A NUMERICAL FRAMEWORK FOR THE SIMULATION OF MOLECULAR DIFFUSION IN THE MICRO-VASCULAR SYSTEM

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Introduction

Cerebral microcirculation is linked to a large number of applications: angiogenesis and neo-angiogenesis, long term remodeling in ageing and/or disease (hypertension, metabolic syndrome, neurological disease such as Alzheimer's), patho-physiology (cerebro-vascular disease -stroke-, brain tumors), and functional neuroimaging. In this context, direct numerical simulation of molecule transfer (e.g. tracers, nutrients) in the brain microcirculatory system where diffusion and transport processes are fully coupled between the vessels and tissue is of a great interest. Although direct simulations of the whole cerebral microcirculation is computationally cumbersome, we will show that they can be carried out on a smaller scale (about 50 to 10000 vessels).

Simulations of mass transfer at this intermediate scale enable a fine comparison with experiments. Indeed, experiments of tracer or oxygen diffusion are avaliable at that scale and make a direct comparison possible with matching geometries. Such simulations can thus be used to validate models, as for example the coupling model for diffusion between vessels and tissue (often expressed as boundary conditions) or exctract parameters of a given model (e.g. diffusion coefficients).

Some works have been done to model the mass transfer from capillaries to tissue taking into account the coupled interaction on very simple geometries [1,2]. Other works used more complex networks, where the vessels were segmented and the cross-sectional variations of concentration were either neglected [3] or fitted from other simulations [4].

Methods

We introduce a numerical framework able to solve the fully coupled problem: tissue-diffusion and vessels-advection/diffusion. The equations are solved by finite element method, using the library Feel++ [5]. Several boundary conditions are tested to model the coupled interaction between vessels and tissue. The simulation method uses a two-domains approach to differentiate tissue and vessels domains. Two methods have been derived to construct the geometries of these domains:

1) two different sub-domains are automatically defined and meshed by scripting the mesh generator Gmsh

2) the vascular and tissue are pure fictitious domains: in that case a cubic mesh is generated and a distance function to the segmented network is computed efficiently through the use of fast algorithms.

The later method can incorporate a mesh refinement process in order to better match some regions of interest.

Results

The simulation using both methods will be compared on simple test cases as in [1]. Results of tracer diffusion on anatomical geometries (figures 1) will be presented and compared to experimental results.

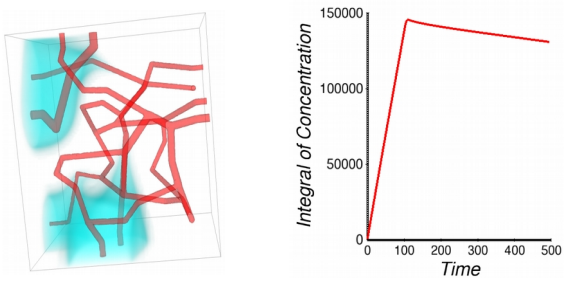

Figure 1

Figure 1: (left) Concentration of tracer (in blue) diffusing into a cerebral capillary network where the vessels (in red) are taken into account through a fictitious domain approach. (right) Integral of concentration over time following a transient injection. After time T=100, where injection stops, the wash-out is observed.

Discussion

The advantages and drawbacks of this numerical approach will be discussed from several points of view, including: performances, error estimations, algorithm complexity. Moreover the boundary conditions at the vessel/tissue interface will also be examined.

References

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