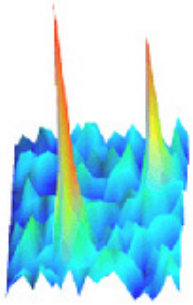
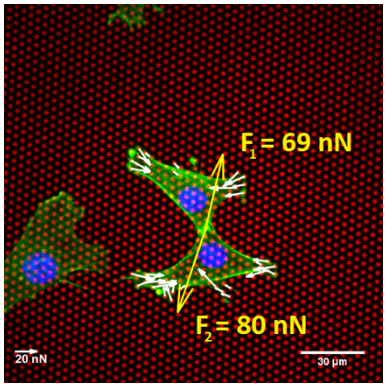
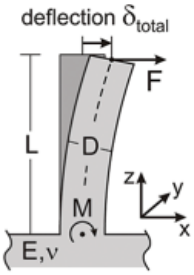
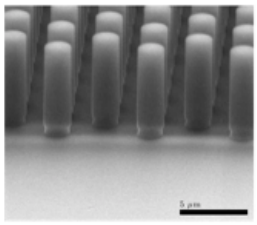


Euler-beams at the Micron-scale

We use micron-sized elastic beams to measure the forces that cells exert on their substrates. Lately, the concept that mechanical cues are a leading signals in processes like embryogenesis, immunology and cancer has been largely adapted, and lead to a paradigm-shift in biology. Yet, currently it is unclear how large those forces exactly are, and measurements of different groups – all using slightly different techniques – come to controversial results. One of the reason might be that calibration of mechanical response at the (sub-)micron scale is difficult to calibrate. In our experimental approach we use microfabricated pillar arrays from a biocompatible polymer to assess cellular force response. The elastic response of our force sensors (2 μm diameter, 4-10 μm height) we extrapolated from bulk-modulus measurements, and Euler's beam theory. We intend to set up experiments using the atomic-force microscope (AFM) for calibration of our microfabricated pillar arrays *in situ*. Those experiments should further answer the question of whether the force-response of such small structures is still linear.

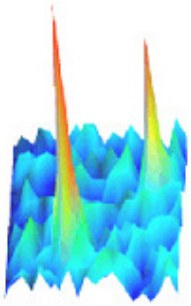






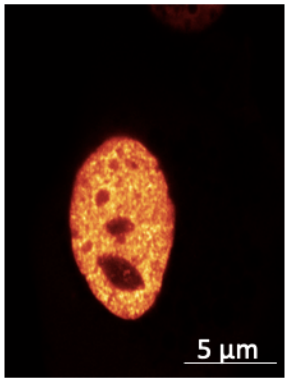
You will have to develop experimental skills to use AFMs in the Institute's AFM-facility to quantitatively perform (shear-)force measurements including their analysis on micropillar arrays you will produce in our lab.

Contact: Julia Eckert, eckert@physics.leidenuniv.nl
Prof Thomas Schmidt

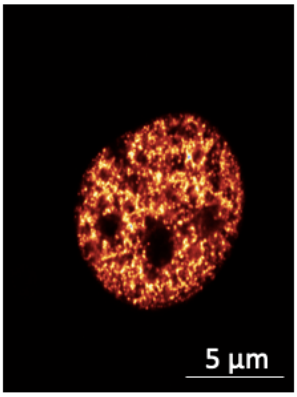


Are ‘Speckles’ Nuclear Hormone-Receptor Factories?

The project is about how transcription factors (proteins that bind to specific sites in the DNA to switch on the RNA synthesis) distribute inside the nucleus of a cell. It appears that some transcription factors distribute randomly, whereas others preferably localize in specific focal domains, also called 'speckles'. To study this, we use a specific class of transcription factors, which are steroid receptors (receptors for hormones like testosterone, estradiol and cortisol). We labeled these receptors with a fluorescent protein (GFP), and imaged their distribution inside the nuclei of cultured cells. We found that the Estrogen Receptor (ER, the receptor for estradiol) speckles quite heavily, whereas the Glucocorticoid Receptor (GR, the receptor for cortisol) only shows a few speckles and is more randomly distributed over the nucleus. We would like to perform a quantitative analysis of these different distributions, and we are particularly interested in these 'speckles'.



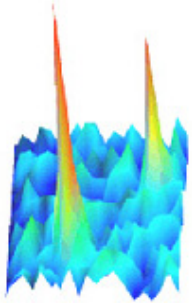
glucocorticoid receptor (GR)



estrogen receptor (ER)

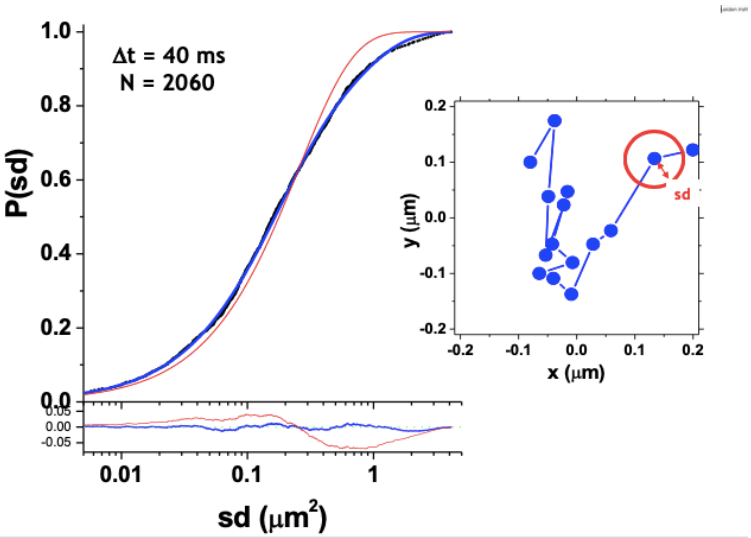
This project is a collaboration with Marcel Schaaf’s group from Cell Biology. Your task will be to develop robust methods for quantitative data analysis in Matlab or Python. Further, you will be acquiring high-resolution images to complete available data sets.

Contact: Prof Thomas Schmidt, schmidt@physics.leidenuniv.nl



Machine-learning Approaches for the Analysis of Diffusional Mobility.

We have shown in the past that relevant biological information may be obtained by a detailed analysis of trajectories from individual molecules. Yet in high-density situations or due to intermittent observation during imaging, the analysis of such data is a major undertaking. So-far we applied models based on statistical underpinning to analyze mobility data of membrane receptors and nuclear hormone receptors. Such analysis subsequently allowed us to conclude on changes and modes of protein mobility in cells. In this project we want to analyze whether machine-learning approaches could be utilized as a potential robust method for the analysis of tracking data.



You will develop machine-learning approaches to automatically analyze mobility data, and compare it's performance with respect to classical approaches available in the lab. The implementation will be done in Python or Matlab.

Contact: Prof Thomas Schmidt