A new method to measure local stiffness in epithelial cells

Introduction

For living organisms, it is crucial to have a clear border between “inside" and “outside". This border is formed by so-called ‘epithelial cells’, which cover the outer surfaces of our organs, form a layer around our body (which we usually call our skin), and line our blood vessels, lungs and intestines. Because of their function, these epithelial cells have a well-defined structure, with a basal side that is oriented inwards, and an apical side that is oriented outwards. Accordingly, the organelles within the cells are also organized, where for example the (relatively large) cell nucleus is always found at the basal side of the cell, while the smaller organelles are found closer to the apical side. In earlier studies, it has been shown that protein signalling lies at the root of this polarity.

The hypothesis in this project is that there is, in addition to protein signalling, also a *physical* origin for the polar organization of the organelles. For example, if the cytoskeleton of the cell is stiffer at the apical side of the cell, this could drive the nucleus towards the basal side. A difference in motor activity could also have a similar effect.

Project approach

To study mechanical properties within a cell, we use active and passive microrheology in our lab. The principle is that a small (micrometer-sized) bead is taken up by the cell. We trap these bead in the focus of a laser, and apply a force to the bead by moving the laser (optical tweezers). By detecting the movement of the bead in response to this force, we then learn whether the bead sits in a soft (it will easily follow the laser) or a stiff environment (Figure 1a). For this measurement, it is important that the apical-basal axis is oriented left-right, while in normal growth conditions the cells would form a layer with the apical-basal axis vertical.

In this project, you will start by making a micro-patterned structure [1] on which epithelial cells can grow vertically (Figure 1b). Once this is established, you will perform the optical tweezers measurements to probe the mechanical properties in the epithelial cell. If it can be established that there is a mechanical difference between the apical and basal side, you can manipulate the cytoskeleton of the cell, to establish what component(s) of the cytoskeleton lie at the origin of the cell polarity.

Qualifications

The project is open to a highly motivated student with a background in physics, chemistry, biology, or a related field, who is interested in participating in an interdisciplinary project. Experience with cell culture, microscopy and/or micropatterning is preferred. You are available for at least 3 months, although longer is preferable.

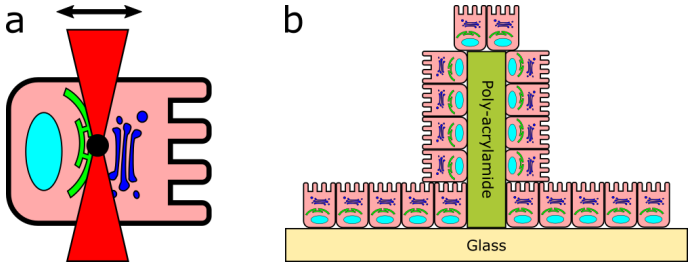

Figure 1: **(a)** A sketch of an optical tweezers measurement in a cell. **(b)** A sketch of epithelial cells growing vertically on the micro-patterned surface.

References

[1] Philippe Nghe, Sarah Boulineau, Sebastian Gude, Pierre Recouvreux, Jeroen S. van Zon, and Sander J. Tans. Microfabricated Polyacrylamide Devices for the Controlled Culture of Growing Cells and Developing Organisms. *PLoS ONE*, 8(9):e75537, sep 2013.