PDE-constrained optimization problem for a tumor invasion in 2D using Adaptive Finite Element Method.

C. Turner A.A.I.Quiroga D.R. Fernández G.A. Torres

FaMAF-UNC, CIEM - CONICET, Medina Allende s/n, 5000 Córdoba, Argentina.

Abstract:

In this work we present a method for estimating unknown parameter that appear in a two dimensional non-linear reaction-diffusion model of cancer invasion. This model considers that tumor-induced alteration of micro-enviromental pH provides a mechanism for cancer invasion. A coupled system reaction-diffusion describing this model is given by three partial differential equations for the 2D non-dimensional spatial distribution and temporal evolution of the density of normal tissue, the neoplastic tissue growth and the excess concentration of H^+ ions. Each of the model parameters has a corresponding biological interpretation, for instance, the growth rate of neoplastic tissue, the diffusion coefficient, the reabsorption rate and the destructive influence of H^+ ions in the healthy tissue.

After solving the direct problem, we propose a model for the estimation of parameters by fitting the numerical solution with real data, obtained via in vitro experiments and fluorescence ratio imaging microscopy. We define an appropriate functional to compare both the real data and the numerical solution using the adjoint method for the minimization of this functional.

We apply a splitting strategy joint with Adaptive Finite Element Method (AFEM) to solve the direct problem and the adjoint problem. The minimization problem (the inverse problem) is solved by using a trust-region-reflective method including the computation of the derivative of the functional.

Moreover, in the work of Gatenby et all, the authors suppose that transformation-induced reversion of neoplastic tissue to primitive glycolytic metabolic pathways, with resultant increased acid production and the diffusion of that acid into surrounding healthy tissue, creates a peritumoral microenvironment in which the tumor cells survive and proliferate, while normal cells may not remain viable. The following temporal sequence would derive: (a) a high concentration of H^+ ions in tumors will diffuse chemically as a gradient to adjacent normal tissue, exposing these normal cells to an interstitial pH like in the tumor, (b) normal cells immediately adjacent to the edge of the tumor are unable to survive in chronically this acid environment, and (c) progressive loss of normal cell layers in the tumor-host interface facilitates tumor invasion. Key elements of this mechanism of tumor invasion include low pH due to primitive metabolism and reduced viability of normal tissue in an acidic environment. Due to this fact, with this methodology we can estimate important parameters of the model.

Bibliography

R.A. Gatenby, E.T. Gawlinski ,A reaction-diffusion model of cancer invasion, Cancer Research, vol. 56,1996, 5745–5753.

G.R. Martin, R.K. Jain, Noninvasive measurement of interstitial ph profiles in normal and neoplastic tissue using fluorescence ratio imaging microscopy, Cancer research, vol. 54, 1994,5670–5674.