Project summary

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 mechanisms leading to disease (stroke, neurodegenerative diseases, ...).

In the last decade, cutting edge technologies, including two-photon scanning laser microscopy (TPSLM) and optical manipulation of blood flow, 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.

In this context, our first aim is to develop a general methodological framework for physiologically informed microvascular fluid dynamics modeling, understood in a broad meaning, i.e. blood flow, molecule transport and resulting functional imaging signals or signal surrogates.Our second aim is to validate this methodological framework by direct comparison of in vivo anatomical and functional TPSLM measurements with the simulation results based on the same anatomical data.

The third objective is to exploit these methodologies in order to identify the logic of the structure/function relationships of brain microcirculation and neurovascular coupling, in human health and disease, with a focus on the role of vascular factors in AD. Specific hypotheses on how vascular changes in AD affect both vascular function and neurovascular coupling can be experimentally tested in animal models of AD.

Crucially, similar anatomical (but not functional) data can be acquired in healthy and AD humans. This will enable us to model how AD-induced vascular alterations could affect human patients. Ultimately, it provides us with new avenues for design and/or evaluation of improved diagnosis/preventive/treatment strategies.