Université de Rennes

IMFT INSTITUT DE MECANIQUE DES FLUIDES DE TOULOUSE

PhD position at the Centre National de la Recherche Scientifique on **the physics of solute transport in brain micro-vascular networks**

Subject description : Blood microcirculation supplies neurons with oxygen and clears their neurotoxic waste through a dense capillary network connected to a tree-like network of arterioles and venules (Fig. 1). This microvascular architecture results in highly heterogeneous blood flow and travel time distributions [Jes12,Sak14], whose consequences on brain pathophysiology begin to be uncovered. To explore this question, the University of Rennes and the Toulouse Institute for Fluid Mechanics have bridged together their expertise on the physics of transport in disordered media, e.g. [LeB08], and on cerebrovascular structure/function relationships, e.g. [Lor11]. This has lead to the first physics-based upscaling framework describing the dynamics of solute transport in brain microvascular networks [Goi21]. This new representation uses random network and dipole flow theories to derive a stochastic model for solute transport in microvascular networks (Fig. 2). It predicts the appearance of critical regions under reduced perfusion, i.e. with insufficient oxygen or excessive waste, which may play a key role in the onset of Alzheimer' disease. This advance opens new opportunities for understanding the physics of solute transport in the brain and its impact on neurovascular diseases.

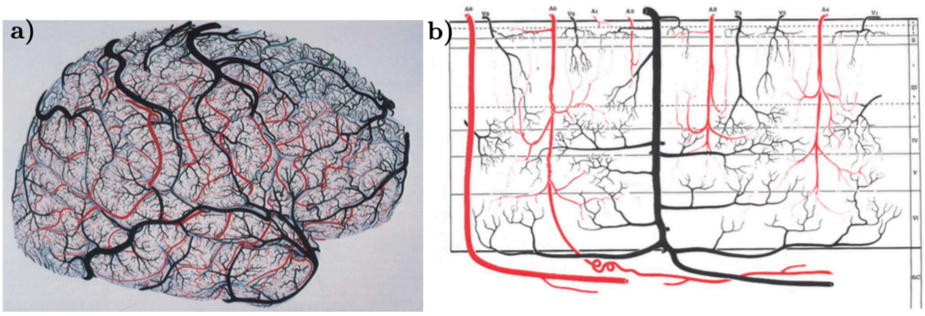

Figure 1: spatial organization of the arterial and venous systems in the cortical layer of the human brain [Duv81]: a. lateral view of the arterial and venous systems running over the cortical surface **b.** arteriolar and venular sub-branches in depth of the cortical layer. Arterioles are shown in red, venules in black. The deepest region correponds to sub-cortical white matter.

Based on this new modeling framework, the objective of this PhD project is to investigate how the spatial organization of arterioles/venules controls the appearance and growth of critical regions of reduced oxygenation and waste clearance. The project will include three goals:

1. We will first simulate blood flow and solute transport in different brain microvascular architectures (density, evolution of diameter with depth, proportion of arterioles versus venules, Fig. 2) across various brain areas and mammal species. We will thus analyze the localization and density of critical regimes in these different structures to establish the structural controls on the resilience of brain microvascular networks to reduced perfusion.
2. We will then develop synthetic biomimetic networks whose structure can be modified [Lin19], to reproduce and generalize the link between network structure and transport properties.
3. Finally, we will use random walk theories [Goi21] to quantify the impact of network structure on upscaled transport laws driving oxygen perfusion and metabolic waste clearance

Depending on the candidate profile, she/he may also participate to on-going experiments using 3D printing to investigate flow and transport in brain microvascular networks.

Academic context : This PhD project is part of a collaboration between two teams developing complementary approaches. The Geosciences Rennes laboratory develops stochastic models for transport and reaction in porous media [LeB08,LeB13,Aqu21]. The Porous and Biological Media group of IMFT is a pioneer in the multiscale modeling of brain microvascular networks, based on mixed-dimensional Eulerian descriptions [Ber20,Pey18]. The successful candidate is expected to spend a significant amount of time in both groups. International collaborations will be developed with CSIC Barcelona and the University of Munich.

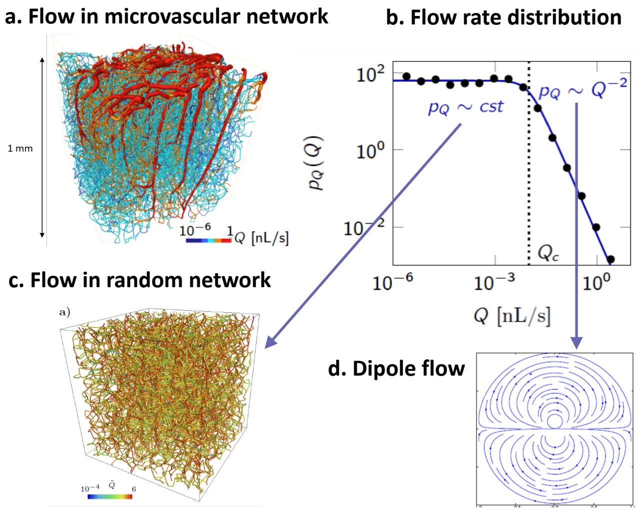

Figure 2: dipole on networks framework for transport in microvascular networks [Goi21]: a. simulation of flow in a microvascular network from mouse cortex, where arterioles and venules drive flow in a dipolar fashion; **b.** statistics of flow rates showing broad distributions, explained by **c.** flow in random networks in the low flow range and **d.** dipole flow in the high flow range.

Profile: Strong background in physics or fluid mechanics. Demonstrated motivation for work at the interface between disciplines, in a collaborative environment. Experience in stochastic modeling of transport phenomena in porous media of porous models welcomed. A Master Degree in Physics, Fluid Mechanics or related disciplines is required, as well as fluency in English.

Academic supervisors: Tanguy Le Borgne, Professor (Observatoire des Sciences de l'Univers de Rennes), Sylvie Lorthois, Directrice de Recherche CNRS (IMFT).

Administrative aspects: 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 September/October 2023.

References:

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For more information, 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, to: tanguy.le-borgne@univ-rennes.fr and sylvie.lorthois@imft.fr.