Research Article

Mathematical Methods in the Applied Sciences

Received 8 October 2010 Published online 6 May 2011 in Wiley Online Library

(wileyonlinelibrary.com) DOI: 10.1002/mma.1473
MOS subject classification: 47 H 06; 35 F 31; 47 H 20

Well-posedness of a nonlinear evolution equation arising in growing cell population

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Communicated by M. Lachowicz

We prove that a nonlinear evolution equation which comes from a model of an age-structured cell population endowed with general reproduction laws is well-posed. Copyright © 2011 John Wiley & Sons, Ltd.

Keywords: accretive operators; cell population dynamics; mild solutions; integral solutions

1. Introduction

Many models of structured population dynamics with inherited properties have been proposed especially in cell biology. Many cell biologists believe that the inheritance of generation time is important for modeling proliferating cell populations.

In this paper we are concerned with the following nonlinear model:

$$\begin{cases} \dfrac{\partial}{\partial t}f(t,a,l)=-\dfrac{\partial}{\partial a}f(t,a,l)+\sigma(a,l,f(t,a,l)), \\ f(t,0,l)=K(f(t,l,l)), \end{cases} \tag{1}$$

where $l\in(l_1,l_2)$, $0\leqslant l_1<l_2<\infty$ and $a\in[0,l]$ and where K denotes a nonlinear operator defined between two suitable function spaces.

Equations of type (1) were introduced in 1974 by Lebowitz and Rubinow [1] for modeling microbial populations by an age and cycle length formalism. The variable a represents age, while l is the cycle length of cells and represents the time between cell birth and cell division. The function $f(t,a,l)$ is the density of the population with respect to the age a and the cell cycle length l at time t. The cell cycle length l of individual cells is an inherent characteristic determined at birth, i.e. the duration of the cycle from cell birth to cell division is determined at birth. The constant l_1(resp. l_2) denotes the minimum cycle length (resp. the maximum cycle length). The function $\sigma(\cdot,\cdot,\cdot)$ is the rate of cell mortality or loss due to causes other than division. All biological laws of the transition for distribution of mothers cycle length to daughters cycle length are mathematically described by the following general boundary conditions:

$$f(t,0,l)=[K(f(t,\cdot,\cdot))](l), \tag{2}$$

where K is an operator on suitable trace spaces called the transition operator. The case when K is a linear operator was studied for instance in [2–4]. The nonlinear case has been studied in [5] although for the stationary equation. In fact, it was observed by Rotenberg [6] that the linear model seems not adequate. Indeed, the cells are in contact with a nutrient environment and fluctuations in nutrient concentration and other density-dependent effects such as contact inhibition of growth make the transition rate functions of population density, thus creating a nonlinear problem. On the other hand, the biological boundaries l_1 and l_2 are fixed and tightly coupled throughout mitosis. The conditions present at the boundary are left throughout the system and cannot be omitted. This fact suggests that at mitosis the daughter cells and mother cells are related by nonlinear reproduction rule. (A mathematical model for age-dependent dynamics with nonlinear boundary conditions was considered in [7]). Examples of transition operators were exploited in [8–10]. Here, we prove that this model for the parabolic case is well-posed in the natural framework like L^1-space, since $f(t,a,l)$ has the meaning of a density of the population with respect to time t, to the age a and the cell cycle length l i.e. the purpose of this note is to obtain an existence and uniqueness result for Equation (1) although K becomes nonlinear.

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2. Preliminaries

We start this section by supposing that $0<l_1<l_2<\infty$ and that Ω is the set $\Omega:=\{(a,l)$ such that $0<a<l,\ l_1<l<l_2\}$. We consider the Banach space $X:=L^1(\Omega)$ with its natural norm, which is given by

$$\|\varphi\|_1=\int_\Omega |\varphi(a,l)|\,\mathrm{d}a\,\mathrm{d}l=\int_{l_1}^{l_2}\left(\int_0^l |\varphi(a,l)|\mathrm{d}a\right)\mathrm{d}l.$$

We introduce the partial Sobolev space $W^1(\Omega):=\{\varphi\in L^1(\Omega):\frac{\partial}{\partial a}\varphi\in L^1(\Omega)\}$, which is a Banach space with the norm:

$$\|\varphi\|_{W^1(\Omega)}=\|\varphi\|_1+\left\|\frac{\partial\varphi}{\partial a}\right\|_1.$$

Now we define the following boundary spaces: $X^1=L^1(\Gamma_1,dl)$ and $X^2=L^1(\Gamma_2,dl)$ where $\Gamma_1:=\{(0,l):l\in(l_1,l_2)\}$ and $\Gamma_2:=\{(l,l):l\in(l_1,l_2)\}$.

It is well known (see Theorem 3.3 of [2]) that every function $\psi\in W^1(\Omega)$ has traces on both spaces X^1 and X^2. Moreover, the trace mappings γ_0 and γ_1 are linear continuous mappings and they are given by

$$\gamma_0(\psi)(l):=\psi(x,l)-\int_0^x\frac{\partial\psi(s,l)}{\partial a}\,\mathrm{d}s,$$

and

$$\gamma_1(\psi)(l):=\psi(x,l)+\int_x^l\frac{\partial\psi(s,l)}{\partial a}\,\mathrm{d}s.$$

Let $(X,\|\cdot\|)$ be a real Banach space. A mapping $A:D(A)\subseteq X\to X$ is said to be *accretive* if the inequality $\|x-y+\lambda(A(x)-A(y))\|\geqslant\|x-y\|$ holds for all $\lambda\geqslant 0$, $x,y\in D(A)$. If, in addition, $\mathscr{R}(I+\lambda A)$ (i.e. the range of the operator $I+\lambda A$), is for one, hence for all, $\lambda>0$, precisely X, then A is called *m*-accretive. Accretive operators were introduced by Browder [11] and Kato [12] independently.

Finally, A is said to be *w*-accretive (*w*-*m*-accretive), where $w\in\mathbb{R}$, if $A+wI$ is accretive (respectively *m*-accretive). Notice that A is accretive if and only if A is *w*-accretive with $w=0$.

Those operators which are *w*-*m*-accretive play an important role in the study of nonlinear partial differential equations.

Consider the Cauchy problem

$$\begin{cases}u'(t)+A(u(t))=f(t), & t\in(0,T),\\ u(0)=x_0\in\overline{D(A)},\end{cases}\tag{3}$$

where A is *w*-*m*-accretive on X and $f\in L^1(0,T,X)$.

Given $\varepsilon>0$. An ε-discretization on $[0,T]$ of the equation $u'(t)+A(u(t))=f(t)$ consists of a partition $0=t_0\leqslant t_1\leqslant t_2\leqslant\cdots\leqslant t_N$ of the interval $[0,t_N]$ and a finite sequence $(f_i)_{i=1}^N\subseteq X$ such that

$$t_i-t_{i-1}<\varepsilon\quad\text{for } i=1,\ldots,N,\quad T-\varepsilon<t_N\leqslant T,$$
$$\sum_{i=1}^N\int_{t_{i-1}}^{t_i}\|f(s)-f_i\|\,\mathrm{d}s<\varepsilon.$$

A $D_A^\varepsilon(0=t_0\leqslant t_1\leqslant t_2\leqslant\cdots\leqslant t_N;\ f_1,\ldots,f_N)$ solution to (3) is a piecewise constant function $z:[0,t_N]\to X$ whose values z_i on $(t_{i-1},t_i]$ satisfy the finite difference equation

$$\frac{z_i-z_{i-1}}{t_i-t_{i-1}}+A(z_i)=f_i,\quad i=1,2,\ldots,N.\tag{4}$$

Such a function $z=(z_i)_{i=1}^N$ is called an ε-approximate solution to the Cauchy problem (3) if it further satisfies

$$\|z(0)-x_0\|\leqslant\varepsilon.$$

It is well known (see Corollary 4.1 of [13]) that (3) has a unique mild solution in the sense that there exists a unique continuous function $u:[0,T]\to\overline{D(A)}$ such that $u(0)=x_0$, and moreover, for each $\varepsilon>0$ there is an ε-approximate solution z of $u'+A(u)=f$ on $[0,T]$ such that $\|u(t)-z(t)\|\leqslant\varepsilon$ for all $t\in[0,T]$.

If u is the mild solution of Problem (3), then for each $(x,y)\in A$ and $0\leqslant s\leqslant t\leqslant T$, we have

$$\|u(t)-x\|\leqslant \mathrm{e}^{w(t-s)}\|u(s)-x\|+\int_s^t \mathrm{e}^{w(t-\tau)}[f(\tau)-y,u(\tau)-x]_s\,\mathrm{d}\tau.\tag{5}$$

Here the function $[\cdot,\cdot]_s:X\times X\to\mathbb{R}$ is defined by $[y,x]_s=\sup\{x^*(y):x^*\in J(x)\}$, where $J:X\to 2^{X^*}$ is the duality mapping on X, i.e. $J(x)=\{x^*\in X^*:x^*(x)=\|x\|,\|x^*\|=1\}$. This means that u is an integral solution to Equation (3) in the sense of Benilan [14] and moreover both concepts of solution coincide within our context.

If u, v are integral solutions of $u'(t)+A(u(t))=f(t)$ and $v'(t)+A(v(t))=g(t)$, respectively, with $f,g\in L^1(0,T,X)$, then

$$\|u(t)-v(t)\|\leqslant e^{wt}\|u(0)-v(0)\|+\int_0^t e^{w(t-s)}\|f(s)-g(s)\|ds.$$

We now recall some important facts regarding accretive operators which will be used in our paper (see for example [13]).

Proposition 1
Let $A:D(A)\to X$ an operator on X. The following conditions are equivalent.

- A is a w-accretive operator,
- The inequality $[A(x)-A(y),x-y]_s\geqslant -w\|x-y\|$, holds for every $x,y\in D(A)$,
- For each $0<\lambda<1/w$ the resolvent $J_\lambda:=(I+\lambda A)^{-1}:R(I+\lambda A)\to D(A)$ is a single-valued $1/(1-w\lambda)$-Lipschitzian mapping.

3. General existence results

Our first step in this section will be to associate an m-accretive operator with the boundary value problem (1) whenever $K:X^2\to X^1$ is a nonexpansive mapping, i.e.

(H1) $\|K(f_1)-K(f_2)\|_{X^1}\leqslant\|f_1-f_2\|_{X^2}$.

As a trivial consequence of (H1) we obtain that K is a continuous operator from X^2 into X^1.
Let us define the following operator:

$$\begin{cases} T_K:D(T_K)\subseteq L^1(\Omega)\to L^1(\Omega),\\ \varphi\to T_K(\varphi(a,l))=\dfrac{\partial\varphi}{\partial a}(a,l), \end{cases}\tag{6}$$

where $D(T_K):=\{\varphi\in W^1(\Omega):\gamma_0(\varphi)=K(\gamma_1(\varphi))\}$.

Theorem 1
The operator $T_K:D(T_K)\subseteq L^1(\Omega)\to L^1(\Omega)$ is m-accretive on $L^1(\Omega)$.

Proof
Let φ_1, φ_2 two elements of $D(T_K)$. We claim that T_k is accretive. Indeed, if we introduce the function $sgn_0:\mathbb{R}\to\mathbb{R}$ by

$$\mathrm{sgn}_0(r)=\begin{cases} 1 & \text{if } r>0,\\ 0 & \text{if } r=0,\\ -1 & \text{if } r<0.\end{cases}$$

We obtain that

$$\begin{aligned}[T_K(\varphi_1)-T_K(\varphi_2),\varphi_1-\varphi_2]_s &\geqslant \int_{l_1}^{l_2}\left(\int_0^l\left(\frac{\partial}{\partial a}(\varphi_1(a,l)-\varphi_2(a,l))\mathrm{sgn}_0(\varphi_1(a,l)-\varphi_2(a,l))\,da\right)dl\right.\\ &=\int_{l_1}^{l_2}\left(\int_0^l\left(\frac{\partial}{\partial a}(|\varphi_1(a,l)-\varphi_2(a,l)|)da\right)dl.\right.\end{aligned}\tag{7}$$

By using that the trace mappings are linear and continuous, we have the last term of inequality (7) greater than or equal to

$$\int_{l_1}^{l_2}(|\gamma_1(\varphi_1)(l)-\gamma_1(\varphi_2)(l)|-|\gamma_0(\varphi_1)(l)-\gamma_0(\varphi_2)(l)|)dl.\tag{8}$$

Since φ_1, $\varphi_2\in D(T_K)$, we obtain that expression (8) is greater than or equal to

$$\int_{l_1}^{l_2}(|\gamma_1(\varphi_1)(l)-\gamma_1(\varphi_2)(l)|-|K(\gamma_1(\varphi_1))(l)-K(\gamma_1(\varphi_2))(l)|)dl.\tag{9}$$

Finally, since K is a nonexpansive mapping, we conclude that

$$[T_K(\varphi_1)-T_K(\varphi_2),\varphi_1-\varphi_2]_+\geqslant\|\gamma_1(\varphi_1)-\gamma_1(\varphi_2)\|-\|K(\gamma_1(\varphi_1))-K(\gamma_1(\varphi_2))\|\geqslant 0.\tag{10}$$

Inequality (10) implies that T_K is accretive, as we claimed.

By definition of m-accretive operator we only have to see that $\mathscr{R}(I+T_K)=L^1(\Omega)$, i.e., given a function $g\in L^1(\Omega)$ we have to find a function $\varphi\in D(T_K)$ such that

$$\varphi+T_K(\varphi)=g.$$

Thus, we look for the general solution of the following differential equation:

$$\varphi(a,l)+\frac{\partial\varphi}{\partial a}(a,l)=g(a,l). \tag{11}$$

Since Equation (11) is linear with respect to the variable a, the general solution will be given by the following formula:

$$\varphi(a,l)=\mathrm{e}^{-a}\chi(l)+\int_0^a g(s,l)\mathrm{e}^{s-a}\,\mathrm{d}s.$$

If we call $\varepsilon(a,l)=\mathrm{e}^{-a}$ we have that

$$\varphi(a,l)=\varepsilon(a,l)\chi(l)+\int_0^a g(s,l)\mathrm{e}^{s-a}\,\mathrm{d}s. \tag{12}$$

First, let us show that if $\chi\in L^1(l_1,l_2)$, then $\varphi\in W^1(\Omega)$. Indeed,

$$\begin{aligned}\|\varphi\|_1 &= \|\varepsilon\chi+\int_0^a g(s,l)\mathrm{e}^{s-a}\,\mathrm{d}s\|_1\\ &=\int_{l_1}^{l_2}\left(\int_0^l |\mathrm{e}^{-a}\chi(l)+\left(\int_0^a g(s,l)\mathrm{e}^{s-a}\,\mathrm{d}s\right)|\mathrm{d}a\right)\mathrm{d}l\\ &\leqslant \|\chi\|_{L^1(l_1,l_2)}+\int_{l_1}^{l_2}\left(\int_0^l\left(\int_0^a |g(s,l)|\mathrm{e}^{s-a}\,\mathrm{d}s\right)\mathrm{d}a\right)\mathrm{d}l\\ &\leqslant \|\chi\|_{L^1(l_1,l_2)}+l_2\|g\|_1. \end{aligned}\tag{13}$$

On the other hand,

$$\left\|\frac{\partial\varphi}{\partial a}\right\|_1=\|g-\varphi\|_1\leqslant\|g\|_1+\|\varphi\|_1. \tag{14}$$

It is clear that if $\chi\in L^1(l_1,l_2)$, inequalities (13) and (14) yield that $\varphi\in W^1(\Omega)$.

Now, our next step will be to prove that there exists a function $\varphi\in D(T_K)$ such that it satisfies Equation (12). In this case $\gamma_0(\varphi)=\chi$. Furthermore, if we call $h(a,l)=\int_0^a g(s,l)\mathrm{e}^{s-a}\,\mathrm{d}s$, the following condition should be satisfied:

$$\gamma_1(\varphi)=\gamma_1(\varepsilon\chi)+\gamma_1(h)=\mathrm{e}^{-l}\gamma_0(\varphi)+\gamma_1(h).$$

Since $\varphi\in D(T_K)$ we know that $\gamma_0(\varphi)=K(\gamma_1(\varphi))$. Consequently,

$$\gamma_1(\varphi)(l)=\mathrm{e}^{-l}K(\gamma_1(\varphi))(l)+\gamma_1(h)(l).$$

At this moment we may introduce the operator $S:L^1(l_1,l_2)\to L^1(l_1,l_2)$ defined by $S(\rho)(l))=\varepsilon(l,l)K(\rho)(l)$,

We claim that S is a strict contraction. Indeed,

$$\begin{aligned}\|S(\rho_1)-S(\rho_2)\|_{L^1(l_1,l_2)} &= \int_{l_1}^{l_2}|\mathrm{e}^{-l}K(\rho_1)(l)-\mathrm{e}^{-l}K(\rho_2)(l)|\mathrm{d}l\\ &=\int_{l_1}^{l_2}\mathrm{e}^{-l}|K(\rho_1)(l)-K(\rho_2)(l)|\mathrm{d}l\\ &\leqslant \mathrm{e}^{-l_1}\|K(\rho_1)-K(\rho_2)\|_{L^1(l_1,l_2)}\\ &\leqslant \mathrm{e}^{-l_1}\|\rho_1-\rho_2\|_{L^1(l_1,l_2)}. \end{aligned}\tag{15}$$

Thus, if $l_1>0$ we obtain that S is a strict contraction as claimed.

In this case, it is not difficult to prove that the operator $I-S:L^1(l_1,l_2)\to L^1(l_1,l_2)$ is bijective and moreover $(I-S)^{-1}$ is continuous (for instance see [15]), then given $\gamma_1(h)\in L^1(l_1,l_2)$ there exists a unique function $\psi\in L^1(l_1,l_2)$ such that $(I-S)(\psi)=\gamma_1(h)$.

The above argument allows us to define

$$\varphi(a,l)=\varepsilon(a,l)K(I-S)^{-1}\gamma_1(h)(l)+h(a,l)\in W^1(\Omega)m$$

which yields that $\mathscr{R}(I+T_K)=L^1(\Omega)$, i.e. T_K is m-accretive. □

3.1. A general condition on K

In this section our goal will be to associate an w-m-accretive operator for an appropriate $w>0$) to the boundary value problem (1) when the operator $K:L^1(l_1,l_2)\to L^1(l_1,l_2)$ satisfies a Lipschitz condition:

(H1)′ There exists $\alpha>1$ such that $\|K(f_1)-K(f_2)\|\leqslant\alpha\|f_1-f_2\|$, for all f_1, $f_2\in L^1(l_1,l_2)$.

Let us introduce the weighted space $X_w^1=L^1(\Omega,h_w)$ with the norm

$$\|\varphi\|_{1,w}=\int_\Omega|\varphi h_w)(a,l)|\,\mathrm{d}a\,\mathrm{d}l=\int_{l_1}^{l_1}\left(\int_0^l|\varphi h_w|(a,l)\mathrm{d}a\right)\mathrm{d}l,\tag{16}$$

where h_w is given by

$$h_w(a,l)=\mathrm{e}^{-w(l-a)}.$$

We also consider the partial Sobolev space

$$W_w^1(\Omega):=\left\{\varphi\in X_w^1:\frac{\partial\varphi}{\partial a}\in X_w^1\right\}.$$

Using the trace theorem (see Theorem 2.1 of [3]) it is possible to give a sense to the following operator:

$$\begin{cases}T_K:D(T_K)\subseteq X_w^1\to X_w^1,\\ \varphi\to T_K(\varphi(a,l))=\dfrac{\partial\varphi}{\partial a}(a,l),\end{cases}\tag{17}$$

where $D(T_K):=\{\varphi\in W_w^1(\Omega):\gamma_0(\varphi)=K(\gamma_1(\varphi))\}$.
In what follows we will take a fixed $w>\frac{1}{l_1}\ln(\alpha)$.

Theorem 2
The operator T_K is a w-m-accretive operator on X_w^1.

Proof
Given $g\in X_w^1$ and $\lambda\in(0,1/w)$ there exists a function $\varphi\in D(T_K)$ such that $\varphi+\lambda T_K(\varphi)=g$. Using the same argument develops in proof of Theorem (1) we look for a function φ such that

$$\varphi(a,l)=\mathrm{e}^{-\frac{a}{\lambda}}\chi(l)+\frac{1}{\lambda}\int_0^a g(s,l)\mathrm{e}^{-\frac{a-s}{\lambda}}\,\mathrm{d}s.$$

Let us show that if $\chi\in L^1(l_1,l_2)$, then $\varphi\in W_w^1(\Omega)$. Indeed,

$$\begin{aligned}\|\varphi\|_{1,w}&=\int_{l_1}^{l_2}\left(\int_0^l\mathrm{e}^{-w(l-a)}\left|\mathrm{e}^{-\frac{a}{\lambda}}\chi(l)+\frac{1}{\lambda}\left(\int_0^a g(s,l)\mathrm{e}^{\frac{s-a}{\lambda}}\mathrm{d}s\right|\right)\mathrm{d}a\right)\mathrm{d}l\\
&\leqslant\int_{l_1}^{l_2}\left(\int_0^l\mathrm{e}^{(w-\frac{1}{\lambda})a}|\chi(l)|\mathrm{d}a\right)\mathrm{d}l+\frac{1}{\lambda}\int_{l_1}^{l_2}\left(\int_0^l\mathrm{e}^{-w(l-a)}\left(\int_0^a|g(s,l)|\mathrm{e}^{w(s-a)}\mathrm{d}s\right)\mathrm{d}a\right)\mathrm{d}l\\
&\leqslant\frac{\lambda}{1-w\lambda}\|\chi\|_{L^1(l_1,l_2)}+\frac{1}{\lambda}\int_{l_1}^{l_2}\mathrm{e}^{-wl}\left(\int_0^l\left(\int_0^l|g(a,l)|\mathrm{e}^{wa}\mathrm{d}a\right)\mathrm{d}a\right)\mathrm{d}l\\
&\leqslant\frac{\lambda}{1-w\lambda}\|\chi\|_{L^1(l_1,l_2)}+\frac{1}{\lambda}\int_{l_1}^{l_2}l\left(\int_0^l|g(a,l)|\mathrm{e}^{-w(l-a)}\mathrm{d}a\right)\mathrm{d}l\\
&\leqslant\frac{\lambda}{1-w\lambda}\|\chi\|_{L^1(l_1,l_2)}+\frac{l_2}{\lambda}\|g\|_{1,w}.\end{aligned}\tag{18}$$

On the other hand,

$$\|\frac{\partial\varphi}{\partial a}\|_{1,w}=\frac{1}{\lambda}\|g-\varphi\|_{1,w}\leqslant\frac{1}{\lambda}(\|g\|_{1,w}+\|\varphi\|_{1,w}).\tag{19}$$

It is clear that if $\chi\in L^1(l_1,l_2)$, from inequalities (18) and (19) we obtain that $\varphi\in W_w^1(\Omega)$.

Now, our next step will be to prove that there exists a function $\varphi\in D(T_K)$ such that it satisfies Equation (12). In this case $\gamma_0(\varphi)=\chi$. Furthermore, if we call $h(a,l)=\int_0^a g(s,l)\mathrm{e}^{-\frac{a-s}{\lambda}}\,\mathrm{d}s$, the following condition should be satisfied:

$$\gamma_1(\varphi)=\gamma_1(\varepsilon_\lambda\chi)+\frac{1}{\lambda}\gamma_1(h)=\mathrm{e}^{-\frac{l}{\lambda}}\gamma_0(\varphi)+\frac{1}{\lambda}\gamma_1(h),$$

where $\varepsilon_\lambda(a,l)=\mathrm{e}^{-\frac{a}{\lambda}}$.

Since $\varphi \in D(T_K)$ we know that $\gamma_0(\varphi)=K(\gamma_1(\varphi))$. Consequently,

$$\gamma_1(\varphi)(l)=\mathrm{e}^{-\frac{l}{\lambda}}K(\gamma_1(\varphi))(l)+\frac{1}{\lambda}\gamma_1(h)(l).$$

At this moment we may introduce the operator $S_\lambda : L^1(l_1,l_2)\to L^1(l_1,l_2)$ defined by $S_\lambda(\rho)(l))=\varepsilon_\lambda(l,l)K(\rho)(l)$,
We claim that S_λ is a strict contraction. Indeed,

$$\begin{aligned}\|S_\lambda(\rho_1)-S_\lambda(\rho_2)\|_{L^1(l_1,l_2)} &= \int_{l_1}^{l_2}|\mathrm{e}^{-\frac{l}{\lambda}}K(\rho_1)(l)-\mathrm{e}^{-\frac{l}{\lambda}}K(\rho_2)(l)|\mathrm{d}l\\ &=\int_{l_1}^{l_2}\mathrm{e}^{-\frac{l}{\lambda}}|K(\rho_1)(l)-K(\rho_2)(l)|\mathrm{d}l\\ &\leqslant \mathrm{e}^{-\frac{l_1}{\lambda}}\|K(\rho_1)-K(\rho_2)\|_{L^1(l_1,l_2)}\\ &\leqslant \mathrm{e}^{-\frac{l_1}{\lambda}}\alpha\|\rho_1-\rho_2\|_{L^1(l_1,l_2)}.\end{aligned} \tag{20}$$

Since we have taken $w>\frac{1}{l_1}\ln(\alpha)$ and $\lambda\in(0,1/w)$ it is clear that $\mathrm{e}^{-\frac{l_1}{\lambda}}\alpha<1$, which means that S_λ is a strict contraction.

In this case, following the same argument as in Theorem 1 we have that given $\frac{1}{\lambda}\gamma_1(h)\in L^1(l_1,l_2)$ there exists a unique $\psi\in L^1(l_1,l_2)$ such that $(I-S_\lambda)(\psi)=\frac{1}{\lambda}\gamma_1(h)$.

The above argument allows us to define

$$\varphi(a,l):=(I+\lambda T_K)^{-1}(g)=\varepsilon_\lambda(a,l)K(I-S_\lambda)^{-1}\left(\frac{1}{\lambda}\gamma_1(h)\right)(l)+\frac{1}{\lambda}h(a,l)\in W^1_w(\Omega),$$

which yields that $\mathscr{R}(I+\lambda T_K)=L^1_w(\Omega)$ whenever $\lambda\in(0,1/w)$.

Now, consider $g_1,g_2\in L^1_w(\Omega)$, by the above argument we can obtain φ_1, $\varphi_2\in D(T_K)$ such that

$$\varphi_1=(I+\lambda T_K)^{-1}(g_1),\quad \varphi_2=(I+\lambda T_K)^{-1}(g_2).$$

Hence,

$$\begin{aligned}\|\varphi_1-\varphi_2\|_{1,w} &= \|(I+\lambda T_K)^{-1}(g_1)-(I+\lambda T_K)^{-1}(g_2)\|_{1,w}\\ &\leqslant -\lambda\int_\Omega \mathrm{sgn}_0(\varphi_1-\varphi_2)h_w\frac{\partial(\varphi_1-\varphi_2)}{\partial a}\mathrm{d}a\,\mathrm{d}l+\int_\Omega \mathrm{sgn}_0(\varphi_1-\varphi_2)h_w(g_1-g_2)\mathrm{d}a\,\mathrm{d}l\\ &\leqslant -\lambda\int_{l_1}^{l^2}\int_0^l\frac{\partial}{\partial a}|h_w(\varphi_1-\varphi_2)|\mathrm{d}a\,\mathrm{d}l+w\lambda\int_\Omega|h_w(\varphi_1-\varphi_2)|\mathrm{d}a\,\mathrm{d}l+\int_\Omega h_w(a,l)|g_1(a,l)-g_2(a,l)|\mathrm{d}a\,\mathrm{d}l\\ &\leqslant \lambda\left(\int_{l_1}^{l_2}(\mathrm{e}^{-wl}|K(\gamma_1(\varphi_1))-K(\gamma_1(\varphi_2))|-|\gamma_1(\varphi_1)-\gamma_(\varphi_2)|\right)\mathrm{d}l+w\lambda\|\varphi_1-\varphi_2\|_{1,w}+\|g_1-g_2\|_{1,w}\\ &\leqslant \lambda(\mathrm{e}^{-wl_1}\alpha-1)\|\gamma_1(\varphi_1)-\gamma_1(\varphi_2)\|_1+w\lambda\|\varphi_1-\varphi_2\|_{1,w}+\|g_1-g_2\|_{1,w}\\ &\leqslant w\lambda\|\varphi_1-\varphi_2\|_{1,w}+\|g_1-g_2\|_{1,w}.\end{aligned} \tag{21}$$

From this inequality we conclude that

$$\|(I+\lambda T_K)^{-1}(g_1)-(I+\lambda T_K)^{-1}(g_2)\|_{1,w}\leqslant\frac{1}{1-w\lambda}\|g_1-g_2\|_{1,w}.$$

□

3.2. *The evolution equation*

In this section, we are concerned with the existence and uniqueness result for Problem (1). For our subsequent analysis, we need the following hypothesis:

(H2) $\sigma:\Omega\times\mathbb{R}\to\mathbb{R}$ is a Carathéodory function,
(H3) there exists $h\in L^\infty(\Omega)$ such that $|\sigma(a,l,x)-\sigma(a,l,y)|\leqslant|h(a,l)||x-y|$.

Given the equation:

$$\begin{cases} \dfrac{\partial}{\partial t}f(t,a,l) = -\dfrac{\partial}{\partial a}f(t,a,l) + \sigma(a,l,f(t,a,l)), \\ f(t,0,l) = K(f(t,l,l)), \\ f(0,\cdot,\cdot) \in L^1(\Omega,h_w), \end{cases} \tag{22}$$

where $w=0$ if K is a nonexpansive mapping and w is a fixed number bigger than $\frac{1}{l_1}\ln(\alpha)$ if K is α-Lipschitzian mapping with $\alpha>1$. We may consider the Banach space $X_w^1 = L^1(\Omega,h_w)$ and $u(t):=f(t,\cdot)\in X_w^1$. Define $\mathcal{N}_\sigma : X_w^1 \to X_w^1$ by $\mathcal{N}_\sigma(\varphi)(a,l) := \sigma(a,l,\varphi(a,l))$. Thus, we may interpret and rewrite Problem (22) as follows:

$$\begin{cases} u'(t) + T_K(u(t)) = \mathcal{N}_\sigma(u(t)), \\ u(0) = g \in X_w^1. \end{cases} \tag{23}$$

Now we try to show that if assumptions (H2), (H3) and either (H1) or (H1)′ hold, then Equation (23) has a unique mild solution. Hence the main result of this section reads as follows.

Theorem 3
Under conditions (H2), (H3) and either (H1) or (H1)′, Equation (23) has a unique mild solution.

Proof
First, we claim that $L^1(\Omega,h_w) = \overline{D(T_K)}^{L^1(\Omega,h_w)}$. In order to see this, it is enough to prove that $\mathcal{C}_0^\infty(\overline{\Omega}) \subseteq \overline{D(T_K)}^{L^1(\Omega,h_w)}$. Let v be an element of $\mathcal{C}_0^\infty(\overline{\Omega})$. For each $n\in\mathbb{N}$, define de function:

$$u_n(a,l) = \begin{cases} v(a,l), & (a,l)\in\Omega \quad \text{with } a \geqslant \dfrac{l_1}{n}, \\ K(v(l,l)), & (a,l)\in\Omega \quad \text{with } 0\leqslant a < \dfrac{l_1}{n}. \end{cases}$$

It is clear that $|u_n(a,l)| \leqslant \max\{|v(a,l)|, |K(v(l,l))|\}$ and both functions belong to $L^1(\Omega)$. It is also clear that $h_w u_n \to h_w v$ a.e. in Ω. Thus, by the dominated convergence theorem we have that $\|u_n - v\|_{1,w} \to 0$.

On the other hand,

$$\frac{\partial u_n}{\partial a} = \begin{cases} \dfrac{\partial v}{\partial a}(a,l), & (a,l)\in\Omega \quad \text{with } a \geqslant \dfrac{l_1}{n}, \\ 0, & (a,l)\in\Omega \quad \text{with } 0\leqslant a < \dfrac{l_1}{n}. \end{cases}$$

Therefore, it is not difficult to see that $u_n \in D(T_K)$. Since $u_n \in W_w^1(\Omega)$, $\gamma_1(u_n)(l) = v(l,l)$, and $\gamma_0(u_n)(l) = K(v(l,l)) = K(\gamma_1(u_n)(l))$.

Second, let us see that $\mathcal{N}_\sigma : L^1(\Omega,h_w) \to L^1(\Omega,h_w)$ is a Lipschitzian mapping.

$$\begin{aligned} \|\mathcal{N}_\sigma(\varphi) - \mathcal{N}_\sigma(\psi)\|_{1,w} &= \int_\Omega h_w(a,l)|\mathcal{N}_\sigma(\varphi)(a,l) - \mathcal{N}_\sigma(\psi)(a,l)|\,\mathrm{d}a\,\mathrm{d}l \\ &= \int_\Omega h_w(a,l)|\sigma(a,l,\varphi(a,l)) - \sigma(a,l,\psi(a,l))|\,\mathrm{d}a\,\mathrm{d}l \\ &\leqslant \int_\Omega h_w(a,l)|h(a,l)||\varphi(a,l) - \psi(a,l)|\,\mathrm{d}a\,\mathrm{d}l. \end{aligned}$$

By using Hölder's inequality we have that

$$\begin{aligned} \|\mathcal{N}_\sigma(\varphi) - \mathcal{N}_\sigma(\psi)\|_{1,w} &\leqslant \int_\Omega |h(a,l)|h_w(a,l)|\varphi(a,l) - \psi(a,l)|\,\mathrm{d}a\,\mathrm{d}l \\ &\leqslant \|h\|_\infty \|\varphi - \psi\|_{1,w}. \end{aligned}$$

Let T be a positive number. Consider the subset $\mathcal{K} := \{u \in C(0,T;X_w^1) : u(0) = g\}$. Given $v\in\mathcal{K}$, the problem

$$\begin{cases} u'(t) + T_K(u(t)) = \mathcal{N}_\sigma(v(t)), & t\in(0,T), \\ u(0) = g \end{cases} \tag{24}$$

has a unique mild solution, namely $S(v)\in\mathcal{K}$. This fact allows us to introduce a mapping $S:\mathcal{K}\to\mathcal{K}$ defined as follows: given $v\in\mathcal{K}$, $S(v)$ is the unique mild solution of the above problem.

From the properties of mild solutions, it follows that

$$\|S(v)(t)-S(w)(t)\| \leqslant \int_0^t e^{w(t-\tau)}\|h\|_\infty \|v(\tau)-w(\tau)\| d\tau$$
$$\leqslant e^{wt}\|h\|_\infty t \max\{\|v(s)-w(s)\|:\ s\in[0,t]\}.$$

Using an inductive process, we deduce that for each $n\in\mathbb{N}$,

$$\|S^n(v)(t)-S^n(w)(t)\|\leqslant \frac{(e^{wt}\|h\|_\infty t)^n}{n!}\max\{\|v(s)-w(s)\|:s\in[0,t]\}.$$

Hence $\|S^n(v)-S^n(w)\|_\infty\leqslant\frac{(e^{wT}\|h\|_\infty T)^n}{n!}\|v-w\|_\infty$. This means that there exists $n_0\in\mathbb{N}$ such that S^{n_0} is a strict contraction on $\mathscr{K}$. Since $\mathscr{K}$ is closed, S has a unique fixed point in $\mathscr{K}$ by Banach's fixed point theorem. This is fixed point is the unique mild solution of Equation

$$\begin{cases} u'(t)+T_K(u(t))=\mathscr{N}_\sigma(u(t)), & t\in(0,T),\\ u(0)=g. \end{cases} \tag{25}$$

In order to finish the proof, given $t>0$, we define $u(t):=u_T(t)$ where u_T is the unique integral solution of Problem (25) with $T>t$. It is clear that u is the unique mild solution of Problem (23). □

Finally, if we assume that $0\in D(T_K)$, i.e. if $K(0)=0$ and replace assumption (H3) by the assumptions:

(H3)′ For every $s>0$ there exists $L(s)>0$ such that $\|\mathscr{N}_\sigma(\varphi)-\mathscr{N}_\sigma(\psi)\|_{1,w}\leqslant L(s)\|\varphi-\psi\|_{1,w}$ whenever $\varphi,\psi\in B_s(0)$,
(H4) there exists $r>0$ such that for every $\psi\in X_w^1$ with $\|\psi\|_{1,w}\geqslant r$ then $[\mathscr{N}_\sigma(\psi),\psi]_s\leqslant 0$.

Corollary 1
If assumptions (H2), (H3)′, (H4) and either (H1) or (H1)′ hold, Equation (23) has a unique mild solution.

Proof
Let us see that Equation (23) has a unique mild solution. Indeed, given $g\in X_w^1$ consider $r>0$ such that $\|g\|_{1,w}\leqslant r$ and assumption (H4) hods for this $r>0$.

Let us introduce the following function:

$$\rho(x)=\begin{cases} x, & \|x\|\leqslant r,\\ \dfrac{r}{\|x\|}x, & \|x\|\geqslant r. \end{cases}$$

It follows from condition (H3)′ that the function $\mathscr{N}_\sigma(\rho(.))$ is $2L(r)$-Lipschitz.

Therefore, by Theorem 3, the equation

$$\begin{cases} u'(t)+T_K(u(t))=\mathscr{N}_\sigma(\rho(u(t))),\\ u(0)=g \end{cases} \tag{26}$$

has a unique mild solution u.

Since we are assuming that $0=T_K(0)$ and $\mathscr{N}_\sigma$ satisfies condition (H4), we can apply Lemma 3.1 of [16] to obtain that $u\in B_r(0)$ then $\rho(u)=u$ and thus we may conclude that Equation (23) has a unique mild solution. □

4. Comments

The condition $l_1=0$ means that there are cells which are born as mothers and daughters simultaneously. This presents a biological pathology which corresponds to the mathematical difficulty that the operator S in Theorem 1 is not a strict contraction and then we cannot assume that $(I-S)^{-1}$ exists. This could be fixed assuming that K is a strict contraction.

In the structured population dynamics framework, we have in general a proliferation of the population, thus it is more appropriate to consider boundary conditions of the type $\|K(u)\|\geqslant\|u\|$ for all $u\in L^1(l_1,l_2)$, which was the reason to study, in Section 3.1, the boundary value problem (1) when the operator $K:L^1(l_1,l_2)\to L^1(l_1,l_2)$ is α-Lipschizian with $\alpha>1$. In particular, we may consider as transition operators the following examples: Proliferating cell is related to the transfer of the cycle length between each mother cell and its daughters. During each mitosis, it is possible that there exists a correlation between the cycle length of a mother cell l' and that of a daughter cell l. The general mathematical description of such correlation is given by the following boundary condition:

$$f(t,0,l)=\int_{l_1}^{l_2} r(l,l',f(t,l',l'))dl',$$

where $r(\cdot,\cdot,\cdot)$ is Lipschitzian with respect to the third coordinate. In this sense we can take $r(l,l',f(t,l',l'))=\beta k(l,l')g(f(t,l',l'))$ where

(1) The function $k(\cdot,\cdot)$ is essentially bounded on $[l_1,l_2]\times[l_1,l_2]$. We denote by $\|k\|_\infty$ its essential norm,
(2) $g:\mathbb{R}\to\mathbb{R}$ is γ-Lipschitz mapping,
(3) β is a positive constant.

The operator $K:L^1(l_1,l_2)\to L^1(l_1,l_2)$ defined by

$$K(\varphi)(l)):=\beta\int_{l_1}^{l_2}k(l,l')g(\varphi(l'))\mathrm{d}l'$$

is $\beta\gamma\|k\|_\infty(l_2-l_1)$ Lipschitzian. Indeed,

$$\begin{aligned}\|K(\phi)-K(\varphi)\|_1&=\beta\int_{l_1}^{l_2}\left|\int_{l_1}^{l_2}k(l,l')(g(\phi(l'))-g(\varphi(l')))\mathrm{d}l'\right|\mathrm{d}l\\&\leqslant\beta\|k\|_\infty\int_{l_1}^{l_2}\left(\int_{l_1}^{l_2}|g(\phi(l'))-g(\varphi(l')|\mathrm{d}l'\right)\mathrm{d}l\\&\leqslant\beta\|k\|_\infty(l_2-l_1)\gamma\|\phi-\varphi\|_1.\end{aligned}$$

The above transition operator allows us to recapture the example of the transition operator given in [3], where $k(l,l')$ is a positive kernel and $\beta\geqslant 0$ is the average number of daughter cells viable per mitotic.

When there is no correlation but there is an inheritance between cycle length of a mother cell and that of its daughters, then the biological rule of this inheritance is mathematically described by

$$f(t,0,l)=r(f(t,l,l)),$$

where many times r is Lipschitzian. In particular , when there is a perfect inheritance we can describe this taking $r(f(t,l,l)=\alpha f(t,l,l)$ where $\alpha\geqslant 0$ is the average number of daughter cells viable per mitotic (see [3]). At this point, we refer to [8, 7, 9, 10], where the reader will find a study of several types of nonlinear transition operators.

Finally, in Theorem 3 of Section 3.2 we see that Equation (22) admits a unique solution for every initial function of density of population whenever the rate of cell mortality or loss due to causes other than division satisfies Conditions ((H2) and (H3)) which are quite usual (for instance see [5]). On the other hand, from the biological point of view it seems quite natural that if the density of the population of the cell cycle length l at mitosis is zero, i.e, $f(t,l,l)=0$, then the transition for the distribution of mothers cycle length to daughters cycle length should be also zero, this is mathematically described by assuming that the transition operator K satisfies that $K(0)=0$. We have studied this case in Corollary 1 and thus we can replace the condition $(H3)$ by assumptions $(H3)'$ and $(H4)$ which allow us to consider more general functions describing the rate of cell mortality (see [16]).

Acknowledgements

The author was partially supported by MTM2009-10696-C02-02.

References

1. Lebowitz JL, Rubinow SI. A theory for the age and generation time distribution of microbial population. *Journal of Mathematical Biology* 1974; **1**:17–36.
2. Boulanouar M. A mathematical study in the theory of dinamic population. *Journal of Mathematical Analysis and Applications* 2001; **225**:230–259.
3. Boulanouar M. A model of proliferating cell population with infinite cell cycle length: Semigroup existence. *Acta Applicandae Mathematicae* 2010; **109**:949–971.
4. Latrach K, Mokhtar-Kharroubi M. On an unbounded linear operator arising in the theory of growing cell population. *Journal of Mathematical Analysis and Applications* 1997; **211**:273–294.
5. Jeribi A. A nonlinear problem arising in the theory of growing cell population. *Nonlinear Analysis*: *Real World Applications* 2002; **3**:85–105.
6. Rotenberg M. Transport theory for growing cell population. *Journal of Theoretical Biology* 1983; **103**:181–199.
7. Gurtin ME, Maccamy RC. Nonlinear age-dependent population dynamics. *Archive for Rational Mechanics and Analysis* 1983; **82**:13–25.
8. Boulanouar M. Un modèle de Rotenberg avec des vitesses de maturité nulles. *Comptes Rendus de l'Académie des Sciences. Série I* 1998; **326**:443–446.
9. Webb GF. A model of proliferating cell populations with inherited cycle length. *Journal of Mathematical Biology* 1986; **23**:269–282.
10. Webb GF. Dynamics of structured populations with inherited properties. *Computers and Mathematics with Applications* 1987; **13**:749–757.
11. Browder FE. Nonlinear mappings of nonexpansive and accretive type in Banach spaces. *Bulletin of the American Mathematical Society* 1967; **7**(3):875–882.
12. Kato T. Nonlinear semigroups and evolution equations. *Journal of the Mathematical Society of Japan* 1967; **19**:508–520.
13. Barbu V. *Nonlinear Differential Equations of Monotone Types in Banach Spaces*. Springer: Berlin, 2010.
14. Bénilan Ph. Équations d'évolution dans un espace de Banach quelconque et applications. *Thèse de doctorat d'État*, Orsay, 1972.
15. Garcia-Falset J. Existence of fixed points for the sum of two operators. *Mathematische Nachrichten* 2010; **283**(12):1736–1757.
16. Garcia-Falset J, Reich S. Integral solutions to a class of nonlocal evolution equations. *CCM* 2010; **12**(6):1031–1054.