A Finite Element Method for the Interaction between Microcirculation and Tissue Interstitium

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1 Introduction

We aim at performing large scale simulations of microcirculation. In the context of blood flow, the application of geometrical model reduction techniques plays an essential role, see for example [8, 18]. In particular, small vessels embedded into a continuum can be described as one-dimensional (1D) concentrated sources, in order to reduce the computational cost of simulations. Although the coupling of three-dimensional (3D) continua with embedded (1D) networks arises in applications of paramount importance such as microcirculation, flow through perforated media and the study of reinforced materials, it has not been well investigated yet.

Two remarkable examples of methods that were previously proposed to overcome the challenges of simulating small objects into a continuum are the *immersed boundary methods* [13, 17, 22] and the *fictitious domain methods* [9, 10, 21]. Although they share some similarities with the approach that we pursue here, they have never been applied for solving coupled partial differential equations on embedded domains.

In the particular case of microcirculation, many ad-hoc approaches have been proposed. Since capillaries can be modelled as long and narrow cylindrical vessels, asymptotic expansions that exploit the large aspect ratio of the channel can be derived to approximate the fluid exchange from one capillary to the surrounding tissue. This idea has been successfully exploited to study the microvascular flow in simple arrays of capillaries [1, 6, 7]. However, vascular networks are characterized by a complex, possibly irregular geometry. The previous semi-analytic methods may be hardly applied to realistic configurations. We believe that numerical methods may override this obstacle. For example, the method of Green's functions, has been extensively applied to the study complex vascular networks of tumors [11, 19, 20].

In this work we aim to move away from ad-hoc approaches and cast the microcirculation problem into a new unified framework to formulate and approximate coupled partial differential equations (PDEs) on manifolds with heterogeneous dimensionality. The main computational barrier consists in the ill-posedness of restriction operators (such as the trace operator) applied on manifolds with co-dimension larger than one. Following the approach introduced in [5, 12, 4], we will overcome the computational challenges of approximating PDEs on manifolds with high dimensionality gap [16]. The main idea consists of introducing nonlocal restriction operators that combine standard traces with mean values of the solution on low dimensional manifolds, in order to couple the problem solution in

3D with the one in 1D. This new approach has the fundamental advantage to enable the approximation of the problem using Galerkin projections on Hilbert spaces, which could not be otherwise applied, because of regularity issues.

Within this general framework, the specific objective of this work is to formulate the microcirculation problem as a system of coupled 1D and 3D partial differential equations governing the flow through the capillary network and the interstitial volume, respectively. In order to obtain a good approximation of pressure and velocity fields, and in particular to satisfy mass conservation, we formulate the problem in mixed form. Then, we derive a discretization method based on mixed finite elements. We will also address applications of the method to study pathologies related to microcirculation, such as cancer [3, 2, 14, 15].

2 Methodology

We propose a mathematical model for fluid transport in a permeable biological tissue perfused by a capillary network. The domain where the model is defined is composed by two parts, Ω and Λ, denoting the interstitial volume and the capillary bed respectively. We assume that the capillaries can be described as cylindrical vessels and Λ denotes the centerline of the capillary network. The capillary radius, R, is for simplicity considered to be constant. We decompose the network Λ into individual branches Λ_i. Branches are parametrized by the arc length s_i; a tangent unit vector $\boldsymbol{\lambda}_i$ is also defined over each branch, defining in this way an arbitrary branch orientation. Differentiation over the branches is defined using the tangent unit vector as $\partial_{s_i} := \nabla \cdot \boldsymbol{\lambda}_i$ on Λ_i, i.e. ∂_{s_i} represents the projection of ∇ along λ_i. The blood flow along each branch is described by Poiseuille's law for conservation of momentum and mass:

$$\mathbf{u}_v^i = -\frac{R^2}{8\mu}\frac{\partial p_{v,i}}{\partial s_i}\boldsymbol{\lambda}_i, \quad -\pi R^2 \frac{\partial \mathbf{u}_v^i}{\partial s_i} = g_i \qquad \text{on} \quad \Lambda_i, \tag{1}$$

where g_i is the transmural flux leaving the vessel. As a consequence of the geometrical assumptions, the vessel velocity has fixed direction and unknown scalar component along the branches, namely $\mathbf{u}_v^i = u_v^i \boldsymbol{\lambda}_i$. We shall hence formulate the vessel problem using the scalar unknown u_v. The governing flow equations for the whole network Λ are obtained by summing (1) over the index i.

We consider the interstitial volume Ω as an isotropic porous medium, described by the Darcy's law, namely

$$\mathbf{u}_t = -\frac{1}{\mu}\mathbb{K}\nabla p_t, \tag{2}$$

where $\mathbf{u}_t$ is the average velocity vector in the tissue, $\mathbb{K} = k\mathbb{I}$ is the isotropic permeability tensor, μ is the viscosity of the fluid and p_t is the fluid pressure.

The coupled problem for microcirculation and interstitial flow reads as follows

$$\begin{cases} \dfrac{\mu}{k}\,\mathbf{u}_t + \nabla p_t = 0 & \text{in} \quad \Omega, \\ \nabla \cdot \mathbf{u}_t - f(p_t, p_v)\delta_\Lambda = 0 & \text{in} \quad \Omega, \\ \dfrac{8\mu}{R^2}\,u_v + \dfrac{\partial p_v}{\partial s} = 0 & \text{in} \quad \Lambda, \\ \dfrac{\partial u_v}{\partial s} + \dfrac{1}{\pi R^2} f(p_t, p_v) = 0 & \text{in} \quad \Lambda. \end{cases} \tag{3}$$

The constitutive law for blood leakage from the capillaries to the tissue is provided by means of Starling's law of filtration,

$$f(p_t, p_v) = 2\pi R L_p (p_v - \bar{p}_t), \tag{4}$$

with

$$\bar{p}_t(s) = \frac{1}{2\pi R} \int_0^{2\pi} p_t(s, \theta) R d\theta. \tag{5}$$

3 Results and conclusions

The numerical solution of a simplified problem is visualized in Figure 1. Unitary parameters $\kappa_v = 1$, $R' = 1$, $Q = 1$ are used. These simulations confirm that the model captures the characteristic traits of microcirculation. More advanced numerical simulations will be presented and thoroughly discussed, with particular focus on the cancer treatments based on the delivery of nanoparticles [15, 14].

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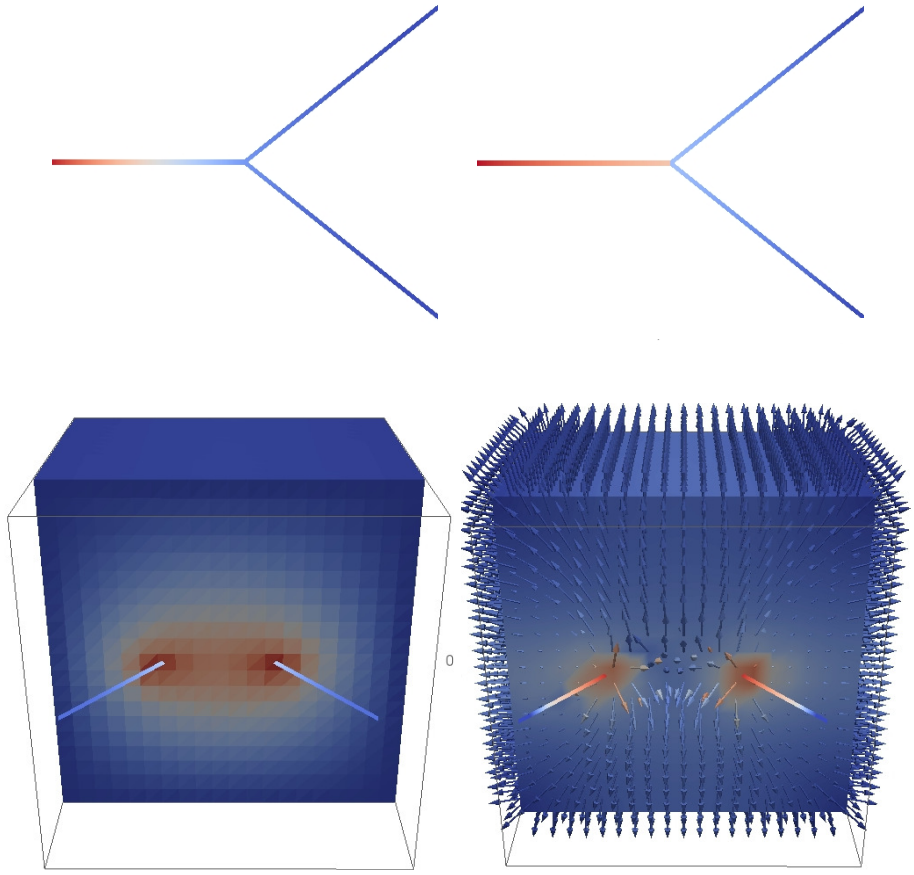

Figure 1: Visualization of the 3D/1D coupled pressure and velocity fields.

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