Comparison of Two Sensitivity Analysis Methods in a Tumor Growth Model

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Abstract. The aim of this work is to compare two different sensitivity analysis methods, used to investigate the influence of the input parameters of a tumor model on its outcome. The first method uses a Monte Carlo approach to produce Scatterplots and the second uses the Elementary Effects method. Numerical experiments are conducted to highlight the main strengths of each approach.

Keywords. Tumor Growth, Sensitivity Analysis, Scatterplots, Elementary Effects.

Introduction

It is recognized that tumor growth and invasion results from an intricate interplay of many phenomena that occur at different biological, spatial and temporal scales, although sometimes the precise agents involved are not well understood and many mechanisms remain unfolded. Mathematical models can help to elucidate the dynamics of the tumor growth, its key components, the role of parameters and the crosstalk among different agents at different scales. Sensitivity analysis (SA) is a useful tool to assess, qualitatively and quantitatively, how changes in input parameters affect the variation and uncertainty in the model quantity of interest (QoI) [1]. In this work we make a step towards tumor growth model assessment with respect to the evolution of the tumor volume and invasion front, chosen as the most important QoIs. SA is performed in a one-dimensional vascular tumor growth model, represented here by the deterministic reaction-diffusion type model studied in [2]. It consists of a nonlinear coupled system of seven reaction-diffusion equations with more than a dozen parameters. Although simple, this model encompasses several aspects and mechanisms underlying tumor progression.

A wide range of SA approaches are available in the literature [4]. In this work, two model-free sensitivity analysis methods are investigated. The first method, based on the

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construction of scatterplots, is a rather simple and informative way to perform sensitivity analysis. In this method, the parameters are sampled through a Monte Carlo approach and scatterplots are built by projecting the resulting values of the selected QoIs against the sampled values of each parameter. Each scatterplot depicts clouds of points over the range of the respective uncertain parameter. A more defined pattern indicates a more important correlation between the uncertain parameter and the QoIs, providing a straightforward way to visualize the relation between them. Being a qualitative measure, the challenge for this analysis is the quantification of such relationships, by ranking the most important parameters of the model, for example. Other difficulties of the scatterplot approach appear when there are too many input parameters or when group of parameters have to be analised [4].

To evaluate the extent of these limitations regarding the tumor growth model, a screening SA method is also used in this work, the so called Elementary Effect (also known as Morris method [3]). The whole parametric space is screened according to an One-(parameter)-At-a-Time (OAT) sampling strategy, tracking the elementary effect, defined as the difference ratio between the variation of the QoI and the variation of the input parameter. Special techniques are available to guarantee an unbiased screen for the parametric space, while yielding a relatively small number of model evaluations. Finally, global SA measures are obtained by averaging the elementary effects, allowing to rank the parameters [4]. This methodology is numerically efficient and can be easily applied to group of parameters. More interestingly, it is a good proxy for the total effects of variance-based models [1] and it is proven to be useful when the number of input parameters is large.

Those two different techniques are compared through a series of computational experiments and their roles in the assessment of the tumor progression (tumor volume and position of the invasion front) are discussed.

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