Dear participants,

welcome to the *7th Annual "Physics of Cancer" Symposium* held at the *University of Leipzig*. This fall, we look forward to a meeting again assembling scientists worldwide pioneering in the investigation of the physical mechanisms underlying cancer progression.

The scientific program consists of invited talks as well as contributed talks and posters. This booklet contains the schedule and abstracts for the three conference days. For more information, please visit our conference website:

conference.uni-leipzig.de/poc/2016/

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City of Leipzig

Leipzig is a vibrant metropolis in the heart of former East Germany. It is well known for its cultural, especially musical, history and famous for its trade fairs and exhibitions. Leipzig played a significant role in the peaceful revolution of 1989, which led to the fall of the Berlin Wall and finally of communism in Eastern Europe.


Photo: Michael Bader, CC-BY

The *University of Leipzig*, being one of Europe's oldest universities, looks back to a long tradition. Many famous names, including Bach, Mendelssohn, Goethe, Lessing, Leibniz, Debye, Ostwald, Bloch, Hertz, and Heisenberg, are associated with Leipzig and its university.

In 2010, Leipzig was included in the top 10 cities to visit by the New York Times. While you are in town attending the *"Physics of Cancer"* symposium, we hope that you will also find the time to see some highlights of Leipzig. The city offers many different sightseeing destinations and activities.

Leipzig's Public Transport System

The city of Leipzig and its surrounding areas are part of *MDV local public transport association*. It consists of **tram and bus lines** as well as a metro-like railway called **S-Bahn** (and some regional trains). Trams and buses are operated by the *LVB*, while the S-Bahn is operated by *DB (Deutsche Bahn)*. However, they all share the same ticket system. Ticket fees are distance-based (zones). Here are some examples:

- *"Kurzstrecken-Fahrkarte"* (short distance ticket) is valid for a maximum of four stops with tram or bus within the city of Leipzig (zone 110) without interchange option or for a maximum of one stop with the S-Bahn (fee 1.80 EUR).
- *"Einzelfahrkarte - 1 Zone Stadt Leipzig"* (full single ticket for 1 zone city of Leipzig) is valid for 1 hour for travel within the city of Leipzig (zone 110) with the option to interchange to any other tram, bus, and S-Bahn lines (fee 2.60 EUR).
- There also options for day or week tickets which are also distance-based.

Tickets are bought at ticket machines located on most platforms and in some trams (not S-Bahn!) as well as directly from bus drivers. The machines accept cash. Tickets have to be validated prior travelling using the stamping machines located on the platforms (S-Bahn) or inside the vehicle (trams and buses).

General information on Leipzig's public transportation system, timetables, and a connection planner can be found at **www.lvb.de**. There, you also find network maps for day and night.

(Note: The *DB (Deutsche Bahn)* additionally operates inter-city trains (called "IC" and "ICE") and some regional trains (called "RB" and "RE") which are included in the *MDV local public transport association*. These trains have a separate DB ticket system. DB ticket machines offer both, MDV tickets and DB tickets. LVB and MDV ticket machines, on the other hand, offer MDV tickets only.)

Conference Venue

The "Physics of Cancer" symposium will take place in Leipzig, Germany, at the *Haus des Buches*.

Haus des Buches - Literaturhaus Leipzig
Gerichtsweg 28
04103 Leipzig, Germany


Photo: Vermietung und Hausverwaltung GbR Haus des Buches

You quickly reach the *Haus des Buches* from the main train station ("Hauptbahnhof") or from the city center at *Augustusplatz* via tram line 15 in direction *Meusdorf*. You have to travel just 3 or 2 stops respectively. Your target stop is called *Gutenbergplatz* which is directly in front of the *Haus des Buches*.
The opposite direction for your way back to *Augustusplatz* or the main train station is called *Miltitz*.

If you arrive by car, you may use the underground parking at *Gutenbergplatz*, which is open 24/7.

The following map shows a detailed view of the area around the conference venue (marked in red) including the stops and tracks of tram lines (depicted as black lines) as well as the mentioned underground parking.

For more information on how to get to Leipzig, have a look at the travel information on our conference website.

General Information

Presentations

Scientific presentations will be held either orally (talk) or by poster.

Talk sessions will take place in the large auditory ("Großer Konferenzraum") of the *Haus des Buches*. The room is equipped with a video projector with VGA input. Contributed talks are allocated 15 min (including discussion), whereas invited talks are allocated 20 min plus 10 min discussion.

The poster session will be on Wednesday, October 5th, 2016 at 13:00. During this session, a lunch buffet will be provided for all participants. Authors can already mount their posters on Tuesday, October 4nd, starting from 11:00. Poster boards will be marked with numbers according to the scientific program. Push pins for mounting will be provided. Please remove your poster before Thursday, October 6th, 14:00. Any posters that are left will be discarded by the organizers.

Weekend and National Holiday

In case you arrive some days earlier, please note that in Germany most shops including grocery stores and supermarkets are closed on Sundays. However, most restaurants will be open.

Moreover, on Monday, October 3, there is the national holiday of Germany ("Day of German Unity"). Hence, most shops including grocery stores and supermarkets will be closed on that day.

In Case of Questions...

... or any problems, do not hesitate to ask the conference organizers and assistants for help. You will recognize them by their name badges with names printed in red (in contrast to the black printing of normal name badges).

Tuesday, October 4, 2016

11:00 – 13:00 *Conference check-in and on-site registration*

13:00 – 13:15 *OPENING | WELCOME*

Session I: Functional Mechanics of Cancer Cells

13:15 – 13:45 **Effect of Hyaluronic Acid on Mechanoresponse of Cancer Cells**
PAUL JANMEY (University of Pennsylvania, USA)

13:45 – 14:15 **Phenotyping Single Cell Derived Microtissues by Time-Resolved Imaging and Molecular Sequencing**
ROLAND EILS (German Cancer Research Center, Heidelberg, Germany)

14:15 – 14:30 **Change Matters: a Time-Varying Parameter Model for Cell Migration**
CHRISTOPH MARK (Friedrich-Alexander University Erlangen-Nuremberg, Germany)

14:30 – 14:45 **TA Instruments - High Performance Thermal and Rheological Characterization**
MATTHIAS QUAIßER (TA Instruments AG, Germany)

14:45 – 15:15 **Micro-Structured Surfaces for Assessment of Migratory Phenotypes**
JOACHIM RÄDLER (Ludwig Maximilians University of Munich, Germany)

15:15 – 15:45 *Coffee break*

15:45 – 16:15 **Cytoskeleton Mechanics and Forces in Cancer**
ALLEN EHRLICHER (McGill University, Montréal, Canada)

16:15 – 16:45 **Liver Mechanics and Hepatocellular Carcinoma**
REBECCA WELLS (University of Pennsylvania, USA)

16:45 – 17:15 **Probing the Physical Properties of the Microenvironment Niche**
KANDICE TANNER (National Cancer Institute, USA)

17:15 – 17:30 **Insights about the Role of Single- and Double-Strand Breaks in Cancer Radiotherapy**
FABRIZIO CLERI (Lille University I, France)

17:30 – 18:00 **Physical Dynamics of Cancer Response to Chemotherapy in 3D Micro-environments: A Platform to Examine Complex Physical and Chemical Microenvironments**
LISA J. MCCAWLEY (Vanderbilt-Ingram Cancer Center, Nashville, USA)

18:00 – 18:15 **LINC-ing the Nucleus, the Cytoskeleton and Cancer**
PATRICIA M. DAVIDSON (Institut Curie, France)

18:30 ***Round table: All participants are invited to join a barbecue!***
(Faculty of Physics and Earth Sciences, Linnéstr. 5, 04103 Leipzig)

Session II: Membranes and the Cytoskeleton

08:30 – 09:00 **Cancer Metastasis in Bone: Investigating the Role of Cancer Cell Interaction with Bone Matrix Proteins and Mesenchymal Stem Cells on the Single Cell Level**
HAUKE CLAUSEN-SCHAUMANN
(Center for Applied Tissue Engineering and Regenerative Medicine, Germany)

09:00 – 09:30 **Measuring and Modeling Collective Cell Migration**
WOLFGANG LOSERT (University of Maryland, USA)

09:30 – 10:00 **Cytoskeletal Intermediate Filaments – from Self-Assembly to Cell Mechanics**
SARAH KÖSTER (GEORG AUGUST UNIVERSITY GÖTTINGEN, GERMANY)

10:00 – 10:15 **Multiparametric of Collagen I Self-Assembly, and Cytoskeleton Reorganisation in Living Cells**
DIMITAR STAMOV (JPK INSTRUMENTS AG)

10:15 – 10:45 *Coffee break*

10:45 – 11:15 **The Mechanical Control of CNS Development and Disease**
KRISTIAN FRANZE (University of Cambridge, United Kingdom)

11:15 – 11:30 **Matrix Adhesion Sites Drive 3D Cancer Cell Migration through Direct Force Coupling to the Nucleus**
TOBIAS ZECH (University of Liverpool, United Kingdom)

11:30 – 11:45 **Fiber Slippage in Collagen Matrices Enables Long-range Transmission of Mechanical Signals Between Local Cells**
HAMID MOHAMMADI (The Francis Crick Institute, London, United Kingdom)

11:45 – 12:15 **Mechanics of Cancer Cell Invasion in Vivo**
PETER FRIEDL (The University of Texas, Houston, USA)

12:15 – 12:30 **Investigating Heterogeneity of Tumor Mechanical Properties with Super-Resolution Multifrequency Magnetic Resonance Elastography**
ERIC BARNHILL (Charité Berlin, Germany)

12:30 – 13:00 **Bacteria-Associated Cancer Theranostics: When Bacteria Meet Cancer**
JUNG JOON MIN (Chonnam National University Medical School, Republic of Korea)

Poster Session

13:00 – 15:30 *Presentation of the contributed posters with discussions and lunch buffet.*

1 **Change Matters: a Time-Varying Parameter Model for Cell Migration**
CHRISTOPH MARK (Friedrich-Alexander University Erlangen-Nuremberg, Germany)

2 **TA Instruments - High Performance Thermal and Rheological Characterization**
MATTHIAS QUAIßER (TA Instruments, Germany)

3 **Insights about the Role of Single- and Double-Strand Breaks in Cancer Radiotherapy**
FABRIZIO CLERI (Lille University I, France)

4 **Multiparametric of Collagen I Self-Assembly, and Cytoskeleton Reorganisation in Living Cells**
DIMITAR STAMOV (JPK INSTRUMENTS AG)

5 **Matrix Adhesion Sites Drive 3D Cancer Cell Migration through Direct Force Coupling to the Nucleus**
TOBIAS ZECH (University of Liverpool, United Kingdom)

6 **Fiber Slippage in Collagen Matrices Enables Long-Range Transmission of Mechanical Signals Between Local Cells**
HAMID MOHAMMADI (The Francis Crick Institute, London, United Kingdom)

7 **Investigating Heterogeneity of Tumor Mechanical Properties with Super-Resolution Multifrequency Magnetic Resonance Elastography**
ERIC BARNHILL (Charité Berlin, Germany)

8 **Mechanobiology, Migration and Coordinated Cell-Remodeling in Invading Breast-Cancer Cells**
DAPHNE WEIHS (Technion-Israel Institute of Technology, Israel and CSPO journal)

9 **Novel Tools for Discovery, Development and QC of Therapeutic (Bio)Molecules**
TOBIAS PFLÜGER (NanoTemper Technologies GmbH, Germany)

10 **LINC-ing the Nucleus, the Cytoskeleton and Cancer**
PATRICIA M DAVIDSON (Laboratoire Physico-Chimie, France)

11 **The Role of p130Cas – PKN3 Interaction in Proliferation and Invasiveness**
GEMPERLE JAKUB (Charles University in Prague, Czech Republic)

12 **Cellular Contractile Forces and Migration Measured with a Multi-Well Silicone Device and Gradient Silicone Assay Reveal Physical Changes During Cancer Disease**
HARUKA YOSHIE (McGill University, Canada)

13 **Characterizing Single Cell Migration and Crossing of Chemical Barriers on Ring-Shaped Microlanes**
CHRISTOPH SCHREIBER (Ludwigs-Maximilians-Universität München, Germany)

14 **The Role of Long Non-Coding RNA MALAT1 in the Invasive Behavior of Tumor Cells**
LADISLAV MERTA (Charles University in Prague, Czech Republic)

15 **Membrane-Spanning DNA Channel with Lipid Domain and Ion Selectivity**
AHMED SAYED (University of Leipzig, Germany)

16 **Oligocellular Systems for Accessing Adhesion and Contractility Parameters**
MATTHIAS ZORN (Ludwigs-Maximilians-Universität München, Germany)

17 **Connecting Cell Jamming with Adhesion, Contractility and Cell Stiffness**
JÜRGEN LIPPOLDT (University of Leipzig, Germany)

18 **Microstructure of Sheared Entangled Solutions of Semiflexible Polymers**
MARC LÄMMEL (University of Leipzig, Germany)

19 **TiO_2 Nanotube Scaffolds for Long-Term Organotypic Culture of Adult Mammalian Tissue**
SABRINA FRIEBE (Leibniz Institut für Oberflächenmodifizierungen, Germany)

20 **Construction of a Multifunctional DNA-Based Carrier System for Antisense Oligonucleotide Delivery**
ALEXANDER SPAETH
(Fraunhofer Institute for Cell Therapy and Immunology, Germany)

21 **Toxicity and Biodistribution of Nanoparticle-Delivered Gene Therapeutics In Vitro and In Vivo**
SUSANNE PRZYBYLSKI
(Fraunhofer Institute for Cell Therapy and Immunology, Germany)

22 **DNA-templated Multivalency as a Tool to Regulate Binding and Activation of Cancer Cell Pathways**
CHRISTIN MÖSER
(Fraunhofer Institute for Cell Therapy and Immunology, Germany)

23 **Reptation in Semiflexible Polymer Networks**
TINA HÄNDLER (University of Leipzig, Germany)

24 **Altering Synthetic Semiflexible DNA Nanotube Networks by Tunable Cross-linking**
MARTIN GLASER (University of Leipzig, Germany)

25 **Cellular Jamming in 3D Cancer Aggregates**
LINDA OSWALD (University of Leipzig, Germany)

26 **Synthetic Actin Cross-linkers Slow Down 3D Cell Migration and Invasion**
JESSICA LORENZ (Fraunhofer Institute for Cell Therapy and Immunology, Germany)

27 **Investigations of Single Squamous Cell Carcinoma Cells**
MAJA STRUGACEVAC (Institute of Applied Physics, Germany)

28 **Variability and Reproducibility of Cell Mechanical Measurements with Microconstriction Arrays: Influence of Pressure, Strain, Measurement Parameters and Protein Expression**
JANINA RENATE LANGE (University of Erlangen-Nuremberg, Germany)

29 **Advanced Thermorheology of Living Cells**
ENRICO WARMT (University of Leipzig, Germany)

30 **Occupancy and Stochastic Transitions of Single Cells on Double-Well Micropatterns**
ALEXANDRA FINK (Ludwig-Maximilians-Universität München, Germany)

Afternoon ***City tour:*** *Leipzigs city centre with Josef Käs*

Evening ***Social Event for Invited Speakers: Dinner at "Auerbachs Keller"***

Convergent Science
Physical Oncology

Session III: Cell Migration in Cancer

08:30 – 09:00 **Novel Methods to Study Cancer Cell Migration and Invasion**
Ben Fabry (Friedrich-Alexander University of Erlangen-Nuremberg, Germany)

09:00 – 09:30 **Mechanical Aspects of Angiogenesis**
Stefan Zahler (Ludwig Maximilian University of Munich, Germany)

09:30 – 10:00 **Basement Membrane Fragments Contribute to the Regulation of the Epithelial-to-Mesenchymal Transition**
Christine-Maria Horejs (Karolinska Institutet, Sweden)

10:00 – 10:30 *Coffee break*

10:30 – 11:00 **Mechanobiology, Migration and Coordinated Cell-Remodeling in Invading Breast-Cancer Cells**
Daphne Weihs (Technion-Israel Institute of Technology, Israel and CSPO journal)

11:00 – 11:30 **Gene Therapy Coming of Age**
Dietger Niederwieser (University Hospital Leipzig, Germany)

11:30 – 12:00 **Programming the Mechanical Properties of Bionic Networks**
Jörg Schnauß (University of Leipzig, Germany)

12:00 – 12:30 **Employing Nanostructured Scaffolds for Long-Term Adult Tissue Culture and Investigation of Tissue Mechanics at the Nanoscale**
Mareike Zink (University of Leipzig, Germany)

12:30 – 14:00 *Lunch break*

Session IV: Micro Tools in Cancer Research

14:00 – 14:30 **Condensing DNA into Nanostructures**
Friedrich Simmel (Technical University Munich, Germany)

14:30 – 15:00 **Why Do Rigid Tumors Contain Soft Cancer Cells?**
Josef A. Käs (University of Leipzig, Germany)

15:00 – 15:30 **Dynamics of Circular Dorsal Ruffles and their Role in Cancer**
Hans-Günther Döbereiner (University of Bremen, Germany)

15:30 – 16:00 **Cell Binding Peptides from Statistical Analysis of Random Peptide Phage Display Libraries**
MICHAEL SZARDENINGS
(Fraunhofer Institute for Cell Therapy and Immunology, Leipzig, Germany)

16:00 – 16:30 *Coffee break*

Special Focus Session: Programming Nanomaterials Against Cancer

16:30 – 17:00 **Spatial Signalling at the Membrane**
ANA TEIXEIRA (Karolinska Institutet, Sweden)

17:00 – 17:30 **Bottom-up Engineering of Nanoscale Devices to Program Biological Materials**
DAVID M. SMITH
(Fraunhofer Institute for Cell Therapy and Immunology, Leipzig, Germany)

17:30 – 17:45 **Novel Tools for Discovery, Development and QC of Therapeutic (Bio)Molecules**
TOBIAS PFLÜGER (NanoTemper Technologies GmbH, Germany)

17:45 – 18:15 **Membrane - Targeting DNA Nanostructures**
RALF SEIDEL (University of Leipzig, Germany)

18:15 – 18:45 **Death by Gold: Targeting Invasive Glioblastoma Cells by Peptide - Functionalized Gold Nanorods**
DIANA GONCALVES-SCHMIDT (Leibniz-Institut for Polymer Research Dresden, Germany)

19:00 *Prospective end*

Session I: Functional Mechanics of Cancer Cells

Invited Talk Tue 13:15

Effect of Hyaluronic Acid on Mechanoresponse of Cancer Cells — PAUL JANMEY — University of Pennsylvania, IME & Department of Physiology 1010 Vagelos Research Labs, 3340 Smith Walk Philadelphia, PA 19104-6393, U.S.A.

Changes in cancer cell phenotype in response to the mechanical properties of their substrate are well-documented, but also highly dependent on the chemistry of the cell-matrix adhesion site. They also vary strongly between different cell types. By studying the response of 30 different human cancer cell lines to seven different substrates, certain patterns of mechanical response emerge. Different cell lines derived from human breast and colorectal cancers respond strongly to changes in substrate stiffness, but often very differently when they are bound to collagen-coated surfaces compared to fibronectin-coated surfaces. In contrast, cells derived from prostate and pancreatic tumors appear to have diminished response to the mechanical features of their substrate. Perhaps most striking is the response of the cell lines to substrates that contain both an integrin ligand and hyaluronic acid, a common extracellular matrix polymer that is often upregulated in cancer. Even very soft (200 Pa) substrates made from a cross-linked network of hyaluronic acid linked to an integrin ligand can stimulate many cancer cell types to spread, locomote and proliferate much more than they do on equally soft polyacrylamide gels coated with the same ligand, and often as much as they do on very stiff substrates or glass.

Invited Talk Tue 13:45

Phenotyping Single Cell Derived Microtissues by Time-Resolved Imaging and Molecular Sequencing

— ROLAND EILS, STEPHAN M. TIRIER, JULIA NEUGEBAUER, ZUGUANG GU, JAN-PHILIPP MALLM AND CHRISTIAN CONRAD — German Cancer Research Center, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany

Recent developments in DNA sequencing technology now enable sequencing of the human genome for less than US$1,000 making whole genome sequencing affordable for routine diagnostics for increasingly larger sets of cancer patients. Hundreds of thousands of patient genomes will become sequenced in the next few years, and in Germany alone we expect completion of >25,000 individual cancer genomes by 2018. While those estimates are made on the basis that for each tumor only one sample is sequenced it has become clear that averaging over millions of cells in a given tumor sample may hide subtle, but clinically important genomic alterations that are only present in a small fraction of cells. Here, I will report on our recent development of an integrated imaging and sequencing pipeline that allows growing of microtissues from single patient derived cancer cells, dynamic phenotyping of those microtissues over many days and subsequent harvesting of individual cells followed by molecular sequencing. By this strategy, we aim to integrate sequencing with image-based phenotyping and drug profiling ex vivo of patient derived single cancer cells to comprehensively tackle intratumour cellular heterogeneity.

Contributed Talk Tue 14:15

Change Matters: a Time-Varying Parameter Model for Cell Migration — CHRISTOPH MARK, CLAUS METZNER, JULIAN STEINWACHS, LENA LAUTSCHAM, BEN FABRY — Friedrich-Alexander University Erlangen-Nürnberg, Department of Physics, Biophysics group, Henkestraße 91, Erlangen, Germany

Depending on cell type and the local environment, tumor cells show a variety of different migration modes, including mesenchymal and amoeboid motion. As the cell interacts with a spatially changing extracellular matrix, cell movements are highly heterogeneous in space and time and thus do not comply with conventional statistical models. Common measures of cell motility which regard cell migration as a homogeneous random walk (like the step width distribution or the mean squared displacement) may therefore fail to distinguish between cell migration in different environments as well as the migration patterns of different cell

types. To provide a more sensible measure of cell motility, we build stochastic models for cell migration that explicitly allow for temporal changes of its parameters. As the parameters of such models may change at each time step, the number of parameter values to infer from measured data is proportional to the number of recorded cell movements. The two existing approaches to fit such high-dimensional models (Hamiltonian Monte Carlo and Variational Bayes) either do not scale well for long time series, or do not provide an objective measure of goodness-of-fit or require expert knowledge to adapt them to different models. To overcome these issues, we use a sequential inference approach, effectively breaking down one high-dimensional inference problem into many low-dimensional ones. We subsequently solve these low-dimensional inference problems by approximating the probability distributions of the parameters on a discrete, regular grid. This grid-based approach allows for an efficient calculation of the model evidence, i.e. the probability that the data is produced by the model. The model evidence as an objective measure of goodness-of-fit is essential to test the existence and infer the magnitude of temporal parameter changes. Our method can be applied to a large class of time-varying parameter models and is available as open-source Python code. Here, we reconstruct the time-varying directional persistence and migratory activity from measured migration paths of tumor cells in 1-, 2- and 3-dimensional environments. First, we show that our estimates of cell persistence and activity highly correlate with the local micro-environment of the cell, using a micro-structured array of narrow channels and wide chambers. We demonstrate that the temporal changes in persistence and activity, rather than their mean values, provide a distinct fingerprint of the strategies that cells employ to cope with different environments. For example, persistence is positively correlated with activity in a 3-dimensional collagen matrix over much longer time periods compared to migration on 2-dimensional substrates, supporting the hypothesis that cells are able to pull themselves along collagen fibers and hence use the surrounding matrix to their advantage. To test this hypothesis, we measure cell pulling forces in a collagen gel with 3D traction force microscopy. We find that directional persistence of invading MDA-MB-231 breast carcinoma cells is highly correlated with contractility and cell elongation. Finally, we analyze the migration of four different cell types (A125, MDA-MB-231, HT1080, IFDUC) on a 2-dimensional substrate. We show that the cross-correlation between persistence and activity allows to accurately classify the cell type based only on its dynamics. Furthermore, the prevalence of phases with simultaneously high/low persistence and activity shows an intriguing connection to the respective invasivity of these four cell types in 3-dimensional collagen gels.

Contributed Talk Tue 14:30

TA Instruments - High Performance Thermal and Rheological Characterization — MATTHIAS QUAIßER — TA Instruments, Germany

Many of you have long known TA Instruments for expertise in DSC, TGA and DMA thermal equipment, as well as the popular ARES and DHR rheometers. In 2013, TA Instruments made a bold statement about its commitment to the rubber and elastomer industry with the acquisition of Scarabaeus GmbH (a supplier of high quality RPA, MDR, Mooney, hardness and density equipment and software). Additionally, last year, TA announced the acquisition of certain assets related to the ElectroForce® Systems Group, from the Bose Corporation. The ElectroForce group manufactures dynamic mechanical testing systems used to characterize a wide variety of engineered materials, including plastics, polymers and elastomers.

In 2016, TA Instruments launched a brand new Thermal analysis line that includes the Discovery DSC and Discovery TGA. Incorporating many patented TA technologies, these products once again set new standards in performance, reliability, and ease of use. Backed by TA's global service organization and in house application expertise, TA has solidified its position as the leader in the Thermal Analysis product space.

Additionally, In 2016 TA announced the acquisition of Rubotherm GmbH. The patented magnetic balance technology of Rubotherm extends TA's capability in TGA to now include high pressure and high temperature applications in challenging environments.

TA Instruments – a subsidiary of Waters Corporation (NYSE: WAT) – is the leading manufacturer of analytical instruments for thermal analysis, rheology and microcalorimetry. The company is headquartered in New Castle, Delaware, USA, and has direct operations in 24 countries.

Invited Talk Tue 14:45

Micro-Structured Surfaces for Assessment of Migratory Phenotypes — J. O. RÄDLER — Ludwig-Maximilians-University Munich, Geschwister-Scholl-Platz 1, 80539 München, Germany

Collective cell migration is a hallmark in cancer development and progression. One of the challenges in the field is to bridge collective cell dynamics to single cell migration. The talk provides a perspective on how micro-structured surfaces, which confine cell migration, facilitate quantitative assessment of migratory phenotypes. Using time-lapse microscopy we first analyze the directed flow of Madin–Darby canine kidney (MDCK) cells in micro-channels and examine velocity correlations and spontaneous formation of vortices. We compare the collective behavior with the distinct modes of rotational migration found in confined mesoscopic systems consisting of a small number of cells on circular micro-pattern. The particular vortex states are reproduced in computer simulations based on a generalized Potts model. In agreement with experiment the model shows that vortex stability depends on the interplay of the spatial arrangement and internal polarization of neighboring cells. We then report on novel modes of migration observed in ring-shaped micro-lanes with artificial barriers and dumbbell-like structures. We demonstrate that micro-patterned surfaces open up novel approaches to probe multiple motility parameters with potential applications in cancer research and drug screening.

[1] A. K. MAREL, M. ZORN, C. KLINGNER, R. WEDLICH-SOLDNER, E. FREY AND J.O. RÄDLER, *Biophysical Journal 107(5), 1054 (2014)*

[2] F. J. SEGERER, F. THÜROFF, A. P. ALBEROLA, E. FREY, AND J.O. RÄDLER, *Physical Review Letters 114, no 22 228102 (2015)*

[3] C. SCHREIBER, F. J. SEGERER, E. WAGNER, A. ROIDL, AND J. O. RÄDLER, *Scientific Reports 6 26858 (2016)*

Invited Talk Tue 15:45

Cytoskeleton Mechanics and Forces in Cancer — ALLEN J. EHRLICHER — McGill University, Department of Bioengineering, 817 Sherbrooke Street West, Montreal QC H3A 0C3, Canada

Cell migration and force generation are ubiquitous and essential elements of biology throughout development, and their dysfunction plays a critical role in disease. Cancer progression and metastasis while linked to hundreds of specific mutations in different cell types may share similar changes in their physical attributes that contribute to the process of dispersion into new tissues. I will discuss our ongoing efforts to understand how these underlying changes that are related to the cytokseleton are linked to mechanics, movement, and the progression of disease.

Invited Talk Tue 16:15

Liver Mechanics and Hepatocellular Carcinoma — REBECCA G. WELLS — University of Pennsylvania, 421 Curie Boulevard, Philadelphia, PA 19104, U.S.A.

Hepatocellular carcinoma (HCC) is the second most common cause of death from cancer in the world. Approximately 90% of HCCs occur in cirrhotic (advanced fibrotic) livers, which are highly abnormal mechanically, and the risk of HCC increases dramatically in parallel with increased liver stiffness. HCC is the cancer most strongly associated with increased tissue stiffness. Our goal has been to determine the tissue mechanics of the normal and cirrhotic liver and to define the impact of these mechanical changes on hepatocytes, the major cells of the liver and the source cells for HCC. We have demonstrated in both rat models of liver fibrosis and in human livers that shear modulus increases significantly as fibrosis increases, although not linearly with increased matrix content. Livers demonstrated shear strain softening and compression stiffening, the latter of which increased significantly in advanced fibrosis and appeared to be secondary to a combination of proteoglycan content and cell-matrix interactions. Advanced fibrosis and cirrhosis are architectural definitions, and we show that the large-scale architectural arrangements associated with these stages of fibrosis are secondary to the mechanical properties of liver cells and matrix. Human HCCs were significantly stiffer than the cirrhotic tissue surrounding them and had increased proteoglycans and hyaluronic acid. Our data highlight the complex mechanics of the normal liver and the changes that occur in cirrhosis. Consistent with the hypothesis that these mechanical and matrix changes drive the development or progression of HCC, changes in the matrix and mechanical environment had a significant impact on hepatocyte phenotype in vitro.

Invited Talk Tue 16:45

Probing the Physical Properties of the Microenvironment Niche — KANDICE TANNER — Laboratory of Cell Biology, Center for Cancer Research, National Cancer Institute (NIH), Bethesda, MD 20892-4256, U.S.A.

Tissue microenvironment is composed of heterogeneous biological components and physical parameters, and nanometric topography in 3D is one of crucial factors that influence on cell phenotype, tissue morphogenesis and cancer progression. . Here we aim to distinguish the contributions of the physical from those due to chemical properties on cell fate as it relates to malignancy and normal tissue homeostasis. However, delineating the complex interplay between cells and their physical microenvironment is challenging using current techniques. What is needed is the ability to resolve and quantitate minute forces that cells sense in the local environment (on the order of microns) within thick tissue (in mm). 3D culture models approximate in vivo architecture and signaling cues, allowing for real time characterization of cell-ECM dynamics. We employ two approaches where we recreate diverse nanoscale topographies of protein distributions in 3D matrix for the purpose of mimicking tissue microenvironment. To achieve this, we chemically immobilize the proteins on the surface of magnetic nanoparticles then using an applied magnetic field –to program self-assembly. Using this simple technique, we achieved diverse 3D topography by varying fibril diameter, spacing and localized or interfaced architecture of proteins, and independent of other material parameters of the matrix, such as stiffness. Next, we employ a novel method to quantitate absolute physical properties of tissue. We present active Microrheology by optical trapping in vivo, using in situ calibration to accurately apply and measure forces to quantitate tissue mechanics. With micrometer resolution at broadband frequencies and depths approaching 0.5 mm, aMotiv applies differential stresses and strains on force, time and length scales relevant to cellular processes in living zebrafish. We determined that proxy calibration methods overestimate complex moduli by ~20 fold. While ECM hydrogels displayed rheological properties predicted for polymer networks, new models may be needed to describe the behavior of tissues observed. We believe that this platform can be used in elucidating the basic mechanisms that govern the role of material properties in mechanobiology.

Contributed Talk Tue 17:15

Insights about the role of single- and double-strand breaks in cancer radiotherapy — FABRIZIO CLERI[1], DOMINIQUE COLLARD[2], HIROYUKI FUJITA[3], ERIC LARTIGAU[4], CORINNE ABBADIE[5] — [1]Universite de Lille I, IEMN, Av. Poincare, 59652 Villeneuve d'Ascq, France — [2]CNRS and IRCL, SMMIL-E Project, Place de Verdun, 59045 Lille, France — [3]University of Tokyo, CIRMM, 4-6-1 Komaba, Meguro-ku, Tokyo, Japan — [4]Regional Cancer Center, Rue F. Combemale, 59000 Lille, France — [5]Universite de Lille I and Institut de Biologie, Rue Calmette, 59021 Lille, France

Among the defects produced in DNA by various endogenous and external agents, single- and double-strand breaks (SSB and DSB) stand out as the most critical for cell survival and multiplication. Controlled production of such defects, and most notably DSBs, is indeed at the heart of cancer radiotherapy. However, the detailed microscopic mechanisms of production of SSB and DSB defects in DNA is not well understood: practically, all the information is currently obtained from chemical methods, by post-processing at much later stages after the time of irradiation, and the clinical relevance of such defects is empirically deduced from "cell survival" radiobiological curves, to be further interpreted with few-parameter phenomenological models (such as the venerable Linear-Quadratic model).
In the past few years, we started a wide-scoped biophysical program, involving biophysicists, engineers, biologists and clinicians, dedicated to the investigation of SSB and DSB production in both isolated DNA and in live cells by means of therapeutic photon beams. We demonstrated the first ever causal observation of DNA degradation in real-time by a custom developed micro-electro mechanical device (MEMS) [1], and developed a theoretical framework based on the statistical mechanics of damaged fibre bundles [2]. In our approach, DNA bundles of a few thousand parallel molecules are captured between the vibrating tips of the MEMS with a few micrometer opening, and irradiated by a 20-MeV Cyberknife photon beam; by monitoring in real-time the variation of resonant frequency and quality factor, the number (and possibly, the quality) of defects produced in the DNA bundle can be detected. The biophysical analysis with a second-order kinetics equation allows interpreting the experimental observations.

In parallel, we developed a program of in-vitro irradiation of live fibroblast cells under the 6-MeV Varian LINAC photon beam, to investigate the differential production of SSBs and DSBs according to the distance of the cells from the beam center, as well as other biological and physical parameters. The production of DNA defects is monitored by fixing the irradiated cells at different times, and correspondingly detecting the fluorescence of XRCC1 and 53BP1 repair proteins, as well as by comet assays. In this case, an agent-based Monte Carlo simulation model has been developed [3], to test different hypotheses of cell population evolution under irradiation, and compare the results to the experimental observations.

In a third, parallel line of research, we are developing molecular simulations by both classical and ab-initio molecular dynamics, to describe the early stages of strand-break defect formation and evolution. We study the role of oxidative and reducing pathways in attacking the DNA backbone by hybrid quantum/classical dynamics, while by large-scale classical simulations we attempt at following the complex defect evolution, after the initial breaking of O-P-O backbone covalent bonds. Another companion experimental program based on singe-molecule spectroscopy with optical tweezers, to couple to such microscopic simulations, is just starting.

The ensemble of such coupled theoretical/experimental actions is providing numerous new insights about the relative role and efficacy of DNA defects in cancer radiobiology. We are starting to formulate some novel hypotheses, also at variance with the common wisdom, which will be main subject of discussion of this talk, after a brief overview of our program.

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Invited Talk Thu 17:30

Physical Dynamics of Cancer Response to Chemotherapy in 3D Microenvironments: A Platform to Examine Complex Physical and Chemical Microenvironments — Lisa J. McCawley[1], Katarzyna A. Rejniak[2], Rahul Telange[1], Aleksandra Karolak[2], Phillip Fryman[1], Gloria Bazilevich[1], Dmitry A. Markov[1] — [1]Vanderbilt-Ingram Cancer Center, 2220 Pierce Ave, 738 Preston Building Nashville, TN 37232-6840, U.S.A. — [2]H. Lee Moffitt Cancer Center & Research Institute – IMO, Tampa, Florida, USA

Recent advances and successes in microfabricated organs-on-chips and human organ constructs have made it possible to design scaled and interconnected organ systems that may significantly augment the current development of new model systems for toxicology, systems biology and oncology allowing for dynamic monitoring of tissue behavior. Tissue microenvironment, especially within the tumor, is highly complex and can evolve not only during tumor outgrowth but also when anticancer treatments are administered.

In vivo, tumor behavior is modified by its own microenvironment receiving cues through structural information by surrounding extracellular matrix (ECM), and through the surrounding chemical nature such as the state of oxygenation or acidity. The microenvironment of advanced tumors is frequently hypoxic due to a variety of factors that result in abnormal vasculature with reduced oxygen transport and increased diffusional space between tissue compartments. Another defining feature of malignant tumors is enhanced glycolysis that leads to production of lactate and H+ ions, resulting in an increasingly acidic environment. As a result, the type of tumor microenvironmental selects for tumor cells that can thrive within these harsh conditions and profoundly impacts anti-tumor drug efficacy. We are developing a new computationally driven platform to examine these complex physical and chemical microenvironments utilizing organ-on-chip microfluidic bioreactor technology coupled with a predictive mathematical model of tumor growth and therapeutic response. This integrated platform combines the power of organ-on-chip 3D tissue bioreactor, developed to include uniform and non-uniform fully controlled physical and chemical microenvironments, together with a 3DMultiCel math model that allows predictive testing of a broad range of microenvironmental combinations around the experimentally validated baseline. We are applying this technology to applications of anti-tumor drug efficacy of mammary tumors under mixed microenvironments as well as toxicant evaluation on normal mammary development including hyperplasia assessment.

Contributed Talk Tue 18:00

LINC-ing the Nucleus, the Cytoskeleton and Cancer — PATRICIA M DAVIDSON[1], BRUNO CADOT[2], TIMO BETZ[3], CÉCILE SYKES[1] — [1]Laboratoire Physico-Chimie, UMR 168, Institut Curie, Paris, France — [2]Institut de Myologie, Paris, France — [3]Center for Molecular Biology of Inflammation-ZMBE Cell Biology, Münster, Germany

Cancer is now the leading cause of death in economically developed countries. The presence of secondary tumors (also called metastases) are a poor prognostic factor, and the cause of 90% of cancer deaths.[1] A promising strategy to reduce mortality is to target the mechanisms by which cells leave the primary tumour and disseminate through the body. To migrate through tissues, cells have to overcome the mechanical resistance of their large and rigid nucleus, which I (and others) have shown to be a limiting factor during 3-D migration.[2] Considerable force needs to be applied by the cytoskeleton to the nucleus, yet many aspects of mechanical linkage and force transmission from the cytoskeleton to the nucleus are still poorly understood. Many nuclear envelope proteins, including nesprins, which mechanically link the actin cytoskeleton to the nuclear membrane have been implicated in cancer.[3] The cytoskeletal actors that mediate force exertion on the nucleus to translocate it through narrow constrictions have yet to be fully identified. However, non-muscle myosin IIB is necessary for cell migration through constrictions in breast cancer[4] and glioma cells,[5] strongly implying that actomyosin contractility is the major contributor. Furthermore, actin-associated proteins which bind nesprins such as FHOD1 are necessary for nuclear movement[6] and fascin[7] is required for nuclear translocation through narrow constrictions.

My hypothesis is that nesprin expression is altered in migrating cancer cells, allowing more efficient transmission of forces to the nucleus and therefore more efficient 3D migration. To verify this hypothesis, I am investigating the nesprin isoform composition of metastatic cells, verifying the ability of these cells to migrate through narrow 3-D constrictions more efficiently, and rebuilding and studying the nesprin-actin physical connection in vitro.

Nesprin isoform composition of metastatic cells.

The nesprin family is comprised of four genes that encode many different isoforms.[8] Giant nesprin isoforms of nesprins-1 and 2 (~1mDa and 800 kDa, resp.) anchor into the nuclear envelope through their KASH domain by binding SUN proteins (themselves anchored into the nuclear lamina)[9] and they bind actin fibers directly through calponin homology (CH) domains. These connections are crucial for many processes that involve force transmission to the nucleus.[10] SYNE1 and 2, which encode nesprin-1 and 2, are candidate cancer genes, and an antibody for the actin-binding domain of nesprin 2 showed increased expression in tumours,[11] but the expression of nesprins in metastatic cells has yet to be fully investigated.

Using an antibody that recognizes the KASH domain of nesprins-1 and 2, I used western blot to identify the expression levels of two patient metastatic cell lines and MCF-10A cell (healthy breast cell line). The highest molecular weight bands detected (presumably the giant isoforms) were clearly labelled for both metastatic cell lines, but only faintly detectable for nesprin-2 for the control cells. The control cells predominantly expressed lower molecular weight isoforms.

Ability of metastatic cells to migrate through narrow constrictions.

I compared the migration ability of these cells in devices that I developed.[12] By comparing the migration time of the nucleus through 3 µm constrictions to the time required to pass through a 15 µm control channel, I obtain the normalized migration time indicative of the barrier that the nucleus represents during migration. The two metastatic cell lines had shorter normalized migration times than the control cells, indicating that they passed their nucleus through constrictions more easily than control cells, despite equivalent or higher lamin A/C levels (and consequently increased nuclear stiffness). Thus, the metastatic cells appear to have an increased ability to deform their nucleus through narrow constrictions compared to the control cells, independently of stiffness.

Rebuilding actin-nucleus interactions in vitro.

I isolated nuclei from fibroblasts using a hypotonic buffer and a shearing protocol. I showed that nesprins at the nuclear membrane are recognized using antibod-

ies for the calponin homology domain, indicating that these domains are intact following the isolation procedure. In vitro reconstitution of actin filaments in the presence of isolated nuclei shows that filaments coat the surface of the nuclei. Using an antibody that masks the actin-binding site of nesprin significantly reduces this interaction, implying that we are specifically observing actin binding to nesprins.

Future experiments to characterize the biophysical properties of the nesprin-actin interaction are planned. These include measuring the mobility and recruitment of nesprins in presence and absence of actin (FRAP experiments, actin shell peeling, deposition of nuclei on actin patches). I will also characterize the amount of force that can be transferred to the nesprin-actin connection using optical tweezers, and determine whether nesprins bind more strongly to actin architectures that resemble peri-nuclear actin, and whether nesprins can induce actin organization.

I demonstrate here that metastatic patient cells are able to deform their nucleus more efficiently to migrate in 3-D small spaces and show increased levels of the giant isoforms of nesprins-1 and 2, indicating an increased ability to mechanically link their nucleus to the actin cytoskeleton for force exertion. By rebuilding the interactions between the nucleus and reconstituted actin filaments in vitro, I will characterize the biophysical interactions between nesprins and actin.

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Round Table **Tue 18:30**

Discussion of students, junior academics, and senior professors on future developments.

Barbecue at Faculty of Physics and Earth Sciences, Linnéstr. 5, 04103 Leipzig.

Session II: Membranes and the Cytoskeleton

Invited Talk Wed 08:30

Cancer Metastasis in Bone: Investigating the Role of Cancer Cell Interaction with Bone Matrix Proteins and Mesenchymal Stem Cells on the Single Cell Level — Ediz Sariisik[1,2,3,4], Stefanie Sudhop[1,2,3], Domenik Zistl[1,2], Daniela Padula[2,3], Cvetan Popov[3,4], Jan Oper[3,4], Cem Saracel[1,6], Matthias Schieker[1,5], Denitsa Docheva[1,5], Arndt Schilling[1,6], Martin Benoit[3,4], Hauke Clausen-Schaumann[1,2,3] — [1]Center for Applied Tissue Engineering and Regenerative Medicine (CANTER), Munich University of Applied Sciences, Munich, Germany — [2]Department of Applied Sciences and Mechatronics, Munich University of Applied Sciences, Munich, Germany — [3]Center for NanoScience, Ludwig-Maximilians-University, Munich, Germany — [4]Chair of Biophysics and New Materials, Ludwig-Maximilians-University, Munich, Germany — [5]Experimental Surgery and Regenerative Medicine, Department of Sugery, Ludwig-Maximilians-University, Munich, Germany — [6]Experimental Plastic Surgery, Clinic for Plasic and Hand Surgery, Klinikum Rechts der Isar, Technical University of Munich. Munich Germany

For some of the most common cancer types, including prostate cancer and breast cancer, the formation of bone metastases is a frequent complication. The spread of the cancer cells into the skeleton is associated with a poor prognosis for the patient. Although the molecular mechanisms of cancer cell growth in the bone microenvironment have been an area of active investigation, the initial steps of tumor cell-to-bone interaction, that lead to cancer cell colonization, remain to be elucidated. In any case, a complex, bidirectional interplay between cancer cells with bone matrix proteins and with cell types residing in the bone tissue is supposed to be involved: Cancer cells express adhesion molecules (e. g. Integrins) that may facilitate their interaction with bone matrix proteins and therefore contribute to their invasive capability and progression into the bone. These adhesion molecules may also play a role in cross-talk between tumor cells with mesenchymal stem cells (MSC) residing in the bone marrow. It is assumed, that MSCs stimulate the invasion of tumor cells into the bone by remodeling the bone microenvironment and thus creating a physical space where the cancer cells can enter. In this study we investigated the adhesive capacity of the two prostate carcinoma cell lines PC3 (bone marrow specific) and LnCAP (lymph node specific). Using atomic force microscopy (AFM) based force spectroscopy, the adhesion patterns on bone-marrow derived stem cells (SCP1) and collagen type I, the major bone matrix protein, for both cell line have been analyzed. PC3 cells have a higher affinity to SCP1 cells as well as to collagen type I compared to LnCAP cells. By β1-Integrin-antibody-blocking the adhesion events were reduced, indication a role of these adhesion molecules in cancer cell-to-bone interaction.

An additional factor that may have influence metastasis development might be the mineralization state of the bone tissue. In case of breast cancer, epidemiological studies have correlated calcium and/or vitamin deficiencies in patients with increased tumor metastatic growth. On the other hand, Vitamin D treatment increases survival rates and prolongs disease-free intervals of the patients. The biological mechanisms underlying the effect of Vitamin D in cancer therapy is not well understood. Recent studies mainly focused on the response of cancer cells on Vitamin D treatment. In contrast, we put the effect of Vitamin D on bone mineralization to the fore and investigated the adhesion of the invasive and non-invasive breast cancer cell lines MDA-MB-231 and MCF-7 on poorly mineralized matrix compared to mineralized matrix.

Invited Talk Wed 09:00

Measuring and Modeling Collective Cell Migration — Wolfgang Losert — University of Maryland, Department of Physics, Physical Sciences Complex, College Park, MD 20742, U.S.A.

The metastatic process begins when cells migrate away from the primary tumor in small groups. Thus the long process of metastasis starts with changes in the collective behavior of primary tumor cells. I will describe our recent effort to capture and measure these changes in collective migration using metrics that capture a broad

range of lengthscales and timescales. By analyzing migration dynamics from multiple scales and perspectives, we are able to make a clear comparison of our experimental results to a simulation of collective cell migration, and provide a nuanced phenotype of collective behavior. To further elucidate basic mechanisms that can underly collective behavior, we analyze how changes in cytoskeletal dynamics, cell cell adhesion and cell-substrate adhesion alter collective cell migration in a simple cell model system.

Invited Talk Wed 09:30

Cytoskeletal Intermediate Filaments - from Self-Assembly to Cell Mechanics — Sarah Köster — Georg-August-University Göttingen, Institute for X-Ray Physics, Friedrich-Hund-Platz 1, 37077 Göttingen, Germany

Biological cells are pervaded by a dense biopolymer network of fibrous proteins, collectively called the cytoskeleton. The exact structures comprising this composite network are majorly important for the mechanical properties of the cells, which in turn support their physiological function. The cytoskeleton consists of three filamentous systems, actin filaments, microtubules and intermediate filaments (IFs) along with a plethora of binding proteins and molecular motors. Among the three filamentous systems, IFs self-assemble in a highly hierarchical manner giving rise to a very particular molecular architecture. IFs are expressed in a cell type specific manner and are thus being discussed as strong candidates for the precise definition of the different mechanical properties of different cell types. Interestingly, during epithelial-to-mesenchymal transition (EMT), which plays a role for example in cancer metastasis, keratin IF proteins are down-regulated while vimentin IF proteins are up-regulated. Our research focuses on the relation between molecular structure and mechanical properties of filaments and cells. I will present state-of-the art experiments and recent results on the self-assembly of the proteins into filaments and networks. The relevant length scales for these processes range between few nanometers and many micrometers. Therefore, we employ small angle x-ray scattering (SAXS), x-ray nano-diffraction, static and dynamic light scattering (SLS/DLS), fluorescence correlation spectroscopy (FCS), and fluorescence microscopy. As some of these methods are inherently slow and thus provide only a low time resolution, we combine the observation techniques with microfluidics to obtain in situ data.

Contributed Talk Wed 10:00

Multiparametric of Collagen I Self-Assembly, and Cytoskeleton Reorganisation in Living Cells — Dimitar R. Stamov[1], Sandra Kostrowski[1], Clemens M. Franz[2], Torsten Jähnke[1], Heiko Haschke[1] — [1]JPK Instruments AG, Department of Application Science, Colditzstr. 34-36, 12099 Berlin, Germany — [2]DFG-Center for Functional Nanostructures (CFN), Karlsruhe Institute of Technology (KIT), Wolfgang-Gaede-Str. 1a, 76131 Karlsruhe, Germany

Living cells are highly dynamic systems, and feature ensembles of well-integrated macromolecular and signalling networks, used for their function and communication with the environment. Conventional high-resolution microscopy techniques, such as TEM, SEM, or fluorescence microscopy typically require sample treatment, thus inherently affecting relevant cell characteristics, such as morphology, adhesion, and mechanical properties. In turn this hinders the study of important cellular functions and state, namely morphogenesis, differentiation, or cell division.

Studying the single macromolecule dynamics and the function of complex biological systems, such as living cells, requires a tool that can meet the requirements for both high spatial and temporal resolution. Atomic force microscopy (AFM) still remains the only technique that offers premium resolution of the analysed biological systems, while being able to simultaneously acquire information about the sample's mechanical properties at near physiological/native sample conditions. Very recent high-speed AFM developments have also made possible the acquisition of single images on the time-scale of seconds, and even milliseconds.

We will give examples of applying fast AFM for imaging of membrane dynamics of KPG-7 fibroblasts, and the cytoskeleton reorganisation of living CHO cells, demonstrated by realtime videos reaching 1 frame per second. We will also show how AFM can be combined with super-resolution optical techniques, such as D-STORM and STED, to study high-resolution cytoskeleton structure simultaneous to AFM. This will be extended to tuning the in vitro fibril formation dynamics of collagen type I, a common scaffold used in cell culture scenarios.

We have recently developed, a quantitative imaging force tool, which allows the combination of nanotopographical resolution and the multiparametric mechanical characterisation (stiffness, adhesion) of the specimens.
The demonstrated combination of an AFM setup with advanced optical microscopy allows the long-term and non-invasive study of dynamic macromolecular processes, further supplemented by complex data analysis including Young´s modulus images, topography at different indentation forces resulting in 3D tomographic sample reconstruction.

Invited Talk Wed 10:45

The Mechanical Control of CNS Development and Disease — Kristian Franze — University of Cambridge Department of Physiology, Development and Neuroscience, Downing Street Anatomy Building, Cambridge CB2 3DY UK

During the development of the nervous system, neurons migrate and grow over great distances. During these processes, they are exposed to a multitude of signals determining how they grow. Currently, our understanding of neuronal development and function is, in large part, based on studies of biochemical signaling. Despite the fact that forces are involved in any kind of cell motion, mechanical aspects have so far rarely been considered. Here we show how Xenopus neurons respond to their mechanical environment. Axonal growth patterns in vitro strongly depended on substrate stiffness. In vivo atomic force microscopy measurements revealed stiffness gradients in developing brain tissue, which axons followed towards soft. This turning away from stiffer substrates was reproduced in vitro – in the absence of chemical gradients. Globally and locally interfering with brain stiffness, blocking mechanotransduction pharmacologically, and knockdown of the mechanosensitive ion channels Piezo1 in vivo all led to similar aberrant neuronal growth patterns with reduced fasciculation and pathfinding errors, strongly suggesting that neuronal growth is not only controlled by chemical signals – as it is currently assumed – but also by the tissue's local mechanical properties. Importantly, the mechanics of CNS tissue changed after mechanical trauma and demyelination. Furthermore, primary human glioblastoma cells showed distinct mechanical features depending on their location within the tumor. Our results thus suggest an important role of mechanical signals in health and disease of the nervous system.

Contributed Talk Wed 11:15

Matrix adhesion sites drive 3D cancer cell migration through direct force coupling to the nucleus — Tobias Zech[1], Daniel Newman[1], Iben Ronn-Vehland[2], Vineetha Vijayakumar[3], Gareth E. Jones[3], Patrick T. Caswell[4], Mark R. Morgan[1], Laura M. Machesky[2] — [1]University of Liverpool, Institute of Translational Medicine, Cellular and Molecular Physiology, Crown Street, Liverpool, L69 3BX, UK — [2]The Beatson Institute for Cancer Research, Switchback, Rd., Bearsden, Glasgow, G61 1BD, UK — [3]King's College London, Randall Division of Cell & Molecular Biophysics, London WC2R 2LS, UK — [4]University of Manchester,3Wellcome Trust Centre for Cell Matrix Research, Faculty of Life Sciences, Manchester, M13 9PT, UK

The nucleus is a major constraint on cells migrating through a dense 3D matrix, as cells must actively squeeze their nuclei through matrix pores. Using a novel Nesprin-2 based FRET/FLIM force biosensor we provide the first indication that the nucleus is being actively pulled forward when cells migrate through 3D matrices in a Nesprin-2 dependant manner. This study set out to identify how cells pull their nuclei forward to achieve 3D invasive migration. Cancer cells invading into 3D matrices form adhesion structures, which share properties of focal/fibrillar adhesions and invadopodia. Using novel proximity labelling (BioID) based interaction screens of 3D matrix adhesion site composition we have identified a novel interaction module consisting of N-WASP/WIP → ARHGEF7 → Myosin18 that is present in invasive 3D adhesion sites. The disruption of this protein interaction module alters the force dynamics and composition of adhesion sites and concomitantly inhibits nuclear force coupling required for effective invasive migration, but did not affect protrusions dynamics or matrix degradation. Loss of nuclear force coupling – from either the adhesion or nuclear site- lead to a loss of polarised migration and tension dependant pro-invasive gene transcription by YAP/TAZ. This leads us to hypothesise that actin based nuclear force coupling from adhesion sites determines the axis of polarity in migration and is the basis of adhesion based cellular motility in 3D matrix.

Contributed Talk Wed 11:30

Fiber Slippage in Collagen Matrices Enables Long-range Transmission of Mechanical Signals Between Local Cells — HAMID MOHAMMADI[1], ANTON ZILMAN[2], CHRIS MCCULLOCH[3] — [1]The Francis Crick Institute, Tumor Microenvironment, London UK — [2]Department of Physics, University of Toronto, Toronto, Canada — [3]Matrix Dynamics Group, University of Toronto, Toronto, Canada

Long-range mechanical signaling between local cells is essential for many biological processes including wound healing and tumor progression. In these processes, extracellular matrices transmit cell-generated forces across networks, thereby mediating long-range mechanosensing. While several discrete mechanical properties of matrices are implicated in long-range force transmission, the role of inelasticity, an unusual but universal feature of natural biopolymers, is undefined. Here we examine force transmission and propagation of matrix deformation across reconstituted collagen networks using quantitative experiments and mathematical modeling. We find that linear and nonlinear elastic properties of matrix networks are insufficient to explain long-range force transmission. In contrast, cell-induced inelastic deformation enables long-range mechanosensing. This counter-intuitive requirement of matrix inelasticity in mechanosensing is supported by permanent reorganization of collagen fibers, which arises from fiber slippage and the formation of new configurations that favor long-range force transmission. Our findings provide a novel mechanism for force transmission in fibrillar biological networks.

Invited Talk Wed 11:45

Mechanics of Cancer Cell Invasion in Vivo — PETER FRIEDL[1,2] — [1]The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd. Unit Number: 18-2 Houston, TX 77030, U.S.A. — [2]Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands

Single-cell or collective invasion results from coordination of cell shape, deformability and actin dynamics relative to the tissue environment. When monitored in vivo, using intravital multiphoton second and third harmonic generation and fluorescence microscopy, tissue microniches provide invasion-promoting tracks that enable collective migration along tracks of least resistance. As main routes, non-destructive contact-guidance is mediated by preformed multi-interface perimuscular, vascular and –neural tracks of 1D, 2D and 3D topography. 3D ultrastructural analysis reveals predefined tissue conduits ("highways") of defined geometry, nanotropography and molecular composition as predominant routes of invasion by contact guidance combined with a cell "jamming" mechanism. Targeting of beta1/beta3 integrins induces profound plasticity of invasion, including collective and amoeboid single-cell dissemination, followed by enhanced systemic dissemination and micrometastasis. In conclusion, cancer invasion is maintained by physicochemical programs that balance cell-intrinsic adhesion and mechanocoupling with encountered physical space and molecular cues.

Contributed Talk Wed 12:15

Investigating Heterogeneity of Tumor Mechanical Properties with Super-Resolution Multifrequency Magnetic Resonance Elastography — BARNHILL ERIC[1], BRAUN JÜRGEN[2], SACK INGOLF[1] — [1]Radiological Sciences, Charité Universitätsmedizin Berlin, 1 Charitéplatz, Berlin, 10117 — [2]Medical Informatics, Charité Universitätsmedizin Berlin, 1 Charitéplatz, Berlin, 10117

Tumorigenesis is sensitive to tissue spatial structures and tissue mechanical parameters. Magnetic Resonance Elastography (MRE) is an MRI-based method of measuring gross-scale soft tissue mechanical properties such as elasticity and viscosity. In MRE, simultaneous with an MRI scan acquisition, soft tissue of interest is vibrated with steady state waves, and the waves are encoded in the MRI phase image, enabling determination of wave speed and damping by wave inversion. MRE viscoelasticity maps have been shown to be sensitive to alterations in tissue microstructure and to mechanical pressures. Recently, multifrequency MRE (MMRE), which exploits wave scaling properties across MRE scans at multiple frequencies, was shown to enable super-resolution.

In this initial investigation, elasticity images of glioblastoma and metastases patients were acquired with MMRE, and for the first time, super-resolved. In our initial findings, mechanical property maps of the tumours revealed heterogeneities not visible in the conven-

tional-resolution acquisitions, as well as sharply resolved spatial boundaries. The dual-parameter inversion enables a rich characterisation of the mechanical properties of these newly visible details.

Invited Talk Wed 12:30

Bacteria-Associated Cancer Theranostics : When Bacteria Meet Cancer — JUNG-JOON MIN — Institut Lumière Matière – UMR CNRS 5306, Université Lyon 1, Domaine Scientifique de la Doua - Bâtiment Léon Brillouin 43 Boulevard du 11 novembre 1918,Villeurbanne, France — Institute for Molecular Imaging & Theranostics, Department of Nuclear Medicine, Chonnam National University Medical School, Republic of Korea

Current cancer therapies, including chemotherapy and radiotherapy, cannot completely destroy all cancer cells and are toxic to normal tissue. Three major causes of these problems are (1) incomplete tumor targeting, (2) inadequate tissue penetration and (3) limited toxicity to all cancer cells. These drawbacks prevent effectual treatment and are associated with increased morbidity and mortality. For example, chaotic vasculature and large intercapillary distances in tumors impede the delivery of therapeutic molecules. Low levels of oxygen and glucose create quiescent cells that are unresponsive to chemotherapeutics that are designed to target rapidly growing cells. Besides, the concentration of chemotherapeutic molecules drops as a function of distance from vasculature. Therefore, proper intratumoral targeting enables direct drug delivery to these distal, unresponsive cells that are far from the tumor vasculature.
Some strains of bacteria have unique capabilities: (1) the ability to specifically target tumors, (2) preferential growth in tumor-specific microenvironment, (3) intratumoral penetration, (4) native bacterial cytotoxicity. Motility is the key feature of bacterial therapies that enables intratumoral targeting. Bacteria can actively swim away from the vasculature and penetrate deep into tumor tissue. Within tumor, bacteria actively proliferate, resulting in 1000-fold or even higher increases in bacterial numbers in tumor tissue relative to normal organs. Because their genetics can be easily manipulated, bacteria can be engineered to synthesize drugs at sufficient concentrations to induce therapeutic effects. Although this strategy led to significantly greater therapeutic effects, they still have significant limitations; for example, multiple injections of bacteria are required, the tumors tend to recur quickly, and efficacy is unclear in the treatment of metastatic disease.
Our group developed an attenuated strain of S. typhimurium, which was defective in guanosine 5′-diphosphate-3′-diphosphate synthesis (ΔppGpp S. typhimurium) and genetically engineered this strain to express diverse cargo molecules that can provoke anticancer immunogenicity or direct cell killing. In this lecture, I will introduce several strategies of genetic engineering of bacteria for cancer treatment and describe unique mechanisms related to bacteria-mediated cancer therapy.

Poster Session

Poster 1 Wed 13:00

Change Matters: a Time-Varying Parameter Model for Cell Migration — CHRISTOPH MARK, CLAUS METZNER, JULIAN STEINWACHS, LENA LAUTSCHAM, BEN FABRY — Friedrich-Alexander University Erlangen-Nürnberg, Department of Physics, Biophysics group, Henkestraße 91, Erlangen, Germany

See abstract of the corresponding contributed talk on Tuesday 14:15.

Poster 2 Wed 13:00

„TA Instruments - High Performance Thermal and Rheological Characterization". — MATTHIAS QUAIßER — TA Instruments, Germany

See abstract of the corresponding contributed talk on Tuesday 14:30.

Poster 3 Wed 13:00

Insights about the Role of Single- and Double-Strand Breaks in Cancer Radiotherapy — FABRIZIO CLERI[1], DOMINIQUE COLLARD[2], HIROYUKI FUJITA[3], ERIC LARTIGAU[4], CORINNE ABBADIE[5] — [1]Universite de Lille I, IEMN, Av. Poincare, 59652 Villeneuve d'Ascq, France — [2]CNRS and IRCL, SMMIL-E Project, Place de Verdun, 59045 Lille, France — [3]University of Tokyo, CIRMM, 4-6-1 Komaba, Meguro-ku, Tokyo, Japan — [4]Regional Cancer Center, Rue F. Combemale, 59000 Lille, France — [5]Universite de Lille I and Institut de Biologie, Rue Calmette, 59021 Lille, France

See abstract of the corresponding contributed talk on Tuesday 17:15.

Poster 4 Wed 13:00

Multiparametric of Collagen I Self-Assembly, and Cytoskeleton Reorganisation in Living Cells — DIMITAR R. STAMOV[1], SANDRA KOSTROWSKI[1], CLEMENS M. FRANZ[2], TORSTEN JÄHNKE[1], HEIKO HASCHKE[1] — [1]JPK Instruments AG, Department of Application Science, Colditzstr. 34-36, 12099 Berlin, Germany — [2]DFG-Center for Functional Nanostructures (CFN), Karlsruhe Institute of Technology (KIT), Wolfgang-Gaede-Str. 1a, 76131 Karlsruhe, Germany

See abstract of the corresponding contributed talk on Wednesday 10:00.

Poster 5 Wed 13:00

Matrix Adhesion Sites Drive 3D Cancer Cell Migration through Direct Force Coupling to the Nucleus — TOBIAS ZECH[1], DANIEL NEWMAN[1], IBEN RONN-VEHLAND[2], VINEETHA VIJAYAKUMAR[3], GARETH E. JONES[3], PATRICK T. CASWELL[4], MARK R. MORGAN[1], LAURA M. MACHESKY[2] — [1]University of Liverpool, Institute of Translational Medicine, Cellular and Molecular Physiology, Crown Street, Liverpool, L69 3BX, UK — [2]The Beatson Institute for Cancer Research, Switchback, Rd., Bearsden, Glasgow, G61 1BD, UK — [3]King's College London, Randall Division of Cell & Molecular Biophysics, London WC2R 2LS, UK — [4]University of Manchester,3Wellcome Trust Centre for Cell Matrix Research, Faculty of Life Sciences, Manchester, M13 9PT, UK

See abstract of the corresponding contributed talk on Wednesday 11:15.

Poster 6 Wed 13:00

Fiber Slippage in Collagen Matrices Enables Long-range Transmission of Mechanical Signals Between Local Cells — HAMID MOHAMMADI[1], ANTON ZILMAN[2], CHRIS MCCULLOCH[3] — [1]The Francis Crick Institute, Tumor Microenvironment, London UK — [2]Department of Physics, University of Toronto, Toronto, Canada — [3]Matrix Dynamics Group, University of Toronto, Toronto, Canada

See abstract of the corresponding contributed talk on Wednesday 11:30.

Poster 7 Wed 13:00

Investigating Heterogeneity of Tumor Mechanical Properties with Super-Resolution Multifrequency Magnetic Resonance Elastography — BARNHILL ERIC[1], BRAUN JÜRGEN[2], SACK INGOLF[1] — [1]Radiological Sciences, Charité Universitätsmedizin

Berlin, 1 Charitéplatz, Berlin, 10117 — [2]Medical Informatics, Charité Universitätsmedizin Berlin, 1 Charitéplatz, Berlin, 10117

See abstract of the corresponding contributed talk on Wednesday 12:15.

Poster 8 Wed 13:00

Mechanobiology, Migration and Coordinated Cell-Remodeling in Invading Breast-Cancer Cells — DAPHNE WEIHS — Technion-Israel Institute of Technology, Israel and CSPO journal, Haifa 32000, Israel

See abstract of the corresponding contributed talk on Thursday 10:30.

Poster 9 Wed 13:00

Novel Tools for Discovery, Development and QC of Therapeutic (Bio)Molecules — TOBIAS PFLUEGER — Nano Temper Technologies, Flößergasse 4, 81369 Munich, Germany

See abstract of the corresponding contributed talk on Thursday 17:30.

Poster 10 Wed 13:00

LINC-ing the Nucleus, the Cytoskeleton and Cancer — PATRICIA M DAVIDSON[1], BRUNO CADOT[2], TIMO BETZ[3], CÉCILE SYKES[1]— [1]Laboratoire Physico-Chimie, UMR 168, Institut Curie, Paris, France — [2]Institut de Myologie, Paris, France — [3]Center for Molecular Biology of Inflammation-ZMBE Cell Biology, Münster, Germany

See abstract of the corresponding contributed talk on Tuesday 18:00.

Poster 11 Wed 13:00

The Role of p130Cas – PKN3 Interaction in Proliferation and Invasiveness — GEMPERLE JAKUB[1,2], DIBUS MICHAL[1,2], BRABEK JAN[1,2], ROSEL DANIEL[1,2] — [1]Department of Cell Biology, Faculty of Science, Charles University in Prague, Vinicna 7, Prague, Czech Republic — [2]BIOCEV - Biotechnology and Biomedicine Center of the Academy of Sciences and Charles University in Vestec, Prumyslova 595, Vestec, Czech Republic

Crk associated substrate (p130Cas/BCAR1) is a major Src substrate implicated in integrin-mediated control of cell behavior including mechanosensing. Re expression of p130Cas in p130Cas deficient mouse embryo fibroblasts (MEFs) transformed by oncogenic Src promotes enhanced cell invasiveness while in non-transformed cells elevated expression of p130Cas enhances cell survival and proliferation. The p130Cas protein structure contains one Src homology SH3 domain followed by regions rich in tyrosine and Ser/Thr phosphorylations. This SH3 domain interacts with many different kinases and phosphatases and is indispensable for p130Cas phosphorylations and signaling.
Because majority of studies are focused on the p130Cas signaling directed by its tyrosine phosphorylation, less is known about its Ser/Thr phosphorylation. We have identified a Ser/thr kinase PKN3 previously implicated in regulating malignant prostate and breast cell growth downstream of activated phosphoinositide 3-kinase as direct interaction partner of p130Cas. This interaction which occurs between polyproline sequence of PKN3 and p130Cas SH3 domain seems to drive p130Cas phosphorylation on several serines and could be responsible for PKN3 dependent increased proliferation rate and invasiveness of MEFs.

Poster 12 Wed 13:00

Cellular Contractile Forces and Migration Measured with a Multi-Well Silicone Device and Gradient Silicone Assay Reveal Physical Changes During Cancer Disease — HARUKA YOSHIE[1], ROSA KAVIANI[1], HOSEEIN KHADIVI[1], NEWSHA KOUSHKI[1], ADELE KHAVARI[2], RAMASWAMY KRISHNAN[3], PETER SIEGEL[4], ALLEN EHRLICHER[1] — [1]McGill University, Department of Bioengineering, Pavillon des Sciences biologiques (SB), 141 Avenue du Président-Kennedy, Montréal, Canada [2]Chalmers University of Technology, Department of Chemical and Biological Engineering, Kemigarden 4, Kemi 3022, Goteborg, Sweden [3]Harvard Medical School, Beth Israel Deaconess Medical Center, Center for vascular biology research 99 Brookline Ave, room 280b, Boston, USA [4]McGill University, Rosalind and Moris Goodman Cancer Research Center, 1160 Avenue des Pins, Montréal, Canada

Cell migration is a highly integrated process and basic to many biological functions ranging from development

to immune response and wound healing, to metastasis in cancer. For cells to migrate, they must generate and transduce traction forces to their environment, however, no technology to date has provided a high throughput solution for measuring these traction forces. Here we present a new assay for measuring cellular contractile forces employing robust multiwell culture plates: Using a 96-well plate format, we fabricate soft (~1-10 kPa) elastic silicone rubbers with embedded fiduciary particles; by measuring the cell-induced deformation of these particles we calculate the cellular traction stresses and work using Fourier transform cytometry. We utilize this system to quantify the traction mechanics underlying cellular migration in cancer diseased settings including cancer metastasis and induced epithelial to mesenchymal transition (EMT); in both instances, we find significant changes in the contractile stresses and work, suggesting that contractile force screening may become a valuable biophysical diagnostic addition. Additionally, we study cancer cell motilities on the silicone substrate with the continuous range of elastic moduli (~2 kPa-30 kPa). This gradient assay is further combined with traction force assay to investigate the cellular contractile forces and work of the cells migrating on the substrate with the continuous stiffness gradient. Our 96-well format traction assays along with gradient assays and the use of a non-degrading soft silicone rubber create simple and stable assays, and we anticipate that this technology will be of broad utility in diverse quantitative biological and health sciences.

Poster 13 Wed 13:00

Characterizing Single Cell Migration and Crossing of Chemical Barriers on Ring-Shaped Microlanes — Christoph Schreiber[1], Felix Segerer[1], Ernst Wagner[2], Andreas Roidl[2], Joachim Rädler[1] — [1]Ludwigs-Maximilians-Universität München, Fakultät für Physik, Geschwister-Scholl-Platz 1, 80539 München — [2]Ludwigs-Maximilians-Universität München, Department für Pharmazie, Butenandtstraße 5-13, 81377 München

Deviations from the typical migratory behavior of a cell can often be an indicator for pathological conditions. Hence, in order to detect anomalies in the migration pattern of a cell, finding suitable metrics to characterize cell motility is of fundamental importance in pathology as well as in drug screening. Here, we investigate the quasi-one-dimensional migration of single cancer cells on ring-shaped microlanes. We find bimodal behavior with states of directional migration (run state) and reorientation (rest state). Both states show exponential lifetime distributions with characteristic persistence times which, in combination with the measured velocity of cells in the run state, provide a well-defined set of parameters quantifying cell motion. Introducing PEGylated barriers of different widths into the setup, this set is extended by quantifying the sensitivity of a migrating cell to abrupt changes in the composition of the underlying substrate. We observe that cells either reverse at the interface or traverse the barriers. The traversal probability decreases as a function of barrier width thus revealing a characteristic invasion depth of the leading lamellipodia. Together this results in a fingerprint-like set of parameters characterizing cell migration that can be used to distinguish the movement patterns of different cell lines as well as to quantify the effects of motility affecting drugs like salinomycin. Hence the migration assay provides a differentiated view on cell motility with potential for cell classification and drug screening.[1]

[1] Schreiber et al., Scientific Reports, 6, 26858 (2016)

Poster 14 Wed 13:00

The Role of Long Non-Coding RNA MALAT1 in the Invasive Behavior of Tumor Cells — Ladislav Merta[1,2], Vladimír Čermák[1,2], Aneta Gandalovičová[1,2], Daniel Rösel[1,2], Jan Brábek[1,2] — [1]Faculty of Science, Charles University, Viničná 7, 128 00 Prague 2, Czech Republic — [2]BIOCEV, Průmyslová 595, 25250 Vestec, Czech Republic

Several million people die annually due to cancer metastases. The ability of cancer cells to migrate through tissues and colonize distant sites in an organism is a critical step in this process. There are at least two distinct invasion strategies – amoeboid and mesenchymal. Metastatic cells switch between these strategies in specific environmental conditions. Modification of the conditions can induce transition between the two strategies (i.e. mesenchymal to amoeboid or amoeboid to mesenchymal transition – MAT and AMT, respectively). The understanding of the transitions at molecular level is essential for anti-metastatic cancer treatment. Our results indicate that long non-coding RNA MALAT1 may have a crucial role in these processes. Although MALAT1 has

already been known for 10 years, its exact function is poorly understood.
Our project aims to clarify the role of MALAT1 in the plasticity of cancer cell migration and to characterize molecules influenced by MALAT1, which are potentially involved in controlling cell migration mode in 3D environment. So far, we have observed an increased level of MALAT1 in HT1080 cells undergoing mesenchymal to amoeboid transition. Furthermore, we have established MALAT1 knock-down clones derived from largely amoeboid A375m2 cell line using zinc-finger nucleases. These clones exhibit a more mesenchymal morphology in comparison with the control ones.
Taken together, these results suggest that MALAT1 is an important regulator (direct or indirect) of cancer cells' mode of invasion.

Poster 15 Wed 13:00

Membrane-Spanning DNA Channel with Lipid Domain and Ion Selectivity — AHMED SAYED, RALF SEIDEL — Molecular Biophysics group, Institute of Experimental physics I, Universität Leipzig, Linnéstr. 5, 04103 Leipzig, Germany

Several diseases, such as Wilson and neurodegenerative disorders, are caused by disruptions in the cellular transition metal homeostasis due to the dysfunction of the relevant transporter proteins. Developing a new and innovative approach becomes urgent to deal with such diseases. Recently DNA origami has emerged as a powerful and versatile method to fabricate highly stable 3-dimensional structures at the nanometer-scale. Here the ongoing project, inspired by the heavy metal-transporter proteins, aims to fabricate controllable DNA nanopores which are able to 1) target a specific lipid composition and 2) to transport particular metal ions across membrane lipids.
The DNA channels consist of six DNA double helices arranged in parallel with a 10-nm-length and 2-nm-wide pore and conjugated with metal-biding domains which have varying affinity and selectivity towards heavy metal ions (such as Copper and Zinc ions). Innovative hydrophobic modifications to DNA structure have been developed in order to anchor the highly negatively charged DNA nanostructure into giant unilamellar vesicles (GUVs). Docking sites are introduced at the entrance of DNA nanopore in order to hybridize with "lock strand" forming a duplex across the channel opening in "lock state". This lock strand could be removed by hybridizing with a "key strand", consequently activating the transport activity. Thus, we are able to regulate the translocation of small-molecule cargo across membrane lipid using lock/key system. Moreover, the selectivity of DNA nanopore toward liquid-ordered (lo) and liquid-disordered (ld) lipid phases is improved by controlling the number and positions of lipid anchor. So, the DNA nanopore could potentially be used in drug delivery.

Poster 16 Wed 13:00

Oligocellular Systems for Accessing Adhesion and Contractility Parameters — MATTHIAS ZORN, JOACHIM RÄDLER — Ludwigs-Maximilians-Universität München, Fakultät für Physik, Geschwister-Scholl-Platz 1, 80539 München

The Vertex model is a simple, yet elegant model that can make predictions about the arrangement of epithelial cell sheets, such as monolayers of MDCKs or the Drosophila wing disc. Though the model makes use of energy terms proportional to elastic properties of the cell (e.g. cell contractility), it is hard to, in turn, directly access these cell properties from experimental observations. This is in part due to the complexity of the typically used experimental systems. In recent years, micropatterning techniques (e.g. microcontactprinting) have widely been used to confine cells to predefined areas and thus reduce the degree of freedom. When attempting to make use of this sort of approach to create a setting where the Vertex model can be used to more readily access the cells' elastic parameters, one is quickly faced with the problem that small-numbered cell assemblies confined in circular or even square geometries begin to collectively rotate. Such a dynamic scenario is problematic, because it is possible that the cells never reach the static equilibrium predicted by the model, making it a poor choice for extracting parameters from the experimental observations.
To this end, we have developed a new adhesion geometry that suppresses this collective rotation for systems of four MDCK cells to a large extent simply due to its boundary conditions. In this geometry, each cell is given an individual "island" to adhere to. Even though the area between the cells is passivated by Pll-PEG, the MDCK cells nonetheless spread out and connect, forming junctions. From their general positioning and junction shape, the cells on this new pattern seem to

arrange much the same as four MDCK cells do on a large square adhesion pattern. Comparing the angular velocity in both cases, we find that despite the same general cell arrangement, collective rotation in clearly suppressed on our new geometry once the four cells have moved into a configuration where each cell sits on its own island. Analysis of the two-dimensional mean squared displacement shows that although each cell still moves around on its individual square, the cells have reached a quasi-stable state where the cells remain in the same general arrangement. Each cell remains on its own adhesion island, with switching of places rarely occurring. In this quasi-stable configuration, the cells seem to arrange in an asymmetric manner. Instead of forming one vertex where all four cells meet, two vertices form, connected by a junction. Two of the cells have two neighbors, while the other two have contact with three neighbors. The junction connecting the vertices fluctuates in length over time, however, we could demonstrate that these fluctuations are reduced on our new geometries compared to four cells rotating on a large square. Furthermore, we can show that the average length of this junction depends on the distance between the four small adhesion sites for the individual cells. This assay should prove useful in extracting the cell mechanical parameters with help of the Vertex model, as it reduces the degree of freedom in the system, while at the same time ensuring the cells reach a quasi-stable equilibrium state necessary for the Vertex model approach to make sense. At the same time, by increasing the distance between the adhesive sites, we can influence the system, similar to pulling on the cells mechanically. This should enable testing of hypothesis on the cell arrangements, as well as decoupling of cell parameters that could otherwise not be measured independently of one another. In addition this assay could prove useful in studying T1 transitions, providing the minimal system necessary for them to occur.

Poster 17 Wed 13:00

Connecting Cell Jamming with Adhesion, Contractility and Cell Stiffness — JÜRGEN LIPPOLDT, STEFFEN GROSSER, LINDA OSWALD, PAUL HEINE, JOSEF KÄS — University of Leipzig, Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, Soft Matter Physics Division, Linnéstraße 5, 04103 Leipzig, Germany

Understanding cancer metastasis could lead to major advances in cancer therapy, since metastases are statistically the main cause of death for cancer patients. An interesting hypothesis is that tumours are jammed cell aggregates and locally unjam in metastatic events. Following this line of thought, a better understanding of the physics of cell jamming could, in the long run, lead to advances in cancer therapies.

Our collaborators, Lisa Manning and Cristina Marchetti have developed a coarse grained model of cell jamming in elastic tissues. The constitutive equation has a harmonic term for the cell area, which promotes volume conservation due to cell stiffness and osmotic pressure, and one for the cell perimeter, which expresses the interplay between cell adhesion and cell contractility. This leads to an effective shape parameter, which is the ratio between the preferred perimeter and the square root of the preferred area. In simulations with self-propelled cells and Voronoi tessellation a phase transition between a jammed and an unjammed phase was observed at critical value of 3.8 in two-dimensional sheets.

We examine this model with cancer cell lines, which undergo the epithelial-mesenchymal transition. To determine, whether the cell layers are jammed or not, we will use standard glassy metrics like the mean-square displacement, the non-Gaussian parameter $\alpha 2$ and a dynamical 4-point susceptibility $\chi 4$ as well as Bayes statistics of individual tracks. The shape of the cells can be determined by image analysis of phase contrast or actin labelled fluorescence images. Additionally, the information of centre points of the cells is required. These are obtained from fluorescence images with a stained nucleus. The image segmentation is then performed with the help of entropy filters and a watershed algorithm.

This framework is well suited to explore changes in collective cell migration for different cell types, varying conditions and the use of drugs. Changing physical properties of the cells will lead to a different target shape parameter and should change their motility. This could give hints, how cells can change their collective behaviour by altering their individual properties and how observed collective phenomena like cellular streaming emerge.

Poster 18 Wed 13:00

Microstructure of Sheared Entangled Solutions of Semiflexible Polymers — Marc Lämmel[1], Evelin Jaschinski[2], Rudolf Merkel[2], Klaus Kroy[1] — [1]University of Leipzig, Institute of Theoretical Physics, Theory of Condensed Matter, Postfach 100920, 04009 Leipzig, Gemrnay — [2]Forschungszentrum Julich, Institute of Complex Systems 7: Biomechanics, 52425 Julich, Germany

We study the influence of finite shear deformations on the microstructure and rheology of solutions of entangled semiflexible polymers theoretically and by numerical simulations and experiments with filamentous actin. Based on the tube model of semiflexible polymers, we predict large finite shear deformations to stronlgy affect the average tube width and curvature, thereby exciting considerable restoring stresses. In contrast, the associated shear alignment is moderate, with little impact on the average tube parameters, and thus expected to be long-lived and detectable after cessation of shear. Similarly, topologically preserved hairpin configurations are predicted to leave a long-lived fingerprint in the shape of the distribtutions of tube widths and curvatures. Our numerical and experimental data support the theory.

Poster 19 Wed 13:00

TiO_2 Nanotube Scaffolds for Long-Term Organotypic Culture of Adult Mammalian Tissue — Sabrina Friebe[1,2], Solveig Weigel[4,5], Mike Francke[4,5], Mareike Zink[3], Stefan G. Mayr[1,2] — [1]Leibniz Institut für Oberflächenmodifizierungen (IOM) e.V., Permoser Str. 15, 04318 Leipzig, Germany — [2]Division of Surface Physics, Faculty of Physics and Earth Sciences, University of Leipzig, Linnéstr. 5, 04103 Leipzig, Germany — [3]Soft Matter Physics Division, Faculty of Physics and Earth Sciences, University of Leipzig, Linnéstr. 5, 04103 Leipzig, Germany — [4]Paul-Flechsig-Institute for Brain Research, University of Leipzig, Liebigstr. 19, 04103 Leipzig, Germany — [5]Sächsischer Inkubator für klinische Translation (SIKT), Universität Leipzig, Philipp-Rosenthal-Str. 55, 04103 Leipzig, Germany

Organotypic tissue cultures not only offer possibilities to study the complex structure of explants in vitro, but can also be employed to investigate pathological changes, their correlation with variation in tissue mechanics, as well as the effect of drugs. Conventional culture methods do not allow to preserve adult mammalian tissues alive for more than a few days, as adult explants undergo rapid morphological changes and degenerate due to cell death and out-migrating cells. As we have shown previously, biocompatible and self-organized TiO_2 nanotube scaffolds composed of parallel aligned nanotubes with highly tunable surface geometry in terms of tube diameter and surface roughness are ideally suited for adult tissues and maintain tissue integrity of at least 14 days [1]. While the biophysical origins of this behavior are the focus of current research, we could show that good adhesion from tissue explants to the scaffold plays a central role. After culture, TiO_2 nanotube scaffolds can be cleaned by UV-light irradiation and reused for organotypic tissue cultures. As we demonstrate for the example of rabbit retina explants, TiO_2 nanotube scaffolds are ideally suited for environmental scanning electron microscopy (ESEM) studies to visualize complex tissue structures. Since we have shown that TiO_2 nanotube scaffolds can be employed for long-term culture of various tissue types, fundamental biological questions, from cancer progression to the effect of reagents in combination with mechanical properties investigations can be addressed in vitro [2].

[1] V. Dallacasagrande, M. Zink, S. Huth, A. Jakob, M. Müller, A. Reichenbach, J.A. Käs, S.G. Mayr, Advanced Materials 24, 2399-2403 (2012)

[2] S.M. Rahman, A. Reichenbach, M. Zink, S. Mayr, Soft Matter12, 3431-3441 (2016)

Poster 20 Wed 13:00

Construction of a Multifunctional DNA-Based Carrier System for Antisense Oligonucleotide Delivery — Alexander Spaeth[1,2], Jessica Lorenz[1,3], Nadja Hilger[1], Stephan Fricke[1], David Smith[1] — [1]Fraunhofer Institute for Cell Therapy and Immunology, AG DNA Nanodevices, Perlickstr. 1, 04103 Leipzig, Germany — [2]Martin-Luther University Halle-Wittenberg, Institute for Biochemistry and Biotechnology, Kurt-Mothes-Str. 3, 06120 Halle (Saale), Germany — [3]University of Cologne, Department of Chemistry, Insitute of Biochemistry, Albertus-Magnus-Platz, 50923 Cologne, Germany

Single stranded DNA is suitable for constructing three dimensional carriers by forming double stranded DNA, giving a predictable shape. This project deals with the

design and assembly of DNA-based carriers for the delivery of antisense oligonucleotides (ASO) against microRNA-155 (miR-155) in MV4-11 acute myeloid leukemia (AML) cells. MV4-11 cells contain a mutation in the FLT3-rececptor and are thus characterized by blocked myeloid differentiation while proliferation is induced [1, 2]. The delivered ASO is intended to knock-down miR-155 by steric blocking or induced enzymatic degradation, thereby leading MV4-11 cells to differentiate and to undergo apoptosis [3].
The nanometer-scale DNA-based carriers are designed to contain free 5'-ends for the functionalization with desired biomolecules such as fluorophores, peptides and the ASO in a covalent manner using copper free click chemistry [4]. Fluorophores will help to track the carriers in cells while peptides for endosomal escape may support the cellular uptake into the cytosol. In order to prevent the internalized DNA from degradation through endo- and exonucleases we are using phosphorothioate (PTO) modified DNA. The introduction of sulfur into the phosphodiester backbone makes the DNA more stable against digestion by nucleases, thus the PTO-carrier system can resist degradation in cells much longer after internalization. We could show that PTO-modified DNA-nanostructures survive Exonuclease III digestion and incubation in fetal calf serum over several days. Additionally, we are able to attach the ASOs to our DNA-carriers in high yields.
MiR-155 knock-down is known to cause MV4-11 cells to regain their differentiation ability, reduced proliferation and apoptosis. Thus, the effects after the application of ASO-conjugated carriers will be observed by apoptosis assays and differentiation assays using cell staining methods and flow cytometry analysis. Furthermore the anti-proliferative effect will be investigated in proliferation assays in comparison to non-treated cells.

[1] B. Löwenberg, J. R. Downing and A. Burnett, The New England Journal of Medicine; 341: 1051-1062 (1999)

[2] S. Fricke, N. Hilger, D. Gerloff, G. Behre, *Regeneration of normal hematopoiesis from leukemic stem cells: MIR-155 inhibition and anti-CD4 antibody therapy,* TRM Application Form, University Leipzig (2014)

[3] D. Gerloff, R. Grundler, A. A. Wurm, D. Bräuter-Hartmann, C. Katzerke, J.-U. Hartmann, V. Madan, C. Müller-Tidow, J. Duyster, D. G. Tenen, D. Niederwieser, G. Behre, Leukemia; 29(3): 535-547 (2015)

[4] N. J. Agard, J. A. Prescher and C. R. Bertozzi, Journal of the American Chemical Society; 126(46): 15046-15047 (2004)

Poster 21 Wed 13:00

Toxicity and Biodistribution of Nanoparticle-Delivered Gene Therapeutics In Vitro and In Vivo — Susanne Przybylski[1], Alexander Ewe[2], Daniela Rudolf[1], Marcus Ebert[1], Achim Aigner[2], Jana Burkhardt[1] — [1]Fraunhofer Institute for Cell Therapy and Immunology, Perlickstr.1, Leipzig, Germany — [2]Rudolf-Boehm-Institute for Pharmacology and Toxicology, Clinical Pharmacology, University of Leipzig, Härtelstr.16/17, Leipzig, Germany

Gene Therapy is the most promising and innovative therapeutic technology in modern medicine with a perspective to treat even incurable diseases such as malignant cancers. However, the successful transfer of therapeutic nucleid-acid drugs into the target cells or tissue is challenging, especially in terms of facilitating efficient cellular uptake without compromising viability or function of cells unspecifically. To confer safe and efficient transfer of nucleic acid based drugs in vivo, transfection nanoparticles (NP) might be applied. For development of an optimal gene therapeutic drug candidate, the design of the potentially bioactive sequence and possible chemical modifications of the nucleic-acid-based drug or transfection NPs with regard to bioactivity, bioavailability and toxicity in vitro and in vivo, has to be considered. The nucleic acid – NP complex should be strictly tested for a sufficient and safe biodistribution pattern in vivo in addition to preliminary in vitro studies.
Here, we investigated various nanoparticle-based transfection methods in relation to transfection rate, cytotoxicity and possible side-effects of transfected NPs on immunological parameters, such as cytokine production and cell populations (immunoprofiling), in vitro and in vivo. To estimate toxicity of NP conjugates in vivo, we applied nonsense antisense oligonucleotides (AON, 2' O-methyl PTO RNA) complexed with polyethylenimine (PEI-F25) in wildtype animals and an irradiated murine GvHD model. We measured serum parameters, analysed cytokine levels and histological tissue sections.

We also analysed tissue- specific biodistribution of differently labelled nucleic acid based drugs in vivo. To assess biodistribution, wildtype mice were injected i.v. or i.p. with AON or siRNA complexed with different modified PEI- variations. Organs were harvested after 1 to 7 days and isolated cells were measured for oligonucleotide uptake by flow cytometry.
While direct application of PEI in vivo was not toxic at therapeutic levels to untreated wildtype animals, animals irradiated prior to treatment seemed to show symptoms of toxicity. Additionally, biodistribution of in vivo applied NPs revealed a varied organ specific transfection pattern with lung, liver and bone marrow being preferably transfected.
Hence, NP mediated targeted gene therapy might be an interesting option especially for cancer types in preferentially transfected tissues such as lung or liver. In the future, cell type specificity of NPs needs to be investigated further.

Poster 22 Wed 13:00

DNA-templated Multivalency as a Tool to Regulate Binding and Activation of Cancer Cell Pathways — Christin Möser[1,2], Jessica S Lorenz[1,3], Maik Herbig[4], Oliver Otto[4], Jochen Guck[4], Frank Bier[2,5], David M Smith[1] — [1]Fraunhofer Institute for Cell Therapy and Immunology, DNA Nanodevices unit, Leipzig, Germany — [2]University of Potsdam, Institute of Biochemistry and Biology, Potsdam, Germany — [3]University of Cologne, Department of Chemistry, Institute of Biochemistry, Cologne, Germany — [4]Biotechnology Center TU Dresden, Cell Mechanics, Dresden, Germany — [5]Fraunhofer Institute for Cell Therapy and Immunology, Department of Biosystem Integration & Automation, Potsdam, Germany

EphrinA2 receptors (EphA2) are overexpressed in many types of cancer (breast, pancreatic, ovarian, prostate and lung cancer) whereas tumor suppressor properties are reported when their signaling ability is activated by ephrin ligands. This project focuses on the attachment of EphA2 ligands on DNA nanostructures, which facilitates the creation of many parallel and thus collectively strong interactions with EphA2. We examine the effect that parameters such as inter-ligand distance, valency and orientational flexibility have upon the binding kinetics between EphA2-postive cells and DNA nanostructures containing EphA2-binding peptides via flow cytometry.
DNA nanostructures consist of partially complementary oligonucleotide sequences that self-assemble into discrete objects of pre-defined shape and size. Since the underlying DNA sequence is known, it is possible to attach EphA2 binding peptides to nearly any unique location on the structure. Due to the resolution provided by DNA-based nanostructures, spatial arrangements of ligands on the size scale of dimeric and trimeric cell-surface receptors can be created and closely controlled.
In detail, we study not only the attachment but also the activation of EphrinA2 receptors (EphA2) upon multivalent presentation of small EphA2-binding peptides.
The degree of ephrin pathway activation as a function dose and the above template parameters can be determined by immunolabeling. Activation and signaling are already known to be accompanied by structural changes in the underlying cytoskeleton, which we measure using real-time deformability cytometry [1]. Our preliminary results indicate a nearly 100-fold increased potency of pathway activation for DNA-templated dimeric structures, and work currently is underway in order to optimize both binding and signaling properties through close control of further structural parameters.
Ultimately, control over these multivalent interactions can be used to enhance the effect of the ligands on the target acceptors.

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Poster 23 Wed 13:00

Reptation in Semiflexible Polymer Networks — Tina Händler[1,2], Tom Golde[1], Martin Glaser[1,2], Carsten Schuldt[1,2], Jörg Schnauß[1,2], David Smith[2], Josef Käs[1] — [1]University of Leipzig, Soft Matter Physics Division, Linnéstraße 5, 04103 Leipzig — [2]Fraunhofer Institute for Cell Therapy and Immunology, Perlickstraße 1, 04103 Leipzig

Studying the mechanics and dynamics of biopolymers has inspired many ideas and theories in polymer physics. One prominent example is actin, being the best-studied semiflexible polymer. Nanotubes formed from synthetic DNA strands are ideal model polymers: they are semiflexible over their typical length scale and can be hybridized to have characteristics such as persis-

tence length which are similar to actin filaments or can be varied in a controllable way. Additionally, DNA nanotubes are extremely stable, making them both favorable for polymer physics experiments and material science applications.
We use this model system to measure the mesh size of entangled networks by directly observing the reptation of single filaments. The results show a concentration scaling in good agreement with theoretical predictions. These findings are the first intrinsic proof of mesh size scaling with concentration and demonstrate the applicability of this method. Furthermore, reptation analysis with our „programmable" filaments enables the test of central assumptions and predictions from the theory of semiflexible polymer networks.

Poster 24 Wed 13:00

Altering Synthetic Semiflexible DNA Nanotube Networks by Tunable Cross-linking — Martin Glaser[1,2], Paul Mollenkopf[1,2], Christin Möser[2], Carsten Schuldt[1,2], Jörg Schnauß[1,2], Tina Händler[1,2], Josef Käs[1], David Smith[2] — [1]Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, Leipzig University, Leipzig, Germany — [2]Fraunhofer Institute for Cell Therapy and Immunology IZI, DNA Nanodevices Group, Leipzig, Germany

The mechanical properties of complex soft matter have been subject to various experimental and theoretical studies in the past years. The underlying constituents often cannot be modeled in the classical physical frame of flexible polymers or rigid rods. Polymers in the semiflexible regime, where the finite bending stiffness leads to a non-trivial mechanical contribution, are a highly interesting subclass and can be found in the cytoskeleton of every living cell. A natural occurring model system for such polymers is the protein actin [1].
However, experimental studies of actin networks to validate existing theories [2], are limited since the persistence length cannot be altered. Here, we establish a tunable system of cross-linked, synthetically DNA nanotubes to overcome this limitation. We present first results of the impact tunable cross-linking has on the well characterized entangled DNA nanotube networks [3]. These studies enable investigations of the impact of a crucial parameter of semiflexible polymers, namely the persistence length, on resulting network properties.
Also, the study will allow a deeper insight into the underlying mechanics of biomaterials, such as hydrogels, which are extensively used for in vitro as well as in vivo applications [4].

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[4] N. Reddy, R. Reddy and Q. Jiang, Trends Biotechnol. 33 362–9 (2015)

Poster 25 Wed 13:00

Cellular Jamming in 3D Cancer Aggregates — Linda Oswald[1], Steffen Grosser[1], Jürgen Lippoldt[1], Steve Pawlizak[1], Anatol Fritsch[2], Josef A. Käs[1] — [1]University of Leipzig, Faculty of Physics and Earth Sciences, Institute for Experimental Physics I, Soft Matter Physics Division, Linnéstr. 5, 04103 Leipzig, Germany — [2]Max Planck Institute of Molecular Cell Biology and Genetics - Kreysing Group, Pfotenhauerstr. 108, 01307 Dresden, Germany

Traditionally, tissues are treated as simple liquids, which holds e.g. for embryonic tissue. However, recent experiments have shown that this picture is insufficient for other tissue types, suggesting possible transitions to solid-like behaviour induced by cellular jamming. The coarse-grained self-propelled Voronoi (SPV) model predicts such a transition depending on cell shape [1]. We observe non-liquid behaviour in 3D breast cancer spheroids of varying metastatic potential and correlate single cell shapes and collective dynamic behaviour via the SPV model.

[1] M. Merkel, M. L. Manning, *Glassy dynamics in a model for confluent 3D tissues*, Aspen Winter Conference (2016)

Poster 26 Wed 13:00

Synthetic Actin Cross-linkers Slow Down 3D Cell Migration and Invasion — Jessica Lorenz[1,2,3], Jörg Schnauß[1,3], Martin Glaser[1,3], Martin Sajfutdi-

NOW[1,4], CARSTEN SCHULDT[1,3], INES NEUNDORF[2], JOSEF A. KÄS[3], DAVID M. SMITH[1] — [1]Fraunhofer Institute for Cell Therapy and Immunology (IZI), DNA Nanodevices Unit, Leipzig, Germany, Perlickstraße 1, 04103 Leipzig, Germany — [2]University of Cologne, Department of Chemistry, Institute of Biochemistry, Cologne, Germany, Albertus-Magnus-Platz, 50923 Köln, Germany — [3]University of Leipzig, Institute of Experimental Physics I, Soft Matter Physics Division, Germany, Linnéstraße 5, 04103 Leipzig, Germany — [4]Leibniz Institute for Surface Modification (IOM), Leipzig, Germany, Permoserstraße 15, 04318 Leipzig, Germany

The cytoskeleton is a crucial cellular element and one of its key components is the protein actin, which polymerizes into helical filaments under physiological conditions. These filaments form extensive networks and are not only responsible for dynamic functions (e.g. cell motility) but also fulfill static tasks (e.g. cell stability). These somehow contradictory functions are tightly interconnected, dependent on each other and are based on the fact that actin networks are highly tunable. A central tuning mechanism is the cross-linking of filaments within the network to alter dynamics as well as mechanical properties of the cytoskeleton. Nature provides us with a set of cross-linking proteins specifically designed to fulfill distinct cellular tasks.

However, to interfere with properties of these natural cross-linkers to alter, for instance, cell dynamics or to precisely tune mechanical properties of the cytoskeleton is tedious since extensive genetic modifications are required.

Here, we overcome this limitation by creating bionic cross-linkers, which are based on DNA templates defining the topology of the linker. These templates can be conjugated to actin binding peptides to facilitate binding to two or more filaments. In a physical frame, we can design these cross-linkers with well-defined parameters, which can be readily altered to study the impact of different binding affinities, lengths, or valencies on the overall actin network in a decoupled manner.

In a first test, we used one distinct DNA template to investigate the role of the cross-linker's binding affinity in reconstituted actin networks via bulk rheology. Within these studies we were able to show that these constructs not only bind to actin, but also resemble complex mechanical fingerprints of naturally occurring cross-linkers such as alpha-actinin and fascin [1, 2].

Additionally, we found mechanical regimes, which have been differently reported previously [3].

Since mechanical properties of the cytoskeleton and its dynamic behaviors are tightly connected, we further investigated the influence of our cross-linkers on cellular systems. We internalized these constructs into different cancer cell lines and evaluated alterations via 2D/3D migration and invasion assays. Our results show that cells are inherently slowed down in migration due to the additional cross-linking, which retards the dynamics of the actin cytoskeleton. Furthermore, the invasiveness of these cells was not only retarded but drastically reduced. We speculate that the cross-linkers diminish the depolymerization of actin as reported for naturally occurring cross-linkers [4]. Actin polymerization/depolymerization is known to regulate the expressions of certain enzymes, which indicates that these cross-linkers not only alter mechanical properties but also influence biochemical expression pathways [5]. In principle, this rather general concept can be transferred to literally every cell type and potentially impedes the epithelial to mesenchymal transition (EMT).

In summary, we have proven that these bionic cross-linkers indeed alter mechanical properties of actin networks and further allow to controllably explore the entire phase space of cross-linked networks by specifically changing the cross-linker topology, binding strength, or valency. By identifying binding domains to other naturally occurring filaments, this concept can be transferred to literally every biopolymeric system. A library of these cross-linkers would potentially enable us to precisely alter dynamics and mechanical properties of entire cells and even tissues.

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Poster 27 Wed 13:00

Investigations of Single Squamous Cell Carcinoma Cells — Maja Strugacevac[1], Susanne Steeger[1], Nina Bartels[1], Jan Lietz[1], Julia Kristin[2], Marcel Glaas[2], Jörg Schipper[2], Mathias Getzlaff[1] — [1]Institute of Applied Physics, Heinrich-Heine Universität Düsseldorf, Universitätsstr. 1, Düsseldorf, Deutschland — [2]Universitäts-HNO-Klinik Düsseldorf, Moorenstrasse 5, Düsseldorf, Deutschland

Considering that the number of cancer patients increases every day, it is important to develop new treatment techniques. Our group's research deals with hardness and elasticity of carcinoma cells in comparison to benign cells. In our work we use two different techniques in the study of cells, Atomic Force Microscopy (AFM) and fluorescence microscopy.

Mechano-elastic properties of carcinoma cells were investigated using AFM. The Young's Modulus calculated by the Hertzian Model was determined in order to quantify the elasticity of the cells. The differences between carcinoma and benign cells can - in part - be attributed to the modified cytoskeleton of cancer cells. The new results will be utilized in order to improve cancer treatment.
Colonies of Squamous cell carcinoma cells (UD01) are examined in confocal fluorescence microscopy. Different markers allow us to selectively observe specific parts of a given cell. The objective is to destroy cancer cells by physical means. Meaningful results require us to differentiate intentionally induced cell death from unintentional causes. Thermal fluctuations introduced by measurement setup provide a challenge since cells are sensitive to temperature changes. A separate cell colony dish serves as a control group during measurements. An oxidative stress detection marker can be used to distinguish between intentionally caused and unwanted stress. The latter may be induced by thermal fluctuations, sample transportation or environmental factors. Our latest results focus on the cytoskeleton with a future inclusion of other cell parts as well as on the comparison of carcinoma and benign cells.

Poster 28 Wed 13:00

Variability and Reproducibility of Cell Mechanical Measurements with Microconstriction Arrays: Influence of Pressure, Strain, Measurement Parameters and Protein Expression — Janina Renate Lange[1], Claus Metzner[1], Sebastian Richter[1], Werner Schneider[1], Monika Spermann[1], Thorsten Kolb[2], Graeme Whyte[3], Ben Fabry[1] — [1]University of Erlangen-Nuremberg, Institut of Physics, Biophysics Group, Henkstrasse 91, 91052 Erlangen, Germany — [2]German Cancer Research Center (DKFZ), Division of Molecular Genetics, Im Neuenheimer Feld 280, 69120 Heidelberg, Germany — [3]Heriot-Watt University, Department of Physics, IB3: Institute of Biological Chemistry, Biophysics and Bioengineering, Edinburgh, Scotland, EH14 4AS, United Kingdom

We describe a quantitative, high-precision, high-throughput method for measuring the mechanical properties of cells in suspension with a microfluidic device, and to relate cell mechanical responses to protein expression levels. Using a high-speed (750 frames/s) CCD camera, we measure the driving pressure, maximum cell deformation and entry time of cells in an array of microconstrictions. From these measurements, we estimate the average elasticity and fluidity of the cell population. We find that cell elasticity increases linearly with increasing strain and increasing pressure. Variable cell stress due to driving pressure fluctuations and variable cell strain due to cell size fluctuations therefore cause significant variability between measurements. To reduce measurement variability, we use a histogram matching method that selects and analyzes only those cells from different measurements that have experienced the same pressure and strain. With this method, we investigate the influence of measurement parameters on the resulting cell stiffness and fluidity. We find a small but significant stiffening of cells with increasing time after cell harvesting. Cells harvested from confluent cultures are softer compared to cells harvested from sub-confluent cultures. Moreover, cell stiffness increases with decreasing concentration of the adhesion-reducing surfactant pluronic. Lastly, we correlate protein expression levels with cell mechanical properties in mixed cell populations. We simultaneously measure cell mechanics and fluorescent signals of cells that transiently overexpress the GFP-tagged nuclear envelope protein lamin A. We find that increasing lamin A levels

increase cell stiffness and decrease cell fluidity. Together, our findings demonstrate that histogram matching of pressure, strain and protein expression levels greatly reduces the variability between measurements and enables us to reproducibly detect small differences in cell mechanics.

Poster 29 Sat 13:00

Advanced Thermorheology of Living Cells — ENRICO WARMT, TOBIAS KIEßLING, SEBASTIAN SCHMIDT, JOSEF KÄS — Universität Leipzig, Soft Matter Physics Division, Linnéstr. 5, Leipzig, Germany

Temperature has a reliable and nearly instantaneous influence on biomechanical responses of cells. As recently published, MCF10 normal epithelial breast cells, behave thermorheological simple i.e. creep compliance curves superpose just by shifting the time axis [1]. Additionally, we measured thermorheological behaviour of eight common cell types within physiologically relevant temperatures and applied thermorheological time-temperature superposition (TTS) to creep compliance curves. Our results showed that superposition is not a universal feature, and is only applicable in four of the eight investigated cell types [2]. For the other cell types, transitions of thermorheological responses around 36°C were observed. Even without a rigorous applicability of TTS to all cell types, the quality how creep curves superpose reveal valuable information about relaxation processes in response to mechanical load. For various cell lines, different thermorheological characteristics can be observed indicating differences in relevant load bearing structures. Now we focused on certain cytoskeletal structures and its influence on thermorheological cell response. With the help of various cytoskeletal drugs we strengthened or weakened the actin- and microtubule network. Preliminary data showed that superposition of creep compliance curves was easier for cells with disrupted cytoskeletal networks. This is intuitive, since cells loose particular rheological properties of individual structure filaments and behave more fluid like. The exact contribution of diverse cytoskeletal filaments to cell mechanical behaviour can be calculated by this model. So we are able to explain characteristic rheological cell response of certain cell lines due to particular cell assembly of these cell lines.

[1] TOBIAS KIEßLING, ROLAND STANGE, JOSEF KÄS AND ANATOL FRITSCH, *Thermorheology of living cells—impact of temperature variations on cell mechanics*, NJP (2013)

[1] SEBASTIAN SCHMIDT TOBIAS KIEßLING, ENRICO WARMT, ANATOL FRITSCH, ROLAND STANGE AND JOSEF KÄS, *Complex thermorheology of living cells*, NJP (2015)

Poster 30 Sat 13:00

Occupancy and Stochastic Transitions of Single Cells on Double-Well Micropatterns — ALEXANDRA FINK[1], PETER RÖTTGERMANN[1], CHRISTOPH SCHREIBER[1], CHASE BROEDERSZ[2], JOACHIM RÄDLER[1] — [1]Faculty of Physics and Center for NanoScience, Ludwig-Maximilians-Universität, Geschwister-Scholl-Platz 1, 80539 München, Germany — [2]Arnold-Sommerfeld-Center for Theoretical Physics and Center for NanoScience, Faculty of Physics, Ludwig-Maximilians-Universität, Theresienstraße 37, 80333 München, Germany

Micropatterns have become a standard tool to confine and immobilise living cells. They allow the study of cell elasticity, cell adhesion and internal cellular organisation. Micropatterns have also been found to induce cell polarization and guide cell migration. While static cell shapes on micropatterns have been described theoretically, correctly predicting observed cell shapes, little is known about cell dynamics on micropatterns.

Here, we report on a new phenomenon, "cell hoping", on "dumbbell-like" micropatterns consisting of two square single cell adhesion sites. The sites have dimensions of 35 µm x 35 µm and are connected by a 5 µm wide adhesive bridge. The migration of MDA-MB-231 human breast cancer cells on these micropatterns is studied by time-lapse fluorescence microscopy.

A single cell on a dumbbell-pattern is found to occupy one of the square adhesion sites most of the time. The cells are observed to constantly produce random membrane protrusions, and the bridge provides a guidance cue for these protrusions, resulting in the occasional formation of a stable lamellipodium along the bridge. Subsequently, a cell may transit from one adhesion site to the other. We have evaluated the stay time of cells on the square islands depending on the length of the connecting bridges. The inverse of the mean stay time, which is the hopping rate, shows an exponential dependence on the bridge length.

In the next step, we have changed the dimensions of one of the two terminal adhesion sites while keeping the bridge length constant. We analyze the occupancy

probability function over all cells and all times. In the symmetric case of equally sized adhesion sites the result is a symmetric double peak distribution. For asymmetric dumbbells, the relative amplitudes of these peaks change. The asymmetry of the occupancy distribution is quantified using the ratio of total stay times on each adhesion site. To test the dependence of the stay probabilities on cell area and perimeter, we have constructed further asymmetric dumbbell geometries: one of the two square adhesion sites is replaced by a circular adhesion site of the same area or perimeter as the corresponding square adhesion site. We discuss the measured probabilities using an effective Hamiltonian comprising line tension, area elasticity and adhesive energy, and find a good agreement between our observations and predicted occupancies.

In summary, we have created an artificial two-state system, providing a dynamical assay for testing the theoretical concepts of effective elastic energies which govern cell behaviour. Potentially, the setup can be used to probe cell surface affinities by changing the nanoscopic or chemical structure of the adhesion sites. Moreover, it can be utilised as a lab-on-a-chip device to quantify cellular response to drug treatment.

Session III: Cell Migration in Cancer

Invited Talk Thu 08:30

Novel Methods to Study Cancer Cell Migration and Invasion — Ben Fabry — University of Erlangen-Nuremburg, Department of Physics, Henkestrasse 91, 91052 Erlangen, Germany

To migrate and metastasize in complex environments, tumor cells display a set of elementary activities, such as protrusion and retraction of cellular extensions, adhesion and de-adhesion, generation of tractions, or the chemical degradation of the surrounding matrix. However, an efficient and persistent cell migration on longer time scales requires coordination of these activities in close response to the local environmental conditions. As tumor cells can metastasize to different organs, an adaptation process must occur initially in the primary tumor. Despite numerous recent studies that have attempted to relate the metastatic potential of cancer cells to bio-mechanical measurements, no single cell parameter has emerged that can reliably predict how cancer cells invade or otherwise behave in a 3D matrix.
We therefore utilize a combined approach to evaluate multiple biophysical and functional properties that the cell can "tune" to adapt its migration strategies to the local environment. These properties include adhesion strength, contractility, visco-elastic cell properties, protrusion morphodynamics, and the activity and persistence of migration. We measure these properties in cells grown on 2D matrices with different adhesive ligand functionalization and stiffness, and in 3D matrices where we can modify the pore size, adhesive ligand composition and concentration, and stiffness. Our results demonstrate that not just a single biophysical attribute but rather a complex biophysical signature correlates with the ability of tumor cells to migrate in a complex 3D environment. In my presentation, I will focus on novel methods that we have recently developed to measure these biophysical properties with high accuracy, sensitivity and throughput, including 3-D traction force microscopy in highly non-linear biopolymer networks, Bayesian inference of migration parameter, and histogram-matching for bias-free microfluidic cell mechanical analysis.

Invited Talk Thu 09:00

Mechanical aspects of angiogenesis — Stefan Zahler — Ludwig-Maximilians-University Munich, Pharmaceutical Biology, Center for Drug Research, Butenandtstr. 5-13, 81377 Munich

In order to evade logistic limits of growth set by supply with oxygen and nutrients, tumors have to organize a vascular system of their own. This process of vascularization is termed angiogenesis, and has become an integral target of current cancer therapy. The underlying mechanisms of cell behavior and pattern formation have, to date, mainly been investigated on a biochemical level, not in terms of mechanotransduction.
Using microstructured surfaces, we dissected the specific roles of cell shape, adhesion surface, cell-cell contacts and dynamical changes for the activation of the mechanosensitive transcription regulators MRTF and YAP. Adhesion surface and cell-cell contacts turned out to be the major regulators for the activity of both signaling pathways, while cell shape played no role. Both transcription factors responded quickly (within minutes). Dynamic studies showed that MRTF is also quickly deactivated, while YAP responds much slower. This indicates that the two mechanosensitive pathways are not just redundant, but serve different purposes (quick response vs. sustained activation).
In a second setup we investigated the role of forces for vascular pattern formation. We found that the initial finding process between cells is not necessarily induced by chemotactic gradients, but depends on mechanical communication by matrix deformation. This communication turned out to crucially depend on the biophysical properties of the matrix (stiffness, topography).

Invited Talk Thu 09:30

Basement Membrane Fragments Contribute to the Regulation of the Epithelial-to-Mesenchymal Transition — Christine-Maria Horejs — Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Scheeles väg 2, Stockholm, 17177, Sweden

The epithelial-to-mesenchymal transition (EMT) enables cells of epithelial phenotype to become motile and

change to a migratory mesenchymal phenotype. EMT is known to be a fundamental requisite for tissue morphogenesis, and EMT-related pathways have been described in cancer metastasis and tissue fibrosis. Epithelial cells deposit a sheet-like extracellular matrix, the basement membrane, which is assembled from two major proteins, laminin and collagen type IV. This specialized matrix is essential for tissue function and integrity, and provides an important barrier to the potential pathogenic migration of cells. The profound phenotypic transition in EMT involves the proteolytic breakdown of the basement membrane. Matrix metalloproteinases (MMPs) are known to cleave components of basement membranes and a variety of basement membrane fragments have been shown to be released by specific MMPs in vitro and in vivo exhibiting distinct biological activities.

We have recently reported a previously unidentified laminin fragment that is released during EMT by MMP2 and that modulates key EMT-signaling pathways. Specifically, interaction of the laminin fragment with $\alpha 3\beta 1$-integrin triggers the down-regulation of MMP2 expression and a decrease in cell migration, thereby constituting a cell-matrix-cell feedback mechanism that contributes to the regulation of EMT and MMP activity. We explored this feedback mechanism to target pathological EMT in vivo, and developed an electrospun synthetic membrane that is functionalized with the recombinant laminin fragment and that can be directly interfaced with epithelial tissue to interfere with EMT pathways and inhibit MMP2 expression. Interaction of the functionalized synthetic membrane with peritoneal tissue inhibits TGFβ1-induced mesothelial EMT in vivo by decreasing active MMP2 levels and therefore, preventing basement membrane breakdown. Specifically, the functionalized synthetic membrane triggers changes in EMT-related transcription factor expression and nuclear translocation through the specific interaction of the laminin fragment with α3-integrin, suggesting a novel mechanism of how the basement membrane is involved in EMT regulation.

Invited Talk Thu 10:30

Mechanobiology, Migration and Coordinated Cell-Remodeling in Invading Breast-Cancer Cells — DAPHNE WEIHS — Technion-Israel Institute of Technology, Israel and CSPO journal, Haifa 32000, Israel

Invited Talk Thu 11:00

Gene Therapy Come of Age — DIETGER NIEDERWIESER — University Hospital Leipzig, Department of Hematology and Medical Oncology, Johannisallee 32 A, 04103 Leipzig, Germany

The ability to introduce genes into mammalian cells has contributed much to our knowledge of the mechanism and regulation of gene expression. A variety of methods have been used to transfer foreign genetic material into cells ranging from calcium-phosphate-mediated gene-transfer, micro-injection into target cells and the use of viral vectors to direct gene expression. The SV40 vectors used in the 80ties had a number of limitations, many of which were overcome with the development of retrovirus packaging mutants that could be used to produce helper-free, defective retrovirus. These more efficient delivery systems offered the first real promise of gene therapy. This may be used to restore the function of defect genes, to mark cells and even to treat cancer. The first attempt to modify human cells in this way was performed in 1980, but the first successful procedure to be reported involved the marking of infiltrating lymphocytes with a G418 resistant gene in 1989. Treatment of ADA deficient patients was reported in 1990. Since then, over 2300 clinical trials have been conducted, more than half of them in phase I studies. This intense period of investigation into gene therapy and the successful treatment of a number of patients served to demonstrate both the high potential benefits and the risks involved. The high potential is obvious: Natural and chimeric genes can produce products to restore homeostasis and provide clinical benefit. The question now is how to reduce the risk and broaden the appeal so that gene therapy can enter into the mainstream of clinical practice.

Important developments in this respect include the recent use of lentiviral vectors to replace mutated genes in blood stem cells of patients with leukodystrophy and Wiskott Aldrich syndrome, apparently without causing harmful side effects, and the introduction of chimeric antigen receptors (CAR) in T-cells to treat hematological cancer.

The introduction of chimeric antigen receptors into T-cells has been of interest for decades. However it was only recently that scientists recognized that the intracellular T-cell receptor wasn't enough to induce cell death of the antigen-bearing tumor cell. The early clinical trials using CAR T cells showed only modest results. However,

after modifying the intracellular domain, several trials of CD19-targeted CAR T-cells in the treatment of patients with B-cell malignancies have reported impressive outcomes, resulting in increased enthusiasm for this approach. Unprecedented remission rates of 70%–90% have been observed in adult and pediatric patients with relapsed and refractory acute lymphoblastic lymphoma. Remissions have been sustained in many patients without subsequent therapy, a phenomenon often correlating with CAR T-cell persistence. In other CD19+ malignancies including chronic lymphocytic leukemia and B cell Non-Hodgkin Lymphomas, response rates of 50%–80% have been observed even in heavily pretreated and refractory patients. Cytokine release syndrome is the most significant treatment related toxicity. Neurologic toxicity with encephalopathy is another important side effect. On target, off tumor effects of CD19-CAR T-cells are fortunately limited to B-cells and B-cell aplasia occurs in patients with CAR T-cell persistence. Given the successes of these early phase trials, larger Phase II studies are underway to assess the feasibility of expanding this treatment modality to multiple centers and to evaluate outcomes among larger numbers of patients. Important lessons have been learned from clinical trials of CD19-specific CAR T cells, and ongoing clinical trials are testing CAR designs directed at novel targets involved in hematological and solid malignancies. However questions regarding the persistence of transduced cells and tumor escape remain to be solved in the future.

Invited Talk Thu 11:30

Programming the Mechanical Properties of Bionic Networks — JÖRG SCHNAUß[1,2], JESSICA LORENZ[1,2,3], CARSTEN SCHULDT[1,2], TINA HÄNDLER[1,2], MARTIN GLASER[1,2], MARTIN SAJFUTDINOW[1], TOM GOLDE[2], JOSEF A. KÄS[2], DAVID M. SMITH[1] — [1]Fraunhofer Institute for Cell Therapy and Immunology, Perlickstraße 1, 04103 Leipzig, Germany — [2]University of Leipzig, Faculty of Physics and Earth Sciences, EXP, Soft Matter Division, Linnéstr. 5, 04103 Leipzig, Germany — [3]Department of Chemistry, Institute of Biochemistry, University of Cologne, Zülpicher Str. 47, 50674 Cologne, Germany

All living organisms are built up by semiflexible polymers. To understand the fundamental functional principles that enable the active complexity of living systems, we have to explore and uncover the physics of this special polymer class to be able to precisely alter their exclusive mechanical properties.

Here we use DNA-based, bionic constructs to explore the rich phase space of entangled as well as crosslinked networks of semiflexible polymers. Using biomimetic DNA nanotubes with similar mechanical properties as actin, we are able to directly test and determine the influence of the stiffness of the underlying polymer on the overall network elasticity. In contrast to predominant theories of entangled semiflexible polymer networks, we show proof that these networks stiffen upon increasing the persistence length of the underlying filaments. I.e., these networks stiffen without changing the underlying mesh size of this hydrogel, which is an unavoidable side effect for current cell experiments based on collagen matrices.

In addition to these purely artificial systems, we also directly target actin networks to precisely influence their mechanical properties by introducing DNA-based crosslinkers. Although cells do employ crosslinking proteins, they can be hardly compared since they vary in many different parameters. Our constructs are readily tuneable and allow us, for instance, to explore the impact of a crosslinker's binding affinity decoupled from any other parameters. Measurements with bulk rheology revealed that the bionic crosslinkers indeed recreate the mechanical fingerprints of naturally occurring crosslinkers such as fascin and show a non-trivial, concentration dependent stiffening of actin networks.

Invited Talk Thu 12:00

Employing Nanostructured Scaffolds for Long-Term Adult Tissue Culture and Investigation of Tissue Mechanics at the Nanoscale — MAREIKE ZINK[1], SADDAM RAHMAN[2], VALENTINA DALLACASAGRANDE[1,2,5], ANDREAS REICHENBACH[2], JOSEF KÄS[1], STEFAN G. MAYR[3,4] — [1]University of Leipzig, Faculty of Physics and Earth Sciences, EXP, Soft Matter Division, Linnéstr. 5, 04103 Leipzig, Germany — [2]Paul Flechsig Institute for Brain Research, University of Leipzig, Liebigstr. 19, 04103 Leipzig, Germany — [3]Leibniz Institute for Surface Modification (IOM), Permoser Str. 15, 04318 Leipzig, Germany — [4]Division of Surface Physics, Department of Physics and Earth Sciences, University of Leipzig, Leipzig, Germany — [5]Weill Cornell Medical College, Cornell University, New York, USA

Tissue properties such as morphology, organization of cells and the extracellular matrix, as well as the distribution of mechanical properties can often only be accessed ex vivo. However, organotypic culture of adult tissues is still an unsolved task since tissue survival of adult fully differentiated tissues is limited to a few days in vitro. Here we show that TiO2 nanotube scaffolds with tissue-specifically tailored characteristics can serve as ideal substrates for long-term cultures of different adult tissues with high viability for at least two weeks in contrast to tissue cultures on standard PTFE membranes [1]. Prerequisite for long-term tissue survival is an improved adhesion of the tissue to the underlying nanotube scaffold which strongly depend on the nanotube geometry in terms of tube diameter and surface roughness. Additionally, on the example of complex neural tissues such as the retina, we employ a self-designed mechanical spectroscopy setup and show that the nanotube scaffolds can be employed as vibrating reed to investigate the mechanical properties of tissue at the nanoscale, viz. protein level. Here the nanotube scaffold is clamped at one end and excited to perform free damped oscillations with the retina on top. The detected oscillation parameters represent a fingerprint of the frequency-dependent mechanical tissue properties that are derived in combination with sandwich beam analysis and finite element calculations [2]. We found that the Young's modulus of the retina on the scale of 10 nm is of the order of a few GPa, much higher than values obtained on micrometer length scales. In our study, individual biopolymers and proteins on the photoreceptor side of the retina in contact with the nanostructured reed are stretched and compressed during vibration of the underlying scaffold and the acting intramolecular forces are probed at the protein level. We reveal that the Young's moduli of individual protein chains from serum – a major component of the used tissue culture medium – are about 16 times higher compared to the average modulus of the porous TiO2 nanostructure when probed at the nanoscale (38 GPa vs. 2 GPa). In fact, computer simulations of various biomolecules already demonstrated polymer stiffnesses up to 200 GPa. Since pathology and many diseases are related to changes on molecular level, e.g. during cancer progression and remodeling of the extracellular matrix, our biotechnological approach offers new perspectives in studying the relation of tissue mechanics to tumor spreading and effect of medications.

[1] V. Dallacasagrande, M. Zink, S. Huth, A. Jakob, M. Müller, A. Reichenbach, J.A. Käs, S.G. Mayr, Adv. Mater. 24, 2399–2403 (2012)

[2] S.M. Rahman, A. Reichenbach, M. Zink, S. Mayr, Soft Matter 12, 3431 – 3441 (2016

Session IV: Micro Tools in Cancer Research

Invited Talk Thu 14:00

Condensing DNA into Nanostructures — FRIEDRICH C. SIMMEL — Technical University, Munich, Am Coulombwall 4a, 85748 Garching, Germany

In nature, DNA molecules often have to be packed into confined spaces such as the cell nucleus, sperm heads, or virus capsids. This condensation process is facilitated by cationic condensing agents, which help to overcome the strong electrostatic repulsions between closely packed DNA duplexes. In this talk, we will present two applications of such condensing agents in an artificial context. First, we demonstrate how the polyamine spermidine can be used to create and stabilize DNA origami nanostructures under low ionic strength conditions. The structures turn out to be resistant to strong electric field pulses and can even be electrotransfected into cells. Second, we show how condensation of micrometer long DNA molecules can be directed along one-dimensional lines on a lithographically structured biochip. The resulting linear DNA condensates may find use in the control of cell-free gene expression processes on a chip.

Invited Talk Thu 14:30

Why Do Rigid Tumors Contain Soft Cancer Cells? — FRANZISKA WETZEL*[1], ANATOL FRITSCH*[1], DAPENG BI*[7], ROLAND STANGE[1], TOBIAS KIEßLING[1], STEVE PAWLIZAK[1], MAREIKE ZINK[1], LARS-CHRISTIAN HORN[3], KLAUS BENDRAT[4], MAJA OKTAY[5], AXEL NIENDORF[4], JOHN CONDEELIS[6], MICHAEL HÖCKEL[2], M. CRISTINA MARCHETTI[8], LISA MANNING[8], JOSEF KÄS[1] — [1]University of Leipzig, Faculty of Physics and Earth Sciences, EXP, Soft Matter Division, Linnéstr. 5, 04103 Leipzig, Germany — [2]Department of Obstetrics and Gynecology, Women`s and Children`s Center, Leipzig University, Leipzig, 04103 Leipzig, Germany — [3]Division of Breast, Urogenital and Perinatal Pathology, Institute of Pathology, Leipzig University, 04103 Leipzig, Germany — [4]Pathology, Hamburg-West, 22767 Hamburg, Germany — [5]Montefiore Medical Center, Bronx, NY 10467, U.S.A. — [6]Albert Einstein College of Medicine, Bronx, NY 10461, U.S.A. — [7]Center for Studies in Physics and Biology, Rockefeller University, 1230 York Avenue, NY 10065, U.S.A. — [8]Departement of Physics, Syracuse University, Syracuse, NY 13244, U.S.A

As early as 400 BCE, the Roman medical encyclopaedist Celsus recognized that solid tumours are stiffer than surrounding tissue. However, cancer cell lines are softer, which facilitates invasion. This paradox raises several questions: Does softness emerge from adaptation to mechanical and chemical cues in the external microenvironment, or are soft cells already present inside a primary tumour? If the latter, how can cancer tissue be more rigid than normal tissue and yet contain more soft cells? Here we show that in primary samples from patients with mammary and cervix carcinomas, cells do exhibit a broad distribution of rigidities, with a higher fraction of softer and more contractile cells compared to normal tissue. Mechanical modelling based on patient data reveals that tumours with a significant fraction of very soft cells can still remain solid. Moreover, in tissues with the observed distributions of cell stiffness, softer cells spontaneously self-organize into multicellular streams, possibly facilitating cancer metastasis.
* These authors contributed equally to this work.

Invited Talk Thu 15:00

Dynamics of circular dorsal ruffles and their role in cancer — ERIK BERNITT[1,2,3], JULIA LANGE[1], MALTE OHMSTEDE[1], NIR GOV[2], ARIK YOCHELIS[3], HANS-GÜNTHER DÖBEREINER[1] — [1]Institut für Biophysik, Universität Bremen, 28359 Bremen, Germany — [2]Department of Chemical Physics, Weizmann Institute of Science, 76100 Rehovot, Israel — [3]Department of Solar Energy and Environmental Physics, Ben-Gurion University of the Negev, 849900 Midreshet Ben-Gurion, Israel

Cells utilize the actin cytoskeleton to actively remodel their morphologies. This enables them to internalize extracellular fluid and activated membrane receptors via macropinocytosis. To form large vesicles this endocytotic mechanism relies on the contraction and closure of actin-based, ring-shaped vertical protrusions at the dorsal cell membrane that are known as Circular Dorsal Ruffles (CDRs). CDRs are essential to a range of vital and pathogenic processes alike. For cancer cells CDRs

seem to play two oppositional roles: Loss of CDRs is associated with failure of the shut down of signalling by activated growth factor receptors, which leads to uncontrolled cell growth. On the other hand CDRs also serve the dissociation of the cytoskeleton, which facilitates the ability of cancer cells for mesenchymal migration.

Despite much scientific attention, the mechanism of how proteins self-organize to form these dynamic ring-shaped structures remains unknown. We show that CDRs are propagating fronts of actin polymerization in a bistable system. A new model assigns the expansion and contraction of waves to distinct counter-propagating fronts of different velocities. Under a change in biochemical conditions, CDR may be pinned and fluctuate near the cell boundary or result in complex spiral wave dynamics due to a wave instability. Indeed, both phenomena are found in our data [1] pointing at the conditions for which macropinocytosis is suppressed. The latter scenario is valid for, e.g., confined CDRs on quasi one-dimensional tracks. We investigate the stochastic dynamics of these states as a function of biochemical conditions and find evidence of stochastic resonance.

[1] E.Bernitt, C.G.Koh, N.Gov, HG Döbereiner, PLOS One 10 (1), e0115857 (2015)

Invited Talk Thu 15:30

Cell Binding Peptides from Statistical Analysis of Random Peptide Phage Display Libraries — Michael Szardenings — Fraunhofer Institute for Cell Therapy and Immunology (IZI), Perlickstraße 1, 04103 Leipzig, Germany

An innovative, highly diverse (>109) peptide phage library has been generated with a novel tri-nucleotide synthesis approach, with less than 20 codons per position, perfectly statistically distributed and a peptide diversity outnumbering most any present library. This diversity, in combination with next generation sequencing and novel software allows for the first time that phage display results are interpreted on a completely statistical basis in silico. For example it allows determining epitopes after single round panning directly on complete sera from allergy patients or on polyclonal antibodies. In collaboration with CNUHH we started looking at peptides binding to general tumor tissues. In another project together with partners from the pharmaceutical industry we have identified kidney tissue specific peptides. These approaches have led to several insights into how statistical search for binding motifs in large data sets can be accomplished. We have now several peptides in the pipeline for further development and multiple applications.

Special Focus Session: Programming Nanomaterials Against Cancer

Invited Talk Thu 16:30

Spatial Signalling at the Membrane — Ana Teixeira — Karolinska Institute, Department of Medical Biochemistry and Biophysics, Scheeles väg 2, 171 77 Stockholm, Sweden

Membrane proteins are key sensor components in cells and form the largest class of proteins in the druggable genome. Dyregulation in membrane protein mediated signaling is involved in allowing cells to acquire abnormal functions in cancer such as aberrant proliferation and invasion of neighboring tissues.
The significance of the biophysical context of ligands and receptors at the membrane for downstream signalling pathways is widely accepted but poorly understood due to difficulties in controlling and analysing membrane protein microenvironments at the nanoscale. DNA origami is a nanofabrication technology that uses DNA self-assembly to drive the precise formation of nanostructures. We have recently shown that DNA origami can be used to tailor the spatial distribution of protein assemblies [1]. This new tool allows for display of well-defined protein nanoclusters in solution and is therefore amenable to the study of 3D in vitro tissue models and presents an opportunity for future translational applications. Therefore, DNA origami/ligand nanoclusters form a nanotool that is well suited to investigate the roles of the biophysical properties of ligand/receptor interactions on downstream signaling and cellular outcomes.
We have previously shown that the levels of EphA2 receptor activation depend on the spatial distribution of ephrinA5 ligands at the nanoscale [1]. To investigate the morphological and dynamical aspects of the assembly of receptor on the cell membrane, we are using Stochastic Optical Reconstruction Microscopy (STORM). In order to identify the downstream signaling pathways modulated by receptor spatial distribution and lateral mobility, we are using RNA-sequencing and functional assays.
We developed tailor-made ligand nanoclusters that have the potential to contribute to understanding of the fundamental mechanisms of action of physical variables at the membrane in ligand/receptor signaling. This work has the potential to provide insights relevant for the development of new types of pharmacological interventions that target the biophysical context of the ligand-receptor interaction

[1] A. Shaw, V. Lundin, E. Petrova, F. Fordos, E. Benson, A. Al-Amin, A. Herland, A. Blokzijl, B. Hogberg, A. I. Teixeira, Nature Methods 11:841-846 (2014)

Invited Talk Thu 17:00

Bottom-up Engineering of Nanoscale Devices to Program Biological Materials — David Smith — Fraunhofer Institute for Cell Therapy and Immunology, Perlickstraße 1, 04103 Leipzig, Germany

Biologically evolved materials are often used as inspiration in the design and development of new materials; however, the molecular toolbox provided by biological systems has been evolutionarily optimized to carry out the necessary functions of cells. The resulting inability to systematically modify such fundamental properties such as size, binding strength and valency in experimentally available model systems hinders a meticulous examination of parameter space. We circumvent these limitations using model systems and components assembled from programmable nanomaterials such as DNA and peptides.
Synthetic constructs for crosslinking actin filaments are fabricated from DNA strands which have been conjugated to different actin-binding peptides. These were shown to modulate bulk network elasticity in accordance with binding strength, concentration and size of the crosslinking construct, and can mimic certain non-canonical behaviors of crosslinked biopolymer systems. Introduction of these synthetic constructs into living cells hinders their motility, indicating a controllable slowing or suppression of their internal actin network dynamics. In invasive (mesenchymal) cancer cells, these constructs selectively inhibit the invasion of cells into a collage network in comparison to simple migration through micrometer-sized pores, also indicating an inhibitory effect on biochemical invasion processes. Indeed, in non-malignant epithelial cells that are stimulated to undergo the epithelial-to-mesenchymal transition (EMT), these constructs fully inhibit key indicators of the transition such as the formation of actin-based stress fibers. This points towards the biasing of mechanotransductive

biochemical pathways, triggered by an interplay between local network stiffening and actin depolymerization dynamics, which can be programmed in an entirely deterministic manner.
A similar approach is used to engineer "synthetic antibodies" that can be used to influence cell behavior by activating receptor-mediated pathways on the cell surface. Here, we target the Ephrin A2 recpetor, which is over-expressed in certain types of cancer, yet paradoxically triggers anti-oncogenic effects in malignant cells. By linking short (12 a.a.), Ephrin-activating peptides through DNA-based scaffolds, a valency-dependent effect on binding to EphA2-expressing cells can be controlled. Furthermore, these multivalent, synthetic antibodies can be used to cause a two-fold enhancement phenotypic expression on targeted cells.

Contributed Talk Thu 17:30

Membrane-Targeting DNA Nanostructures — Tobias Pflueger — Nano Temper Technologies, Flößergasse 4, 81369 Munich, Germany

NanoTemper Technologies develops highly innovative instrument and software solutions for biomolecular analytics with focus on affinity, stability and conformation. Our collaborative approach, science-driven insights, our high-quality, proprietary instruments and analytical technologies focus on helping researchers to make the greatest impact - with maximum speed, efficiency and precision.
This scientific presentation will give an overview about experimental setup, common and exceptional applications and latest developments and publications linked to drug discovery and development.

Invited Talk Thu 17:45

Membrane-Targeting DNA Nanostructures — Ralf Seidel — Molecular Biophysics group, Institute of Experimental physics I, Universität Leipzig, Linnéstr. 5, 04103 Leipzig, Germany

Almost one third of the genes in most genomes encode for membrane proteins. Sitting at the interface between cell interior and exterior, these types of molecules are important drug targets. One approach in order to understand the mechanisms of membrane proteins is to build artificial mimics that reconstitute certain functionalities of their natural counterparts. Recent developments in DNA nanotechnology provide now a powerful toolbox too build multifunctional and complexly shaped macromolecules with atomic precision. Here we show how DNA nanostructures assembled by the origami technique can be attached to lipid membranes and how functional membrane protein mimics can be obtained. Examples include large scale membrane deformations in analogy to coat-forming proteins, e.g. from the I-/F-BAR family, as well as DNA-based nanopores. Furthermore, fundamental properties of the DNA nanostructure lipid membrane interaction, such as the two-dimensional diffusive motion and the domain localization of these structures are characterized. Finally we show how DNA nanostructures can be integrated into carrier systems assembled by the layer-by-layer method providing a new approach for the assembly of multi-compartment drug delivery systems.

Invited Talk Thu 18:15

Death by Gold: Targeting Invasive Glioblastoma Cells by Peptide-Functionalized Gold Nanorods — Diana P.N. Goncalves[1], Raul D. Rodriguez[2], Thomas Kurth[3], Laura J. Bray[1,4], Marcus Binner[1], Christiane Jungnickel[5], Fatih N. Gür[6], Steve W. Poser[7], Thorsten Schmidt[6], Dietrich R. T. Zahn[2], Andreas Androutsellis-Theotokis[7], Michael Schlierf[5], Carsten Werner[1] — [1]Leibniz Institute of Polymer Research Dresden, Max Bergmann Center of Biomaterials Dresden, Hohe Str. 6, 01069 Dresden, Germany — [2]Institute of Physics, Technische Universität Chemnitz, 09107 Chemnitz, Germany — [3]Electron Microscopy Facility, DFG - Center of Regenerative Therapies Dresden, Technische Universität Dresden, Fetscherstr. 105, 01307 Dresden, Germany — [4]Institute of Health and Biomedical Innovation, Queensland University, 60 Musk Avenue, Kelvin Grove, QLD 4059, Australia — [5]B CUBE - Center of Macromolecular Bioenineering, Technische Universität Dresden, 01307 Dresden, Germany — [6]Cluster of Excellence Center of Advancing Electronics Dresden (cfaed), Technische Universität Dresden, 01062 Dresden, Germany — [7]University Clinic Carl-Gustav Carus, Technische Universität Dresden, 01062 Dresden, Germany

Cancer stem cells (CSCs) are known to be responsible for drug resistance and tumor recurrence in several cancer types, making their eradication a primary objective in cancer therapy. Glioblastoma multiforme

(GBM) tumors are usually composed of a highly infiltrating CSC subpopulation, which has Nestin as a putative marker. Since the majority of these infiltrating cells are able to elude conventional therapies, we have developed a gold nanorod- (AuNR) peptide-biosensor capable of specific recognition and selective eradication of Nestin-positive GBM (GBM-Nes+) infiltrating cells, by photohermolysis. The AuNR-peptide biosensor was evaluated regarding heating abilities, cell selectivity, cell uptake pathway, and photohthermal activity in mono- and co-culture systems containing Nes+ and Nestin-negative (Nes-) GBM cells. Biodegradable three dimensional (3D) hydrogels, composed of star shaped poly(ethyleneglycol) (starPEG) covalently connected to matrix metalloproteinase-susceptible peptides and heparin (starPEG-MMP-heparin), were used to recreate GBM tumor microenvironments, and for the assessment of AuNR photothermal activity. Finally, the obtained 3D culture results were then compared with two dimentional monolayer cultures.

7th Symposium

PHYSICS OF CANCER

October 4- 6, 2016 | Leipzig, Germany

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Program Overview

Time	Tuesday, Oct. 4, 2016
11:00	Conference check-in
13:00	Welcome
	Session I: Functional Mechanics of Cancer Cells
13:15	Paul Janmey
13:45	Roland Eils
14:15	Christoph Mark (CT)
14:30	TA Instruments (CT)
14:45	Joachim Rädler
15:15	Coffee break
15:45	Allen Ehrlicher
16:15	Rebecca Wells
16:45	Kandice Tanner
17:15	Fabrizio Cleri (CT)
17:30	Lisa J. McCawley
18:00	Round Table: Barbecue for all participants Faculty of Physics and Earth Sciences Linnéstr.5, 04103 Leipzig

Time	Wednesday, Oct. 5, 2016
	Session II: Membranes and the Cytoskeleton
08:30	Hauke Clausen-Schaumann
09:00	Wolfgang Losert
09:30	Sarah Köster
10:00	Dimitar Stamov (CT)
10:15	Coffee break
10:45	Kristian Franze
11:15	Tobias Zech (CT)
11:30	Hamid Mohammadi (CT)
11:45	Peter Friedl
12:15	Eric Barnhill (CT)
12:30	Jung Joon Min
13:00	**POSTER SESSION** Presentation of contributed posters with discussions and lunch/ large lecture hall
16:00	Guided City Tour with Josef Käs
	Social Event for Invited Speakers: Dinner at "Auerbach´s Keller"

Time	Thursday, Oct. 6, 2016
	Convergent Science Physical Oncology
	Session III: Cell Migration in Cancer
08:30	Ben Fabry
09:00	Stefan Zahler
09:30	Christine-Maria Horejs
10:00	Coffee break
10:30	Daphne Weihs
11:00	Dietger Niederwieser
11:30	Jörg Schnauss
12:00	Mareike Zink
12:30	Lunch
	Session IV: Micro Tools in Cancer Research
14:00	Friedrich Simmel
14:30	Josef A. Käs
15:00	Hans-Günther Döbereiner
15:30	Michael Szardenings
16:00	Coffee break
	Special Focus Session: **Programming Nanomaterials Against Cancer**
16:30	Ana Teixeira
17:00	David M. Smith
17:30	Tobias Pflüger (CT)
17:45	Ralf Seidel
18:15	Diana Goncalves-Schmidt
19:00	Prospective end