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

Quantification and analysis of three-dimensional brain microvascular architecture in human health and disease

Keywords: Blood microcirculation, Microvascular networks, 3D Image Processing, Anatomical variability, Inter-species comparison.

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. For example, while the vascular component of Alzheimer's disease (AD) is now clearly established, with microvascular lesions, abnormal vascular topology, reduced total microvascular density and reduction in blood flow, the question whether these vascular abnormalities participate in the onset or progression of the disease is still totally open. To answer this question, quantitative knowledge of the three-dimensional brain microvascular network anatomy and large-scale structuration in healthy and diseased humans is needed.

Project summary: Our group has previously developed new methodologies for reconstruction and quantitative analysis of microvascular networks from 3D anatomical data spanning large fields of view (~ mm^3 to 10 mm^3) of the human cortex imaged *post-mortem* at unprecedented spatial resolution (~ 1 to 3 µm). However, the large quantitative data library on human brain microcirculation analyzed so far only concerns a few number of cortical areas and individuals. No equivalent library has been obtained in pathological conditions, including AD. Thus, in close collaboration with the researchers preparing the anatomical material, the successful applicant will participate to the acquisition of new microscopic data representative of several brain areas and several conditions, including AD. Alongside the optimization of tools used for image registration, thresholding and vessel skeletonization, he/she will perform a statistical analysis of morphometric, topologic and multi-scale parameter variations between brain areas and conditions. Comparison with data from corresponding rodent models acquired at Cornell University will be performed. This will allow a longitudinal study of the brain vascular network in the same animal over several months and of the corresponding functional changes (blood flow, transfers).

Student profile: Strong background in C++, numerical algorithms in 3D image processing, demonstrated motivation for work at the interface between disciplines. Knowledge in graph theory is welcomed. A university Master Degree or equivalent in Computer Science, 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 Frédéric Lauwers, Professor (INSERM "Cerebral Imaging and Neurological Handicaps Laboratory").

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 PhD4" in the subject line, to: Sylvie Lorthois, PhD, HDR (lorthois@imft.fr).