Quantitative analysis and simulation of fluid flows powered by cilia in vivo

Host teams
Laurent Kodjabachian / IBDM / laurent.kodjabachian@univ-amu.fr
Annie Viallat / CINAM / viallat@cinam.univ-mrs.fr
Julien Favier / M2P2 / julien.favier@univ-amu.fr

Scientific background
Ciliated epithelia are present throughout evolution and serve functions ranging from locomotion of marine larvae to mucociliary clearance of pathogens from human airways. These functions are supported by the coordinated beating of myriads of motile cilia at the surface of multiciliated cells (MCCs), which generates robust and regular waves of fluid. The production of such waves depends on multiple parameters integrated across micrometric to millimetric scales, such as MCC density and cilia orientation. These parameters can be adequately studied in the larval mucociliary skin of the amphibian Xenopus, which is organized like the human airway epithelium, but is much easier to manipulate and film. This project will bridge the gap between biology, physics and numerical simulation to bring a new perspective to the understanding of respiratory diseases characterized by altered cilia-driven mucociliary transport, such as COPD or cystic fibrosis.

PhD Objectives
The aim of this PhD project is to link quantitative experimental analysis to numerical simulation to build a global model of ciliated epithelium organization and activity. The ambition is to generate a multi-parametric model able to explain the emergence of cilia-driven fluid flows at the level of an entire organ. To this aim quantitative live imaging of cilia will be implemented on the 3D Xenopus embryo, which has never been done before. Numerical models will be challenged in silico and through experiments to test their predictive capacity.

Proposed approach
Live imaging (teams 1 and 2): The PhD student will adapt light-sheet microscopy to film fluorescent beating cilia in all MCCs of the Xenopus embryo at various developmental stages.
Image processing (teams 1 and 2): Methods developed in team 2 will be applied to extract quantitative information regarding cilia beating frequency and orientation, so as to build a global map of the embryo.
Numerical simulation (team 3): The quantitative experimental parameters thus acquired will be used to feed Lattice Boltzmann-based simulations, with the aim of generating numerical paradigms to explain the emergence of metachronal ciliary beat waves and spatial flow patterns.
Validation (teams 1, 2 and 3): In silico challenges (changes in ciliated cell density or orientation) will be introduced to predict outcomes on flow patterns, which will be verified through our experimental pipeline.

PhD student’s expected profile
The selected PhD student must have a keen interest in interdisciplinary and quantitative approaches to study biological problems. The ideal candidate will have a solid theoretical background in biological physics. Experience in microscopy techniques and image processing and a strong interest in modeling will be favorably considered.