Hemodynamics modeling and advection-reaction simulation in a capillary network. Focus on liver micro architecture

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Mots-clés : microcirculation, capillary network, hemodynamics modeling, advection-reaction equation simulation

Establishing mathematical models of tissue function in relation with medical applications is a subject of growing interest. Models of the whole body metabolism, assuming organs are well mixed compartments, have been thoroughly studied and are widely used in drug development. Yet, for blood detoxifying organs, such as the liver, the micro architecture, spatial model has a strong impact on the simulated tissue function. This impact is strongly linked to the flow distribution patterns at the micro-scale. Several imaging techniques precisely analyzing a tissue micro architecture permit to extract geometrical feature values such as lengths or radii. In this study, we propose to focus on hemodynamics and compound advection-reaction modeling in capillary networks, restricting our study of the architecture of a liver functional unit, called a liver lobule.

Blood vessel hemodynamics are modeled as a resistive network at steady state, with boundary conditions set within physiological ranges and, when possible, such that the average blood flow speed is within measurement ranges. This results in an algebraic system of equations solved by an iterative linear solver. First, the effect of red blood cells on blood effective viscosity is investigated, applying Pries law [1]. We show that, when neglecting the effect of red blood cells on viscosity, it is only possible to reproduce the highest speed measurements under physiological pressure boundary conditions. To reproduce the average speed measurements, Pries law has to be included in the model.

To further improve this model, the effect of plasma skimming, [2] an observed phenomenon that corresponds to uneven distribution of red blood cells at bifurcations, is investigated. Two different plasma-skimming models are compared. This results in a system of non-linear equations solved by a fixed-point algorithm with a stopping criterion set on flow speeds. This system has several solutions that have been observed [3] and that can be reproduced with only one of the two studied plasma skimming models.

The simulated flow speeds finally feed a model of transport and metabolism written as a 1D advection-reaction equation in each vessel, coupled at multi-furcations to ensure mass conservation. To extend the simulation of tissue function, this system can be coupled with a system of ODEs accounting for the metabolism inside each cell. We propose an extension of a finite volume explicit numerical scheme including flux limiters to reduce numerical diffusion and handle multi-furcations, and therefore a network. We introduce fluxes at the inlet and outlet of a numerical cell dealing with several neighboring numerical cells and successive multi-furcations. First, this scheme is studied on simple bifurcations before considering the case of a network. The considered reaction term corresponds to the uptake of a substance from blood by a cell. Several regimes of advection-reaction are considered showing different behaviors depending on the blood flow speed vs. reaction parameters.

Références

[1] Pries, AR and Secomb, TW and Gaehtgens, P, *Biophysical aspects of blood flow in the microvasculature*, Cardiovascular research, 32(4) 654-667,1996.

[2] Krogh, A, *Studies on the physiology of capillaries: II. The reactions to local stimuli of the blood-vessels in the skin and web of the frog*, The Journal of physiology, 55, 1921.

[3] Kiani, MF and Pries, AR and Hsu, LL and Sarelius, IH and Cokelet, GR, *Fluctuations in microvascular blood flow parameters caused by hemodynamic mechanisms*, American Journal of Physiology-Heart and Circulatory Physiology, 266(5), H1822-H1828, 1994.

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