



# Computational modelling of multiscale, multiphase fluid mixtures with application to tumour growth

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## Abstract

In this work we consider the discretization of a recently formulated (Collis et al., [22]) multiscale model for drug- and nutrient-limited tumour growth. The key contribution of this work is the proposal of a discontinuous Galerkin finite element scheme which incorporates a non-standard coupling across a singular surface, and the presentation of full details of a suitable discretization for the coupled flow and transport systems, such as that arising in Collis et al. [22] and other similar works. We demonstrate the application of the proposed discretizations via representative numerical experiments; furthermore, we present a short numerical study of convergence for the proposed microscale scheme, in which we observe optimal rates of convergence for sufficiently smooth data.

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## 1. Introduction

Over many years, mathematicians have sought effective means of incorporating effects occurring on multiple spatial and temporal scales into mechanistic models, whether this is in the classical settings of homogenization via asymptotic expansions and volume averaging [1], or the more contemporary setting of multiscale numerical methods, see e.g. [2–4]. Multiscale effects are of interest to many communities of applied mathematicians, such as those studying groundwater flow [5,6] or biological systems [7–9]. As these techniques become better developed, we observe an increased level of their application across an ever greater range of physical and biological systems, inevitably driving further development of both analytical and computational techniques.

A specific application that has garnered much interest is the study of cancer as a multiscale system. There have been extensive developments in the mathematical and computational modelling of tumour growth since the middle portion of the last century [10]. However, in the last few decades there has been an increased focus on incorporating mechanisms occurring on multiple scales in an effective manner, see e.g. [11–21] and the references

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therein. Understanding the dependence of a tumour's evolving microstructure and microvasculature is vital for making predictions regarding the potential efficacy of a drug in its treatment [17,18].

In the companion article to this work [22], we consider an asymptotic analysis of a multiphase fluid dynamics model for avascular tumour growth of the type exploited in [23,24]. This analysis allows us to derive a system of equations that describes tumour growth at a lengthscale associated with the full extent of the tumour tissue, that is explicitly dependent on a microscale formulation describing the microstructural properties of the tumour. The resulting microscale problem comprises a system of coupled tensor Stokes problems, the macroscale problem, a coupled system of nonlinear hyperbolic transport equations, further coupled to an elliptic flow equation. The analysis of [22] represents an extension of the multiscale analyses of [7,20,25], as we consider growth that is dependent on the tissue composition in a multiscale framework as a means of incorporating interstitial growth. However, the relative complexity of the micro- and macroscale systems obtained in [22], compared to those in [7,20,25], necessitates increased sophistication in their discretization.

In this article, we address the challenges associated with defining suitable discretizations for both systems of equations. For the microscale system, we consider a means of incorporating the non-standard coupling of flow across a quasi-stationary internal surface into a discontinuous Galerkin (dG) finite element (FE) discretization which, to the authors' knowledge, has not been considered elsewhere in the literature (cf. [26] and references cited therein). For the macroscale system, the primary difficulty arises in obtaining a suitably stable discretization for the complex coupled system of nonlinear partial differential equations (PDEs), that does not suffer from spurious numerical oscillations. As such, we present a full description of the dG FE and mixed Raviart–Thomas (RT)/dG FE discretizations employed in [22]. Additionally, we present a short numerical study of the convergence of the method proposed for the microscale problem as well as a selection of representative numerical experiments for the macroscale problem.

This article is organized as follows. In Section 2 we recall the microscale and macroscale models presented in [22] governing tumour growth together with passive transport of drug and nutrient, and in Section 3 we introduce the discretization employed in their solution. In Section 4 we present a short numerical study of the convergence of the discretization of microscale model and a selection of numerical experiments demonstrating the dynamics of the macroscale system. Finally, in Section 5 we make some concluding remarks and highlight ongoing and future work.

## 2. Model description

In this section we provide a brief summary of the underlying conceptual model describing drug- and nutrient-regulated growth and response of a tumour, and transport of passive solutes as described in [22], as well as brief details of the formulation arising from a multiple scales analysis contained therein, the solution of which forms the principal focus of the current work.

### 2.1. Conceptual model

We consider a multiphase fluid dynamics model of avascular tumour growth and transport of passive solutes based on that employed in [23,24], in which detailed justification for the application of models of this type is provided. We consider a formulation that is characterized by two lengthscales that are strongly separated, referred to as the microscale and the macroscale. Under this assumption, described formally below, and strong interphase drag so that all phases move with a common velocity (motivated by such works as [27,28]), we are able to derive an effective description of growth and transport on the macroscale (corresponding to the lengthscale of the tumour tissue), explicitly incorporating microscale tumour dynamics.

We consider a region of tumour tissue,  $\Omega_L \subset \mathbb{R}^d$  ( $d = 2, 3$ ), as an idealized porous medium that consists of a multicomponent mixture, comprising  $N_\theta$  interacting phases, saturated with a viscous Newtonian fluid, and subsequently referred to as the mixture and interstitial fluid, respectively. We assume that within  $\Omega_L$  there is a spatially periodic microstructure, which we denote  $\Omega_\ell$ , that further defines two subdomains  $\Omega_1$  and  $\Omega_2$ , corresponding to the regions that contain the multicomponent mixture and the interstitial fluid, respectively. We further assume that the free interface between  $\Omega_1$  and  $\Omega_2$ , denoted  $\Gamma$ , is sharp, and that phase transition may occur on this singular surface; where the movement of  $\Gamma$  is determined by tissue growth. A schematic diagram of this geometry is shown in Fig. 1. Additionally, we assume that the porous medium may be characterized by two distinct lengthscales ( $\ell$ , corresponding

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