BP 38: Focus: Biological Cells in Microfluidics II

Microfluidic devices have a great potential to enable precise label-free analysis and manipulation of heterogeneous cell suspensions based on the intrinsic properties of the cell. This focus session will discuss recent advances in the behavior of biological cells and cell-mimicking systems in microfluidic flow, and represent a forum of theoretical and experimental contributions.

Time: Friday 9:30–12:00 Location: HÜL 386

Invited Talk BP 38.1 Fri 9:30 HÜL 386

Physical phenotyping of cells in microfluidic systems — •Jochen Guck — Max-Planck-Institut für die Physik des Lichts & Max-Planck-Zentrum für Physik und Medizin, Erlangen, Germany

While most current biological research focuses on molecular, biochemical aspects of cell processes, we are interested in the physical properties of cells, their importance for biological function, and ultimately transfer of insights to medical application. One major roadblock has been a paucity of appropriate tools for the convenient quantification of such properties. Recently, we have introduced real-time deformability cytometry (RT-DC) to address this need. RT-DC permits the continuous physical single-cell characterization of large populations (> 100.000 cells) with analysis rates of 1,000 cells/s - approaching that of conventional fluorescence-based flow cytometers. Using RT-DC we can sensitively detect physiological and pathological changes in cell function by image-based parameters such as size, shape, deformability, and any other information contained in an image. Combined with machine learning, conventional fluorescence detection and sorting, this constitutes a novel discovery machine specifically well suited to identify and characterize cell populations and states invisible to marker-based techniques. Physical phenotyping adds a new functional, marker-free and unbiased dimension to flow cytometry with diverse applications in biology, biotechnology and medicine.

BP 38.2 Fri 10:00 HÜL 386

Lingering dynamics of microvascular blood flow in Syrian hamsters — •Alexander Kihm[1], Stephan Quint[1], Matthias Laschke[2], Michael Menger[2], and Christian Wagner[1] — [1]Department of Experimental Physics, Saarland University, Saarbruecken, Germany — [2]Institute for Clinical and Experimental Surgery, Saarland University, Homburg, Germany

The microvascular networks in the body of vertebrates consist of the smallest vessels, such as arterioles, venules, and capillaries. The flow of red blood cells (RBCs) through these networks ensures the gas exchange in, as well as the transport of nutrients towards the tissues. Any alterations in this blood flow may have severe implications on the health state. Since the vessels in these networks obey dimensions similar to the diameter of RBCs, dynamic effects on the cellular scale play a key role. The steady progression in numerical modelling of RBCs even in complex networks has led to novel findings in the field of hemodynamics, especially concerning the impact and the dynamics of lingering events. However, these results are yet unmatched by a detailed analysis of the lingering in experiments in vivo. To quantify this lingering effect in in vivo experiments, we analyse branching vessels in the microvasculature of Syrian hamsters via intravital microscopy and the use of an implanted dorsal skinfold chamber. We present a detailed analysis of these lingering effects of cells at the apex of bifurcating vessels, affecting the temporal distribution of cell-free areas in the branches and even causing a partial blockage in severe cases.

BP 38.3 Fri 10:15 HÜL 386

Hydrogel-based cell mimics and applications — •Salvatore Girardo[1], Ruchi Goswami[1], Nicole Träber[2,3], Anna Taubenberger[2], Katrin Wagner[2], and Jochen Guck[1] — [1]MPL,Erlangen,Germany — [2]Biotec,Dresden,Germany — [3]IPF,Dresden,Germany

In recent decades it has become increasingly obvious that cell mechanical properties can be used to monitor physiological and pathological changes in cells. It has been reported that mechanical properties measured by using different techniques on the same cell type span a wide range of values, making hard the comparison of the obtained results. Therefore, a mechanical standard is needed to validate and calibrate mechanical measurements. Furthermore, quantification of stresses exerted and experienced by cells at the cell-scale level in in vivo and in vitro systems is fundamental to improve the understanding of the role of mechanics in biology and medicine. This quantification is still a challenge due to the lack of the availability of appropriate measurement tools. All these aspects can be addressed by using elastic, compressible and homogeneous spheres whose shape, size, mechanical properties and functionalization with specific adhesion sites are well established before use. Here we illustrate the production, characterization and functionalization of standardized microgel beads covering all these features. We demonstrate that these beads can be used as mechanical standards, as cell-scale stress sensors able to sense forces through their deformation and as building blocks of novel 3D scaffolds to investigate mechanosensing.

BP 38.4 Fri 10:30 HÜL 386

Sensorimotor processing and navigation in confined microswimmers — Samuel Bentley, Vasileios Anagnostidis, Fabrice Gielen, and •Kirsty Y. Wan — Living Systems Institute, Exeter, United Kingdom, EX4 4QD

All living organisms are environmentally intelligent. This is the fundamental distinction between life, and other forms of matter. Even unicellular organisms are capable of complex behaviours, for they can sense as well as respond to changes in the environment. Here, we study spontaneous and constrained motor actions in algal microswimmers, using motility as a dynamic read-out of behaviour and physiology. Previous studies have focussed on locomotion transients over short timescales ranging from milliseconds to minutes. We present a novel microfluidic platform which allowed us for the first time to monitor and analyse algal cell motility over hours, and even developmental timescales. We focus on two species, a biflagellate which exhibits a form of run-and-tumble, and an octoflagellate which which exhibits a tripartite behavioural repertoire termed run-stop-shock. Excitability and stochastic transitions in swimming gait are projected onto a low-dimensional state space. We reveal how flagellar mechanosensitivity mediates repetitive boundary interactions, and discuss the discovery of a light-dependent quiescent regime. Finally, we conduct pharmacological perturbations within these microenvironments, to shed new light on the physiological origins of excitable flagellar dynamics.

BP 38.5 Fri 10:45 HÜL 386

DNA-mediated programmable functionalization and symmetry break in microfluidic droplets — •Kevin Jahnke[1,2] and Kerstin Göpfrich[1,2] — [1]Biophysical Engineering Group, Max Planck Institute for Medical Research, Jahnstraße 29, 69120 Heidelberg, Germany — [2]Department of Physics and Astronomy, Heidelberg University, 69120 Heidelberg, Germany

Droplet-based microfluidics has emerged as a powerful tool in synthetic biology. For many applications, chemical functionalization of the droplets is a key process. Therefore, we developed a straight-forward and broadly applicable approach to functionalize the inner periphery of microfluidic droplets with diverse reactive groups and components. This method relies on cholesterol-tagged DNA that self-assembles at the droplet periphery [Jahnke et al., Adv. Funct. Mat. 2019]. The cholesterol-tagged DNA serves as an attachment handle for the recruitment of complementary DNA, which can carry diverse functional groups. We demonstrate that the attachment is thermo-responsive and exemplify the versatility of our approach. Further, we employ our DNA-linker system to engineer light-activated directional contractility of a minimal actomyosin network inside microfluidic cell-sized compartments. Ultimately, symmetry breaking is achieved using the DNA link between the actin network and the compartment periphery.

We envision that droplet functionalization via DNA handles will help to tailor interfaces for diverse applications – featuring programmable assembly, unique addressability, and stimuli-responsiveness – hence increasing the complexity of synthetic cellular systems.

30 min. coffee break

BP 38.6 Fri 11:30 HÜL 386

Bayesian parameter estimation and model selection for bio-

physical models of leukocyte cell extensions during leukocyte rolling — •Mats Leif Moskopp[1], Philipp Rosendahl[2,3], Jochen Guck[2,4], Andreas Deussen[1], and Peter Dieterich[1] — [1]Institut für Physiologie, TU Dresden, Dresden, Germany — [2]Biotechnology Center, TU Dresden, Dresden, Germany — [3]Zellmechanik Dresden GmbH, Dresden, Germany — [4]MPL & MPZ-PM, Erlangen, Germany

The leukocyte adhesion cascade describes the extravasation of leukocytes from the blood stream into tissue. We focus on the initial process of leukocyte rolling, which is driven by shear stress and (passive) restoring forces in leukocyte cell extensions (microvilli, tethers and slings). We investigate the biomechanical properties of cell extensions based on experimental data combined with mathematical modelling and Bayesian inference. High speed (2000 fps) video sequences of rolling leukocytes (THP-1) were used to obtain cell positions as a function of time over a periode of about 10 s. Bayesian inference allows for model selection and parameter estimation of visco-elastic models (Maxwell, Kelvin-Voigt, Standard linear solid) for the fast deceleration of cell extensions during leukocyte rolling. This new technique identified differences in the biomechanical stress responses of cell extensions according to isoforms of selectins. These findings correlate to distinct rolling dynamics on P- and E-selectin isoforms regarding overall velocity and fast deceleration events. Further, this approach allows to quantify model parameters. This was tested using Glutaraldehyde (tissue fixation) and Cytochalasin D (inhibitor of actin polymerization).

BP 38.7 Fri 11:45 HÜL 386

Synthetic cells: De novo assembly with microfluidics and DNA nanotechnology — Yannik Dreher[1,2], Julius Fichtler[1,2], Kevin Jahnke[1,2], and •Kerstin Göpfrich[1,2] — [1]Biophysical Engineering Group, Max Planck Institute for Medical Research, Jahnstraße 29, 69120 Heidelberg, Germany — [2]Department of Physics and Astronomy, Heidelberg University, 69120 Heidelberg, Germany

Bottom-up synthetic biology has been successful at isolating components from cells and reconstituting subcellular functions in vitro. Progress towards a fully functional synthetic cell, however, requires strategies to recombine and arrange a multitude of components in space and time. Here, we merge two precision technologies, microfluidics and DNA nanotechnology, to position and manipulate various components in synthetic cells [K. Göpfrich *et al., Trends Biotechnol.*, 2018; Jahnke *et al., Adv. Funct. Mater.*, 2019]. After encapsulation, we actuate DNA nanostructures in microfluidic or lipid-based compartments [K. Göpfrich *et al., ACS Synth. Biol.*, 2019] to assemble dynamic systems with structural reconfigurability. By the integration of plasmonic probes we achieve real-time optical feedback to monitor the dynamics upon external stimulation. Moreover, we demonstrate the division of lipid vesicles relying on physical mechanisms and show that it can be regulated by metabolic activity. These unique tools, bridging the micro- and nanoscale, enrich the complexity and diversity of functional synthetic cellular systems.