2 years postdoc

Epithelial mat of active cilia: collective dynamics and complex fluid transport. Application to mucociliary clearance in respiratory diseases

Keywords: physics of living systems, active matter, self-organization, ciliated epithelium, rheology, hydrodynamics, COPD

Context & aim of the project:

The airways are protected by mucus, a complex fluid carried along the epithelial surface, from the lung to the throat, by the coordinated beating of millions of microscopic cilia, hence the name mucociliary clearance. Dysfunction of this essential function is associated with all chronic respiratory diseases such as cystic fibrosis, chronic obstructive pulmonary disease (COPD) and severe asthma. These diseases affect hundreds of millions of people worldwide and are in constant evolution due to many environmental factors and pollution.

Mucus transport depends on its rheology and the propulsive force exerted by the cilia mat. We have recently shown that this force in turn depends on the rheology of the mucus, as the necessary long-range coordination of ciliary beats emerges through the active response of individual cilia (notably the orientation of beats) to the hydrodynamic interactions they exert on each other via the mucus. The aim of this project is to establish the quantitative relationship between mucus rheology, self-organization and dynamics of beating cilia and mucus transport. We want to identify the critical mechanical conditions that lead to the arrest of mucus.

This project is part of a consortium that involves 3 research labs, one hospital and two start-ups which develop instruments for the diagnosis and monitoring of pulmonary diseases and develop a new CE Medical device for airway clearance therapy.

Experimental approach:

The experimental approach relies on various techniques of optical microscopy performed on in-vitro reconstituted bronchial epithelia. We will use native and synthetic mucus with controlled rheology to 1) quantify the hydrodynamic coupling between mucus and cilia, responsible for long range transport and 2) Establish the relation between mucus transport velocity and mucus rheology, to determine the critical rheology that leads to an arrest of mucus transport. Experimental data will be used to calibrate a numerical model developed by our collaborators to simulate complex configuration (bronchi geometry...)

Expected profile of the candidate: a PhD in physics (soft matter, biological physics...)

Contacts & how to apply

Send a detailed cv and a cover letter to: Etiene Loiseau - <u>etienne.loiseau@univ-amu.fr</u> Annie Viallat - <u>annie.viallat@univ-amu.fr</u>

References:

O Mesdjian et al., Longitudinal to transverse metachronal wave transitions in an In Vitro model of ciliated bronchial epithelium, *Physical Review Letters*, 2022

E. Loiseau, et al, Active mucus-cilia hydrodynamic coupling drives the self-organisation of human bronchial epithelium. *Nature Physics*, 2020.

S. Gsell et al., Hydrodynamic model of directional ciliary-beat organization in human airways, *Scientific reports*, 2020

MK. Khelloufi et al., Spatiotemporal organization of cilia drives multiscale mucus swirls in model human bronchial epithelium, *Scientific Reports*, 2018.