Biophysics of Epithelial Barrier function

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Research areas: Biophysics, cell biology, tissue biology, tissue engineering

The Charras lab focuses on understanding the interplay between cytoskeletal organization, intercellular adhesion and the mechanics of cells and tissues. In our research, we combine techniques from physics and engineering with molecular cell biology, microscopy, optogenetics, and image analysis to study questions relevant to cell and developmental biology. More information about the laboratory can be found here: https://charraslab.com/.

We propose to investigate the interplay between mechanical stresses and epithelial barrier function. Epithelial monolayers are amongst the simplest tissues in the body, yet they act as essential barriers between the internal and external environment. One challenge to this barrier function is the mechanical stress that monolayers experience as part of their physiological function. For example, the lung epithelium stretches as we breathe and the intestinal epithelia deform during bowel movements. Therefore, to resist rupture and preserve barrier integrity, epithelia must adapt to their environment by finely adjusting their mechanical properties. At the molecular level, the mechanics of epithelia are governed by the cytoskeleton and the adhesive proteins that link cells to integrate them into a tissue-scale mechanical syncytium. This organisation leads to complex emergent rheological behaviours.

Disease and mutations can prevent establishment of appropriate tissue mechanical properties, leading to septicaemia and haemorrhage in adult tissues. For example, mutations in cytoskeletal and adhesive proteins lead to diseases presenting frequent fractures in the tissue, suggesting the epithelia have become fragilised. Other diseases (such as cancer and inflammatory bowel disease) lead to profound changes in gene transcription that affect cytoskeletal and adhesive proteins, likely impacting tissue mechanics. While it is recognized that pathologies affect epithelial mechanics, a lack of understanding of the exact nature of the mechanical changes induced and how these contribute to disease aetiology prevents the development of appropriate treatment strategies.

This project will investigate the link between epithelial mechanics and barrier integrity in health and disease. For this, we will develop methods to characterise tissue mechanics and barrier integrity across all relevant time- and length-scales based on those previously published by the lab (Duque J et al, Nature Materials, 23:1563-1574, 2024). Using computational simulations, we will determine how the properties and organisation of the cytoskeleton and adhesions combine across scales to control tissue rheology, rupture properties, and barrier integrity in epithelia.

The successful candidate will be a highly-motivated scientist with an MSc in Physics, Life Sciences or other relevant degree. Experience in working in interdisciplinary teams, biophysics, and programming is desired. Additional experience in microscopy, and biology will be an advantage.

Interested applicants can get in touch with Prof Guillaume Charras, who will be supervising the research.