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WELL-POSEDNESS OF A NONLINEAR MODEL OF PROLIFERATING CELL POPULATIONS WITH INHERITED CYCLE LENGTH*

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Abstract This paper deals with a nonlinear initial boundary values problem derived from a modified version of the so called Lebowitz and Rubinow's model [16] discussed in [8, 9] modeling a proliferating age structured cell population with inherited properties. We give existence and uniqueness results on appropriate weighted L^p-spaces with $1 \le p < \infty$ in the case where the rate of cells mortality σ and the transition rate k are depending on the total density of population. General local and nonlocal reproduction rules are considered.

Key words evolution equation; local and nonlocal boundary conditions; quasi-accretive operators; mild solutions, strong solutions; local and global solutions

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1 Introduction

In the works [8, 9], the author discussed the well-posedness and various mathematical aspects of solution to the Cauchy problem

$$\begin{cases} \dfrac{\partial f}{\partial t}(t,a,l) = -\dfrac{\partial f}{\partial a}(t,a,l) - \sigma(a,l)f(t,a,l) + (Pf)(t,a,l), \\ f(0,a,l) = f_0(a,l), \end{cases} \tag{1.1}$$

where

$$(Pf)(t,a,l) = \int_{l_1}^{l_2}\int_0^{l'} k(a,l,a',l')f(t,a',l')\mathrm{d}a'\mathrm{d}l',$$

$t > 0$, $0 < a, a' < l$, $0 < l_1 < l, l' < l_2$ and f_0 stands for the initial data. The function $f := f(t,a,l)$ denotes the cell density with respect to cell cycle length l, and age a at time t, and $\sigma(a,l)$ denotes the rate of cell mortality. By cell cycle length we mean the time between cell birth and cell division. It is an inherent characteristic of cells 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 lenght). The function

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$k(a,l,a',l')$ denotes the transition rate at which cells change their cell cycle length from l' to l and their age from a' to a. The problem (1.1) is complemented with a general biological reproduction rule given by

$$f(t,0,l) = \big(Kf(t,\cdot,\cdot)\big)(l), \tag{1.2}$$

where K is a bounded linear operator on suitable function spaces.

In the case where $P = 0$ and $\big(Kf(t,\cdot,\cdot)\big)(l) = \int_{l_1}^{l_2} r(l,l')f(t,l',l')\mathrm{d}l'$, where $r(\cdot,\cdot)$ is a measurable function, we find a model originally introduced by Lebowitz and Rubinow [16] for modeling proliferating microbial populations. It was extensively studied by many authors and various mathematical aspects concerning the Cauchy problem: well-posedness (generation results), spectral analysis, time asymptotic behavior of solution (when it exists) were discussed in many papers (see, for example, the works [7, 15, 17, 21, 22] and the references therein).

As it was observed by Rotenberg [19], 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. On the other hand, the biological boundaries at l_1 and l_2 are fixed and tightly coupled through out mitosis. The conditions present at the boundaries are left throughout the system and cannot be remote. This phenomena suggests that at mitosis the daughter cells and parent cell are related by a nonlinear reproduction rule. At mitosis, the daughter and mother cells are related by a nonlinear reproduction rule which describes the boundary conditions.

We point out that the well-posedness of nonlinear initial boundary value problems derived from Rotenberg model were already discussed in [12, 20] and [1]. However, it seems that the well-posedness of nonlinear time dependent versions derived from (1.1) has not yet been investigated. The main goal of this work is to present and to discuss two nonlinear versions of the model (1.1) in a weighted L^p-spaces, $1 \le p < \infty$, on the set $\Omega := \{(a,l);\ 0 < a < l,\ l_1 < l < l_2\}$ where the total cross section σ and the transition rate k are assumed to be nonlinear functions of the total density of population f and, at the mitosis, daughter and mother cells are related by a nonlinear reproduction rule which describes constraints at boundaries.

The structure of this work is as follows. In the next section we introduce the functional setting of the problem and the main assumptions. In Section 3 we study the initial boundary value problem (3.1) in the case where $\sigma(\cdot,\cdot,\cdot)$ and $k(\cdot,\cdot,\cdot,\cdot,\cdot)$ are nonlinear functions of the density of population f, and K is a nonlinear operator on suitable trace spaces modeling the biological rule. Following the same strategy as in the works [12, 20] for Lebowitz-Rubinow's model (also see [4] and [13]) we discuss existence and uniqueness of solutions to problem (3.1). The main result of this section is Theorem 3.5 which asserts that, under reasonable assumptions, problem (3.1) has a unique mild solution on appropriate weight L^p spaces where $1 \le p < \infty$. If $p > 1$, then this solution is also a weak solution of the problem. Further, if the initial data belongs to the domain of T_K^ω (see Section 2 for the definition of T_K^ω), then we obtain a strong solution. Further, we derive sufficient conditions guaranteeing that problem (3.1) possesses a unique global strong solution.

Section 4 focuses on problem (4.1) where $\sigma_1(\cdot,\cdot,\cdot)$ is a nonlinear function of $\langle f\rangle(t)$ with