Project Details	
Project Code	MRC23IIAREx Wan
Title	Mapping pathogen transport and retention near ciliated surfaces
Research Theme	Infection, Immunity, Antimicrobial Resistance and Repair
Summary	Cilia fulfil numerous physiological functions. From protists to mammals, cilia have highly conserved structure and function. In humans, motile cilia beating in our airways are a critical first line of defence against bacterial, fungal and viral infections. This interdisciplinary PhD will provide the first comprehensive biophysical study of how the rich dynamics and topology of different ciliated surfaces conspire to control the fate of foreign particles/pathogens.
Description	BACKGROUND – The current global pandemic highlights the enormous threat posed by respiratory infections. The orderly beating of motile cilia in the upper respiratory tract is essential to prevent severe disease –by filtering and stopping pathogens from gaining entry into host epithelia. Impaired ciliary function greatly increases our susceptibility to these infections. Exactly how inhaled particles first make contact and then interact with ciliated surfaces is unclear and deserves in-depth and systematic study. Recently, non-human models have proven indispensable for studying ciliary structure and dynamics, due to the highly conserved nature of these organelles as well as shared physics (Wan & Jekely, On the Unity & Diversity of Cilia, Phil Trans Roy Soc B, 2020). AIMS – This truly interdisciplinary project will elucidate the basic fluid physical processes that underlie particle deposition and penetration into a ciliated epithelium. We will use a set of single-celled eukaryotes and ciliated marine invertebrate larvae as novel experimental models for natural ciliated surfaces. These small, non-mammalian systems are much easier to handle, culture, and are more amenable to targeted experimentation and manipulation. PLAN – The student will: 1) Establish a live-cell, high-speed imaging pipeline for visualizing and recording the dynamics of ciliary arrays in protists (ciliates and flagellates), concurrently with deposited tracer particles of different aspect ratios and sizes; 2) From these large datasets, analyse and mine single-particle trajectories and timeseries to estimate retention probabilities and decouple effects of ciliary activity, frequency, coordination, and interciliary spacing. These particle-flow interaction assays will be repeated for both passive and active particles (to mimic situations where both host and pathogen are motile); 3) Develop data-driven mathematical models of ciliary arrays to understand and predict the effect of different cilia coordination patterns and stress profiles on the trajectories of nearby particles, using novel boundary element methods for simulation with physical ingredients such as elasticity (with supervisor Bennett); 4) Extending these wet- and dry-lab approaches to invertebrate animal larvae exhibiting more complex arrangements and topologies of cilia (e.g. bands, rings, spirals) (with supervisor Williams). This is a highly feasible project with many innovative elements. All of the key approaches required for the successful realisation of the project including lab techniques, flow measurement approaches, mathematical/computational models, and detailed biological knowledge of the study organisms, are already well-established in the host lab and collectively in those of the supervisory team. TRAINING: The student

	will be based at the University of Exeter's world-leading Living Systems Institute where they will join a rapidly growing and vibrant student community, and have access to state-of-the-art resources, equipment (brightfield, confocal, superresolution microscopes), and excellent training facilities. They will spend time at another top GW4 institution through routine meetings and learn key modelling skills through interactions with Dr Bennett (Bristol). Meanwhile Dr Williams (Exeter Biosciences) will provide key, complementary expertise through a more biologically oriented perspective. The student will also engage with cross-disciplinary training and public outreach activities throughout their PhD. This unique and ambitious project will transform our understanding of how the dynamic fluid physical landscape around ciliated surfaces impact their ability to retain or reject foreign pathogens, with many potential downstream consequences for further exploration in clinical settings. Achieving a thorough understanding of these interactions will also inform the design of next-generation antimicrobial surface treatments using artificial cilia.
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