Nonlinear Analysis 143 (2016) 1–18

Contents lists available at ScienceDirect

Nonlinear Analysis

www.elsevier.com/locate/na

On the solutions for a nonlinear boundary value problem modeling a proliferating cell population with inherited cycle length

Abdul-Majeed Al-Izeri, Khalid Latrach*

Université Blaise Pascal, Laboratoire de Mathématiques, CNRS (UMR 6620), Campus Universitaire des Cézeaux, 3 place Vasarely, TSA 60026 CS 60026, 63178 Aubière Cedex, France

A R T I C L E I N F O

Article history:
Received 1 February 2016
Accepted 4 May 2016
Communicated by Enzo Mitidieri

MSC:
92B05
34B15
45K05

Keywords:
Boundary value problem
Nonlinear boundary operator
Measure of weak noncompactness
Fixed point theorems
Existence results

A B S T R A C T

This paper deals with existence results for a nonlinear boundary value problem derived from a model introduced by Lebowitz and Rubinow (1974) describing a proliferating cell population. Cells are distinguished by age a and cycle length l. The cycle length is viewed as an inherited property determined at birth. The boundary condition models the process of cell division of mother cells and the inheritance of cycle length by daughter cells. In our framework, daughter cells and mother cells are related by a general reproduction rule which covers all known biological ones. In this work, the cycle length l is allowed to be infinite, that is, $l \in [l_1, +\infty)$. This hypothesis introduces some mathematical difficulties which are overcome by using domination arguments (in the lattice sense) and recent fixed point theorems involving continuous weakly compact operators on non reflexive Banach spaces.

1. Introduction

The purpose of this paper is to establish some existence results for the following nonlinear integro-differential equation

$$\frac{\partial \psi}{\partial a}(a,l) + \lambda\psi(a,l) + \sigma(a,l,\psi(a,l)) = \int_{l_1}^{+\infty} \kappa(a,l,l')f(a,l',\psi(a,l'))\chi_\Omega(a,l')dl', \tag{1}$$

where λ is a real number and χ_Ω denotes the characteristic function of the set

$$\Omega := \{(a,l);\, 0 < a < l,\ 0 < l_1 < l < +\infty\}.$$

* Corresponding author.
E-mail addresses: Abdul_Majeed.Al_izeri@math.univ-bpclermont.fr (A.-M. Al-Izeri), Khalid.Latrach@math.univ-bpclermont.fr (K. Latrach).

http://dx.doi.org/10.1016/j.na.2016.05.001
0362-546X/

This equation is derived from an age-structured proliferating cell population model with inherited properties introduced by Lebowitz and Rubinow [17]. The variable l denotes the cycle length of individual cells which is the time between cell birth and cell division. The cell cycle length of individual cells is an inherent characteristic determined at birth. The variable a is the age of the individual cells. It is defined so that cells born at $a = 0$ (daughter cells) and divide at $a = l$ (mother cells). The constant l_1 is the minimum cycle length of cells while the maximum cycle length of cells is allowed to be infinite ($l_2 = +\infty$). Here $\psi(a, l)$ denotes the density of the population with respect to age a and cell cycle length l. The function $\sigma(\cdot, \cdot, \cdot)$ is the rate of cells mortality or loss due to causes other than division, $f(\cdot, \cdot, \cdot)$ is a measurable function from $\Omega \times \mathbb{R}$ into $\mathbb{R}$ and $\kappa(\cdot, \cdot, \cdot)$ is a measurable function from $\mathbb{R}^+ \times [l_1, +\infty) \times [l_1, +\infty)$ into $\mathbb{R}$.

The model originally proposed by Lebowitz and Rubinow [17] is a linear partial differential equation, but as observed by Rotenberg [21], it seems that the linear model is not adequate. Indeed, 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 functions of the population density, thus creating a nonlinear problem. So the rate of cell mortality $\sigma(\cdot, \cdot, \cdot)$ and the function $f(\cdot, \cdot, \cdot)$ are assumed to be nonlinear functions of the density of cells $\psi(\cdot, \cdot)$. On the other hand, the biological boundary is fixed and tightly coupled through out mitosis and the conditions present at the boundaries are felt throughout the system and cannot be remote. This phenomena suggest that at mitosis daughter cells and parent cells are related by a nonlinear reproduction rule which describes the boundary conditions. It writes in the shape

$$\psi(0, l) = (\mathbf{R}\psi)(l, l), \tag{2}$$

where $\mathbf{R}$ stands for a nonlinear operator which is intended to model the transition from mother cells of cycle length l to daughter cells of cycle length l. It covers, in particular, the usual biological models (cf. [17,23,24, 13,19] and the references therein).

The model (1)–(2) has been analyzed in [11] in L^p-spaces, $1 < p < \infty$, in the case where the maximum cycle length ($l_2 < +\infty$) is finite. The analysis follows the same strategy as that used by the second author in [12] in the context of rarefied gas dynamics. It is based essentially on compactness results established only for $1 < p < \infty$ and uses the Schauder and Krasnosel'skii fixed point theorems. Due to the lack of compactness in L^1-spaces, this approach fails in the L^1 context (which is the convenient and natural setting of the problem because $\psi(a, l)$ has the meaning of a density of cells with respect to the age a and the cells cycle length l). The case of L^1-spaces was considered in [15]. The approach is based on topological methods and uses the specific properties of weakly compact sets in L^1-spaces. Note also that the well-posedness of nonlinear evolution equations derived from the model of Lebowitz and Rubinow was discussed in the works [22,10,1,2]. The main purpose of this paper is to present an existence theory for the boundary value problem (1)–(2) on L^1-spaces in the case where the maximum cycle length is infinite ($l_2 = +\infty$).

The organization of this paper is as follows. In Section 2 we introduce the functional setting of the problem and we establish some preliminary results. We recall some facts from functional analysis and two fixed point theorems established in [14,16] needed in the sequel. We also introduce a measure of weak noncompactness adapted to the problem. In Section 3, establish an existence result for the boundary value problem (1)–(2) (cf. Theorem 3.1) in the special case where $\sigma(a, l, \psi(a, l)) = \sigma(a, l)\psi(a, l)$ (σ is not relabeled) is a multiplication operator. The proof of this result consists in writing problem (1)–(2) as a fixed point problem involving a nonlinear ws-compact operator, depending on the real $\lambda, \mathsf{G}_\lambda$, and we show that it satisfies the hypotheses of Theorem 2.1 on an appropriate subset of $L^1(\Omega)$. Existence results for the general boundary value problem (1)–(2) (i.e. $\sigma(\cdot, \cdot, \cdot)$ is a nonlinear function of $\psi(\cdot, \cdot)$) is the subject of Theorem 3.2. In order to transform (1)–(2) into a fixed point problem, the additivity of the transition operator $\mathbf{R}$ (and consequently its linearity because it is continuous) is required. Under this hypothesis, we first transform (1)–(2) into a fixed point problem involving two nonlinear operators depending on the real number λ, say, $\psi = \mathcal{F}(\lambda)\psi + \mathcal{H}(\lambda)\psi$.