Subject: Quantitative imaging of cytoskeletal crosstalk at the nanoscale

Project type: MEP/Intern (4+ month)

Supervision: Kristin Grussmayer, k.s.grussmayer@tudelft.nl, Bionanoscience/AS and Gijsje Koenderink, G.H.Koenderink@tudelft.nl, Bionanoscience/AS

Contact: James Conboy, J.P.Conboy@tudelft.nl and Moritz Engelhardt, M.L.K.Engelhardt@tudelft.nl

Start date: available immediately

Project background

A cell's ability to both actively deform and withstand mechanical stress is a result of the scaffolding that maintains a cell's structure, known as the cytoskeleton. This actively driven polymer network is exciting to investigate because of these seemingly paradoxical properties. The cytoskeleton consists of three distinct protein filaments: actin, intermediate filaments and microtubules. The actin cytoskeleton is the engine behind cell migration because it generates the forces necessary to drive the cell forward. Microtubules play a steering role by establishing front-rear cell polarity necessary for directional migration. Intermediate filaments (IFs) were traditionally considered merely a reinforcing network, but recent evidence indicates that they contribute to cell migration by regulating the architecture of the actin and microtubule cytoskeletons through physical and signaling interactions. However, the high density and nanoscale dimensions of these cytoskeletal networks in cells hinder quantitative analysis of structural details and prevent direct observation of network interactions or co-assembly using conventional confocal microscopy.

This is a joint Kavli Institute for Nanotechnology Delft funded project between the Koenderink Lab and the Grussmayer Lab @Bionanoscience/Applied Science.

Project goals and activities

We want to establish new multicolor super-resolution imaging to unveil the nanoscopic cytoskeletal structures (actin, microtubules and intermediate filaments) of cells as well as their interaction (crosstalk) and relate it to their active mechanical behaviour. You will focus on quantitative network analysis of multicolor super-resolved networks at the nanoscale and investigate how different adhesive micropatterns of varying size and geometry influence cytoskeletal crosstalk. Alternatively, you can focus on extending imaging from 2D to 3D, depending on your own preference.

For you?

You will learn mammalian cell culture and fluorescent labeling, state-of-the-art super-resolution microscopy methods and advanced image analysis as well as visualization and presentation of experimental data. You will work with cellular model systems from the Koenderink Lab and image them using multicolor single-molecule localization microscopy (SMLM) on a home-built microscope in the Grussmayer Lab. You will either focus on image analysis or on modifying the detection optics to implement PSF engineering for 3D SMLM. Depending on your background, the project may include micropatterning of surfaces for controlled cell adhesion. We are looking for students with a background in nanobiology, (bio-) physics/engineering/chemistry or related that are interested to work on a collaborative project between two Bionanoscience labs. If you are an TU Nanobiology or Applied Physics master student, this could be a great fit for you!

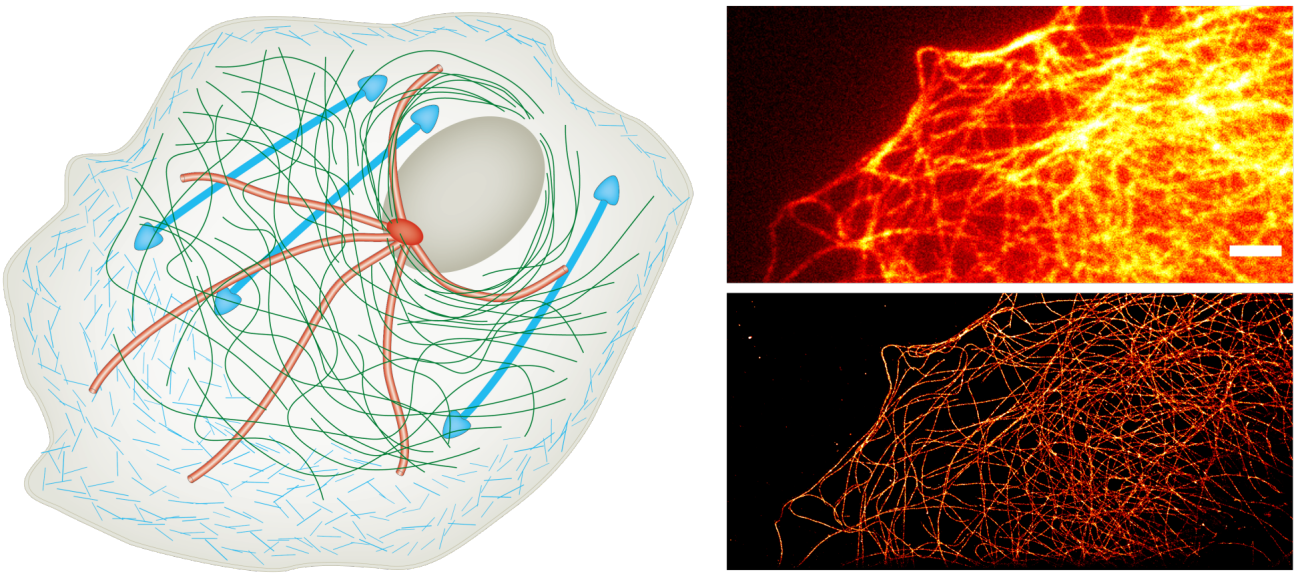

Figure 1: Left: Cytoskeleton of a cell: Microtubules in red, vimentin intermediate filaments in green and actin filaments in blue. Right top and bottom: Widefield and super-resolved STORM image of the microtubule network of a COS-7 cell, scalebar 5um.