Simulation of abnormal colonic cell dynamics using a multiscale method

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Abstract

It is generally accepted that colorectal cancer is initiated in colonic crypts as a consequence of several genetic mutations in normal cells. Clusters of abnormal crypts, called Aberrant Crypt Foci (ACF), are thought to be the first manifestation of a possible carcinogenic process. Assuming that ACF result from the accumulation of abnormal cells, we simulate the ACF evolution by using a multiscale model, which characterizes the dynamics of abnormal cells. This multiscale model results from a system that couples the evolution of both normal and abnormal colonic cells, during their propagation along the crypt walls and the colon [1, 2, 3]. Inside the crypts, the dynamics of the abnormal cells is governed by a convective-diffusive model, whose solution is the cell density and the pressure exerted by the cells on the crypt wall. Outside the crypts, in the inter-cryptal region, a proliferative-diffusive model is assumed for the dynamics of abnormal cells.

For the numerical implementation of this model, it is used a technique based on heterogeneous multiscale methods [4]. Two scales are employed : a macro-scale and a micro-scale. The macro-scale corresponds to the region of the colon where the evolution of ACF is taking place, whilst the micro-scale is related to the region occupied by each crypt and its inter-cryptal region.

Pressure and cell density are computed at the macro-scale level, using a full finite element discretization of the model, but with the model parameters (diffusion and proliferation coefficients) defined at the micro-scale. The micro-scale finite element discretization is performed only in a neighborhood of the quadrature points used in the macro-scale finite elements operators [5]. This strategy reduces the computational cost of the simulations.

Numerical results, simulating the ACF evolution, are shown and discussed.

Keywords: Convective-diffusive model, multiscale methods, colonic crypts.

References

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