Numerical analysis of a cell dwarfism model

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We analyze, from a numerical point of view, a cell population balance model (CPBM) in which cells are distinguished by their cell-size. The CPBM we consider is based upon the model developed by Diekmann, Heijmanns and Thieme [1] and studied theoretically in [2],

$$u_t(x,t) + (x\,u(x,t))_x = (\nu(x) - \mu(x) - b(x))\,u(x,t) + 4\,b(2\,x)\,u(2\,x,t),$$
$$0 < x < 1,\, t > 0, \tag{1}$$
$$u(x,0) = \varphi(x), \quad 0 \le x \le 1. \tag{2}$$

The population of cells is described by a density function $u(x,t)$, t represents time and x the measure of the cell-size. Functions μ, b and ν represents the mortality, division and migration processes which take place within the population and φ is the initial state of the population density. We assume that the environment is unlimited and all possible nonlinear mechanisms are ignored.

In this model, cells grow exponentially, $x'(t) = x(t)$, as in a petri dish experiment, and die with death rate $\mu(x)$ depending on cellular size. The cell division is considered into two equal cells [1]. Note that the exponential growth introduces the unavailability of a boundary condition at size $x = 0$, thus cell renewal is introduced through the division $b(x)$ and immigration $\nu(x)$ rates. We want to point out that a proper combination of growth, division and mortality rates would introduce a natural maximum cell size [3], otherwise we could fix it as one (normalized) and we would consider that larger cells may only grow and die.

The usual CPBM, as developed in [1], assumes the existence of a minimal cell size $a > 0$ for cellular division to take place which generates a minimal cellular size $a/2$. However, the model we study allows cell of any size in the interval $(0, 1]$ to divide. Therefore, the minimal cellular size is $a = 0$. Although the idea of a cell with size zero is biologically unrealistic, we use it as the limiting value to describe an abnormality in the cellular division process: the production of unfunctional "dwarf" cells. These kind of cells are

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observed in a group of inherit blood disorders that affect the body's ability to produce hemoglobin and red blood cells: thalassemia. These hereditary blood disorders (anemias) are one of the most common human genetic abnormalities known and prevalent in tropical and subtropical world regions where malaria was and still is epidemic. In healthy persons, the synthesis of α and β-globin chains is finely balanced during terminal erythroid differentiation, giving rise to red blood cells of consistent size (reflected in the mean corpuscular volume (MCV)) and hemoglobin content (mean corpuscular hemoglobin (MCH)). On the contrary, the disorders are caused by the absent or decreased production of the α-chain of hemoglobin. Major α-thalassemia disorder (hydrops fetalis) has a high lethality rate and it has become an important public health problem due to population migrations. Besides, carriers of (minor) α-thalassaemia are found at high frequencies and they are usually asymptomatics. These minor forms of thalassemia are associated with smaller red blood cells than normal, a condition known as microcytosis which are only distinguishable through MCV. These diseases are also associated to other blood disorders as the myelodysplastic syndrome [4, 5, 6].

Some theoretical properties of the model (1)-(2) were developed in [2]. The author addressed the existence and uniqueness of generalized solutions and their stability and unstability. On the one hand, he established the conditions on the data functions bounds to obtain a strongly stable solution, that biologically arrived to the extinction of the population. On the other hand, he proposed the data functions properties that arrived to the topological transitivity of the different cellular generations. It includes the erratic behaviour customarily associated with chaos.

These theoretical properties can be studied without a solution expression. However, the knowledge of their qualitative or quantitative behaviour in a more tangible way is sometimes necessary. Therefore, numerical methods provide a valuable tool to obtain such information. In the case of the study of CPBMs, different techniques have been used for both symmetric and asymmetric division rates (see [3, 7, 8] and the references therein). However, all of them are proposed for the solution of models with minimal cell division age, and it is very important to design numerical schemes specially adapted to the characteristics of this particular CPBM.

In this work, we present and analyze three first-order methods: natural grid, semi-lagangian and upwind schemes which are specially adapted to obtain the solution to the problem (1)-(2). We will compare them, study their convergence and show their ability to reproduce the behaviour of the solution.

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