De Oosterpoort, Groningen
Friday, 7 April 2017

Focus Session: Physics & Biology

Programme:

- Patrick van Rijn (UMCG): Mechanics, Topography, and Chemistry: How to determine multi-parameter influences on cell behavior
- 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:

Patrick van Rijn (UMCG): Mechanics, Topography, and Chemistry: How to determine multi-parameter influences on cell behavior

Cell-surface interactions are influenced by various factors including surface chemistry, mechanics and nano-/micro-topography [1]. A lot of investigations show that these surface parameters can be used to direct cellular behavior. However, there is still little known about how combined surface parameters affect cellular behavior as there are so many different parameter combinations. Screening platforms of surface parameter in a gradient fashion [2,3] are being developed to elucidate which cellular behaviors are affected. The screening platform, based on silicone rubber (PDMS), combines four orthogonal double gradients of wettability, topography, and stiffness connected to automated cell imaging and analysis which allows to generate substantial insights into multi-parameter influences on cell behavior. These screenings are expected to facilitate translation of basic cellular behavior towards clinical applications related to implant materials and tissue engineering scaffolds.

[1] A.M. Schaap, P.T. Kuhn, T.G. van Kooten, P. van Rijn, *RSC Adv.*, **2014**, *4*, 53307
[2] Q. Zhou, P. T. Kühn, T. Huisman, E. Nieboer, C. van Zwol, T. G. van Kooten, P. van Rijn, *Sci. Rep.* **2015**, *5*, 16240.
[3] P. T. Kuhn, Q. Zhou, T. van der Boon, A. M. Schaap-Oziemlak, T. G. van Kooten, P. van Rijn, *ChemNanoMat*, **2016**, *2*, 407.

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.

<u>Kees Storm (TU/e): Cell adhesion and motility: The physics of biological mechanosensing and mechanoresponse</u>

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.

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

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.