



De Oosterpoort, Groningen Friday, 7 April 2016

Focus Session: Physics & Biology

Programme:

- Gijs Wuite (VU): Frontiers in Single Molecule Manipulation and Imaging of DNA-protein transactions
- Marcel Janson (WUR): Linking microtubule polymers into functional cellular networks
- Kees Storm (TU/e): Cell adhesion and motility: The physics of biological mechanosensing and mechanoresponse
- Doris Heinrich (UL / Fraunhofer Institute for Silicate Research): Cell Dynamics in Complex Environments

Session organisers: Patrick Onck, Wouter Roos, Erik van de Giessen, Thorben Cordes (RUG)

Abstracts:

Gijs Wuite (VU): Frontiers in Single Molecule Manipulation and Imaging of DNA-protein transactions

The genetic information of an organism is encoded in the base pair sequence of its DNA. Many specialized proteins are involved in organizing, preserving and processing the vast amounts of information on the DNA. In order to do this swiftly and correctly these proteins have to move quickly and accurately along and/or around the DNA constantly rearranging it. In order to elucidate these kind of processes we perform single-molecule experiments on model systems such as RNA polymerases, DNA polymerases and repair proteins. The data we use to extract forces, energies and mechanochemistry driving these dynamic transactions. The results obtained from these model systems are then generalized and thought to be applicable to many DNA-protein interactions. In particular, I will report experiments that use a combination of (super-resolution) fluorescence microscopy and optical tweezers to investigate DNA organisation.

Marcel Janson (WUR): Linking microtubule polymers into functional cellular networks

Microtubules are long and rigid biopolymers with two distinct ends. They are interconnected inside cells to form large-scale filamentous networks. We investigate how the design principles of these networks relate to their diverse cellular functions. In particular, we focus on lateral connections between the ends of oppositely oriented microtubules. The location and length of these contacts turns out to be a determining factor in the positioning of cell division planes. Connections are formed and maintained by a fascinating interplay between microtubule length dynamics and the presence of both active and passive microtubule linker proteins. Actively stepping molecular motors push overlapping microtubules apart whilst a gas of diffusely bound passive linkers generates opposing entropic forces. Using cellular observations and in vitro reconstitution of microtubule networks we demonstrate how,



within overlaps, feedback can be established between filament sliding and filament growth. In this way cells may fine-tune microtubule connections to control cell division.

Kees Storm (TU/e): Cell adhesion and motility: The physics of biological mechanosensing and mechanoreponse

Cells are acutely aware of the mechanical properties of their environment, and base some of the most important decisions of their lives on these properties. What basic physical mechanism allows cells to translate external mechanical information into the biochemical language they understand? A family of proteins called the integrins, which connect the cell to the outside world, was recently demonstrated to possess some curious physical properties that may provide mechanosensory functionality.

These integrins form so-called catch bonds: cellular receptor-ligand pairs whose lifetime, counterintuitively, increases with increasing load. While their existence was initially pure theoretical speculation, recent years have seen several experimental demonstrations of catch behavior in biologically relevant protein-protein bonds. I discuss the implications of single catch-bond characteristics for the behavior of a load-sharing cluster of such bonds: these are shown to possess a regime of strengthening with increasing applied force. I will discuss the implications of stiffness-dependent integrin binding for the persistence of durotactic motility, which in recent experiments was shown to correlate with substrate stiffness.

Doris Heinrich (UL / Fraunhofer Institute for Silicate Research): Cell Dynamics in Complex Environments

For the survival of living organisms, a coordinated control of each living cells is vital. All cells in the human body are exposed to diverse external mechano-chemical cues. These cues are coordinated in a spatio-temporal pattern and trigger specific cell functions. This complex interplay between external chemical cues and nanostructured 3D cell environments is translated into intracellular signalling loops and far from being understood.

The aim here is to investigate multi-scale mechanisms for specific guiding of cell migration. Profound understanding of contradicting and superimposing stimuli acting on cells will help to identify dominant cues and to ultimately generate a cell environment mimicking the human body.

Mechanical stimuli can be exerted by 3D scaffolds that guide or hinder cell migration to shuttle cells to the desired destinations and/or to keep them in place. Chemical stimuli in the form of chemotactic gradients add further stimuli to the mechanical cues, to advance or hinder targeted cell migration. This approach mimicks the amount of information a cell has to compute while migrating and surviving in a real organism.