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Drug Release from polymeric platforms: numerical analysis of a second order method on nonuniform grids with low regularity assumptions

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Polymeric platforms are one of the main devices that has been used for active and passive target drug release due to their optimum control properties. When this device is in contact with a solvent, the fluid enters in the polymer that swells and then a drug dissolution starts. Afterwards, the molecules of the dissolved drug diffuse through the relaxed polymeric structure [1]. Let c_l, c_d and c_s be the solvent, dissolved drug and solid drug concentrations in a spherical polymer of radius R. The behaviour of these concentrations is described by the following system of nonlinear integro-differential equations:

$$\begin{cases} \dfrac{\partial c_\ell}{\partial t} = \dfrac{\partial}{\partial x}\Big(\tilde{D}_\ell(c_\ell)\dfrac{\partial c_\ell}{\partial x}\Big) + \dfrac{\partial}{\partial x}\Big(\displaystyle\int_0^t q(t,s,c_\ell(s),c_\ell(t))\dfrac{\partial c_\ell}{\partial x}(s)ds\Big), \\ \dfrac{\partial c_d}{\partial t} = \dfrac{\partial}{\partial x}(\tilde{D}_d(c_\ell)\dfrac{\partial c_d}{\partial x}) + f(c_s,\, c_d,\, c_\ell), \\ \dfrac{\partial c_s}{\partial t} = -f(c_s,\, c_d,\, c_\ell) \end{cases} \tag{1}$$

is defined in $(0,R)\times(0,T]$, with initial and boundary conditions

$$\begin{cases} c_\ell(0) = c_{l,0} \\ c_d(0) = 0 \\ c_s(0) = c_{s,0} \end{cases}, \begin{cases} \dfrac{\partial c_\ell}{\partial x}(0) = \dfrac{\partial c_d}{\partial x}(0) = 0 \\ c_\ell(R) = c_{ext} \\ c_d(R) = 0 \end{cases} \tag{2}$$

In (1) the nonlinear reaction term $f(c_s,\, c_d,\, c_\ell) = H(c_s)k_d\dfrac{c_{sol}-c_d}{c_{sol}}c_\ell$ is the dissolution rate expressed by a Noyes-Whitney model where k_d denotes the dissolution rate, c_{sol} is the solubility limit and $H(\cdot)$ is the Heaviside function. The term $q(t,s,c_\ell(s),c_\ell(t))$ describes the nonlinear viscoelasticity polymer properties.

Our goal is to prove the stability and convergence properties of a finite difference method (that is as a semi-discrete Galerkin finite element method [2]) to solve numerically (1) -(2) in non-uniform grid. The analysis is performed using low space regularity assumptions for the solutions:

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$c_l(t)$, $c_d(t)$ and $c_s(t)$ are only in $H^3(0, R)$ at each time t. This low regularity guarantees a second order convergent method in space. Then by using a method of lines based on a Crank-Nicolson approach we prove that the method has also a second convergence order in time. The nontrivial proof for the second order in non-uniform space grid is based on the authors work [2] and [3, 4].

Referências

[1] J. S. Borges. "Numerical Modelling and Analysis of Drug Release from Viscoelastic Polymers". Tese de doutorado. IMECC/UNICAMP, 2019.

[2] J.A. Ferreira e R.D. Grigorieff. "Supraconvergence and Supercloseness of a Scheme for Elliptic Equations on Nonuniform Grids". Em: **Numerical Functional Analysis and Optimization** (2006), pp. 539–564.

[3] J. S. Borges, J.A. Ferreira, G. Romanazzi e E. Abreu. "Drug release from viscoelastic polymeric matrices - a stable and supraconvergent FDM". Em: **Computers and Mathematics with Applications** 99 (2021), pp. 257–269.

[4] G. C. M Campos, J.A. Ferreira e G. Romanazzi. "Density-pressure IBVP: Numerical analysis, simulation and cell dynamics in a colonic crypt". Em: **Applied Mathematics and Computation** 424.127037 (2022).

