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PARAMETER RELEVANCE IN A THREE DIMENSIONAL COLONIC CRYPT MODEL

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Colorectal cancer is one of the most frequent type of cancer in the western world [1]. Different scientific communities have studied its morphogenesis from geneticists to computing scientists. This cancer is thought to originate in the colon epithelium (a structure consisting of millions of small orifices, called crypts), where an intense cellular activity occurs.

It is generally accepted that the tumorigenesis, that elapses for a period of 20-40 years, starts with genetic mutations of the APC pathway that leads to an increase of the cellular rate of proliferation [2, 3]. Due to these mutations, normal cells transform into abnormal cells. A clear evidence of the presence of abnormal cells in the crypts is the appearance of the so called Aberrant Crypt Foci (ACF), which are clusters of colonic crypts exhibiting a different shape from the normal ones. ACF can be detected by colonoscopy since they react to certain dyes differently from normal crypts (these latter are filled with normal cells). It is believed that ACF evolve to adenoma (benign tumour) that if removed can stop in many cases the cancerogenesis [6].

Recent research on modelling and numerical simulation for the dynamics of ACF, based on different theories proposed to describe the formation of an ACF (such as the top-down [5] and bottom-up theories [4]), can be found in [7, 8, 9, 10]. In this work we describe the dynamics of abnormal cells within a colonic crypt in a three dimensional (3D) setting. The intention is to show, based on the top-down and bottom-up theories and using numerical simulations, the important role of some parameters, such as the cell rate proliferation and the cell diffusion coefficient. In addition we remark that these parameters are very difficult or impossible to determine *in vivo* and that only a qualitative information is available in the literature (see [11] for a related work).

The proposed 3D crypt model is a generalization, for the 3D setting, of that described in [9], where a reduced multiscale two dimensional model, derived from the original 3D

model, is proposed for simulating the ACF dynamics (briefly, it involves a parabolic reaction diffusion equation, describing the cell density, coupled with an elliptic equation, defining the cell pressure). By considering the real 3D scenario, for a colonic crypt, the main goal is to analyze and compare *in silico* the possible different behavior induced in its morphogenesis and cell dynamics, by changing in the model, both the diffusion coefficients and rate of proliferation parameters of the colonic cells.

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