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Selection and Validation of Predictive Models of Radiation Effects on Tumor Growth Based on Noninvasive Imaging Data

E. A. B. F. Lima[a], J. T. Oden[a,1,*], B. Wohlmuth[b], A. Shahmoradi[a], D. A. Hormuth II[a], T. E. Yankeelov[a,c,d], L. Scarabosio[b], T. Horger[b]

[a]Institute for Computational Engineering and Sciences (ICES), The Center of Computational Oncology (CCO), The University of Texas at Austin
[b]Technical University of Munich, Germany, Department of Mathematics, Chair of Numerical Mathematics (M2)
[c]Department of Biomedical Engineering, The University of Texas at Austin
[d]Department of Internal Medicine, Livestrong Cancer Institutes, Dell Medical School, The University of Texas at Austin

Abstract

The use of mathematical and computational models for reliable predictions of tumor growth and decline in living organisms is one of the foremost challenges in modern predictive science, as it must cope with uncertainties in observational data, model selection, model parameters, and model inadequacy, all for very complex physical and biological systems.

In this paper, large classes of parametric models of tumor growth in vascular tissue are discussed including models for radiation therapy. Observational data is obtained from MRI of a murine model of glioma and observed over a period of about three weeks, with X-ray radiation administered 14.5 days into the experimental program. Parametric models of tumor proliferation and decline are presented based on the balance laws of continuum mixture theory, particularly mass balance, and from accepted biological hypotheses on tumor growth. Among these are new model classes that include characterizations of effects of radiation and simple models of mechanical deformation of tumors.

The Occam Plausibility Algorithm (OPAL) is implemented to provide a Bayesian statistical calibration of the model classes, 39 models in all, as well as the determination of the most plausible models in these classes relative to the observational data, and to assess model inadequacy through statistical validation processes. Discussions of the numerical analysis of finite element approximations of the system of stochastic, nonlinear partial differential equations characterizing the model classes, as well as the sampling algorithms for Monte Carlo and Markov chain Monte Carlo (MCMC) methods employed in solving the forward stochastic problem, and in computing posterior distributions of parameters and model plausibilities are provided. The results of the analyses described suggest that the general framework developed can provide a useful approach for predicting tumor growth and the effects of radiation.

Keywords: MRI imaging, radiotherapy, phenomenological models, calibration, validation, model plausibilities, Bayesian inference, Monte Carlo methods, statistical sampling.

1. Introduction

The development of computational models that reliably predict the growth or decline of tumors in living tissue is one of the great challenges in modern predictive science. It is a mission made difficult not only because of the considerable physical and biological complexity of heterogeneous interacting media in which tumors exist and evolve, but also because of the presence of uncertainties. Uncertainty in the observational data, in the selection of reliable models, in model parameters, in combination with errors in the computed approximations result in uncertainties in the predicted quantities of interest.

*Corresponding author

Email addresses: lima@ices.utexas.edu (E. A. B. F. Lima), oden@ices.utexas.edu (J. T. Oden), wohlmuth@ma.tum.de (B. Wohlmuth), amir@ices.utexas.edu (A. Shahmoradi), david.hormuth@utexas.edu (D. A. Hormuth II), thomas.yankeelov@utexas.edu (T. E. Yankeelov), scarabos@ma.tum.de (L. Scarabosio), horger@ma.tum.de (T. Horger)