BP 5: Focus Session NanoAgents

Time: Monday 15:00–17:30 Location: TOE 317

Invited Talk BP 5.1 Mon 15:00 TOE 317

Repurposing nucleic acids as high-resolution force sensors: From fundamental mechanotransduction to translational biophysics — •Khalid Salaita — Emory University, Department of Chemistry, Atlanta, Georgia, USA

Cells are highly dynamic structures that are constantly converting chemical energy into mechanical work to pull and push on one another and on their surroundings. These pulls and pushes are mediated by tiny molecular forces at the scale of tens of piconewtons. For context, 7 pN applied a distance of 1 nm is ~1 kcal/mol. Nonetheless, these forces can have profound biochemical consequences. For example, the rapidly fluctuating forces between immune cells and their targets can drastically tune immune response and function. Despite the importance of mechanics there are limited methods to study forces at the molecular scale and particularly within living cells.

In this talk, I will discuss my group's efforts at addressing this gap in knowledge by developing tools to map the molecular forces applied by cells. I will describe the development of a suite of DNA tension probes which offer significant improvements in S/N and lead to enhanced spatial and temporal resolution. I will also describe a series of force-triggered reactions that enable signal amplification. Fluorescence polarization spectroscopy and super-resolution imaging offer the highest resolution maps of cell traction forces reported to date. Finally, armed with these new tools, I will describe the advent of translational mechanobiology where we predict the bleeding risk in patients by measuring the mechanical activity of their platelet adhesion receptors.

BP 5.2 Mon 15:30 TOE 317

Remodelling DNA filaments for bottom-up synthetic biology — •Maja Illig[1], Kevin Jahnke[1,2], Marlene Scheffold[1], Hauke Drechsler[3], Stefan Diez[3], and Kerstin Göpfrich[1] — [1]MPI for Medical Research, Heidelberg, Germany — [2]Harvard University, School of Engineering and Applied Sciences (SEAS), Cambridge, MA, USA — [3]TU Dresden, Center for Molecular Bioengineering (B CUBE), Dresden, Germany

The control of filamentous cytoskeletal systems is one of the dedicated aims of bottom-up synthetic biology to engineer self-dividing synthetic cells and equip them with mechanical cell-to-cell communication pathways. A molecular engineering approach to achieve specific functionality from the nanoscale to the microscale requires programmability in order to design self-assembly.

This work reinforces how DNA nanotechnology paves the way to create biocompatible nanostructures that can mimic cellular entities. Here, we demonstrate the remodelling of entirely synthetic filaments made from DNA nanotubes: (i) Towards bottom-up synthetic cell division, we can rationally design a ring structure made from bundled filaments. We can control the ring formation by engineering of a synthetic crosslinking peptide and we further constrict the ring diameter by external triggers. (ii) Towards mechanotactic synthetic cells, a transmembrane signalling pathway enables the reconfiguration of the cytoskeleton made from DNA filaments. The stimulus-induced clustering of transmembrane entities results in mechanical remodelling of the internal DNA cytoskeleton (Jahnke, Illig et al. Biorxiv 2022).

BP 5.3 Mon 15:45 TOE 317

Einfluss von Kohlenstoff-Nanoteilchen auf die Funktion von Lysosomen — •Carla Sprengel, Cathrin Nollmann, Lena Berning, Thomas Lenz, Björn Stork und Thomas Heinzel — Heinrich-Heine-Universität Düsseldorf

Die Verwendung von Nanopartikeln als Wirkstoffträger in Drug Delivery Systemen gewinnt besonders bei der Tumortherapie an Bedeutung. Die zielgenaue Medikamentenfreisetzung in pathologischen Zellen könnte bei gleichbleibender therapeutischer Wirkung starke Nebenwirkungen durch Schädigung gesunder Zellen vermeiden. Kohlenstoff-Nanopartikel (CNDs) eignen sich aufgrund ihrer Fluoreszenzeigenschaften, geringen Zytotoxizität und Möglichkeit zur Funktionalisierung besonders gut als Carrier für ein solches Drug Deliver System. Durch die Fluoreszenz der CNDs im blauen Bereich nach UV-Anregung können die CNDs in Zellen nachgewiesen werden und auf zellulärer Ebene lokalisiert werden. Bisherige Untersuchungen zeigen, dass die CNDs über Endozytose in die Zelle aufgenommen und in den Endosomen und Lysosomen angelagert werden. Da wichtige metabolische Prozesse wie die Autophagie abhängig von Lysosomen sind, werden die Auswirkungen der CNDs auf diese lysosomalen Prozesse mittels verschiedener Methoden untersucht und diskutiert.

BP 5.4 Mon 16:00 TOE 317

Aufnahme von Kohlenstoff-Nanopartikeln in humane AML-Zellen im Vergleich zu primären hämatopoetischen Zellen — •Cathrin Nolllmann[1], Thomas Heinzel[1] und Rainer Haas[2] — [1]Institut für Physik der kondensierten Materie, Heinrich-Heine-Universität, Düsseldorf, Deutschland — [2]Klinik für Hämatologie, Onkologie und Klinische Immunologie, Universitätsklinikum Düsseldorf, Deutschland

Kohlenstoff-Nanopartikel (CNDs) sind eine vielversprechende Klasse von Nanopartikeln. Diese kohlenstoffbasierten, nanometergroßen Partikel bieten ein breites Spektrum potenzieller biomedizinischer Anwendungen wie Bioimaging, Krebsdiagnostik und Drug-Delivery. Im Zusammenhang mit Drug Delivery ist eine selektive Aufnahme durch maligne Zellen entscheidend. Unser Ziel war es zu untersuchen, ob es ein unterschiedliches Aufnahmeverhalten von AML-Zellen im Vergleich zu primären hämatopoetischen Zellen gibt. Dazu wurden aus Zitronensäure und Diethylentriamin hergestellte CNDs 24 Stunden lang mit Zellen von fünf Patienten mit de novo AML und primären hämatopoetischen Zellen von drei gesunden Spendern inkubiert. Die differentielle Aufnahme der CNDs wurde mittels Durchflusszytometrie und monoklonalen Antikörpern untersucht. [1]

[1] C. Nollmann et al., Uptake of carbon nanodots into human AML cells in comparison to primary hematopoietic cells, RSC Adv., (11), pp. 26303-26310, 2021.

15 min. break

BP 5.5 Mon 16:30 TOE 317

DNA origami agents for the efficient treatment of solid tumors — •Johann Moritz Weck[1], Merve-Zeynep Kesici[1], Cornelia Monzel[2], and Amelie Heuer-Jungemann[1] — [1]Max Planck Institut für Biochemie, Am Klopferspitz 18, 82152 Martinsried — [2]Heinrich Heine Universität Düsseldorf, Universitätsstraße 1, 40225 Düsseldorf

We previously used DNA origami as a platform to pre-cluster Fas ligands (FasL) of the tumor necrosis factor receptor superfamily (TNFRSF) with nanometer precision in varying patterns and presented those to HeLa cells in a 2D cell culture model. We found up to a 100x increase of potency upon pre-clustering FasL in hexagonal geometries, a high sensitivity towards inter-ligand distance and a dependency on linker rigidity. In order to use this knowledge for the advancement of TNRSF ligand-based therapeutics, we investigated the interactions of DNA origami nanoagents with solid tumors. Certain aspects of cancer cell biology, such as the complex biological environment of solid tumors cannot be efficiently simulated in regular 2D cell culture systems. Using a 3D tumor spheroid model, we here show that FasL-DNA origami nanoagents are able to strongly affect the growth of 3D tumor spheroids. Partial dissolution of 3D tumoroids is observed after exposure to the nanoagents. We provide insights into DNA origami tumor spheroid penetration ability as well as a threshold like behavior of signaling initiation, and design rules for nanomaterial based therapeutics.

BP 5.6 Mon 16:45 TOE 317

Monitoring the Switching dynamics of Photolipid Membranes with Plasmonic Nanorods — •Jinhua Zhang, Francis Schuknecht, Ludwig Habermann, Alexander Pattis, Stefanie Pritzl, and Theobald Lohmüller — Chair for Photonics and Optoelectronics, Nano-Institute Munich, Department of Physics, Ludwig-Maximilians-Universität, Königinstraße 10, 80539 Munich, Germany

Photoswitchable lipids (i.e. photolipids) are intriguing nanoagents for controlling lipid membrane properties with light. However, analyzing the switching dynamics in a single lipid bilayer locally and in situ is challenging due to a lack of sensitive tools for detecting the very small changes in membrane thickness (< 1 nm). Here, we demonstrate a new approach to monitor the photoisomerization of photolipid membranes on the nanoscale via plasmonic sensing.

In our experiment, gold nanorods are deposited on a glass substrate and coated with a supported photolipid bilayer. The photosensitive

azobenzene group in the lipid tails is switched between a trans and cis form by an illumination sequence with UV and blue light, while scattering spectra of individual nanorods are simultaneously measured. We find that the photoisomerization process of azobenzene leads to a reversible shift of the nanorod's plasmon resonance over many switching cycles. Our study shows that single nanorods may thus be used as sensitive probes to study isomerization dynamics and photostationary states of photolipid bilayer membranes within nanoscale environments.

BP 5.7 Mon 17:00 TOE 317

Bio-inspired Magnetic Nanoprobes For Subcellular Manipulation Studies in Single Cells — •Andreas Neusch[1], Iuliia Novoselova[1], Liesa Zitzke[1], Sarah Sadik[1], Michael Farle[2], Ulf Wiedwald[2], and Cornelia Monzel[1] — [1]Heinrich-Heine-University, Düsseldorf — [2]University of Duisburg-Essen, Duisburg

Probing and manipulating biological functions requires tools to target and modify the proteins involved in the respective process. In recent years Magnetogenetics emerged as an approach where magnetic nanoparticles (MNPs) and external magnetic fields are used to realize such manipulation (Lisse et al., Adv. Mater., 29, 1700189 (2017)). The advantages of this combination lies within the deep tissue penetration of magnetic fields and the possibility to apply stimuli on nanoscales leading to spatial redistribution, force application, or heat generation of proteins. However, a precise active perturbation requires MNPs to be monodisperse, biocompatible, tunable with regard to their magnetic properties, as well as exhibiting a modifiable molecular shell (Monzel et al., Chem. Sci. 8, 7330-7338 (2017)). Here, we synthesize a bioinspired semisynthetic MNP - Magnetoferritin (MFt) -, which fulfils these demands. MFt is based on the globular iron storage protein complex ferritin that converts iron ions to a ferrihydrite core but can be synthetically loaded with a magnetic iron oxide core (Novoselova et al., Nanomaterials, 11, 2267 (2021)). MFt was chemically, physically and magnetically characterized both in vitro and in vivo. We demonstrate how MFt can be used to target proteins on living cells as well as to spatially manipulate MFts in a single cell environment.

BP 5.8 Mon 17:15 TOE 317

Precise micro-manipulations via multiplexed feedback-controlled thermoviscous flows — •Elena Erben[1], Nicola Maghelli[1], Weida Liao[2], Antonio Minopoli[1], Eric Lauga[2], and Moritz Kreysing[1] — [1]Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany — [2]DAMTP, University of Cambridge, UK

Methods for precise micro-manipulation are highly relevant for many problems in biological research such as cell patterning and controlled droplet fusion. Thermoviscous flows [1] hold great potential for manipulations in biological systems since they can be induced optically and enable non-invasive in-vivo perturbations [2]. Recently, we developed a novel optofluidic manipulation method based on feedback-controlled thermoviscous flows. This technique facilitates the automatic positioning of a single micro-particle, with a precision of up to 24 nm [3]. Our approach can be multiplexed to the parallel manipulation of multiple particles, thus facilitating dynamic micropatterning. Furthermore, we found that positioning of multiple particles can be greatly accelerated by leveraging highly complex flow patterns that result from multiplexing. We anticipate that combining our approach with elaborate theoretical modelling will increase the precision and speed of this manipulation method even more, facilitating translation onto applications in the life sciences and beyond.

[1] Weinert et al. Phys. Rev. Lett. 2008; [2] Mittasch et al. Nat. Cell Biol. 2018; [3] Erben et al. Opt. Express 2021.