PhD position at the Centre National de la Recherche Scientifique,
Institut de Mécanique des Fluides de Toulouse (UMR CNRS-INPT-UPS 5502)

How do targeted vessel occlusions impair brain microcirculation? Numerical modeling and experimental validation

Keywords: Biofluid Mechanics, Porous Media, Blood microcirculation, Microvascular Networks, Transport, Transfers.

Academic context: This PhD position is part of the interdisciplinary Brain Micro Flow project (2014-2019) awarded to Sylvie Lorthois (www.imft.fr/LORTHOIS-Sylvie,126) under the European Research Council *Consolidator* grant scheme (http://erc.europa.eu/consolidator-grants). Her group at the Institut de Mécanique des Fluides de Toulouse focuses on modelling the structure and function of brain microcirculation at various scales. The Brain Micro Flow project also involves the Department of Biomedical Engineering of Cornell University (USA) for advanced *in vivo* optical imaging and manipulation of cerebral blood flow and the INSERM "Cerebral Imaging and Neurological Handicaps Laboratory", Toulouse, for its unique expertise in human intra-cortical micro-anatomy.

Scientific context: The cerebral microvascular system is essential to a large variety of physiological processes in the brain, including blood delivery and blood flow regulation as a function of neuronal activity (neuro-vascular coupling). It plays a major role in the associated processes leading to disease (stroke, neurodegenerative diseases) but the comprehension of the basic mechanisms involved is still largely incomplete. In the last decade, cutting edge experimental technologies, including two-photon scanning laser microscopy (TPSLM) and optically-induced single-vessel occlusions, have produced huge amounts of anatomic and functional experimental data in normal and Alzheimer Disease (AD) mice. These require accurate, highly quantitative, physiologically informed modeling and analysis for any coherent understanding and for translating results between species.

Project summary: Our first goal is to extend the non-linear network model previously developed for blood flow simulation at IMFT by coupling a boundary integral method for computing molecule transport and transfers. Here, the coefficient describing the physics at the scale of capillary vessels (blood rheology, diffusion of relevant molecules) will be obtained by global optimization of the numerical results, based on experimental anatomical data, with the associated *in vivo* functional TPSLM measurements (red blood cell velocities, non-metabolizable fluorescent tracer distributions). Our second goal is to validate this approach by direct comparison of the functional consequences of single-vessel occlusions in normal mice with the simulation results based on the same anatomical data. These new methods, validated with an unprecedented level of accuracy, will be used to model how the vascular alterations observed in AD affect the microvascular functions. In particular, we will study how much these alterations impact the mean cerebral blood flow and its heterogeneity, the appearance of hypoxic regions and the clearance of metabolic waste.

Student profile: Strong background in numerical methods for fluid mechanics. Demonstrated motivation for work at the interface between disciplines, in close collaboration with researchers performing advanced *in vivo* experiments in live anesthetized mice. Experience in C++ and high performance computing is welcomed. A university Master Degree or equivalent in Fluid Mechanics, Applied Mathematics or related disciplines is required, as well as fluency in English and in French (or willingness to learn French).

Academic supervisors: Sylvie Lorthois, Chargée de Recherches CNRS (IMFT), in collaboration with Yohan Davit, Chargé de Recherches CNRS (IMFT) and Nozomi Nishimura (Assistant Professor, Cornell University, http://nishimura.research.engineering.cornell.edu).

Administrative aspects: The PhD will be awarded by *Université de Toulouse*, Doctoral School "Mechanics, Energetics, Civil and Process Engineering" (www.ed-megep.fr). The employer is the *Centre National de la Recherche Scientifique* (National Center for Scientific Research, www.cnrs.fr), the largest fundamental research organization in Europe. This PhD project is funded for 3 years, starting on October 1st 2014 (Gross salary: ~ 21 000 €/year; Net salary, including social security: ~ 17 000 €/year).

For more information or to apply, please submit via email your curriculum vitae, copies of recent transcripts, a statement of your future career goals, and the names and email addresses of two references, with "ERC BrainMicroFlow PhD1" in the subject line, to: Sylvie Lorthois, PhD, HDR (lorthois@imft.fr).