BP 26: Focus: Biological Cells in Microfluidics I

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: Wednesday 15:00–17:30 Location: SCH A251

BP 26.1 Wed 15:00 SCH A251

Numerical Investigation of Cell Deformation during Bioprinting — •Sebastian Johannes Müller and Stephan Gekle — Universität Bayreuth, Bayreuth, Deutschland

In 3D bioprinting, cells suspended in hydrogel are deposited through a fine nozzle, creating three dimensional biological tissues. Due to the high viscosity of the hydrogel, the cells experience hydrodynamic stresses that deform or damage the cells and can ultimately affect the viability and functionality of the cells in the printed construct.
Using numerical methods, we quantify these deformations in dependency of the flow parameters and cell elasticity. We consider shear thinning fluid rheology and validate our Lattice Boltzmann flow calculations with microfluidic flow experiments of typical hydrogel materials. Our hyperelastic cell, modeled as purely elastic continuum with neo-Hookean force calculations, is validated with experimental data for cells obtained via AFM indentation measurements.
By coupling our cell model with the fluid simulations, we investigate the cell deformation in typical flow scenarios, like capillary and shear flow. As essential part of the printing process, we further simulate the cell flowing through the transition from the printer nozzle into the free hydrogel strand, where additional radial flow components stretch the cell at short time scale.

BP 26.2 Wed 15:15 SCH A251

Geometry-induced focusing of red blood cells in a contraction-expansion microfluidic device — •Steffen Michael Recktenwald[1], Asena Abay[1,2], Thomas John[1], Lars Kaestner[1,3], and Christian Wagner[1] — [1]Saarland University, Saarbruecken, Germany — [2]Landsteiner Laboratory, Amsterdam, Netherlands — [3]Saarland University Medical Center, Homburg, Germany

Constrictions in blood vessels of the cardiovascular system can dramatically change the spatial distribution of passing cells or particles. To study the flow of red blood cell (RBC) suspensions in obstructed vessels, constricted microfluidic devices are commonly used. However, the three-dimensional nature of cell focusing in the channel cross-section remains poorly investigated. Here, we explore the cross-sectional distribution of living and rigid RBCs passing a constricted microfluidic channel. Therefore, individual cells are tracked in multiple layers across the channel depth and across the channel width. While cells are homogeneously distributed in the channel cross-section pre-contraction, we observe a strong geometry-induced focusing post-contraction. The magnitude of this cross-sectional focusing effect increases with increasing Reynolds number for both living and rigid RBCs. We discuss how this non-uniform cell distribution results in an apparent double-peaked velocity profile in particle image velocimetry analysis and show that trapping of RBCs in the recirculation zones of the abrupt constriction depends on cell deformability, highly relevant for biomedical cell-sorting applications.

BP 26.3 Wed 15:30 SCH A251

Optical Detection, Characterization and Sorting of Cells and Vesicles in Microfluidics — •Tobias Neckernuss[1,2], Daniel Geiger[1,2], Jonas Pfeil[1,2], Lisa Kwapich[1], Patricia Schwilling[1], and Othmar Marti[1] — [1]Institute of Experimental Physics, Ulm University — [2]Sensific GmbH

High-speed video microscopy is used for many particle or cell detection applications. In order to measure the mechanical properties of cells or to identify their type. With standard equipment none of these tasks can be accomplished in a real-time and in a label-free environment, let alone if a subsequent sorting step is required.
With our new ODIN technology, we are able to assess important parameters like size, shape, velocity, and morphology of different kinds of particles in microfluidic channels and in Lab-on-a-Chip environments. The optical and label-free measurement delivers relevant parameters immediately after the particle passes the sensor. Due to the fixed latency times we are able to set a trigger signal as soon as the particle or cell matches freely configurable, predefined parameters. ODIN enables new measurement applications for particles and cells, leading to potentially groundbreaking changes in Lab-on-a-Chip designs and their throughputs. We present different experiments and sorting tasks regarding cell stiffness, droplet size, particle encapsulation, bacterial analysis, and antibiotic screening performed with ODIN. Simultaneous real-time detection, categorization and sorting enables novel multifunctional Lab-on-a-Chip designs leading to a multifunctional microfluidic factory.

BP 26.4 Wed 15:45 SCH A251

Microfluidic platforms to study forces on model cells — •Tom Robinson — Max Planck Institute of Colloids and Interfaces, Potsdam, Germany

Biological cells in their natural environment experience a variety of external forces such as fluidic shear stresses, osmotic pressures, and mechanical loads. The response of cell membranes to such forces is of great interest and model systems such as giant unilamellar vesicles (GUVs) offer the chance to investigate individual components without interference from cellular complexity (Robinson, Adv Biosyst., 2019). However, being able to handle and apply forces to these delicate objects in a controllable manner is non-trivial. Therefore, we present several microfluidic platforms to capture, analyse, and apply forces to GUVs. First, we present microfluidic devices for their high capacity capture and isolation (Yandralli & Robinson, Lab Chip, 2019). Lipid rafts are thought to play an important role in the spatial organization of membrane proteins. Therefore, GUVs with membrane domains are used as models to explore their behaviour in response to external forces. We use a valve-based system to apply precise fluidic shear stresses to vesicles (Sturzenegger, Robinson, et al. Soft Matter, 2016) and a device with an integrated micro-stamp to mechanically compress GUVs to study the effects that deformation has on lipid rafts (Robinson & Dittrich, ChemBioChem 2019).

BP 26.5 Wed 16:00 SCH A251

High Throughput Microfluidic Characterization of Erythrocyte Shapes and Mechanical Variability — •Felix Reichel[1,2], Johannes Mauer[3], Ahsan Nawaz[1], Gerhard Gompper[3], Jochen Guck[1], and Dmitry Fedosov[3] — [1]Max Planck Institute for the Science of Light and Max-Planck-Zentrum für Physik und Medizin, Erlangen — [2]Biotechnology Center, Center for Molecular and Cellular Bioengineering, Technische Universität Dresden, Dresden — [3]Theoretical Soft Matter and Biophysics, Institute of Complex Systems and Institute for Advanced Simulation, Forschungszentrum Jülich, Jülich

The circulation of red blood cells (RBCs) in microchannels is important in microvascular blood flow and biomedical applications such as blood analysis in microfluidics. Current understanding of the complexity of RBC shapes and dynamical changes in microchannels is mainly formed by a number of simulation studies, but there are few systematic experimental investigations. Here, we present a first systematical mapping of experimental RBC shapes and dynamics for a wide range of flow rates and channel sizes. Results are compared with simulations and show good agreement. A key difference to simulations is that in experiments there is no single well-defined RBC state for fixed flow conditions, but rather a distribution of states. This result can be attributed to the inherent variability in RBC mechanical properties, which is confirmed by a model that takes the variation in RBC shear elasticity into account. These results make a significant step toward a quantitative connection between RBC behavior in microfluidic devices and their mechanical properties.

15 min. coffee break

Invited Talk BP 26.6 Wed 16:30 SCH A251

3 D Classification of Red Blood Cells in microchannels — •Christian Wagner — Universität des Saarlandes

Red blood cells (RBCs) are very soft objects that can pass capillaries smaller than the cells diameter. Due to their high deformability, they couple strongly with the flow and can adopt many different shapes. For their quantitative characterization we developed a new confocal 3D imaging technique for fluorescent stained RBCs. We found two equilibrium cell shapes under certain flow condition: the so called 'slipper' and the 'croissant' shape. Numerical simulations are in good agreement with experimental observations. In addition, high throughput data of classical 2-D microscopy combined with an adaptive neural network allow us to obtain the full phase diagram of red blood cell shapes as a function of the flow rate. In larger channels, we use the confocal technique to characterize the margination of single rigidified RBCs in a suspension of healthy RBCs. Margination of e.g. white blood cells or platelets at the vessel walls is a haemodynamic key mechanism of our immune system. Our confocal observation technique allows us to characterize the distribution of hard vs. soft cells in full time and space resolution for the first time. Again numerical simulations are in good agreement although some quantitative differences remain that need further investigations.

BP 26.7 Wed 17:00 SCH A251

Simulation of cell deformation inside a microfluidic channel under the influence of a non-Newtonian fluid. — •Ralf Schuster[1], Bob Fregin[2], Oliver Otto[2], and Othmar Marti[1] — [1]Institute of Experimental Physics, Ulm University, D-89081 Ulm — [2]Humorale Immunreaktionen bei kardiovaskulären Erkrankungen, Universität Greifswald, D-17489

The mechanical characterization of certain cell types is important to obtain physiological insights. For instance, tumor and normal cells can be distinguished by elasticity, indicated by the amount of deformation under given stress. Simulations help to understand, verify and improve the analysis of deformation-based cell characterization such as flow-based cytometry. We achieve efficient computations using a 2D-rotational symmetric model, based on Fluid-Structure-Interaction with a hyper-elastic material. The deformation of a cell along an entire microfluidic channel can be tracked for a variety of elasticities, viscosities, cell sizes, channel geometries and flow rates. The aim is to model typical experimental conditions [1] and compare simulated and measured results. In the study HL60 cells undergo a shear stress in a fluid with shear dependent viscosity, which can be described by a power law. Simulations are carried out for three different flow rates and additionally for Newtonian fluids with constant viscosity. The results help to find appropriate parameters and models to describe and interpret the behavior of certain cell types.

[1]Fregin et al, High-throughput single-cell rheology in complex samples by dynamic real-time deformability cytometry. Nat Com(2019)

BP 26.8 Wed 17:15 SCH A251

ROS induces intracellular acidosis associated with increased cell stiffening — •Yesaswini Komaragiri[1], Huy Tung Dau[1], Doreen Biedenweg[2], Ricardo H Pires[1], and Oliver Otto[1] — [1]Biomechanics, ZIK-HIKE, University of Greifswald, Greifswald, Germany — [2]University medicine Greifswald, Greifswald, Germany

Reactive oxygen species (ROS) are a primary source of superoxides associated with important alterations in cell physiology. Here, it is accepted that ROS affect the cytoskeleton, however, the interplay with cell mechanics has not been thoroughly investigated. This study focuses on understanding the impact of oxidative stress on the mechanical properties of the human myeloid precursor cell line (HL-60). Generation of ROS was induced by exposing cells to varying concentrations of hydrogen peroxide (H2O2). Using real-time fluorescence deformability cytometry we coupled the mechanical characterization of cells with simultaneous fluorometric assessment of intracellular ROS levels. Our work reveals a direct correlation between the elastic modulus of cells and increased levels of superoxides. Interestingly, the changes in the mechanical phenotype cannot be explained by altered structured of F-actin and microtubule. We demonstrate that cell stiffening at elevated levels of ROS is driven by intracellular acidosis and a corresponding decrease in the cytoplasmic pH of our model system.