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Application of fast isogeometric L2 projection solver for tumor growth simulations

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Highlights

- We derive the isogeometric model of the melanoma growth.
- We model tumor cell density, extracellular matrix and, tumor angiogenic factor.
- We couple continuous model with discrete vasculature growth model.
- We apply isogeometric L2 projections implementing alternative directions method.
- We point out the potential of the model for GPGPU acceleration.

Abstract

To employ computer models of tumor proliferation for planning cancer treatment, extremely fast numerical solvers are in high demand at least for two reasons: data adaptation and multiscale character of growth dynamics. The number of complex and non-linear phenomena influencing tumor dynamics involves hundreds of variable parameters. Its matching using incoming data requires reverse optimization or learning procedures, which are very demanding computationally. We present here the fast algorithm for isogeometric L2 projection, which we propose as a numerical engine for tumor modeling. First, we introduce the continuous–discrete model of melanoma described by the system of PDEs in a simplified computational layout of a fragment of skin. Apart from the continuous density fields such as tumor cell density, flux pressure, extracellular and degraded extracellular matrices, we also introduce a discrete model of the vasculature, which is the source of oxygen and nutrients. The discrete vasculature is coupled every given time interval with the continuous model influencing the vasculature remodeling. Our tests and the results of 2-D simulations of melanoma progression clearly show that isogeometric L2 projection utilizing the alternating directions solver is superior over classical approaches in terms of computational complexity, what makes it an excellent candidate for a numerical engine for continuous–discrete models of complex biological systems.

Keywords: Tumor model; Isogeometric solver; Computer simulations

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1. Introduction

Recent reports on the global cancer burden [1] show that over 14 million new cancer cases were diagnosed in 2012 worldwide. Moreover, over 4 million people died of cancer in 2012 in economically developing countries. The expectations are even more alarming. They predict 21.7 million new cancer cases to be diagnosed in 2030 with over 13 million deaths.

Even though a tremendous intellectual and financial effort were spent on understanding cancerogenesis and developing effective anticancer therapies, the neoplasm remains resistant to all currently used drugs. The anticancer therapies must be planned on a case by case basis. Therefore, personalization of tumor dynamics monitoring and simulations becomes crucial in modern oncology.

An interdisciplinary effort that brings clinicians and biologists together with mathematicians and computational modelers is necessary to develop simulations of the tumor growth [2]. These simulations investigate the behavior and response of tumors to various environment conditions and possible therapies [3]. If brought to a high enough level of sophistication, this kind of technology could possibly revolutionize medicine and bring a new paradigm into the treatment and prevention of cancer [4–6].

However, the success of the application of computer simulations in planning cancer treatment depends critically on the efficiency of numerical solvers. There are at least two reasons of that: data adaptation and multiscale character of growth dynamics. The number of complex and non-linear phenomena influencing tumor dynamics involves hundreds of parameters of high spatio-temporal variability. The data adaptation and parameters matching by incoming data require reverse optimization or complicated learning procedures, which are extremely demanding computationally. On the other hand, multiscale and multiphysics of cancer growth require to break another serious barrier in computational complexity [7–10]. The continuous model needs to be very fast computationally for scales bridging and matching parameters to lower in spatio-temporal scale discrete (particle or cellular automata) tumor models.

In this paper, we derive the isogeometric model of melanoma growth. The mathematical model of cancer and its parametrization is based on the previously published research [11–13] with some modification to enable continuous modeling by isogeometric finite element method. We also introduce a discrete model of vasculature which is the source of oxygen and nutrients. The system is solved using fast isogeometric L^2 projections, utilizing the alternating directions method.

The alternating directions method was originally introduced in [14–17] to solve parabolic and hyperbolic partial differential equations by using finite difference methods. The method has been recently generalized for the case of isogeometric finite element method, for regular geometries [18] as well as a preconditioner for iterative solvers such as the conjugated gradient method in the case of complicated geometries [19].

The motivation for using isogeometric FEM is the tensor product structure of the B-spline based functions over 2D regular grids. The tensor product structure is necessary for the application of alternating directions algorithm. Other possible basis functions that fulfill the tensor product structure over the 2D grids would be B-splines with C^0 separators, introduced between patches of elements, like defined in [20]. In the one limiting case (C^0 separators between all the elements) they are equivalent to standard finite elements. In the other case (no C^0 separators) they are equivalent to B-spline basis functions. Finally, when C^0 separators are introduced between some number of elements, they minimize the computational cost of the multi-frontal solver executed over the entire 2D mesh [20]. However, in the case of the alternating directions solver, we solve two 1D problems with multiple right-hand-sides, and the cost of the 1D solver grows linearly when increasing the number of the basis functions. In such the case the introduction of C^0 separators will only increase the number of the basis functions in one direction, so it will increase the number of right-hand sides, and the overall computational cost. Thus, selection of the limiting case of the B-spline basis functions seems to be a natural choice, since they minimize the cost of the 1D solvers (it is a minimal number of functions that span polynomial basis of order p).

The plan of the paper is the following. In Section 2 we present a detailed description of the melanoma growth model, including the vasculature discrete growth model in Section 2.3. In Section 3 we present an overview of the isogeometric L^2 projections solver. We present numerical results in Section 4. Finally, we discuss the conclusions and outline the future work.

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