Nonlinear Analysis 97 (2014) 210–227

Contents lists available at ScienceDirect

Nonlinear Analysis

journal homepage: www.elsevier.com/locate/na

Existence and uniqueness results for a nonlinear evolution equation arising in growing cell populations

J. Garcia-Falset[a], K. Latrach[b,*], A. Zeghal[c]

[a] Departament d'Anàlisi Matemàtica, Universitat de València, Dr. Moliner 50, 46100, Burjassot, València, Spain
[b] Université Blaise Pascal, Laboratoire de Mathématiques, UMR 6620 - CNRS, Complexe des Cézeaux, BP 80026, 63171 Aubière Cedex, France
[c] Université Sultan Moulay Slimane, Laboratoire de Mathématiques et Applications, B.P. 523, 23000 Beni-Mellal, Morocco

ARTICLE INFO

Article history:
Received 31 May 2013
Accepted 29 November 2013
Communicated by Enzo Mitidieri

MSC:
47H06
34A12
35F20

Keywords:
Evolution equation
Local and nonlocal boundary conditions
Quasi-accretive operators
Local and global solutions

ABSTRACT

The present paper is concerned with a nonlinear initial–boundary value problem derived from a model introduced by Rotenberg (1983) describing the growth of a cell population. Each cell of this population is distinguished by two parameters: its degree of maturity μ and its maturation velocity v. At mitosis, the daughter cells and mother cells are related by a general reproduction rule. We prove existence and uniqueness results in the case where the total cross-section and the boundary conditions are depending on the total density of population. Local and nonlocal reproduction rules are discussed.

1. Introduction

In 1983, Rotenberg [1] presented a model for growing cell population in which each cell is distinguished by two parameters. The first parameter is the degree of maturity μ and a cell in the process evolution has a degree of maturity $\mu \in [0, 1]$. Thus, during each cell mitotic, the degree of maturity of a mother cell is $\mu = 1$ and its daughter cells is $\mu = 0$. The second parameter is the velocity of maturation v. The positivity of velocities comes from the fact that a cell may not become less mature with the time and then $v \in (a, b)$ $(0 < a < b < \infty)$. If the function $\psi(t, \mu, v)$ represents the density of the population with respect to the maturation μ and the velocity of maturation v at time t, Rotenberg derived the following partial differential equation

$$\begin{cases} \dfrac{\partial}{\partial t}\psi(t, \mu, v) + v\dfrac{\partial}{\partial \mu}\psi(t, \mu, v) = -\sigma(\mu, v)\psi(t, \mu, v) + \displaystyle\int_a^b \kappa(\mu, v, v')\psi(t, \mu, v')dv' \\ \psi(0, \mu, v) = \psi_0(\mu, v). \end{cases} \tag{1}$$

The kernel $\kappa(\mu, v, v')$ is the transition rate. It specifies the transition of cells from the maturation velocity v' to v while $\sigma(\mu, v) = \int_a^b \kappa(\mu, v', v)dv'$ denotes the total transition cross section. It is the rate of cell mortality or cell loss due to other causes than division. During each cell division, it can be assumed that there is a correlation between the maturation velocity

---

[*] Corresponding author. Tel.: +33 473 407 896.
E-mail addresses: garciaf@uv.es (J. Garcia-Falset), Khalid.Latrach@math.univ-bpclermont.fr (K. Latrach), a.zeghal@fstbm.ac.ma (A. Zeghal).

0362-546X/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.na.2013.11.027

of mother cells v' and that of daughter cells v. This correlation is governed by a transition biological rule mathematically described by the boundary condition

$$v\psi(t,0,v) = \beta \int_a^b k(v,v')\psi(t,1,v')v'dv', \tag{2}$$

where β is the average number of daughter cells viable per mitotic (see [1]).

It is also possible that there are cells which degenerate and in this case there is a total inheritance of the maturation velocity between mother and its daughters. This biological rule is mathematically described by

$$\psi(t,0,v) = \alpha\psi(t,1,v), \tag{3}$$

where $\alpha \geq 0$ is the average number of daughter cells viable per mitotic. However, in reality there are always cells which degenerate and other cells which respect the previous correlation with its daughter cells. One of the most observed biological consideration is described by the boundary conditions (see, for instance, [2] or [3, p. 476]).

$$\psi(t,0,v) = \alpha\psi(t,1,v) + \frac{\beta}{v}\int_a^b k(v,v')\psi(t,1,v')v'dv'. \tag{4}$$

Rotenberg discussed essentially the Fokker–Planck approximation of the Problem (1)–(2) for which he obtained numerical solutions. Using the eigenfunction technique, Van der Mee and Zweifel [4] obtained analytical solutions of (1) for a variety of boundary conditions. Using Lebowitz and Rubinow's boundary conditions, it was established in [3, Chapter XIII, Section 5] that the associated Cauchy problem to (1) is governed by a positive C_0-semigroup and an estimate of the type of the semigroup was derived on the space L^1 which allowed to describe the time asymptotic behavior of the solution of the Cauchy problem. Similar results were obtained for various boundary conditions (see, for example, [5,2,6]). In [7] a detailed spectral analysis of the Problem (1) supplemented with general (linear) transition rule relating mother and daughter cells at mitosis covering, in particular, all classical ones considered in [3,8,1,4], was given.

In the introduction of his paper, Rotenberg has pointed out that the adequate formulation of the model (1) seems to be a nonlinear one. Actually, the cells under consideration are in contact with a nutrient environment which is not part of the mathematical formulation. Fluctuations in nutrient concentration and other density-dependent effects such as contact inhibition of growth make the transition rates $\sigma(\cdot,\cdot)$ and $\kappa(\cdot,\cdot,\cdot)$ functions of the population density, thus creating a nonlinear problem. On the other hand, the biological boundary at $\mu = 0$ and $\mu = 1$ is fixed and tightly coupled throughout mitosis. The conditions present at the boundaries are felt throughout the system and cannot be removed. This phenomena suggest that at mitosis daughter cells and parent cells are related by a nonlinear nonlocal reproduction rule. Motivated by these observations, in [9], the authors have considered a modified nonlinear stationary version of the Rotenberg model. The transition rate and the total cross-section were assumed to depend on the density of population and, at mitosis, the daughter and mother cells are related by a nonlinear rule which describes the boundary conditions. More precisely, they considered the problem

$$v\frac{\partial\psi}{\partial\mu}(\mu,v) + \lambda\psi(\mu,v) + \sigma(\mu,v,\psi(\mu,v)) = \int_0^c \kappa(\mu,v,v',\psi(\mu,v'))\,dv', \tag{5}$$

where $\sigma(\cdot,\cdot,\cdot)$ and $\kappa(\cdot,\cdot,\cdot,\cdot)$ are nonlinear functions of ψ and λ is a complex number. The boundary conditions are modeled by

$$\psi_{|\Gamma_0} = K(\psi_{|\Gamma_1}), \tag{6}$$

where $\Gamma_0 = \{0\} \times [a,b]$ and $\Gamma_1 = \{1\} \times [a,b]$, $\psi_{|\Gamma_0}$ (resp. $\psi_{|\Gamma_1}$) denotes the restriction of ψ to Γ_0 (resp. Γ_1). The function K is a nonlinear operator from a suitable function space on Γ_1 to a similar one on Γ_0.

In [9] several existence theorems for Eq. (5) supplemented with the boundary conditions (6) were obtained in L^p spaces with $1 < p < \infty$. The analysis was carried out via topological arguments and uses compactness results, established in L^p-spaces with $1 < p < \infty$, of the operators involved in the problem. Due to the lack of compactness of these operators on the space L^1, in [10], the second and third authors extended the analysis to the case $p = 1$ using essentially the specific properties of weakly compact sets on L^1-spaces. Despite these works, to our knowledge, the time-dependent Problem (5) even for simple reproduction laws has not yet been investigated. The main purpose of this work is to fill this gap. The paper is organized as follows:

- Introduction,
- Main results,
- Proofs and consequences,
- Comments,
- Annex.