Section 2 as

$$C_2(u,v) = \int_0^1 b(x,y)u(y)dy \quad \text{for } (u,v) \in X,$$

and let $C_1(u,v)$ be as before. We note that the redefined operator $C(u,v) = (C_1(u,v), C_2(u,v))$ is bounded on X. Similar arguments as that in Section 2 yield that the redefined operator $L = A + B + C$ generates a strongly continuous semigroup $(T_2(t))_{t\geq 0}$ on X. Then we can obtain the same assertion as Theorem 1.1 about model (4.1).

Second, we will obtain the asynchronous exponential growth for (4.1). Note that the redefined operator C is still positive on X. Then a similar argument as in the proof of Lemma 3.1 shows that the semigroup $(T_2(t))_{t\geq 0}$ is positive. The proofs of the eventual compactness and the irreducibility of this semigroup have some differences from those given in Lemmas 3.3 and 3.4. We thus give them in the following two lemmas.

Lemma 4.1. *The semigroup $(T_2(t))_{t\geq 0}$ is eventually norm continuous and eventually compact.*

Proof. In view of the Fréchet-Kolmogorov compactness criterion in L^1 we conclude from

$$\begin{aligned} \Big| \int_0^1 b(x,y)u(y)dy - \int_0^1 b(x',y)u(y)dy \Big| &\leq \int_0^1 |b(x,y) - b(x',y)||u(y)|dy \\ &\leq \|b(x,y) - b(x',y)\|_\infty \|u(y)\|_{L^1} \end{aligned} \tag{4.6}$$

and the continuity of b that the operator C is compact. From (2.5) and (2.6), we can easily see that the semigroup $(T_1(t))_{t\geq 0}$ generated by the operator $A + B$ is compact for $t > \max\{G_1(1), G_2(1)\}$. Hence, the semigroup $(T_2(t))_{t\geq 0}$ is compact for $t > \max\{G_1(1), G_2(1)\}$; see [11, Lemma III.1.14]. By [11, Lemma II.4.22], the semigroup $(T_2(t))_{t\geq 0}$ is norm continuous for $t > \max\{G_1(1), G_2(1)\}$. That completes the proof. □

Lemma 4.2. *The semigroup $(T_2(t))_{t\geq 0}$ is irreducible.*

Proof. The proof of this lemma is similar as that in Lemma 3.4 except for the definition of the operators H_λ. Here for each $\lambda \in \mathbb{C}$, we define

$$H_\lambda(f_1(x), f_2(x)) = \Big(\int_0^x \frac{\varepsilon_{1\lambda}(x)\mu(s)f_2(s)}{\varepsilon_{1\lambda}(s)\gamma_1(s)} ds, \int_0^x \frac{\varepsilon_{2\lambda}(x)}{\varepsilon_{2\lambda}(s)\gamma_2(s)} \int_s^1 b(s,y)f_1(y)\, dy\, ds \Big)$$

$$
\begin{aligned}
&= \Big(\int_0^x \frac{\varepsilon_{1\lambda}(x)\mu(s)f_2(s)}{\varepsilon_{1\lambda}(s)\gamma_1(s)} ds, \int_0^x f_1(y) \int_0^y \frac{\varepsilon_{2\lambda}(x)b(s,y)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}\, ds\, dy \\
&\quad + \int_x^1 f_1(y) \int_0^x \frac{\varepsilon_{2\lambda}(x)b(s,y)}{\varepsilon_{2\lambda}(s)\gamma_2(s)}\, ds\, dy \Big),
\end{aligned}
$$

where $\varepsilon_{1\lambda}(x)$ and $\varepsilon_{2\lambda}(x)$ are correspondingly the same with those appearing in the proof of Lemma 3.4. We also note that (4.2), (4.3) and the assumption on $B(x)$ play a important role to obtain that $\pi_1(R(\lambda, L)F)(x) > 0$ and $\pi_2(R(\lambda, L)F)(x) > 0$ for almost all $x \in [0, 1]$. □

We also have that there exist an eigenvalue λ of the redefined operator L (which is also the spectral bound of the redefined operator L) and the strictly positive associated eigenvector $(\hat{m}(x), \hat{n}(x))$; i.e.,

$$
\begin{gathered}
(\gamma_1(x)\hat{m}(x))' + \lambda\hat{m}(x) = -\nu(x)\hat{m}(x) - B(x)\hat{m}(x) + \mu(x)\hat{n}(x), \quad 0 < x < 1, \\
(\gamma_2(x)\hat{n}(x))' + \lambda\hat{n}(x) = -\nu(x)\hat{n}(x) - \mu(x)\hat{n}(x) + \int_0^1 b(x,y)\hat{m}(y)dy, \quad 0 < x < 1, \\
\hat{m}(0) = 0, \quad \hat{n}(0) = 0,
\end{gathered} \tag{4.7}
$$

The conjugate problem of (4.8) is as follows

$$
\begin{gathered}
-\gamma_1(x)\varphi'(x) + \lambda\varphi(x) = -\nu(x)\varphi(x) - B(x)\varphi(x) + \int_0^1 b(y,x)\psi(y)dy, \quad 0 < x < 1, \\
-\gamma_2(x)\psi'(x) + \lambda\psi(x) = -\nu(x)\psi(x) - \mu(x)\psi(x) + \mu(x)\varphi(x), \quad 0 < x < 1, \\
\varphi(1) = 0, \quad \psi(1) = 0,
\end{gathered} \tag{4.8}
$$

The rest argument is similar to that in Section 3 and is therefore omitted. Hence, we can obtain the same assertion as Theorem 1.2 about model (4.1).

Acknowledgements. The authors are greatly in debt to the anonymous referee for his/her valuable comments and suggestions on modifying this manuscript.

References

[1] B. Perthame and L. Ryzhik; Exponential decay for the fragmentation or cell-division equation, *J. Diff. Equ.*, 210(2005), 155-177.

[2] P. Michel, S. Mischler and B. Perthame; General entropy inequality: an illustration on growth models, *J. Math. Pures et Appl.*, 84(2005), 1235–1260.

[3] P. Michel; Existence of a solution to the cell division eigenproblem, *Model. Math. Meth. Appl. Sci.*, vol.16, suppl. issue 1(2006), 1125–1153.

[4] B. Perthame and T. M. Touaoula; Analysis of a cell system with finite divisions, *Bol. Soc. Esp. Mat. Apl.*, no. 44 (2008), 53-77.

[5] J. Z. Farkas and P. Hinow; On a size-structured two-phase population model with infinite states-at-birth, arXiv:0903.1649, March 2009.

[6] J. Z. Farkas; Note on asychronous exponential growth for structured population models, *Nonlinear Analysis: TMA*, 67(2007), 618-622.

[7] H. R. Thieme; Balanced exponential growth of operator semigroups, *J. Math. Anal. Appl.*, 223(1998), 30-49.

[8] 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.

[9] 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.

[10] B. Perthame; *Transport Equations in Biology*, Birkhäuser Verlag, Basel, 2007.
[11] K-J. Engel and R. Nagel; One-Parameter Semigroups for Linear Evolution Equations, Springer, New York, 2000.
[12] Ph. Clément, H. Heijmans, S. Angenent, C. van Duijin, and B. de Pagter; One-Parameter Semigroups, North-holland, Amsterdam, 1987.
[13] 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.
[13] A. Pazy; Semigroups of Linear Operators and Applications to Partial Differential Equations, Springer, New York, 1983.
[14] T. D. Pollard and W. C. Earnshaw; *Cell Biology*, Elsevier Science, New York, 2002.
[15] J. Celis; *Cell Biology*, third edition, Elsevier Academic Press, 2006.

Meng Bai
Department of Mathematics, Sun Yat-Sen University, Guangzhou, Guangdong 510275, China
E-mail address: baimeng.clare@yahoo.com.cn

Shangbin Cui
Department of Mathematics, Sun Yat-Sen University, Guangzhou, Guangdong 510275, China
E-mail address: cuisb3@yahoo.com.cn