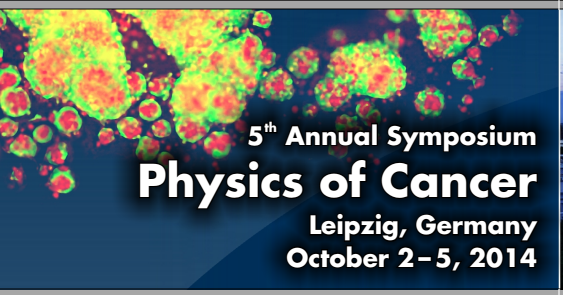

Program

Invited Speakers

Patricia Bassereau (France) • Joel Beaudouin (Germany) • Timo Betz (France)
Daria Bonazzi (France) • Jasna Brujic (USA) • Giovanni Cappello (France)
Dino Di Carlo (USA) • Ben Fabry (Germany) • Claudia Fischbach-Teschl (USA)
Daniel Fletcher (USA) • Karin Forsberg Nilsson (Sweden) • Kristian Franze (UK)
Annica Gad (Sweden) • Rhoda Hawkins (UK) • David Helfman (South Korea)
Sylvie Hénon (France) • Michael Höckel (Germany) • Lance Munn (USA)
Inke Näthke (UK) • Timothy Newman (UK) • Matthieu Piel (France)
Jacques Prost (France) • Cynthia Reinhart-King (USA) • Ana-Suncana Smith (Germany)
Melda Tozluoglu (UK) • Krystyn Van Vliet (USA) • Raphael Voituriez (France)
Angelika Vollmar (Germany) • Franziska Wetzel (France)

Organizing Committee

Franziska Lautenschläger (Germany) • Harald Herrmann (Germany)
Paul Janmey (USA) • Josef A. Käs (Germany)

General Information

Dear participants,

welcome to the *5th 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:

www.uni-leipzig.de/poc/2014

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City of Leipzig


Photo: Michael Bader, CC-BY

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.
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. On the interactive map on our website, we marked some sights which are worth visiting.

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***. Trams and buses are operated by the *LVB*, while the S-Bahn is operated by the *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 (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 with tram, bus, or S-Bahn within one zone (e.g. the city of Leipzig) with the option to interchange to any other tram, bus, and S-Bahn lines (fee 2.40 EUR).
- *"Einzelfahrkarte - 3 Zonen"* (full single ticket for 3 zones) is valid for 2 hours for travel within three zones with the option to interchange to any other tram, bus, and S-Bahn lines (fee 4.30 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 (but not in S-Bahns!) as well as directly from bus drivers. Ticket machines accept cash. Tickets have to be validated prior

travelling using the stamping machines located on the platforms (for S-Bahn travel) or inside the vehicle (for tram or bus travel).
Detailed information on Leipzig's public transportation system including network maps, timetables, and a connection planner can be found at **www.lvb.de**.

(Note: The *DB (Deutsche Bahn)* additionally operates regional trains (called "RB" and "RE") as well as inter-city trains (called "IC" and "ICE") neither of 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.)

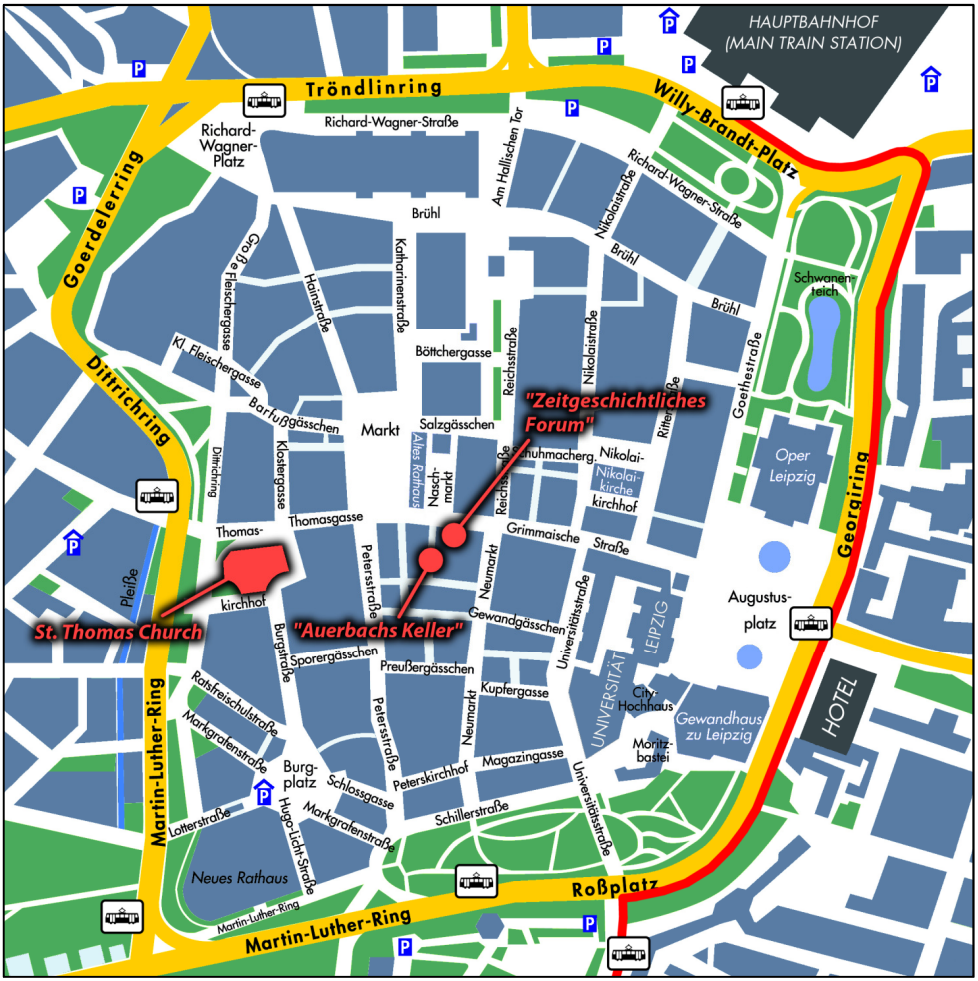
Conference Venue

The *"Physics of Cancer"* symposium will take place at the *University of Leipzig*, more precisely at the building of the *Center for Biotechnology and Biomedicine (BBZ)*.

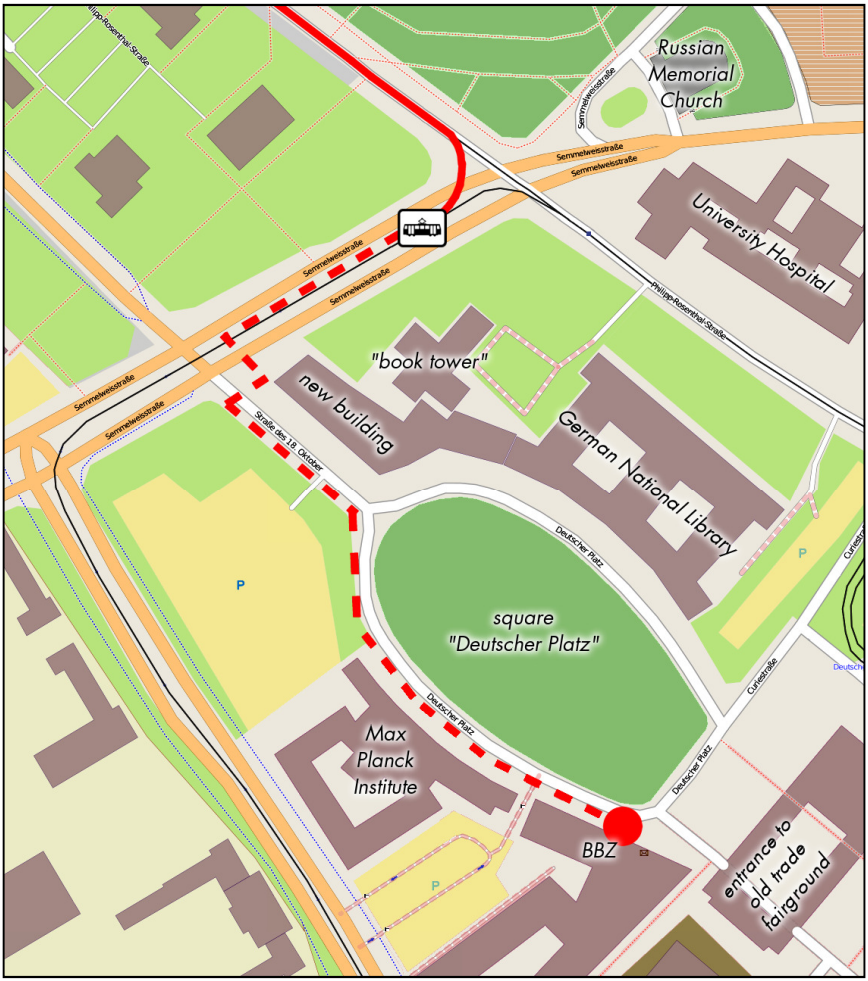
Biocity Leipzig – University of Leipzig
Center for Biotechnology and Biomedicine (BBZ)
Deutscher Platz 5
04103 Leipzig, Germany


Photo: Steve Pawlizak

The easiest way to get from the main train station ("Hauptbahnhof"), the city center at "Augustusplatz", or the "Bayerischer Bahnhof" to the conference site is to take **tram line 16** in direction "Lößnig" or **tram line 2** in direction "Naunhofer Straße" (see map 1 below). Your target stop is called "Deutsche Nationalbibliothek". From there, it is a 5-minute walk to the BBZ building which lies opposite to German National Library and next to the Max Planck Institute (see map 2 below).
On your way back, you have to travel with tram line 16 in the opposite direction called "Messegelände". For detailed information, please have a look at the interactive map on our website.



Map 1: Detailed view of the city center of Leipzig. The solid red line depicts the track of tram line 16 from the main train station via "Augustusplatz" and "Bayerischer Bahnhof" (not shown on this map) to the conference site (shown on this map). The locations visited as a social event on Friday, October 3, are also marked on the map: St. Thomas Church ("Thomaskirche"), the restaurant "Auerbachs Keller" and the museum "Zeitgeschichtliches Forum". (Map source: University of Leipzig)



Map 2: Detailed view of the area around the square "Deutscher Platz". The solid red line depicts the track of tram line 16 coming from the main train station via "Augustusplatz" and "Bayerischer Bahnhof" (not shown on this map) to your target stop called "Deutsche Nationalbibliothek" (German National Library). The dashed red line depicts the walk from the tram stop to the conference site (BBZ). (Map source: OpenStreetMap)

Presentations

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

Talk sessions will be in the large auditory (ground floor, SR 1.1 to 1.3) of the BBZ. 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 Saturday, October 4th, 2014 at 19:00 in the foyer of the BBZ. During this session, a snack buffet will be provided for all participants. Authors can already mount their posters at Thursday, October 2nd, 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 Sunday, October 5th, 12:00. Any posters that are left will be discarded by the organizers.

Wireless Internet Access

For the time of the conference, a special wireless network called "**eduevent**" will be available at the conference site and almost all other facilities of University of Leipzig. Use the following information to connect your Wi-Fi capable device to the network:

Wireless network name:	**eduevent**	IP address:	obtain automatically (DHCP)
Password (PSK):	[redacted]	DNS server:	obtain automatically (DHCP)
Encryption:	WPA2/AES		

Pay attention to the correct (case-sensitive) spelling of the password.
After successful connection, open your web browser (e.g. Internet Explorer, Mozilla Firefox) to view the terms of use. You have to accept these terms in order to unlock the network access for your device. This procedure is necessary only once a day.
Note that this conference wireless network does only support HTTP, POP3, IMAP, VPN, and SSH protocols.

If you are a member of an institution (e.g. a university) which is a member of the international eduroam community, you may also connect to the wireless network called "**eduroam**" provided by the University of Leipzig. In most cases, you can use this network in the same way you are used to connect to the eduroam network at your home institution.

National Holiday and Weekend

Please note that on Friday, October 3, there is the national holiday of Germany ("Day of German Unity"). Hence, most shops including grocery stores and supermarkets will be closed. Additionally, most shops will be also closed on Sundays.

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 special name badges which have a green background (in contrast to the white background of normal name badges).

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

13:00 – 13:15 *Welcome and opening*
JOSEF A. KÄS (University of Leipzig)

Session I: Mechanical Properties of Cancer Cells I

13:15 – 13:45 **Mechanical sensing by normal and transformed cells**
PAUL JANMEY (University of Pennsylvania, USA)

13:45 – 14:15 **Individual and collective metastatic cell migration behaviors**
CYNTHIA REINHART-KING (Cornell University, USA)

14:15 – 14:45 **Applying controlled mechanical pressure on tumor cells aggregates**
GIOVANNI CAPPELLO (Institut Curie, France)

14:45 – 15:15 *Coffee break*

15:15 – 15:45 **Mechanical constraints and cancer**
DANIEL FLETCHER (University of California, Berkeley, USA)

15:45 – 16:15 **Early changes in tissue organisation and structure in colorectal cancer**
INKE NÄTHKE (University of Dundee, UK)

16:15 – 16:45 **Biomechanical processes and topological dynamics in tumors**
LANCE L. MUNN (Massachusetts General Hospital & Harvard Medical School, USA)

16:45 – 17:15 **Caveolae-mediated mechanotransduction in single cells and imaging of confined spheroids**
FRANZISKA WETZEL (Institut d'Optique Graduate School, France)

17:15 – 17:30 **Biomechanics of human primary tissue cells in tumor progression**
ANATOL FRITSCH (University of Leipzig, Germany)

17:30 – 17:45 **Cell deformability during passage through micron-scale constrictions**
JANINA LANGE (University of Erlangen-Nuremberg, Germany)

17:45 – 18:00 **Epithelial closure dynamics**
PHILIPPE MARCQ (Institut Curie, France)

Evening *Enjoy the evening at your own disposal.*

Session II: Membranes and the Cytoskeleton

08:30 – 09:00 **Pulling with filopodia: high forces on weak connections**
PATRICIA BASSEREAU (Institut Curie, France)

09:00 – 09:30 **Oncogenic signaling and the cytoskeleton**
DAVID M. HELFMAN (KAIST, South Korea)

09:30 – 10:00 **Mechanism of CD95 clustering and activation at the single cell level**
JOEL BEAUDOUIN (German Cancer Research Center & BioQuant, Germany)

10:00 – 10:30 **Mimicking tissues with densely packed lipid droplets**
JASNA BRUJIC (New York University, USA)

10:30 – 11:00 *Coffee break*

11:00 – 11:30 **The mechanics of invasion: How contraction sets the stage for invasive migration**
TIMO BETZ (Institut Curie, France)

11:30 – 12:00 **Chemomechanics of cell migration and activation in the cancer microenvironment**
KRYSTYN J. VAN VLIET (Massachusetts Institute of Technology, USA)

12:00 – 12:30 **Oncogenic cell transformation changes the nanoscale organization of adhesions, vimentin filaments and cell stiffness**
ANNICA K. B. GAD (Karolinska Institutet, Sweden)

12:30 – 12:45 **The role of vimentin in cell migration under confinement**
LUIZA STANKEVICINS (Saarland University, Germany)

12:45 – 13:00 **Cancer cell behaviours on a culture substrate imprinted with their own features**
TIFFANY TAN (University of Otago, New Zealand)

13:00 – 14:30 *Lunch for all participants*

Afternoon *Get-together with visit to the museum "Zeitgeschichtliches Forum" (free admission). For all invited speakers, there will be a guided tour starting at 16:00.*

18:00 *Motet at St. Thomas church (2.00 EUR admission). Note that doors already open at 17:15. No reservations possible. Free admission for all invited speakers.*

19:00 *Dinner at "Auerbachs Keller" for all invited speakers*

Session III: Mechanical Properties of Cancer Cells II

08:30 – 09:00 **Analysis of a few *in vitro* experiments**
JACQUES PROST (Institut Curie, France)

09:00 – 09:30 **Mechanotransduction in developing cell systems**
KRISTIAN FRANZE (University of Cambridge, UK)

09:30 – 10:00 **Association between embryonic development and locoregional cancer progression**
MICHAEL HÖCKEL (University of Leipzig, Germany)

10:00 – 10:30 *Coffee break*

10:30 – 11:00 **Biophysical characterization of the myxobacterial compound Soraphen A: an innovative option to fight invasive cancer**
ANGELIKA M. VOLLMAR (Ludwig-Maximilians-Universität München, Germany)

11:00 – 11:30 **Actin-based transport adapts polar cap size to local curvature**
DARIA BONAZZI (Institut Jacques Monod, France)

11:30 – 12:00 **Modeling glioma and targeting the glioma niche**
KARIN FORSBERG NILSSON (Uppsala University, Sweden)

12:00 – 12:15 **Is cell segregation governed by cellular adhesion?**
STEVE PAWLIZAK (University of Leipzig, Germany)

12:15 – 12:30 **Mesenchymal migration cannot be described as a persistent random walk**
CHARLOTTE RIVIERE (Université Lyon 1, France)

12:30 – 14:30 *Lunch for all participants*

Session IV: Microtools for Study and Diagnostics in Cancer Research

14:30 – 15:00 **Measuring cell mechanics for medicine**
DINO DI CARLO (University of California, Los Angeles, USA)

15:00 – 15:30 **Quantifying metastasis using rare events**
TIMOTHY NEWMAN (University of Dundee, UK)

15:30 – 16:00 **Plasticity of cancer cell migration: Extracellular matrix enables the optimisation of blebbing, adhesions, and spreading**
MELDA TOZLUOGLU (University College London, UK)

16:00 – 16:15 **New elasticity-patterned substrates for bi-dimensional organization of cells**
CAMILLE MIGDAL (iRTSV, CEA Grenoble, France)

16:15 – 16:30 **Emergence of collective cell migration on circular micropatterns**
FELIX JAKOB SEGERER (Ludwig-Maximilians-Universität München, Germany)

16:30 – 17:00 *Coffee break*

17:00 – 17:30 **Micromechanical tools to study the role of vimentin in cells**
FRANZISKA LAUTENSCHLÄGER (Saarland University, Germany)

17:30 – 18:00 **Role of serum response factor in the mechanotransduction of myoblasts**
SYLVIE HÉNON (Université Paris Diderot, France)

Poster Session

19:00

1 **Intracellular stresses in patterned cell assemblies**
ALICE NICOLAS (Université Joseph Fourier, France)

2 **Modulation of membrane rigidity impacts cell migration and invasion**
SEBASTIAN SCHMIDT (University of Leipzig, Germany)

4 **The interactions of hERG1 potassium channels and ß1 integrins in pancreatic ductal adenocarcinoma cells**
STEFANO COPPOLA (Sapienza University of Rome, Italy)

5 **Mechanical cues in Ewing sarcoma metastasis**
ELENA BELETKAIA (Leiden University, The Netherlands)

6 **Plasma membrane softening in human breast and cervical cancer cells**
CHRIS HÄNDEL (University of Leipzig, Germany)

7 **The native root extract of Linum usitatissimum: stress fiber induction by increased profilin-1 expression results in reduced motility of MCF-7 breast cancer cells**
NADJA ENGEL-LUTZ (University Medical Center Rostock, Germany)

8 **Mechanosensation in Constrained Collagen Matrices**
HAMID MOHAMMADI (University of Toronto, Canada)

9 **Heterogeneity and dynamics of cancer cells at the interface of step-gradients of 3D collagen matrices**
JIRANUWAT SAPUDOM (University of Leipzig, Germany)

10 **Biophysical method for early cancer detection**
JELENA MUNCAN (University of Belgrade, Serbia)

11 **Contractile actin bundle without molecular motors**
JÖRG SCHNAUSS (University of Leipzig, Germany)

12 **Control of cancer cell invasion by lamin-mediated nuclear deformability**
KATARINA WOLF (Radboud University Nijmegen Medical Centre, The Netherlands)

13 **Effect of x-irradiation on cell morphology, cytoskeleton network, and adhesion**
SABATO FUSCO (Istituto Italiano di Tecnologia, Italy)

14 **Intracellular mechanics of normal and cancer cells**
JEAN-BAPTISTE MANNEVILLE (Institut Curie, France)

15 **Higher ordered assembly of rigid biopolymers induced by depletion forces**
MARTIN GLASER (University of Leipzig, Germany)

16 **Surface tension-based model of epithelial folds**
MATEJ KRAJNC (Jozef Stefan Institute, Slovenia)

17 **Mechanics of tumor growth in an *in vitro* model system**
KRISTEN MILLS (Max Planck Institute for Intelligent Systems, Germany)

18 **Building minimal cells to understand cell shape control**
MULLA YUVAL (FOM Institute AMOLF, The Netherlands)

19 **Cell motility at the leading edge: Measuring membrane fluctuations with an optical tweezer setup**
LIPPOLDT JÜRGEN (University of Leipzig, Germany)

20 **Mechanobiology of cellular trafficking across membranes**
SABYASACHI DASGUPTA (Forschungszentrum Jülich, Germany)

21 **Polymer Physics 2.0: Exploiting programmable nanomaterials to control material properties of soft matter**
CARSTEN SCHULDT (University of Leipzig, Germany)

22 **How biophysical and nanomedical tools support therapeutical improvements in neurooncology**
RUIYAN ZHANG (Christian-Albrechts-Universität, Germany)

23 **Models for angiogenesis on microstructured surfaces**
SIMON SCHUSTER (Ludwig-Maximilians-Universität München, Germany)

24 **Composite networks of actin and intermediate filaments**
TOM GOLDE (University of Leipzig, Germany)

25 **Xenograft draining lymph nodes have alterations within the structural reticular network and collagen fibres**
FREJA ALBJERG VENNING (University of Copenhagen, Denmark)

26 **Resolving the mechanobiology of the epithelium on native basement membranes**
MARIJA PLODINEC (University of Basel, Switzerland)

27 **Taking the atomic force microscopy to the clinic: Predicting the prognosis and recurrence of breast cancer by integrating the nanomechanical profiles of primary tumor and its adjacent tissue**
ELLEN OBERMANN (University Hospital Basel, Switzerland)

28 **Investigating cell mechanics by atomic force microscopy**
ALEXANDER DULEBO (Bruker Nano Surfaces Division, Germany)

29 **Cell deformability during passage through micron-scale constrictions**
JANINA LANGE (University of Erlangen-Nuremberg, Germany)

30 **Epithelial closure dynamics**
PHILIPPE MARCQ (Institut Curie, France)

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LUIZA STANKEVICINS (Saarland University, Germany)

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34 **New elasticity-patterned substrates for bi-dimensional organization of cells**
CAMILLE MIGDAL (iRTSV, CEA Grenoble, France)

35 **Emergence of collective cell migration on circular micropatterns**
FELIX JAKOB SEGERER (Ludwig-Maximilians-Universität München, Germany)

36 **Dynamics and heterogeneity in tumor cell migration**
CHRISTOPH MARK (University of Erlangen-Nuremberg, Germany)

Session V: Cell Migration in Cancer

08:30 – 09:00 **Active gels, cell motility and cell trajectories**
RAPHAËL VOITURIEZ (Pierre-and-Marie-Curie University, France)

09:00 – 09:30 **Tissue Engineering approaches and their relevance to studying tumor-stroma interactions**
CLAUDIA FISCHBACH-TESCHL (Cornell University, USA)

09:30 – 10:00 **Toward the understanding of the growth of model epithelial tissues**
ANA-SUNCANA SMITH (University of Erlangen-Nuremberg, Germany)

10:00 – 10:30 **Modelling cell motility using active gel theory**
RHODA J. HAWKINS (University of Sheffield, UK)

10:30 – 11:00 *Coffee break*

11:00 – 11:30 **Tumor cell migration is a superstatistical process**
BEN FABRY (University of Erlangen-Nuremberg, Germany)

11:30 – 12:00 **Cell migration in confining spaces: pushing off the walls and squeezing through small holes**
MATTHIEU PIEL (Institut Curie, France)

12:00 – 12:30 **The cytoskeleton significantly impacts invasive behavior of biological cells**
JOSEF A. KÄS (University of Leipzig, Germany)

12:30 – 12:45 **Dynamics and heterogeneity in tumor cell migration**
CHRISTOPH MARK (University of Erlangen-Nuremberg, Germany)

12:45 – 13:00 *Prospective end*

Session I: Mechanical Properties of Cancer Cells I

Invited Talk Thu 13:15

Mechanical sensing by normal and transformed cells — PAUL JANMEY — University of Pennsylvania, School of Engineering and Applied Science, 220 South 33rd Street, 107 Towne Building, Philadelphia, PA 19104-6391, USA

There is now abundant evidence that the viscoelastic properties of tumors and other diseased tissues differ from those of normal tissues. In many cases cancerous tissues are stiffer than normal tissues but individual transformed cells are often softer than their non-transformed counterparts. These observations have led to the concept that tumor stiffness arises from changes in extracellular matrix and genetically normal stromal cells and by imposition of pathological levels of mechanical stress generated, for example, by abnormal interstitial pressure gradients. The response of 20 different human cancer cell lines to changes in substrate stiffness and composition have been compared to those of several different classes of normal human cell types. The results show that there are large differences in the response to substrate stiffness among different cancer cell lines even when they are derived from the same type of cancer. Mechanosensing also depends strongly on the type of integrin or other adhesion receptor by which the cell engages its substrate. In aggregate these studies also show that cancer cell lines are less affected by the stiffness of the substrate than genetically normal cell types, especially cells such as mesenchymal stem cells, fibroblasts, or myocytes. The origin of tissue stiffening in disease appears to arise from both changes in matrix cross-linking and by imposition of compressional stresses. These mechanical changes are likely to affect different cell types in fundamentally different ways and suggests that strategies for modulating stromal cells might differ from those directed at genetically transformed cells.

Invited Talk Thu 13:45

Individual and collective metastatic cell migration behaviors — CYNTHIA REINHART-KING — Cornell University, Department of Biomedical Engineering, Ithaca, NY 14853, USA

During metastasis, cells have been described as displaying "follow-the leader" movement, where a leading cell guides the collective movements of trailing cells. It remains unclear how the leader cell is determined (i.e. what makes a leader into a leader?) and how follower cells maneuver to follow the leader cell. To probe the differences between leader and follower cells and the intratumor heterogeneity that gives rise to these separate roles, we developed a 1. tissue-engineered multicellular spheroid (MCS) co-culture model that that recapitulates the fully three-dimensional cell-cell and cell-matrix interactions that characterize carcinomas, and 2. micromolded collagen tracks to mimic the tunnels follower cells create and migrate within during metastasis. We show that "invasion-competent" malignant cells induce the collective invasion of otherwise "invasion-incompetent" epithelial cells, and that these two cell types consistently exhibit distinct leader and follower roles during invasion. Malignant cell invasion is accompanied by extensive extracellular matrix remodeling including matrix alignment and proteolytic track-making. Inhibition of cell contractility- and proteolysis-mediated matrix reorganization prevents leader-follower behavior. Using micromolded collagen tracks made to mimic the tracks formed by leader cells, we find that cells can migrate quickly and unidirectionally in pre-formed tracks and this mode of migration is distinct from both conventional 2D and 3D migration. Overall, our approach demonstrates how experimental models designed to mimic microscale phenomena can provide cues to mechanisms driving tissue disruption in cancer.

Invited Talk Thu 14:15

Force-dependent and -independent integrin regulation of ROS-production — M. DELARUE, F. MONTEL, J. ELGETI, M. BASAN, T. RISLER, J. PROST, J.-F. JOANNY, B. CABANE, C.-E. LEROUX, C. BOCCARA, D. VIGNJEVIC, G. CAPPELLO — Institut Curie, 26 rue d'Ulm 75248 Paris CEDEX 05, France

Two key elements control the proliferation of tumors. On the one hand, cancer cells accumulate gene mutations. On the other hand, tumors have to interact with neighboring cells and to push on their surrounding in order to grow. Therefore, mechanical stress is one of the im-

portant parameters that have to be taken into account to understand the influence of the tumor microenvironment. We developed a quantitative approach to apply a constant mechanical stress on spherical aggregates of cancer cells and to evaluate the effect of such a stress on their long term growth. Our results indicate that the tumor growth rate strongly depends on the applied pressure. In particular, we show that a small mechanical pressure (500 Pa) reduces drastically the growth of a model tumor spheroid, whereas it has no impact on the growth of single cells. We also show that this pressure affect cell proliferation, preferentially in the core of the spheroid. On the contrary, the mechanical stress has no effect on cell apoptosis.
Using only mechanical ingredients, we develop a model to simulate numerically the cancer progression in the presence of a mechanical stress and to reproduce the behavior of tumor spheroids growing under (and without) pressure.

Coffee Break Thu 14:45

Invited Talk Thu 15:15

Mechanical constraints and cancer — DANIEL A. FLETCHER — Bioengineering & Biophysics, UC Berkeley Physical Biosciences, Lawrence Berkeley National Laboratory, 648 Stanley Hall MC 1762, Berkeley, CA, 94720, USA

Tumors are characterized by disorganized growth of normally organized tissue. During mammary morphogenesis, normal epithelial cells form highly organized and growth-arrested structures known as acini, while tumorigenic mammary epithelial cells form disorganized structures that do not growth arrest. Exposure of pharmacological agents to tumorigenic cells have been shown to rescue the formation of normal acini, but the role of stresses and strains on this process, known as 'phenotypic reversion', are poorly understood. We investigated the effect of transient external forces on tumor reversion by compressing mammary epithelial cells embedded in laminin-rich extracellular matrices and tracking them over multiple days as they formed multi-cellular acini. We found that compression applied to tumorigenic mammary epithelial cells promoted formation of organized and growth-arrested acini rather than the disorganized acini observed without compression. This mechanically-induced tumor reversion occurred without the use of exogenous pharmacological agents, indicating a key role for mechanical constraints and mechanotransduction in tumorigenesis.

Invited Talk Thu 15:45

Early changes in tissue organisation and structure in colorectal cancer — INKE NÄTHKE — Cell & Developmental Biology, University of Dundee, DD15EH, UK

Background: Colorectal cancer is the second most common cause of cancer deaths in the developed world. Despite detailed knowledge about molecular events that accompany this disease, therapeutic options are limited. Mutations in a single gene, Apc are common to most sporadic colorectal cancers and are also responsible for a familial form, familial adenomatous polyposis (FAP). Cancer originates from defects in single cells; however, its clinical effects result from malfunction of tissues. Therefore, it is essential to know how single gene defects like mutations in Apc impact on cell behaviour and organization and function of tissues during initiation and progression of tumours. Understanding this relationship will provide better insight into development of cancer to develop new tools for early detection and treatment.

Aims: My work aims to develop a comprehensive understanding of the relationship between tissue and cell behaviour in cancer initiation and progression and associated molecular changes. To this end we measure tissue behaviour in normal, precancerous, and cancerous gut epithelium at high resolution and identify critical changes during early tumour development. A recent focus has been to understand how changes in mechanical properties of cells contribute to tissue changes that accompany altered tissue growth characteristic of tumour formation in the intestinal tract. A specific interest is to determine how crypt fission, the process that drives normal tissue growth in the intestine and colon, is affected by altered mechanical properties of cells carrying mutations in Apc.

Invited Talk Thu 16:15

Biomechanical processes and topological dynamics in tumors — LANCE L. MUNN — Massachusetts General Hospital & Harvard Medical School, 149 13th Street, Charlestown, MA 02129, USA

In contrast to normal tissue, the mechanical environment of a solid tumor is dynamic, heterogeneous and unstable. With tumor progression, tissue mechanical properties and compartment topologies change as cancer cells, macrophages and fibroblasts modify the extracellular matrix and the tissue "mixes". At the same time, mechanical stresses and fluid flows within the tumor are altered. We are interested in how mechanical signals influence the phenotype of cancer cells and the recruitment of blood vessels in tumors. Using animal models, *in vitro* tissue analogues and mathematical modeling, we have identified a number of biomechanical mechanisms that can affect tumor and normal cells. For example, cancer cells growing in a confined space tend to proliferate at the boundary of the cell mass, but apoptose at the center where the solid pressure is highest. Furthermore, forces experienced by cells at the boundary can induce matrix production and faster migration, especially in cancer cells with higher metastatic potential. Fluid forces can also play an important role in tumor angiogenesis. We have found that fluid flow through the interstitium can accelerate angiogenic sprouting and vascular anastomosis. This likely contributes to the recruitment of new blood vessels by the growing tumor. Once formed, the blood vasculature is exposed to shear stresses that direct remodeling in normal tissues, but this seems to be absent in tumor vasculature. Thus, mechanical perturbations and fluid forces prevalent in tumors can have significant roles in progression. We are also interested in detecting and quantifying progression using physical principles. A potentially useful set of metrics are the topologies of the various compartments comprising the tumor. We have developed a methodology for quantifying tissue compartmentalization and connectivity using the Euler characteristic number, which describes key topological features such as fragmentation, looping and cavities. The analysis predicts a number of regimes in which the cancer cells can encapsulate normal tissue, form a co-interdigitating mass, or become fragmented and encapsulated by endothelial or epithelial structures. This topological analysis could be useful for tumor diagnosis or monitoring response to therapy and would only require high resolution, 3D image data to resolve and track the various cell compartments.

Invited Talk Thu 16:45

Caveolae-mediated mechanotransduction in single cells and imaging of confined spheroids — FRANZISKA WETZEL — Institut d'Optique Graduate School, Laboratoire de Photonique Numérique et Nanosciences (LP2N), UMR 5298, IOA - rue François Mitterrand, 33400 Talence, France

During cancer development, tumor cells encounter various mechanical constraints. When the tumor expands, cells experience resistance from the basement membrane surrounding the tumor. Active and passive remodelling of the extracellular matrix (ECM) increases the tissue's stiffness. These stimuli influence cell behavior: Cells probe and adapt to their surrounding matrix by changing their mechanical properties. Already within the tumor, cells display biomechanical characteristics that are different from those of normal cells. The question remains, how mechanical stimuli on tumor cells trigger signaling pathways. Recent studies showed that caveolae constitute membrane reservoirs and play a key role in cellular response to mechanical stresses. Using a membrane stretching device and high resolution TIRF microscopy we study the caveolae-mediated mechanotransduction in single cells. Light-sheet imaging of microcapsules mimicking a tumor spheroid and its microenvironment will give new insights on collective cell response to mechanical constraints.

Contributed Talk Thu 17:15

Biomechanics of human primary tissue cells in tumor progression — ANATOL FRITSCH[1], STEVE PAWLIZAK[1], LARS-CHRISTIAN HORN[2], MICHAEL HÖCKEL[3], WOLF MÜLLER[4], MARTIN REISS-ZIMMERMANN[5], INGOLF SACK[6], JOSEF A. KÄS[1] — [1]University of Leipzig, Institute of Experimental Physics I, Soft Matter Physics Division, Leipzig — [2]University of Leipzig, Institute of Pathology, Division of Breast, Urogenital and Perinatal Pathology, Leipzig — [3]University of Leipzig, Women's and Children's Center, Department of Obstetrics and Gynecology, Leipzig — [4]University of Leipzig, Division of Neuropathology, Department of Diagnostics, Leipzig — [5]University of Leipzig, Division of Neuroradiology, Leipzig — [6]Charité, Institut of Radiology, Berlin

Biomechanical phenotyping of single cells is an emerging field as the cellular cytoskeleton, responsible for the cell's stability and organization, is known to reflect the biological state of a cell. To establish an unbiased and statistically significant view on single cell biomechanics, we use a fully automated optical stretcher system capable to process high cell numbers. This tool at hand, we are able to screen primary tumor samples of different origin in different stages of tumor progression. Furthermore, in cooperation with the Charité Berlin and the medical department of the University of Leipzig, we combined *in vivo* magnetic resonance elastography data and optical stretcher measurements to directly compare single cell deformation to whole tissue properties of the same patient, opening a unique possibility to validate and connect single cell data to its original properties inside the tissue.

Contributed Talk Thu 17:30

Cell deformability during passage through micron-scale constrictions — JANINA LANGE, THORSTEN KOLB, JONAS HALLMEN, GRAEME WHYTE, BEN FABRY — University of Erlangen-Nuremberg, Department of Physics, Center for medical physics and technology, Henkestraße 91, 91052 Erlangen

During metastasis formation, single cells or clusters of cells can leave the primary tumor, intravasate into the blood system and form secondary tumors at distant sites. To do so, the cells need to migrate through small pores of the extracellular matrix. Similar processes are also important for mesenchymal cells and immune cells during wound healing and inflammation. Therefore, the cells' ability to deform and penetrate through small constrictions plays a crucial role in many diseases. Here, we investigate the deformability of cells during the passage through micron-scale constrictions, and how it depends on nuclear and cytoskeletal filaments, including actin, microtubuli, vimentin, chromatin condensation and the nuclear lamina. Using a microfluidic device, cells are pushed through multiple parallel 5µm constrictions, and the cells' transit time through these constrictions is monitored with a high-speed camera. From the cell radius, pressure drop over the constriction and transit time, we compute the stiffness and viscosity for each cell population. For K562 leukemia cells, we find that cell resistance against large deformations is mostly governed by the actin cytoskeleton, with only minor contributions from microtubuli, and vimentin. Moreover, cells with higher Lamin A expression levels are less deformable. Remarkably, also increased expression levels of $\alpha v \beta 3$ integrins reduce cell deformability through enhancement of the actin cytoskeleton. In summary, we present a highly sensitive high-throughput microfluidic method to evaluate the deformability of cells during the passage through micron-scale constrictions which are similar to those found in the blood stream and connective tissue.

Contributed Talk Thu 17:45

Epithelial closure dynamics — OLIVIER COCHET-ESCARTIN, JONAS RANFT, PASCAL SILBERZAN, PHILIPPE MARCQ — Physico-Chimie Curie, Institut Curie, CNRS, Université Pierre et Marie Curie, 26 rue d'Ulm, 75005 Paris, France

We study the closure dynamics of a large number of well-controlled circular apertures within an epithelial monolayer, where the collective cell migration responsible for epithelization is triggered by the removal of a spatial constraint rather than by scratching.
Based on experimental observations, we propose a physical model that takes into account border forces, friction with the substrate, and tissue rheology. Border protrusive activity drives epithelization despite the presence of a contractile actomyosin cable at the periphery of the wound. The closure dynamics is quantified by an epithelization coefficient, defined as the ratio of protrusive stress to tissue-substrate friction, that allows to classify different phenotypes.
The same analysis evidences a distinct signature for human cells bearing the oncogenic RasV12 mutation, demonstrating the potential of the approach to quantitatively characterize metastatic transformations.

[1] O. COCHET-ESCARTIN, J. RANFT, P. SILBERZAN, P. MARCQ: *How filopodia pull: Border forces and friction control epithelial closure dynamic*, Biophys. J. 106, 65 (2014)

Session II: Membranes and the Cytoskeleton

Invited Talk Fri 08:30

Pulling with filopodia: high forces on weak connections — THOMAS BORNSCHLÖGL[1], STÉPAHNE ROMERO[2], CHRISTIAN VESTERGAARD[1,3], JEAN-FRANÇOIS JOANNY[1], GUY TRAN VAN NHIEU[2], PATRICIA BASSEREAU[1] — [1]Laboratoire PhysicoChimie Curie, Institut Curie, Paris, France — [2]Unité de Communications Intercellulaires et Infections Microbienne, Collège de France, Paris, France — [3]Department of Micro- and Nanotechnology, Technical University of Denmark, Lyngby, Denmark

Filopodia are dynamic, finger-like plasma membrane protrusions, which can sense the cells' surroundings and exert forces on a substrate [1]. Their retraction can be induced by adhesion to their tip, a process utilized by pathogens to invade cells [2]. Retraction of filopodia can be induced by attaching beads to their tips and counteracting mechanical forces can stall or even invert filopodia retraction [3-5]. Here, we show that in epithelial cells, filopodial dynamics are determined by the difference in the rates of actin polymerization at the filopodial tip and the cortical retrograde flow. Our measurements indicate tight coupling between the filopodial and cortical actin networks as a force generator for filopodial retraction. Consistently, retraction of filopodia bound via their tip to an optically trapped bead occurred at constant speed against counteracting forces of up to 50 pN. Retraction, however, could be mechanically stalled, due to a weak connection between filopodial actin filaments and the membrane at the tip. Upon rupture of the tip connection, filopodia exerted a passive inwards force of 15 pN via their plasma membrane. Our measurements show that the tip region determines filopodia dynamics allowing tip bound filopodia to continuously probe its surroundings in a load-and-fail manner [6].

[1] T. BORNSCHLÖGL: *How filopodia pull: What we know about the mechanics and dynamics of filopodia*, Cytoskeleton 70, 590-603 (2013)

[2] S. ROMERO, G. GROMPONE, N. CARAYOL, J. MOUNIER, S. GUADAGNINI, M.-C. PREVOST, P.J. SANSONETTI, G. TRAN VAN NHIEU: *ATP-Mediated Erk1/2 Activation Stimulates Bacterial Capture by Filopodia, which Precedes Shigella Invasion of Epithelial Cells*, Cell Host & Microbe 9, 508-519 (2011)

[3] H. KRESS, E.H.K. STELZER, D. HOLZER, F. BUSS, G. GRIFFITHS, A. ROHRBACH: *Filopodia act as phagocytic tentacles and pull with discrete steps and a load-dependent velocity*, Proc. Natl Acad. Sci. USA 104, 11633-11638 (2007)

[4] A. ZIDOVSKA, E. SACKMANN: *On the Mechanical Stabilization of Filopodia*, Biophys. J. 100, 1428-1437 (2011)

[5] S. ROMERO, A. QUATELA, T. BORNSCHLÖGL, S. GUADAGNINI, P. BASSEREAU, G. TRAN VAN NHIEU: *Filopodium retraction is controlled by adhesion to its tip*, J. Cell Sci. 125 4999-5004 (2012)

[6] T. BORNSCHLÖGL, S. ROMERO, C. VESTERGAARD, J.F. JOANNY, G. TRAN VAN NHIEU, P. BASSEREAU: *Filopodia retraction force is generated by cortical actin dynamics and controlled by reversible tethering at the tip*, Proc. Natl Acad. Sci. USA 110, 18928-18933 (2013)

Invited Talk Fri 09:00

Oncogenic signaling and the cytoskeleton — DAVID M. HELFMAN[1], CHEOLWON CHOI[2], DAYOUNG KIM[2], SUKYEONG JEONG[2], GRACE SHIN[2], SUNYOUNG LIM[2] — [1]Korean Advanced Institute of Science and Technology, Graduate School of Nanoscience & Technology, Daejeon 305-701, Republic of Korea — [2]Korean Advanced Institute of Science and Technology, Department of Biological Sciences, Daejeon 305-701, Republic of Korea

Activation of oncogenic signaling pathways results in changes in cell shape and cytoarchitecture. Abnormal changes in cell morphology are an important criterion used by pathologists to identify cancerous tissue. The three-dimensional architecture of cells and tissues is important to normal cellular function and regulation. Underlying the 3-D organization of cells and tissues is the actin cytoskeleton. Alterations in the organization of the actin cytoskeleton and its associated adhesive structures (e.g., cadherins and integrins), are linked to abnormal features of cancer cells including unregulated cell proliferation and programmed cell death (apoptosis), anchorage independent cell growth, cell adhesion, invasion, and metastasis. We still lack a complete

understanding of how the cytoskeleton is targeted during oncogenesis and how changes in the cytoskeleton contribute to the characteristics of cancer cells. We are studying the molecular mechanisms by which oncogenic signaling pathways target the organization of the cytoskeleton and how changes in the cytoskeleton and 3-D architecture of cells contributes to the various properties of tumor cells, including aberrant signaling, motility, invasion and metastasis. I will discuss the nature of the interactions and cross talk between the cytoskeleton and oncogenic signaling pathways in tumor cells and their potential to provide new targets for the therapeutic intervention of cancer.

Invited Talk Fri 09:30

Mechanism of CD95 clustering and activation at the single cell level — JOEL BEAUDOUIN, CLARISSA LIESCHE, JOHANNA BERNDT, ROLAND EILS — DKFZ / IPMB Heidelberg, Germany

CD95 is a member of the tumor necrosis factor receptor superfamily that was originally identified as an apoptosis inducing receptor, and as a potential target for anticancer therapy. However, further studies showed that CD95 can also transmit pro-survival signals, and that tumor cells actually use this receptor for tumor growth. The complex assembled on ligand-bound receptors is formed by different types of multivalent interactions, allowing signal control and amplification. We aim at characterizing how CD95 translates a ligand form and dose into caspase-8 activity, which corresponds to the initiation of apoptotic signal. On one hand, we use fluorescence-based biophysical approaches to characterize the level of oligomerization of different recombinant ligands and receptors, and on the other hand, we use quantitative fluorescent live cell imaging to characterize and correlate ligand binding, receptor crosslinking and activation and caspase-8 activity. To characterize protein oligomerization, we used different molecule counting approaches, including step photobleaching, brightness measurement and calibrated single molecule imaging with normal and super resolution microscopy. In particular, we observed that while the soluble ligand is trimeric, the receptor, generally thought to be trimeric as well, is less oligomerized. Furthermore, we could show that the ligand capacity to crosslink receptors, and not directly ligand binding, correlate with receptor activation. Especially the natural soluble CD95 ligand can interact with receptors without inducing significant apoptotic signal, offering a possible mechanism for switching between apoptotic and alternative survival signaling.

Invited Talk Fri 10:30

Mimicking tissues with densely packed lipid droplets — JASNA BRUJIC — New York University, Center for Soft Matter Research, Meyer Hall, 4 Washington Place, New York, NY 10003, USA

Emulsion droplets are a versatile system whose interactions can be tuned to mimic cellular functions, such as lipid domain formation, cell-cell adhesion or even hemifusion. For example, immiscible lipids on the surface of emulsion droplets create stable patterns of circular or stripy domains, reminiscent of lipid rafts in cell membranes. Functionalizing the lipids with biotins allows them to bind to each other either irreversibly through streptavidin or reversibly through cadherins or complementary DNA strands. We show that these mobile adhesion patches self-assemble linear chains of thermal droplets into well-defined compact structures. The size of adhesion is predicted by the balance between the binding energy and the energy of deformation of the droplets. Applying an external pressure to the system strengthens adhesions, which highlights the importance of homeostatic pressure on cell-cell adhesion and tissue integrity *in vivo*. Alternatively, functionalizing the lipids with E-cadherin proteins unexpectedly leads to droplets fusing together up to a given droplet size. Microscopically, we find that the lateral cis-interaction of cadherins clusters them into rings upon adhesion, which in turn ruptures the adjacent lipid monolayers to cause fusion. Emulsions are therefore not only a new class of liquid patchy particles for self-assembly, but also a model system for important problems in biophysics.

Coffee Break Fri 10:30

Invited Talk Fri 11:00

The mechanics of invasion: How contraction sets the stage for invasive migration — KATARZYNA KOPANSKA, TIMO BETZ — Institut Curie, Biomimetism of cellular movement, 26 rue d'Ulm, 75248 Paris, France

To move out of the primary tumor, cells start a complex process of migration in the surrounding tissue called invasion. The overall mechanisms of the onset of invasion are key elements to understand and hopefully prevent malignant invasion and hence one of the critical factors in the prognosis of cancer. We focus on the mechanical events that can be observed before and during invasion of a mouse colon cancer cell line CT26. The experimental systems consists of a spheroid comprising about 2000 cells that is embedded in a collagen I matrix. Before the onset of invasion a contraction of the collagen gel is observed, and we will discuss the hypothesis that an increase in mechanical tension in the collagen matrix facilitated the outgrowth of cells and hence triggers invasion. Hence, the cells in the spheroid may themselves optimize the environment by force application until the mechanical properties of the ECM allow invasion.

Invited Talk Fri 11:30

Chemomechanics of cell migration and activation in the cancer microenvironment — Krystyn J. Van Vliet — Massachussetts Institute of Technology (MIT), Department of Materials Science & Engineering Department of Biological Engineering, 77 Massachusetts Ave., Cambridge, MA 02139, USA

The physical environment at tumor sites can differ markedly from healthy tissues in the acidity of the extracellular fluids as well as the mechanical properties of the extracellular matrix. Additionally, contractile cells can provide mechanical and chemical cues to noncontractile cells within tumors or associated vasculature. The impact of such chemomechanics on cell behaviors relevant to cancer tumor growth and angiogenesis is increasingly amenable to both experiments and computational modeling. Here, we will discuss the effects of such physical stimuli on cell migration and phenotypic differentiation. In the case of extracellular pH, we use integrated simulations and experiments to show how acidity modulates the conformation of cell surface receptors that, as a result, promotes migration of cells along acidic pH gradients. In the case of cell-generated mechanical strains, we show how such cues can promote blood vessel sprouting that could facilitate tumor growth and metastasis. By describing such coupling between chemistry and mechanics at the cell-material interface, we aim to understand and modulate biological cell responses through the lens of material physics.

Invited Talk Fri 12:00

Oncogenic cell transformation changes the nanoscale organization of adhesions, vimentin filaments and cell stiffness — Annica K. B. Gad[1], Li-Sophie Z. Rathje[1], Niklas Nordgren[2], Torbjörn Pettersson[2], Daniel Rönnlund[3], Hans Blom[3], Jerker Widengren[3], Pontus Aspenström[3] — [1]Karolinska Institutet, Dpt of MTC, Nobels v 17, Stockholm, Sweden — [2]KTH Royal Institute of Technology, School of Chemical Science and Engineering, Stockholm, Sweden — [3]KTH Royal Institute of Technology, Dpt of Applied Physics, Stockholm, Sweden

The molecular control of the mechanical properties of cells and the role these have in carcinoma formation have not been fully described to date. Using super-resolution STED microscopy, we show that at nanoscale resolution, oncogenes induce a spatial reorganization of both nanoscale adhesions and vimentin intermediate filament fibres, as detected as a reduced parallel arrangement and increased width of these fibres. Using collodial probe atomic force microscopy, we could further observe that oncogene expression also increased the cell stiffness. Oncogenes also increased cell invasion and the levels of the HDAC6, which was found to be required for the increased cell stiffness of oncogene-expressing cells. To determine the underlying causes and the consequences of the vimentin reorganization for cell shape and stiffness, we have analysed further the role of HDAC6 and actomyosin contraction in this system. Taken together, our data are consistent with the possibility that oncogenes can alter cell adhesion and induce cellular stiffness via an HDAC6-induced reorganization of the vimentin intermediate filament network.

[1] Rathje LS, Nordgren N, Pettersson T, Rönnlund D, Widengren J, Aspenström P, Gad AK: *Oncogenes induce a vimentin filament collapse mediated by HDAC6 that is linked to cell stiffness*, PNAS 111 (2014)

[2] Gad A.K., Rönnlund D., Xu L., Blom H., Aspentröm P., Widengren J.: *Spatial organization of proteins in metastasizing cells*, Cytometry A (2013)

Contributed Talk Fri 12:30

The role of vimentin in cell migration under confinement — LUIZA STANKEVICINS, EMMANUEL TERRIAC, FRANZISKA LAUTENSCHLÄGER — Saarland University, FR 7.2 Experimentalphysik, Campus Saarbrücken, Gebäude E 2.6, 3.OG, Germany

Cell migration is a fundamental biological process which requires an active cytoskeleton remodelling. During migration, cells often perform long distance displacements passing through obstructive 3D tissues, constrictions, or even in between other cells and therefore continuously need to adjust their shape. The intermediate filaments are the most stretchable components of the cytoskeleton and are organized as a network comprising both cytoplasmatic and nuclear proteins. It is not well established if and how alterations in the extracellular matrix can have an impact in intermediate filaments organization and cell movement. Considering this scenario, we subjected cells to confinement using microfabricated channels with the objective to analyse cell migration and the cytoplasmatic intermediate filament vimentin network. In this given context we analysed two models of cell migration- the low adherent amoeboid performed by Jurkat cell lines and the mesenchymal migration using RPE-1 cells. Both cell lines were stable transfected with wild type vimentin coupled with GFP. Cell movement in the channels was recorded by fluorescence and phase contrast video microscopy for 24 hours under controlled humidity and temperature. The acquired data was analysed by a custom-built cell tracking software. The analysed parameters during both amoeboid and mesenchymal cell migration were the speed, persistence as well as the localization of vimentin network and cell morphology (length, shape, symmetry, nuclear position, and nuclear shape).

Contributed Talk Fri 12:45

Cancer cell behaviours on a culture substrate imprinted with their own features — TIFFANY TAN[1], PETER SYKES[1], MAAN ALKAISI[2,3], JOHN EVANS[1,3,4] — [1]University of Otago, Christchurch Women's Hospital, Department of Obstetrics and Gynaecology, Level 3, 2 Riccarton Avenue, Christchurch, New Zealand — [2]University of Canterbury, Department of Electrical and Computer Engineering, Private Bag 4800, Christchurch, New Zealand — [3]Macdiarmid Institute of Advanced Materials and Nanotechnology, Laby 410, Gate 6 Kelburn Parade, Kelburn, Wellington, New Zealand — [4]University of Otago, Department of Physiology, Centre for Neuroendocrinology, Po Box 913, Dunedin, New Zealand

It is known that cancer development and progression is partly due to disruption of mechanical signals in the tumour microenvironment. However, conventional *in vitro* studies on 2D surfaces do not reproduce 3D physiological tissues with inherent topographical mechanical signals. Consequently, many drug candidates that show promising activity in 2D pre-clinical models fail in clinical trials.

We use a cell imprinting technique to replicate cell features onto culture surfaces as an improved platform for investigating biomechanical effects on cells; the high resolution replication of cells offer the micro and nano environment experienced in typical cell-cell interactions, we called this platform a Bioimprint [1]. Cells of an endometrial adenocarcinoma cell line, Ishikawa, were cultured on a Bioimprint, and compared to cells cultured on flat surfaces. Characteristics of cells, including morphology, activation of adhesion molecules and cell proliferation, were studied.

We observed that cells were smaller in size and had restricted spreading on Bioimprint which implied that cells responded to Bioimprint by changing their attachment to the surface. This restricted spreading was shown to be related to decreased cell expression of adhesion molecules and downstream kinase. Furthermore, we showed that a reduction in cell size was associated with slower proliferation of cells on Bioimprint.

This study of cell behaviours on patterned surfaces provides information on how cancer cells respond to surface topology. Bioimprint, which is a platform with cell-like-topography, contains mechanical signals that restricted endometrial cancer cell spreading, reduced cell expression of adhesion molecules and downstream kinase, and additionally slowed down cell proliferation. The observations support the emerging concept that understanding the physical environment of cells may lead to discovering new cancer treatments in which behaviours of cancerous cells may be altered through targeting pathways related to mechanical sensing.

[1] SAMSURI, ALKAISI, MITCHELL, EVANS: *Replication of Cancer Cells Using Soft Lithography Bioimprint Technique*, Microelectronic Engineering 87, 5-8, 699-703 (2010)

Session III: Mechanical Properties of Cancer Cells II

Invited Talk Sat 08:30

Analysis of a few *in vitro* experiments — JACQUES PROST — Institut Curie, ESPCI, 26 rue d'Ulm 75248 Paris CEDEX 05, France

I will analyze experiments performed both on multicellular spheroids and on tissues growing in alginate cylinders in view of theories of active tissues close to homeostatic conditions.

Invited Talk Sat 09:00

Mechanotransduction in developing cell systems — KRISTIAN FRANZE — University of Cambridge, Department of Physiology, Development and Neuroscience, Downing Street, Cambridge, UK

As motion requires forces, cell motility strongly depends on the mechanical interaction between cells and their environment. Cells actively probe their mechanical environment, and transduce mechanical signals into intracellular, biochemical signaling. Here we illuminate two different mechanotransduction pathways. First, we investigate how neurons probe and respond to their mechanical environment. While the growth rate of *Xenopus* retinal ganglion cell axons was increased on stiffer substrates, their tendency to bundle (i.e., fasciculate) was significantly enhanced on more compliant substrates. If grown on substrates incorporating stiffness gradients, neuronal axons were repelled by stiff substrates. Mechanosensing involved the application of forces driven by the interaction of actin and myosin II, and the activation of stretch-activated ion channels leading to calcium influxes into the cells. *In vivo* atomic force microscopy revealed stiffness gradients in developing *Xenopus* brain tissue; turning angles of axons strongly correlated with gradient strength. The application of chondroitin sulfate, which is a major extracellular matrix component in the developing brain, changed tissue mechanics and disrupted axonal pathfinding. Ultimately, blockers of mechanosensitive ion channels also disrupted axon guidance *in vivo*, strongly indicating an involvement of mechanosensitive ion channels in mechanotransduction and pathfinding in developing neurons. Secondly, we found unique mechanical properties of stem cell nuclei in a transition phase. In contrast to pluripotent and committed stem cell nuclei, which have a positive Poisson's ratio, transition nuclei are auxetic. Auxeticity (i.e., an increase in cross-sectional area under stretch and a decrease under compression) leads to tremendous changes in nuclear volume when the cells are exposed to forces. These volume changes are accompanied by an influx or efflux of small molecules, suggesting that nuclei could work as auxetic pumps, significantly increasing the turnover of transcription factors and signaling molecules, and thus directly coupling external forces to internal gene expression.

Invited Talk Sat 09:30

Association between embryonic development and locoregional cancer progression — MICHAEL HÖCKEL — Department of Gynecology, University of Leipzig, Liebigstraße 20a, 04103 Leipzig, Germany

Locoregional tumor control is necessary and for most patients with early diagnosed cancer sufficient to cure the disease. The ontogenetic compartment theory of locoregional tumor spread (HÖCKEL *et al.*, Lancet Oncol. 2005, 2009, 2014) considers cancer, the progressive destruction of the body by neoplastic tissue, as clinical manifestation of the pathological reactivation of the developmental programs that have controlled the morphogenesis of the tissue from which the cancer originated. During malignant progression these programs run in retrograde sequence.
As the developmental programs are executed in defined tissue domains, local tumor propagation is confined to permissive compartments determined by the state of malignant progression. Common positional information of secondary peripheral lymphatic tissues and their tributary regions essential for the adaptive immune response links the local to the regional propagation field of the neoplasm. Hence, the tissue domains of potential local and regional tumor spread can be precisely outlined for a given state of malignant progression. The theory has been substantiated for carcinoma of the uterine cervix by its successful translation into a new tumor staging system and new cancer operations based on ontogenetic anatomy. Work is in progress to investigate its potential for improving the outcome of patients with other cancers of the female genital tract.

Coffee Break Sat 10:00

Invited Talk Sat 10:30

Biophysical characterization of the myxobacterial compound Soraphen A: an innovative option to fight invasive cancer — ANGELIKA M. VOLLMAR — Ludwig-Maximilians-Universität München, Department of Pharmacy, Center for Drug Research Pharmaceutical Biology, Butenandtstr. 5-13 81377 Munich, Germany

Background: The fatty acid metabolism is found to play a key role in oncogenic transformation. First metabolic investigations of human tumors revealed that malignant cells were characterized by a high rate of de novo fatty acid synthesis. In accordance with this discovery it was found that lipogenic enzymes, like the fatty acid synthase and acetyl-CoA carboxylase (ACC1) were overexpressed [1]. Soraphen A, which is a secondary metabolite isolated from the myxobacterial strain Sorangium cellulosum is a potent ACC1 inhibitor. The aim of our proposal is to characterize the effect of Soraphen A on breast cancer cells and biophysically disclose its mechanism of action.
Preliminary data and hypothesis: First experiments in breast cancer cells revealed that Soraphen A significantly reduces migration and invasion of MDA-MB-231 cells after short stimulation times of 6 h whereas the proliferation of cells is inhibited only after very long treatment (120 h). Interestingly, we observed inhibitory effects of Soraphen A on directed migration in chemotaxis experiments in 2D as well 3D settings accompanied by effects on major players of migration (such as Rac-GTPase, FAK, pSCR). Moreover as mechanical stiffness was found to grade metastatic potential of cells [2], one of our first working hypotheses was that Soraphen A alters membrane stiffness and membrane fluidity, thus affecting invasiveness of cells. So far we could show that after short stimulation times the lipid composition was changed, whereas after longer treatment the total amount of phospholipids decreased. In cooperation with the group of PROF. KÄS (Soft Matter Physics Division, University of Leipzig), we aimed to investigate cell stiffness employing the optical stretcher [3] and to decipher whether Soraphen A acts mainly by influencing the cytoskeleton or rather changes the membrane composition. The respective results will be demonstrated in detail and the potential of Soraphen as lead substance and cell stiffness as an innovative tumor target will be discussed.

[1] ABRAMSON HN: *The lipogenesis pathway as a cancer target*, J. Med Chem. 54 (16): 5615-38 (2011)

[2] SWAMINATHAN V, MYTHREYE K, O'BRIEN ET, BERCHUCK A, BLOBE GC, SUPERFINE R: *Mechanical stiffness grades metastatic potential in patient tumor cells and in cancer cell lines*, Cancer Res. 71 (15): 5075-80 (2011)

[3] GUCK J, ANANTHAKRISHNAN R, MAHMOOD H, MOON TJ, CUNNINGHAM CC, KÄS J: *The optical stretcher: a novel laser tool to micromanipulate cells*, Biophys. J. 81 (2): 767-84 (2001)

Invited Talk Sat 11:00

Actin-based transport adapts polar cap size to local curvature — DARIA BONAZZI, DELPHINE SALORT, NICOLAS MINC — Institut Jacques Monod, Université Paris Diderot, 15 Rue Helene Brion, 75205 Paris Cedex 13, France

Cells come in a wide range of size and shapes and usually assemble polarized cortical domains that scale to their cell size. Work in yeast and other systems, has suggested that the establishment of a single polarity domain, of active Cdc42p for instance, involves a combination of actin-mediated transport and reaction-diffusion mechanisms, both of which function in positive-feedback loops, in a "winner-take-all" situation [1]. How these elements may mediate cell size sensing to assemble a polar cap with the correct width of successive oscillating active-Cdc42p caps in rounded fission yeast spores which change sizes and shapes over time [2]. Quantitative measurements and cell shape manipulation reveal that cap size scales with local radii of curvature, and not with absolute cell volume or Cdc42 concentration. This scaling depends on formin-mediated actin cable nucleation and on the fusion of vesicles transported along these cables. These data in conjunction with modeling, suggest that a reaction-diffusion based mechanism may set a minimal polar cap size, and that actin functions in spreading that cap and adapting its width to local curvature. Thus, this work may uncover a general principle for how cortical functional domains scale with cell size.

[1] N.S. SAVAGE, A.T. LAYTON, D.J. LEW: *Mechanistic mathematical model of polarity in yeast*, Mol Biol Cell 23 (10): 1998-2013 (2012)

[2] D. BONAZZI, *et al.*: *Symmetry breaking in spore germination relies on an interplay between polar cap stability and spore wall mechanics*, Developmental Cell 28 (5): 543-46 (2014)

Invited Talk Sat 11:30

Modeling glioma and targeting the glioma niche — KARIN FORSBERG-NILSSON — Uppsala University, Department of Immunology, Genetics and Pathology and Science for Life Laboratory, Rudbecklaboratoriet 75185 Uppsala, Sweden

Glioblastoma (GBM) is the most frequent and malignant primary brain tumor. Despite advances in understanding the molecular mechanisms of GBM, these tumors continue to be fatal. The concept of cancer stem cells in solid tumors has attracted a lot of interest, and a glioma-initiating cell bearing stem cell characteristics has been proposed, with the ability to seed new tumors through the capacity to evade chemotherapy and irradiation. Basic cancer research, including preclinical tumor models and testing of candidate drugs needs optimized *in vitro* models that better reflect the patient's disease, including modeling of the cancer stem cell compartment. We have set up a biobanking effort to culture and characterize a new panel of GBM stem cells from patients, using stem cell culture conditions, and classify them according to the TCGA subtypes. In our recently published study [1], these cell cultures were screened to identify cellular processes amendable for development of targeted treatments. A small molecule, Vacquinol-1, induced glioblastoma cell death but spared normal cells. It displayed excellent *in vivo* pharmacokinetics and brain exposure, and attenuated GBM progression in animal models. This is the first example of how the new platform can be used successfully towards novel therapeutic opportunities.

Neural progenitors and glioma-initiating cells have several common traits, such as sustained proliferation and a highly efficient migratory capacity in the brain. There are also similarities between the neurogenic niche where adult neural stem cells reside, and the tumorigenic niche. Heparan sulfate (HS) proteoglycans are main components of the ECM where they interact with a large number of physiologically important macromolecules, thereby influencing biological processes. HS modulate growth factor activities, and we have shown a vital role for HS biosynthetic enzymes in the formation of the neural lineage [2]. The major enzymatic activity degrading HS is Heparanase. The activity of this HS-editing enzyme is thus an important regulator of ECM remodeling, and has also been suggested to promote cancer growth by generating a supportive microenvironment. I will discuss the role of heparanase in glioma development.

[1] KITAMBI, *et al.*: *Vulnerability of Glioblastoma Cells to Catastrophic Vacuolization and Death Induced by a Small Molecule*, Cell 157 (2): 313-28 (2014)

[2] M. FORSBERG, *et al.*: *Under-sulfation of heparan sulfate restricts the differentiation potential of mouse embryonic stem cells*, J Biol Chem 287 (14): 10853-10862 (2012)

Contributed Talk Sat 12:00

Is cell segregation governed by cellular adhesion? — STEVE PAWLIZAK[1], ANATOL FRITSCH[1], STEFFEN GROSSER[1], DAVE AHRENS[1], TOBIAS THALHEIM[1], M. LISA MANNING[2], JOSEF A. KÄS[1] — [1]University of Leipzig, Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, Soft Matter Physics Division, Linnéstr. 5, 04103 Leipzig, Germany — [2]Syracuse University, Department of Physics, Syracuse, NY 13244, USA

The segregation of different cell populations and the formation of cellular boundaries is a fundamental process in every higher organism. During the embryonic development, the basis for cellular organization is established when the first cells differentiate into several populations which eventually segregate into different compartments. These compartments are "subunits" of the further development and will persist for life. As a general rule, cells do not cross the well-defined lineage boundaries between different compartments. However, some cells may break ranks: At some point in their development, malignant cells become able to invade adjacent tissues, which is a well-known hallmark of cancer. This raises the question, what physical properties may have changed in such cells to let them eventually overcome compartment boundaries, or in other words, what mechanism drives cellular segregation?

The *differential adhesion hypothesis* gives a first explanation by differences in surface tension and adhesiveness of the interacting cells. In this context, we are

investigating whether cellular adhesion is in fact a necessary or even sufficient factor to characterize compartmentalization and tumor spreading. A simple model system for cellular segregation involves mixing together two different populations of suspended cells. After a certain time, this mixture will eventually segregate into two phases, whereas mixtures of the same cell type will not. A newly developed setup for long-term observation of such suspension cultures provides first insights into the cluster dynamics. These experiments are accompanied by different techniques to characterize the mechanical properties and interactions of the participating cells. In particular, two new approaches were chosen to correlate cellular adhesiveness with the observed segregation behavior: *atomic force microscopy* to directly measure cell-cell adhesion forces and high-resolution *STED* microscopy to determine the adhesion molecule density at the cell-substrate interface. Additionally, cellular elasticity is probed using an *Optical Stretcher*.

Contributed Talk Sat 12:15

Mesenchymal migration cannot be described as a persistent random walk — ANTOINE CONFAVREUX[1], CHARLOTTE RIVIERE[1], MAGALIE FAIVRE[2], HICHEM MERTANI[3], ROSARIA FERRIGNO[2], HÉLÈNE DELANOE-AYARI[1], JEAN-PAUL RIEU[1] — [1]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 — [2]Institut des Nanotechnologies de Lyon – UMR CNRS 5270, Université Lyon 1, Domaine Scientifique de la Doua - Bâtiment Léon Brillouin 43 Boulevard du 11 novembre 1918,Villeurbanne, France — [3]Centre de Recherche en Cancérologie de Lyon – UMR Inserm 1052 CNRS 5286, Université Lyon 1, 28 rue Laennec 69373 Lyon Cedex 08, France

Cell movements and migration are of critical importance during the metastatic spread of cancer cells. Even if models for cell migration have been studied extensively since many decades, to our knowledge, little is known yet on mesenchymal migration. In this study, we investigated the interplay between random migration and adhesion for the MDA-MB231 human breast cancer cell line. This cell line exhibits mesenchymal characteristics (i.e., highly mobile), with invasive and tumorigenic properties *in vivo*.

Using multisite time-lapse microscopy and single cell tracking, we were able to track the trajectories of several hundred cells. Our analysis reveals that the classical model of random motion with persistence is only valid for long time behaviour. In addition, we clearly highlight that the cell displacement cannot be modelled as a simple unimodal migration, but is better represented by a bimodal distribution: the cells are switching between a "confined" mode and a "ballistic" mode. At long time, the mean squared displacement is not affected by this bimodal behaviour and the classical parameter for random walk with persistence can be computed, leading to a robust measurement of an effective diffusion coefficient. By varying cell/substrate adhesion using various protein-coated substrates, we also notice a large difference between collagen and fibronectin coatings. Cells exhibit a higher velocity at short times (Delat = 5 min), together with a distribution of speed much wider, and a higher diffusion constant on collagen-coated substrate.

These results were used to screen the optimised conditions for directed migration using chemotaxis chambers. We were able to screen epithelial from mesenchymal cells based on their migration properties in term of instantaneous speed and directionality. All together, these results indicate that cancer cell migration can be used as a new powerful functional diagnostic tool.

Lunch Break Sat 12:30

Session IV: Microtools for Study and Diagnostics in Cancer Research

Invited Talk Sat 14:30

Measuring cell mechanics for medicine — DINO DI CARLO — University of California, Los Angeles (UCLA), Bioengineering Department, Microfluidic Biotechnology Laboratory, 5121E Engineering V, Los Angeles, CA 90095-1600, USA

Biophysical properties (e.g. deformability, size, motility, adhesiveness) of cancer cells are promising markers indicative of underlying integrative molecular changes associated with various disease processes and changes in cell state. We have developed precision microfluidic systems using inertial microfluidic physics to separate and analyze cells based on these properties, towards translational applications in diagnostics and drug discovery. I will briefly discuss one platform we have developed that enables separation and concentration of disseminated tumor cells from body fluids in microscale vortices formed in a microchip, and allows gentle release of these cells for downstream analysis. I will spend the majority of the time discussing another platform we have developed that combines precise focusing of cells with automated high-speed image analysis for high-throughput cell classification based on intrinsic biomechanical and morphological properties. We have applied this approach to label-free diagnosis of body fluids based on the distribution of single-cell biophysical properties. Using this platform we have analyzed over 100 pleural fluid samples and identified unique mechanophenotypes indicative of malignancy or inflammatory processes. The approach correctly identified false negative and atypical samples while maintaining high specificity, and could potentially act as a standalone test or a useful adjunct for cytological examination. Importantly, such an approach yields quantitative readouts and scoring of samples that could enhance cytopathologist decisions. The "deformability cytometer" instrument shows promise in identifying cancer cells, activated white blood cells, and mesothelial cells in mixed populations – without labels - for a variety of clinical applications.

Invited Talk Sat 15:00

Quantifying metastasis using rare events — TIMOTHY NEWMAN — University of Dundee, College of Life Sciences, School of Engineering, Physics and Mathematics, Dow Street Dundee DD1 5EH, Great Britain

I will present some recent work in which a very simple model of metastasis is constructed and analysed using stochastic process theory. The model posits that metastasis may be due to rare event colonisation from incompetent (non-pre-adapted) disseminated cancer cells (which we term "rare dynamics"), rather than from a pre-adapted cadre of genetically distinct cells (which we term "rare genotypes"). Analysis uncovers the surprising result that early colonisation dynamics of rare dynamics and rare genotypes are statistically indistinguishable. The two parameters in the rare dynamics model can be estimated from human data and are shown to be plausible, indicating that rare dynamics may provide a consistent interpretation of cancer metastasis in humans. This has important implications for clinical intervention – implying that we need to target chance rather than key mutations.

Invited Talk Sat 15:30

Plasticity of cancer cell migration: Extracellular matrix enables the optimisation of blebbing, adhesions, and spreading — MELDA TOZLUOGLU — MRC-Laboratory for Molecular Cell Biology, University College London, Gower Street, London WC1E 6BT, UK

The molecular requirements and morphology of migrating cells can vary depending on matrix geometry; therefore, predicting the optimal migration strategy or the effect of experimental perturbation is difficult. We present a model of cell motility that encompasses actin polymerisation based protrusions, actomyosin contractility, variable actin-plasma membrane linkage leading to membrane blebbing, cell-extracellular matrix adhesion, and varying extracellular matrix geometries. This is used to explore the theoretical requirements for rapid migration in different matrix geometries. Confined matrix geometries cause profound shifts in the relationship of adhesion and contractility to cell velocity; indeed cell-

matrix adhesion is dispensable for migration in discontinuous confined environments. The model is challenged to predict the effect of different combinations of kinase inhibitors and integrin depletion *in vivo* and in confined matrices based on *in vitro* 2D measurements. Intravital imaging is used to verify bleb-driven migration at tumour margins, and the predicted response to single and combinatorial manipulations. Further, we investigate the ability of motile cells to adapt changing extracellular matrix geometries, and variable adhesion zones within the cell's path. Here, our model suggests the feedback mechanisms between the forces exerted by cells, and cell-ECM the adhesion strength allows the cells a higher adaptability, at the cost of peak cell velocities.

Contributed Talk Sat 16:00

New elasticity-patterned substrates for bi-dimensional organization of cells — Camille Migdal[1], Alexandre Morel[1], Marie Courcon[1], David Fuard[2], Nicolas Bouchonville[2], Mélanie Charbit[1], Abbas Mgharbel[2], Danielle Gulino-Debrac[1], Alice Nicolas[2] — [1]Laboratoire "Biologie du Cancer et de l'Infection", UMR INSERM 1036/ CEA/ UJF, iRTSV, CEA Grenoble, 17 rue des Martyrs 38054 Grenoble Cedex 9, France — [2]Laboratoire des Technologies de la Microélectronique UMR CNRS 5129, c/o CEA/LETI/D2NT, CEA Grenoble, 17 rue des Martyrs 38054 Grenoble Cedex 9, France

Studies to prevent the evolution of cancers are an important part of the scientific research in the field of biology. Anticipating the locations where cancer cells will migrate and proliferate remains a major challenge in order to implement appropriate treatments. Many mechanical parameters such as rigidity influence biological functions and signaling pathways of living cells. In particular, it is proven that the stiffness of the substrate influences cell spreading, migration, and differentiation.
Using the cell sensitivity property to extracellular matrix (ECM) stiffness, we have developed micro-scale rigidity-patterned substrates to bi-dimensionally organize cells. These chips based on polyacrylamide gels are elaborated using innovative technologies that are derived from micro- and nano-electronic technologies (optical lithography of wet, aqueous resists, masks with micron to millimeter scale gradients of grey). These chips present apposition of regions with distinct elastic moduli, ranging from 0.5 to 200 kPa as attested by atomic force microscopy, and with a control at the micron scale. They are modified at their surface to favor controlled ECM protein grafting, a step absolutely required for promoting cell adhesion. Thus, these chips offer the opportunity to study cell adhesion and migration mechanisms under physical constraints mimicking the physiological environment encountered in most of the tissues.
The design of the chips permits cell confinement or guidance using cell ability to probe the mechanical properties of the extracellular matrix. For instance, on chips exhibiting rigid patterns surrounded by soft matrix, cells adopt the shape of the corresponding rigid surfaces. On chips presenting alternating rigid and soft bands, cells are confined on the rigid bands where they displace along.
Thus, these chips, developed by a joint team project at the interface of cell biology and materials technology, offer promising tools to tackle the mechanisms at the basis of cell mechano-sensitivity. By allowing cell velocity quantification, they are also expected to allow the identification of drugs having the capacity to inhibit the migration of cancer cells, a property that may be used to prevent metastasis formation.

Contributed Talk Sat 16:15

Emergence of collective cell migration on circular micropatterns — Felix Jakob Segerer[1], Florian Thüroff[2], Alicia Piera Alberola[1], Erwin Frey[2], Joachim Oskar Rädler[1] — [1]Ludwig-Maximilians-Universität München, Faculty of Physics and Center for NanoScience, Geschwister-Scholl-Platz 1, 80539 Munich, Germany — [2]Ludwig-Maximilians-Universität München, Department of Physics,Arnold-Sommerfeld-Center for Theoretical Physics and Center for NanoScience, Theresienstrasse 37, 80333 Munich, Germany

Collective cell migration plays a crucial role in various biological contexts, notably morphogenesis, tissue repair, and cancer growth. The spontaneous appearance of vortices is a hallmark of such collective cellular activity. Here, we study the emergence of collective circular motion as a function of the number of cells confined in circular micropatterns. Analyzing the movement of each cell individually, we find distinct states of coherent angular motion (CAMo) and disordered motion (DisMo) within the system. The persistence of CAMo increases with cell number, besides a pronounced discontinuity, resulting from a topological

transition towards a conformation featuring a cell in the system center. Backed up by computer simulations, we suggest that the dipole nature of polarized, migrating cells accounts for the occurrence of vortex states, which reflect the instability of cell configurations that frustrate optimal dipole arrangement.

Coffee Break Sat 16:30

Invited Talk Sat 17:00

Micromechanical tools to study the role of vimentin in cells — FRANZISKA LAUTENSCHLÄGER — Saarland University, Faculty 7, Experimental Physics, Campus A5 1, 66123 Saarbrücken, Germany

The intermediate filament vimentin is a part of the cytoskeleton, and we expect it to play a role in several aspects of cellular behaviour, such as migration, polarity or mechanics. However, the specific aspects of vimentin in cellular behaviour are far from being fully understood. We are using micro-tools to investigate the role of vimentin migration and polarity of cells.
Specifically, we study linear, surface (2D) migration and 3D migration within inverted colloidal structures or micro pillars. We build our migration tools using microfabrication techniques, such as photolithography or micro-patterning. In order to study the role of vimentin in cell polarity, we treat cells adhering to micro-pattern with a variety of cytoskeletal drugs and analyze the appearing cell polarity.

Invited Talk Sat 17:30

Role of serum response factor in the mechanotransduction of myoblasts — SYLVIE HÉNON[1], LORRAINE MONTEL[1], ALESSANDRA PINCINI[1,2], ATHANASSIA SOTIROPOULOS[2] — [1]Matière et Systèmes Complexes, CNRS – University Paris Diderot, 10 rue Alice Domon et Léonie Duquet 75205 Paris cedex 13 France — [2]Institut Cochin, INSERM – CNRS – University Paris Descartes, Paris, France

Mechanosensing is a fundamental property of many living cells. The need to handle mechanical signals is particularly obvious in muscles which are constantly exposed to external forces and generate forces themselves. Skeletal muscle is a highly plastic tissue that can adapt its size to environmental cues. Understanding the molecular pathways that regulate gain and loss of muscle mass is crucial for treating muscle wasting associated to conditions such as cancer and other chronic diseases (cachexia) and aging (sarcopenia). In a search for new factors controlling muscle mass in response to workload, recent findings identified the transcription factor Srf (Serum Response Factor) and its coactivator Mrtf (Myocardin related transcription factor). The nuclear or cytoplasmic localization of MRTF-A in the muscle cell is actin dependent: monomeric G-actin binds to and sequesters Srf co-factor Mrtf thereby preventing Srf activation and gene transcription. Conversely the recruitment of monomeric actin in filaments allows MRTF-A accumulation in the nucleus, where it can bind SRF.
In order to better characterize the inter-relations between Srf and mechanotransduction in muscle cells, we use stretchable substrates to apply *in vitro* controlled global strains on myoblasts transfected with MRTF-A-GFP. We look at the evolution of MRTF-A localization in cells in response to a constant strain and at its correlation with G-actin and F-actin levels. A moderate strain leads to an accumulation of MRTF-A in the nucleus within two hours, whereas a high strain leads to MRTF-A expulsion from the nucleus. We evidence that the localization of MRTF-A is in strong correlation with the concentration in G-actin both in the cytoplasm and in the nucleus.

Break Sat 18:00

Poster Session

Poster 1 Sat 19:00

Intracellular stresses in patterned cell assemblies — Michel Moussus[1], Christelle der Loughian[3], David Fuard[1], Marie Courçon[2], Danielle Gulino-Debrac[2], Hélène Delanoë-Ayari[3], Alice Nicolas[1] — [1]LTM, Université Joseph Fourier, CNRS UMR 5129, 17 av des Martyrs, F-38054 Grenoble cedex, France — [2]Université Joseph Fourier, INSERM U1036, CEA, Dpt des Sciences du Vivant (DSV), IRTSV, 17 av des Martyrs, F-38054 Grenoble cedex, France — [3]Institut Lumière Matière, UMR5306 Université de Lyon 1-CNRS, Université de Lyon, 69622, Villeurbanne cedex, France

We propose a new, very simple and original method to quantify the intracellular stresses, which directly relates the strain the cells impose on the extracellular matrix to the intracellular stress field. We show that the straightforward derivation of the 2D displacement field measured on the top of the extracellular matrix gives a well controlled measure of the stress tensor. This method is used to analyse how adhesive confinement on cellular assemblies influences the intracellular stress field. As a result, we show that the more confined the cells are, the more stressed they will be [1,2].

[1] Moussus, M.; Loughian, C. d.; Fuard, D.; Courcon, M.; Gulino-Debrac, D.; Delanoe-Ayari, H.; Nicolas, A.: *Intracellular stresses in patterned cell assemblies*, Soft Matter 10: 2414-2423 (2014)

[2] Moussus, M.; Loughian, C. d.; Fuard, D.; Courcon, M.; Gulino-Debrac, D.; Delanoe-Ayari, H.; Nicolas, A.: *Reply to the 'Comment on "Intracellular stresses in patterned cell assemblies"' by D. Tambe et al.*, Soft Matter 10 (2014)

Poster 2 Sat 19:00

Modulation of membrane rigidity impacts cell migration and invasion — Sebastian Schmidt[1], Katharina Ferkaljuk[2], Simone Braig[2], Chris Händel[1], Andreas Koeberle[3], Oliver Werz[3], Rolf Müller[4], Stefan Zahler[2], Josef A. Käs[1], Angelika Vollmar[2] — University of Leipzig, Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, Soft Matter Physics Division, Linnéstraße 5, 04103 Leipzig, Germany — [2]Ludwig-Maximilians-Universität München, Department of Pharmacy - Center for Drug Research, Pharmaceutical Biology, Butenandtstraße 5-13, 81377 Munich, Germany — [3]Institute of Pharmacy, Chair of Pharmaceutical/Medicinal Chemistry, Philosophenweg 14 07743 Jena, Germany — [4]Helmholz Institute for Pharmaceutical Research Saarland, PO 151150, 66042 Saarbrücken, Germany

Soraphen A, a myxobacterial compound, is found to change the lipidome of cells and drastically increase membrane stiffness by up regulating short chained membrane lipids. This impacts invasion and migration of human cancer cells in dense environments. Migration hindering effects of Soraphen A are used to investigate biomechanical interactions for two epithelial cancer cell lines. Mechanical measurements of cells and giant plasma membrane vesicles in conjunction with Boyden chamber assays show a decrease of cell invasion under membrane restructuring towards higher rigidity. This effect was even observed without significant changes in the deformation behavior of the cytoskeleton. Increased membrane rigidity and inhibited migration of cancer cells can be attributed to changes in membranes' lipid composition via Soraphen A. While cell stiffness is already known to influence migration, we were able to show that membrane rigidity alone can have a huge impact. Increase of membrane rigidity and cell stiffness are a general way to hinder invasion and might prove useful in cancer treatment.

Poster 4 Sat 19:00

The interactions of hERG1 potassium channels and ß1 integrins in pancreatic ductal adenocarcinoma cells — Stefano Coppola[1], Sagar Manoli[2], Olivia Crociani[2], Thomas Schmidt[3], Annarosa Arcangeli[2] — [1]Sapienza University of Rome, Deparment of Anatomy, Histology, Forensic Medicine and Orthopedics, Piazzale A. Moro 5, 00185, Rome, Italy — [2]Univeristy of Florence, Department of Experimental and Clinical Medicine, Viale GB Morgagni 50, 50134, Florence, Italy — [3]Leiden University, Huygens-Kamerlingh Onnes Laboratory, Physics of Life Processes, Niels Bohrweg 2, 2333 CA Leiden, The Netherlands

Cancer must be viewed as a "tissue", where neoplastic cells are immersed into a peculiar microenvironment (the "tumor microenvironment" - TME) which modulates tumor cell behaviour during the course of multistep tumorigenesis. Based on this concept, antineoplastic therapy must be tuned to target not only tumor cells but also the cellular constituents of the TME.
Ion channels and transporters are increasingly recognized as relevant players in the tumor cell-TME cross-talk [1, 2]. In particular, during tumor progression, both soluble factors and fixed components of the extracellular matrix (ECM) and membrane proteins determine signal exchange between the TME and the implicated cell types. The signalling network is coordinated by functional "hubs", which can be constituted by integrin receptors associated with other proteins to form macromolecular signalling platforms at the adhesive sites [1, 2]. These complexes often include ion channels.
We found that K^+ channels encoded by the human ether-à-go-go related gene (Kv11.1, or hERG1) are frequently overexpressed in human cancers. hERG1 channels are unique for their peculiar molecular and biophysical features. They are mainly expressed in cardiac myocytes, where they strongly contribute to physiological function. Moreover, hERG1 is also aberrantly expressed in several human cancers where it controls different aspects of the neoplastic cell biology. In particular, hERG1 modulates different intracellular signaling cascades, mainly those triggered by cell adhesion, due to a functional cross talk with integrin receptors. This can occur because hERG1 interacts with the $\beta 1$ subunit of integrin receptors [3].
We have characterized the molecular and functional features of the hERG1/$\beta 1$ complex in a reconstituted model consisting in either HEK293 or GD25 (e.g. cells KO for the $\beta 1$ integrin) transfected with different mutants of hERG1 or $\beta 1$ (manuscript in preparation). It emerged that (1) the two proteins co-immunoprecipitate after cell adhesion onto Fibronectin (FN); (2) by applying hyperspectral (HS)-FLIM-FRET we calculated the intermolecular distance between the two proteins, which turned out to be ~1 nm; (3) hERG1/$\beta 1$ interaction is mediated by the transmembrane domains of the two proteins; (4) the conformational modification of hERG1 subsequent to current activation are important to determine hERG1/$\beta 1$ complex formation; (5) the K^+ flux across the channel protein is a crucial determinant to trigger intracellular signalling pathways, such as the phosphorylation of the Focal Adhesion Kinase (FAK).

We then moved to study hERG1 channels expression in pancreatic ductal adenocarcinoma (PDAC) cells, and showed that they are indeed expressed either in PDAC cell lines (i.e. PANC-1, MIAPaCa-2, BxPC-3) and primary tumors. hERG1 turned out to regulate PDAC cell proliferation and migration, through a complex interaction with the intracellular pathway switched on by $\beta 1$ integrins and EGF receptors. In particular, hERG1 turned out to co-immunoprecipitate with $\beta 1$-containing integrins as well as with $\alpha v \beta 5$ integin, which are expressed onto the plasma membrane of PDAC cells.
Finally, making use of confocal fluorescence microscopy, as well as of novel nanoantibodies we developed against either hERG1 or $\beta 1$, we investigated both the plasma membrane and the intracellular localization of fluorescently labeled hERG1 channels and $\beta 1$ integrins and we quantified their co-localization.
The present data can contribute to better deciphering the role of hERG1 channels and integrins in mechanotransduction in PDAC cells and its relevance in driving PDAC aggressive behavior.

[1] Arcangeli A: *Ion channels and transporters in cancer. 3. Ion channels in the tumor cell-microenvironment cross talk*, American Journal of Physiology-Cell Physiology 301 (4): C762-C771 (2011)

[2] Arcangeli A, Crociani O, and Bencini L: *Interaction of tumour cells with their microenvironment: ion channels and cell adhesion molecules. A focus on pancreatic cancer*, American Journal of Physiology-Philosophical Transactions of the Royal Society B: Biological Sciences 369 (1638): 20130101 (2014)

[3] Crociani O1, Zanieri F, Pillozzi S, Lastraioli E, Stefanini M, Fiore A, Fortunato A, D'Amico M, Masselli M, De Lorenzo E, Gasparoli L, Chiu M, Bussolati O, Becchetti A, Arcangeli A: *hERG1 channels modulate integrin signaling to trigger angiogenesis and tumor progression in colorectal cancer*, Scientific Reports 3: 3308 (2013)

Poster 5 Sat 19:00

Mechanical cues in Ewing sarcoma metastasis

— Elena Beletkaia[1], Laurens Sand[2], Olga Iendaltseva[1], Pancras C.W. Hogendoorn[2], Thomas Schmidt[1] — [1]Leiden University, Leiden Institute of Physics, Physics of Life Processes, Niels Bohrweg 2, 2333 CA Leiden, The

Netherlands — [2]Leiden University Medical Center, Pathology Department, Molecular Tumor Genetics, Albinusdreef 2, 2333 ZA Leiden, The Netherlands

Ewing sarcoma is a high-grade aggressive tumor characterized by a chromosomal translocation fusing portion of EWSR1 gene most commonly to the FLI gene: t(11;22)(q24;q12). The resulting chimeric protein, EWS/FLI, was shown to change expression of many different genes among which some responsible for the architecture and adhesion of cells. The changed expression pattern in turn will influence the cellular mechanoresponse to the extracellular matrix. Ewing sarcoma is developing most commonly in bone. However, the metastatic sites are the lungs. Here we investigated whether alteration in the gene expression in combination with external mechanical cues could guide Ewing sarcoma cells to their preferential low-stiffness metastatic site. Cells were plated on the micropillar arrays of different stiffness and tested for their adhesion and force application properties. We compared four different Ewing sarcoma derived cells lines, with slightly different translocation types. All cell lines showed higher forces on stiffer pillar arrays. The cell lines showed a differential average and maximum force dependent on their genetic background. Our results on the mechanical behaviour in relation to the gene expression profiling might give novel insight into Ewing sarcoma metastasis development.

Poster 6 Sat 19:00

Plasma membrane softening in human breast and cervical cancer cells — CHRIS HÄNDEL[1], SEBASTIAN SCHMIDT[1], JÜRGEN SCHILLER[2], UNDINE DIETRICH[1], TOBIAS KIESSLING[1], STEVE PAWLIZAK[1], ANATOL FRITSCH[1], LARS-CHRISTIAN HORN[3], SUSANNE BRIEST[4], MICHAEL HÖCKEL[4], MAREIKE ZINK[1], JOSEF A. KÄS[1] — [1]Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, University of Leipzig, Linnéstr. 5, 04103 Leipzig, Germany — [2]Medical Faculty, Institute of Medical Physics and Biophysics, University of Leipzig, Härtelstr. 16-18, 04107 Leipzig, Germany — [3]Division of Breast, Urogenital and Perinatal Pathology, Institute of Pathology, University of Leipzig, Liebigstr. 26, 04103 Leipzig, Germany — [4]Department of Obstetrics and Gynecology, University Hospital Leipzig, Liebigstr. 20a, 04103 Leipzig, Germany

Determining biomechanical properties of plasma membranes is an important step for understanding cellular behaviors like cell migration and invasion that are characteristic for cancer progression and other diseases, such as the Hermansky-Pudlak syndrome and the Niemann-Pick disease [1]. Mechanical properties of cytoskeleton have been intensively studied in cells and model systems. However, the role of membrane rigidity during cancer progression is not well understood and rigidity measurements exist only for vesicles composed of artificial lipids. In this project, we studied thermal shape fluctuations of giant plasma membrane vesicles (GPMVs) produced from primary cells as well as cell lines by vesiculation or blebbing [2]. GPMVs contain a larger variety of lipids and membrane proteins than any artificial membrane and have to be regarded as more physiological model system. Based on a self-developed gradient-based edge detection algorithm, the bending rigidity was calculated by a Fourier analysis of thermal vesicle shape fluctuations [3]. The experimental data show that membranes of cancer cells are significantly softer than those of their normal counterparts. This cell membrane softening could be attributed to a decrease of fluid raft forming lipids in malignant cells. Moreover, this finding indicates that cancer may directly influence the membrane composition and its mechanical properties.

[1] A. FRITSCH, M. HÖCKEL, T. KIESSLING, K. D. NNETU, F. WETZEL, M. ZINK, J. A. KÄS: *Are biomechanical changes necessary for tumour progression?*, Nat. Phys. 6: 730–732 (2010)

[2] T. BAUMGART, A. T. HAMMOND, P. SENGUPTA, S. T. HESS, D. A. HOLOWKA, B. A. BAIRD, W. W. WEBB: *Large-scale fluid/fluid phase separation of proteins and lipids in giant plasma membrane vesicles*, Proc. Natl. Acad. Sci. U.S.A. 104: 3165–3170 (2007)

[3] H. P. DUWE, J. KÄS, E. SACKMANN: *Bending elastic moduli of lipid bilayers: modulation by solutes*, J. Phys. France 51: 945-962 (1990)

Poster 7 Sat 19:00

The native root extract of Linum usitatissimum: stress fiber induction by increased profilin-1 expression results in reduced motility of MCF-7 breast cancer cells — NADJA ENGEL-LUTZ[1], KARIN KRAFT[2], JULIANE KÜHN[1], BARBARA

NEBE[1] — [1]Dept. of Cell Biology, University Medical Center Rostock, Schillingallee 69, 18057 Rostock, Germany, Johannisallee 21/23, 04103 Leipzig, Germany — [2]Complementary Medicine, Center of Internal Medicine, University Medical Center Rostock, Ernst-Heydemann-Straße 6, 18057 Rostock, Germany

Background: The phytoestrogen-rich, ethanolic flax root extract (Linum usitatissimum, L.) harbors a great source of lignans and isoflavones, components that may possess estrogenic, anti-inflammatory, and hormone modulating effects. The intention of this systematic cell biological study was to analyze the effects of flax root extract on human MCF-7 estrogen receptor positive breast cancer cells in order to identify the main anti-tumor action by focusing on adhesion and migration related features.
Methods: Adhesion-relevant features like cell impedance, initial adhesion capacity, cell migration ability, and actin cytoskeleton formation was determined by live cell monitoring, flow cytometry, scratch assay and confocal microscopy. Detailed expression analyses of adhesion receptors and actin-related proteins were performed by flow cytometry and western blotting, respectively. The effect on anchorage-independent growth of MCF-7 cells was analyzed by colony formation on soft agar.
Results: 50 µg/ml flax root extract reduced cell impedance (50%), initial adhesion capacity (18%), migration ability (72%) and colony formation (83%) in MCF-7 cells significantly. Increased stress fiber formation (9-fold higher filament number and a 12-fold elevation of the total filament length) was initiated by overexpression of profilin-1 and down regulation of arp-2, two important regulators of actin dynamics.
Conclusion: The flax root extract exhibits anti-tumor potential for estrogen receptor positive breast cancer cells mainly by remodeling of the actin cytoskeleton, leading to significant reduction of migration and colony formation *in vitro*.

Poster 8 Sat 19:00

Mechanosensation in constrained collagen matrices — HAMID MOHAMMADI[1], PAUL JANMEY[2], CHRISTOPHER MCCULLOCH[1] — [1]Matrix Dynamics Group, University of Toronto, Toronto, Canada — [2]Institute for Medicine and Engineering, University of Pennsylvania, Philadelphia, USA

Physical interactions of cells with matrix microenvironments are critical steps in many cellular processes such as mechanosensation and metastatic invasion. Mechanosensory processes are strongly influenced by the composition and mechanical properties of the matrix, which in turn determines cell behavior. Several experimental strategies use homogeneous scaffolds to study cell behavior as a function of matrix microstructures. However, native matrix structures are highly heterogeneous in their organization and composition, which complicates understanding mechanosensation. Accordingly, the sensory mechanisms used by cells to interpret matrix heterogeneities, such as tissue boundaries, remain elusive. We developed a new model system to examine how lateral physical boundaries interfere with cell-induced compaction and remodeling of collagen and how these processes drive cell extension formation. The length and number of cell extensions were dependent on the distance of the cell from the physical boundaries. In the absence of physical boundaries, the resistance of thin collagen matrices to cell-generated forces was dependent on deformation rate. At rates similar to cell-induced deformations, native collagen matrices exhibited pronounced inelastic behavior, which in turn reduced tension in the network. Thus strain rate-dependent inelastic properties of collagen matrices may strongly influence cell-matrix interactions and matrix remodeling. Further, we determined that the actin cross-linking protein filamin A is required for cell-induced maintenance of tension and matrix compaction when resisted by physical boundaries. Our findings underline the heterogeneous and complex mechanics of connective tissue matrices as determinants of cellular mechanosensation.

Poster 9 Sat 19:00

Heterogeneity and dynamics of cancer cells at the interface of step-gradients of 3D collagen matrices — JIRANUWAT SAPUDOM, STEFAN RUBNER, STEVE MARTIN, TILO POMPE — University of Leipzig, Institute of Biochemistry, Biophysical Chemistry Group, Johannisallee 21-23, 04103 Leipzig, Germany

Cancer cells have a highly distinctive ability to adapt and communicate to their surrounding microenvironments. The properties of extracellular microenvironments, namely microarchitecture, mechanics as well as the composition, regulate the development and progression of cancer. Moreover, migration and invasion of

cancer cells through extracellular microenvironments are crucial steps for metastasis. It is hypothesized that interfacial boundaries of the heterogeneous extracellular microenvironments can act as a physical barrier for migration and invasion of cancer cells.

To investigate the mechanisms by which migrating cancer cells respond to the change of the characteristics of extracellular microenvironments, we reconstruct step-gradients of 3D collagen matrices. We yield well-defined distinct zones with various combinations of matrix characteristics such as high-low density of collagen, thick-thin collagen fibrils as well as high-low fibronectin levels. Cellular heterogeneity and dynamics of cancer cells, in particular melanoma cells, were monitored at the interface of the step-gradients and analyzed using our 3D label-free single cell tracking platform. First results demonstrated that cancer cells change their migration characteristics while crossing the interface boundary. In this context we observed that fibril orientation of collagen matrices contribute in guiding migration of cancer cells in a size-dependent manner.

The successful development of step-gradients of 3D collagen matrices provide insights into cellular migration in *in vivo* like microenvironments and allow to study metastatic potential of cancer cells *in vitro*.

Poster 10 Sat 19:00

Biophysical method for early cancer detection

— JELENA MUNCAN, LIDIJA MATIJA, DJURO KORUGA — University of Belgrade, Faculty of Mechanical Engineering, Biomedical Engineering, Kraljice Marije 19, 11000 Belgrade, Serbia

Cancer research has been overwhelmingly directed towards the biochemistry, genomics, and cell biology; by contrast, far less attention has been focused on the biophysics of the cancer state. It was recently proposed that important insights pertaining to the key stages in cancer progression are likely to come from the theory of phase transitions [1].

Human tissues and organs are heterogeneous systems primarily consisting of water, proteins, lipids, carbohydrates, nucleic acids, and mineral components. Water is the most mobile and variable component determining functional properties of tissues. Abnormal states of tissues are accompanied by changes in water content and strength of its binding to structural biopolymers [2].

Recent advances in water science have introduced a new idea that water may exist not in just three, but four phases, and this fourth phase of water – so called exclusion zone water, organized water, or gel phase is the type of water with which the healthy living cells are actually filled [3]. On the other hand, cancer cells contain more free water than normal cells, and the degree of malignancy increases with the degree of cell hydration. It follows that intracellular hydration might be a primary factor in carcinogenesis [4,5,6], and that in cancer cells water changes from ordered gel phase to more disorganized – liquid phase.

Changes in water structural organization in cells can thus be used as a diagnostic parameter for existence of certain pathological states [7,8].

The method of Opto-magnetic imaging spectroscopy (OMIS) introduced by Koruga et. al [9,10] is based on the polarization properties of water and in result gives a summarized magnetic properties of the sample, where paramagnetic properties can serve as a measure of organization of water, while diamagnetic properties as a measure of disorganization (paried/unpaired electrons).

The OMIS was first introduced in 2009 [9] as a non-invasive method for characterization of skin. Since then, it has evolved and has been adjusted for wider area of applications in biomedical engineering; polymers, liquids and epithelial tissues (healthy and cancer) [8,10-13].

The method is based on light-matter interaction using light in the range between 400 nm and 700 nm. Interaction with visible light is non-invasive and provides examination process that can be repeatedly conducted without presenting any risks. Finally, numerous advantages that are offered by digital image acquisition further encouraged the design of this technique and customized hardware solution that was used in studies. The OMIS technique has yielded positive results in early detection of cancer of epithelial tissues such as cervix, skin and oral cavity and other biological samples [8].

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Poster 11 Sat 19:00

Contractile actin bundle without molecular motors — Jörg Schnauss, Carsten Schuldt, Tom Golde, Martin Glaser, Sebastian Schmidt, Dan Strehle, Josef Käs — University of Leipzig, Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, Soft Matter Physics, Linnéstraße 5, 04103 Leipzig, Germany

Contractile actin structures are responsible for a variety of crucial cellular functions such as muscle contractions, cell motility and division, as well as force generation on the filament level [1].
Interactions of actin and its molecular motor myosin are known for decades as the fundamental process for biological force generation. These interactions convert chemical energy into mechanical work by ATP hydrolysis [1].
However, we show an alternative force generation in the absence of any molecular motors or any other actin accessory proteins. The system is not driven by ATP hydrolysis and solely relies on minimization of the free energy based on filament - filament interactions. These interactions are induced by a crowded environment in a regime well below the macromolecular content of cells.
We were able to measure contraction velocities ranging from 0.10 to 0.65 µm/s and to approximate a force regime of 0.5 - 3.0 pN. In comparison, single myosin motors can exert up to 5.0 pN.
Thus, the force we observed correspond to a regime of weak active behavior of single myosin motors depending on ATP hydrolysis.

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Poster 12 Sat 19:00

Control of cancer cell invasion by lamin-mediated nuclear deformability — Katarina Wolf[1], Marina Krause[1], Veronika te Boekhorst[1], Ramanil Perera[1], Rene Marke[1], Joost te Riet[1], Celine Marie Denais[2], Monika Zwerger[3], Peter Friedl[1], Jan

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Cell migration into the 3D extracellular matrix (ECM) is a multistep biophysical process that depends on cell deformability and physical tissue constraints, involved in wound healing, inflammation, and metastatic tumor invasion. Cell deformation to transmigrate available tissue spaces is determined by the mechanical flexibility of the nucleus, the largest and stiffest cell organelle. Nuclear stiffness, stability and shape are maintained by the nuclear lamina consisting of intermediary filaments A- and B-type lamins; and it is established that A-type lamins, together with the chromatin state, determine the stiffness (reciprocal: deformability) of the nucleus. However, it remains unclear whether lamin-mediated nuclear rigidity limits cellular adaptation during migration through the confining spaces of 3D connective tissues, such as from skin, and to what extent individual lamins are rate-limiting during this process. We thus aimed to investigate the role of lamin-mediated nuclear stiffness during tumor cell migration through small pores, by both up- and down-regulation of lamin A- as well as B- subtypes. Transient RNA-interference, or stable overexpression of A/C, B1 and B2-type lamins were induced in HT1080 fibrosarcoma and MV3 melanoma cells, and lamin expression rates were controlled by western blotting and fluorescence microscopy. Lamin distribution and nuclear shape changes were quantified, together with cell migration rates in dense versus loose 3D collagen lattices, and confirmed by transwell chamber assays. In parallel, atomic force microscopy was applied to measure nuclear flexibility and deformability. Transient knockdown, as well as stable overexpression of lamins were found to modify both nuclear deformability as well as migration rates of cancer cells. Knockdown of A- and B-type lamins was associated with increased nuclear deformability and migration rates. Lamin overexpression resulted in somewhat irregular lamin distribution and nuclear shape, in association with lower nuclear deformability and migration rates through collagen or transwell chambers when pores were small but not when spaces matched the cellular diameter. In summary, our data indicate a biomechanical lamin-dependent mechanism of nuclear shape adaptation during cell migration through confining skin-like connective tissue equivalents, with implications on the efficacy of cancer cell invasion through skin-like interstitial tissues.

Poster 13 Sat 19:00

Effect of x-irradiation on cell morphology, cytoskeleton network, and adhesion — SABATO FUSCO[1], VALERIA PANZETTA[1], MARTA DE MENNA[2], DEBORA BUCCI[2], VITTORIA GIOVANNINI[2], MARIAGABRIELLA PUGLIESE[3], MARIA QUARTO[3], PAOLO NETTI[1,2,4] — [1]Center for Advanced Biomaterials for Healthcare at CRIB, Istituto Italiano di Tecnologia, Largo Barsanti e Matteucci, 53, 80125 Napoli, Italy — [2]Interdisciplinary Research Centre on Biomaterials, Federico II University of Naples, Piazzale Tecchio, 80, 80126, Napoli, Italy — [3]Dipartimento di Fisica, Università Federico II, and INFN-Sezione di Napoli, Monte S. Angelo, Via Cintia, 80126 Napoli, Italy — [4]Dipartimento di Ingegneria dei Materiali e della Produzione, Universita di Napoli Federico II, Piazzale Tecchio 80, 80126, Napoli, Italy

It's well known the ability of X-irradiation to produce chromosomal damage inducing a decrease of reproductive ability among cell population. Nevertheless, cells, in which a single ionization is not sufficient for death induction, but affect reproductive functions, have many physiological activities that continue. In this paper we investigated the effects of 2 different doses of X-irradiation (1 and 2 Gy) on some of these activities (i. e. spreading, proliferation, migration) focusing the attention on the cytoskeleton (CSK) structure on two cell lines, BALB/c 3T3 and Simian virus 40-transformed BALB/c 3T3 (SVT2)cells. Indeed, CSK is involved in virtually all cellular processes and abnormalities in its function can result in many diseases, such as cancer. Our studies showed that the alteration in the cytoskelatal architecture during malignant transformation is correlated with a less spread morphology, small adhesion plaques (the structures that form a physical link between the extracellular and the intracellular domain of the plasma membrane), an increased motility and an increased deformability. Finally, we investigated how X-irradiation alters cytoskeleton dynamics in both cell lines, assessing cell proliferation, spreading areas and migration ability.

Poster 14 Sat 19:00

Intracellular mechanics of normal and cancer cells — David Guet[2], Kalpana Mandal[1], Charlotte Alibert[1], Mathieu Pinot[1], Bruno Latge[1], Sabine Bardin[1], Kristine Schauer[1], Bruno Goud[1], Jean-Baptiste Manneville[1] — [1]CNRS-Institut Curie, UMR144, Cell Biology Department, Molecular Mechanims of Intracellular Transport team, 26 rue d'Ulm, 75248 Paris cedex 05, France — [2]Unité Pathologie et Virologie Moléculaire INSERM U944 CNRS UMR9212, Institut Universitaire d'Hématologie, Hôpital Saint-Louis, 1 avenue Vellefaux, 75010 PARIS, France

The mechanical properties of cancer cells differ from those of normal cells. Most studies in the field have focused on the mechanics of the extracellular matrix and the plasma membrane. To investigate the contribution of the cell interior to cell mechanics, we have developed an intracellular microrheology technique based on the manipulation of optically trapped beads internalized in living cells and visualized by fast confocal microscopy. Using this technique, we have shown that a mechanical force applied on the Golgi apparatus perturbs Golgi-associated trafficking events and that actin dynamics plays a central role in the rheology of the Golgi apparatus. We now focus on the role of the cytoskeleton in intracellular mechanics in cancer cells and show (i) that kinesin motors contribute to intracellular viscoelasticity in bladder cancer cells and (ii) that the composition of intermediate filaments controls the mechanical properties of astrocytes and glioma cells.

Poster 15 Sat 19:00

Higher ordered assembly of rigid biopolymers induced by depletion forces — Martin Glaser[1], Jörg Schnauss[1], Teresa Tschirner[2], Maximilian Moebius-Winkler[2], Tom Golde[1], Carsten Schuldt[1], David M. Smith[2], Josef A. Käs[1] — [1]University of Leipzig, Faculty of Physics and Earth Sciences, Institute for Experimental Physics I, Linnéstraße 5, 04103 Leipzig, Germany — [2]Fraunhofer Institute for Cell Therapy and Immunology, Perlickstraße 1, 04103 Leipzig, Germany

The function of cells crucially depends on the properties of the underlying cytoskeleton. One of its major components is actin, which can be found in various structures depending on its surrounding. These structures range from loose networks to densely packed bundles and can also form clusters in a higher-level assembly like asters and nematic phases.
Especially the formation of asters was usually attributed to actin associated proteins. We present experimental evidence of bundle arrangements in star-like structures independent of other proteins. For the formation we use established actin bundling mechanisms like counter-ion clouds and depletion forces. Under certain conditions tertiary structures emerge. These structures can be formed solely by altering the concentration of actin and the according bundling agent in the system.
Since no other associated proteins are involved this effect that higher ordered structure formations can be controlled only by self-assembly and accordingly energy minimization within the system. Therefore, this effect is not necessarily limited to actin and systems consisting of other rigid biopolymers, like DNA tubes, are investigated.

Poster 16 Sat 19:00

Surface tension-based model of epithelial folds — Matej Krajnc[1], Nick Storgel[1,2], Polona Mrak[3], Jasna Strus[3], Primoz Ziherl[1,2] — [1]Jozef Stefan Institute, Department of Theoretical Physics, Biophysics group, Jamova cesta 39, 1000 Ljubljana, Slovenia — [2]Faculty of Mathematics and Physics, University of Ljubljana, Jadranska ulica 19, 1000 Ljubljana, Slovenia — [3]Biotechnical Faculty, University of Ljubljana, Jamnikarjeva ulica 101, 1000 Ljubljana, Slovenia

We propose a mechanical model of simple epithelial tissue consisting of incompressible cells, attached to the elastic basement membrane. Each cell carries a surface energy associated with (i) cortical tension, (ii) differential surface tension due to apico-basal polarity, and (iii) cell-cell adhesion. The apical, the basal and the lateral cell faces are each characterized by a specific effective surface tension [1]. We explore the phase diagram of minimal-energy epithelial shapes and obtain 5 qualitatively different morphological classes: flat, condensed, invaginated, evaginated, and wavy. We qualitatively explain the mechanics of our model tissue by deriving the effective elastic functional. Apart from bending and stretching elasticity terms we identify terms that describe the coupling between local curvature and local thickness. We derive Euler-Lagrange equations of the system and solve them to show that our continuum theory is consistent with the discrete model.

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Poster 17 Sat 19:00

Mechanics of tumor growth in an *in vitro* model system — Kristen Mills[1], Asli Akidil[1], Farid Ghasemalizadeh[1], Shiva Rudraraju[2], Ralf Kemkemer[1,3], Krishna Garikipati[2] — [1]Max Planck Institute for Intelligent Systems, Department of New Materials and Biosystems, Stuttgart, Germany — [2]University of Michigan, Mechanical Engineering, Ann Arbor, Michigan — [3]Reutlingen University, Reutlingen, Germany

The biomechanical environment of a solid tumor is in a transformed state in which tumor-associated cells stiffen the environment through increased deposition and rearrangements of matrix fibers. Additionally, the uncontrolled proliferation of tumor cells means that excessive stresses are built up due to tumor expansion. The effects of such an altered mechanical environment are not completely understood, but it is becoming obvious that it plays a role in the progression of the disease. In order to extrapolate the significance of the mechanical interactions between a growing tumor and its environment, we use an *in vitro* tumor growth model whose mechanical and adhesive properties can be tuned.

We have found that, in addition to other effects of the altered mechanical environment, tumor shape is strongly affected. Tumors that have well-defined boundaries, both *in vivo* and *in vitro*, are often described as being ellipsoidal with a high eccentricity factor (as opposed to spheroidal). Using the theory of elasticity we show how certain ellipsoidal shapes minimize the relevant free energy. The significance of tumor shape may prove to be in determining when and where tumor cells are able to escape from the primary tumor. And, results from tumor growth modeling have suggested that the surface tension, together with tumor shape, will be a determining factor in when and where tumor cells escape.

The surface tension of tissues plays an important role in determining tissue form during morphogenesis. There is likely a corresponding importance to surface tension in the development of solid tumors. In order to understand the role that surface tension plays in tumor growth as well as to start addressing the hypothesis arising from tumor growth modeling, we explore the surface tension of the various hydrogels and model tumor tissues—multicellular tumor spheroids (MCTS)—composed of tumor cells used in the *in vitro* tumor growth models.

Poster 18 Sat 19:00

Building minimal cells to understand cell shape control — Mulla Yuval, Szuba Agata, Koenderink Gijsje — FOM Institute AMOLF, Science Park 104, Amsterdam, The Netherlands

Cell shape control is crucial in many biological processes like mitosis, embryonic development and cell migration. The shape of a cell is defined by the plasma membrane and governed by a thin polymer network underneath the plasma membrane, called the actin cortex. Qualitatively it is known that cell shape is controlled by the actin cortex, membrane linkers and motor proteins. These components are tightly regulated, making it difficult to perform quantitative experiments *in vivo*. Therefore we aim to provide quantitative insight into cell shape control by building and characterizing a minimal cell: the *in vitro* reconstitution of the most essential components for cell shape control.

Poster 19 Sat 19:00

Cell motility at the leading edge: Measuring membrane fluctuations with an optical tweezer setup —Jürgen Lippoldt, Melanie Knorr, Dan Strehle, Josef A. Käs — University of Leipzig, Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, Soft Matter Physics Division, Linnéstraße 5 04103 Leipzig Germany

Cell motility is an important research topic in the context of cancer research. The high motility metastasising cancer cells and their ability to cross the endothelium is not only one of their most interesting properties, but also their most lethal. At the moment, there is a lot of effort been put into a better understand these characteristics of metastasising cancer cells. Thereby, almost all studies use standard microscopic imaging to characterise the time-dependent properties of cellular movement. This approach is sufficient to study the overall behaviour of a cell movement, but several of the underlying processes happen on time and length scales to small to detect with microscopic imaging. Therefore, one can expect to learn about cell motility by 'looking closer'.

It is possible to detect the motion of cell membranes with the help of a focused laser spot[1]. In this project we plan to observe the part of the cell membrane, which is most forward in the direction of motion – the leading edge. The laser spot is positioned at this point of the cell membrane. The position of the leading edge can be deduced by analysing the forward scattered light in the back focal plane of the condenser with a quadrant photo diode (back focal plane microscopy). With this technique, high temporal (10-5 s) and spacial (~ 1 nm) resolutions can be achieved [2].
The aim of this project is to study whether or not macroscopic properties of cellular motion are connected to microscopic processes and properties like membrane fluctuations and membrane stiffness. There are earlier studies which support the hypothesis of such a connection. Betz *et.al.* [3], for example, recorded a bistable stochastic process in leading edge fluctuations of neuronal growth cones and suggested that these fluctuations might help with signal detection by statistical resonance.

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Poster 20 Sat 19:00

Mechanobiology of cellular trafficking across membranes — Sabyasachi Dasgupta, Thorsten Auth, Gerhard Gompper — Institute of Complex Systems and Institute for Advanced Simulation, Forschungszentrum Jülich, Germany

Budding of cell membranes initiates intracellular vesicle transport and has been studied for a variety of soft matter systems. Using a continuum model, we study wrapping of a single nano-particle as an interplay of the membrane deformation energy and the adhesion energy of the particle and membrane. With the help of numerical energy minimization using triangulated surfaces, we investigate the role of shape and size of the particle as well as of the membrane's elastic parameters on nano-particle wrapping.
For rod-like and disc-like particles [1,2], we find a higher binding affinity to the membrane compared with spherical particles. However, such particles have a lower uptake to cells, as confirmed by experiments. All more complex particle shapes, such as a Hauser's cube and supereggs [2], have stable partially-wrapped states with shallow and high wrapping fractions for sufficiently high adhesion strengths. Partially-wrapped particles can be advantageous both from an application point of view for interfacing cells with nanostructured interfaces [3] as well as from a biological point of view. Particles can also preferentially bud tip first from the membrane similar to filamentous viruses like Ebola and Marburg.
Similarly, a mechanistic understanding of how the malarial merozoite [4] invades the erythrocyte membrane tip-first is lacking. Assuming an asymmetric egg-like shape for the parasite, we have investigated the role of the different membrane properties on the invasion mechanism. We propose a concentration gradient of adhesive molecules to be responsible for the reorientatioin of the particle towards the tip before invasion and membrane spontaneous curvature from cytoskeletal re-modelling or secretion of unstructured membranes to assist motor forces for the parasite to invade a red blood cell.

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Poster 21 Sat 19:00

Polymer Physics 2.0: Exploiting programmable nanomaterials to control material properties of soft matter — Carsten Schuldt[1,2], Jessica Lorenz[2], Jörg Schnauss[1], Martin Glaser[1], Josef A. Käs[1], David M. Smith[2] — [1]University of Leipzig, Soft Matter Physics Division, Linnéstraße 5, 04103, Leipzig, Germany — [2]Fraunhofer Institute for Cell Therapy and Immunology, Perlickstraße 1, 04103 Leipzig, Germany

Biologically evolved materials are often used as inspiration in the both the development of new materials as well as examinations into the underlying physical principles governing their general behavior. One prominent example stems from the highly dynamic cytoskeleton of eukaryotic cells, where consideration of its biopolymer constituents such as actin and microtubules along with their respective sets of modulatory proteins and motors has inspired a deeper understanding of soft polymer-based materials [1-4]. In this case, a major limitation lies in the molecular toolbox provided by naturally occurring biological systems, which has been highly optimized and streamlined through evolutionary processes to carry out the necessary functions of cells. The inability to deterministically modulate or "program" basic properties such as biopolymer stiffness and interaction strengths hinders a meticulous examination of parameter space, and the subsequent potential for developing new classes of materials.
Using the semiflexible cytoskeletal filamentous polymer actin as inspiration, we seek to overcome these limitations using model systems assembled from programmable nanomaterials such as DNA and peptides. Nanotubes with similar dimensions and mechanical properties as actin filaments can be constructed from small sets of specially designed DNA strands [5]. Properties such as stiffness and inter-filament attraction (i.e. crosslinking) can be controlled through the design of a particular set of DNA strands [6]. In the low concentrated "entangled" regime, networks displaying viscoelastic properties reminiscent of those arising from natural cytoskeletal biopolymers can be generated and systematically modulated according to choice of network constituents. Furthermore, efforts are underway to create complex hybrid networks, where the mechanical properties of reconstituted actin networks are controlled though programmable interactions with DNA-peptide constructs.

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Poster 22 Sat 19:00

How biophysical and nanomedical tools support therapeutical improvements in neuro-oncology — Ruiyan Zhang[1,12], Athanasios K. Petridis[2], Georgios Scheiner-Bobis[3], Monika Burg-Roderfeld[3], Thomas Eckert[3,4], Axel Wehrend[4], Martin Bergmann[5], Lisha Wu[6], Bengt Norden[6], Martin Billeter[7], Axel Scheidig[1], Roland Schauer[8], Sebastian Fraune[9], Thomas C. G. Bosch[9], Hans Wienk[10], Rolf Boelens[10], Barun K. Chatterjee[11], Hans-Christian Siebert[12] — [1]Zoologisches Institut, Strukturbiologie Zentrum für Biochemie und Molekularbiologie, Christian-Albrechts-Universität Kiel, Am Botanischen Garten 1-9, 24118 Kiel, Germany — [2]Neurochirurgie, Klinikum Duisburg GmbH, Zu den Rehwiesen 9, 47055 Duisburg, Germany — [3]Institut für Veterinärphysiolgie und -Biochemie, Fachbereich Veterinärmedizin, Justus-Liebig-Universität Gießen, Frankfurter Str. 100, 35392 Gießen, Germany — [4]Klinik für Geburtshilfe, Gynäkologie und Andrologie, Fachbereich Veterinärmedizin, Justus-Liebig-Universität Gießen, Frankfurter Str. 106, 35392 Gießen, Germany — [5] Institut für Veterinäranatomie, Histologie und Embryologie, Fachbereich Veterinärmedizin, Justus-Liebig-Universität Gießen, Frankfurter Str. 98, 35392 Gießen, Germany — [6]Department of Chemical and Biological Engineering, Chalmers University of Technology, Gothenburg, Sweden — [7]Department of Chemistry and Molecular Biology,

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Nanomedicine and nanopharmacology are rapidly developing scientific fields in which various biophysical methods (e.g. NMR, X-ray crystallography, MS, AFM, EM and SPR) are combined with molecular modeling approaches (including molecular dynamics simulations and ab initio calculations). The resulting data of this arsenal of techniques have to be further combined with biochemical as well as with molecular and cell biological methods in order to address so-far unsolved clinical problems on a nano-scale level. When describing the Coulomb explosion of a nematocyst discharge process theoretical physics itself has to be used for a proper model description of the fastest process in living nature. We apply a plan of attack related to Coulomb explosions on clinical problems in the field of oncology. The theoretical description as well as the computational and experimentally derived results related to the biological properties of Cnidaria especially nematocyst discharge processes are essential for our approach. It is possible to describe the Coulomb explosion in a nematocyst of Cnidaria completely with our physical formulas. Such an approach was first discussed by Alan Turing when describing the chemical basis of morphogenesis in hydras. In our case we are especially interested in the displacement of the stylet as a function of the applied pressure. In order to understand the trigger-process in dependence of the poly sialic acid (polySia) concentration on tumor cell surfaces we are analyzing various cells with increasing polySia concentrations in their glycocalyx (e.g. various fish eggs, neuroblastoma and glioblastoma cells).

Poster 23 Sat 19:00

Models for angiogenesis on microstructured surfaces — Simon Schuster[1], Kerstin Pflieger[1], Florian Gegenfurtner[1], Max Albert[2], Felix Segerer[2], Joachim Rädler[2], Angelika Vollmar[1], Stefan Zahler[1] — [1]Department of Pharmacy, Ludwig-Maximilians-Universität München, Butenandtstraße 5-13, Munich, Germany — [2]Department of Physics, Ludwig-Maximilians-Universität München, Geschwister Scholl Platz 1, Munich, Germany

Angiogenesis, the growth and formation of novel blood vessels from preexisting vessels, is an important physiological and pathophysiological process involved in wound healing but also in cancer progression. However, dynamics of angiogenesis in general and the impact of physical factors are barely understood. We try to model different cellular processes of primary endothelial cells using micro-structured surfaces. With the help of micro contact printing we bring HUVECs (= Human Umbilical Vein Endothelial Cells) into defined cellular shape and stress conditions in order to model 3D migration, tip cell formation and fibronectin-fibrillogenesis. All these processes have been shown to play an important role in angiogenesis.
We use primary endothelial cells, which are not adapted to 2D cell culture, in order to establish an easy accessible model system for imitating 3D migration on a flat surface. This model has been proposed before for 3T3 fibroblast, but HUVECs show some striking differences. Our results reveal that 1D migrating endothelial cells share a lot of properties compared to 3D migrating cells, regarding their overall morphology as well as their cellular response to selected small molecule inhibitors.

Poster 24 Sat 19:00

Composite networks of actin and intermediate filaments — Tom Golde[1], Martin Glaser[1], Carsten Schuldt[1], Jörg Schnauss[1], Harald Herrmann[2], Josef A. Käs[1] — [1]University of Leipzig, Faculty of Physics and Earth Sciences, Institute for Experimental Physics I, Soft Matter Physics Division, Linnéstraße 5, 04103 Leipzig, Germany — [2]German Cancer Research Center, Divison of Molecular Genetics, Heidelberg, Germany

Cell deformability is mainly determined by cytoskeletal filaments like actin and intermediate filaments. Rheological network properties are quite well understood for networks composed of a single filament type. Actin networks are described by common models for semiflexible polymer networks. In contrast, some intermediate filaments like keratin show a high elastic modulus at low protein concentration that cannot be

explained with these simple models. Cells contain not only one but several types of filament networks. Their rheological behavior cannot simply be deduced from single type network properties.
We want to address this problem with a two-step *in vitro* approach. First, we will study actin, keratin, and vimentin networks with shear and microrheology under comparable boundary conditions. The next step in understanding cell deformability is the investigation of composite networks made of these previously examined filament types.

Poster 25 Sat 19:00

Xenograft draining lymph nodes have alterations within the structural reticular network and collagen fibresX — Freja Albjerg Venning, Chris Denis Madsen, Alejandro Guiliani Mayorca, Janine Terra Erler — University of Copenhagen, Biotech Research and Innovation Centre, Erler Research Group, Ole Maaløes Vej 5, 2200 Copenhagen N, Denmark

Cancer affects 1 in 3 people, and 90% of cancer deaths are due to metastasis. The tumour draining lymph nodes are the first sites of metastasis, and lymph node metastasis is the strongest prognostic indicator in multiple cancer types. Lymph nodes filter the incoming lymph fluid drained from a tissue area, and act as communication hubs for the immune system initiating adaptive immunity towards anything recognised as non-self, such as pathogens or aberrant-looking tumour cells. Yet tumour cells succeed in metastasising to the lymph node, suggesting that they are tolerated even if they should be recognised as aberrant. Primary tumours remodel their draining lymph nodes through soluble factors, perhaps preparing the soil for the arrival of tumour cells. One type of pre-metastatic change, lymphangiogenesis, has indeed been found to increase the risk of developing lymph node metastasis.
The aim of this project is to look at pre-metastatic or early metastatic changes to the extracellular matrix (ECM) of lymph nodes draining a tumour, and the biophysical alterations that accompany them. To investigate the morphological changes in lymph nodes we have established an oral squamous cell carcinoma (OSCC) xenograft model in nude mice. Lymph node metastasis has a particularly poor prognosis in OSCC.
Through immunofluorescent labelling of ECM components on sections of pre-metastatic lymph nodes, we have found that lymph nodes draining OSCC xenografts have marked alterations in the reticular network. This network is created by fibroblastic reticular cells (FRCs) and it coordinates the compartmentalisation of the lymph node into discrete areas such as the B-cell follicles and the T-cell zone. In healthy lymph nodes, the reticular network is present within the T-cell zone, and not notable within the B-cell follicles; but in tumour draining lymph nodes the network no longer respects the boundaries of the B-cell follicles, and is present within the entire lymph node after only 3 days of draining a xenograft, and before the presence of overt tumour cell colonisation. This global distribution of the FRC reticular network is tumour specific, and the fact that a FRC-like network has been found to create an immunotolerant tumour microenvironment suggests that the FRC expansion within the lymph nodes may be inducing tolerance here too, permitting the tumour cells to colonise the lymph node.
Using 2-photon microscopy and second harmonic generation imaging of whole-mount tumour draining lymph nodes, we have found trends towards alterations in the collagen fibres around the tumour outgrowths in the lymph nodes; collagen fibres tend to become longer and run in parallel around the tumour cells, compared with healthy lymph nodes.
The future directions of the project are to investigate if alteration in the FRC reticular network promotes lymph node colonisation, and whether cancer cells physically interact with FRCs. We will also be measuring stiffness of the tumour draining lymph nodes to see if the collagen changes are translated into altered stiffness, and investigate how this affects cell behaviour.

Poster 26 Sat 19:00

Resolving the mechanobiology of the epithelium on native basement membranes — Marija Plodinec[1], Philipp Oertle[1], Selim Benayat[1], Wili Halfter[2], Bernhard Henrich[3], Inke Nathke[4], Mohamed Bentires-Alj[5], Roderick Lim[1] — [1]Biozentrum and the Swiss Nanoscience Institute, University of Basel, Basel, Switzerland — [2]Department of Neurobiology, University of Pittsburgh, Pittsburgh, Pittsburgh, USA — [3]Ophthalmology Department of the University Hospital Basel, Basel, Switzerland — [4]Cell & Developmental Biology, Dundee Cancer Centre, University of Dundee, Dundee, UK — [5]Friedrich Miescher Institute for Biomedical Research, Basel, Switzerland

The onset of metastasis occurs when cancer cells invade and breach the basement membrane (BM) that provides mechanical support to epithelial tissues. Yet, it remains unclear what triggers cancer cells to breach the BM, and how 'triggered' cells breach the BM. Here, we have established an *in vitro* invasion assay using inner limiting membranes (ILMs) isolated from human retinas as a native BM interface for culturing MCF10A and MDCK epithelial cells. Using atomic force microscopy (AFM) with other high-resolution microscopies and TER (trans-epithelial resistance), we have correlated the mechano-cellular attributes of the BM/epithelium interface to its biochemical and structural properties. When tumorigenic variants of these cells are used, we show that cancer cell invasion is associated with a decrease in cellular stiffness correlated to changes in cell and BM morphology. Being a native BM, the ILM serves several advantageous over reconstituted Matrigel, an ECM extract that originates from mouse tumor ascites. Besides variations in thickness and biochemical composition, we find that Matrigel is mechanically 50-fold more compliant (i.e., softer) than native BMs. Given the mechano-biological relevance of the ILM allows us to further understand how intracellular signaling occurs via epithelial junctions and the surrounding stromal layers at the BM interface in health and disease.

Poster 27 Sat 19:00

Taking the atomic force microscopy to the clinic: Predicting the prognosis and recurrence of breast cancer by integrating the nano-mechanical profiles of primary tumor and its adjacent tissue — Christian Raez[1], Ellen Obermann[1], Philipp Oertle[2], Roderick Y.H. Lim[2], Marko Loparic[2,3], Marija Plodinec[2] — [1]Institute of Pathology, University Hospital Basel, 4031 Basel, Switzerland — [2]Biozentrum and the Swiss Nanoscience Institute, University of Basel, 4056 Basel, Switzerland — [3]Nuomedis AG, 4410 Liestal, Switzerland

Breast cancer is the most frequent occurring malignancy and the second most frequent cause of cancer death in women in developed countries. Yet, while primary tumors are rarely fatal, metastases are responsible for the majority of cancer-related deaths. There are some parameters which serve as prognostic markers for the development of metastases, but despite considerable efforts, it is still not possible to predict accurately an individual`s risk. Therefore, adjuvant therapy is frequently administered to patients who might have been cured by surgery and anti-hormonal treatment alone. Current classification of breast cancer - including prognostic and predictive markers - is still mainly based on clinical and histopathological criteria. However, risk stratification based on clinico-pathological parameters alone is often misleading and causes under- or overtreatment in a significant number of patients. This is especially valid for early, HER2/neu-negative breast cancer (i.e. stages I, IIA, IIB, and IIIA) where clinico-pathological factors are not sufficient for clinical decision making. Therefore, the main goal of breast cancer clinical research is to develop prognostic markers that are assessed by quality assured certified tests, can be routinely used, and whose costs are acceptable. These markers should help to optimize cancer diagnosis, orientate therapy choice, and support patient follow up. In addition to genetic and microenvironmental factors, recent data show that physical interactions of cancer cells with their environment are critical parameter in the metastatic process. Nevertheless, efforts to understand cancer biomechanics had been largely polarized between tissue-level and single-cell experimentation. As a result, findings have been disputed due to: 1) a lack of the natural tissue context, and 2) insufficient measurements/analysis to account for intratumoral heterogeneities. This highlights that investigating entire tissue segments with sub-cellular resolution provides a more comprehensive understanding of mechanical changes associated with carcinogenesis. This motivated us to develop an atomic force microscope (AFM)-based diagnostic apparatus known as ARTIDIS ("Automated and Reliable Tissue Diagnostics"; US Patent 8756711) to measure the stiffness profiles of unadulterated tissue biopsies from human patients in close to native physiological conditions with an unprecedented stiffness sensitivity resolved at nanometer-scale spatial resolution. Lasting ~2 hours, an ARTIDIS assay uses ~10 nm-sharp stylus or tip that makes ~10000 miniscule indentations across a biopsy surface. In our initial study using transgenic mice as a breast cancer model we could show that the „softest" nanomechanical phenotype (~0.4 – 0.8 kPa) present at the primary tumor site closely corresponded to the stiffness of the metastatic lesions obtained from the lungs of the same mouse (Plodinec et. al; Nature Nanotech. 2012). In order to transfer preliminary results into a clinical setting, the ARTIDIS technology was set up at the Institute of Pathology, USB in Basel and optimized for analysis of unfixed (measured in physiological aqueous

environment) human breast cancer samples obtained by tumor resections. For this purpose, 152 tissue samples, including primary breast cancers of various stage and grade, lymph node metastases, and non-neoplastic human breast tissues were collected from resection specimens of 56 patients. Post-AFM, tissue samples were fixed and paraffin embedded in an oriented manner. ARTIDIS data have confirmed the initial findings that all carcinoma samples display heterogeneous stiffness phenotypes with a characteristic 2-fold softer phenotype in comparison to the surrounding non-neoplastic and morphologically normal breast tissue. Healthy mammary tissue of patients without breast cancer exhibits stiffness values close to 1.6 kPa. Tumor tissues from breast cancer patients exhibit heterogeneous distributions within 0.5 to 1.2 kPa and exponential decay of up to 20 kPa. Most importantly, we identified invasive breast cancer specimens by a characteristic soft peak of 0.4 to 0.8 kPa. Stiffness distribution of corresponding lymph node metastases was characterized by a heterogeneous stiffness profile with a characteristic soft peak of 0.4 to 0.8 kPa similarly to the primary breast tissue. In addition, adjacent tissue of these patients that was histologically rated as "non-malignant" presented soft stiffness peaks ranging from 0.4 to 0.8 kPa We conclude that for assessment of prognosis in breast cancer patients it is important to take into account not just the primary tumor but also the nanomechanical response of the adjacent tissue and local lymph nodes. In addition, ARTIDIS is ideally suited for use in daily practice as it allows fast, on-site assessment of specimen and does not suffer from inter-obeserver variability as assessment of other markers, such as Ki-67 (Obermann *et al.*, Pathologe, 2012). Finally, our data demonstrate applicability of nanomechanical profiling in clinics for predicting the prognosis and recurrence of breast cancer that can give important clues for treatment decisions.

Poster 28 Sat 19:00

Investigating cell mechanics by atomic force microscopy — Alexander Dulebo[1], Andrea L. Slade[2], Bede Pittenger[2] — [1]Bruker Nano Surfaces Division, Östliche Rheinbrückenstr. 49, 76187 Karlsruhe, Germany — [2]Bruker Nano Inc., 112 Robin Hill Road, Santa Barbara, USA

Cell biology has seen a surge in mechanobiology-related research directed towards understanding how cells exert and respond to forces. Examining the effects of forces on cells has a wide-range of applications from understanding disease pathology to the development of tissue engineering devices. Atomic force microscopy (AFM) not only allows direct examination of the nanoscale structure of cell membrane surfaces, it also provides unique opportunities to measure the nanomechanical properties of live cells. Force Volume AFM imaging has been accepted for decades as one of the best ways to study nanomechanical properties of cells. We have used a novel AFM imaging mode, PeakForce QNM®, to map the modulus of live, individual mammalian cells. These two-dimensional spatial maps provide both high-resolution and quantitative measurements of cell mechanics that directly correlate to cell topography. PeakForce QNM has demonstrated improved results in terms of resolution, speed, ease-of-use, and quality of the information delivered. Additionally, the different frequencies accessible with both Force Volume and PeakForce QNM provide new opportunities for examination of viscoelastic properties. Extending our studies to prokaryotes, we successfully used PeakForce QNM to detect variations in the modulus of bacteria cells that occur during cell division. By integrating PeakForce QNM imaging with fluorescence microscopy we were also able to demonstrate a correlation between changes in modulus and bacterial cell viability. With regards to studying the dynamic processes involved with cell mechanics, traditional AFM imaging has been restricted in this area of research due to the typically longer acquisition times required to obtain a single image (on the order of minutes). With recent advances in high-speed AFM imaging, where images are now obtained in a matter of seconds, we have successfully begun to apply AFM imaging to investigate the mechanics of cell migration. Protrusion formation is one of the essential first steps in this process. High-resolution imaging of this step has often been limited using typical optical microscopy techniques. The unique combination of high-resolution and high-speed AFM imaging has now allowed us to directly observe the formation and advancement of individual lamellipodia and fillipodia at the leading edge of live stem cells during migration.

Poster 29 Sat 19:00

Cell deformability during passage through micron-scale constrictions — Janina Lange, Thorsten Kolb, Jonas Hallmen, Graeme Whyte, Ben

Fabry — University of Erlangen-Nuremberg, Department of Physics, Center for medical physics and technology, Henkestraße 91, 91052 Erlangen

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

Poster 30 Sat 19:00

Epithelial closure dynamics — Olivier Cochet-Escartin, Jonas Ranft, Pascal Silberzan, Philippe Marcq — Physico-Chimie Curie, Institut Curie, CNRS, Université Pierre et Marie Curie, 26 rue d'Ulm, 75005 Paris, France

See abstract of the corresponding contributed talk on Thurday 17:45.

Poster 31 Sat 19:00

The role of vimentin in cell migration under confinement — Luiza Stankevicins, Emmanuel Terriac, Franziska Lautenschläger — Saarland University, FR 7.2 Experimentalphysik, Campus Saarbrücken, Gebäude E 2.6, 3.OG, Germany

See abstract of the corresponding contributed talk on Friday 12:30.

Poster 32 Sat 19:00

Cancer cell behaviours on a culture substrate imprinted with their own features — Tiffany Tan[1], Peter Sykes[1], Maan Alkaisi[2,3], John Evans[1,3,4] — [1]University of Otago, Christchurh Women's Hospital, Department of Obstetrics and Gynaecology, Level 3, 2 Riccarton Avenue, Christchurch, New Zealand — [2]University of Canterbury, Department of Electrical and Computer Engineering, Private Bag 4800, Christchurch, New Zealand — [3]Macdiarmid Institute of Advanced Materials and Nanotechnology, Laby 410, Gate 6 Kelburn Parade, Kelburn, Wellington, New Zealand — [4]University of Otago, Department of Physiology, Centre for Neuroendocrinology, Po Box 913, Dunedin, New Zealand

See abstract of the corresponding contributed talk on Friday 12:45.

Poster 33 Sat 19:00

Mesenchymal migration cannot be described as a persistent random walk — Antoine Confavreux[1], Charlotte Riviere[1], Magalie Faivre[2], Hichem Mertani[3], Rosaria Ferrigno[2], Hélène Delanoe-Ayari[1], Jean-Paul Rieu[1] — [1]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 — [2]Institut des Nanotechnologies de Lyon – UMR CNRS 5270, Université Lyon 1, Domaine Scientifique de la Doua - Bâtiment Léon Brillouin 43 Boulevard du 11 novembre 1918,Villeurbanne, France — [3]Centre de Recherche en Cancérologie de Lyon – UMR Inserm 1052 CNRS 5286, Université Lyon 1, 28 rue Laennec 69373 Lyon Cedex 08, France

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

Poster 34 Sat 19:00

New elasticity-patterned substrates for bi-dimensional organization of cells — Camille Migdal[1], Alexandre Morel[1], Marie Courcon[1], David Fuard[2], Nicolas Bouchonville[2], Mélanie Charbit[1], Abbas Mgharbel[2], Danielle Gulino-Debrac[1], Alice Nicolas[2] — [1]Laboratoire "Biologie du Cancer et de l'Infection", UMR INSERM 1036/ CEA/ UJF, iRTSV, CEA Grenoble, 17 rue des Martyrs 38054 Grenoble Cedex 9, France — [2]Laboratoire des Technologies de la Microélectronique UMR CNRS 5129, c/o CEA/LETI/D2NT, CEA Grenoble, 17 rue des Martyrs 38054 Grenoble Cedex 9, France

See abstract of the corresponding contributed talk on Saturday 16:00.

Poster 35 Sat 19:00

Emergence of collective cell migration on circular micropatterns — Felix Jakob Segerer[1], Florian Thüroff[2], Alicia Piera Alberola[1], Erwin Frey[2], Joachim Oskar Rädler[1] — [1]Ludwig-Maximilians-Universität München, Faculty of Physics and Center for NanoScience, Geschwister-Scholl-Platz 1, 80539 Munich, Germany — [2]Ludwig-Maximilians-Universität München, Department of Physics,Arnold-Sommerfeld-Center for Theoretical Physics and Center for

NanoScience, Theresienstrasse 37, 80333 Munich, Germany

See abstract of the corresponding contributed talk on Saturday 16:15.

Poster 36 Sat 19:00

Dynamics and heterogeneity in tumor cell migration — CHRISTOPH MARK, CLAUS METZNER, JULIAN STEINWACHS, LENA LAUTSCHAM, BEN FABRY — University of Erlangen-Nuremberg, Department of Physics, LPMT, Henkestraße 91, Erlangen, Germany

See abstract of the corresponding contributed talk on Sunday 12:30.

Session V: Cell Migration in Cancer

Invited Talk Sun 08:30

Active gels, cell motility and cell trajectories — RAPHAEL VOITURIEZ — Laboratoire de Physique Théorique de la Matière Condensée and Laboratoire Jean Perrin, Universite Pierre et Marie Curie, 4 place Jussieu, 75252 Paris Cedex 05, France

I will first review some aspects of the active gel theory, which was introduced to model the cell cytoskeleton as a viscoelastic medium driven out-of-equilibrium by ATP hydrolysis. I will show that this model of active gel leads to a rich phase diagram and in particular to spontaneous hydrodynamic flows – and therefore macroscopic motion – in absence of external forcing.
Next I will discuss applications to cell motility, and emphasize the role of geometric confinement. Based on recent experiments of cell motility in micro fabricated structures, I will show that geometric confinement can enhance motility, and can even be used to direct cell migration.

Invited Talk Sun 09:00

Tissue engineering approaches and their relevance to studying tumor-stroma interactions — CLAUDIA FISCHBACH-TESCHL — Cornell University, Department of Biomedical Engineering, 157 Weill Hall, Ithaca, NY 14853, USA

Tumor-stroma interactions play a critical role in tumorigenesis, but the underlying physical mechanisms remain largely unclear. Tissue engineering approaches, initially developed for regenerative therapies, may help to overcome these limitations by providing pathologically relevant platforms for mimicry of tumor-associated microenvironmental physics. Here, I will discuss our efforts in this area and describe strategies that permit evaluating the role of tumor-stroma interactions in the pathogenesis of cancer. In particular, I will focus on microfabrication and materials science tools to examine tumor-mediated changes in vascularization and extracellular matrix (ECM) remodeling. Our results indicate that tumors modulate the fate of mesenchymal stem cells and that the resulting differences in ECM physicochemical properties promote malignancy by regulating the behavior of both endothelial and tumor cells. Especially, varied ECM composition, structure, and mechanical properties play a role in this process. These studies suggest that tissue engineered-tumor models may help to identify physical aberrations of the tumor microenvironment that may be explored for more efficacious anticancer therapies.

Invited Talk Sun 09:30

Toward the understanding of the growth of model epithelial tissues — ANA-SUNCANA SMITH — PULS Group, Institute for Theoretical Physics, University of Erlangen-Nuremberg, Nägelsbachstraße 49b, 91052 Erlangen, Germany / Institute Ruđer Bošković, Zagreb, Croatia

Tissue growth is an inherently complex process, the details of which need to be understood not only from a biological standpoint but also in terms of the purely physical and geometrical aspects. In the most common scenario, epithelial tissue exhibits an increase in cell density during the growth of a colony until such time as a steady state is reached. Using the growth of MDCK II epithelial tissue as an example, we show that several millimeter-sized compartments organize radially, within the typically circular colony, over several days. To characterize these compartments, we study the intensity of the cell-cell and cell-substrate adhesion, as well as the structure of the cellular actin cortexes within each compartment. These data are correlated with information about the local cell density and division rate. Furthermore, we show that the cells within the colony divide the space according to a Voronoi tessellation, based on the shape of the cell nuclei. We use this realization to study the development of the morphological measures (the cell area, orientation, elongation and volume) in the process of densification. This reorganization is achieved by positioning the nuclei closer to the centers of mass of the cell bodies and by decreasing the area associated with the intercellular contacts. Based on the experimental findings we construct a model of the tissue that we propagate in time within a simulation of the colony growth. Despite the relatively simple description, the simulation reproduces the statistical distributions obtained in the matured tissue, and provides a prediction of the long term motion of cells within the colony - from the birth of the cells at the periphery of the

cluster until they become a part of a compartment that has undergone the contact inhibition.

Invited Talk Sun 10:00

Modelling cell motility using active gel theory
— RHODA J. HAWKINS — University of Sheffield, Dept. of Physics and Astronomy, E43, Hicks Building, Hounsfield Road, Sheffield S3 7RH, UK

The cytoskeleton can be successfully modelled as an active gel, i.e. a gel that is driven out of equilibrium by the consumption of biochemical energy. I will consider the case of a finite droplet of active fluid as a model for a cell embedded in a surrounding medium. Motility of the droplet depends on flows of the contractile active gel. I will present analytical calculations of velocity fields for imposed polarisation, shape and boundary conditions in two and three dimensions. These solutions will be compared to numerical simulations in which the steady state polarisations, velocities and droplet shape are found.
I will then consider the inverse problem of an active fluid surrounding a passive object as a model for the cell nucleus. I will discuss the behaviour for different mechanical properties of the nucleus as found in normal and cancer cells.

Coffee Break Sun 10:30

Invited Talk Sun 11:00

Tumor cell migration is a superstatistical process
— BEN FABRY — Friedrich-Alexander-Universität Erlangen-Nürnberg, Zentrum für Medizinische Physik und Technik, Physikalisch-Medizinische Technik, Henkestraße 91, 91052 Erlangen, Germany

Over short time scales, cell migration can be well described as a homogeneous correlated random walk with a fixed average step length and a certain degree of directional persistence. On time scales of up to 24 h, however, the migration process is highly inhomogeneous. Superstatistical fluctuations of step length and directional persistence lead to 'anomalous' features, such as an exponential step width distribution (SWD) and a superdiffusive mean squared displacement (MSD). These features are quantitatively reproduced by a correlated random walk with temporally varying persistence. By comparing tumor cell migration on planar substrates, in a 3D collagen matrix and in microchannel arrays, we demonstrate that the globally averaged MSD and SWD are not sensitive to the microscopic migration mechanism of the cells and can therefore yield identical results in these different environments. Using Bayesian inference, we extract both rapid and gradual changes of step length and directional persistence, together with their mutual correlations and joint probability distributions. These data provide a characteristic fingerprint of the migration process of tumor cells in different environments.

Invited Talk Sun 11:30

Cell migration in confining spaces: pushing off the walls and squeezing through small holes
— MATTHIEU PIEL — Institut Curie, UMR 144 IC/CNRS, Biologie systémique de la division et de la polarité cellulaire Systems Biology of Cell Division and Cell Polarity, 26, rue d'Ulm 75248 Paris CEDEX 05, France

The quest to understand how the mechanical and geometrical environment of cells impacts their behavior and fate has been a major force driving the recent development of new technologies in cell biology research. Despite rapid advances in this field, many challenges remain in order to bridge the gap between the classical and simple cell culture plate and the biological reality of actual tissues. In tissues, cells have their physical space constrained by neighboring cells and extracellular matrix. In the recent years, we have developed simple and versatile devices to precisely and dynamically control this confinement parameter in cultured cells. I will present results we obtained on the effect of confinement on cell migration focusing on two questions: how modulating confinement and adhesion of slow mesenchymal migrating cells can make them switch to a fast amoeboid like migration behavior and how cells can squeeze their nucleus when migrating through small gaps. I will conclude presenting intruiguing results showing that large deformations of migrating cells induce strong damages of their nucleus raising the question of how immune cells such as dendritic cells can combine high motility and long term survival.

Invited Talk Sun 12:00

The cytoskeleton significantly impacts invasive behavior of biological cells — JOSEF A. KÄS, ANATOL FRITSCH, STEVE PAWLIZAK, K. DAVID NNETU, FRANZISKA WETZEL, CHRIS HÄNDEL, SEBASTIAN SCHMIDT, DAVE AHRENS — University of Leipzig, Faculty of Physics and Earth Sciences, Institute of Experimental Physics I, Soft Matter Physics Division, Linnéstr. 5, 04103 Leipzig, Germany

Cell migration is a key determinant of cancer metastasis and nerve regeneration. The role of the cytoskeleton for the epithelial-meschenymal transition (EMT), i.e. for invasive behavior of cells, is only partially understood. Here, we address this issue in cells lacking all keratins upon genome engineering. In contrast to prediction, keratin-free cells show a 60% higher deformability compared to less pronounced softening effects for actin depolymerization. To relate these findings with functional consequences, we use invasion and three-dimensional growth assays. These reveal higher invasiveness of keratin-free cells. This study supports the view that downregulation of keratins observed during EMT directly contributes to the migratory and invasive behavior of tumor cells. Cancer cells that effectively move through tissues are softer and more contractile than cells that stay local in tissues. Soft and contractile avoids jamming. Naturally, softness has to have its limits. So neuronal growth cones are too soft to carry large loads to move efficiently through scar tissue, which is required for nerve regeneration. In synopsis, the physical bounds that the functional modules of a moving cell experience in tissues may provide an overarching motif for novel approaches in diagnosis and therapy.

Contributed Talk Sun 12:30

Dynamics and heterogeneity in tumor cell migration — CHRISTOPH MARK, CLAUS METZNER, JULIAN STEINWACHS, LENA LAUTSCHAM, BEN FABRY — University of Erlangen-Nuremberg, Department of Physics, LPMT, Henkestraße 91, Erlangen, Germany

The dynamics of migrating tumor cells is typically modeled by temporally homogeneous random walks, reproducing certain ensemble- and time-averaged statistical features reasonably well, such as the step width distribution or the velocity autocorrelation function. However, experiments show that migrating tumor cells exhibit highly heterogeneous dynamics – in time as well as across the ensemble. While successive steps u_t of the cell's trajectory can locally be described as an autoregressive process of first order, AR(1), with $u_t = q\ u_{t-1} + a\ \eta_t$, the persistence q and the activity a are changing over longer timescales. Probabilistic inference based on Bayesian statistics allows us to infer the complete dynamics of the hidden parameters qt and at from measured trajectories. By simulating cell trajectories based on the inferred parameter values, we demonstrate that anomalous statistical features of the cell trajectories, in particular the non-Gaussian step width distributions and the superdiffusive mean squared displacements (MSD) with fractional power-law exponents are tightly connected to the heterogeneity of the migration process. Applied to data from migrating tumor cells in a microfabricated channel structure, we show that the temporal changes of the hidden parameters strongly correlate with local changes of the cell's environment. In the case of unconstrained migration of tumor cells on flat 2D surfaces and in 3D collagen matrices, we find that the joint distribution and temporal correlations of the hidden parameters reveal distinct migration behavior depending on dimensionality and surface coating.

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