Physiologic Parameter Estimation in Aberrant Crypt Foci

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Abstract

Aberrant Crypt Foci (ACF) are clusters of abnormal colonic crypts (small pits in the colonic epithelium), which are thought to be the precursors of colon cancer. Consequently, any information involving physiologic parameters related to the dynamics and evolution of ACF is of utmost importance. In this talk we describe two *in vivo* parameter estimation problems in ACF. The first one, that we call *chromoscopy based parameter estimation* [1], is motivated by the current medical endoscopy technique (chromoscopic colonoscopy), used to assess ACF. The second problem, that we call *cell crypt based parameter estimation* [2], relies on the cell dynamic mechanism inside the colonic crypts. Both are inverse problems mathematically formulated as PDE-constrained optimization models.

The *chromoscopy based parameter estimation* is an image-driven problem. During chromoscopic colonoscopy a colored substance (a dye) is instilled in the colonic mucosa. The ACF stain darker with some dyes, than normal crypts. Therefore, we first perform a segmentation of the medical endoscopic image, which separates normal and aberrant crypts. In addition, we assume that the dye concentration obeys to a mass diffusion equation and that it is related to the pixel intensity of the medical image, by the Beer-Lambert law. Then, we do a mathematical and dimensionless quantification (medically noninvasive) of the dye absorption and diffusion coefficients, as well as the dye absorbed, in normal and aberrant colonic crypts. This mathematical quantification can be important for clinicians if it is able to provide a distinction between individuals with and without a high carcinogenic potential.

For formulating the *cell crypt based parameter estimation*, we assume that the cellular kinetics, occurring inside the crypts, is governed by a particular convection-diffusion-shape model [3]. This model correlates colonic crypt patterns with the cellular dynamics [3], which has proven to be significant in the context of colon cancer. Moreover, it involves

some important physiologic parameters, as the birth and death rate of proliferative cells, for which only qualitative information is available in the literature. These parameters have a crucial role in ACF dynamics and evolution. By resolving an inverse problem (that minimizes the misfit between two proliferative cell densities: one predicted by the model and the other actually been observed), we estimate the birth rate of proliferative cells (considered as a parameter field), along the colonic crypt wall. The location where the birth rate deviates from normal qualitative values can then be determined, and used for further clinical research and better understanding of the abnormal process leading to the increase or decrease of proliferative cells, and the emergence of ACF.

The two problems are discretized by finite elements, for the space variable, and finite differences, for the time variable. The first model is solved by a gradient descent method and the second by an inexact Newton method. Some test simulations, illustrating the performance of these two physiologic parameter estimation problems and their application to real patient data, will be shown.

Keywords: image segmentation, convection-diffusion equations, inverse problem, optimality system, finite elements.

References

[1] Isabel N. Figueiredo, Pedro Figueiredo, Nuno Almeida: Image-driven parameter estimation in absorption-diffusion models of chromoscopy, SIAM Journal on Imaging Sciences, 4, 3 (2011) 884-904.

[2] Isabel N. Figueiredo, Carlos Leal: Physiologic parameter estimation using inverse problems, Preprint 12-06, Department of Mathematics, University of Coimbra (2012).

[3] Isabel N. Figueiredo, Carlos Leal, Giuseppe Romanazzi, Bjorn Engquist, Pedro N. Figueiredo: A convection-diffusion-shape model for aberrant colonic crypt morphogenesis, Computing and Visualization in Science, 14, 4 (2011) 157-166.