Numerical treatment of reaction-diffusion-taxis equations arising in cancer invasion modeling.

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Motivation. Chemotaxis plays an important role in a plethora of biomedical processes extending from such as bacterial aggregation to wound healing, and to cancer tumour growth. In the case of cancer growth and cancer metastasis, the role of chemotaxis is twofold: first it promotes the vasculirization of the cancer tumour, and secondly it directs the migration of the cancer metastating cells into the circulatory system; leading hence to possible metastasis of the cancer to a another location of the organism.

Mathematical modeling. In mathematical terms, the deterministic modeling of the biological processes taking place during the growth and the metastasis of the cancer has been done mostly in terms of reaction-diffusion-taxis equations, see [1] (and references therein). In this work the authors prescribe a model that describes the cancer cell invasion of tissue. The model that they have developed reads as follows:

$$
\left.\begin{aligned}
\frac{\partial c}{\partial t} &= D_c \frac{\partial^2 c}{\partial x^2} && - \frac{\partial}{\partial x}\left(\chi_c c \frac{\partial u}{\partial x} + \zeta_c c \frac{\partial p}{\partial x} + \xi_c c \frac{\partial v}{\partial x}\right) && + \phi_{13} cu && + \mu_1 c\left(1 - \frac{c}{c_0}\right) && \\
\frac{\partial v}{\partial t} &= && && + \phi_{21} pu - \phi_{22} pv && + \mu_2 v\left(1 - \frac{v}{v_0}\right) - \delta v m \\
\frac{\partial u}{\partial t} &= D_u \frac{\partial^2 u}{\partial x^2} && && - \phi_{31} pu - \phi_{33} cu && && + \alpha_{31} c \\
\frac{\partial p}{\partial t} &= D_p \frac{\partial^2 p}{\partial x^2} && && - \phi_{41} pu - \phi_{42} pv && && + \alpha_{41} m \\
\frac{\partial m}{\partial t} &= D_m \frac{\partial^2 m}{\partial x^2} && && - \phi_{51} pu + \phi_{52} pv && + \phi_{53} cu &&
\end{aligned}\right\}
$$

diffusion — chemo-/hapto-taxis — proliferation — degradation

Notation: c: cancer cell density, v: ECM (vitronectin), u: uPA , p: PAI-1 and, m: the plasmin density. Parameters: D_c, D_u, D_p, D_m: diffusion coefficients, χ_c, ζ_c, ξ_c: chemo-/hapto-taxis coefficients, μ_1, μ_2, ϕ_{ij}: proliferation/inhibition rates, c_0, v_0: maximum sustainable densities of cancer cells and ECM , δ: degradation rate of ECM due to plasmin, α_{31}, α_{41}: production rates of uPA and PAI-1 due to the cancel cells and the plasmin.

Numerical difficulties & treatment. Numerically the problem is challenging due to the complexity of the system itself, but mostly due to the stiffness of the source terms when biologically relevant parameters are chosen.

We present in this talk our study on a series of numerical methods which were initially developed to treat hyperbolic problems with stiff source terms. We analyze the reasons that these "classical" methods fail when resolving the aforementioned model, and propose accordingly proper numerical corrections. We conclude by presenting our findings in parallel to the existing ones in the related numerical and biological literature.

References

[1] M.A.J. Chaplain, G. Lolas: Mathematical modeling of cancer cell invasion of tissue. The role of the urikinase plasminogen activation system. Math. Models Methods Appl. Sciences **15** (2005).

Vocabulary

proteolysis the hydrolysis of proteins or peptides with formation of simpler and soluble products (source: Merriam-Webster dictionary)

vitronectin Vitronectin is an abundant glycoprotein found in serum and the extracellular matrix (ECM) and promotes cell adhesion and spreading. (source: wikipedia)

urokinase (uPA) Urokinase and cancer: Elevated expression levels of urokinase and several other components of the plasminogen activation system are found to be correlated with tumour malignancy. It is believed that the tissue degradation following plasminogen activation facilitates tissue invasion and, thus, contributes to metastasis. (source: wikipedia)

serpins plasminogen activator inhibitor-1 (PAI-1) Is a serine protease inhibitor that functions as the principal inhibitor of tissue plasminogen activator (tPA) and urokinase (uPA), the activators of plasminogen. (source: wikipedia)

plasmin/fibrinolysin A proteolytic enzyme that dissolves fibrin. It is formed from plasminogen in the blood plasma. (source: Mosby's medical dictionary)

haptotaxis Cell haptotaxis describes cell migration toward or along a gradient of chemoattractants or adhesion sites in the extracellular matrix. These gradients are naturally present in the extracellular matrix (ECM) of the body during processes such as angiogenesis. (source: wikipedia)