# Upscaling mass transfer in 3D anatomically accurate brain microvascular networks.

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*Keywords:* microcirculation, mass transfer, upscaling, finite element, fictitious domain

## 1. Introduction

Due to its highly specialized function, the brain is one of the organs with the highest basal energy demand in mammals. With essentially no sustainable energy reserves, it is extremely vulnerable to discontinuities in oxygen and nutrients delivery by the blood. Thus, the blood supply is locally adjusted in correspondence with local variations of underlying neural activity. This local adjustment of blood flow to function is mediated by contractile cells which convert the bio-chemical signals from activated neurons to changes in vascular diameter, and regulate blood flow by modulating the vascular resistance. Thus, studying cerebral blood flow is of a great interest for medical purposes (diagnostic) as well as for research purpose (better understanding of the neural activity).
Several imaging techniques have been developed to measure the spatio-temporal concentration fields of various endogenous or exogenous tracers in the brain. For example, the concentration of radio-labeled water injected transiently in the vascular system can be measured by Positron Emission Tomography (PET), while the presence of paramagnetic deoxy-hemoglobin induces contrast in functional Magnetic Resonance Imaging (fMRI).

The resolution of PET is about $(10\ \mathrm{mm})^3$ while fMRI can achieve resolutions down to $1\ \mathrm{mm}^3$, i.e. much coarser than the diameters of most arterioles and veinules, which are typically below 100 µm, and, of course, of capillaries, which diameters are tenfold smaller.

This implies that deducing the regional blood flow rate out of these large-scale concentration fields has to rely on upscaled models taking into account the micro-structure of the vascular system. Consequently, deriving a strong link between micro-vascular structure and mass transfer at mesoscopic scale is a major issue to better understand and exploit the information obtained by these imaging techniques, as discussed in [2].

In this context, tools developed for upscaling mass transfer in heterogeneous porous media, such as the Volume Averaging Technique [1], can be used to derive the effective parameters describing the spatio-temporal evolution of concentration in the brain at mesoscopic scale.

This method requires to solve closure equations on a Representative Element Volume (REV). The REV is a 3D network of vessels with diameters ranging from 1 to 10 µm embedded in tissue, see Fig. 1, Left. The typical volume of a REV is about 150 to $(300\ \mu\mathrm{m})^3$. The goal of this work is to create a framework for computing the solution of these equations by a finite element method with a fictitious domain approach to accurately represent the complex 3D structure of the vessels (as shown in Fig. 1, Middle).

## 2. Upscaling of brain micro-vascular system

### *2.1. The mass transfer model*

The model describing the mass transfers in vessels and tissue is similar to the one used in [2], i.e. an advection-diffusion equation in the vessels and pure diffusion in tissue. The advection in the vessels is driven by blood flow ($\boldsymbol{v}$). The diffusion coefficients in vessels and tissue are different. A well term is added in both domains to account for possible decay of concentration with time (e.g. radioactive decay for radio-labeled water). If we use the subscript $v$ for quantities related to vessels and $t$ the one for the

tissue, and $C, D$ and $k$ respectively the concentration of tracer, diffusion coefficient and rate of decay, the model reads:

$$\partial_t C_v + \boldsymbol{v} \cdot \boldsymbol{\nabla} C_v = \nabla \cdot (D_v \boldsymbol{\nabla} C_v) - k_v C_v \qquad \text{in } \Omega_v \tag{1}$$

$$\partial_t C_t = \nabla \cdot (D_t \boldsymbol{\nabla} C_t) - k_t C_t \qquad \text{in } \Omega_t \tag{2}$$

$$C_v = C_t \qquad \text{on } \partial\Omega_{vt} \tag{3}$$

$$\boldsymbol{n}_{vt} \cdot D_v \boldsymbol{\nabla} C_v = \boldsymbol{n}_{vt} \cdot D_t \boldsymbol{\nabla} C_t \qquad \text{on } \partial\Omega_{vt} \tag{4}$$

We assume continuity of concentration between vessels and tissue for simplicity, this hypothesis will be discussed.

*2.2. Upscaling mass transfer in anatomically accurate capillary structures*

It has been shown in [3] that below a certain threshold diameter of about 10 µm, the vessels exhibit a mesh-like structure, space filling, for which a REV can be extracted. An example of such a structure is given in Fig. 1, Left, for a volume of about $(300\ \mu\text{m})^3$. The Volume Averaging Technique of the advection diffusion equations is thus applied at the capillary scale.

It has been written theoretically in [4] and the closure equations to obtain the effective coefficients have been derived. In the same work, the numerical solution of the closure problems has been obtained in 2D on simple artificially generated networks sufficiently small to be solved by the commercial software Comsol.

Here, we present a new framework developed for the solution of the closure equations obtaining the effective coefficients on a 3D anatomically accurate REV. This framework is developed in the C++/parallel finite element library Feel++[5]. The method to generate the complex 3D geometry uses a fictitious domain approach where the two domains are defined through the use of a distance function constructed from a segmented network obtained e.g. from experimental data imaging. We will show how to address the different problems arising from such a complex geometry, as the periodicity required by the closure problems in volume averaging, the boundary conditions at the (fictitious) interface between vessel and tissue.

Finally, we will compare results obtained by the upscaling approach with direct simulations of the advection-diffusion problem (eqs (1) to (4)) on domains with volumes ranging from 100 to $(500\ \mu\text{m})^3$. An example of such results is displayed on Fig. 1, Right representing the concentration field computed by a direct simulation in a 50 vessel network in a domain of volume $(140\ \mu\text{m})^3$.

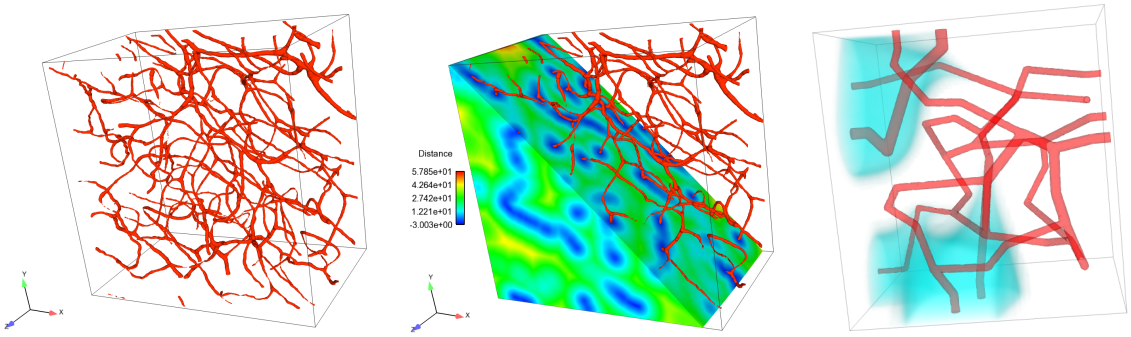


Figure 1: Left and Middle: Space filling capillary structure of $(300\ \mu\text{m})^3$ with vessels of diameters $< 10$ µm. The geometry of the vessels is obtain by computing the distance function to the vessels boundaries. The distance function field is shown in the half-domain of the middle figure. Right: Concentration of tracer (in blue) in a smaller network (in red) of volume $(140\ \mu\text{m})^3$ just after its injection in the vessels located in the bottom and left part of the domain.

## References


[1] Quintard et al, *International Journal of Heat and Mass Transfer*, 38:2779-2796, 1995.
[2] Lorthois et al, *Journal of Theoretical Biology*, 353:157-169, 2014.
[3] Lorthois et al, *Journal of Theoretical Biology*, 262:614-633, 2010.
[4] Billanou, *PhD Thesis*, 2010
[5] Prud'homme et al, *ESAIM: Proc.* 38:429-455, 2012.